National Clinical Guideline Centre

.

Myocardial infarction with ST-segment elevation

The acute management of myocardial infarction with ST-segment elevation

Clinical guideline 167

Appendices A - H

July 2013

November 2020: NICE's original guidance on Myocardial infarction with ST-segment elevation was published in 2013. See the NICE website for the guideline recommendations and for the 2020 Acute coronary syndromes update. This document preserves evidence reviews and committee discussions from the 2013 guideline.

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Appendices

Appendix A: Scope

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Centre for Clinical Practice

SCOPE

Clinical guideline title: Myocardial infarction with ST-segment-elevation: the acute management of myocardial infarction with ST-segment-elevation

Quality standard title: Management of acute coronary syndromes including myocardial infarction

1 Introduction

.1 *Clinical guidelines*

Clinical guidelines are recommendations by NICE on the appropriate treatment and care of people with specific diseases and conditions within the NHS. They are based on the best available evidence.

This scope defines what the guideline will (and will not) examine, and what the guideline developers will consider. The scope is based on the referral from the Department of Health.

.2 *Quality standards*

Quality standards are a set of specific, concise quality statements and measures that act as markers of high-quality, cost-effective patient care, covering the treatment and prevention of different diseases and conditions.

For this clinical guideline a NICE quality standard will be produced during the guideline development process, after the development of the clinical guideline recommendations.

This scope defines the areas of care for which specific quality statements and measures will (and will not) be developed.

The guideline and quality standard development processes are described in detail on the NICE website (see section 8).

2 Need for guidance

.3 *Epidemiology*

a) ST-segment-elevation myocardial infarction (STEMI) is at one end of a spectrum of related conditions called acute coronary syndromes. The underlying common pathophysiology involves either the erosion or sudden rupture of an atheromatous plaque (cholesterol-rich material) within the wall of a coronary artery. This plaque erosion or rupture then stimulates blood clotting (thrombosis) within the affected coronary artery. Complete obstruction to blood flow is usually associated with the appearance of 'ST-segment-elevation' on the electrocardiograph – the defining feature of STEMI. Occlusion of blood flow leads to heart muscle (myocardium) cell death that, without intervention, progressively worsens with time.

b) Typically STEMI causes the onset of acute chest pain, although symptoms may include sweating, nausea and breathlessness. Symptoms may be atypical, particularly in women and people with diabetes. Cardiac arrhythmias may occur early in the onset of STEMI and may cause sudden death before the person is able to access emergency medical care. Certain groups of people, including women and those from ethnic minorities, may be slow to call for medical help.

c) Although the incidence of STEMI has been declining over the past 20 years, it varies between regions of the UK and still averages around 750 cases per million people each year. Over the past 30 years in-hospital mortality following STEMI has fallen from around 20% to less than 5%, this has been attributed to various factors, including improved drug therapy and speed of access to effective treatments.

.4 *Current practice*

a) The overriding concern in the management of STEMI is to rapidly and effectively restore coronary blood flow (reperfusion) because this limits the extent of heart muscle (myocardium) damage and reduces the likelihood of death or future heart failure. In the past, fibrinolysis (that is, reperfusion with fibrinolytic – or 'clot buster' – drugs) was the most common treatment. The treatment of choice now is mechanical reopening of the occluded artery by angioplasty and stent insertion (primary percutaneous coronary intervention [PPCI]).

b) The Department of Health undertook a feasibility study (National Infarct Angioplasty Project) that reported in October 2008 and concluded that PPCI was both feasible and cost effective, and should become the treatment of choice for STEMI in England, although PPCI is more expensive than fibrinolytic therapy. Since 2009, cardiac networks have successfully implemented the new PPCI policy and by the end of 2011 it is estimated that 95% of the population in England and Wales will be covered by a PPCI care pathway. This PPCI strategy needs emergency access to specialist cardiac catheter laboratories and staff at all times.

c) Fibrinolytic therapy is still offered a few people (5%) who live in remote rural surroundings and cannot access PPCI services within current recommended time frames.

d) People may develop symptoms of STEMI and then call the emergency services or self-present to an emergency department. STEMI may also occur in someone already in hospital for a different reason, such as a surgical operation. Whatever the circumstances, care pathways should exist to ensure that PPCI is offered to all who may benefit, in a timely and efficient manner.

e) The prime determinant of clinical benefit following reperfusion therapy for STEMI is the degree of myocardial salvage (a function of timeliness, effectiveness and maintenance of coronary reperfusion). Bleeding complications also play an important part in both morbidity and mortality if combinations of potent antiplatelet and antithrombin agents are used. After successful acute treatment, secondary prevention therapy, lifestyle modification and cardiac rehabilitation recommendations parallel those for non-STEMI acute coronary syndromes, on which NICE recently produced guidance ('Unstable angina and NSTEMI', NICE clinical guideline 94, 2010).

f) This guideline will address the factors that influence the delivery of effective and timely coronary reperfusion treatment for people with STEMI.

3 Clinical guideline

.5 *Population*

.5.1 Groups that will be covered

a) Adults (18 years or older) believed to be having spontaneous onset of STEMI (types 1 and 3 of the 'universal definition of myocardial infarction' categories).

b) Adults with suggestive symptoms of spontaneous onset of STEMI, but whose electrocardiogram may be difficult to interpret because of the presence of left bundle branch block or permanent pacing.

c) Where data exist, guidance will address differences between specific populations, such as older adults, women and people from ethnic minorities.

d) Particular attention will be paid to people with STEMI who remain unconscious following resuscitation.

.5.2 Groups that will not be covered

a) Children and young people (younger than 18 years).

b) Patients initially suspected as having STEMI once this diagnosis is excluded (for example, on cardiac catheterisation).

c) Patients once a diagnosis of STEMI has been excluded (for example, as a complication of coronary revascularisation).

.6 Healthcare settings

Primary, secondary and tertiary healthcare settings, including care from ambulance teams and other paramedical staff before admission to hospital.

.7 Management

.7.1 Key issues that will be covered

The diagnosis of STEMI will be considered to have been made once a patient is identified as having a suggestive clinical presentation and either ST-segment-elevation on the electrocardiograph or an electrocardiograph where interpretation is complicated by the presence of left bundle branch block or permanent pacing. The acute aspects of the following will be addressed, from symptom onset to the point of hospital discharge:

a) Adjunctive pharmacotherapy (for example, antiplatelet and antithrombin agents).

b) Time factors in relation to acute coronary reperfusion.

c) The time interval from onset of STEMI beyond which fibrinolysis may be preferable to PPCI.

d) Drug combinations administered before PPCI (facilitated PPCI).

e) Timing and effectiveness of angiography or PCI following fibrinolytic therapy.

f) Timing and effectiveness of PCI following failed fibrinolysis (rescue PCI).

g) Procedural aspects of PPCI (for example, thrombus extraction).

h) Guideline recommendations will normally fall within licensed indications; exceptionally, and only if clearly supported by evidence, use outside a licensed indication may be recommended. The guideline will assume that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients.

National Clinical Guideline Centre, 2013.

.7.2 Key issues that will not be covered

a) Management of suspected brain injury in those with STEMI who have suffered cardiac arrest.

b) Management of STEMI after hospital discharge, including post-myocardial infarction treatments (we will cross-refer to existing NICE guidance).

.8 *Main outcomes*

a) Major cardiovascular events.

b) Mortality.

c) Stroke.

d) Myocardial re-infarction.

e) Reintervention at various time intervals (for example, in hospital, 30 days, and 1 year).

f) Adverse events including bleeding complications.

g) Length of hospital stay.

h) Quality of life.

.9 *Economic aspects*

Developers will take into account both clinical and cost effectiveness when making recommendations involving a choice between alternative interventions. A review of the economic evidence will be conducted and analyses will be carried out as appropriate. The preferred unit of effectiveness is the quality-adjusted life year (QALY), and the costs considered will usually be only from an NHS and personal social services (PSS) perspective. Further detail on the methods can be found in 'The guidelines manual' (see Section 8).

4 Quality standard

Information on the NICE quality standards development process is available on the NICE website, see section 8.

.10 *Mapped areas of care*

The areas of care of a patient's journey that will inform the development of the quality statements are set out below (see 4.1.1). The content of the final quality standard statements may differ before and after consultation with stakeholders.

.10.1 Areas of care that will be considered

a) Out of hospital presentation of acute chest pain

  a. Assessment and ECG (see www.nice.org.uk/guidance/CG95)

  b. Immediate management, pain relief, aspirin, and oxygen (see www.nice.org.uk/guidance/CG95)

b) In-hospital assessment diagnosis

  a. Clinical assessment and ECG (see www.nice.org.uk/guidance/CG95)

  b. Troponin (see www.nice.org.uk/guidance/CG95)

c) Management of STEMI (this guideline)

  a. PPCI

  b. Facilitated PCI

  c. Rescue PCI

  d. Fibrinolytic therapy

  e. Angiography following fibrinolysis

  f. Antiplatelet agents

  g. Antithrombotic agents

d) Management of unstable angina and NSTEMI

a. Antiplatelets (see www.nice.org.uk/guidance/CG94)

b. Antithrombotic agents (see www.nice.org.uk/guidance/CG94)

c. Angiography (see www.nice.org.uk/guidance/CG94)

e) Discharge Planning (this guideline and CG48 – currently scoping for update)

a. Cardiac rehabilitation

b. Initiation of secondary prevention

.10.2 Areas of care that will not be considered

a) Adherence to secondary-prevention interventions after their initiation in hospital.

b) Uptake of cardiac rehabilitation after discharge from hospital following acute coronary syndromes.

.11 Economic aspects

Developers will take into account both clinical and cost effectiveness when prioritising the quality statements to be included in the quality standard. The economic evidence will be considered, and the cost and commissioning impact of implementing the quality standard will be assessed.

5 Status

.12 *Scope*

This is the final scope.

.13 *Timings*

The development of the guideline recommendations and the quality standard will begin in August 2011.

6 Related NICE guidance

.13.1 NICE guidance that will be incorporated in or updated by the clinical guideline

The guideline will incorporate the following NICE guidance, subject to a technology appraisal review proposal agreement:

- Bivalirudin for the treatment of ST-segment-elevation myocardial infarction. NICE technology appraisal guidance 230 (2011). Available from www.nice.org.uk/guidance/TA230
- Guidance on the use of drugs for early thrombolysis in the treatment of acute myocardial infarction. NICE technology appraisal guidance 52 (2002). Available from www.nice.org.uk/guidance/TA52
- Ticagrelor for the treatment of acute coronary syndromes. NICE technology appraisal. Publication expected October 2011.

.14 *Related NICE guidance*

Published

- Hypertension (update). NICE clinical guideline 127 (2011). Available from www.nice.org.uk/guidance/CG127
- Stable angina. NICE clinical guideline 126 (2011). Available from www.nice.org.uk/guidance/CG126
- Prevention of cardiovascular disease. NICE public health guidance 25 (2010). Available from www.nice.org.uk/guidance/PH25

- Chest pain of recent onset. NICE clinical guideline 95 (2010). Available from www.nice.org.uk/guidance/CG95
- Unstable angina and NSTEMI. NICE clinical guideline 94 (2010). Available from www.nice.org.uk/guidance/CG94
- Clopidogrel and modified-release dipyridamole for the prevention of occlusive vascular events. NICE technology appraisal guidance 210 (2010). Available from www.nice.org.uk/guidance/TA210
- Cardiac resynchronisation therapy for the treatment of heart failure. NICE technology appraisal guidance 120 (2010). Available from www.nice.org.uk/guidance/TA120
- Prasugrel for the treatment of acute coronary syndromes with percutaneous coronary intervention. NICE technology appraisal guidance 182 (2009). Available from www.nice.org.uk/guidance/TA182
- Medicines adherence. NICE clinical guideline 76 (2009). Available from www.nice.org.uk/guidance/CG76
- Smoking cessation services in primary care, pharmacies, local authorities and workplaces, particularly for manual working groups, pregnant women and hard to reach communities. NICE public health guidance 10 (2008). Available from www.nice.org.uk/guidance/PH10
- Familial hypercholesterolaemia. NICE clinical guideline 71 (2008). Available from www.nice.org.uk/guidance/CG71
- Lipid modification. NICE clinical guideline 67 (2008). Available from www.nice.org.uk/guidance/CG67
- Drug-eluting stents for the treatment of coronary artery disease. NICE technology appraisal 152 (2008). Available from www.nice.org.uk/guidance/TA152
- MI: secondary prevention. NICE clinical guideline 48 (2007). Available from www.nice.org.uk/guidance/CG48
- Implantable cardioverter defibrillators (ICDs) for arrhythmias (2006). NICE technology appraisal 95 (2006). Available from www.nice.org.uk/guidance/TA95.
- Statins for the prevention of cardiovascular events. NICE technology appraisal guidance 94 (2006). Available from www.nice.org.uk/guidance/TA94
- Brief interventions and referral for smoking cessation in primary care and other settings. NICE public health guidance 1 (2006). Available from www.nice.org.uk/guidance/PH1

- Off-pump coronary artery bypass (OPCAB). NICE interventional procedure guidance 35 (2004). Available from www.nice.org.uk/guidance/IPG35
- Myocardial perfusion scintigraphy for the diagnosis and management of angina and myocardial infarction. NICE technology appraisal guidance 73 (2003). Available from www.nice.org.uk/guidance/TA73
- Guidance on the use of coronary artery stents. NICE technology appraisal guidance 71 (2003). Available from www.nice.org.uk/guidance/TA71
- Guidance on the use of drugs for early thrombolysis in the treatment of acute myocardial infarction. NICE technology appraisal guidance 52 (2002). Available from www.nice.org.uk/guidance/TA52
- Guidance on the use of glycoprotein IIb/IIIa inhibitors in the treatment of acute coronary syndromes. NICE technology appraisal guidance 47 (2002). Available from www.nice.org.uk/guidance/TA47

NICE guidance under development

NICE is currently developing the following related guidance (details available from the NICE website):

- Hyperglycaemia in patients with acute coronary syndrome. NICE clinical guideline. Publication expected October 2011.

7 Further information

Information on the guideline development process is provided in:

- 'How NICE clinical guidelines are developed: an overview for stakeholders the public and the NHS'
- 'The guidelines manual
- 'Developing NICE quality standards: interim process guide'.

These are available from the NICE website (www.nice.org.uk/GuidelinesManual and www.nice.org.uk/aboutnice/qualitystandards). Information on the progress of the guideline and quality standards are also available from the NICE website (www.nice.org.uk).

Appendix B: Declarations of interest

B.1 Guideline development group members

B.1.1 Sotiris Antoniou

Item declared	Date	Expiry	Classification	Action taken
Chair of cardiac committee for the United Kingdom Clinical pharmacy Association	2005	Ongoing	Personal non-pecuniary	Declare and participate
Member NICE guideline development groups for Stable Angina and NSTEMI		Issued March 2010	Expired	Expired Declare and participate
Attended advisory board meeting for Chiesi Pharmaceuticals on integrated care pathways in ACS. Received honorarium.	26 August 2010	25 August 2011	Personal non-specific pecuniary	Expired
Attended presentation at Heart Rhythm Congress meeting sponsored by Sanofi Aventis.	2 October 2010	1 October 2011	Personal non-specific pecuniary	Declare and participate GDG1 and 2. Expired by GDG3
Attended advisory board meeting for Astra Zenica on ticagrelor. Received honorarium.	23 October 2010	22 October 2011	Personal specific pecuniary	GDG not discussing recommendations for ticagrelor (TA incorporated). Declare and participate GDG1 and 2. Expired by GDG3
Reimbursed for presentation on the role of pharmacy in health care (not specifically related to a drug) by Astra Zenica.	3 November 2010	2 November 2011	Personal specific pecuniary	GDG not discussing recommendations for ticagrelor (TA incorporated). Declare and participate GDG1 and 2. Expired by GDG3
Attended meeting on Ad Review (a drug used for imaging in heart failure). Honorarium received from GE Healthcare.	10 November 2010	9 November 2011	Personal non-specific pecuniary	Declare and participate GDG1 and 2. Expired by GDG3
Attended advisory board on ivabradine in Chronic Heart Failure for Servier. Received honorarium.	16 November 2010	15 November 2011	Personal non-specific pecuniary	Declare and participate GDG1 and 2. Expired by GDG3.
Attended advisory board on prasugrel for Lilly. Received honorarium.	23 November 2010	22 November 2011	Personal specific pecuniary	GDG not discussing recommendations for prasugrel (TA undergoing update).

Item declared	Date	Expiry	Classification	Action taken
				Declare and participate GDG1 and 2
Attended advisory board on HDL increasing prasugrel for Lilly. Received honorarium.	23 February 2011	22 February 2012	Personal specific pecuniary	GDG not discussing recommendations for prasugrel (TA undergoing update). Declare and participate.
Attended advisory board on anti Xa in Atrial Fibrillation (edoxaban - drug in development) for Daiichi Sankyo. Received honorarium.	3 March 2011	2 March 2012	Personal specific pecuniary	Re Daiichi Sankyo as manufacturer - GDG not discussing recommendations for prasugrel (TA undergoing update). Declare and participate.
Attended advisory board on dabigatan for atrial fibrillation. Received honorarium from Boehringer Ingelheim.	8 April 2011	7 April 2012	Personal specific pecuniary	GDG debating strategy only therefore declare and participate
Attended advisory board on prasugrel. Received honorarium from Lilly.	9 May 2011	8 May 2012	Personal specific pecuniary	GDG not discussing recommendations for prasugrel (TA undergoing update). Declare and participate.
Wrote an article for the journal 'Future Prescriber' on ticagrelor.	May 2011		Personal specific non-pecuniary	Declare and participate
Received reimbursement from Bayer for a presentation on the role of pharmacy and cardiac networks (not drug related)	29 June 2011	28 June 2012	Personal non-specific pecuniary	Declare ad participate
Attended advisory board on ticagrelor. Received honorarium from Astra Zeneca.	4 July 2011	3 July 2012	Personal specific pecuniary	GDG not discussing recommendations for ticagrelor (TA incorporated). Declare and participate
Reimbursed for analysis of risk stratification tools in NSTEMI by Daiichi Sankyo.	1 August 2011	31 July 2012	Personal specific pecuniary	Declare and participate
Received accommodation, travel and expenses to attend ESC congress in 2011 from Daiichi Sankyo.	27 August 2011	26 August 2012	Personal specific non-pecuniary	Declare and participate
Attended advisory board on dalcetrapib HDL agent. Received honorarium from Roche.	15 September 2011	14 September 2012	Personal non-specific pecuniary	Declare and participate

Item declared	Date	Expiry	Classification	Action taken
Attended UK antithrombotics meeting. No payment received.	13 October 2011	12 October 2012	Personal specific non-pecuniary	Declare and participate
Attended an advisory board on Integrated care pathway development for stable angina sponsored by Menarini who manufacture ranolazine. Honorarium received.	October 2012	September 2013	Personal, non-specific pecuniary	Declare and participate
Attended an advisory board on Heart failure sponsored by Servier who manufacture ivabradine. Honorarium received.	October 2012	September 2013	Personal, non-specific pecuniary	Declare and participate
Attend an advisory board by DS/Lilly partnership on prasugrel. Honorarium received.	17 December 2012	16 December 2013	Personal specific pecuniary	GDG not discussing recommendations for prasugrel (TA undergoing update). Declare and participate

B.1.2 Charles Deakin

	Date	Expiry	Classification	Action taken
Director, Prometheus Medical Ltd (http://www.prometheusmedical.co.uk) There is no direct link with STEMI management. Not actively engaged in sales or training (more as an advisory role).	24 August 2011	-	Personal non-specific pecuniary	Declare and participate
Divisional Medical Director, South Central Ambulance Service	24 August 2011	-	No conflict of interest	Declare and participate
Consultant in Cardiac Anaesthesia and Cardiac Intensive Care	24 August 2011	-	No conflict of interest	Declare and participate
Member of the Executive Committee, Resuscitation Council (UK)	24 August 2011	-	Personal non-pecuniary	Declare and participate
Board member, European Resuscitation Council	24 August 2011	-	Personal non-pecuniary	Declare and participate
Chair, Advanced Life Support Working Group, European Resuscitation Council	24 August 2011	-	Personal non-pecuniary	Declare and participate
Co-Chair, Advanced Life Support Working Group, International Liaison Committee on Resuscitation	24 August 2011	-	Personal non-pecuniary	Declare and participate
Royal College of Anaesthetists representative, Joint Royal Colleges Ambulance Liaison Committee (JRCALC)	24 August 2011	-	Personal non-pecuniary	Declare and participate
Guidelines Committee, Joint Royal Colleges Ambulance Liaison Committee(JRCALC)	24 August 2011	-	Personal non-pecuniary	Declare and participate

	Date	Expiry	Classification	Action taken
Honorary Civilian Consultant in Pre-Hospital Emergency Care to the British Army.	24 August 2011	-	No conflict of interest	Declare and participate
Deputy Chair (Chair as of January 2012), RNLI Medical & Survival Committee.	24 August 2011	-	Personal non-pecuniary	Declare and participate
Involved in developing the Position statement from JRCALC on paramedic airway management (see CV) - 30/06/11	24 August 2011	-	Personal non-pecuniary	Declare and participate
Various research papers and reviews on ambulance triage of patients with chest pain, management of cardiac arrest, and post-cardiac arrest management.	24 August 2011	-	Personal non-pecuniary	Declare and participate
Resuscitation Council (UK) – Research Grant 2007 – Lead applicant on grant to fund research into the safety of automatic chest compression devices.	24 August 2011	-	Non-personal pecuniary – non-healthcare manufacturer / industry related	Declare and participate
Resuscitation Council (UK) – Research Grant 2007 – Lead applicant to fund study of genetic polymorphism as a factor affecting survival from cardiac arrest. (Administers these funds)	24 August 2011	-	Non-personal pecuniary – non-healthcare manufacturer / industry related	Declare and participate
Resuscitation Council (UK) – Research Grant 2007 – Lead applicant to fund research a comparison of the efficacy of biphasic truncated exponential and rectilinear biphasic waveforms in cardioversion of atrial fibrillation. (Administers these funds)	24 August 2011	-	Non-personal pecuniary – non-healthcare manufacturer / industry related	Declare and participate
Resuscitation Council (UK) – Research Fellowship 2010 – A pilot prospective study of the role of cerebral oximetry in predicting outcomes in in-hospital cardiac arrest Principle Investigator. March 2010 (Administers these funds)	24 August 2011	-	Non-personal pecuniary – non-healthcare manufacturer / industry related	Declare and participate
Resuscitation Council (UK) – Research Fellowship 2010 – Principle Investigator. 'Hands on' Defibrillation – Is it safe? June 2010 (Administers these funds)	24 August 2011	-	Non-personal pecuniary – non-healthcare manufacturer / industry related	Declare and participate

B.1.3 Huon Gray

Item declared	Date	Expiry	Classification	Action taken
President, British Cardiovascular Society (2003-5)	2003	2005	Expired	Not relevant
Lead (Cardiology), London Review of Cardiovascular Services, NHS London 2009-10.			Personal non-pecuniary	Declare and participate
Hon. Civilian Consultant Adviser (Cardiology) to the Army	2008	-	No conflict of interest	Not relevant
Clinical Advisor, NICE Clinical Guideline 95 (Unstable angina & non-ST elevation myocardial infarction) 2007-10		Issue March 2010	Expired	Expired Declare and participate
Chair, International Council (2008-date) & Member of Board of Trustees (2010-date), American College of Cardiology. Travel expenses paid by ACC for attendance at international & board meetings.	2008	-	Non-classifiable - ACC do not provide services to the NHS	Declare and participate
Co-chair of NIAP (with Roger Boyle, the National Director for Heart Disease at DH) from the project's inception to completion. Chaired meetings of the Steering Group, attended data monitoring meetings, and was principal clinical author on the two NIAP reports which appeared in 2008. I did not receive any reimbursement or payment for this work nor was I involved in allocating the £1 million of funds which the DH allocated to the Study. This was done by Civil Servants. I was also a co-author on the cost effectiveness paper which appeared in Heart [Heart 2010; 96:668-672]		2008	Personal non-pecuniary	Declare and participate
Advisory Board Member, Daiichi Sankyo; prasugrel for acute coronary syndromes (2 meetings – December 2010 & July 2011). Remuneration for each.	December 2010	July 2012	Personal specific pecuniary	GDG not discussing recommendations for prasugrel (TA undergoing update). Deputy Chair wrote related NICE guidance chapter of guideline. Declare and participate
Attendance at an Advisory Board meeting for St Jude Medical who are discussing the introduction of their remote monitoring device for the management of heart failure patients in the UK.	24 November 2011	23 November 2012	Pecuniary non-specific	Declare and participate action at the discretion of the Guideline Lead

Item declared	Date	Expiry	Classification	Action taken
Seconded to the Department of Health as interim National clinical director for cardiovascular diseases.	12 March 2012		Non-specific pecuniary	Declare and participate

B.1.4 Robert Henderson

Item declared	Date	Expiry	Classification	Action taken
Sponsored by Edwards Life Science to attend EuroPCR Valve Live meeting. Reimbursed travel and accommodation costs only.	October 2010	October 2011	Expired by GDG2	No action required
Attended 'Cardiology and Diabetes at the Limits Conference' in Feb 2011; sponsored by Pfizer Ltd, F.Hoffman-La Roche Ltd, Novo Nordisk, AstraZenica South Africa, Medtronic Ltd, Saiichi-Sankyo/Lilly UK, Sanofi-Aventis, Lilly UK Ltd. Reimbursed travel and accommodation expenses only.	February 2011	February 2012	Within normal expenses of DOI policy	No action required
Member of council of British Cardiovascular Intervention Society Council member 2006-current Clinical standards lead 2009-current Member, British Cardiovascular Society clinical standards committee 2009-current Member, British Cardiovascular Society programme committee 2010-current			Personal non-pecuniary	Declare and participate No contribution to SH comments from BCIS because answering on behalf of GDG
Member of the steering committee of RITA-3 and co-author of publications			Personal non-pecuniary	Declare and participate
Member of NICE guideline development group for Unstable Angina/NSTEMI and clinical adviser to NICE Stable Angina guideline development group		Unstable Angina published March 2010, Stable Angina July 2011	Expired	No action required
Attended Euro-PCR meeting in Paris. Registration, travel and accommodation expenses paid by Edwards Lifesciences (heart valve manufacturer).	15-18 May 2012	18th May 2013	Within normal expenses of DOI policy	No action required
Attended a one day meeting in London on TAVI on 15 June 2012. The meeting was sponsored by Edwards Lifesciences (heart valve manufacturer) and the company paid for travel and overnight	15 June 2012		Within normal expenses of DOI policy	No action required

Item declared	Date	Expiry	Classification	Action taken
Attended London PCR-valve conference (1-2 October). Edwards Lifesciences paid for travel, accommodation and registration but no honorarium or other financial benefit received.	1-2 October 2012		Within normal expenses of DOI policy	No action required
Attended TCT conference in Miami, USA (21-25 October). Biosensors (coronary stent manufacturer) paid for travel, accommodation and registration but I did not receive any other payment from the company.	21-25 October 2012		Within normal expenses of DOI policy	No action required

B.1.5 Jason Kendall

Item declared	Date	Expiry	Classification	Action taken
Authored a paper in the EMJ related to the management of STEMI in 2007: The Optimum Reperfusion Pathway for ST elevation myocardial infarction: development of a decision framework. Kendall JM. EMJ 2007; 24:52-56 Also published as a web-based interactive tool at: http://www.ddaccess.co.uk/europr/cdrom/index/htm		2007	Expired	No action required
Co-author of publication related to pre-hospital thrombolysis: Does pre-hospital thrombolysis increase the proportion of patients having an aborted myocardial infarction? Jackson L. Kendall JM, Castle N. EMJ 2009; 26:206-209	2009		Expired	No action required
Co-applicant on an NIHR-funded research project evaluating the cost effectiveness of diagnostic strategies for acute coronary syndromes (project based at the University of Sheffield).	2009	2011	Non-personal pecuniary	Declare and participate
Author of a BMJ Learning module on 'The Management of STEMI'.	2009	2010	Expired	Expired Declare and participate
Author of a Department of Health e-learning for Health (elfh) module on 'The Management of STEMI and its complications'.	2009	2010	Expired	Expired Declare and participate
Author of various e-learning modules on the College of Emergency Medicine's e-learning platform (ENLIGHTENme) related to Acute Coronary Syndromes (Pathophysiology, Clinical Assessment, STEMI, UA and NSTEMI)	2008 – on going		Personal non-pecuniary	Declare and participate
Member of NICE guideline development group CG95 on Chest Pain (2008-2010)		Issued March 2010	Expired	No action required
Steering Committee Member of STREAM Trial: Strategic Reperfusion Early after Myocardial Infarction Study. This is an international randomised control trial comparing PPCI with a contemporary lytic-based reperfusion strategy. (24/06/11) - no payment received in previous 12 months	24 June 2011		Personal non-pecuniary	Declare and participate
Attended an advisory board meeting on the diagnosis and treatment of pulmonary embolism, funded by Bayer who manufacture rivaroxaban which is one of the new oral anticoagulants used for the treatment of venous thromboembolic disorders.	September 2012	September 2013	Personal non-specific pecuniary	Declare and participate

B.1.6 Hugh McIntyre

Item declared	Date	Expiry	Classification	Action taken
Received research grant support from Takeda for a 2-year doctorate which HM supervised investigating the epidemiology of heart failure (to Jan 2011)	January 2009	January 2012	Non-personal pecuniary	Declare and participate
Regional acute lead for Heart Failure for the Enhancing Quality Programme run by NHS SE. One session per week reimbursed during secondment to April 2013.	April 2010	April 2013	Non-personal pecuniary	Declare and participate
Attended advisory board meeting for Novartis Pharmaceuticals on the topic of age-related muscular degeneration, therapy Lucentis. Honorarium received.	13 May 2011	12 May 2012	Personal non-specific pecuniary	Declare and participate
Attended advisory board meeting for Pfizer Pharmaceuticals on eplerenone in chronic heart failure (not yet licensed for chronic heart failure but licensed for post MI heart failure). Honorarium received.	9 May 2011	8 May 2012	Personal non-specific pecuniary	Declare and participate
Deputy Divisional Director of Medicine (Conquest Hospital East Sussex HealthcareTrust) recent establishment and ongoing developments in primary PCI service (no direct involvement).	24 August 2011		Personal non-pecuniary	Declare and participate
IVAN Data Safety Monitoring Board member (comparison of bevacizumab and ranibizumab in macular degeneration)	24 August 2011		Personal non-pecuniary	Declare and participate
NICE Heart Failure GDG member (2008-10) and Topic Expert Group Chair (2010-11) – (reimbursed for role as Chair)	24 August 2011	2011	Expired	No action required
Principal investigator to international randomised control trials, including lipid lowering agent (HPS THRIVE), antiplatelet treatment for chronic cardiovascular disease (TRA2P), registry of patients treated for acute coronary syndrome (EPICOR), registry of patients with atrial fibrillation. Does not administer trial funds.	24 August 2011		Personal non-pecuniary	Declare and participate
Sub-investigator for study of antiplatelet agent in ACS (TAO study).	24 August 2011		Personal non-pecuniary	Declare and participate
European Society of Cardiology Annual meeting (from Servier). Travel and accommodation expenses only.	August 2011		Within normal expenses of DOI policy	No action required
Attended advisory board meeting for Boehringer Ingelheim Pharmaceuticals on dabigatran for anticoagulation in atrial fibrillation. Honorarium received.	12 September 2011	11 September 2012	Personal specific pecuniary	Q3, 5 & 6 - debating strategy only therefore declare and participate

Item declared	Date	Expiry	Classification	Action taken
Participated in consensus statement for heart failure meeting for Pfizer pharmaceuticals. Honorarium received.	16 September 2011	15 September 2012	Personal non-specific pecuniary	Declare and participate
Attended advisory board meeting for Servier Pharmaceuticals on ivabradine. Honorarium received.	16 September 2011	15 September 2012	Personal non-specific pecuniary	Declare and participate
Attended Advisory Board meeting on rivaraoxaban (Bayer)	Nov 2011		Personal non-specific pecuniary	Declare and participate
Trust authorisation for two Charitable Funds (managed by East Sussex Healthcare Trust): 1. the Cardiovascular Research Fund - manages reimbursement from RCTs to support Research nurse funding; 2. and to the Hastings Heart Failure fund –supports MD student and heart failure nurses in continuing medical education, equipment and research.	Declared January 2012	-	Non-personal pecuniary	Declare and participate
Attendance at an advisory board for Roche Pharmaceuticals regarding BNP in diagnosis of heart failure. Honorarium received.	13 March 2012	12 March 2013	Personal non-specific pecuniary	Declare and participate
Presented at a regional industry meeting on Chronic Heart Failure (Pfizer pharmaceuticals) on 18th April (Honorarium received).	18 April 2012	17 April 2013	Personal non-specific pecuniary	Declare and participate
Presented at a regional educational meeting in London – Heart Failure New Challenges New solutions. Independent conference. Honorarium received from Servier.	26 April 2012	25 April 2013	Personal non-specific pecuniary	Declare and participate
Received educational grant from Pfizer to support conference attendance (travel, accommodation and registration only)	May 2012		Within normal expenses of DOI policy	No action required
Gave an expert cardiovascular briefing (Gilenya in multiple scleroisis) for Novartis. Honorarium received.	4 May 2012		Personal non-specific pecuniary	Declare and participate
Session chair for the 'from myocardial ischaemia to heart failure conference. (Independent conference – education grant from Servier) Honorarium received.	16 May 2012		Personal non-specific pecuniary	Declare and participate
Attended an advisory board for Novartis on LCZ (trial medication for heart failure not licensed) in Chronic Heart Failure. Honorarium received.	24 May 2012		Personal non-specific pecuniary	Declare and participate
Presented at an educational meeting on Heart Failure and received honorarium from Pfizer.	13 June 2012		Personal non-specific pecuniary	Declare and participate
Presented at RCP Heart Failure Educational Update Lecture.	21 June 2012		Personal non-specific	Declare and participate

Item declared	Date	Expiry	Classification	Action taken
(Independent conference - education grant from Pfizer). Received honorarium.			pecuniary	
Advisory Board on Gilenya in multiple sclerosis for Novartis. Honorarium.	28 June 2012		Personal non-specific pecuniary	Declare and participate
Attended NICE acute heart failure stakeholder group	July 2012		Personal non-pecuniary	Declare and participate
Attended Department of Health cardiovascular disease long term conditions work stream.	July 2012		Personal non-pecuniary	Declare and participate
Presentation to Educational meeting (Pfizer)	July 17 2012		Personal non-specific pecuniary	Declare and participate
Presentation to Educational meeting (Servier)	July 24 2012		Personal non-specific pecuniary	Declare and participate
Presentation on the treatment of heart failure, 27 July 2012. Funded by Servier. ivabaradine.	July 2012		Personal non-specific pecuniary	Declare and participate
Educational grant to support one day development programme for local heart failure service. Pfizer pharmaceuticals reimbursed room hire, refreshments and facilitator.	Sept 2012	Sept 2013	Non-personal pecuniary	Declare and participate
Appointed chair of NICE Quality Standard Advisory Committee	2 September 2012		Personal non-pecuniary	Declare and participate
Attended American Heart Association annual meeting 3rd - 8th November and received accommodation expenses from Boehringer Ingelheim grants toward travel costs from Novartis, Servier and Pfizer.	3 – 8 November 2012		Within normal expenses of DOI policy	No action required
Participation on an advisory board for Novartis (regarding Relaxin for AHF).	28 November 2012	27 November 2013	Personal pecuniary non-specific interest	Declare and participate

B.1.7 Jim McLenachan

Item declared	Date	Expiry	Classification	Action taken
Clinical lead for the development of PPCI in Leeds since 2004.			Personal non-pecuniary	Declare and participate
Clinical lead for the development of PPCI in the West Yorkshire Cardiac Network since 2004.			Personal non-pecuniary	Declare and participate

Item declared	Date	Expiry	Classification	Action taken
Local investigator in the NIAP (National Infarct Angioplasty Project) in 2005.			Personal non-pecuniary	Declare and participate
Attended Lilly symposium on 17/11/10 and accepted the honorarium	17 November 2010	16 November 2011	Personal specific pecuniary	Declaration expires by date of Q4 (March 2012). Declare and participate.
The cardiology department at Leeds General Infirmary (in which I work) receives money from The Medicines Company to fund a research nurse post. Not administering any of these funds.	24 August 2011	-	Non-personal specific pecuniary	Declare and participate
Member (and past Honorary Secretary) of the British Cardiovascular Intervention Society and will attend the society's autumn meeting in October 2011. The society receives money from the British Cardiovascular Industry Association (BCIA) which is made up of a number of cardiac device and pharmaceutical companies. This money is then used to fund the meeting including overnight accommodation costs and travel expenses for invited speakers and chairmen.			Personal non-pecuniary	Declare and participate No contribution to SH comments from BCIS because answering on behalf of GDG
National Clinical Lead for PPCI with NHS Improvement, from September 2008 to date	September 2008	-	Personal non-pecuniary	Declare and participate
Gave presentation on 'Regional and National Roll-Out of PPCI' at a clinical cardiology meeting in York on 2/11/11. The meeting will be sponsored by the pharmaceutical company Lilly Ltd. No honorarium paid.	2 November 2011	1 November 2012	Personal non-pecuniary	Declare and participate
Attendance at ACI 2012 travel and expenses.	25/26 January 2012	24 January 2013	Within normal expenses of DOI policy	No action required

B.1.8 Francesco Palmer

Item declared	Date	Expiry	Classification	Action taken
None declared				No action required

B.1.9 Gerald Robinson

Item declared	Date	Expiry	Classification	Action taken
Member of the Birmingham, Sandwell & Solihull Cardiac and Stroke	29 July 2011	-	Personal non-	No action required

Item declared	Date	Expiry	Classification	Action taken
Network Shadow Board. This is a voluntary position.			pecuniary	

B.1.10 Fiona Sayers

Item declared	Date	Expiry	Classification	Action taken
Member of the NICE guideline development group on the prevention of stroke and systemic embolism in patients with atrial fibrillation	24 August 2011	-	Personal non-pecuniary	Declare and participate
Technology appraisal group member for rivaroxaban	24 August 2011	-	Personal non-pecuniary	Declare and participate

B.1.11 David Smith (Wales)

Item declared	Date	Expiry	Classification	Action taken
Received sponsorship from Biosensors International (who make and sell coronary stents) to attend the TCT conference in Miami from October 22nd to 26th 2012. I received sponsorship for registration, travel and accommodation costs but received no other monies.	22 – 26 October 2012	25 October 2013	Within normal expenses of DOI policy	No action required

B.1.12 LDR Smith

Item declared	Date	Expiry	Classification	Action taken
Attendance at European Society of Cardiology conference – registration, travel and expenses only reimbursed by Boehringer Ingleheim	30/31 August 2010	30 August 2011	Within normal expenses of DOI policy	No action required
Registration, travel and expenses only paid for by BCOS for BCIS Meeting and BCIS Clinical Standards Committee	7/8 October 2010	7 October 2011	Within normal expenses of DOI policy	No action required
Attendance at best practice in Cardiology (London) funded by PriMed, honorarium in addition to travel and accommodation received.	13 October 2011	12 October 2012	Personal non-specific	Declare and participate
Attendance at best practice in Cardiology (Manchester) funded by PriMed, honorarium in addition to travel and accommodation received.	10/11 November 2011	10 November 2012	Personal non-specific	Declare and participate
Accommodation, travel and expenses reimbursed by Boston	26/27 November	26 November	Within normal	No action required

Item declared	Date	Expiry	Classification	Action taken
Scientific to attend SWIG/IWEST in Bath	2010	2011	expenses of DOI policy	
Accommodation, travel and expenses reimbursed by Biosensors to attend meeting on PCI in the CGH in Basingstoke.	2/3 March 2011	2 March 2012	Within normal expenses of DOI policy	No action required
Accommodation, travel and expenses reimbursed by the Royal College of Physicians to attend a meeting on acute general medicine for physicians in Birmingham.	25/26 May 2011	25 May 2012	Within normal expenses of DOI policy	No action required
Accommodation, travel and expenses reimbursed by BCS to attend the BCS annual scientific sessions.	13-15 June 2011	14 June 2012	Within normal expenses of DOI policy	No action required
Member BCIS council			Personal non-pecuniary	Declare and participate No contribution to SH comments from BCIS because answering on behalf of GDG
Member of the International Editorial board for Heart			Personal non-pecuniary	Declare and participate
Member of NIAP being one of 7 hospitals involved in study			Personal non-pecuniary	Declare and participate
Attended TCT conference in Miami, USA (21-25 October). Biosensors (coronary stent manufacturer) paid for travel, accommodation and registration but I did not receive any other payment from the company.	21-25 October 2012	24 October 2013	Within normal expenses of DOI policy	Declare and participate

B.1.13 Mark Whitbread

Item declared	Date	Expiry	Classification	Action taken
Member of the JRCALC guidelines committee			Personal non-pecuniary	Declare and participate
Member of NICE guideline development group for the UA/NSTEMI guideline		Issued March 2010	Expired	No action required

B.2 Invited experts

B.2.1 Keith Fox

Item declared	Date	Expiry	Classification	Action taken
Invited speaker for, and honoraria received from: Bayer, Johnson & Johnson, Astra Zeneca and Sanofi Aventis	September 2012	August 2013	Personal specific pecuniary	No action required – Keith Fox did not attend any GDG meetings and was not involved in discussing recommendations.
Grants received from Lilly and Bayer/Johnson & Johnson	Ongoing		Non-personal pecuniary	No action required – Keith Fox did not attend any GDG meetings and was not involved in discussing recommendations.

B.2.2 Tony Gershlick (Attended one session of GDG 10)

Item declared	Date	Expiry	Classification	Action taken
Support to attend meetings and financial remuneration for advisory boards for ABBOT Vascular, Metronic Corp and Boston Scientific.	September 2012	August 2013	Personal specific pecuniary	No action required – Professor Gershlick was not involved in discussing recommendations.
Remuneration for attendance at Steering Committee and TC re. trial management for the STREAM trial. Boehringer Ingelhiem.	Ongoing		Personal specific pecuniary	No action required – Professor Gershlick was not involved in discussing recommendations.

B.3 Technical team

B.3.1 Daria Bilan

Item declared	Date	Expiry	Classification	Action taken
None declared				No action required

B.3.2 Serena Carville (from October 2012)

Item declared	Date	Expiry	Classification	Action taken
None declared				No action required

B.3.3 Angela Cooper (from December 2011)

Item declared	Date	Expiry	Classification	Action taken
Co-author with Jane S Skinner on BMJ Clinical evidence reviews, Secondary prevention of ischaemic cardiac events, Clinical Evidence 2011; 08:2	2011		No conflict	No action required

B.3.4 Martin Harker (from April 2012)

Item declared	Date	Expiry	Classification	Action taken
None declared				No action required

B.3.5 Taryn Krause (until October 2012)

Item declared	Date	Expiry	Classification	Action taken
None declared				No action required

B.3.6 Kate Lovibond (until August 2012)

Item declared	Date	Expiry	Classification	Action taken
None declared				No action required

B.3.7 Jill Parnham

Item declared	Date	Expiry	Classification	Action taken
Employment contract with the Royal College of Physicians	2001		No conflict	No action required No contribution to SH comments from RCP because answering on behalf of GDG
Accept NICE commissions			Non-personal pecuniary	Declare and participate
Various publications unrelated to STEMI			No conflict	No action required

B.3.8 Robert Pitcher (until January 2012)

Item declared	Date	Expiry	Classification	Action taken
None declared				No action required

B.3.9 Carlos Sharpin

Item declared	Date	Expiry	Classification	Action taken
None declared				No action required

Appendix C: Review protocols

Table 1: Review protocol: Time to reperfusion

Review question	What is the duration of PPCI-related time delay at which fibrinolysis becomes more clinically and cost effective compared to PPCI in people with STEMI and how is this modulated by patient presentation delay and patient risk profile?
Objectives	To determine the duration of PPCI-related time delay at which fibrinolysis becomes more clinically and cost effective compared to PPCI in people with STEMI.
Criteria	**Population:** Adults (≥ 18 years old) with STEMI to be managed by reperfusion therapy. **Intervention:** PPCI. Plus standard adjunctive pharmacotherapies (for example, antiplatelet and antithrombin agents). **Comparison:** Fibrinolytic therapy (in-hospital or pre-hospital; any agent). Plus standard adjunctive pharmacotherapies (for example, antiplatelet and antithrombin agents). **Outcomes (original study definitions will be used and recorded):** • Mortality (all-cause and cardiovascular specific) • Non-fatal and all (non-fatal and fatal) stroke • Non-fatal and all (non-fatal and fatal) myocardial reinfarction • Heart failure • Minor and major bleeding • Revascularisation (unplanned) • Length of hospital stay • Quality of life (report all, inc EQ-5D (EuroQol), SF-36 (Short Form 36), SF6D (Short Form 6-Dimensions), SF-12 (Short Form 12-Dimensions), RAND-36 (Research and Development Medical Outcomes Study Short Form-36)) • Time to equipoise between the treatments for outcomes listed above. **Study design:** RCTs that stratify people based on time to presentation or PPCI-related time delay Meta-regression analyses or other modelling techniques that assess impact of time to presentation or PPCI-related time delay on relative benefits of fibrinolysis and PPCI, based on : ≥10 RCTs or UK registry data or International registry data (n>100,000). **Population size and directness:** No limitations on sample size (unless registry data – n>100,000) Studies with indirect populations will not be considered. **Setting:** Pre-hospital Secondary care
Search	See appendix F

Strategy	
Review Strategy	**Quality of life data** Collect all data for the stated quality of life measure, for meta-analysis and GRADE report only overall scores. **Appraisal of methodological quality** The methodological quality of each study will be assessed using adapted NICE checklists and GRADE. Limitations include the robustness of modelling technique (for example, use of patient/hospital level covariates, sensitivity analyses) and quality of input data (for example, patient/hospital/study-level data; number of studies; RCTs versus registry data; proportion of studies using streptokinase, stents and GPIs; conference abstracts versus full articles). **Data synthesis** We will record results of meta-regression analyses and other modelling techniques. We will also analyse each constituent RCT and where possible, meta-analyse data stratified by time to presentation. **Subgroups:** The following groups will be considered separately if data is present: • People with diabetes • People with renal dysfunction • People aged over 70 years • Ethnicity • Gender • MI location • MI size.

Table 2: Review protocol: Facilitated PPCI

Review question	What is the clinical and cost effectiveness of facilitated PPCI (fPPCI) compared to PPCI in people with STEMI?
Objectives	To compare the clinical and cost effectiveness of facilitated PPCI and PPCI, for the treatment of adults with STEMI.
Criteria	**Population:** Adults (≥ 18 years old) with STEMI eligible for PPCI. **Intervention:** • In people already scheduled to have PCI. Facilitated PCI: use of pharmacological agents (GPIs, fibrinolytics or heparin OR a combination of any of these classes) before an anticipated PPCI to improve coronary patency • pharmacological agents can be given any time before PPCI, before arrival in the cath lab, and given with the intention of facilitation (ambulance, hospital, accident and emergency) • people must also be on a background of at least one oral antiplatelet agent, and may have been given an antithrombin • older studies = aspirin with/without heparin • newer studies = aspirin + clopidogrel (or other ADP antagonists) with/without heparin. **Comparison:** • In people with STEMI where the intended reperfusion strategy is PPCI. PPCI arm: PPCI with or without placebo or adjunctive therapy • adjunctive therapy: GPIs • adjunctive therapy drugs must be given in the cath lab or at time of PPCI, not before

	• they should ideally should be the same drugs as given in the fPPCI arm • newer studies give GPIs as part of standard PPCI therapy, in this case a suitable comparator fPPCI arm must be on combination therapy (GPI + fibrinolytic or heparin) OR they could be given the same drug but at an earlier time (ie. Studies comparing upstream/pre-cath lab administration fPPCI versus downstream/cath-lab administration fPPCI) • people must also be on a background of at least one antiplatelet agent • older studies = aspirin with/without heparin • newer studies = aspirin + clopidogrel (or other ADP antagonists) with/without heparin) • background antiplatelet therapy must be the same as in the fPPCI arm. Additional intervention and comparison • We will also look at studies that assess the effect of early versus later fPPCI. **Outcomes (original study definitions will be used and recorded):** • Mortality (all-cause and cardiovascular specific) • Non-fatal and all (non-fatal and fatal) stroke. • Non-fatal and all (non-fatal and fatal) myocardial reinfarction • Major and minor bleeding. Note intracranial bleeding separately • Heart failure • Repeat revascularisation (this includes TVR, repeat revascularisation, unplanned revascularisation and urgent revascularisation) • Length of hospital stay • Quality of life (report all, including EQ-5D (EuroQol), SF-36 (Short Form 36), SF6D (Short Form 6-Dimensions), SF-12 (Short Form 12-Dimensions), RAND-36 (Research and Development Medical Outcomes Study Short Form-36)). **Study design:** • RCT **Additional inclusion / exclusion criteria including population size and directness:** • Studies with indirect populations will not be considered (population must be 100% STEMI or AMI). • Only studies published after 1990 will be considered. This is to ensure that the extracted evidence is reflective of current practice, especially with regard to the widespread adoption of stenting in place of balloon angioplasty for PCI procedures over the last 15 years. • Rescue PCI in either arm rather than scheduled PCI (this is after failed fibrinolysis, therefore not all people had PCI) • Elective PCI in either arm rather than scheduled PCI (as this is indicative of not being STEMI population). • Old meta-analyses (pre-2008). • If, during sifting of the abstract lists, the abstract does not mention PCI occurring after fibrinolysis (as this is indicative of fibrinolysis NOT facilitated PCI). • Outcomes stated are not post-PCI period - just pre-PCI (as this means results are for the fibrinolysis and not the facilitated PCI). • PCI must have been performed in at least 85% of people in each group. • Exclude trials of n<60 where there are other larger trials using the same class of intervention (for example, GPI or fibrinolytic) and comparison. • Exclude trials that did not use stents or <50% people received stents (as this would not be a good representation of current clinical practice). Also exclude studies if they do not mention the percentage of stent usage.

	Setting: • Pre-hospital (pharmacological component of facilitated PCI) • Secondary care (pharmacological component of facilitated PCI; PCI).
Search strategy	See appendix F
Review strategy	**Quality of life data** • Collect all data for the stated quality of life measure, for meta-analysis and GRADE report only overall scores. **Appraisal of methodological quality** • The methodological quality of each study will be assessed using NICE checklists and GRADE. **Data synthesis of RCT data** Meta-analysis where appropriate will be conducted. **Subgroups:** The following groups will be considered separately if data is present (we will only consider subgroup analyses when people were stratified according to subgroups or the analyses were pre-specified in the study protocol): • People with diabetes • People from black and minority ethnic groups • People with renal dysfunction • People of female gender • People aged over 70 years (70 is an approximate cut-off age, record what age the study uses that is near to 75 years). If heterogeneity is present among studies the following subgroups will be examined. in addition to those stated above: • People receiving balloon angioplasty versus stenting • People using GPIs administered in the catheterisation laboratory immediately before PCI versus selective GPIs versus no GPIs at this time-point.

Table 3: Review protocol: Radial versus femoral access for PPCI

Review question	**What is the clinical and cost effectiveness of radial access compared to femoral access for coronary angiography and, if appropriate, follow-on PPCI in people with STEMI managed by PPCI?**
Objectives	To determine whether it is more clinically beneficial to perform PPCI by radial artery access or femoral artery access.
Criteria	**Population:** Adults (≥ 18 years old) with STEMI eligible for PPCI. **Intervention:** Radial access to perform coronary angiography and PPCI (if clinically indicated); Plus standard adjunctive pharmacotherapies (for example, antiplatelet and antithrombin agents). **Comparison:** Femoral access to perform coronary angiography and PPCI (if clinically indicated); Plus standard adjunctive pharmacotherapies (for example, antiplatelet and antithrombin agents). **Outcomes (original study definitions will be used and recorded):** • Mortality (all-cause and cardiovascular specific) • Non-fatal and all (fatal and non-fatal) stroke

	• Intracranial bleeding • Non-fatal and all (fatal and non-fatal) myocardial reinfarction • Heart failure • Repeat revascularisation • Access site crossover • Inability to cross the lesion with a wire, balloon or stent during PCI • Radiation exposure (X-ray time/fluoroscopic exposure) or procedural time if noted • PCI procedural success • Adverse events (major and minor bleeding) • Length of hospital stay • Patient experience (pain) • Vascular access site complications • Quality of life (report all, including EQ-5D (EuroQol), SF-36 (Short Form 36), SF6D (Short Form 6-Dimensions), SF-12 (Short Form 12-Dimensions), RAND-36 (Research and Development Medical Outcomes Study Short Form-36)). **Study design:** RCT **Population size and directness:** • No limitations on sample size. • Studies with indirect populations will not be considered. • Only studies published after 1990 will be considered. This is to ensure that the extracted evidence is reflective of current practice, especially with regard to the widespread adoption of stenting in place of balloon angioplasty for PPCI procedures over the last 15 years. • Where ≥3 RCTs (with a combined population of ≥500 people) deploy stents in≥50% of PPCI procedures (in which stenting is feasible) we will exclude studies where stents are deployed in <50% of PPCI procedures. • Where <3 RCTs deploy stents in ≥50% of PPCI procedures (or the total population of RCTs deploying stents is <500 people) we will include all studies that began enrolling people after 1996. • If <3 RCTs began enrolling people after 1996 (or the total population is <500 people), we will consider all studies published after 1990. **Setting:** Secondary care
Search strategy	See appendix F
Review strategy	**Quality of life data** Collect all data for the stated quality of life measure, for meta-analysis and GRADE report only overall scores. **Appraisal of methodological quality** The methodological quality of each study will be assessed using NICE checklists and GRADE. **Data synthesis of RCT data** Meta-analysis where appropriate will be conducted. **Subgroups:** The following groups will be considered separately if data is present (we will only consider

	subgroup analyses when people were stratified according to subgroups or the analyses were pre-specified in the study protocol): • People with diabetes • People with renal dysfunction • BMI • People aged > 70 years • Gender • Ethnicity If heterogeneity is present among studies the following subgroups will be examined in addition to those stated above: • Operator expertise • People receiving GPIs versus people not receiving GPIs • BMI.

Table 4: Review protocol: Thrombus extraction during PPCI

Review question	**What is the clinical and cost effectiveness of using thrombus extraction devices (catheter aspiration devices, mechanical thrombectomy devices) during PPCI compared with PPCI alone for the treatment of STEMI in adults?**
Objectives	To determine the clinical and cost effectiveness of thrombus extraction devices in people with STEMI managed by PCI.
Criteria	**Population:** Adults (≥ 18 years old) with STEMI managed by PPCI. **Intervention:** PPCI plus thrombus extraction device. The devices will be sub-grouped: • Thrombus aspiration devices (includes simple, manual, and aspiration devices) • Mechanical thrombus extraction (includes mechanical and non-manual devices). **Comparator:** Standard PPCI. **Outcomes (original study definitions will be used and recorded):** • Mortality (all-cause and cardiovascular specific) • Non-fatal and all (fatal and non-fatal) stroke. • Non-fatal and all (fatal and non-fatal) myocardial reinfarction • Heart failure • Target vessel revascularisation • Major and minor bleeding. Note intracranial bleeding separately. • Length of hospital stay • Quality of life (report all, inc EQ-5D (EuroQol), SF-36 (Short Form 36), SF6D (Short Form 6-Dimensions), SF-12 (Short Form 12-Dimensions), RAND-36 (Research and Development Medical Outcomes Study Short Form-36)). **Study design:** RCT **Population size and directness:** • No limitations on sample size. • Studies with indirect populations will not be considered.

	• Only studies published after 1990 will be considered. This is to ensure that the extracted evidence is reflective of current practice, especially with regard to the widespread adoption of stenting in place of balloon angioplasty for PCI procedures over the last 15 years. • Where ≥3 RCTs (with a combined population of ≥500 people) deploy stents in≥50% of PCI procedures (in which stenting is feasible) we will exclude studies where stents are deployed in <50% of PCI procedures. • Where <3 RCTs deploy stents in ≥50% of PCI procedures (or the total population of RCTs deploying stents is <500 people) we will include all studies that began enrolling people after 1996. • If <3 RCTs began enrolling people after 1996 (or the total population is <500 people), we will consider all studies published after 1990. **Setting:** Secondary care
Search Strategy	See appendix F
Review Strategy	**Quality of life data** Collect all data for the stated quality of life measure, for meta-analysis and GRADE report only overall scores. **Appraisal of methodological quality** The methodological quality of each study will be assessed using NICE checklists and GRADE. **Data synthesis of RCT data:** Meta-analysis where appropriate will be conducted.

Table 5: Review protocol: Culprit versus complete revascularisation
****Updated, see the 2020 evidence review ****

Review question	**What is the clinical and cost effectiveness of multivessel PCI compared to culprit-only PPCI in people with STEMI and multivessel coronary disease undergoing primary PCI (PPCI)?**
Objectives	To compare the clinical and cost effectiveness of multivessel coronary artery, primary percutaneous revascularisation and culprit-only primary percutaneous revascularisation in people with STEMI and multivessel coronary disease.
Criteria	**Population:** Adults (≥ 18 years old) with STEMI and multivessel coronary disease. **Intervention:** Culprit vessel only PPCI. Plus standard adjunctive pharmacotherapies (for example, antiplatelet and antithrombin agents). Culprit vessel only PPCI defined as PPCI confined to culprit vessel lesions only. **Comparison:** • Multivessel PCI during the index procedure). Plus standard adjunctive pharmacotherapies (for example, antiplatelet and antithrombin agents). Multivessel PCI defined as PCI in which lesions in the culprit vessel as well as ≥ 1 non-culprit vessel were treated during the same procedure. • Staged multivessel PCI. Plus standard adjunctive pharmacotherapies (for example, antiplatelet and antithrombin agents). Staged PCI defined as PCI confined to the culprit vessel only after which ≥ 1 non-culprit vessel were treated during planned secondary procedures. The timing of the secondary procedure is during the index hospitalisation for STEMI. The timing of staged PCI procedures was defined as reported in each study. **Outcomes (original study definitions will be used and recorded):**

- Mortality (all-cause and cardiovascular specific)
- Non-fatal and all (fatal and non-fatal) stroke
- Non-fatal and all (fatal and non-fatal) myocardial reinfarction
- Heart failure
- Unplanned revascularisation
- Major and minor bleeding. Note intracranial bleeding separately
- Contrast-induced nephropathy (also note population that goes onto dialysis/renal replacement therapy)
- Length of hospital stay
- Radiation exposure (fluoroscopic time/X-ray time) or if not recorded, procedural time
- PCI procedural success
- Quality of life (report all, including EQ-5D (EuroQol), SF-36 (Short Form 36), SF6D (Short Form 6-Dimensions), SF-12 (Short Form 12-Dimensions), RAND-36 (Research and Development Medical Outcomes Study Short Form-36)).

Study design:

Cohort study > 500 people

RCT.

Population size and directness:

- No limitations on sample size for RCTs; limitation for cohort studies > 500 people.
- Studies with indirect populations will not be considered.
- Only studies published after 1990 will be considered. This is to ensure that the extracted evidence is reflective of current practice, especially with regard to the widespread adoption of stenting in place of balloon angioplasty for PCI procedures over the last 15 years.
- Where ≥ 3 RCTs (with a combined population of ≥ 500 people) deploy stents in≥ 50% of PCI procedures (in which stenting is feasible) we will exclude studies where stents are deployed in < 50% of PCI procedures.
- Where < 3 RCTs deploy stents in ≥\50% of PCI procedures (or the total population of RCTs deploying stents is <\500 people) we will include all studies that began enrolling people after 1996.
- If < 3 RCTs began enrolling people after 1996 (or the total population is < 500 people), we will consider all studies published after 1990.

Setting:

Secondary care

Search strategy

See appendix F

Review strategy

Quality of life data

Collect all data for the stated quality of life measure, for meta-analysis and GRADE report only overall scores

Appraisal of methodological quality

The methodological quality of each study will be assessed using NICE checklists and GRADE.

Data synthesis of RCT data

Meta-analysis where appropriate will be conducted.

Subgroups:

The following groups will be considered separately if data is present (we will only consider subgroup analyses when people were stratified according to subgroups or the analyses were

	pre-specified in the study protocol): • Gender • Black and minority ethnic groups • People with diabetes • People with renal dysfunction • People aged over 70 years. If heterogeneity is present among studies the following subgroups will be examined in addition to those stated above: • People who are haemodynamically compromised versus people who are not • People with cardiogenic shock versus no cardiogenic shock • Stent use • GPI use.

Table 6: Review protocol: Cardiogenic shock

Review question	**In people with cardiogenic shock due to STEMI what is the clinical and cost effectiveness of early revascularisation compared to medical stabilisation?**
Objectives	To compare routine early revascularisation with initial medical stabilisation in people with cardiogenic shock due to STEMI.
Criteria	**Population:** Adults (≥ 18 years old) with cardiogenic shock due to STEMI. **Intervention:** Early revascularisation (undefined time frame). Defined as immediate angiography and PPCI or CABG when indicated. **Comparison:** Initial medical stabilisation (with or without subsequent revascularisation). **Outcomes (original study definitions will be used and recorded):** • Mortality (all-cause and cardiovascular specific) • Non-fatal and all (fatal and non-fatal) stroke. • Non-fatal and all (fatal and non-fatal) myocardial reinfarction • Heart failure • Unplanned revascularisation • Major and minor bleeding. Note intracranial bleeding separately • Renal failure (use of dialysis) • Length of hospital stay • Use of IABP (surrogate haemodynamic measures) • Quality of life (report all, inc EQ-5D (EuroQol), SF-36 (Short Form 36), SF6D (Short Form 6-Dimensions), SF-12 (Short Form 12-Dimensions), RAND-36 (Research and Development Medical Outcomes Study Short Form-36)). **Study design:** RCT. **Population size and directness:** • No limitations on sample size. • Studies with indirect populations will not be considered. • Only studies published after 1990 will be considered. This is to ensure that the extracted evidence is reflective of current practice, especially with regard to the widespread adoption

	of stenting in place of balloon angioplasty for PCI procedures over the last 15 years. • Where ≥3 RCTs (with a combined population of ≥500 people) deploy stents in≥50% of PCI procedures (in which stenting is feasible) we will exclude studies where stents are deployed in <50% of PCI procedures. • Where <3 RCTs deploy stents in ≥50% of PCI procedures (or the total population of RCTs deploying stents is <500 people) we will include all studies that began enrolling people after 1996. • If <3 RCTs began enrolling people after 1996 (or the total population is <500 people), we will consider all studies published after 1990. **Setting:** Secondary care Emergency care.
Search Strategy	See appendix F
Review Strategy	**Quality of life data** Collect all data for the stated QoL measure, for meta-analysis and GRADE report only overall scores. **Appraisal of methodological quality** The methodological quality of each study will be assessed using NICE checklists and GRADE. **Data synthesis of RCT data and subgroups:** Meta-analysis where appropriate will be conducted. The following groups will be considered separately or as subgroups if data is present (we will only consider subgroup analyses when people were stratified according to subgroups or the analyses were pre-specified in the study protocol): • People with diabetes • People with renal dysfunction • People aged over 70 years (or as reported in the studies) • Ethnicity • Gender.

Table 7: Review protocol: People who remain unconscious after a cardiac arrest

Review question	**Does immediate angiography followed by PPCI where indicated improve outcomes of people with presumed STEMI who are resuscitated but remain unconscious after a cardiac arrest?**
Objectives	To determine whether immediate angiography followed by PPCI where indicated improves outcomes in people who are resuscitated but remain unconscious after a cardiac arrest.
Criteria	**Population:** Adults (≥ 18 years old) who are resuscitated but remain unconscious after an out of hospital cardiac arrest due to STEMI. **Intervention:** Upon hospital entry, immediate transfer for coronary angiography followed by PPCI where indicated. Plus standard adjunctive pharmacotherapies (for example, antiplatelet and antithrombin agents) with or without therapeutic hypothermia. **Comparator:** Usual care. Defined as any care not involving immediate angiography followed by PPCI where indicated.

	Outcomes (original study definitions will be used and recorded): • Mortality (all-cause and cardiovascular specific) • Non-fatal and all (fatal and non-fatal) stroke • Non-fatal and all (fatal and non-fatal) myocardial reinfarction • Heart failure • Unplanned urgent target vessel revascularisation • Major and minor bleeding ; note intracranial bleeding separately • Use of intra-aortic balloon pump • Length of hospital stay • Neurologically intact survival at discharge (CPC score) or other measures of neurological disability • Quality of life (report all, inc EQ-5D (EuroQol), SF-36 (Short Form 36), SF6D (Short Form 6-Dimensions), SF-12 (Short Form 12-Dimensions), RAND-36 (Research and Development Medical Outcomes Study Short Form-36)). **Study design:** RCTs and systematic reviews first. Prospective comparative observational prospective and retrospective studies if no RCTs are available. **Population size and directness:** No limitations on sample size. Studies with indirect populations will not be considered. **Setting:** Pre-hospital Hospital.
Search strategy	See appendix F
Review strategy	**Quality of life data** Collect all data for the stated quality of life measure, for meta-analysis and GRADE report only overall scores. **Appraisal of methodological quality** The methodological quality of each study will be assessed using NICE checklists and GRADE. **Data synthesis of RCT data** Meta-analysis where appropriate will be conducted. **Subgroups:** The following groups will be considered separately if data is present (we will only consider subgroup analyses when people were stratified according to subgroups or the analyses were pre-specified in the study protocol): • People with diabetes • People with renal dysfunction • People aged over 70 years • Ethnicity • Gender. If heterogeneity is present among studies the following subgroups will be examined in addition to those stated above: • People receiving GPIs versus people not receiving GPIs

	• Balloon angioplasty versus stenting.

Table 8: Review protocol: Hospital volumes of PPCI

Review question	What is the impact of high volume versus low volume PPCI services on patient outcomes?
Objectives	To consider the clinical and cost effectiveness of volume on PPCI services in people with STEMI.
Criteria	**Population:** Adults (≥ 18 years old) with ST-segment elevation. **Prognostic factor:** Hospital PPCI volume (not rescue, facilitated, elective angiography). **Outcomes at following time intervals: in hospital, 30 days, 6 months, 1 year, longest follow-up (original study definitions will be used and recorded):** • Mortality (all-cause and cardiovascular specific) • Non-fatal and all (non-fatal and fatal) stroke • Non-fatal and all (non-fatal and fatal) myocardial reinfarction • Heart failure • Unplanned revascularisation (where information available we will record whether index lesion or not) • Major and minor bleeding • Length of hospital stay • Quality of life (report all, including EQ-5D (EuroQol), SF-36 (Short Form 36), SF6D (Short Form 6-Dimensions), SF-12 (Short Form 12-Dimensions), RAND-36 (Research and Development Medical Outcomes Study Short Form-36)). **Study design:** Prospective and retrospective observational data. **Population size and directness:** • Majority of the data collected post 1 January 1995 • Studies with >1000 participants • Studies with indirect populations will not be considered • Only data collected after 1995 will be considered with ≥50% of stent use in PCI procedures. This is to ensure that the extracted evidence is reflective of current practice, especially with regard to the widespread adoption of stenting in place of balloon angioplasty for PCI procedures over the last 15 years. **Setting:** Secondary care.
Search Strategy	See appendix F
Review Strategy	**Quality of life data** Collect all data for the stated quality of life measure, for meta-analysis and GRADE report only overall scores. **Appraisal of methodological quality** The methodological quality of each study will be assessed using NICE checklists and GRADE.

	Subgroups: The following groups will be considered separately if data is present (we will only consider subgroup analyses when people were stratified according to subgroups or the analyses were pre-specified in the study protocol): • Gender • Black and minority ethnic groups • People with diabetes • People with renal dysfunction • People aged over 70 years.

Table 9: Review protocol: Pre-hospital versus in-hospital fibrinolysis

Review question	What is the clinical and cost effectiveness of pre-hospital versus in-hospital fibrinolysis?
Objectives	To determine whether it is more beneficial to administer fibrinolysis before a patient arrives at hospital or in-hospital
Criteria	**Population:** Adults (≥ 18 years old) with STEMI to be managed by fibrinolysis. **Intervention:** Pre-hospital fibrinolysis (all agents). Plus standard adjunctive pharmacotherapies (for example, antiplatelet and antithrombin agents). **Comparison:** In-hospital fibrinolysis (all agents). Plus standard adjunctive pharmacotherapies (for example, antiplatelet and antithrombin agents). **Outcomes (original study definitions will be used and recorded):** • Mortality (all-cause and cardiovascular specific) • All-cause stroke (non-fatal and fatal) • Intracranial bleeding • Myocardial reinfarction (non-fatal and fatal) • Heart failure • Major and minor bleeding • Subsequent revascularisation • Length of hospital stay • Quality of life (report all, inc EQ-5D (EuroQol), SF-36 (Short Form 36), SF6D (Short Form 6-Dimensions), SF-12 (Short Form 12-Dimensions), RAND-36 (Research and Development Medical Outcomes Study Short Form-36)). **Study design:** RCTs. **Population size and directness:** • No limitations on sample size. • Studies with indirect populations will not be considered. **Setting:** • Pre-hospital • Secondary care.
Search	See appendix F

Strategy	
Review Strategy	**Quality of life data:** • Collect all data for the stated QoL measure, for meta-analysis and GRADE report only overall scores. **Appraisal of methodological quality:** • The methodological quality of each study will be assessed using NICE checklists and GRADE. **Data synthesis of RCT data and subgroups:** Meta-analysis where appropriate will be conducted. If heterogeneity is present among studies the following subgroups will be examined: • People with diabetes • People with renal dysfunction • People aged > 70 years • Ethnicity • Gender.

Table 10: Review protocol: Use of antithrombin as an adjunct to fibrinolysis

Review question	Does administration of anti-thrombin treatment at the same time as pre-hospital fibrinolysis improve outcomes compared to administration of pre-hospital fibrinolysis alone?
Objectives	To determine whether administration of anti-thrombin treatment at the same time as pre-hospital fibrinolysis improves outcomes compared to administration of pre-hospital fibrinolysis alone.
Criteria	**Population:** Adults (≥ 18 years old) with STEMI managed by pre-hospital fibrinolysis (reteplase or tenecteplase). **Interventions:** • Unfractionated heparin plus antiplatelet therapy. • LMWH plus antiplatelet therapy. • Bivalirudin plus antiplatelet therapy. • Fondaparinux plus antiplatelet therapy. **Comparison:** No pre-hospital anti-thrombin treatment. **Outcomes (original study definitions will be used and recorded):** • Mortality (all-cause and cardiovascular specific) • Non-fatal and all (fatal and non-fatal) stroke. • Non-fatal and all (fatal and non-fatal) myocardial reinfarction • Heart failure • Unplanned revascularisation • Major and minor bleeding. Note intracranial bleeding separately • Length of hospital stay • Quality of life (report all, including EQ-5D (EuroQol), SF-36 (Short Form 36), SF6D (Short Form 6-Dimensions), SF-12 (Short Form 12-Dimensions), RAND-36 (Research and Development Medical Outcomes Study Short Form-36)). **Study design:** RCT.

	Population size and directness: No limitations on sample size Studies with indirect populations will not be considered. **Setting:** Emergency care, secondary care.
Search Strategy	See appendix F
Review Strategy	**Quality of life data** Collect all data for the stated quality of life measure, for meta-analysis and GRADE report only overall scores. **Appraisal of methodological quality** The methodological quality of each study will be assessed using NICE checklists and GRADE. **Data synthesis of RCT data** Meta-analysis where appropriate will be conducted. **Subgroups:** The following groups will be considered separately if data is present (we will only consider subgroup analyses when people were stratified according to subgroups or the analyses were pre-specified in the study protocol): • People with diabetes • People with renal dysfunction • People aged over 70 years.

Table 11: Review protocol: Rescue PCI

Review question	**What is the clinical and cost effectiveness of rescue PCI, repeated fibrinolysis or conservative management compared to each other in people with STEMI who fail to reperfuse after fibrinolytic therapy?**
Objectives	To compare the clinical and cost effectiveness of rescue PCI, repeated fibrinolysis and conservative management in people with STEMI who fail to reperfuse after fibrinolytic therapy.
Criteria	**Population:** Adults (≥ 18 years old) with STEMI who fail to reperfuse after fibrinolytic therapy (any agent). **Intervention:** Rescue PCI; defined as unplanned emergency PCI in people who fail to reperfuse after fibrinolysis. Plus standard adjunctive pharmacotherapies (for example, antiplatelet and antithrombin agents). **Comparison:** • Repeat fibrinolysis (any agent) plus standard adjunctive pharmacotherapies (for example, antiplatelet and antithrombin agents) or • Conservative management. Defined as standard medical therapy for MI without fibrinolysis or PCI. **Outcomes at following time intervals: in hospital, 30 days, 6 months, 1 year, longest follow-up (original study definitions will be used and recorded):** • Mortality (all-cause and cardiovascular specific)

	• Non-fatal and all (non-fatal and fatal) stroke • Non-fatal and all (non-fatal and fatal) myocardial reinfarction • Heart failure • Unplanned revascularisation (Where information is available we will record whether index lesion or not) • Major and minor bleeding • Length of hospital stay • Quality of life (report all, including EQ-5D (EuroQol), SF-36 (Short Form 36), SF6D (Short Form 6-Dimensions), SF-12 (Short Form 12-Dimensions), RAND-36 (Research and Development Medical Outcomes Study Short Form-36)). **Study design:** RCT **Population size and directness:** • No limitations on sample size. • Studies with indirect populations will not be considered. • Only studies published after 1990 will be considered. This is to ensure that the extracted evidence is reflective of current practice, especially with regard to the widespread adoption of stenting in place of balloon angioplasty for PCI procedures over the last 15 years. • Where ≥3 RCTs (with a combined population of ≥500 people) deploy stents in≥50% of PCI procedures (in which stenting is feasible) we will exclude studies where stents are deployed in <50% of PCI procedures. • Where <3 RCTs deploy stents in ≥50% of PCI procedures (or the total population of RCTs deploying stents is <500 people) we will include all studies that began enrolling people after 1996. • If <3 RCTs began enrolling people after 1996 (or the total population is <500 people), we will consider all studies published after 1990. **Setting:** Secondary care
Search Strategy	See appendix F
Review Strategy	**Quality of life data** Collect all data for the stated quality of life measure, for meta-analysis and GRADE report only overall scores. **Appraisal of methodological quality** The methodological quality of each study will be assessed using NICE checklists and GRADE. **Data synthesis of RCT data** Meta-analysis where appropriate will be conducted. **Subgroups:** The following groups will be considered separately if data is present (we will only consider subgroup analyses when people were stratified according to subgroups or the analyses were pre-specified in the study protocol): • Gender • Black and minority ethnic groups • People with diabetes • People with renal dysfunction

	• *People aged over 70 years (or age breakdown as reported in the study). If heterogeneity is present among studies the following subgroups will be examined in addition to those above: • People receiving balloon angioplasty versus stenting • People receiving GPIs with PCI versus no GPIs with PCI.

Table 12: Review protocol: Routine early angiography following fibrinolysis

Review question	What is the clinical and cost effectiveness of routine early angiography following STEMI successfully treated by fibrinolysis compared to routine deferred or selective angiography?
Objectives	To compare the clinical and cost effectiveness of routine early angiography following STEMI treated by fibrinolysis to routine deferred or selective angiography.
Criteria	**Population:** Adults (≥ 18 years old) who were fibrinolysed (any agent) for STEMI. **Intervention:** Early routine angiography (and intervention if indicated) following fibrinolysis. Defined as planned angiography within 24 h after fibrinolysis was administered. **Comparison:** Conservative approach following fibrinolysis. Defined as either routine deferred (≥24 h after fibrinolysis administered) or selective angiography. **Outcomes at following time intervals: in hospital, 30 days and 1 year (or closest to 1 year)(original study definitions will be used and recorded):** • Mortality (all-cause and cardiovascular specific) • Non-fatal and all (non-fatal and fatal) fatal stroke • Non-fatal and all (non-fatal and fatal) myocardial reinfarction • Unplanned revascularisation (Where information is available we will record whether index lesion or not) • Major and minor bleeding. Intracranial bleeding recorded separately • Length of hospital stay • Refractory ischaemia • Heart failure • Quality of life (report all, including EQ-5D (EuroQol), SF-36 (Short Form 36), SF6D (Short Form 6-Dimensions), SF-12 (Short Form 12-Dimensions), RAND-36 (Research and Development Medical Outcomes Study Short Form-36)). **Study design:** RCTs **Population size and directness:** • No limitations on sample size. • Studies with indirect populations will not be considered. • Only studies published after 1990 will be considered. This is to ensure that the extracted evidence is reflective of current practice, especially with regard to the widespread adoption of stenting in place of balloon angioplasty for PCI procedures over the last 15 years. • Where ≥3 RCTs (with a combined population of ≥500 people) deploy stents in≥50% of PCI procedures (in which stenting is feasible) we will exclude studies where stents are deployed in <50% of PCI procedures. • Where <3 RCTs deploy stents in ≥50% of PCI procedures (or the total population of RCTs deploying stents is <500 people) we will include all studies that began enrolling people after

	1996. • If <3 RCTs began enrolling people after 1996 (or the total population is <500 people), we will consider all studies published after 1990. **Setting:** Secondary care
Search Strategy	See appendix F
Review Strategy	**Quality of life data** Collect all data for the stated quality of life measure, for meta-analysis and GRADE report only overall scores. **Appraisal of methodological quality** The methodological quality of each study will be assessed using NICE checklists and GRADE. **Data synthesis of RCT data** Meta-analysis where appropriate will be conducted. **Subgroups:** The following groups will be considered separately if data is present (we will only consider subgroup analyses when people were stratified according to subgroups or the analyses were pre-specified in the study protocol): • Gender • Black and minority ethnic groups • People with diabetes • People with renal dysfunction • People aged over 70 years. If heterogeneity is present among studies the following subgroups will be examined in addition to those above: • High risk versus low risk patients • Mean time interval to angiography after fibrinolysis • People receiving GPIs with PCI versus no GPIs with PCI.

Table 13: Health economic review protocol

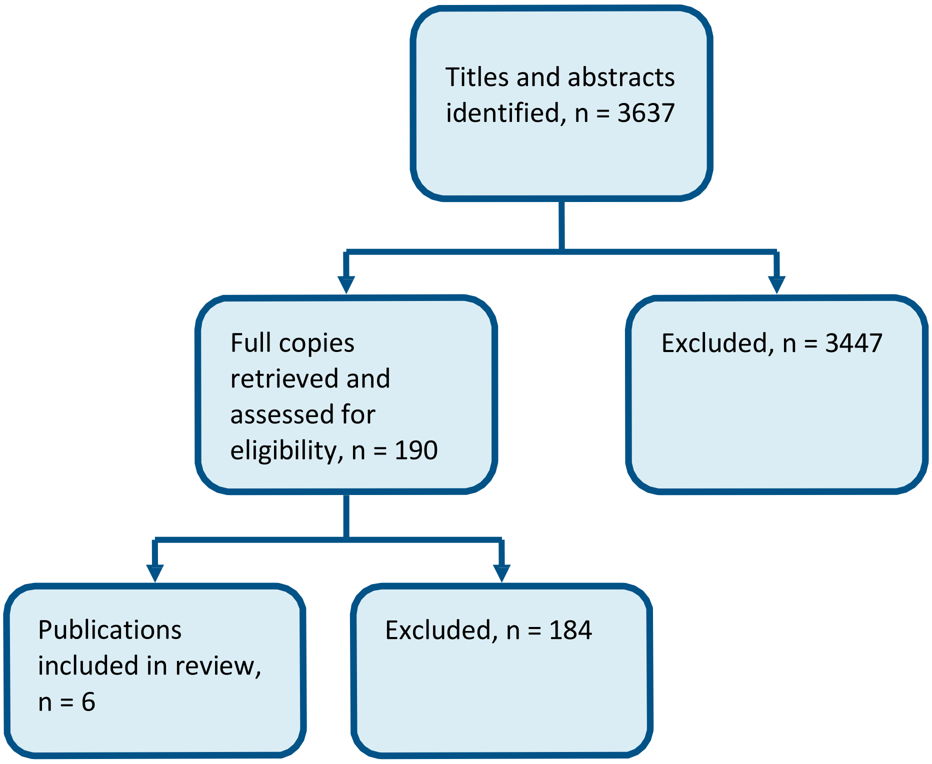
Review question	All review questions – health economic evidence
Objectives	To identify economic studies relevant to the review questions set out above.
Criteria	Populations, interventions and comparators as specified in the individual review protocols above. Must be a relevant economic study design (cost–utility analysis, cost–benefit analysis, cost-effectiveness analysis, cost–consequence analysis, comparative cost analysis).
Search strategy	An economic study search was undertaken using population-specific terms and an economic study filter – see Appendix F.
Review strategy	Each study is assessed using the NICE economic evaluation checklist which can be found in Appendix H of the NICE guidelines manual (2009).[87] **Inclusion and exclusion criteria** • If a study is rated as both 'Directly applicable' and 'Minor limitations' (using the NICE economic evaluation checklist) then it will be included in the guideline. An evidence table will be completed and it should be included in the economic profile. • If a study is rated as 'Partially applicable', 'Potentially serious limitations' or both then there

	is discretion over whether it should be included. The health economist will make a decision based on the relative applicability and quality of the available evidence for that question, in discussion with the GDG if required. The ultimate aim is to include studies that are helpful for decision-making in the context of the guideline and the current NHS setting. Where exclusions occur on this basis this will be noted in the relevant section of the guideline with references. • If a study is rated as 'Very serious limitations' then it will usually be excluded from the guideline. The health economist will make a decision based on the relative quality of the available evidence for that question, in discussion with the GDG if required. • If a study is rated as 'Not applicable' then it will be excluded from the guideline. An evidence table will not be completed and it will not be included in the economic profile. The following will also be excluded: • unpublished reports unless submitted as part of a call for evidence • abstract-only studies • letters • editorials and commentaries • reviews of economic evaluations • articles not in English. **Where there is discretion** The health economist will be guided by the following hierarchies. *Setting:* • UK NHS • OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden) • OECD countries with predominantly private health insurance systems (for example, USA, Switzerland) • non-OECD settings (always 'Not applicable'). *Economic study type:* • cost–utility analysis (QALYs as outcome measure) • other type of full economic evaluation (cost–benefit analysis, cost-effectiveness analysis, cost–consequence analysis) • comparative cost analysis • non-comparative cost analyses including cost of illness studies (always 'Not applicable'). *Year of analysis:* • Studies that are based on resource use and unit costs from more than 10 years ago will be downgraded in terms of applicability. • Studies that are based on resource use and unit costs from more than 20 years ago will be judged 'Not applicable'. *Quality and relevance of effectiveness data used in the economic analysis:* • The more closely the effectiveness data used in the economic analysis matches with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making for the guideline.

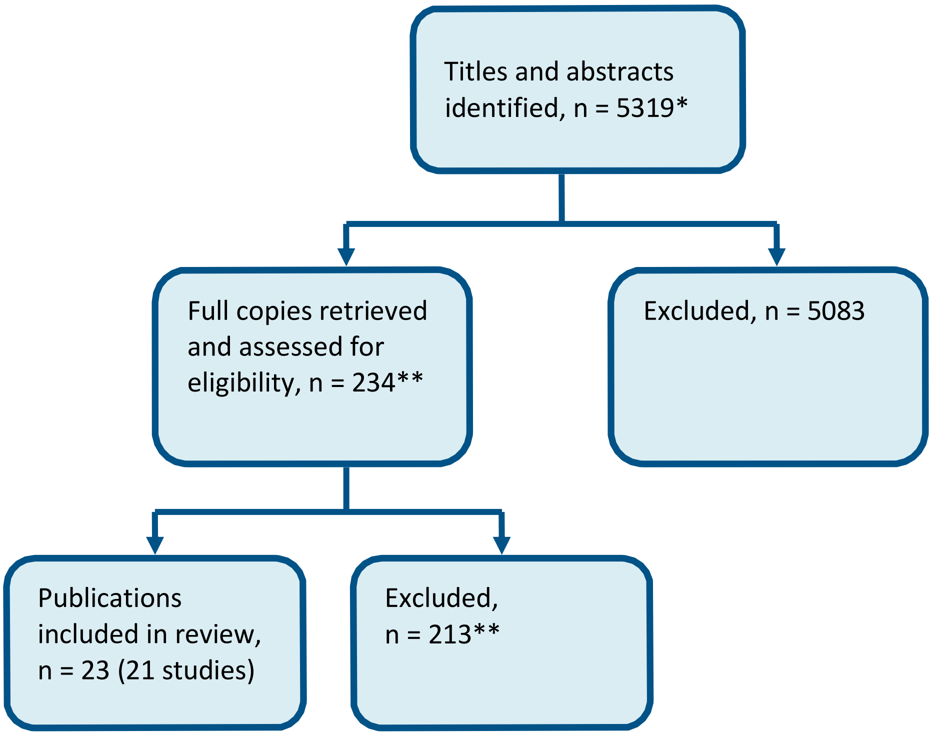
(a) Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered

Appendix D: Clinical article selection

D.1 Time to reperfusion



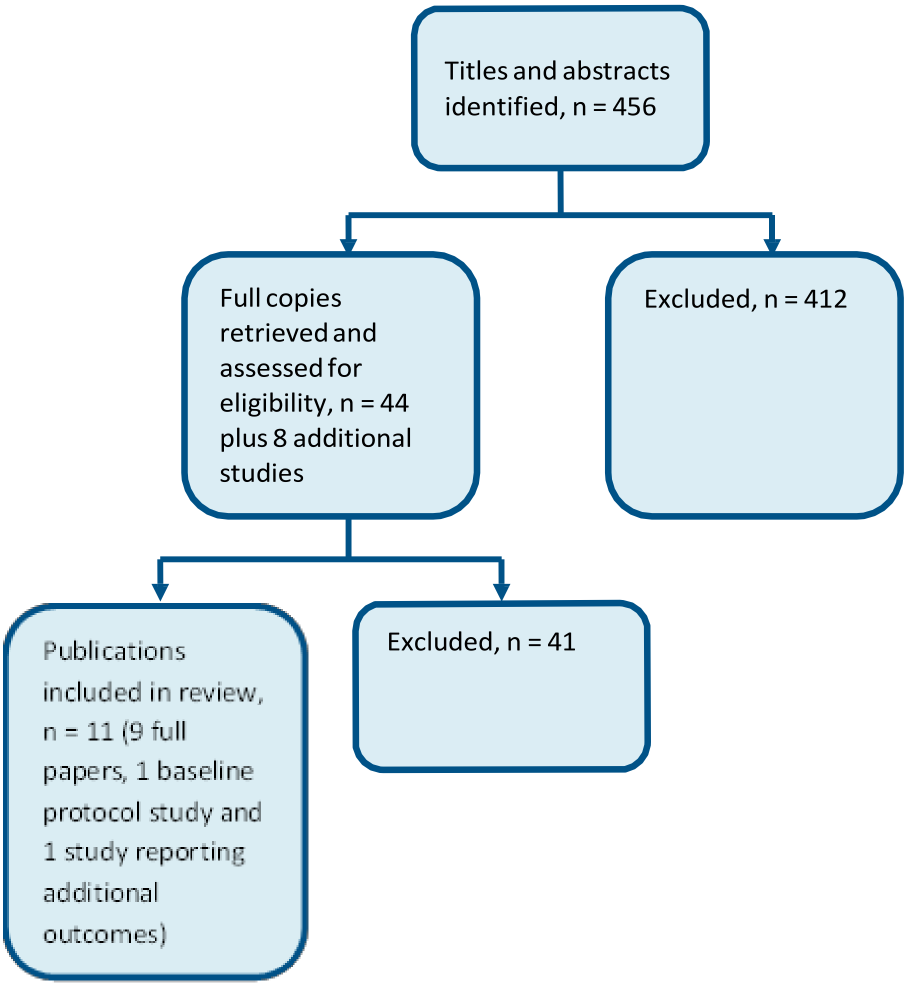
D.2 Facilitated PPCI



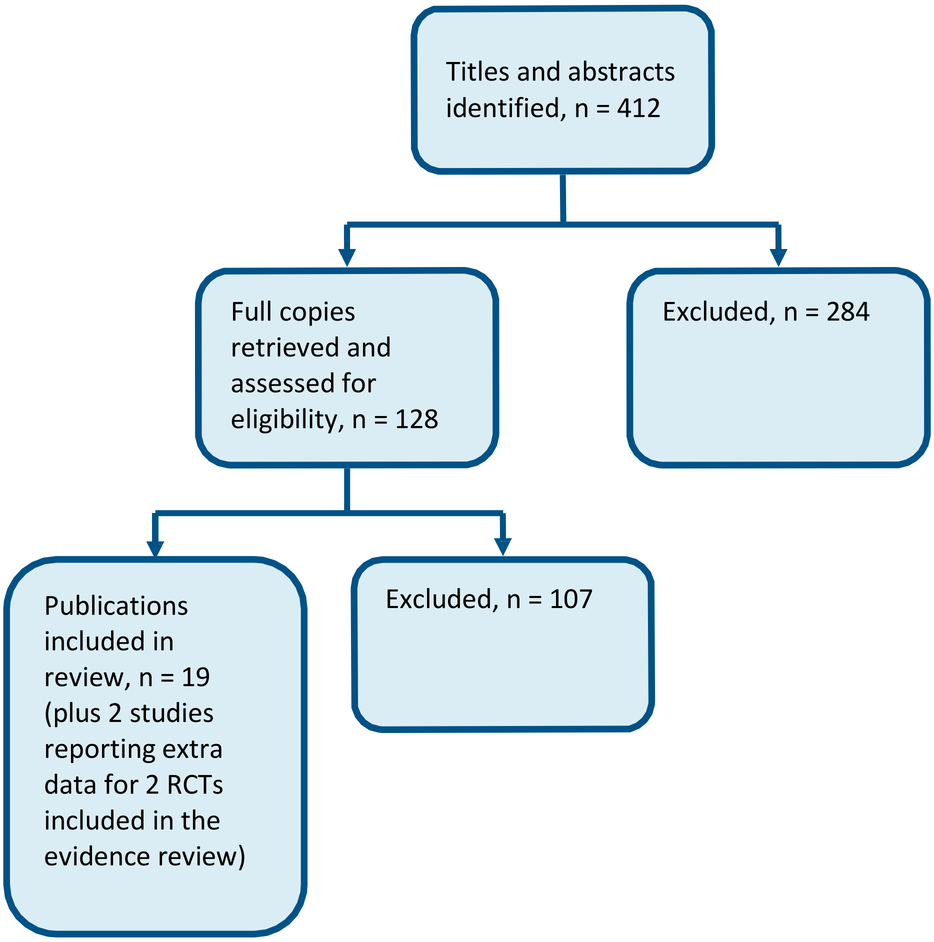
**This includes n = 12 found by cross-referencing*

***Some studies retrieved from the search were duplicates so have not been included in the final (n = 174) number of excluded studies*

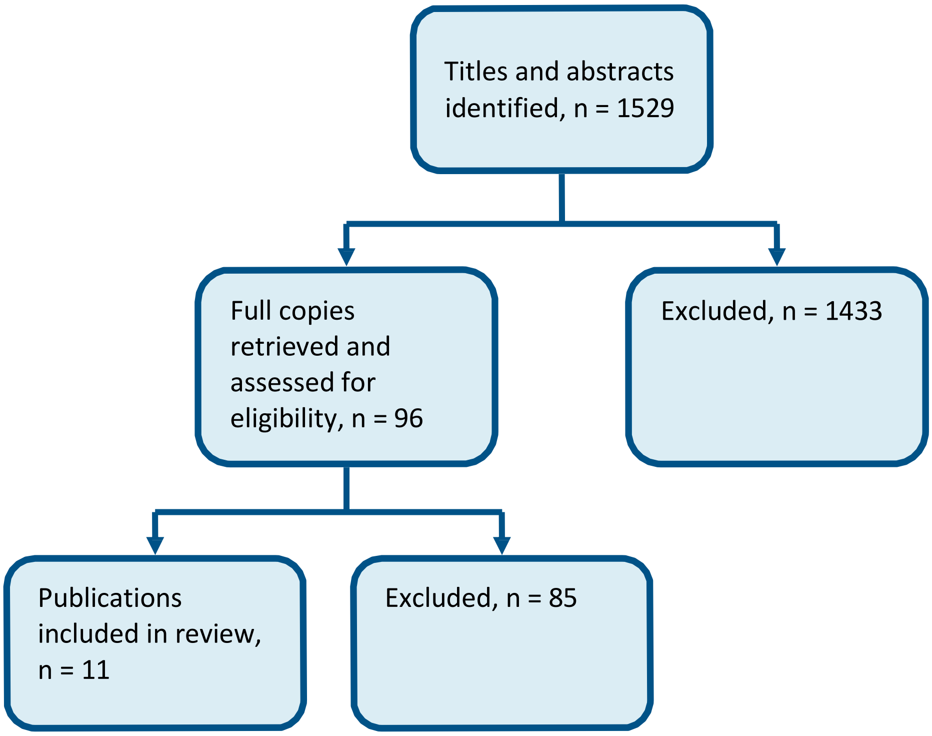
D.3 Radial versus femoral arterial access for PPCI



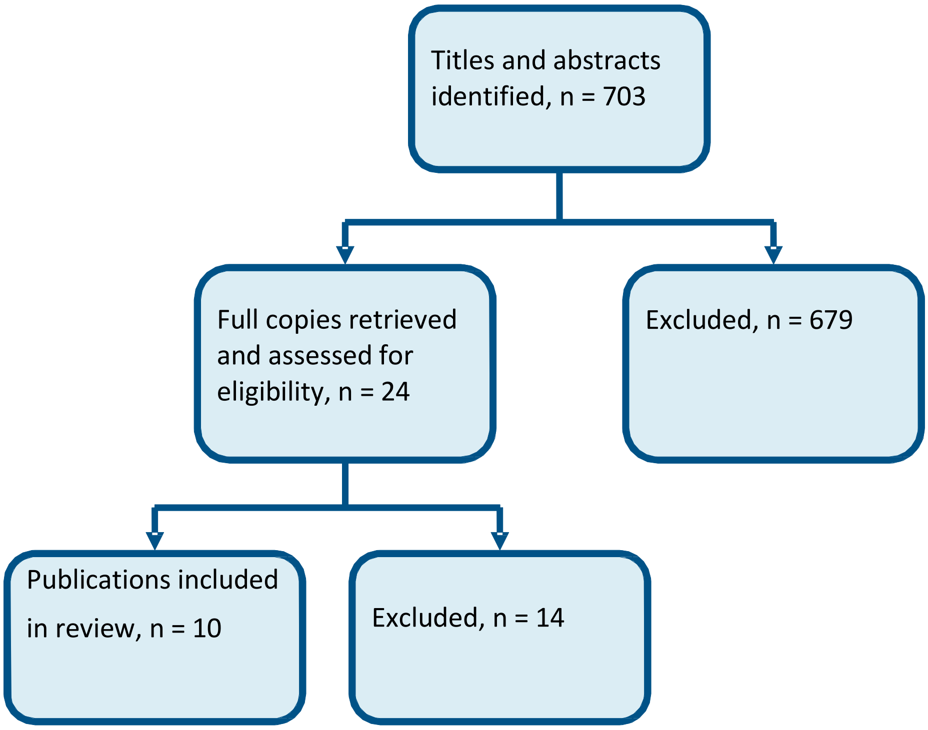
D.4 Thrombus extraction during PPCI



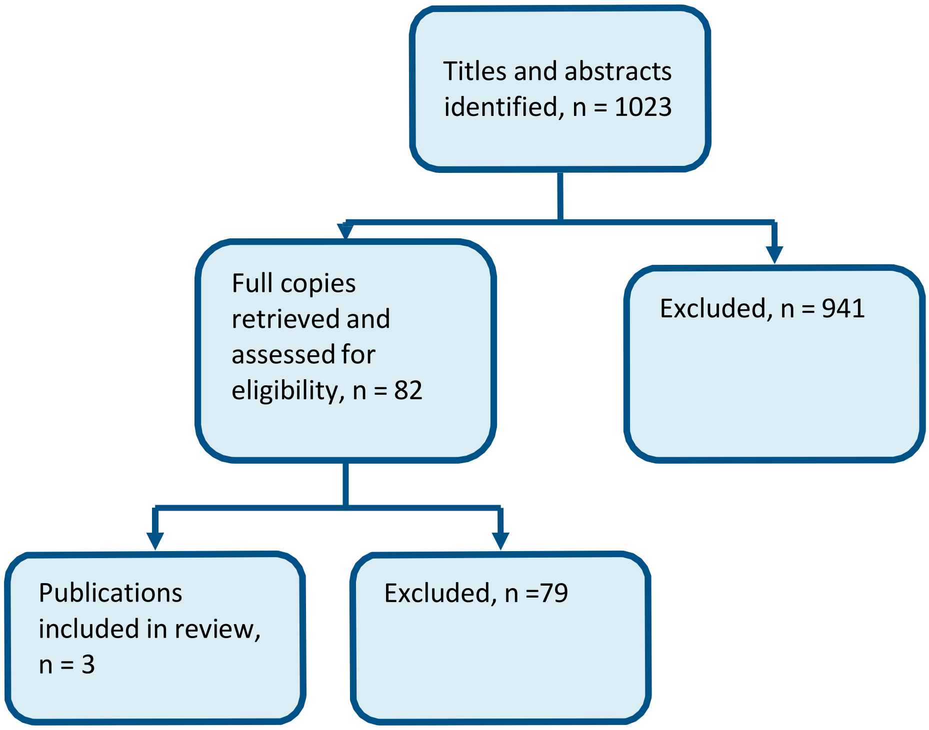
D.5 Culprit versus complete revascularisation **Updated, see 2020 evidence review**



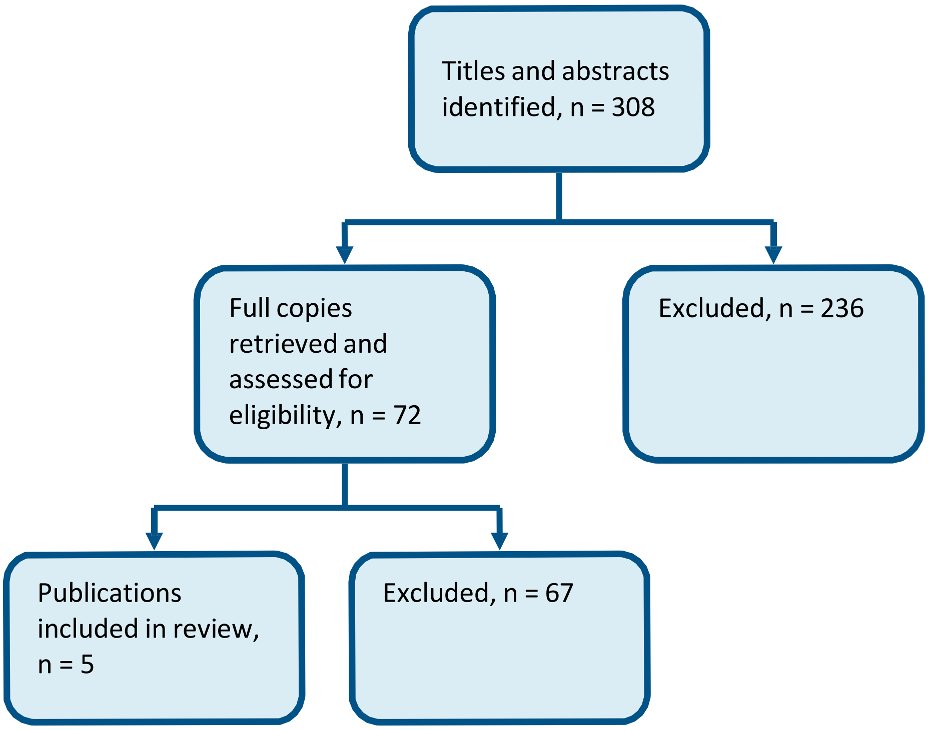
D.6 Cardiogenic shock



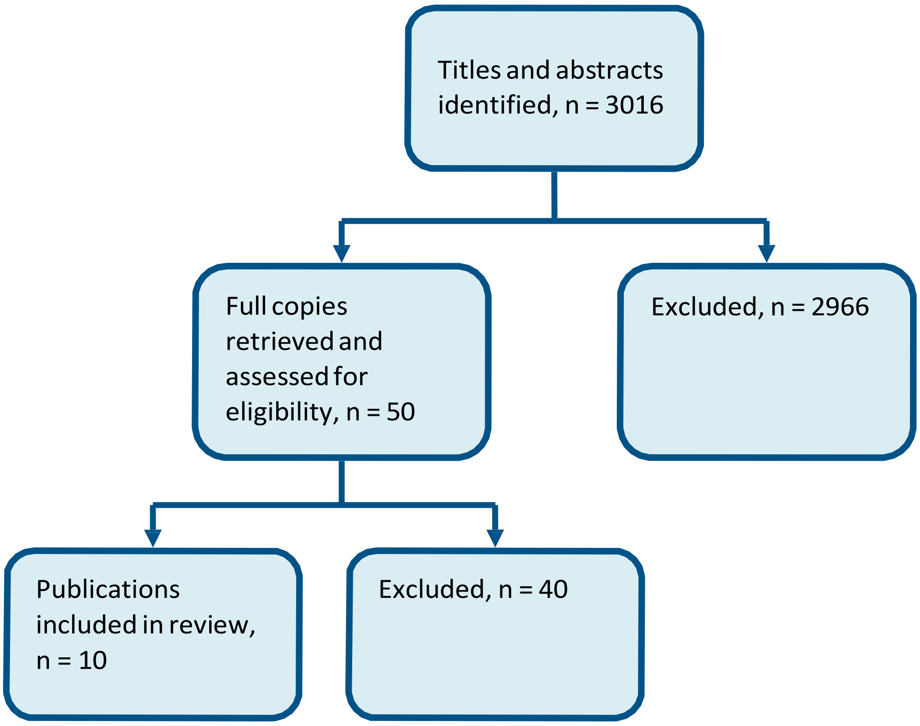
D.7 People who remain unconscious after a cardiac arrest



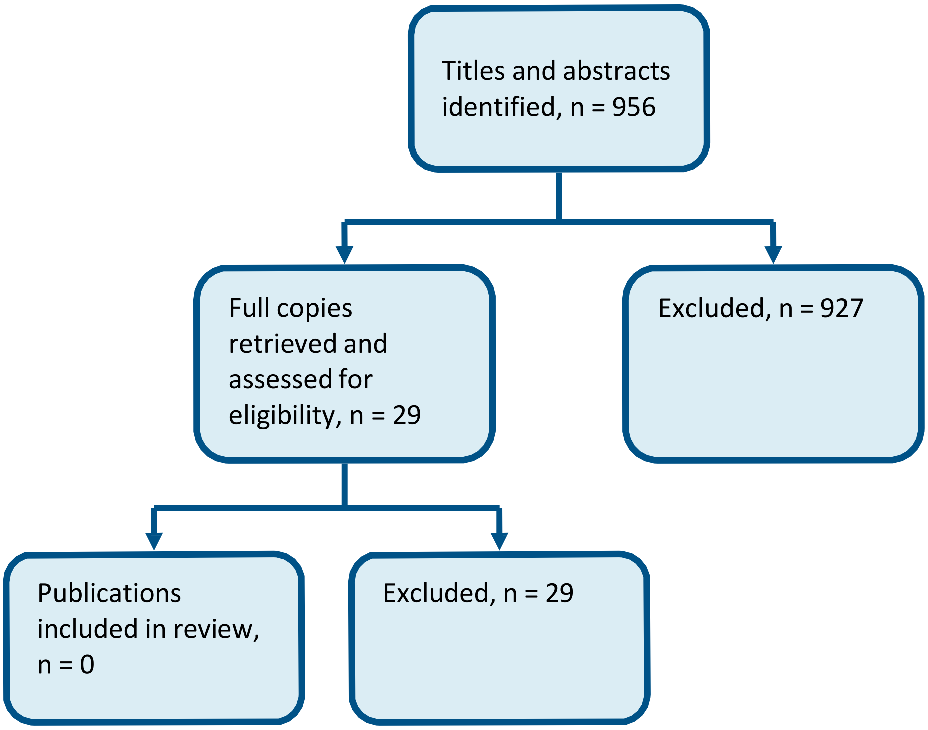
D.8 Hospital volumes of PPCI



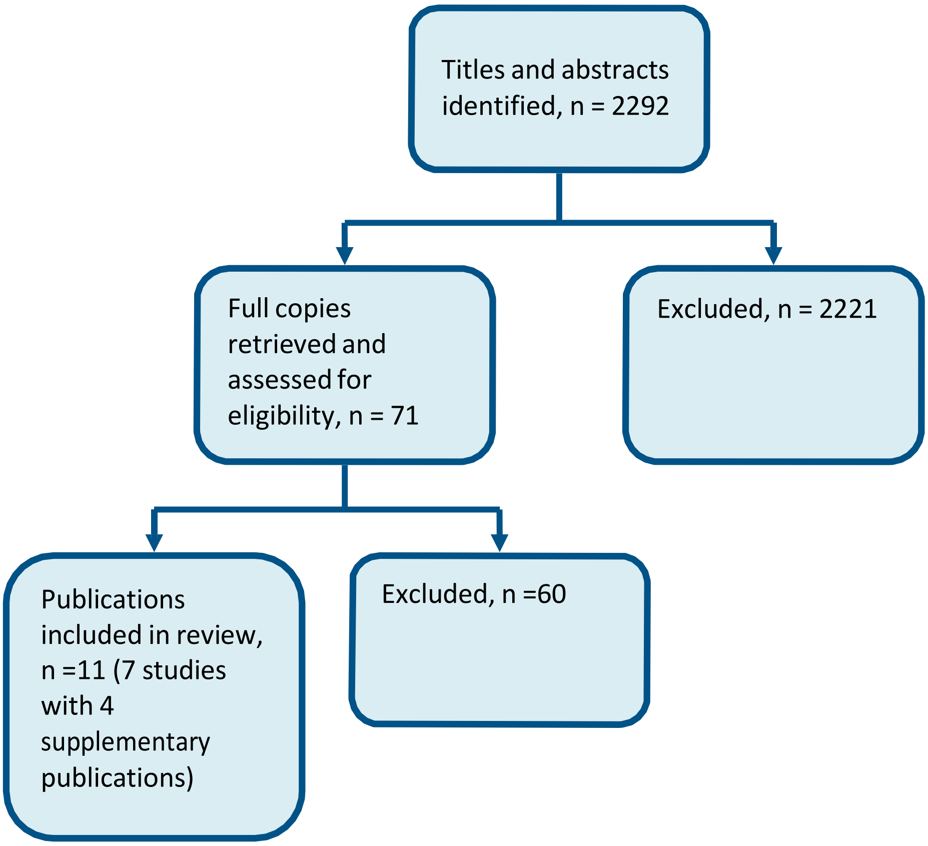
D.9 Pre-hospital versus in-hospital fibrinolysis



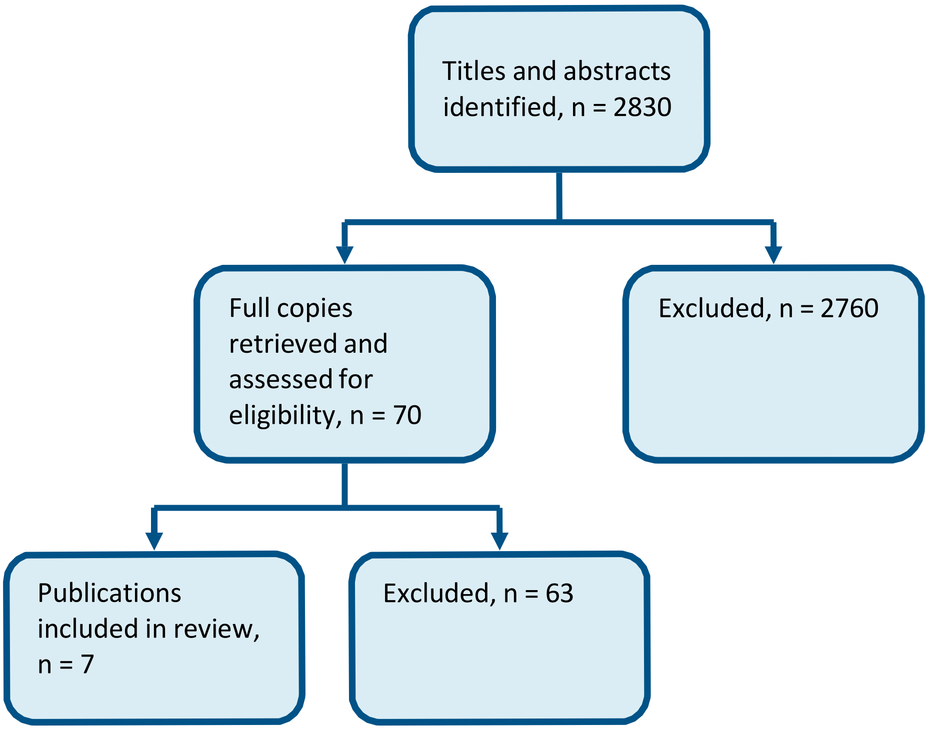
D.10 Use of antithrombin as an adjunct to fibrinolysis



D.11 Rescue PCI

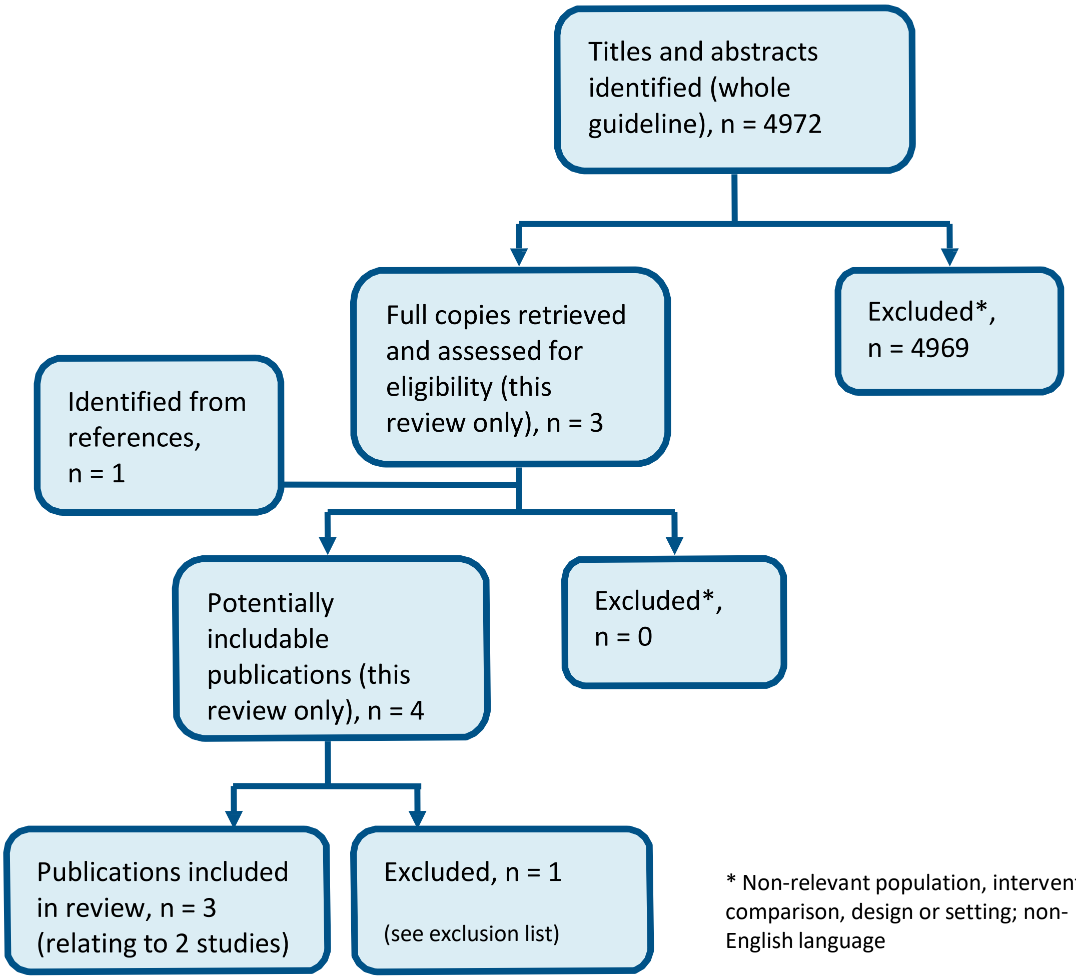


D.12 Routine early angiography following fibrinolysis



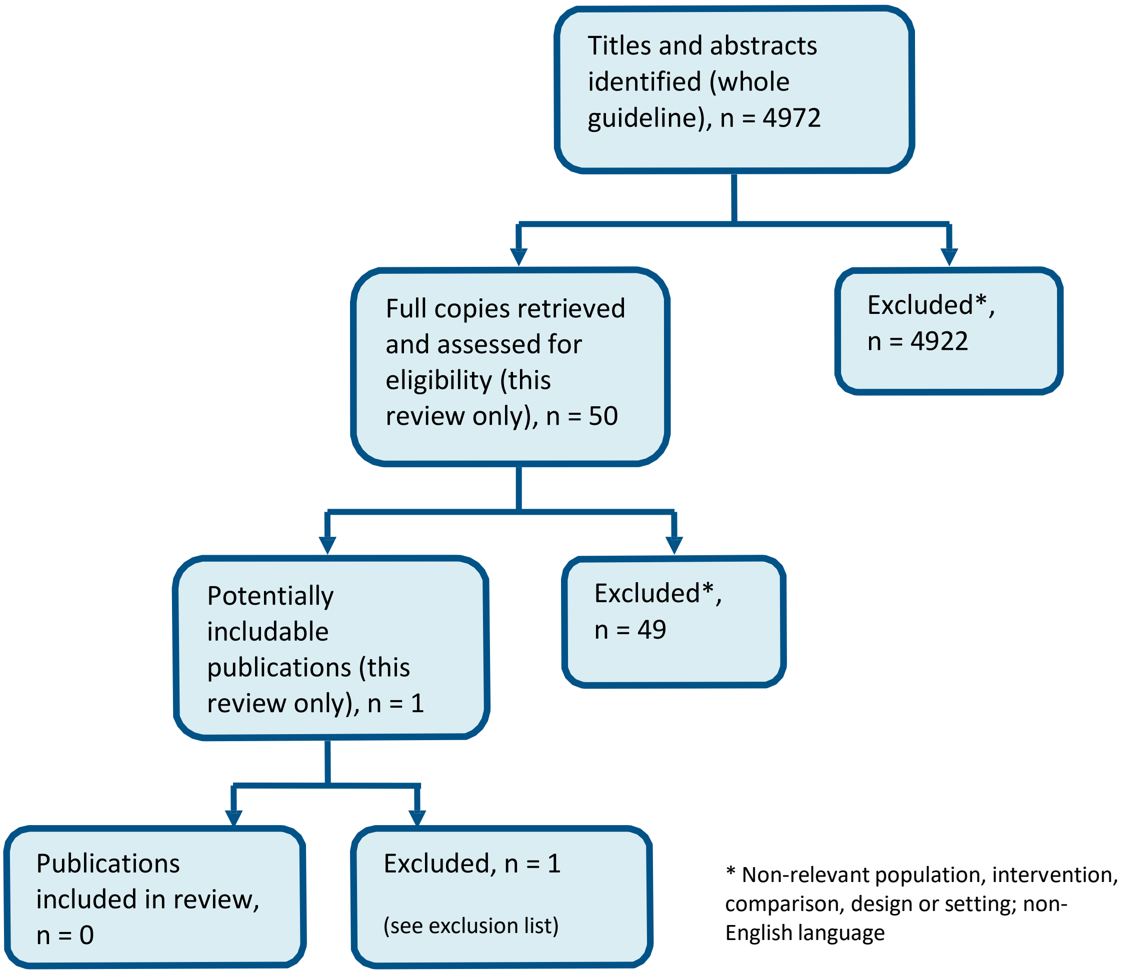
Appendix E: Economic article selection

E.1 Time to reperfusion

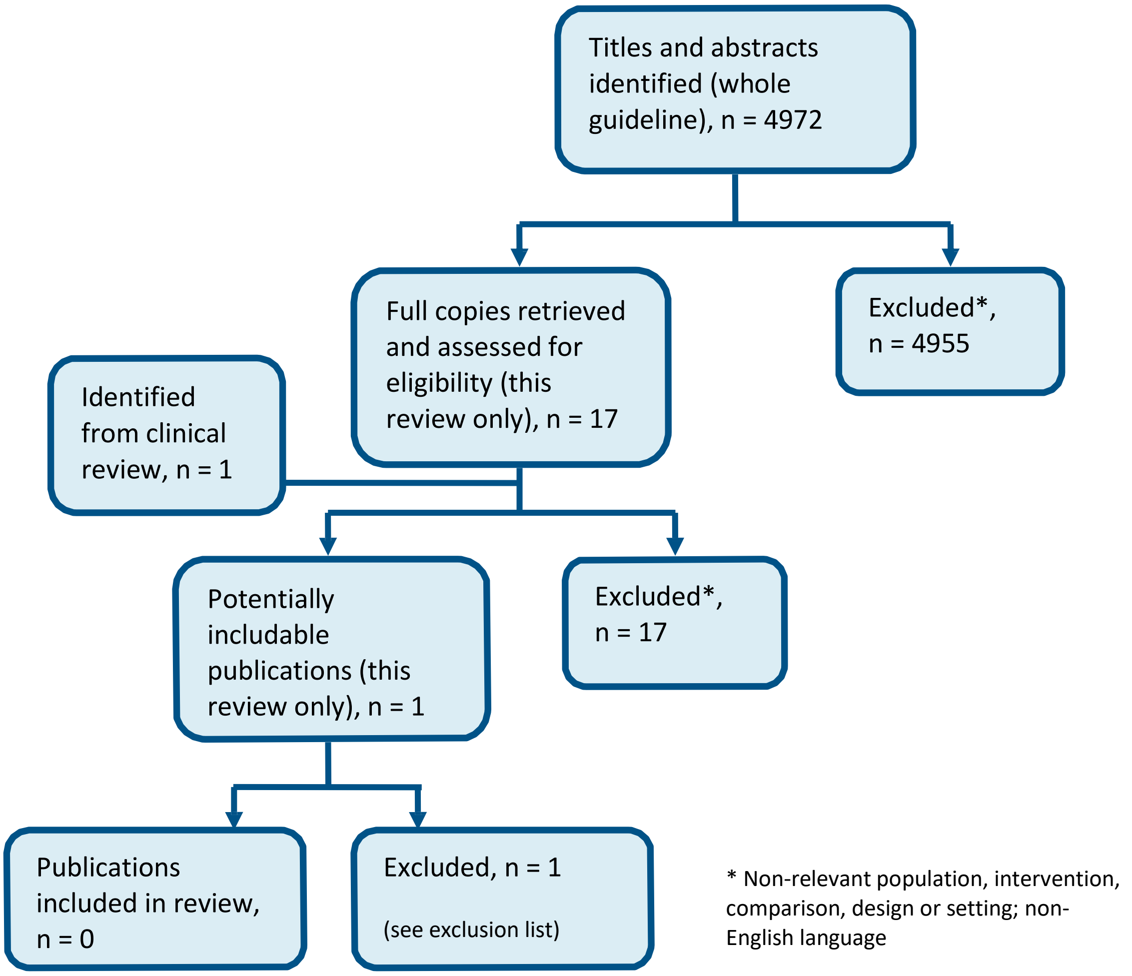


* Non-relevant population, intervention, comparison, design or setting; non-English language

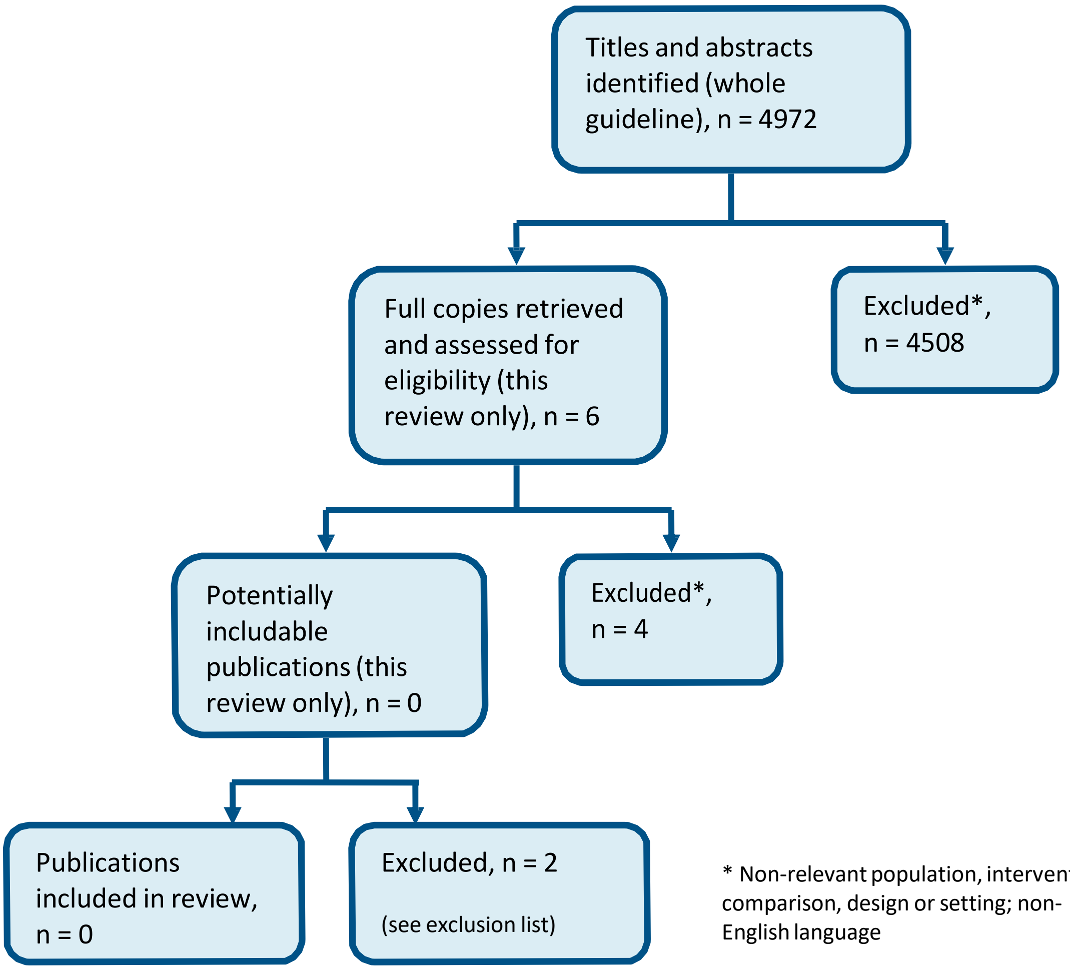
E.2 Facilitated PPCI


Titles and abstracts identified (whole guideline), n = 4972
Full copies retrieved and assessed for eligibility (this review only), n = 50
Excluded*, n = 4922
Potentially includable publications (this review only), n = 1
Excluded*, n = 49
Publications included in review, n = 0
Excluded, n = 1
(see exclusion list)
* Non-relevant population, intervention, comparison, design or setting; non-English language

E.3 Radial versus femoral arterial access for PPCI

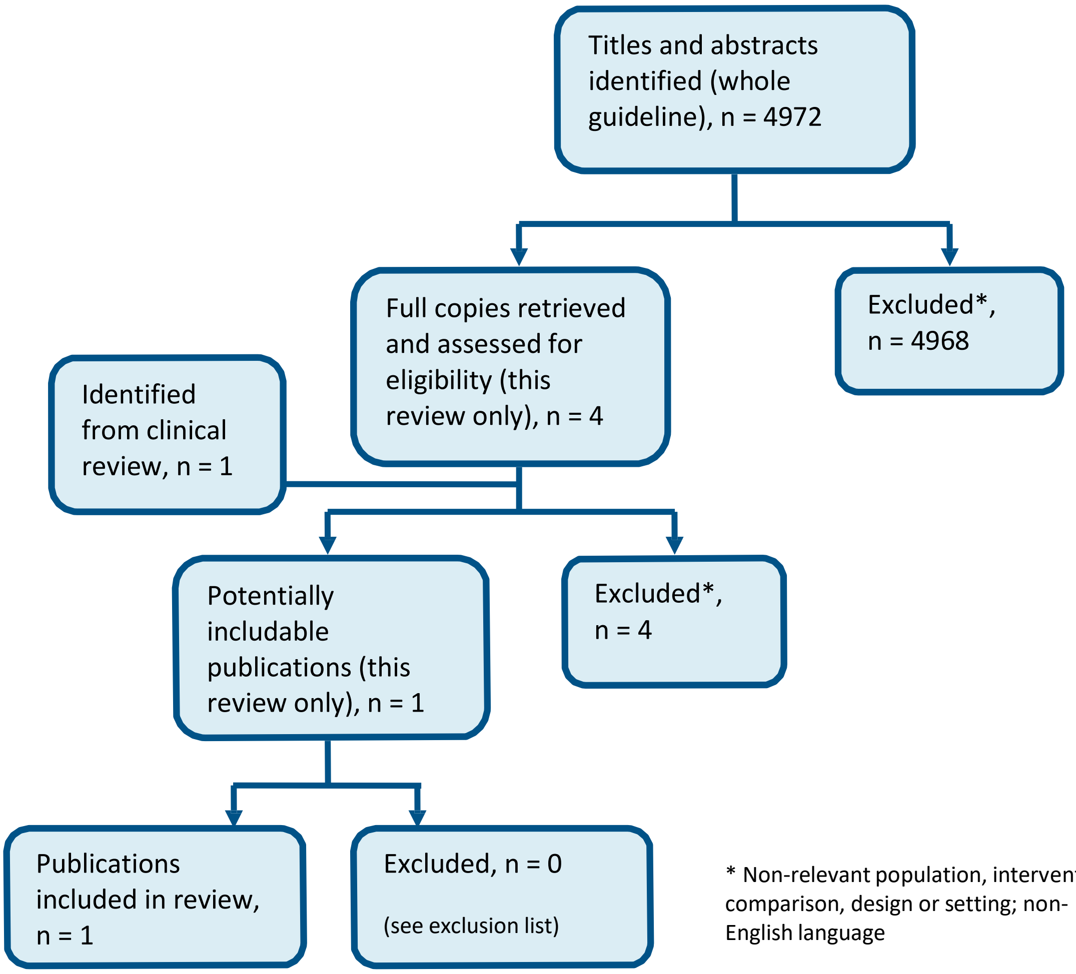


E.4 Thrombus extraction during PPCI



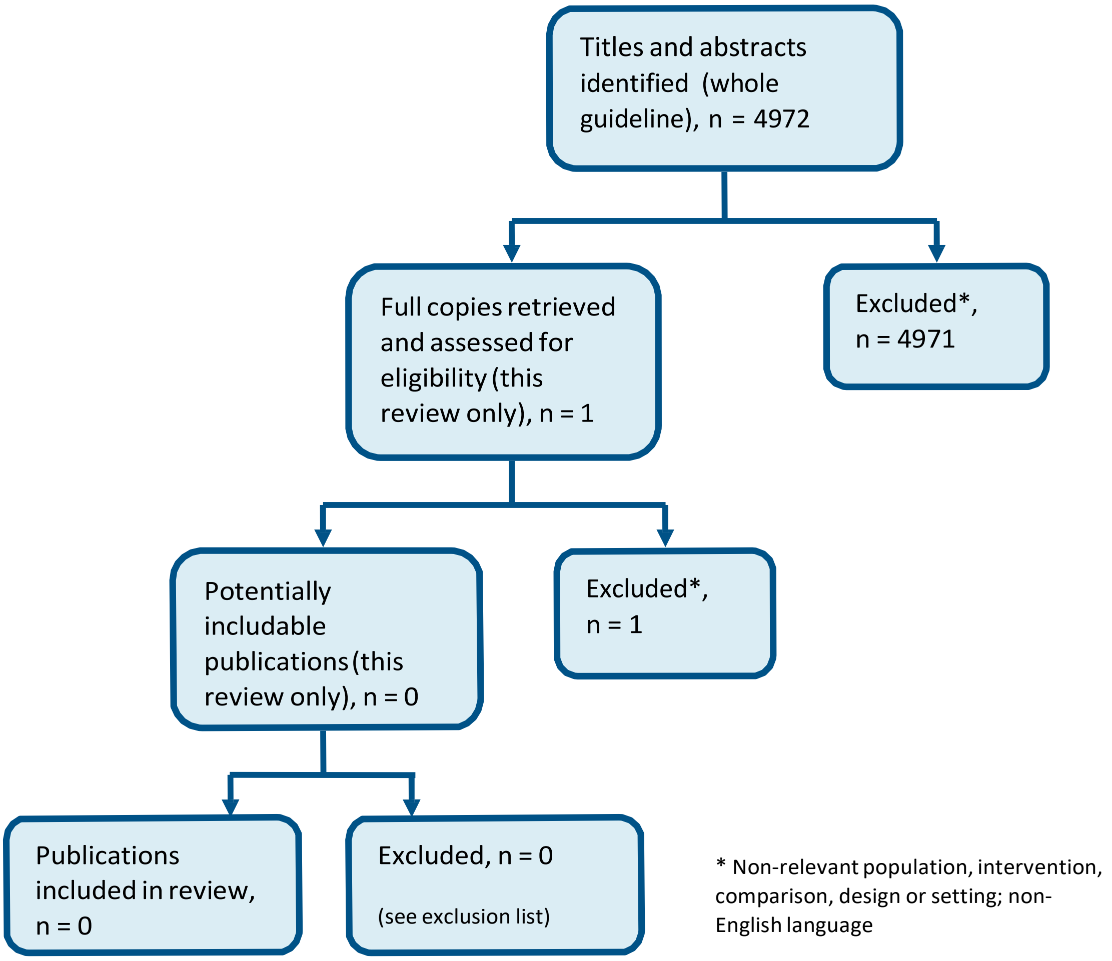
* Non-relevant population, intervention, comparison, design or setting; non-English language

E.5 Culprit versus complete revascularisation **Updated, see the 2020 evidence review**

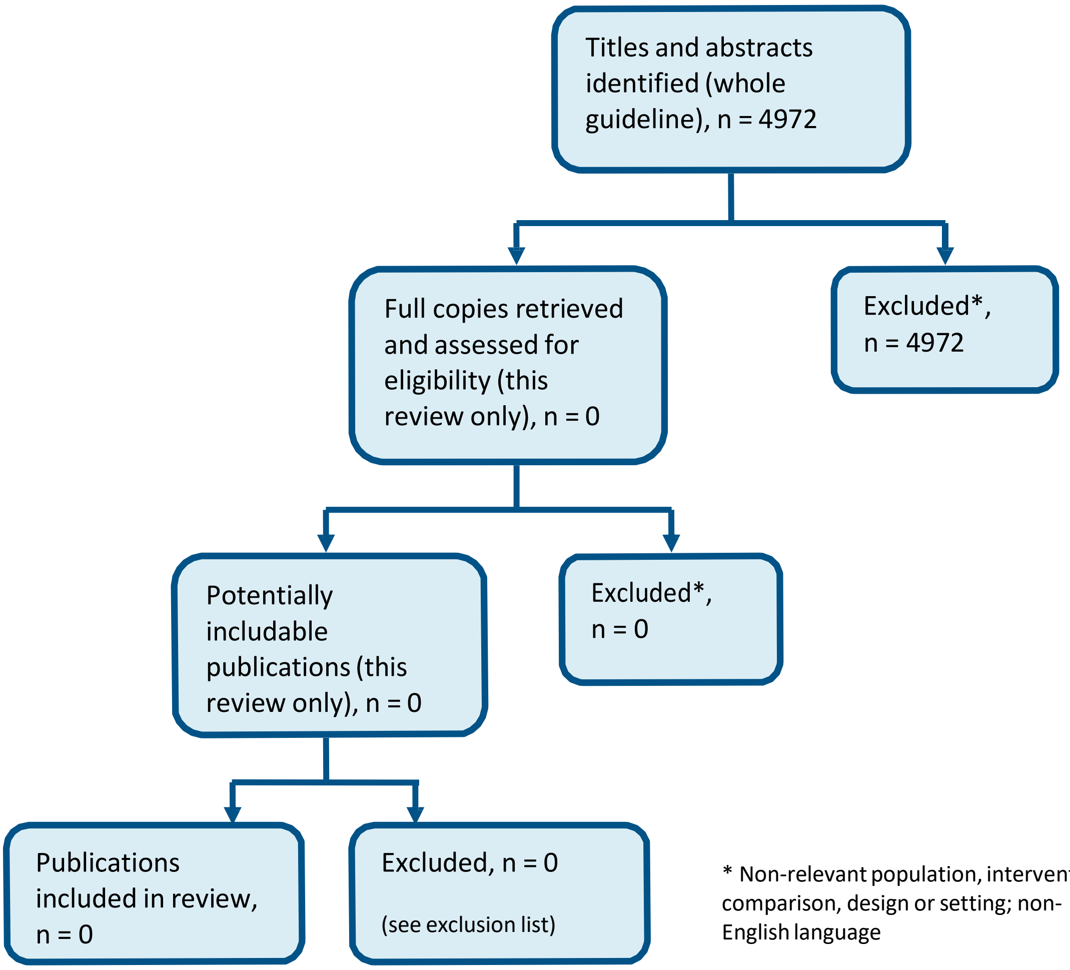


* Non-relevant population, intervention, comparison, design or setting; non-English language

E.6 Cardiogenic shock

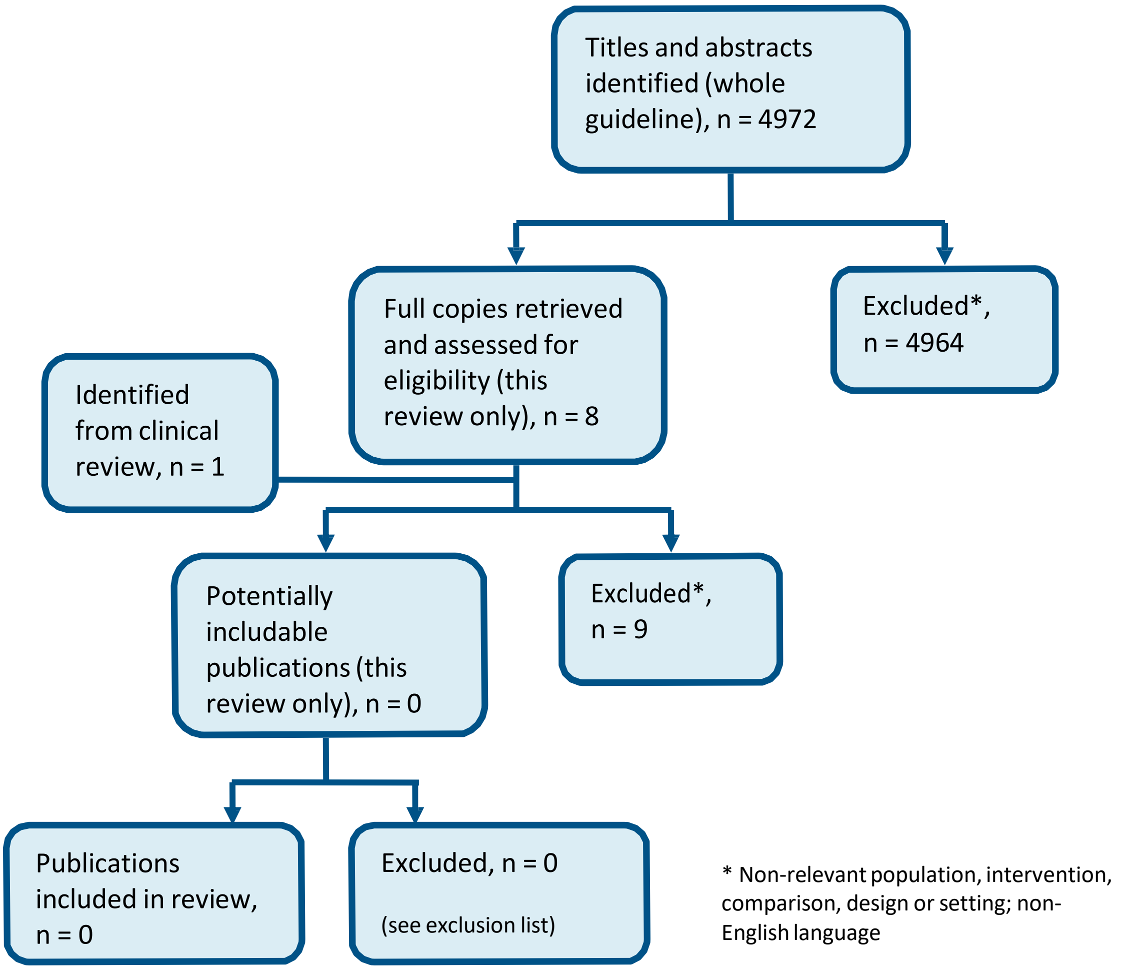


E.7 People who remain unconscious after a cardiac arrest

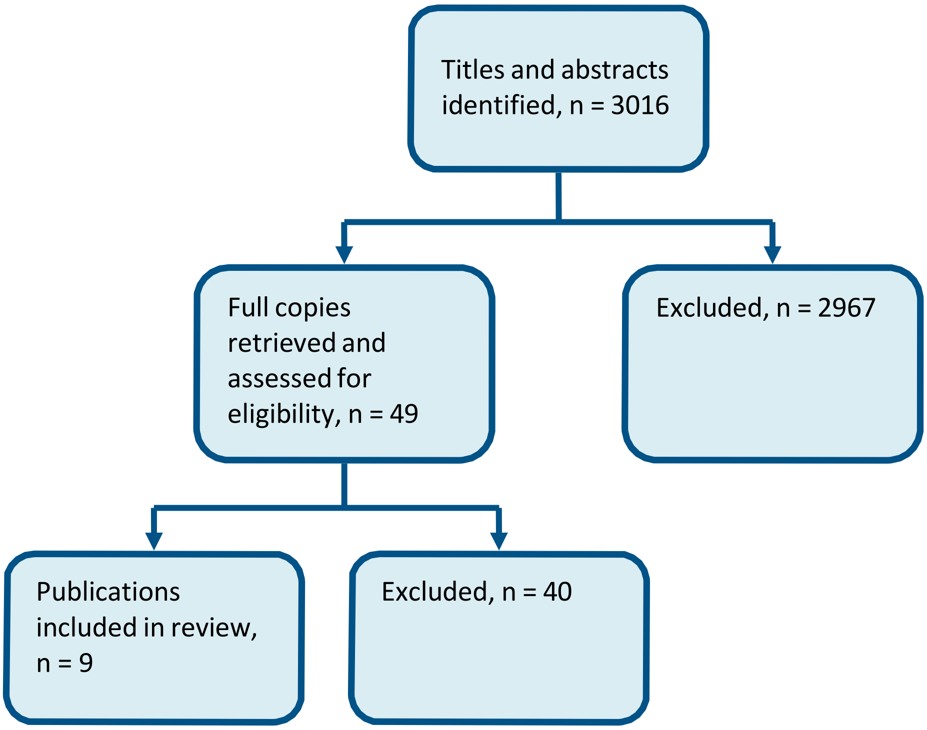


* Non-relevant population, intervention, comparison, design or setting; non-English language

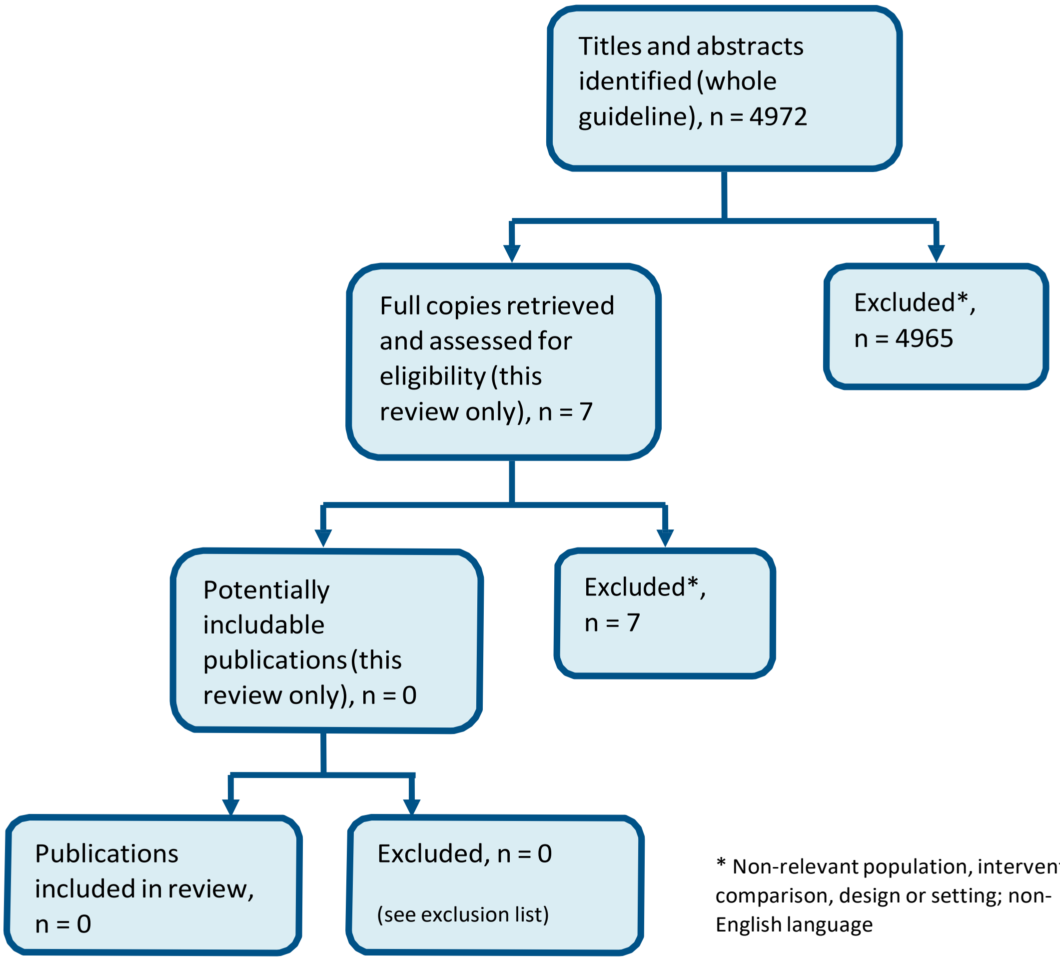
E.8 Hospital volumes of PPCI



E.9 Pre-hospital versus in-hospital fibrinolysis

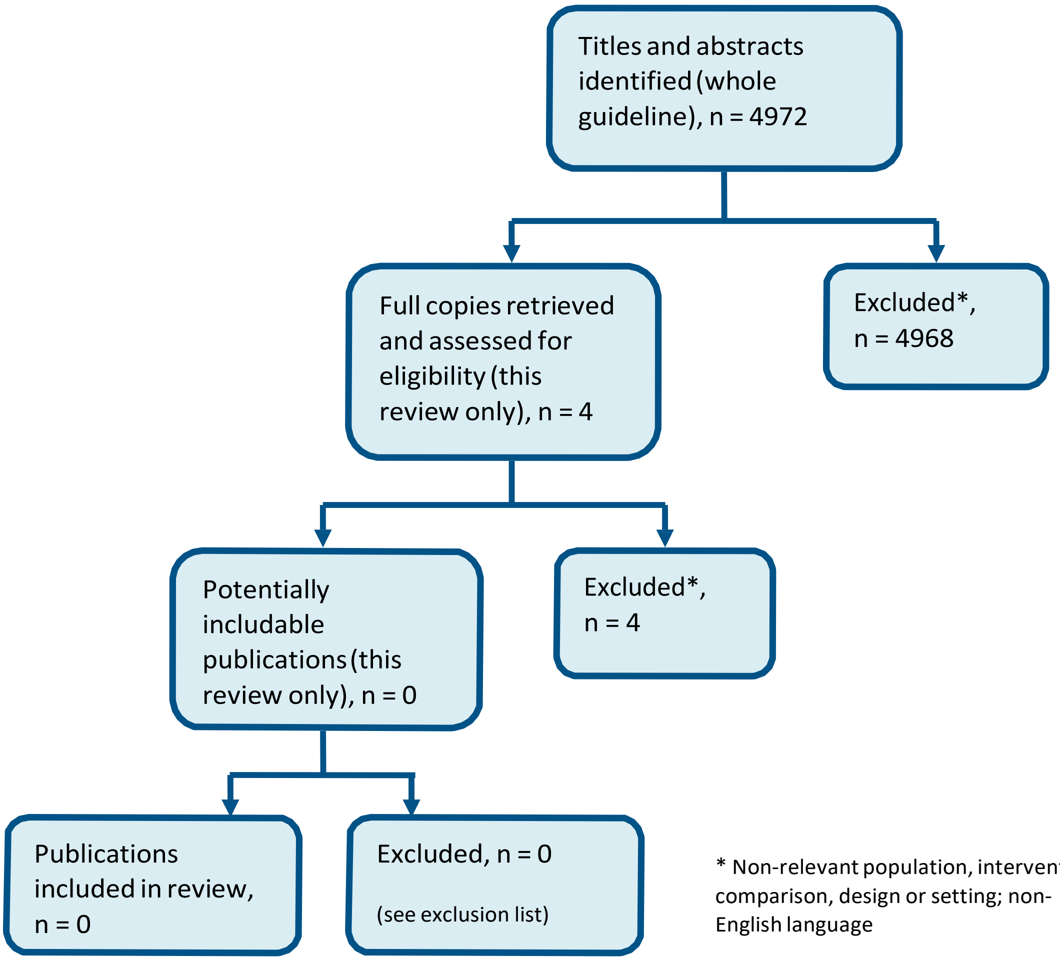


E.10 Use of antithrombin as an adjunct to fibrinolysis



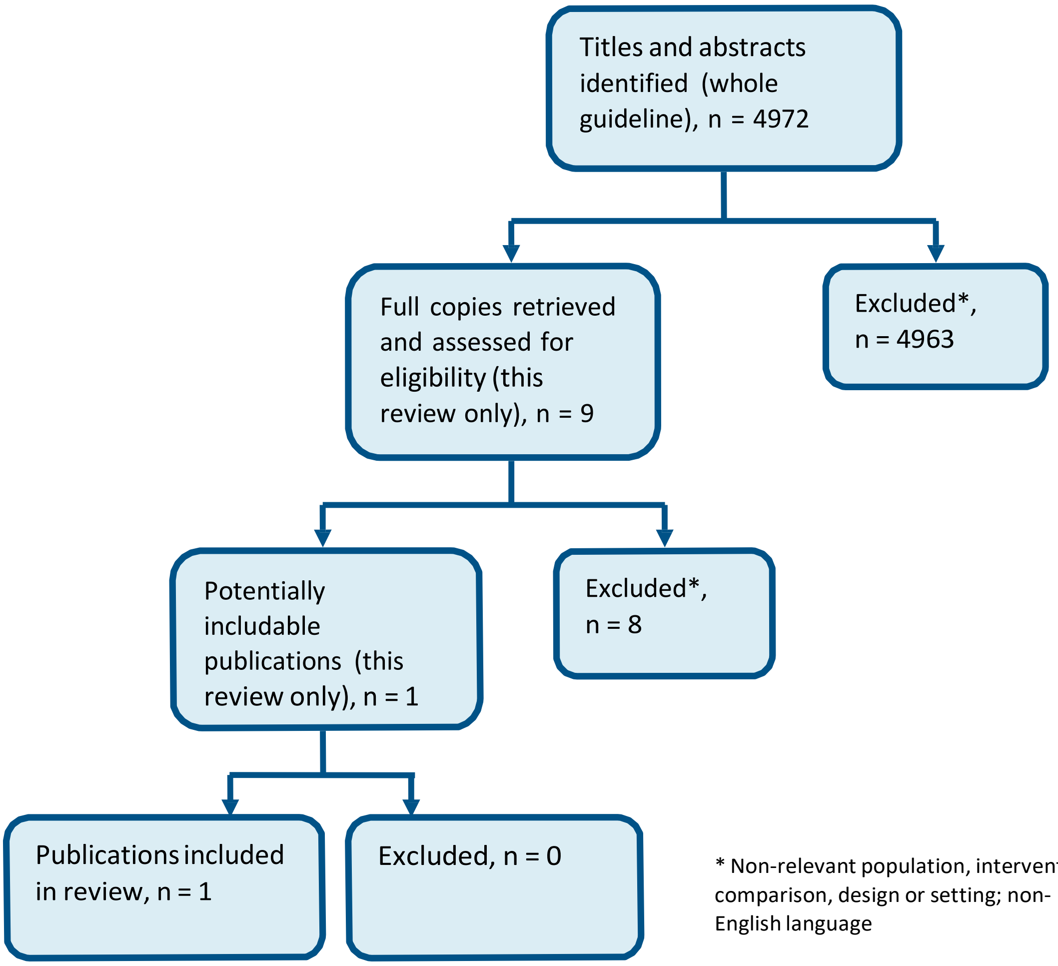
* Non-relevant population, intervention, comparison, design or setting; non-English language

E.11 Rescue PCI



* Non-relevant population, intervention, comparison, design or setting; non-English language

E.12 Routine early angiography following fibrinolysis



* Non-relevant population, intervention, comparison, design or setting; non-English language

Appendix F: Literature search strategies

F.1 Contents

F.2 Introduction

Search strategies used for the STEMI guideline are outlined below and were run in accordance with the NICE guidelines manual (2009).[87]

All searches were run up to 29 November 2012 unless otherwise stated. Any studies added to the databases after this date were not included unless specifically stated in the text. Journal web sites were not searched in addition to the databases. Where possible searches were limited to retrieve material published in English.

Scoping searches

Scoping searches were conducted in January 2011 using the following websites and databases (listed below in alphabetical order). Browsing or simple search strategies were employed. The search results were used to provide information for scope development and project planning.

Guidelines	Website address
Clinical Knowledge Summaries	www.cks.nhs.uk
CMA Infobase (Canadian guidelines)	www.cma.ca/cpgs
Guidelines International Network	www.g-i-n.net
National Guidelines Clearinghouse	www.guideline.gov
New Zealand Guidelines Group	www.nzgg.org.nz
NHMRC (Australian Guidelines)	www.nhmrc.gov.au/guidelines/
NICE Guidelines	guidance.nice.org.uk
Scottish Intercollegiate Guidelines Network	www.sign.ac.uk
TRIP Database	www.tripdatabase.com
Reviews, clinical evidence sources, economic evaluations	**Website address**
BMJ Clinical Evidence	clinicalevidence.bmj.com
Cochrane Library (Systematic Reviews)	www.thecochranelibrary.com
NHS Evidence	www.nelh.nhs.uk
Other sources as agreed by reviewers	**Website address**
British National Formulary (BNF)	www.bnf.org
electronic Medicines Compendium (eMC)	www.medicines.org.uk

Clinical searches

Searches for the **clinical reviews** were run in Medline (OVID), Embase (OVID) and the Cochrane Library. Searches were usually constructed using a PICO format: where population (P) terms were combined with Intervention (I) and sometimes Comparison (C) terms. Outcomes (O) are rarely used in search strategies for interventions. Search filters were also added to the search where appropriate.

Economic searches

Searches for the **health economic reviews** were run in Medline (OVID), Embase (OVID), the NHS Economic Evaluations Database (NHS EED), the Health Technology Assessment (HTA) database and the Health Economic Evaluation Database (HEED). HTA and NHSEED searches were carried out via the Centre for Reviews and Dissemination (CRD) interface. The HTA, NHS EED and HEED databases were accessed via the Wiley interface. Searches in these three databases were constructed using population terms only. For Medline and Embase a health economic filter (instead of a study type filter) was added to the standard population search strategy.

F.3 Population search strategies

F.3.1 Standard population search strategy

Medline search terms

1	exp *myocardial infarction/
2	myocardial infarct*.ti,ab.
3	(cardiac adj (infarct* or attack* or arrest* or event*)).ti,ab.
4	(stemi or st-segment or st segment or st-elevat* or st elevat*).ti,ab.
5	acute coronary syndrome/
6	acute coronary syndrome*.ti,ab,kw.
7	or/1-6

Embase search terms

1	myocardial infarct*.ti,ab.
2	(cardiac adj (infarct* or attack* or arrest* or event*)).ti,ab.
3	(stemi or st-segment or st segment or st-elevat* or st elevat*).ti,ab.
4	acute coronary syndrome/
5	acute coronary syndrome*.ti,ab,kw.
6	exp *heart infarction/
7	exp st segment elevation myocardial infarction/
8	or/1-7

Cochrane search terms

1	MeSH descriptor Myocardial Infarction explode all trees
2	(myocardial next infarct*):ti,ab
3	(cardiac next (infarct* or attack* or arrest* or event*)):ti,ab
4	(st-elevat* or st-segment* or stemi):ti,ab,kw
5	st next elevat*:ti,ab,kw
6	st next segment:ti,ab,kw
7	(("acute coronary") next syndrome*):ti,ab,kw
8	MeSH descriptor Acute Coronary Syndrome, this term only
9	(#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8)

F.3.2 STEMI and Cardiogenic shock

Medline search terms

1.	exp *myocardial infarction/
2.	myocardial infarct*.ti,ab.
3.	(cardiac adj (infarct* or attack* or arrest* or event*)).ti,ab.
4.	(stemi or st-segment or st segment or st-elevat* or st elevat*).ti,ab.
5.	acute coronary syndrome/
6.	acute coronary syndrome*.ti,ab,kw.
7.	or/1-6
8.	shock.ti,ab.
9.	7 and 8
10.	exp shock, cardiogenic/

11.	(cardio* adj3 shock).ti,ab.
12.	9 or 10 or 11

Embase search terms

1.	myocardial infarct*.ti,ab.
2.	(cardiac adj (infarct* or attack* or arrest* or event*)).ti,ab.
3.	(stemi or st-segment or st segment or st-elevat* or st elevat*).ti,ab.
4.	acute coronary syndrome/
5.	acute coronary syndrome*.ti,ab,kw.
6.	exp *heart infarction/
7.	exp st segment elevation myocardial infarction/
8.	or/1-7
9.	shock.ti,ab.
10.	8 and 9
11.	exp cardiogenic shock/
12.	(cardio* adj3 shock).ti,ab.
13.	10 or 11 or 12

Cochrane search terms

1.	MeSH descriptor Myocardial Infarction explode all trees
2.	myocardial infarct*:ti,ab
3.	st next segment:ti,ab
4.	st next elevat*:ti,ab
5.	(cardiac near/3 (infarct* or attack* or arrest* or event*)):ti,ab
6.	stemi:ti,ab
7.	MeSH descriptor Acute Coronary Syndrome explode all trees
8.	(#1 or #2 or #3 or #4 or #5 or #6 or #7)
9.	shock:ti,ab,kw
10.	(#8 and #9)
11.	MeSH descriptor Shock, Cardiogenic explode all trees
12.	(cardio* next shock):ti,ab
13.	(#10 or #11 or #12)

F.3.3 STEMI and Cardiac arrest

Medline search terms

1.	exp *myocardial infarction/
2.	myocardial infarct*.ti,ab.
3.	(cardiac adj (infarct* or attack* or arrest* or event*)).ti,ab.
4.	(stemi or st-segment or st segment or st-elevat* or st elevat*).ti,ab.
5.	acute coronary syndrome/
6.	acute coronary syndrome*.ti,ab,kw.
7.	or/1-6
8.	heart arrest/
9.	((heart or cardiac) adj2 arrest*).ti,ab.
10.	((surviv* or resuscit* or postresuscit* or unconscious*) adj6 arrest*).ti,ab.
11.	or/8-10

12.	7 and 11

Embase search terms

1.	myocardial infarct*.ti,ab.
2.	(cardiac adj (infarct* or attack* or arrest* or event*)).ti,ab.
3.	(stemi or st-segment or st segment or st-elevat* or st elevat*).ti,ab.
4.	acute coronary syndrome/
5.	acute coronary syndrome*.ti,ab,kw.
6.	exp *heart infarction/
7.	exp st segment elevation myocardial infarction/
8.	or/1-7
9.	*heart arrest/ or "out of hospital cardiac arrest"/
10.	((heart or cardiac) adj2 arrest).ti,ab.
11.	((surviv* or resuscit* or postresuscit* or unconscious*) adj6 arrest*).ti,ab.
12.	or/9-11
13.	8 and 12

Cochrane search terms

1.	MeSH descriptor Heart Arrest, this term only
2.	MeSH descriptor Out-of-Hospital Cardiac Arrest, this term only
3.	((heart or cardiac) next arrest*):ti,ab
4.	((unconscious or resuscit* or postresuscit* or surviv*) near/6 arrest):ti,ab
5.	(#1 or #2 or #3 or #4)

F.4 Study filter search terms

F.4.1 Systematic review (SR) search terms

Medline search terms

1	meta-analysis/
2	meta-analysis as topic/
3	(meta analy* or metanaly* or metaanaly*).ti,ab.
4	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
5	((systematic* or evidence*) adj2 (review* or overview*)).ti,ab.
6	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
7	(search* adj4 literature).ab.
8	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
9	cochrane.jw.
10	or/1-9

Embase search terms

1	systematic review/
2	meta-analysis/
3	(meta analy* or metanaly* or metaanaly*).ti,ab.
4	((systematic or evidence) adj2 (review* or overview*)).ti,ab.

1	systematic review/
5	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
6	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
7	(search* adj4 literature).ab.
8	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
9	((pool* or combined) adj2 (data or trials or studies or results)).ab.
10	cochrane.jw.
11	or/1-10

F.4.2 Randomised controlled studies (RCTs) search terms

Medline search terms

1	randomized controlled trial.pt.
2	controlled clinical trial.pt.
3	randomi#ed.ab.
4	placebo.ab.
5	randomly.ab.
6	Clinical Trials as topic.sh.
7	trial.ti.
8	or/1-8

Embase search terms

1	random*.ti,ab.
2	factorial*.ti,ab.
3	(crossover* or cross over*).ti,ab.
4	((doubl* or singl*) adj blind*).ti,ab.
5	(assign* or allocat* or volunteer* or placebo*).ti,ab.
6	crossover procedure/
7	single blind procedure/
8	randomized controlled trial/
9	double blind procedure/
10	or/1-9

F.4.3 Cohort studies

Medline search terms

	epidemiologic studies/
1.	exp case control studies/
2.	exp cohort studies/
3.	cross-sectional studies/
4.	case control.ti,ab.
5.	(cohort adj (study or studies or analys*)).ti,ab.
6.	((follow up or observational or uncontrolled or non randomi#ed or nonrandomi#ed or epidemiologic*) adj (study or studies)).ti,ab.
7.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort*)).ti,ab.

8.	or/1-8

Embase search terms

1.	clinical study/
2.	exp case control study/
3.	family study/
4.	longitudinal study/
5.	retrospective study/
6.	prospective study/
7.	cross-sectional study/
8.	cohort analysis/
9.	follow-up/
10.	cohort*.ti,ab.
11.	9 and 10
12.	case control.ti,ab.
13.	(cohort adj (study or studies or analys*)).ti,ab.
14.	((follow up or observational or uncontrolled or non randomi#ed or nonrandomi#ed or epidemiologic*) adj (study or studies)).ti,ab.
15.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort*)).ti,ab.
16.	or/1-8,11-14

F.4.4 Health economic search terms

Medline search terms

1.	economics/
2.	value of life/
3.	exp "costs and cost analysis"/
4.	exp economics, hospital/
5.	exp economics, medical/
6.	economics, nursing/
7.	economics, pharmaceutical/
8.	exp "fees and charges"/
9.	exp budgets/
10.	budget*.ti,ab.
11.	cost*.ti.
12.	(economic* or pharmaco?economic*).ti.
13.	(price* or pricing*).ti,ab.
14.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
15.	(financ* or fee or fees).ti,ab.
16.	(value adj2 (money or monetary)).ti,ab.
17.	or/1-16

Embase search terms

1.	health economics/
2.	exp economic evaluation/
3.	exp health care cost/

4.	exp fee/
5.	budget/
6.	funding/
7.	budget*.ti,ab.
8.	cost*.ti.
9.	(economic* or pharmaco?economic*).ti.
10.	(price* or pricing*).ti,ab.
11.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
12.	(financ* or fee or fees).ti,ab.
13.	(value adj2 (money or monetary)).ti,ab.
14.	or/1-13

F.4.5 Quality of life search terms

Medline search terms

1.	exp quality-adjusted life years/
2.	quality adjusted life.ti,ab.
3.	exp "quality of life"/
4.	exp "value of life"/
5.	(qaly* or qald* or qale* or qtime*).ti,ab.
6.	disability adjusted life.ti,ab.
7.	daly*.ti,ab.
8.	health status indicators/
9.	(sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw.
10.	(sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw.
11.	(sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw.
12.	(sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw.
13.	(sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw.
14.	(euroqol or euro qol or eq5d or eq 5d).tw.
15.	(hql or hqol or h qol or hrqol or hr qol).tw.
16.	(hye or hyes).tw.
17.	health* year* equivalent*.tw.
18.	health utilit*.tw.
19.	(hui or hui1 or hui2 or hui3).tw.
20.	disutili*.tw.
21.	rosser.tw.
22.	(quality of wellbeing or quality of well being or quality of well-being or qwb).ti,ab.
23.	willingness to pay.tw.
24.	standard gamble*.tw.
25.	(time trade off or time tradeoff or tto).tw.
26.	or/1-25

Embase search terms

1.	quality adjusted life year/
2.	quality of life/
3.	(qaly* or qald* or qale* or qtime*).tw.
4.	daly*.tw.
5.	quality adjusted life.tw.
6.	disability adjusted life.tw.
7.	(sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw.
8.	(sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw.
9.	(sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw.
10.	(sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw.
11.	(sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw.
12.	(euroqol or euro qol or eq5d or eq 5d).tw.
13.	(hql or hqol or h qol or hrqol or hr qol).tw.
14.	(hye or hyes).tw.
15.	health* year* equivalent*.tw.
16.	health utilit*.tw.
17.	(hui or hui1 or hui2 or hui3).tw.
18.	disutili*.tw.
19.	rosser.tw.
20.	(quality of wellbeing or quality of well being or quality of well-being or qwb).ti,ab.
21.	willingness to pay.tw.
22.	standard gamble*.tw.
23.	(time trade off or time tradeoff or tto).tw.
24.	or/1-23

F.4.6 Excluded study designs and publication types

The following study designs and publication types were removed from the retrieved results using the NOT operator.

Medline search terms

1	letter/
2	editorial/
3	news/
4	exp historical article/
5	Anecdotes as Topic/
6	comment/
7	case report/
8	(letter or comment*).ti.
9	or/1-8
10	randomized controlled trial/ or random*.ti,ab.
11	9 not 10
12	animals/ not humans/

13	exp Animals, Laboratory/
14	exp Animal Experimentation/
15	exp Models, Animal/
16	exp Rodentia/
17	(rat or rats or mouse or mice).ti.
18	or/11-17

Embase search terms

1.	letter.pt. or letter/
2.	note.pt.
3.	editorial.pt.
4.	case report/ or case study/
5.	(letter or comment*).ti.
6.	or/1-5
7.	randomized controlled trial/ or random*.ti,ab.
8.	6 not 7
9.	animal/ not human/
10.	nonhuman/
11.	exp Animal Experiment/
12.	exp Experimental Animal/
13.	animal model/
14.	exp Rodent/
15.	(rat or rats or mouse or mice).ti.
16.	or/8-15

F.5 Searches by specific questions with intervention terms

F.5.1 Time to reperfusion

What is the duration of PPCI-related time delay at which fibrinolysis becomes more clinically and cost effective compared to PPCI in people with STEMI and how is this modulated by patient presentation delay and patient risk profile?

Search constructed by combining the columns in the following table using the 'AND' Boolean operator, except for the exclusion filter which is combined with the search using the 'NOT' Boolean operator

Population	Intervention(s) / exposure(s)	Study filters used (Medline & Embase only)	Date parameters
STEMI	PCI terms AND fibrinolysis terms AND timing terms (line 24 below)	Exclusions	1990 to 29/11/12
STEMI	PCI terms AND fibrinolysis terms (line 23 below)	SRs, RCTs, Exclusions	1990 to 29/11/12

Medline search terms

1.	exp *stents/
2.	angioplasty/

3.	exp *angioplasty, balloon, coronary/
4.	*coronary angiography/
5.	exp *catheterization, peripheral/
6.	*myocardial reperfusion/
7.	percutaneous coronary intervention*.ti,ab.
8.	(peripheral adj3 catheter*).ti,ab.
9.	(coronary adj3 angiograph*).ti,ab.
10.	((heart or myocardi*) adj3 reperfusion).ti,ab.
11.	((primary or coronary or transluminal or balloon) adj3 angioplasty).ti,ab.
12.	coronary artery dilat*.ti,ab.
13.	stent*.ti,ab.
14.	or/1-13
15.	exp *thrombolytic therapy/
16.	((thrombolytic or fibrinolytic) adj1 therap*).ti,ab.
17.	(thrombolysis or fibrinolysis).ti,ab.
18.	fibrinolytic agents/
19.	or/15-18
20.	time factors/
21.	(delay* or timing or time).ti,ab.
22.	20 or 21
23.	14 and 19
24.	14 and 19 and 22

Embase search terms

1.	percutaneous coronary intervention*.ti,ab.
2.	((heart or myocardi$) adj3 reperfusion).ti,ab.
3.	((Primary or coronary or transluminal or balloon) adj3 angioplasty).ti,ab.
4.	Coronary artery dilat$.ti,ab.
5.	Stent$.ti,ab.
6.	exp *stent/
7.	exp *transluminal coronary angioplasty/
8.	exp *percutaneous transluminal angioplasty/
9.	angioplasty/
10.	catheterization/
11.	heart muscle reperfusion/
12.	or/9-19
13.	fibrinolytic agent/
14.	exp *fibrinolytic therapy/
15.	((thrombolytic or fibrinolytic) adj1 therap*).ti,ab.
16.	(thrombolysis or fibrinolysis).ti,ab.
17.	or/21-24
18.	(delay$ or timing or time).ti,ab.
19.	time/
20.	26 or 27
21.	12 and 17 and 20

Cochrane search terms

1.	MeSH descriptor Stents explode all trees
2.	MeSH descriptor Angioplasty, Balloon, Coronary explode all trees
3.	MeSH descriptor Coronary Angiography explode all trees
4.	MeSH descriptor Catheterization, Peripheral explode all trees
5.	MeSH descriptor Myocardial Reperfusion explode all trees
6.	(percutaneous NEXT coronary NEXT intervention*):ti,ab
7.	(peripheral NEAR/3 catheter*):ti,ab
8.	((heart or myocardi*) NEAR/3 reperfusion):ti,ab
9.	((coronary or transluminal or balloon) NEAR/3 angioplasty):ti,ab
10.	(Coronary NEXT artery NEXT dilat*):ti,ab
11.	Stent*:ti,ab
12.	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11
13.	MeSH descriptor Thrombolytic Therapy explode all trees
14.	MeSH descriptor Fibrinolytic Agents, this term only
15.	((thrombolytic or fibrinolytic) NEXT therap*):ti,ab
16.	(thrombolysis or fibrinolysis):ti,ab
17.	#13 OR #14 OR #15 OR #16 OR #17
18.	MeSH descriptor Time Factors explode all trees
19.	(delay* or timing or time):ti,ab
20.	#18 or #19
21.	#12 and #17 and #20

F.5.2 Facilitated PPCI

What is the clinical and cost effectiveness of facilitated PPCI (fPPCI) compared to PPCI in people with STEMI?

Search constructed by combining the columns in the following table using the 'AND' Boolean operator, except for the exclusion filter which is combined with the search using the 'NOT' Boolean operator

Population	Intervention(s) / exposure(s)	Study filters used (Medline & Embase only)	Date parameters
STEMI	PCI terms AND Pharmacological agents terms (drugs used to facilitate PCI)	SRs, RCTs, Exclusions	1990 to 29/11/12

Medline search terms

1.	exp *stents/
2.	angioplasty/
3.	exp *Angioplasty, Balloon, Coronary/
4.	*Coronary Angiography/
5.	exp *Catheterization, Peripheral/
6.	*Myocardial Reperfusion/
7.	percutaneous coronary intervention*.ti,ab.
8.	(peripheral adj3 catheter$).ti,ab.
9.	(coronary adj3 angiograph$).ti,ab.

10.	((heart or myocardi$) adj3 reperfusion).ti,ab.
11.	((primary or coronary or transluminal or balloon) adj3 angioplasty).ti,ab.
12.	Coronary artery dilat$.ti,ab.
13.	Stent$.ti,ab.
14.	or/1-13
15.	(Alteplase or Actilyse or Activase or Altepase or Activacin).ti,ab.
16.	(Reteplase or Rapilysin or Retavase or ecokinase).ti,ab.
17.	(Tenecteplase or Metalyse or TNKase).ti,ab.
18.	(Streptokinase or Streptase or Kabikinase or avelysin or celiase or kinalysin or plasmokinase or plasminokinase or stretodecase or zykinase).ti,ab.
19.	(abciximab or ReoPro or abcixi or centorx).ti,ab.
20.	(Eptifibatide or Integrilin or integrelin or intrifiban).ti,ab.
21.	(Tirofiban or Aggrastat or aggrastet).ti,ab.
22.	Tissue plasminogen activator/
23.	Fibrinolytic agents/
24.	Streptokinase/
25.	Platelet Glycoprotein GPIIb-IIIa Complex/
26.	(Glycoprotein* adj2 IIb*).ti,ab.
27.	or/15-26
28.	heparin/ or heparin, low-molecular-weight/ or dalteparin/ or enoxaparin/ or nadroparin/ or heparinoids/
29.	(Calciparine or Monoparin or Calcium Multiparin or Bemiparin or Zibor or Dalteparin or Fragmin or Enoxaparin or Clexane or Lovenox or Tinzaparin or Innohep or Antixarin or CY 222 or Embolex or monoembolex or Fragmin or Tinzaparin or Suleparoide or Ardeparin or Certoparin or Nadroparin or Parnaparin or Reviparin or Tedelparin).mp.
30.	or/28-29
31.	27 or 30
32.	14 and 31

Embase search terms

1.	exp *stent/
2.	Stent$.ti,ab.
3.	*angioplasty/
4.	exp *percutaneous transluminal angioplasty/
5.	exp transluminal coronary angioplasty/
6.	((Primary or coronary or transluminal or balloon) adj3 angioplasty).ti,ab.
7.	Coronary artery dilat$.ti,ab.
8.	*percutaneous coronary intervention/
9.	percutaneous coronary intervention*.ti,ab.
10.	catheterization/
11.	heart muscle reperfusion/
12.	((heart or myocardi$) adj3 reperfusion).ti,ab.
13.	or/1-12
14.	(Alteplase or Actilyse or Activase or Altepase or Activacin).ti,ab.
15.	(Reteplase or Rapilysin or Retavase or ecokinase).ti,ab.
16.	(Tenecteplase or Metalyse or TNKase).ti,ab.
17.	(Streptokinase or Streptase or Kabikinase or avelysin or celiase or kinalysin or plasmokinase or

	plasminokinase or stretodecase or zykinase).ti,ab.
18.	(abciximab or ReoPro or abcixi or centorx).ti,ab.
19.	(Eptifibatide or Integrilin or integrelin or intrifiban).ti,ab.
20.	(Tirofiban or Aggrastat or aggrastet).ti,ab.
21.	(Glycoprotein* adj2 IIb*).ti,ab.
22.	Alteplase/
23.	Plasminogen activator/
24.	reteplase/
25.	tenecteplase/
26.	streptokinase/
27.	Abciximab/
28.	Eptifibatide/
29.	Tirofiban/
30.	fibrinogen receptor antagonist/
31.	or/14-30
32.	heparin/ or low molecular weight heparin/ or dalteparin/ or enoxaparin/ or nadroparin/ or heparinoid/
33.	(Calciparine or Monoparin or Calcium Multiparin or Bemiparin or Zibor or Dalteparin or Fragmin or Enoxaparin or Clexane or Lovenox or Tinzaparin or Innohep or Antixarin or CY 222 or Embolex or monoembolex or Fragmin or Tinzaparin or Suleparoide or Ardeparin or Certoparin or Nadroparin or Parnaparin or Reviparin or Tedelparin).mp.
34.	or/32-33
35.	31 or 34
36.	13 and 35

Cochrane search terms

1.	MeSH descriptor Stents explode all trees
2.	MeSH descriptor Angioplasty, Balloon, Coronary explode all trees
3.	MeSH descriptor Coronary Angiography explode all trees
4.	MeSH descriptor Catheterization, Peripheral explode all trees
5.	MeSH descriptor Myocardial Reperfusion explode all trees
6.	(percutaneous NEXT coronary NEXT intervention*):ti,ab
7.	(peripheral NEAR/3 catheter*):ti,ab
8.	((heart or myocardi*) NEAR/3 reperfusion):ti,ab
9.	((coronary or transluminal or balloon) NEAR/3 angioplasty):ti,ab
10.	(Coronary NEXT artery NEXT dilat*):ti,ab
11.	Stent*:ti,ab
12.	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #10 OR #11
13.	(Alteplase or Actilyse or Activase or Altepase or Activacin):ti,ab
14.	(Reteplase or Rapilysin or Retavase or ecokinase):ti,ab
15.	(Tenecteplase or Metalyse or TNKase):ti,ab
16.	(Streptokinase or Streptase or Kabikinase or avelysin or celiase or kinalysin or plasmokinase or plasminokinase or stretodecase or zykinase):ti,ab
17.	(abciximab or ReoPro or abcixi or centorx):ti,ab
18.	(Eptifibatide or Integrilin or integrelin or intrifiban):ti,ab
19.	(Tirofiban or Aggrastat or aggrastet):ti,ab
20.	(Glycoprotein* NEAR/2 IIb*):ti,ab

21.	MeSH descriptor Tissue Plasminogen Activator, this term only
22.	MeSH descriptor Fibrinolytic Agents, this term only
23.	MeSH descriptor Streptokinase explode all trees
24.	#13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24
25.	MeSH descriptor Heparin explode all trees
26.	MeSH descriptor Dalteparin, this term only
27.	MeSH descriptor Enoxaparin, this term only
28.	MeSH descriptor Nadroparin, this term only
29.	(Calciparine or Monoparin or Calcium Multiparin or Bemiparin or Zibor or Dalteparin or Fragmin or Enoxaparin or Clexane or Lovenox or Tinzaparin or Innohep or Antixarin or CY 222 or Embolex or monoembolex or Fragmin or Tinzaparin or Suleparoide or Ardeparin or Certoparin or Nadroparin or Parnaparin or Reviparin or Tedelparin):ti,ab
30.	#25 OR #26 OR #27 OR #28 OR #29 OR #30
31.	#24 or 30
32.	#12 and #31

F.5.3 Radial versus femoral arterial access for PPCI

What is the clinical and cost effectiveness of radial access compared to femoral access for coronary angiography and, if appropriate, follow-on PPCI in people with STEMI managed by PPCI?

Search constructed by combining the columns in the following table using the 'AND' Boolean operator, except for the exclusion filter which is combined with the search using the 'NOT' Boolean operator

Population	Intervention(s) / exposure(s)	Study filters used (Medline & Embase only)	Date parameters
STEMI	PCI terms AND femoral or radial artery terms	SRs, RCTs, Exclusions	1990 to 29/11/12

Medline search terms

1.	exp *stents/
2.	exp *angioplasty, balloon, coronary/
3.	exp *coronary artery bypass/
4.	*coronary angiography/
5.	exp *catheterization, peripheral/
6.	*myocardial reperfusion/
7.	percutaneous coronary intervention*.ti,ab.
8.	(aortocoronary adj3 bypass).ti,ab.
9.	((coronary or heart) adj3 bypass*).ti,ab.
10.	(peripheral adj3 catheter*).ti,ab.
11.	(coronary adj3 angiograph*).ti,ab.
12.	((heart or myocardi*) adj3 reperfusion).ti,ab.
13.	((coronary or transluminal or balloon) adj3 angioplasty).ti,ab.
14.	coronary artery dilat*.ti,ab.
15.	stent*.ti,ab.
16.	or/1-15
17.	femoral artery/
18.	radial artery/

19.	(radial or femoral or (trans adj radial) or (trans adj femoral)).ti,ab.
20.	or/17-19
21.	16 and 20

Embase search terms

1.	percutaneous coronary intervention*.ti,ab.
2.	(aortocoronary adj3 bypass).ti,ab.
3.	((coronary or heart) adj3 bypass*).ti,ab.
4.	(peripheral adj3 catheter*).ti,ab.
5.	(coronary adj3 angiograph*).ti,ab.
6.	((heart or myocardi*) adj3 reperfusion).ti,ab.
7.	((coronary or transluminal or balloon) adj3 angioplasty).ti,ab.
8.	coronary artery dilat*.ti,ab.
9.	stent*.ti,ab.
10.	exp *stent/
11.	exp *transluminal coronary angioplasty/
12.	exp *percutaneous transluminal angioplasty/
13.	coronary artery bypass graft/
14.	catheterization/
15.	heart muscle reperfusion/
16.	or/1-15
17.	radial artery/
18.	exp femoral artery/
19.	(radial or femoral or (trans adj radial) or (trans adj femoral)).ti,ab.
20.	or/17-19
21.	16 and 20

Cochrane search terms

1.	MeSH descriptor Stents explode all trees
2.	MeSH descriptor Angioplasty, Balloon, Coronary explode all trees
3.	MeSH descriptor Coronary Angiography explode all trees
4.	MeSH descriptor Coronary Artery Bypass explode all trees
5.	MeSH descriptor Catheterization, Peripheral explode all trees
6.	MeSH descriptor Myocardial Reperfusion explode all trees
7.	(aortocoronary near/3 bypass*):ti,ab
8.	((coronary or heart) near/3 bypass*):ti,ab
9.	(peripheral near/3 catheter*):ti,ab
10.	(coronary near/3 angiograph*):ti,ab
11.	((heart or myocardi*) near/3 reperfusion):ti,ab
12.	((coronary or transluminal or balloon) near/3 angioplasty):ti,ab
13.	(coronary next artery next dilat*):ti,ab
14.	(percutaneous next coronary next intervention*):ti,ab
15.	stent*:ti,ab
16.	(#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15)
17.	MeSH descriptor Radial Artery explode all trees
18.	MeSH descriptor Femoral Artery explode all trees

19.	(radial or femoral or (trans next radial) or (trans next femoral)):ti,ab
20.	(#17 or #18 or #19)
21.	#16 and #20

F.5.4 Thrombus extraction during PPCI

What is the clinical and cost effectiveness of using thrombus extraction devices (catheter aspiration devices, mechanical thrombectomy devices) during PPCI compared with PPCI alone for the treatment of STEMI in adults?

Search constructed by combining the columns in the following table using the 'AND' Boolean operator, except for the exclusion filter which is combined with the search using the 'NOT' Boolean operator

Population	Intervention(s) / exposure(s)	Study filters used (Medline & Embase only)	Date parameters
STEMI	PCI AND thrombectomy terms	SRs, RCTs, Exclusions	1990 to 29/11/12

Medline search terms

1.	exp heart catheterization/
2.	exp stents/
3.	myocardial reperfusion/
4.	exp angioplasty/
5.	exp myocardial revascularization/
6.	percutaneous coronary intervention*.ti,ab.
7.	((heart or cardiac) adj3 catheter*).ti,ab.
8.	((heart or myocardi*) adj3 reperfusion).ti,ab.
9.	((primary or percutaneous or coronary or transluminal or balloon) adj3 angioplasty).ti,ab.
10.	(ppci or pci or ptca).ti,ab.
11.	coronary artery dilat*.ti,ab.
12.	stent*.ti,ab.
13.	revasc*.ti,ab.
14.	or/1-13
15.	exp thrombectomy/
16.	mechanical thrombolysis/
17.	suction/
18.	embolectomy/
19.	(thrombectomy or thrombectomies or embolectomy or embolectomies).ti,ab.
20.	(emboli* adj2 protect*).ti,ab.
21.	thromboaspiration.ti,ab.
22.	((thrombus or clot* or embol*) adj2 (remov* or extract* or aspirat*)).ti,ab.
23.	((mechanical or manual) adj2 (clot disrupt* or thrombolysis or aspirat*)).ti,ab.
24.	((catheter* or thrombo*) adj2 aspirat*).ti,ab.
25.	(quickcat or thromcat or angiojet or x-sizer).ti,ab.
26.	or/15-25
27.	14 and 26

Embase search terms

1.	percutaneous coronary intervention*.ti,ab.
2.	((heart or myocardi*) adj3 reperfusion).ti,ab.
3.	((coronary or transluminal or balloon) adj3 angioplasty).ti,ab.
4.	coronary artery dilat*.ti,ab.
5.	stent*.ti,ab.
6.	exp *stent/
7.	exp *transluminal coronary angioplasty/
8.	exp *percutaneous transluminal angioplasty/
9.	catheterization/
10.	heart muscle reperfusion/
11.	or/1-10
12.	artificial embolism/
13.	exp thrombectomy/
14.	coronary artery thrombosis/
15.	exp percutaneous thrombectomy/
16.	embolectomy/
17.	(thrombus adj2 (aspirat* or extracti*)).ti,ab.
18.	thrombectomy.ti,ab.
19.	thromboaspiration.ti,ab.
20.	(emboli* adj2 protect*).ti,ab.
21.	embolectomy.ti,ab.
22.	emboli#ation.ti,ab.
23.	(export or pronto or diver or angiojet or (x adj sizer) or rescue).ti,ab.
24.	or/12-23
25.	11 and 24

Cochrane search terms

1.	MeSH descriptor Heart Catheterization explode all trees
2.	MeSH descriptor Stents explode all trees
3.	MeSH descriptor Myocardial Reperfusion, this term only
4.	MeSH descriptor Angioplasty explode all trees
5.	MeSH descriptor Myocardial Revascularization explode all trees
6.	"percutaneous coronary intervention*":ti,ab
7.	((heart or cardiac) near/3 catheter*):ti,ab
8.	((heart or myocardi*) near/3 reperfusion):ti,ab
9.	((percutaneous or primary or coronary or transluminal or balloon) near/3 angioplasty):ti,ab
10.	(PPCI or PCI or PTCA):ti,ab
11.	(revasc* or stent*):ti,ab
12.	(coronary next artery next dilat*):ti,ab
13.	(#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12)
14.	MeSH descriptor Thrombectomy explode all trees
15.	MeSH descriptor Suction, this term only
16.	MeSH descriptor Embolectomy, this term only
17.	MeSH descriptor Mechanical Thrombolysis, this term only
18.	(thrombectomy or thrombectomies or embolectomy or embolectomies or thromboaspiration or quickcat or thromcat or angiojet or x-sizer):ti,ab

19.	(emboli* near/2 protect*):ti,ab
20.	((thrombus or clot* or emboli*) near/2 (remov* or extract* or aspirat*)):ti,ab
21.	((mechanical or manual) near/2 ("clot disrupt*" or thrombolysis or aspirat*)):ti,ab
22.	((catheter* or thrombo*) next aspirat*):ti,ab
23.	(#14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22)
24.	(#13 and #23)

F.5.5 Culprit versus complete revascularisation **Updated, see the 2020 evidence review**

What is the clinical and cost effectiveness of multivessel PCI compared to culprit-only PPCI in people with STEMI and multivessel coronary disease undergoing PPCI?

Search constructed by combining the columns in the following table using the 'AND' Boolean operator, except for the exclusion filter which is combined with the search using the 'NOT' Boolean operator

Population	Intervention(s) / exposure(s)	Study filters used (Medline & Embase only)	Date parameters
STEMI	PCI terms AND culprit or multivessel terms	SRs, RCTs, Observational study, Exclusions	1990 to 29/11/12

Medline search terms

1.	exp *stents/
2.	percutaneous coronary intervention*.ti,ab.
3.	((primary or coronary or percutaneous or transluminal or balloon) adj3 angioplasty).ti,ab.
4.	coronary artery dilat*.ti,ab.
5.	stent*.ti,ab.
6.	(PPCI or PCI or PTCA).ti,ab.
7.	exp angioplasty/
8.	or/1-7
9.	(culprit or non-culprit or nonculprit).ti,ab.
10.	((infarct-related or infarct related or non-infarct-related) adj2 (artery or arteries)).ti,ab.
11.	(complete adj2 revasc*).ti,ab.
12.	((multivessel or multi-vessel or single-vessel or single vessel) adj3 (percutaneous coronary intervention* or PCI or stent* or revasc* or recanali* or angioplast*)).ti,ab.
13.	or/9-12
14.	8 and 13

Embase search terms

1.	percutaneous coronary intervention*.ti,ab.
2.	coronary artery dilat*.ti,ab.
3.	stent*.ti,ab.
4.	exp *stent/
5.	*percutaneous transluminal angioplasty/ or *angioplasty/ or *laser angioplasty/
6.	exp *percutaneous coronary intervention/
7.	(PPCI or PCI or PTCA).ti,ab.
8.	((primary or percutaneous or coronary or transluminal or balloon) adj3 angioplasty).ti,ab.
9.	or/1-8

10.	(culprit or non-culprit or nonculprit).ti,ab.
11.	((infarct-related or infarct related or non-infarct-related) adj2 (artery or arteries)).ti,ab.
12.	(complete adj2 revasc*).ti,ab.
13.	((multivessel or multi-vessel or single vessel or single-vessel) adj3 (percutaneous coronary intervention* or PCI or stent* or revasc* or recanali* or angioplast*)).ti,ab.
14.	or/10-13
15.	9 and 14

Cochrane search terms

1.	MeSH descriptor Stents explode all trees
2.	MeSH descriptor Angioplasty explode all trees
3.	stent*:ti,ab
4.	(PCI or PCTA or PPCI):ti,ab
5.	"percutaneous coronary intervention":ti,ab
6.	(("coronary artery") next dilat*):ti,ab
7.	((primary or coronary or percutaneous or transluminal or balloon) near/3 angioplasty):ti,ab
8.	#1 or #2 or #3 or #4 or #5 or #6 or #7
9.	(culprit or nonculprit or non-culprit):ti,ab
10.	((infarct-related or "infarct related" or non-infarct-related) next (artery or arteries)):ti,ab
11.	(complete next revasc*):ti,ab
12.	((multivessel or multi-vessel or "single vessel" or single-vessel) near/3 (angioplas* or pci or stent* or "percutaneous coronary intervention" or recanali* or revasc*)):ti,ab
13.	#9 or #10 or #11 or #12
14.	#8 and #13

F.5.6 Cardiogenic shock

In people with cardiogenic shock due to STEMI what is the clinical and cost effectiveness of early revascularisation compared to medical stabilisation?

Search constructed by combining the columns in the following table using the ‘AND’ Boolean operator, except for the exclusion filter which is combined with the search using the ‘NOT’ Boolean operator

Population	Intervention(s) / exposure(s)	Study filters used (Medline & Embase only)	Date parameters
STEMI OR cardiogenic shock terms	PCI terms OR revascularisation terms OR catheter terms OR bypass terms	SRs, RCTs, Exclusions	1990 to 29/11/12

Medline search terms

1.	exp *stents/
2.	*myocardial reperfusion/
3.	percutaneous coronary intervention*.ti,ab.
4.	((heart or myocardi*) adj3 reperfusion).ti,ab.
5.	coronary artery dilat*.ti,ab.
6.	stent*.ti,ab.
7.	((primary or coronary or percutaneous or transluminal or balloon) adj3 angioplasty).ti,ab.
8.	(PPCI or PCI or PTCA).ti,ab.

9.	exp myocardial revascularization/
10.	exp angioplasty/
11.	revasc*.ti,ab.
12.	CABG.ti,ab.
13.	((heart or coronary or aortocoronary or cardio*) adj2 bypass).ti,ab.
14.	(bypass adj2 (surg* or graft*)).ti,ab.
15.	exp *heart catheterization/
16.	((heart or coronary) adj3 catheter*).ti,ab.
17.	or/1-16

Embase search terms

1.	percutaneous coronary intervention*.ti,ab.
2.	coronary artery dilat*.ti,ab.
3.	stent*.ti,ab.
4.	exp *stent/
5.	(PPCI or PCI or PTCA).ti,ab.
6.	((primary or percutaneous or coronary or transluminal or balloon) adj3 angioplasty).ti,ab.
7.	heart muscle revascularization/
8.	*heart muscle reperfusion/
9.	exp coronary artery surgery/
10.	*heart catheterization/
11.	((heart or coronary) adj3 catheter*).ti,ab.
12.	exp percutaneous coronary intervention/
13.	angioplasty/ or percutaneous transluminal angioplasty/
14.	revasc*.ti,ab.
15.	CABG.ti,ab.
16.	((heart or coronary or aortocoronary or cardio*) adj2 bypass).ti,ab.
17.	(bypass adj2 (surg* or graft*)).ti,ab.
18.	or/1-17

Cochrane search terms

1.	MeSH descriptor Stents explode all trees
2.	MeSH descriptor Myocardial Reperfusion explode all trees
3.	MeSH descriptor Myocardial Revascularization explode all trees
4.	MeSH descriptor Angioplasty explode all trees
5.	("percutaneous coronary intervention"):ti,ab
6.	((heart or myocardial or coronary) near/3 reperfusion):ti,ab
7.	(("coronary artery " or coronary arteries") next dilat*):ti,ab
8.	stent*:ti,ab
9.	((primary or coronary or percutaneous or transluminal or balloon) near/3 angioplast*):ti,ab
10.	(PCI or PPCI or PTCA or CABG or revasc*):ti,ab
11.	(bypass near/2 (surg* or graft*)):ti,ab
12.	((heart or cardiac or coronary or aortocoronary or cardio*) next bypass):ti,ab
13.	MeSH descriptor Myocardial Infarction explode all trees
14.	MeSH descriptor Heart Catheterization explode all trees
15.	((heart or coronary) near/3 catheter*):ti,ab

16.	(#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9or #10 or #11 or #12 or #13 or #14or #15)

F.5.7 People who remain unconscious after a cardiac arrest

Does immediate angiography followed by PPCI where indicated improve outcomes of people with presumed STEMI who are resuscitated but remain unconscious after a cardiac arrest?

Search constructed by combining the columns in the following table using the 'AND' Boolean operator, except for the exclusion filter which is combined with the search using the 'NOT' Boolean operator

Population	Intervention(s) / exposure(s)	Study filters used (Medline & Embase only)	Date parameters
STEMI AND cardiac arrest	PCI terms	SRs, RCTs, Exclusions	1990 to 29/11/12

Medline search terms

1.	percutaneous coronary intervention*.ti,ab.
2.	((heart or myocardi*) adj3 reperfusion).ti,ab.
3.	((primary or percutaneous or coronary or transluminal or balloon) adj3 angioplasty).ti,ab.
4.	coronary artery dilat*.ti,ab.
5.	stent*.ti,ab.
6.	exp stents/
7.	exp angioplasty/
8.	myocardial reperfusion/
9.	exp myocardial revascularization/
10.	revasc*.ti,ab.
11.	(PPCI or PCI or PTCA).ti,ab.
12.	((heart or cardiac) adj3 catheter*).ti,ab.
13.	exp heart catheterization/
14.	coronary angiography/
15.	(coronary adj3 angiograph*).ti,ab.
16.	or/1-15

Embase search terms

1.	percutaneous coronary intervention*.ti,ab.
2.	((heart or myocardi*) adj3 reperfusion).ti,ab.
3.	((primary or percutaneous or coronary or transluminal or balloon) adj3 angioplasty).ti,ab.
4.	coronary artery dilat*.ti,ab.
5.	stent*.ti,ab.
6.	exp *stent/
7.	exp *percutaneous coronary intervention/
8.	*percutaneous transluminal angioplasty/
9.	*angioplasty/
10.	*heart muscle reperfusion/
11.	heart muscle revascularization/
12.	revasc*.ti,ab.
13.	(PPCI or PCI or PTCA).ti,ab.
14.	((heart or cardiac) adj3 catheter*).ti,ab.

15.	*heart catheterization/
16.	angiocardiography/
17.	(coronary adj3 angiograph*).ti,ab.
18.	or/1-17

Cochrane search terms

1.	MeSH descriptor Heart Catheterization explode all trees
2.	MeSH descriptor Stents explode all trees
3.	MeSH descriptor Myocardial Reperfusion, this term only
4.	MeSH descriptor Angioplasty explode all trees
5.	MeSH descriptor Myocardial Revascularization explode all trees
6.	(percutaneous next coronary next intervention*):ti,ab
7.	((heart or cardiac) near/3 catheter*):ti,ab
8.	((heart or myocardi*) near/3 reperfusion):ti,ab
9.	((percutaneous or primary or coronary or transluminal or balloon) near/3 angioplasty):ti,ab
10.	(PPCI or PCI or PTCA):ti,ab
11.	(revasc* or stent*):ti,ab
12.	(coronary next artery next dilat*):ti,ab
13.	(coronary next angiograph*):ti,ab
14.	MeSH descriptor Coronary Angiography, this term only
15.	(#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14)

F.5.8 Hospital volumes of PPCI

What is the impact of high volume versus low volume PPCI services on patient outcomes?

Search constructed by combining the columns in the following table using the 'AND' Boolean operator, except for the exclusion filter which is combined with the search using the 'NOT' Boolean operator

Population	Intervention(s) / exposure(s)	Study filters used (Medline & Embase only)	Date parameters
No population	PCI and volume terms	Exclusions	1990 to 29/11/12

Medline and Embase search terms

1.	workload/
2.	((surg* or physician* or operat* or procedure* or hospital* or cardiol*) adj4 (volume* or workload* or caseload*)).ti,ab.
3.	1 or 2
4.	exp Angioplasty/
5.	percutaneous coronary intervention*.ti,ab.
6.	((primary or coronary or transluminal or balloon) adj3 angioplast*).ti,ab.
7.	or/4-6
8.	3 and 7

Cochrane search terms

1.	MeSH descriptor Workload, this term only
2.	(surg* or physician* or operat* or procedure* or hospital* or cardiol*) near/4 (volume* or workload* or caseload*):ti,ab
3.	(#1 or #2)

4.	MeSH descriptor Angioplasty explode all trees
5.	("percutaneous coronary intervention" or "percutaneous coronary interventions"):ti,ab
6.	((primary or coronary or transluminal or balloon) near/3 angioplast*):ti,ab
7.	(#4 or #5 or #6)
8.	(#3 and #7)

F.5.9 Pre-hospital versus in-hospital fibrinolysis

What is the clinical and cost effectiveness of pre-hospital versus in-hospital fibrinolysis?

Search constructed by combining the columns in the following table using the 'AND' Boolean operator, except for the exclusion filter which is combined with the search using the 'NOT' Boolean operator

Population	Intervention(s) / exposure(s)	Study filters used (Medline & Embase only)	Date parameters
STEMI	(General fibrinolysis terms AND prehospital terms) OR Fibrinolysis agent terms	SRs, RCTs, Exclusions	All years up to 29/11/12

Medline search terms

1.	(tissue adj2 plasminogen activator*).ti,ab.
2.	(alteplase or actilyse or activase).ti,ab.
3.	(tenecteplase or metalyse or tnkase).ti,ab.
4.	(reteplase or rapilysin or retavase).ti,ab.
5.	duteplase.ti,ab.
6.	(monteplas* or cleactor).ti,ab.
7.	(streptokinase or streptase or kabikinase or mutose or heberkinasa).ti,ab.
8.	(urokinase adj2 plasminogen activator*).ti,ab.
9.	(urokinase or abbokinase or (syner adj kinase)).ti,ab.
10.	(saruplase or (pro adj urokinase) or rescupase).ti,ab.
11.	plasminogen streptokinase activator*.ti,ab.
12.	(anistreplas* or eminase).ti,ab.
13.	tissue plasminogen activator/
14.	urokinase-type plasminogen activator/
15.	streptokinase/
16.	exp plasminogen activators/
17.	or/1-16
18.	fibrinolysis/
19.	thrombolytic therapy/
20.	(fibrinoly* or thromboly*).ti,ab.
21.	or/18-20
22.	(pre-hospital or prehospital).ti,ab.
23.	21 and 22
24.	17 or 23

Embase search terms

1.	(tissue adj2 plasminogen activator*).ti,ab.
2.	(alteplase or actilyse or activase).ti,ab.
3.	(tenecteplase or metalyse or tnkase).ti,ab.
4.	(reteplase or rapilysin or retavase).ti,ab.
5.	duteplase.ti,ab.
6.	(monteplas* or cleactor).ti,ab.
7.	(streptokinase or streptase or kabikinase or mutose or heberkinasa).ti,ab.
8.	(urokinase adj2 plasminogen activator*).ti,ab.
9.	(urokinase or abbokinase or (syner adj kinase)).ti,ab.
10.	(saruplase or (pro adj urokinase) or rescupase).ti,ab.
11.	plasminogen streptokinase activator*.ti,ab.
12.	(anistreplas* or eminase).ti,ab.
13.	tissue plasminogen activator/
14.	alteplase/
15.	urokinase/
16.	tenecteplase/
17.	plasminogen activator/
18.	reteplase/
19.	duteplase/
20.	monteplase/
21.	streptokinase/
22.	saruplase/
23.	anistreplase/
24.	or/1-23
25.	*fibrinolytic therapy/
26.	*fibrinolysis/
27.	(fibrinoly* or thromboly*).ti,ab.
28.	or/25-27
29.	(pre-hospital or prehospital).ti,ab.
30.	28 and 29
31.	24 or 30

Cochrane search terms

1.	(tissue near/2 (plasminogen activator*)):ti,ab
2.	(alteplase or actilyse or activase):ti,ab
3.	(tenecteplase or metalyse or tnkase):ti,ab
4.	(reteplase or rapilysin or retavase):ti,ab
5.	duteplase:ti,ab
6.	(monteplas* or cleactor):ti,ab
7.	(streptokinase or streptase or kabikinase or mutose or heberkinasa):ti,ab
8.	(urokinase near/2 (plasminogen activator*)):ti,ab
9.	(urokinase or abbokinase or (syner next kinase)):ti,ab
10.	(saruplase or (pro next urokinase) or rescupase):ti,ab
11.	("plasminogen streptokinase activator*"):ti,ab
12.	(anistreplas* or eminase):ti,ab

13.	MeSH descriptor Tissue Plasminogen Activator explode all trees
14.	MeSH descriptor Urokinase-Type Plasminogen Activator explode all trees
15.	MeSH descriptor Streptokinase explode all trees
16.	MeSH descriptor Anistreplase explode all trees
17.	MeSH descriptor Plasminogen Activators explode all trees
18.	(#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17)
19.	MeSH descriptor Thrombolytic Therapy, this term only
20.	MeSH descriptor Fibrinolysis, this term only
21.	(fibrinoly* or thromboly*):ti,ab
22.	(#19 or #20 or #21)
23.	(pre-hospital or prehospital):ti,ab
24.	(#22 and #23)
25.	(#18 or #24)

F.5.10 Use of antithrombin as an adjunct to fibrinolysis

Does administration of antithrombin treatment at the same time as pre-hospital fibrinolysis improve outcomes compared to administration of pre-hospital fibrinolysis alone?

Search constructed by combining the columns in the following table using the 'AND' Boolean operator, except for the exclusion filter which is combined with the search using the 'NOT' Boolean operator

Population	Intervention(s) / exposure(s)	Study filters used (Medline & Embase only)	Date parameters
STEMI	Antithrombin agents OR prehospital terms	SRs, RCTs, Exclusions	All years up to 29/11/12

Medline search terms

1.	(reteplase or rapilysin or retavase).ti,ab.
2.	(tenecteplase or TNKase or metalyse).ti,ab.
3.	(pre-hospital or prehospital).ti,ab.
4.	or/1-3

Embase search terms

1.	reteplase/
2.	tenecteplase/
3.	(reteplase or rapilysin or retavase).ti,ab.
4.	(tenecteplase or TNKase or metalyse).ti,ab.
5.	(pre-hospital or prehospital).ti,ab.
6.	or/1-5

Cochrane search terms

1.	(reteplase or rapilysin or retavase or tenecteplase or TNKase or metalyse):ti,ab
2.	(pre-hospital or prehospital):ti,ab
3.	(#1 or #2)

F.5.11 Rescue PCI

What is the clinical and cost effectiveness of rescue PCI, repeated fibrinolysis or conservative management compared to each other in people with STEMI who fail to reperfuse after fibrinolytic therapy?

Search constructed by combining the columns in the following table using the 'AND' Boolean operator, except for the exclusion filter which is combined with the search using the 'NOT' Boolean operator

Population	Intervention(s) / exposure(s)	Study filters used (Medline & Embase only)	Date parameters
STEMI	(PCI terms OR fibrinolysis terms) AND rescue terms	SRs, RCTs, Exclusions	1990 to 29/11/12

Medline search terms

1.	exp *stents/
2.	exp *angioplasty, balloon, coronary/
3.	percutaneous coronary intervention*.ti,ab.
4.	((rescue or emergency or unplanned) adj4 (percutaneous or angioplast*)).ti,ab.
5.	(rescue adj1 (PPCI or PCI)).ti,ab.
6.	exp *thrombolytic therapy/
7.	((thrombolytic or fibrinolytic) adj1 therap*).ti,ab.
8.	(thrombolysis or fibrinolysis).ti,ab.
9.	exp *tissue plasminogen activator/
10.	exp *urokinase-type plasminogen activator/
11.	exp *streptokinase/
12.	(alteplase or actilyse or reteplase or rapilysin or tenecteplase or metalyse or urokinase or syner-?kinase or streptokinase or streptase).ti,ab.
13.	or/1-12
14.	recurrence/
15.	retreatment/
16.	treatment failure/
17.	((fail* or after or repeat* or rescue) adj2 (reperfus* or treat* or therap* or thromb* or fibrino*)).ti,ab.
18.	or/14-17
19.	13 and 18

Embase search terms

1.	exp *stent/
2.	exp *transluminal coronary angioplasty/
3.	exp *percutaneous transluminal angioplasty/
4.	percutaneous coronary intervention*.ti,ab.
5.	((rescue or emergency or unplanned) adj4 (percutaneous or angioplast*)).ti,ab.
6.	(rescue adj1 (PPCI or PCI)).ti,ab.
7.	exp *fibrinolytic therapy/
8.	((thrombolytic or fibrinolytic) adj1 therap*).ti,ab.
9.	(thrombolysis or fibrinolysis).ti,ab.
10.	exp *tissue plasminogen activator/

11.	exp *urokinase/
12.	exp *streptokinase/
13.	(alteplase or actilyse or reteplase or rapilysin or tenecteplase or metalyse or urokinase or syner-?kinase or streptokinase or streptase).ti,ab.
14.	or/1-13
15.	exp recurrent disease/
16.	exp treatment failure/
17.	exp retreatment/
18.	((fail* or after or repeat* or rescue*) adj2 (reperfus* or treat* or therap* or thromb* or fibrino*)).ti,ab.
19.	or/15-18
20.	14 and 19

Cochrane search terms

1.	MeSH descriptor Stents explode all trees
2.	MeSH descriptor Angioplasty, Balloon, Coronary explode all trees
3.	percutaneous next coronary next intervention*:ti,ab
4.	((rescue or emergency or unplanned) near/4 (percutaneous or angioplast*)):ti,ab
5.	(rescue next (PPCI or PCI)):ti,ab
6.	MeSH descriptor Thrombolytic Therapy explode all trees
7.	((thrombolytic or fibrinolytic) next therap*):ti,ab
8.	(thrombolysis or fibrinolysis):ti,ab
9.	MeSH descriptor Tissue Plasminogen Activator explode all trees
10.	MeSH descriptor Urokinase-Type Plasminogen Activator explode all trees
11.	MeSH descriptor Streptokinase explode all trees
12.	(alteplase or actilyse or reteplase or rapilysin or Tenecteplase or metalyse or urokinase or syner-kinase or Streptokinase or streptase):ti,ab
13.	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11or #12
14.	MeSH descriptor Recurrence explode all trees
15.	MeSH descriptor Retreatment explode all trees
16.	MeSH descriptor Treatment Failure explode all trees
17.	((fail* or after or repeat* or rescue*) near/2 (reperfus* or treat* or therap* or thromb* or fibrino*)):ti,ab
18.	#14 or #15 or #16 or #17
19.	#13 and #18

F.5.12 Routine early angiography following fibrinolysis

What is the clinical and cost effectiveness of routine early angiography following STEMI successfully treated by fibrinolysis compared to routine deferred or selective angiography?

Search constructed by combining the columns in the following table using the ‘AND’ Boolean operator, except for the exclusion filter which is combined with the search using the ‘NOT’ Boolean operator

Population	Intervention(s) / exposure(s)	Study filters used (Medline & Embase only)	Date parameters
STEMI	Fibrinolyis terms AND angiography terms	SRs, RCTs, Exclusion	1990 to 29/11/12

Medline search terms

1.	exp *thrombolytic therapy/
2.	exp *fibrinolytic agents/
3.	(antithrombic or antithrombotic or anti-thrombic or anti-thrombotic or thrombolytic or thrombolysis or fibrinolytic or fibrinolysis).ti,ab.
4.	or/1-3
5.	*coronary angiography/
6.	(angiogram or angiograph* or angioplasty or stent*).ti,ab.
7.	exp *angioplasty/
8.	exp *stents/
9.	or/5-8
10.	4 and 9

Embase search terms

1.	exp *fibrinolytic therapy/
2.	exp *fibrinolytic agent/
3.	(antithrombic or antithrombotic or anti-thrombic or anti-thrombotic or thrombolytic or thrombolysis or fibrinolytic or fibrinolysis).ti,ab.
4.	or/1-3
5.	exp *angiocardiography/
6.	exp *angioplasty/
7.	exp *stent/
8.	(angiogram or angiograph* or angioplasty or stent*).ti,ab.
9.	or/5-8
10.	4 and 9

Cochrane search terms

1.	MeSH descriptor Thrombolytic Therapy explode all trees
2.	MeSH descriptor Fibrinolytic Agents explode all trees
3.	(antithrombic or antithrombotic or anti-thrombic or anti-thrombotic or thrombolytic or thrombolysis or fibrinolytic or fibrinolysis):ti,ab,kw
4.	(#1 or #2 or #3)
5.	MeSH descriptor Coronary Angiography explode all trees
6.	MeSH descriptor Angioplasty explode all trees
7.	MeSH descriptor Stents explode all trees
8.	(angiogram or angiograph* or angioplasty or stent*):ti,ab,kw
9.	(#5 or #6 or #7 or #8)
10.	(#4 and #9)

F.6 Economics search

F.6.1 General economic search

Search constructed by combining the columns in the following table using the 'AND' Boolean operator, except for the exclusion filter which is combined with the search using the 'NOT' Boolean operator.

Population	Intervention(s) / exposure(s)	Study filters used (Medline & Embase only)	Date parameters
STEMI OR PCI terms OR angioplasty terms (search terms below)	*none*	Economic, Exclusions	Medline & Embase 2010 to 29/11/12 NHS EED and HEED all years to 29/11/12

Medline search terms

1.	exp *myocardial infarction/
2.	myocardial infarct*.ti,ab.
3.	(cardiac adj (infarct* or attack* or arrest* or event*)).ti,ab.
4.	(stemi or st-segment or st segment or st-elevat* or st elevat*).ti,ab.
5.	acute coronary syndrome/
6.	acute coronary syndrome*.ti,ab,kw.
7.	or/1-6
8.	*angiography/
9.	angiocardiography/
10.	*coronary angiography/
11.	(angiograph* or arteriograph* or angiocardiograph* or angiogram* or cardioangiograph* or angiocardiogram* or angio cardiograph* or coronarograph*).ti,ab.
12.	*myocardial revascularization/
13.	*myocardial reperfusion/
14.	((myocardi* or coronary or heart or cardiac) adj2 (revasculari* or reperfus*)).ti,ab.
15.	pci.ti,ab.
16.	ptca.ti,ab.
17.	exp angioplasty/
18.	blunt microdissection.ti,ab.
19.	angioplast*.ti,ab.
20.	((percutaneous or balloon or coronary or transluminal or primary) adj3 (dilation or dilatation or intervention*)).ti,ab.
21.	((coronary or drug-eluting or "bare metal") adj2 stent*).ti,ab.
22.	or/8-21
23.	7 or 22

Embase search terms

1.	myocardial infarct*.ti,ab.
2.	(cardiac adj (infarct* or attack* or arrest* or event*)).ti,ab.
3.	(stemi or st-segment or st segment or st-elevat* or st elevat*).ti,ab.
4.	acute coronary syndrome/

5.	acute coronary syndrome*.ti,ab,kw.
6.	exp *heart infarction/
7.	exp st segment elevation myocardial infarction/
8.	or/1-7
9.	*Angiography/
10.	Angiocardiography/
11.	Coronary Angiography/
12.	Angiograph*.ti,ab.
13.	Arteriograph*.ti,ab.
14.	Angiocardiograph*.ti,ab.
15.	Coronary Arteriogra*.ti,ab.
16.	Angiogram*.ti,ab.
17.	Cardioangiograph*.ti,ab.
18.	Angiocardiogram*.ti,ab.
19.	Angio Cardiograph*.ti,ab.
20.	Coronary Arteriogra*.ti,ab.
21.	Coronarograph*.ti,ab.
22.	*Heart Muscle Revascularization/
23.	Angioplasty, Transluminal, Percutaneous Coronary/
24.	(Myocardial adj (revascularisation or revascularization)).ti,ab.
25.	PCI.ti,ab.
26.	Percutaneous coronary intervention.ti,ab.
27.	Percutaneous transluminal coronary angioplasty.ti,ab.
28.	PTCA.ti,ab.
29.	exp Angioplasty/
30.	Blunt Microdissection.ti,ab.
31.	((laser or patch) adj angioplasty).ti,ab.
32.	Percutaneous Transluminal Angioplasty.ti,ab.
33.	Transluminal Coronary Angioplasty.ti,ab.
34.	(Balloon adj3 coronary).ti,ab.
35.	(Balloon adj3 angioplasty).ti,ab.
36.	(Coronary adj2 stent*).ti,ab.
37.	or/9-36
38.	8 or 37

CRD search terms

1.	MeSH DESCRIPTOR Acute Coronary Syndrome IN NHSEED,HTA
2.	MeSH DESCRIPTOR Myocardial Infarction EXPLODE ALL TREES IN NHSEED,HTA
3.	MeSH DESCRIPTOR Coronary Thrombosis IN NHSEED,HTA
4.	(acute coronary syndrome*) OR (myocardial infarct*) OR (coronary NEAR thrombos*) IN NHSEED, HTA
5.	(heart NEAR infarct*) OR (heart NEAR attack) OR (heart NEAR arrest) OR (heart NEAR event) IN NHSEED, HTA
6.	(STEMI) OR (st-segment) OR (st segment) OR (st-elevation) OR (st elevation) IN NHSEED, HTA
7.	#1 OR #2 OR #3 OR #4 OR #5 OR #6
8.	MeSH DESCRIPTOR Angiography IN NHSEED,HTA

9.	MeSH DESCRIPTOR Angiocardiography IN NHSEED,HTA
10.	MeSH DESCRIPTOR Coronary Angiography IN NHSEED,HTA
11.	(Angiograph*) OR (Arteriograph*) OR (Angiocardiograph*) OR (Coronary Angiograph*) OR (Angiogram*) IN NHSEED, HTA
12.	(Cardioangiograph*) OR (Angiocardiogram*) OR (Angio Cardiograph*) OR (Coronary Arteriogra*) OR (Coronarograph*) IN NHSEED, HTA
13.	MeSH DESCRIPTOR Myocardial Revascularization EXPLODE ALL TREES IN NHSEED,HTA
14.	(Myocardial NEAR revascularization) OR (Myocardial NEAR revascularisation) OR (PCI) OR (Percutaneous coronary intervention) OR (Percutaneous AND Transluminal Coronary angioplasty) IN NHSEED, HTA
15.	MeSH DESCRIPTOR angioplasty EXPLODE ALL TREES IN NHSEED,HTA
16.	(PTCA) OR (Blunt Microdissection) OR (Laser NEAR angioplasty) OR (Patch NEAR angioplasty) OR (Percutaneous Transluminal Angioplasty) IN NHSEED, HTA
17.	(Transluminal Coronary Angioplasty) OR (Balloon NEAR coronary) OR (Balloon NEAR angioplasty) OR (coronary NEAR stent*) IN NHSEED, HTA
18.	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17

HEED search terms

1.	AX=Acute coronary syndrome or acute coronary syndromes
2.	Ax=myocardial infarction or myocardial infarct or myorcardial
3.	Ax=Coronary thrombosis
4.	Ax=Heart infarction or heart infarct or heart infarcts
5.	AX=Heart attack or heart attacks
6.	Ax=heart arrest or heart arrests
7.	Ax=heart event or heart events
8.	AX=STEMI
9.	AX= st-segment
10.	AX=st-elevation
11.	Ax=st segment
12.	Ax=st elevation
13.	CS=1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12
14.	Ax=angiography
15.	Ax=Angiocardiography
16.	Ax=Coronary angiography
17.	AX=Angiograph or angiographs
18.	AX=Arteriography or arteriograph or arteriographs
19.	AX=Angiogram or angiograms
20.	Ax=myocardial revascularization
21.	Ax=myocardial revascularisation
22.	Ax=PCI
23.	Ax=Percutaneous coronary intervention
24.	AX=Percutaneous transluminal coronary angioplasty
25.	Ax=PCTA
26.	AX=Angioplasty
27.	AX=Balloon and coronary
28.	AX=Balloon and Angioplasty

29.	Ax=Coronary and Stent
30.	Ax=coronary and stents
31.	CS=14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30
32.	CS=13 and 31

F.6.2 Quality of life reviews

These searches were carried out on Medline and Embase only.

Population	Intervention(s) / exposure(s)	Study filters used (Medline & Embase only)	Date parameters
STEMI	*none*	Quality of life, Exclusions	all years to 29/11/12

Appendix G: Clinical evidence tables

G.1 Time to reperfusion

Table 14: Asseburg 2006[5]

Reference/funding	Methods	Outcomes	RCTs
Asseburg C, et al. Assessing the effectiveness of primary angioplasty compared with fibrinolysis and its relationship to time delay: a Bayesian evidence synthesis. Heart. 2007; 93(10):1244-50. Funding: Unrestricted educational grant from Cordis Ltd; NHS	Updated previously published meta-analysis http://www.ncbi.nlm.nih.gov/pubmed/12517460 (Keeley et al 2003) by searching: Cochrane Controlled Trials Register, UK National Research Register, Medline, Embase, Database of Abstracts of Reviews of Effects, UK National Health Service Economic Evaluation Databases, and the Health Technology Assessment Database for English language RCTs published between 2002 and 2004 New meta-analysis was calculated by Bayesian statistical methods using random effects model (study-level data were used on an ITT basis). Meta-regression was used to estimate the relative treatment effect of PPCI and fibrinolysis as a function of the covariate PPCI-related time delay PPCI-related time delay was defined as the difference between time to balloon in PPCI and time to needle in fibrinolytic treatment, to avoid problems of different timing definitions across RCTs. Mean times (and SD) to treatment were preferred, when unavailable medians (and IQR) were used. A sensitivity analysis was undertaken to determine the effect of uncertainty around input parameters (prior distributions) and differences between fibrinolytic drugs.	Mortality, non-fatal strokes, non-fatal reinfarctions; all at 1 and 6 months PPCI-related time delay associated with equipoise between both reperfusion strategies Outcomes are presented as absolute probabilities of specific events and odds ratios (ORs; with 95% credible intervals (CrI)) as a function of the additional time delay associated with PPCI.	22 RCTs (n = 3760 PPCI; n = 3758 fibrinolysis) Zijlstra 1993; 1997 Ribeiro 1993 de Boer 1994; 2002 Berrocal 2003 Widimsky 2000; 2003 DeWood 1990 Grines 1993; 2002 Gibbons 1993 Ribichini 1998 Garcia 1999 GUSTO IIb 1997 Le May 2001 Bonnefoy 2002 Schomig 2000 Vermeer 1999 Kastrati 2002 Aversano 2002 Andersen 2003 --------------------- 22/22 trials reported outcomes at 30 days or 6 weeks (grouped as '1 month') 10/22 trials reported outcomes at 6 months ---------------------

Reference/funding	Methods	Outcomes	RCTs
			1/22 used pre-hospital fibrinolysis 8/22 trials used streptokinase 14/22 used tPA 13/22 trials used stents 8/22 used GPIs

Table 15: Boersma 2006[10]

Reference/funding	Methods	Outcomes	RCTs
Boersma E, et al. Primary Coronary Angioplasty vs. Thrombolysis Group. Does time matter? A pooled analysis of randomized clinical trials comparing primary percutaneous coronary intervention and in-hospital fibrinolysis in acute myocardial infarction patients. Eur Heart J. 2006; 27(7):779-88. Funding: Boehringer Ingelheim (the Netherlands)	Based on patient-level data – All RCTs (n > 50) published between January 1990 and December 2002 were considered (non-English articles were not excluded). They were identified by OVID MEDLINE and ISI Web of Science using a broad range of key words; References of identified papers and abstract listings of annual meetings of the American Heart Association, American College of Cardiology and European Society of Cardiology were also examined. Individual patient data from 22 RCTs were pooled, and multi-level logistic regression assessed the relationship among treatment, treatment delay, and 30-day mortality. Treatment delay was divided into 'presentation delay' (symptom onset to randomisation; categorised as 0–1, >1–2, >2–3, >3–6, >6 hours) and 'PPCI-related time delay' (median time from randomisation to PPCI minus median time to FT per hospital). PPCI-related time delay was calculated for each of the 153 hospitals and assigned to each patient within that hospital. PPCI-related time delay was then grouped into: 0–35, >35–50, >50–62, >62–79, and >79 minutes. At the patient level, age, gender, weight, diabetes mellitus, previous MI, prior revascularisation (PCI or CABG), anterior MI at presentation, heart rate, systolic blood pressure, presentation delay, and study treatment (FT or PPCI) were considered fixed effects. At hospital level, the PPCI-related time delay and the average annual PCI volume (grouped into tertiles of its distribution: <10, 10–23, ≥24 PPCI/year) were considered.	30-day all-cause mortality, stroke and re-MI Outcomes are presented as OR and 95% CI Further analyses of how presentation delay affected PPCI benefit were performed in patient-, hospital- and study-level subgroups selected in advance (< 65 versus ≥ 65-years-old; gender; ± diabetes mellitus; ± previous MI; anterior versus non-anterior MI; systolic blood pressure (< 130 versus ≥ 130 mmHg); heart rate (< 70 versus ≥ 70 bpm), hospital-level average annual PCI volume and study-level type of fibrinolytic agent used.	22 RCTs (n = 6763) Zijlstra 1993; 1997 Ribeiro 1993 Grinfeld 1996 Akhras 1997 Kedev 1997 de Boer 2002 Widimsky 2000; 2003 Grines 1993; 2002 Gibbons 1993 Ribichini 1998 Garcia 1999 GUSTO IIb 1997 Le May 2001 Schomig 2000 Vermeer 1999 Kastrati 2002 Aversano 2002 Andersen 2003 Aoki 1997 --------------------- 0/22 used pre-hospital fibrinolysis

Reference/funding	Methods	Outcomes	RCTs
	At the study level, the likelihood of PCI within 30 days after initial FT, use of stents, use of GPIs, type of fibrinolytic agent used (streptokinase, t-PA, or accelerated t-PA), single-centred versus multicentred trial, and the year of publication were considered. Two sensitivity analyses were performed: (i) impact of exclusion of 3 trials without patient data; (ii) fibrinolytic agent used.		9/22 used streptokinase 1/22 used duteplase 12/22 used t-PA 10/22 used accelerated t-PA 10/22 used stents 6/22 used GPIs

Table 16: Kent 2001[63]

Reference/funding	Methods	Outcomes	RCTs
Kent DM, et al. Balancing the benefits of primary angioplasty against the benefits of thrombolytic therapy for acute myocardial infarction: the importance of timing. Eff Clin Pract. 2001; 4(5):214-20. Funding: New England Medical Centre Research Fund Award	Based on study-level data from 10 RCTs included in a previously published meta-analysis (Weaver 1997). For each RCT this analysis calculated PPCI-related time delay (median 'door-to-balloon' time minus median 'door-to-needle' time) and survival benefit (30-day mortality after fibrinolytic therapy minus 30-mortality after PPCI) Linear meta-regression was used to assess the relationship between PPCI-related time delay and treatment benefit by estimating: 1) the decrease in benefit for each additional minute of delay in receipt of PCI and 2) the delay expected to lead to equipoise between PCI and fibrinolytic therapy. The magnitude and statistical significance of the relationship were estimated by weighting each RCT's results by the square root of the number of patients in that trial. A sensitivity analysis was performed by excluding the trials with the longest and the shortest PPCI-related time delay.	PPCI-related time delay associated with equipoise between both reperfusion strategies (Outcomes are presented as relative and absolute reduction in 30-day mortality, both as a function of the PPCI-related time delay) Reduction in mortality benefit for each additional 10 minutes of PPCI-related time delay.	10 RCTs (n = 2628) Zijlstra 1993; 1997 Ribeiro 1993 DeWood 1990 Grines 1993 Gibbons 1993 Ribichini 1996 Garcia 1997 GUSTO IIb 1997 Grinfeld 1996 --------------------- 10/10 trials reported outcomes at 30 days No details on longer follow-up data --------------------- 5/10 trials used streptokinase 5/10 used tissue plasminogen activator 0/10 used stents 0/10 used glycoprotein IIb/IIIa antagonists (GPIs)

Table 17: Pinto 2006[90]

Reference/funding	Methods	Outcomes	Registry
Pinto DS, et al. Hospital delays in reperfusion for ST-elevation myocardial infarction: implications when selecting a reperfusion strategy. Circulation. 2006; 114(19):2019-25. Funding: Genentech, Inc	Based on patient-level data from the National Registry of Myocardial Infarction (NRMI) 2, 3, and 4 NRMI 2–4 were voluntary, prospective registries that collected data from June 1994 to August 2003 on consecutive patients with documented STEMI (or LBBB on initial ECG) and < 12 hours after pain onset who received either fibrinolytic therapy or PPCI as initial reperfusion therapy. Patients transferred to an NRMI hospital for reperfusion were included, but patients transferred out of an NRMI hospital to a non-NRMI hospital were excluded because mortality data were unavailable. Patients with missing time-interval data were also excluded. Participating hospitals were required to manage ≥ 20 patients with STEMI (≥ 10 PPCI and ≥ 10 fibrinolysis). PPCI-related time delay was calculated by subtracting the median DN time from the median DB time at each hospital. For transfer patients, the point of reference to calculate DB and DN times was the first hospital arrival date/time. Hospitals were divided into 4 categories of PPCI-related time delays (< 60, 60–89, 90–120, and > 120 minutes). Then, the mean time delay within each of these 4 categories was calculated with the median PPCI-related time delay at each hospital. Hierarchical models that adjusted simultaneously for both patient-level risk factors and hospital-level covariates were used to evaluate the relationship between PPCI-related time delay, patient risk factors, and in-hospital mortality. Patient covariates included: treatment type (PPCI versus fibrinolysis), age, gender, race, diabetes mellitus, hypertension, angina, Killip class 2/3, Killip class 4, previous infarction, current smoking, stroke, pulse, systolic blood pressure, payer, pre-hospital delay, and discharge year. Hospital covariates included STEMI volume, PPCI volume, transfer-in rate, rural location, and status as a teaching hospital.	In-hospital mortality (before discharge) PPCI-related time delay associated with equipoise between both reperfusion strategies Relationship between DB-DN time delay and the mortality difference in patient subgroups stratified by age (< 65 versus ≥ 65 years), infarct location (anterior versus other), and time from symptom onset to hospital presentation (≤ 120 or > 120 minutes) Outcomes are presented as OR and 95% CI.	The selection criteria yielded 192,509 patients with STEMI and 645 hospitals eligible for analysis. PPCI was performed in 65,600 patients, and FT was administered to 126,909 patients (Fibrin-specific agents were administered in 92% (n = 117,256) of patients). > 65% of patients (n = 125,737) presented within 2 hours of symptom onset.

Table 18: Tarantini 2010[110]

Reference/funding	Methods	Outcomes	RCTs
Tarantini G, et al. Acceptable reperfusion delay to prefer primary angioplasty over fibrin-specific thrombolytic therapy is affected (mainly) by the patient's mortality risk: 1 h does not fit all. Eur Heart J. 2010; 31(6):676-83. Funding: None stated	Based on study-level data – All RCTs (n ≥ 50), published and unpublished (non-English articles were not excluded) comparing fibrin-specific fibrinolysis to PPCI. MEDLINE, CENTRAL, EMBASE, and the Cochrane Central Register of Controlled Trials were searched (Jan. 1990–Dec. 2008) using a broad range of keywords. Also searched for abstracts in the New England Journal of Medicine, Circulation, European Heart Journal, Journal of the American College of Cardiology, and Heart. References of identified papers, relevant studies, and meta-analyses were additionally scanned. Oral presentations and expert slide presentations identified from www.theheart.org, www.tctmd.com, www.crtonline.com, www.clinicaltrialresults.org, www.esccardio.org, www.europcr.com, and www.acc.org were also examined. Weighted meta-regression was used to explore the relationship, (adjusted for pre-hospital time delay) between the mortality risk and the PPCI-related time delay which leads to equivalent 30-day mortality between PPCI and fibrin-specific fibrinolysis. A multiple linear regression analysis considered the absolute risk reduction as a linear function of fibrinolytic mortality, time to treatment and PPCI-related time delay. Mortality benefit was calculated as fibrinolysis 30-day mortality minus PPCI 30-day mortality. PPCI-related time delay was calculated as the difference between mean or median DB time minus DN time. Presentation delay was calculated as mean or median time from the symptom onset to door (randomisation or first medical contact) that was not influenced by the allocated treatment. Because the outcome was mortality, the control (lytic arm) mortality rate was interpreted as a proxy for baseline mortality risk. This rate can be considered as a surrogate of the underlying baseline risk and has the advantage of being a measure that reflects multiple factors contributing to outcome occurrence. Sensitivity analyses alternatively excluded from the set of studies the RCT with the minimum effect and the RCT with the maximum effect.	30-day mortality risk leading to equipoise between treatments.	16 RCTs (n = 6281) DeWood 1992 Grines 1993; 2002; 2005 Gibbons 1993 Ribichini 1998 Garcia 1999 GUSTO IIb 1997 Le May 2001 Bonnefoy 2002 Schomig 2000 Vermeer 1999 Kastrati 2002 Aversano 2002 Andersen 2003 Armstrong 2006 --------------------- 1/16 used pre-hospital fibrinolysis 0/16 stents 10/16 trials used stents 7/16 used GPIs

Table 19: Zjilstra 2002[122]

Reference/funding	Methods	Outcomes	RCTs
Zijlstra F, et al. Clinical characteristics and outcome of patients with early (<2 h), intermediate (2-4 h) and late (>4 h) presentation treated by primary coronary angioplasty or thrombolytic therapy for acute myocardial infarction. Eur Heart J. 2002; 23(7):550-7. Funding: None stated	Based on patient-level data from 9/10 RCTs included in a previously published meta-analysis (Weaver 1997) plus Akhras 1997 (identified subsequent to Weaver meta-analysis) The analysis examined the effects of presentation delay on outcomes after PPCI and fibrinolytic therapy using individual patient data on an ITT basis according to randomised groups. Time to presentation was measured from the outset of symptoms to randomisation in 6 RCTs and from symptom onset to hospital admission in 3 RCTs (unavailable in 1 RCT). Patients were classified into 3 categories according to the time delay from symptom onset to presentation (< 2 hours, 2–4 hours, ≥ 4 hours) Subgroups were investigated to allow multivariate analysis (lytic regimen; age [<50, 50–60, 60–70 and >70 years); gender, diabetes, infarct location, prior MI, heart rate on admission [<65, 65–75, 75–85, and >85 beats per minute] and SBP on admission [<115, 115–130, 130–150 and >150 mmHg].	Mortality, non-fatal reinfarction and total stroke at 30 days Mortality and non-fatal reinfarction at 6 months Both as a function of time to presentation	10 RCTs (n = 2635; n = 1302 PPCI; n = 1333 fibrinolysis) Zijlstra 1993; 1997 Ribeiro 1993 Grinfeld 1996 Grines 1993 Gibbons 1993 Ribichini 1998 Garcia 1999 GUSTO IIb 1997 Akhras 1997 --------------------- 0/10 used pre-hospital fibrinolysis 5/10 trials used streptokinase 5/10 used tPA 0/10 trials used stents 0/10 used GPIs

G.2 Facilitated PPCI

FINESSE[41,42]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
SG. Ellis, M Tendera, MA. de Belder, AJ. van Boven, P Widimsky et al., and FINESSE Investigators FINESSE. Facilitated PCI in patients with ST-elevation myocardial infarction. N.Engl.J.Med. 358 (21):2205-2217, 2008. 1 year follow-up paper: S G. Ellis, M Tendera, M A. de Belder, Ad J. van	**Design:** RCT (20 sites – international: Europe, Argentina, Canada and USA) **Enrolment:** Aug 2002 – Dec 2006 **Setting** NO DETAILS GIVEN **Randomisation** Good: central randomisation (1:1:1 ratio) **Allocation concealment** Unclear: central randomisation **Blinding:** Double bind, double dummy: dummy (placebo) medications used	n = 2452 Drop-outs (during the 90 days – not available for follow-up at 90 days): fPPCI: n = 8 (1%) Combination fPPCI: n = 15 (1.8%) PPCI: n = 13 (1.6%) Drop-outs (at 1 year follow-up): fPPCI: 1.6%	**Inclusion criteria** Adults ≥21 years Presented within 6 hours after the onset of signs and symptoms of cardiac ischaemia. Had ST-segment elevation suggestive of an acute MI eligible for fibrinolytic therapy or PPCI estimated time to diagnostic catheterisation was 1-4 hours after randomisation **Exclusion criteria** Low risk (<60 years and had localised inferior infarction) had risk factors for bleeding planned use of a direct thrombin inhibitor during PCI MI precipitated by a condition other than atherosclerotic coronary artery disease, recent (within 14 days) use of fibrinolytic, administration of low-molecular–weight heparin (LMWH) within 24 hours PCI within 7 days	fPPCI (n = 818) (Abciximab EARLY) Administered in the emergency department. Abciximab: IV bolus 0.25 mg / kg ---------------- Combination fPPCI (n = 828) Administered in the emergency department Reteplase + abciximab Reduced-	PPCI (Abciximab LATER) (n = 806) PPCI with abciximab initiated in the cardiac cath lab, immediately before PCI Abciximab (an IV bolus of 0.25 mg /kg). 'Dummy' placebo medications were administered at all time points to ensure that the study remained	90 days, 1 year For death and complications of MI: 90 days (maximum 100 days) after randomisation; 1 year (long-term follow-up)	1° Combined death (all causes), AND complications of MI [ventricular fibrillation (> 48 hours after randomisation), cardiogenic shock, HF (requiring hospitalisation or an emergency room visit through 90 days)]. 2° complications of MI through 90 days (as in the primary end pint) Death (all causes through 90 days)	Centocor and Eli Lilly

Boven, P Widimsky, H R. Andersen, A Betriu, et al. and Investigators FINESSE. 1-year survival in a randomized trial of facilitated reperfusion: results from the FINESSE (Facilitated Intervention with Enhanced Reperfusion Speed to Stop Events) trial. JACC Cardiovasc Interv 2 (10):909-916, 2009. Methods paper – ELLIS 2004 how shall I reference this?) SG. Ellis, P Armstrong	to maintain the abciximab and reteplase bolus blind. Central adjudication (for cardiogenic shock, congestive HF and stroke – in all patients; and ST segment resolution – in random selection of 50% of patients) by people blinded to treatment assignment Sample size calculation: NOT POWERED: aim was 3000 patients but recruitment terminated early due to slow recruitment and substantial cost overruns. Analysis aimed for was to detect a difference between combination fPPCI and PPCI in primary end point (82% power)	Combination fPPCI: 1.4% PPCI: 2.4%	known or suspected bleeding confirmed uncontrolled hypertension, and other contraindications to fibrinolytic treatment. If the protocol-specified ceiling dose of unfractionated heparin (40 U/kg, 3000U maximum) or an activated partial thromboplastin time (70 seconds) is exceeded before enrolment Demographics and baseline characteristics see below	reteplase: 2 5-U boluses separated by 30 minutes, for those <75 years old, or 1 5-U dose, for those ≥75 years old) Abciximab (IV bolus 0.25 mg / kg) Notes: IN PATIENTS AGED ≥75 YEARS: a novel regimen of reteplase 5U single bolus in combination with abciximab was studied. NOTE: Before catheterisation – aspirin: 81 - 325 mg orally or 250 to 500 mg IV. heparin: to 40 U /kg (maximum dose,	blinded	ST-segment resolution (>70% from baseline as assessed at 60–90 minutes after randomisation) Safety: Non-intracranial major or minor bleeding (TIMI) Intracranial haemorrhage (through discharge or day 7 whichever was sooner) Cardiogenic shock Congestive heart failure Stroke ST-segment resolution (see below for definitions)

A Betriu, B Brodie, H Herrmann, et al., and FINESSE Investigators. Facilitated percutaneous coronary intervention versus primary percutaneous coronary intervention: design and rationale of the Facilitated Intervention with Enhanced Reperfusion Speed to Stop Events (FINESSE) trial. Am.Heart J. 147 (4):E16, 2004.	ITT analysis: ITT for efficacy outcomes; As-treated analysis (treatment received) for safety outcomes		3000 U), with a target activated clotting time of 200 - 250 seconds At sites that participated in the low-molecular weight heparin sub-study, 0.5 mg /kg enoxaparin IV was administered, and 0.3 mg /kg was administered subcutaneous, with no target for the activated clotting time. Post-PCI – 0.125 µg/kg/minute abciximab (maximum dose, 10 µg / min) for 12 hours Stent type used – choice of stent at discretion of investigator PCI – 92% overall (91 and 92% in each group) Stents used – not mentioned			

	fPPCI (n = 818)	Combination fPPCI (n = 828)	PPCI (n = 806)
Mean age, years (SD)	61.9 (11.8)	62.6 (11.4)	62.5 (11.4)
Age <75 years (%)	695 (85)	691 (83.5)	678 (84.1)
Age ≥75 years (%)	123 (15)	137 (16.5)	128 (15.9)

Men (%)	602 (73.6)	609 (73.6)	599 (74.3)
Hypertension (%)	405 (49.5)	894 (47.6)	374 (46.4)
Hypercholesterolemia (%)	119 (14.5)	128 (15.5)	276 (34.2)
Diabetes mellitus (%)	249 (30.4)	291 (35.1)	133 (16.5)
Family history of CAD diagnosed at <55 years if age (%)	149 (18.5)	187 (22.9)	190(22.9)
Current smoker (%)	363 (44.4)	347 (41.9)	357 (44.3)
Previous MI (%)	82 (10.2)	80 (9.8)	104 (12.6)
Previous congestive heart failure (%)	13 (1.6)	9 (1.1)	12 (1.4)
Previous treatment (%)	NOT GIVEN	NOT GIVEN	NOT GIVEN
Anterior infarction (%)	370 (45.9)	403 (49.3)	40 (48.3)

*Activated clotting time

Definitions of end points

Complications of MI: Complications are defined as resuscitated ventricular fibrillation occurring 48 hours after randomisation, rehospitalisation or emergency department visit for congestive heart failure, or cardiogenic shock.

Other end points not described further.

Outcomes

Outcomes at 90 days (unless specified)	fPPCI (n = 818)	Combination fPPCI (n = 828)	PPCI (n = 806)	Statistical significance / p value	p value (Kaplan-Meier)
Primary composite end point at 90 days, %	9.8	10.5	10.7	Combination versus fPPCI: HR 0.91 (95% CI 0.67 to 1.23)	Combination versus PPCI: p = 0.55 Facilitated versus PPCI: p = 0.86 Combination versus facilitated: p = 0.68
Complications of MI, %	7.4	7.5	9.0	NS differences (data not given)	
Death from all causes, %	5.2	5.5	4.5	NS differences (data not given)	
Ventricular fibrillation occurring > 48 hours after randomisation, %	0.6	0.2	0.4	NS differences (data not given)	
Cardiogenic shock, %	5.3	4.8	6.8	NS differences (data not given)	
Rehospitalisation or emergency room visit for	1.9	2.9	2.2	NS differences (data not given)	

congestive HF, %					
Heart failure - Index hospitalisation, n (%)	45 (5.5)	54 (6.5)	52 (6.5)	not given	not given
Recurrent MI	16 (2.0)	17 (2.1)	15 (1.9)	not given	not given
Any subsequent revascularisation, n (%) PCI CABG	111 (13.6) 85 (10.4) 26 (3.2)	111 (13.4) 81 (9.8) 31 (3.7)	111 (13.8) 78 (9.7) 37 (4.6)	not given not given not given	not given not given not given
SAFETY END POINTS (through discharge or day 7)	n = 814	n = 805	n = 795		
Non-intracranial TIMI bleeding, n (%) Major Minor	118 (14.5) 39 (4.8) 79 (9.7)	81 (10.1) 33 (4.1) 48 (6.0)	55 (6.9) 21 (2.6) 34 (4.3)	Combination versus PPCI (p < 0.001); fPPCI versus PPCI (p < 0.05) Combination versus PPCI: p < 0.05 Combination versus fPPCI: p < 0.05	
Stroke, n (%) Intracranial haemorrhage Ischaemic	9 (1.1) 5 (0.6) 4 (0.5)	4 (0.5) 0 (0) 4 (0.5)	8 (1.0) 1 (0.1) 7 (0.9)	data not given	
Fatal stroke, n (%)	3 (3.7)	0 (0)	0 (0)	data not given	
ST-segment resolution (>70%) in 60–90 minutes, %	43.9	33.1	31.0	p = 0.003 (combination versus PPCI) p = 0.01 (combination versus fPPCI)	
TIMI flow grade 3 before PCI performed, %	32.8	14.1	12.0	p < 0.001(combination versus PPCI) p < 0.001 (combination versus fPPCI)	
TIMI flow grade after PCI	not given	not given	not given	No substantial difference between groups (data not given)	
TIMI flow grade for ST-segment resolution at 180–	not given	not given	not given	No substantial difference between groups (data not given)	

240 minutes					
1 year follow-up					
Death from all causes at 1 year follow-up, %	7.4	6.3	7.0	NS differences (data not given)	Combination versus PPCI: p = 0.603 fPPCI versus PPCI: p = 0.765 Combination versus fPPCI: p = 0.415
Median door to balloon time (all patients): 2.2 hours (IQR 1.8 to 2.8)					
92% of patients underwent PCI					
SUBGROUPS					
AGE 75: No intracranial haemorrhages occurred in patients aged ≥75 years					
Cardiac procedures					

n, %	fPPCI (n = 818)	Combination fPPCI (n = 828)	PPCI (n = 806)	n, %
Catheterisation	96%	93%	95%	Catheterisation
PCI	92% overall (91 and 92% in each group)		-	PCI
Transfer and timing, and hospital stay				
No details given				

Table 20: ASSIST TRIAL[69]

Reference	Study type	Patient characteristics	Intervention	Comparison	Outcome measures	Source of funding
LeMay M. et al. Primary percutaneous coronary angioplasty with and without eptifibatide in ST-segment elevation myocardial infarction. A safety end efficacy study of integrilin-facilitatyed versus primary percutaneous coronary intervention in ST_segment elevation myocardial infarction (ASSIST)	**Design:** RCT (prospective) **Enrolment:** August 2005- March 2008 **Setting** Hospital (3 Ottawa hospitals). **Randomisation:** Yes. Randomly assigned in a 1:1 ratio to intervention or comparison group, in blocks of 10 at each site. Allocation concealment: Not mentioned / unclear. Blinding: No. The intervention group received open-label drug. Corrected TIMI frame counts and Myocardial perfusion grades were evaluated by independent blinded investigators. Sample size calculation: The sample size to detect a	**Number of patients:** n = 400 Drop-outs: 1 patient lost to follow-up. **Inclusion criteria** <12 hours of the onset of ischaemic chest discomfort ≥30 minutes ≥1mm (0.1mV) ST-elevation in 2 or more contiguous leads **Exclusion criteria** Active bleeding Stroke within 90 days Intracranial bleeding at any time Major surgery or trauma within 6 weeks Systolic blood pressure >200mmHg or diastolic blood pressure >110mmHg Prolonged cardiopulmonary resuscitation PCI within 30 days Fibrinolytic agents within 7 days Any glycoprotein IIb/IIIa within 7 days Low-molecular weight heparin within 12 hours Coagulation disorder Current warfarin treatment Intolerance to aspirin or clopidogrel Other illness likely to result in death	PPCI with heparin + eptifibatide (n = 201) 180 microgram/kg of body weight bolus, followed by (after 10 minutes) a continuous infusion of 2.0 microgram/kg/minute with a second bolus of 180 microgram/kg. Eptifibatide initiated before catheterisation and continued for 18 hours after PCI. Note: Before catheterisation: oral aspirin (160mg), oral clopidogrel (600mg) and IV unfractionated heparin (60U/kg up to max 4000U).	PPCI with heparin (n = 199) Note: Before catheterisation: oral aspirin (160mg), oral clopidogrel (600mg) and IV unfractionated heparin (60U/kg up to max 4000U). 9 (4.5%) patient were given abciximab and 6 (3.0%) were given eptifibatide during PCI. PCI performed in 184 (92.5%) patients. Stent insertion in 183 (92.0%) patients.	1° Death from any cause, recurrent MI, recurrent severe ischaemia at 30 days. Other: Stroke, congestive heart failure cardiogenic shock **Length of follow-up:** 30 days, 6 months	Schering-Plough Canada Inc provided an unrestricted grant and free distribution of eptifibatide, and Medtronic Canada Ltd provided free stents for the study.

	difference between 15% and 5.0%, with a level of significance of 0.05 and 90% power using a χ2 test, was determined to be 187 per group. With an anticipated loss to follow-up rate of 5%, the minimum number of patients required was 200 per group. ITT analysis: Yes	within 12 months Pregnancy Creatine >200micromol/L Cardiogenic shock Severe contrast allergy Demographics and baseline characteristics see below	PCI performed in 190 (94.5%) patients. Stent insertion in 187 (93.0%) patients.	

Demographics and baseline characteristics

	Heparin + eptifibatide (n = 201)	**Heparin (n = 199)**
Age, years	60.4±12.1	60.6±11.8
Male gender	162 (80.6)	143 (71.9)
Hypertension	92 (45.8)	99 (49.8)
Diabetes mellitus	29 (14.4)	36 (18.1)
Current smoking	90 (44.8)	76 (38.2)
Hyperlipidimia	67 (33.3)	77 (38.7)
Prior MI	21 (10.5)	27 (13.6)
Prior angioplasty	16 (8.0)	16 (8.0)
Prior bypass surgery	10 (5.0)	8 (4.0)
Anterior MI	73 (36.3)	75 (37.7)
Heart rate, bpm	74±16	76±18
Systolic blood pressure, mmHg	130±23	134±24
Diastolic blood pressure	77±14	80±15
Killip class		
I	182 (90.6)	172 (86.4)
II	19 (9.5)	27 (13.6)
III or IV	0 (0.0)	0 (0.0)

BMI, KG/m^2	28.4±4.9	27.5±4.6
Eptifibatide started before initial catheterisation	189 (94.0)	0
Baseline creatine clearance, mL/min	93.3±35.2	87.3±31.1
Peak CK (creatine kinase), U/L	2009±1879	2047±1628

Data are presented as mean±SD or n (%)

Definitions of end points

Reinfarction:

Presence of recurrent ischaemic symptoms at rest, lasting at least 30 minutes and accompanied by any of the following:

New or recurrent ST-segment elevation of ≥1mm (0.1mV) in any contiguous leads

New left bundle branch block

Reelevation in serum creatine kinase level more than twice the upper limit of normal and at least more than 50% of the lowest level measured post-infarction.

Recurrent severe ischaemia:

Recurrent symptoms of ischaemia at rest associated with any of the following:

new ST-segment deviation (elevation at least 0.1mV or depression >0.05mV measured 80 ms after the J-point in at least 2 contiguous leads)

an episode of acute pulmonary edema, sustained ventricular arrhythmia, or haemodynamic instability

the need for urgent revascularisation within 30 days

recurrent myocardial infarction.

Effect Size / Outcomes

	Heparin + eptifibatide (n = 201)	**Heparin (n = 199)**	**p value**	**Relative Risk (95% CI)**
30 days				
Death	7 (3.5)	4 (2.0)	0.54	1.76 (0.51–6.11)
Reinfarction	3 (1.5)	1 (0.5)	0.62	3.00 (0.31–29.09)
Congestive heart failure	15 (7.5)	22 (11.1)	0.22	0.65 (0.33–1.29)
Stroke	0 (0.0)	1 (0.5)	0.50	
6 months				
Death	9 (4.6)	6 (3.1)	0.44	1.52 (0.53–4.34)
Reinfarction	4 (2.0)	2 (1.0)	0.69	2.01 (0.36–11.11)

Congestive heart failure	15 (7.7)	24 (12.3)	0.12	0.59 (0.30–1.16)
Stroke	0 (0.0)	4 (2.0)	0.06	
Repeat target vessel revascularisation †	8 (4.0)	6 (3.0)	0.60	-
CABG	10 (5.0)	6 (3.0)	0.32	1.68 (0.60–4.73)
Repeat PCI of infarct-related artery	5 (2.5)	2 (1.0)	0.45	2.51 (0.48–13.11)
Repeat target vessel revascularisation †	8 (4.0)	4 (2.0)	0.38	1.76 (0.51–6.11)
Major bleeding	19 (9.5)	11 (5.5)	0.14	1.78 (0.83–3.85)
Major bleeding, non-CABG related	11 (5.5)	5 (2.5)	0.20	2.25 (0.77–6.59)
Minor bleeding	26 (12.9)	18 (9.1)	0.21	1.49 (0.79–2.82)
Minor bleeding, non-CABG related	25 (12.4)	18 (12.4)	0.27	1.43 (0.75–2.71)

Table 21: van't Hof et al. 2004[116]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Outcome measures	Source of funding
AWJ. van't Hof, N Ernst, M Jan de Boer, R de Winter, E Boersma, T Bunt, S Petronio, A. T. Marcel Gosselink, W Jap, F Hollak, JCA. Hoorntje, H Suryapranata, JH Dambrink, F Zijlstra, and On-TIME study group. Facilitation of primary coronary angioplasty by early start of a glycoprotein 2b/3a inhibitor: results of the ongoing tirofiban in myocardial infarction evaluation	**Design:** RCT (multicentre - Netherlands) **Enrolment:** June 2001-November 2002 **Setting** Recruitment and randomisation in the ambulance or referring hospital; transported to tertiary hospital for angiography and PCI (PCI centres were experienced cardiology centres). **Randomisation:** Blocks per institution. Randomised by selecting sealed study drug kits in sequential order **Allocation concealment:** Not mentioned / unclear. **Blinding:** Double blind (mentioned, but details	n = 507 Drop-outs: 0 days: 3% (n = 15); 1 year: 4% (n = 18). n = 15 patients withdrew consent most often on the 2nd day of admission.	**Inclusion criteria** Presence of chest pain (>30 minutes) together with >0.2 mV (anterior MI) or 0.1 mV (non-anterior MI) of ST-elevation in 2 contiguous ECG leads Ability to perform primary angioplasty within 6 hours after the onset of symptoms **Exclusion criteria** >80 years of age Women <50 years of age Treatment with fibrinolytic therapy in previous 24 hours On warfarin or acenocoumarol within last 7 days Contraindication to GPIs Severe heart failure or cardiogenic shock (Killip class III or IV) On haemodialysis Demographics and baseline characteristics see below	fPPCI (early tirofiban treatment – pre-hospital) (n = 251) IV bolus Tirofiban (10 microgram/kg) followed by maintenance infusion (0.15 mg/kg/min) Note: Before transportation all patients received IV bolus 5000 IU unfractionated heparin + 250 mg aspirin IV. Emergency transportation performed after arrival of pt at the cath lab. After angiography, and before angioplasty, all patients received a second bolus of study drug IV (tirofiban in patients initially given placebo, and placebo in patients initially given tirofiban). After this second bolus of drug, all patients were given open-label tirofiban (maintenance infusion 0.15 microgram/kg/min)	Placebo (later tirofiban treatment - in cath lab) (n = 256) IV bolus and infusion of placebo; tirofiban given later (see 'note' below) until 24 hours post-PCI	1° increase in incidence of TIMI grade 3 flow at initial angiography prior to PCI TIMI flow components Presence of thrombus fresh occlusion at initial angiography pre-PCI myocardial blush grade Other: Death Re-MI Stroke Major bleeding (non-CABG related	Educational grant from Merck and Co.

(On-TIME) trial. Eur.Heart J. 25 (10):837-846, 2004.	not given of patient blinding). Outcome assessors blinded to treatment allocation for all angiographic parameters **Sample size calculation:** Yes: powered study. A sample size of 438 patients (80% power to show a significant difference in the incidence of the primary end point: increase in incidence of TIMI grade 3 flow at initial angiography prior to PCI). Trial recruited approx. 500 patients to allow for drop-outs and false-positive infarct diagnoses in the ambulance. ITT analysis: Yes		for 24 hours. Post-PCI all ts were treated with clopidogrel (300 mg loading dose followed by 75 mg daily for 1 month), aspirin, BB, statin therapy and ACEi. NOTE: Before catheterisation – all patients had heparin (5000U) and aspirin (500 mg) Post-PCI – antithrombin therapy of ticlopidine (25o mg bds, 4 weeks) and aspirin (100 mg bds, throughout study) Stent type used – different types of slotted-tube stents (evenly distributed between the study groups) PCI – 100% Stents used – 100%	major bleeding) Minor bleeding Composite (death/re-MI/stroke/major or non-CABG related major bleeding) (see below for definitions) **Length of follow-up:** 30 days, 1 year	

	Early tirofiban (n = 251)	Later tirofiban (n = 256)
Age, years; mean (SD)	63 (10)	61 (11)
Male gender, %	79	80
Hypertension. %	10	11
Diabetes, %	27	30

Smoking (current or previous), %	62	68
Anterior MI, %	44	47
Previous MI, %	6	10
Previous CABG, %	2	2
Previosu PCI, %	5	6
Multivessel disease, %	58	53
Killip class >1, %*	17	15
TIMI, n(%) out of 243 and 244 total patients for each group respectively		
2 or 3	104 (43)	82 (34)
0	107 (44)	143 (59)
1	32 (13)	19 (8)
2	58 (24)	46 (19)
3	46 (19)	36 (15)
Treatment, %		
Angioplasty	88	90
CABG	3.6	2.3
Other	8.4	8.2

*defined as SBP <100 mmHg or HR >100/min

Definitions of end points

Successful angioplasty: < 50% diameter stenosis and TIMI 3 flow of the IRV.

Presentation delay: Time from symptom-onset to infarct diagnosis (first ECG).

Major bleeding: Fall in Hb of ≥2.0 mmol/L and the need for transfusion of 2 or more units of blood, corrective surgery or both. OR bleeding that resulted in documented intra-cranial or retro-peritoneal haemorrhage

Minor bleeding: Fall in Hb ≥2.0 mmol/L without the need for a transfusion.

Recurrent MI: A new increase in creatine kinase (CK)-MB fraction of >3 times the upper limit of normal, whether accompanied by chest pain or ECG changes and present in 2 separated blood samples or not.

	Early tirofiban	**Later tirofiban**	**p value**
Presentation delay*	88 (58–137)	104 (55–155)	0.25
In-outdoor time†	26 (19–33)	25 (19–33)	0.49
Transportation delay	30 (17–47)	33 (18–46)	0.70

Door to angio time	25 (15–40)	24 (15–36)	0.29
Angio to balloon time	16 (12–21)	15 (12–20)	0.37
Ichaemic time**	196 (155–252)	199 (159–266)	0.48
Pre-treatment time††	79 (65–92)	15 (12–20)	-

Time delays, minutes; median (25–75% IQR)

*Defined as time from symptom onset to infarct diagnosis (1st ECG)

†Defined as time from infarct diagnosis to start of transportation

**Defined as time from symptom onset to 1st balloon inflation

††Defined as time between 1st active bolus of study drug and 1st balloon inflation

Effect Size / Outcomes

After initial angiography, 89% patients underwent PCI and 3% were candidates for bypass surgery due to severe 3-vessel disease. Remainder of patients (8%) treated conservatively.

30 days:

Major bleeding in 44/492 (9%) patients, from which 25 events (57%) were blood transfusions related to the CABG procedure.

No differences in bleeding were observed between the groups.

No intracranial bleeding event occurred during treatments with tirofiban.

1 year:

Mortality no longer a difference between the groups

Combined incidence of death or re-MI was the same (7%) in both groups.

	Early tirofiban (n = 251)	**Later tirofiban (n = 256)**	**p value**
PCI success, % patients	90	91	-
Stents, % patients	72	74	0.71
At 30 days, n (%)	n = 245	n = 247	
Death	9 (3.7)	2 (0.8)	0.03
Re-MI	3 (1.2)	2 (0.8)	0.65
Stroke	0	1 (0.4)	1.00
Major bleeding*	11 (4.5)	8 (3.2)	0.47
Composite**	21 (8.6)	11 (4.4)	0.06
1 year, n (%)	n = 245	n = 244	

Death	11 (4.5)	9 (3.7)	0.66
re-MI	6 (2.4)	9 (3.7)	0.43
Death or re-MI	17 (7.0)	17 (7.0)	0.99
Post-PCI	n = 217	n = 228	
TIMI 3, n(%)	196 (90)	208 (91)	0.74

*Non-CABG related major bleeding

**combined incidence of death/re-MI/stroke or major non-CABG-related major bleeding

Cardiac procedures

			In-hospital	
	TNK only n = 100)	**Invasive strategy (n = 104)**		
Cardiac catheterisation	Not reported	102 (within 24 h)	Not reported	Not reported
Revascularisation	60	89*	65	90*
Rescue PCI	14, at a median of 197 minute after randomisation (IQR 172–280 min).	38 (29 protocol-mandated; 6 ECG criteria)	Not reported	Not reported

* Of these 9 patients received CABG

48% of the 91 patients undergoing PCI within 24 hours of randomisation in the invasive strategy arm received abciximab; 81% of these patients had TIMI 3 and 12% had TIMI 2 flow at the end of the procedure

Coronary stents were used in over 97% of all patients undergoing PCI

Transfer: There were no significant differences (in the primary end point) across the treatment groups in either setting (pre-hospital or in-hospital)

SUBGROUPS – TIMI3 flow (NS difference between the treatment groups)

AGE < 62: 22% (early) versus 11% (later) - NS

AGE ≤ 62: 16% (early) versus 12% (later) - NS

MALE: 20% (early) versus 15% (later) - NS

FEMALE: 16% (early) versus 12% (LATER) - NS

DIABETES (YES): 24% (early) versus 8% (later) - NS

DIABETES (NO): 18% (early) versus 16% (later) - NS

Table 22: van't Hof et al. 2008[111,115,117]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Outcome measures	Source of funding
A W. J. van't Hof, J ten Berg, T Heestermans, T Dill, R C. F, W van Werkum, J H Dambrink, H S, G van Houwelingen, J Paul O, P Stella, E Giannitsis, C Hamm, and Ongoing Tirofiban In Myocardial infarction Evaluation (On-TIME). Prehospital initiation of tirofiban in patients with ST-elevation myocardial infarction undergoing primary angioplasty (On-TIME 2): a multicentre, double-blind, randomised controlled trial. Lancet 372 (9638):537-546, 2008. A. W. van't Hof, C. Hamm, S. Rasoul, S. Guptha, J. F. Paolini, and J. M. Ten Berg. Ongoing tirofiban in myocardial infarction evaluation (On-TIME) 2 trial: rationale and study design. EuroIntervention 3 (3):371-380, 2007.	**Design:** RCT (multicentre – 24 centres in Netherlands, Germany and Belgium) **Enrolment:** June 2006-November 2007 **Setting:** Recruitment and randomisation in the ambulance or referring hospital; transported to tertiary hospital for angiography and PCI (PCI centres were experienced cardiology centres). **Randomisation:** Random permuted blocks at each site; stratified by intended place of recruitment **Allocation concealment:** Unclear – assignment	n = 984 Drop-outs (acceptable): Clinical follow-up at 30 days: fPPCI – 4% and PPCI 3%; 1 year: 4.8% overall.	**Inclusion criteria** Age 21–85 years Symptoms of AMI (>30 minutes but <24 hours) and ST-elevation >1 mV in 2 adjacent ECG leads **Exclusion criteria** known severe renal dysfunction therapy resistant cardiogeniuc shock persistent severe HT contraindication to anticoagulation or increased risk of bleeding left bundle branch block pregnant or breastfeeding women life expectancy <1 year Demographics and baseline characteristics see below	fPPCI (early tirofiban treatment – pre-hospital) (n = 491) NOTE: given pre-hospital (ambulance or referring centre) Tirofiban – bolus 25 mg/kg; bail-out tirofiban could be given where needed Heparin – 5000U bolus given IV NOTE: Before catheterisation – aspirin IV (500 mg) clopidogrel orally (600 mg loading dose) UFH IV (5000 U) Post-PCI – tirofiban infusion 0.15 microgram/kg/minute for 18 hours post-PCI Stent type used –DES	PPCI (Placebo) (n = 493) IV bolus and infusion of placebo; tirofiban given post-PCI for 18 hours (see 'note' below) Heparin – 5000U bolus given IV	1°: extent of ST-segment deviation at 1 hour after PCI. Other: composite Death; Recurrent MI; Major and minor bleeding; stroke **Length of follow-up** In-hospital, 30 days, 1 year	Educational grant from Merck and Co.

(methods) and J. M. Ten Berg, A. W. J. Van 't Hof, T. Dill, T. Heestermans, J. W. Van Werkum, A. Mosterd, Houwelingen G. Van, P. C. Koopmans, P. R. Stella, E. Boersma, and C. Hamm. Effect of Early, Pre-Hospital Initiation of High Bolus Dose Tirofiban in Patients With ST-Segment Elevation Myocardial Infarction on Short- and Long-Term Clinical Outcome. J.Am.Coll.Cardiol. 55 (22):2446-2455, 2010. (3 year results)	given by each investigator Blinding: Double blind Sample size calculation: Yes: powered study. A sample size of 814 patients (80% power for primary outcome) ITT analysis: Yes	(approx. 25%) and BMS (approx 75%) PCI – 99% in both groups Stents used – 90% in both groups	

%	fPPCI (early tirofiban – pre-hospital) (n = 491)	Placebo PPCI (n = 493)	p value
Age, years; mean	62	62	-
Male gender	77	75	-
Diabetes	12	11	-
Hypertension	34	35	-
Current smoking	45	49	-
Hypercholesterolemia	29	25	-
Previous MI	9	8	-

Previous CABG or PCI	12	9	-
Killip Class >1	11	13	-
TIMI flow (%)			0.069
0	42	50	
I	14	11	
II	22	20	
III	22	20	
Critical time intervals, minutes; median (IQR)			
antithrombotic pre-treatment and study drug, to angiography		55 (43–70)	-

Effect Size

Angioplasty

Overall 99% (people had PCI and 90% in had stents (in both arms)

Outcomes

	In-hospital (after procedure)			**At 30 days**			**1 year**		
N (%)	**fPPCI (early tirofiban – pre-hospital) (n = 491)**	**Placebo PPCI (n = 493)**	**p value**	**fPPCI (early tirofiban – pre-hospital) (n = 491)**	**Placebo PPCI (n = 493)**	**p value**	**N (%)**	**fPPCI (early tirofiban – pre-hospital) (n = 491)**	**p value Placebo PPCI (n = 493)**
ST-segment			0.03				ST-segment		
recovery, %	286/436	264/440		-	-	-	recovery, %	286/436	264/440
Complete	(65.6)	(60.0)		-	-	-	Complete	(65.6)	(60.0)
Intermediate	10/436 (22.9)	104/440		-	-	-	Intermediate	10/436 (22.9)	104/440
None	50/436 (11.5)	(23.6)					None	50/436 (11.5)	(23.6)
		72/440 (16.4)							72/440 (16.4)
Normalised ST segment	160/451 (35.5)	132/455 (29.0)	-	-	-	-	Normalised ST segment	160/451 (35.5)	132/455 (29.0)
Stroke	-	-	-	1/473 (0.2)	7/477 (1.5)	0.07	Stroke	-	-
Death	-	-	-	11/473 (2.3)	19/477 (4)	0.14	Death	-	-
Cardiac death	-	-	-	-	-	-	Cardiac death	-	-
Non-cardiac death	-	-	-	-	-	-	Non-cardiac death	-	-

Recurrent MI	-	-	-	13/473 (2.7)	14/477 (2.9)	0.86	Recurrent MI	-	-
Major bleeding	-	-	-	19/473 (4.0)	14/477 (2.9)	0.36	Major bleeding	-	-
Minor bleeding	-	-	-	29/473 (6.1)	21/477 (4.4)	0.23	Minor bleeding	-	-
TIMI flow grade 0–2 or slow reflow	29/488 (5.9)	45/492 (9.1)	0.58	-	-	-	TIMI flow grade 0–2 or slow reflow	29/488 (5.9)	45/492 (9.1)
Urgent TVR	-	-	-	20/477 (4.2)	18/473 (3.8)	0.7614	Urgent TVR	-	-
	In-hospital (after procedure)	p value	At 30 days	p value	1 year	p value		In-hospital (after procedure)	p value

Cardiac procedures

%	**fPPCI (early tirofiban – pre-hospital) (n = 491)**	**%**	**p value**
Coronary angiogram	99%		-
PCI	99%		-

Transfer and timing, and hospital stay

No details given

Table 23: Kanakakis et al. 2009[62]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Outcome measures	Source of funding
J Kanakakis, J N. Nanas, E P. Tsagalou, G D. Maroulidis, S G. Drakos, A S. Ntalianis, P Tzoumele, E Skoumbourdis, P Charbis, S Rokas, and M Anastasiou-Nana. Multicenter randomized trial of facilitated percutaneous coronary intervention with low-dose tenecteplase in patients with acute myocardial infarction: the Athens PCI trial. Catheter Cardio vasc.Interv. 74 (3):398-405, 2009.	Design: RCT (Greece, 1 area, multiple hospitals) Enrolment: April 2005 – October 2006 Setting Patients were directly admitted or transferred to tertiary care hospital with PPCI facilities Randomisation: Not mentioned (just 'randomised') Allocation concealment: Not mentioned Blinding: [illegible] assessors only were blinded to treatment assignment	n = 284 Drop-outs/missing patients/ineligible: In-hospital: n = 0 (some deaths but this was the clinical outcome measure)	INCLUSION CRITERIA: Age ≥18 years <6hrs between symptom onset and randomisation ≥0.1 mV STE in ≥2 limb leads or ≥0.2 mV in 2 contiguous precordial leads or presence of left bundle branch block EXCLUSION CRITERIA expected arrival to cathlab <30 mins after randomisation SBP >180 mmHg or DBP >110 mmHg, or both, on multiple measurements use of GPIs within preceding 7 days major surgery, biopsy of parenchymal organ or severe trauma within 2 months head injury or trauma occurring after the onset of ongoing MI history of stroke, TIA, dementia or structural damage to the CNS ongoing treatment with oral anticoagulants, LMWH administered <12h before randomisation or platelet count <100.000 ul-1	fPCI (Tenecteplase) (n = 143) Tenecteplase – 10 mg (quarter of the standard dose) NOTE: Before catheterisation – all patients had UFH (single bolus, 70 U/kg, IV) and aspirin (150-300 mg p.o). Heparin could be added in the cath lab to reach and activated clotting time of 250-300 sec. Immediately before PCI – all patients undergoing PCI received infusion of GPI (eptifibatide) in the cath lab. 180 ug/kg initial bolus followed by 2ug/kg/min dose-adjusted infusion for 21hrs Patients with stents received 300mg clopidogrel Post-PCI – Patients with stents received clopidogrel 75mg/day	PPCI (n = 141)	Primary: TIMI flow grade 2 or 3 Secondary: composite of death, congestive HF and cardiogenic shock during hospitalisation Non-cerebral bleeding complications death congestive HF cardiogenic shock Length of follow-up: In-hospital	Not stated

	Sample size calculation: Slightly underpowered study: 80% power using approximately 150 patients in each arm to demonstrate a 15% absolute increase in TIMI flow grade 2 or 3 (primary end point). ITT analysis: Not mentioned – it appears so (no drop-outs but there were deaths!) – numbers given were always out of the total randomised	>10 mins of cardiopulmonary resuscitation in previous 2 weeks pregnancy, lactation or parturition in previous 30 days anticipated difficulties with vascular access participation in another drug or device investigation in previous 30 days any other disorder that would expose the pt at inordinate risk inability or unwillingness to follow the protocol Demographics and baseline characteristics see below	

	Facilitated PCI (tenecteplase) (n = 143)	PPCI (n = 141)	p value
Age, yrs; mean (SD)	61 (12)	59 (12)	0.16
Age >75 yrs, n	13	11	0.34
Male gender, %	92	89	0.23
Killip Class, %			
I	75	76	0.63
II/III	17	16	
IV	8	8	
History of hypertension, %	54	50	0.58
History of diabetes, %	21	31	0.12

Anterior	46	44	0.25
Inferior	50	47	
Other	4	9	
SBP, mmHg; mean (SD)	125 (24)	127 (26)	0.83
Pre-PCI TIMI flow, n (%)			
0/I	54 (38)	81 (58)	0.0001
II/III	85 (59)	52 (37)	
Not measurable	4 (3)	8 (6)	
Previous PCI, %	16.7	23.2	0.35
Previous CABG, %	5	3	0.49
Previous MI, %	13	13	0.94
Onset of symptoms to hospital arrival	100 (60-169)	120 (30-240)	-
Onset of symptoms to tenecteplase	135 (90-228)	-	-
Onset of symptoms to 1st coronary angiogram (target lesion)	224 (172-306)	259 (172-368)	-
Door to 1st coronary angiogram (target lesion)	108 (75-150)	99 (68-54)	-
Onset of symptoms to 1st balloon	232(185-315)	275 (190-380)	-
Door to 1st balloon	122 (91-175)	120 (89-175)	-
Tenecteplase to 1st balloon	121 (90-168)	-	-
Before catheterisation			
tenecteplase	100	0	-
bolus heparin	100	100	1.00
During catheterisation			
GPI	91.2	93.5	0.55
Clopidogrel	88.2	90.4	0.85
After catheterisation			
clopidogrel or ticlopidine	88.2	90.4	0.85

Angioplasty

Higher use of PCI in the fPCI group – 94% versus 88%

Outcomes

	Inhospital		**p value**
n (%)	**Facilitated PCI, tenecteplase (n = 143)**	**PCI (n = 141)**	
Death	8 (6)	5 (3.5)	0.57
Congestive HF	24 (17)	5 (3.5)	1.00
Cardiogenic shock	12 (8)	11 (8)	0.91
Intracranial haemorrhage	0	0	1.00
Haemorrhagic stroke	0	0	1.00
Primary (non-fatal) ischaemic stroke	1 (0.7)	0	0.93
Unclassified stroke	0	0	1.00
All strokes	1 (0.7)	0	0.92
Major bleeding complications	8 (6)	5 (3.5)	0.55
Death + HF + shock	39 (27)	34 (24)	0.59
Patency / post-PCI TIMI flow			
0/I	13 (10)	13 (11)	NS
II/III	122 (90)	52 (37)	
Not measurable	1 (3)	8 (6)	

Transfer: No details

Table 24: LIPSIA-STEMI trial[112]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Outcome measures	Source of funding
H. Thiele, I. Eitel, C. Meinberg, S. Desch, A. Leuschner, D. Pfeiffer, A. Hartmann, U. Lotze, W. Strauss, and G. Schuler. Randomized comparison of pre-hospitalinitiated facilitated percutaneous coronary intervention versus primary percutaneous coronary intervention in acute myocardial infarction very early	Design: RCT (12 centres in 1 region of Germany) Enrolment: August 2006 – August 2009 Setting Ambulance to interventional centre for PCI Randomisation: Poor/unclear: sealed envelopes Allocation concealment: Good: contacted the study co-ordinating centre Blinding: No mention of blinded patients or	n = 162 Drop-outs/ missing data/ ineligible: Excluded due to no infarction: n = 1 (fPCI) and n = 3 (PPCI) None lost to follow-up at 30 days OVERALL acceptable losses (<20%): primary end point analysis fPCI – n = 12 (14.8%) missing and PPCI n = 10 (12%) missing. Secondary	**Inclusion criteria:** Peoplewith presence of ischaemic symptoms <3hours ST-segment elevation ≥0.1 mV in 2 or more extremity leads or ≥0.2 mV in 2 or more precordial leads **Exclusion criteria:** Contraindications to fibrinolysis (eg. previous stroke, active bleeding, history of major trauma or surgery <30 days, active peptic ulcer, neoplasms, uncontrolled HT >200 mmHg, chronic oral anticoagulation, cardiogenic shock and pregnancy) typical contraindications for MRI such as pacemakers, defibrillators and intracerebral metallic clips Demographics and baseline characteristics see below	fPCI (tenecteplase +clopidogrel background) (n = 81) NOTE: given pre-hospital Tenecteplase – weight-adjusted IV dose (as per ASSENT trial) During PCI: Heparin - dose calculated to achieve activated clotting time of 200-250 seconds GPIs – recommended at standard dose for 12h	PPCI (clopidogrel background) (n = 81) During PCI: Heparin - dose calculated to achieve activated clotting time of 200-250 seconds GPIs – recommended at standard dose for 12h	Primary: infarct size. Secondary: composite of death, reinfarctiona nd new congestive HF <30days after randomisation; post-hospital outcomes at 30 days follow-up: reinfarction; death; new HF; severe of life-threatening, moderate or minor bleeding; occurrence of ischaemic stroke Length of follow-up: Inhospital; 30 days	Supported in part by German Heart Research foundation and Boehringher Ingelheim GmbH, Germany..

after symptom onset: The LIPSIA-STEMI trial (Leipzig Immediate Prehospital Facilitated Angioplasty in ST-segment myocardial infarction). JACC: Cardiovascu l ar Intervention s 4 (6):605-614, 2011.	physicians TIMI flow and clinical end points had blinded observers/adjudicati on committee Sample size calculation: Powered study: 80% power using at least 64 patients for infarct size outcome. ITT analysis: Yes	end point analysis fPCI – n = 1 (1%) and PPCI – n = 3 (4%) missing.			

%	fPCI (tenecteplase +clopidogrel background) (n = 80)	PPCI (clopidogrel background) (n = 78)	p value
Age, yrs; median (IQR)	63 (54-73)	61 (53-72)	0.57
Male gender	76	82	0.48
Diabetes mellitus	36	24	0.15
Hypertension	66	64	0.91
Current smoking	41	48	0.43
Hypercholesterolemia	40	26	0.12
Previous MI	3	5	0.65

Previous CABG	0	1	0.99
Killip Class			0.36
1	71	74	
2	14	18	
3	6	5	
4	9	3	
TIMI flow (%)			<0.001
II	26.6	10.3	
III	44.3	24.4	
Concomitant medications			
BB	96	99	0.63
ACEi	98	97	0.63
Aspirin	99	100	0.99
Clopidogrel	100	100	1.00
Statins	98	97	0.63
Aldosterone antagonists	6	4	0.74
GPIs	29	88	<0.001
Critical time intervals, mins; median (IQR)			
Symptom onset to first balloon inflation	Symptom onset to first balloon inflation	Symptom onset to first balloon inflation	Symptom onset to first balloon inflation
Door to balloon	Door to balloon	Door to balloon	Door to balloon

Effect size

Angioplasty

Overall 93% and 98% (fPCI and PPCi respectively) people had PCI and 100% in each arm had stents

Outcomes

	Inhospital (after procedure)			**At 30 days**		**p value**
N (%)	**fPCI (tenecteplase +clopidogrel**	**PPCI (clopidogrel background)**	**p value**	**fPCI (tenecteplase +clopidogrel**	**N (%)**	**fPCI (tenecteplase +clopidogrel background)**

	background) (n = 80)	(n = 78)		background) (n = 80)		(n = 80)
ST-segment recovery,			0.18		ST-segment recovery,	
%	42.9	57.7		-	%	42.9
Complete	40.2	29.5		-	Complete	40.2
Intermediate	16.9	12.8		-	Intermediate	16.9
None					None	
Ischaemic stroke	-	-	-	1	Ischaemic stroke	-
Death	-	-	-	5 (6.1)	Death	-
Nonfatal reinfarction	-	-	-	5 (6.1)	Nonfatal reinfarction	-
New congestive HF	-	-	-	6 (7.4)	New congestive HF	-
Bleeding:	-	-	-		Bleeding:	-
severe/life threatening				2.5%	severe/life threatening	
moderate				2.5%	moderate	
mild				4.9%	mild	
TIMI flow grade III (in IRA), %	83.2	88.5	0.44	-	TIMI flow grade III (in IRA), %	83.2

Cardiac procedures

%	**fPCI (tenecteplase +clopidogrel background) (n = 80)**	**PPCI (clopidogrel background) (n = 78)**	**p value** **%**
Coronary angiogram	100%	-	Coronary angiogram
PCI	93%	98%	PCI

Transfer and timing, and hospital stay: No details given

Table 25: Mehilli et al. 2009[81,99]

Reference	Study type	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Mehilli J. et al. 2009 Abciximab in patients with acute ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention after clopidogrel loading. and S. Schulz, K. A. Birkmeier, G. Ndrepepa, W. Moshage, F. Dotzer, K. Huber, J. Dirschinger, M. Seyfarth, A. Schomig, A. Kastrati, and J.	Design: RCT (double blind) Enrolment: June 2003 – January 2008 Setting Hospital (5 PCI centres). Randomisation: Yes. Computer-generated random sequence Allocation concealment: Yes, sealed envelopes. Blinding: Yes. Patients, medical staff and investigators were blinded. Sample size calculation: The assumptions	**Number of patients:** n = 800 Drop-outs: None **Inclusion criteria** <24 hours of the onset symptoms Chest pain ≥ 20 min ≥ 0.1mV ST-elevation in 2 or more limb leads, ≥ 0.2mV in 2 or more contiguous precordial leads **Exclusion criteria** Received fibrinolytic therapy for the index infarction Previous stroke (within last 3 months) Active bleeding or bleeding diatheses Recent trauma or major surgery (during the last month) Suspected aortic dissection Oral anticoagulation therapy with coumarin derivatives (within the last 7 days) Recent use of glycoprotein IIb/IIIa (within the last 14 days) Severe uncontrolled hypertension (>180mm Hg, unresponsive to therapy) Relevant hematologic deviations (haemoglobin <100g/L or hematocrit <34%, platelet count < 100x109/L or > 600 x109/L) Malignancies	Abciximab (n = 401) PPCI Abciximab dose: 0.25 mg/kg, bolus, followed by infusion of 0.125microgram/kg/minute (max dose: 10 microgram/min) for 12 hours Note: Before catheterisation: All patient received clopidgrel 600mg orally; aspirin bolus 500mg; heparin 60U/kg (max dose: 5000U) intravenous. After reperfusion all patients were treated with clopidogrel 75mg twice daily for 3 days and 75 mg/d thereafter for 30	Placebo (n = 399) PPCI Dose: Intravenous bolus of 70U heparin/kg followed by infusion of placebo for 12 hours.	30 days; 1 year	1° Infarct size Other: Death, recurrent MI, stroke, urgent revascularisation, in-hospital incidence of major and minor bleeding complications	BRAVE-3 was supported by grants from Deutsches Herzzentrum, Munich, Germany.

Mehilli. One-year clinical outcomes with abciximab in acute myocardial infarction: Results of the BRAVE-3 randomized trial. Clin.res.cardiol. 99 (12):795-802, 2010. (1 year results)	used for this purpose included an infarct size of 16.9% (SD, 13.9%) of the left ventricle in the placebo group and a 20% reduction with abciximab. Choosing a 2-sided α level of 0.05 and power of 90%, we needed 353 patients with scintigraphic follow-up study in each group. We allowed for the possibility that not all patients would have a follow-up SPECT and included a total of 800 patients. ITT analysis: Yes	Prolonged cardiopulmonary resuscitation or cardiogenic shock >80 or <18 years of age Known or suspected pregnancy Allergy to study drugs Demographics and baseline characteristics see below	days and with aspirin 100mg twice daily indefinitely. All patients were sent to the cath lab for coronary angiography and PCI. The decision to perform a coronary intervention was at the discretion of the operator. The recommended intervention was coronary stenting.		

	Abciximab (n = 401)	Placebo (n = 399)	p value
Age, years	62.4±11.7	61.58±12.2	0.50
Women, n(%)	98 (24)	109 (27)	0.35

Arterial Hypertension, n(%)	280 (70)	282 (71)	0.79
Hypercholesterolemia, n(%)	167 (42)	177 (44)	0.44
Diabetes mellitus, n(%)	76 (19)	65 (16)	0.32
Current smoking, n(%)	168 (42)	162 (41)	0.71
BMI, Kg/m^2	27.1±3.8	27.0±4.1	0.74
History of MI, n(%)	38 (10)	43 (11)	0.54
History of CABG surgery, n(%)	15 (4)	8 (2)	0.14
Infarct localisation, n(%)			0.81
Anterior	168 (42)	174 (44)	
Inferior	174 (43)	172 (43)	
Lateral	59 (15)	53 (13)	
Killip class, n(%)			0.89
I	304 (76)	307 (77)	
II	75 (19)	74 (19)	
III	15 (4)	11 (3)	
IV	7 (2)	7 (2)	
Arterial blood pressure, mm Hg			
Systolic	138±23	139±22	0.39
Diastolic	79±13	80±14	0.62
Heart rate, bpm	73±17	73±16	0.50
Peak CK (creatine kinase)-MB, U/L, U/L	258.9±251.5	265.5±240.5	0.72

Data are presented as mean±SD when appropriate

Definitions of end points

Recurrent infarction

Diagnosis of recurrent infarction was based on the following criteria:

If the biomarkers of the index MI were still increasing or the peak had not been reached, the patients had to have both new ECG changes consistent with MI (new or re-elevation of ST segments≥0.2 mV in ≥2 contiguous precordial leads, ≥0.1 mV in ≥2 adjacent limb ECG leads, or development of new, abnormal Q waves considered distinct from the evolution of the index MI) and recurrent ischaemic discomfort lasting >20 minutes at rest or ischaemia-triggered haemodynamic instability;

If the biomarkers of the index MI were falling but still above the upper limit of normal, the patients had to have either an increase in creatine kinase-MB (creatine kinase) ≥50% over the nadir level or new ECG changes consistent with MI;

If the biomarkers of the index MI were normalised, the patients had to have a new increase in creatine kinase-MB (creatine kinase) ≥3 times the upper limit of normal.

Stroke

The diagnosis of stroke required confirmation by computed tomography or magnetic resonance imaging of the head.

Bleeding

A bleeding complication was defined as major if it was intracranial or if clinically significant overt signs of haemorrhage were associated with a drop in haemoglobin of >5 g/dL (or, when haemoglobin was not available, an absolute drop in hematocrit of at least 15%).

Effect Size

	30 day results			**1 year results**		
n(%)	**Abciximab (n = 401)**	**Placebo (n = 399)**	**n(%)**	**Abciximab (n = 401)**	**Placebo (n = 399)**	**n(%)**
Death	13 (3.2)	10 (2.5)	0.53	27 (6.8)	16 (4)	0.09
Recurrent MI	6 (1.5)	6 (1.5)	0.99	12 (3.1)	11 (2.8)	0.83
IRA revascularisation	3 (0.8)	4 (1)	0.70	62 (16.3)	86 (22.3)	0.04
Stroke	1 (0.3)	1 (0.3)	1.0	3 (0.8)	1 (0.3)	0.32
TIMI major bleeding	7 (1.8)	7 (1.8)	0.99	-	-	-
TIMI minor bleeding	15 (3.7)	7 (1.8)	0.09	-	-	-
Repeat revascularisation of Target lesion	-	-	-	53 (13.9)	76 (19.7)	0.04
TIMI (post PCI, not 30 days or 1 year) - overall NS (p = 0.49)						
0	11 (3)	6 (1)	0.49 overall	-	-	-
1	4 (1)	7 (2)				
2	16 (4)	18 (5)				
3	370 (92)	368 (92)				
Repeat revascularisation of Target lesion	-	-	-	53 (13.9)	76 (19.7)	0.04

Table 26: Gabriel et al. 2006[47]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Outcome measures	Source of funding
H. Mesquita Gabriel, Joaquim A. Oliveira, Pedro Canas da Silva, J. Marques da Costa, and J. A. C. da Cunha. Early administration of abciximab bolus in the emergency department improves angiographic outcome after primary PCI as assessed by TIMI frame count: results of the early ReoPro administration in myocardial infarction (ERAMI) trial.	**Design:** RCT (prospective) **Enrolment:** August 2001-September 2002 **Setting** Hospital (Santa Maria Hospital, Lisbon). **Randomisation:** Yes. Randomly assigned in a 1:1 ratio to intervention or comparison group. **Allocation concealment:** Unclear. **Blinding:** 2-way blinding. The study packages were labelled in a way to preserve 2-way blinding.	n = 80 Drop-outs: 6 in total did not receive PCI. 4 from the early group and 2 from the later group	**Inclusion criteria:** Clinical picture suggestive of AMI of <12 hours duration Presence of an ST-segment elevation of >0.2mV in 2 or more adjunctive leads and suitability for angiographic evaluation **Exclusion criteria:** Admitted >12 hours from onset of symptoms Had received fibrinolytic agent for the treatment of the current episode Experienced cardiogenic shock, Had known bleeding diathesis Demographics and baseline characteristics see below	Early group (n = 36) Early described as administration in the emergency room of abciximab bolus in MAI patients undergoing PCI. 0.25 mg/kg abciximab bolus in the emergency room (given placebo in the catherisation lab (CL)) Both groups: Pre-PCI Recommended to received 250 mg aspirin and 5000 U bolus of heparin Other medications such as nitrates, morphine and beta-blockers used at the discretion of the emergency department cardiologist. In the CL dose adjusted heparin was administered to achieve an activated clotting time (ACT) of ≥250 sec Post PCI In patients who received PCI coronary stenting was used liberally and 1 of 2 antithrombotics was associated to aspirin:	Later group (n = 38) Later described as administration in the catheterisation lab (CL) of abciximab bolus in MAI patients undergoing PCI. 0.25 mg/kg abciximab bolus in the CL (given placebo in the emergency room) Both groups: Pre-PCI Recommended to received 250 mg aspirin and 5000 U bolus of heparin Other medications such as nitrates, morphine and beta-blockers used at the discretion of the emergency department cardiologist. In the CL dose adjusted heparin was administered to achieve an activated clotting time (ACT) of ≥250 sec Post PCI	TFG 2 or 3 Death Re-MI Urgent TVR TIMI-defined bleeding **Length of follow-up** 30 days	Not reported

Catheter.Cardiovasc.Interv. 68 (2):218-224, 2006.	**Sample size calculation:** The study was powered to have an 85% power to detect 23% difference in coronary patency at initial angiography with an overall type I error rate of 0.05 (2-sided). Sample size was calculated to be 78 patients. ITT analysis: No. Per protocol analaysis			clopidogrel 300mg, followed by 75 mg orally for ≥24 days or ticlopidine 500 mg, followed by 250 mg orally twice daily for ≥ 26 days	In patients who received PCI coronary stenting was used liberally and 1 of 2 antithrombotics was associated to aspirin: clopidogrel 300mg, followed by 75 mg orally for ≥ 24 days or ticlopidine 500 mg, followed by 250 mg orally twice daily for ≥ 26 days		

Demographics and baseline characteristics		
	Early group (n = 36)	**Later group (n = 38)**
Age, years	60±12	63±16
Male gender	23 (64)	30 (79)
Hypertension	23 (64)	23 (61)
Diabetes	9 (25)	7 (18)
Smoker	19 (53)	16 (42)
Hypercholesterolemia	19 (53)	19 (50)
Prior MI	3 (8)	4 (11)
Anterior MI location	16 (44)	24 (63)
Treatment in emergency department Aspirin (250mg) Heparin (5,000 U)	 35 (97) 27 (75)	 37 (97) 31 (82)
First angiography		

TFG 2 or 3	11 (31)	10 (26)
TFG 3	4 (11)	3 (8)
TFG 2	7 (19)	7 (18)
TFG 1	4 (11)	2 (5)
TFG 0	21 (58)	26 (68)

Data are presented as mean±SD or n (%)

Effect Size / Outcomes

30 days	**Early group (n = 36)**	**Later group (n = 38)**	**p value**	**Details**
Final angiography				
TFG 2 or 3	35 (97)	34 (90)	0.18	
TFG 3	32 (89)	29 (76)	0.08	
Death	4 (11%)	5 (13%)	0.78	Causes of death: heart failure (5); mechanical complications (2) (free wall rupture and ventricular septal defect); stroke (1) sudden death after discharge (1). groups not specified
Re-MI	0	1 (3%)	0.32	
Urgent target vessel revascularisation	1 (3%)	0	0.3	
TIMI-defined bleeding				
Significant	4 (11%)	2 (5%)	0.37	
Major	1 (3%)	0	0.51	
Minor	3 (8%)	2 (5%)	0.53	

Table 27: Bellandi et al. 2006[8]

Reference	Study type	Patient characteristics	Intervention	Comparison	Outcome measures	Source of funding
Bellandi, 2006 F Bellandi, M Maioli, M Leoncini, A Toso, and R P. Dabizzi. Early abciximab administration in acute myocardial infarction treated with primary coronary intervention. Int.J.Cardiol. 108 (1):36-42, 2006.	**Design:** RCT (prospective) **Enrolment:** June 2003 – January 2004 **Setting** Hospital. **Randomisation:** Yes. Computerised randomisation. **Allocation concealment:** Blinded envelopes **Blinding:** No. Open label **Sample size calculation:** Not reported. ITT analysis: Yes	**Number of patients:** n = 55 Drop-outs: None. **Inclusion criteria:** Presenting within 6 hours of symptom onset with ST-segment elevation of more than 1 mm in at least 2 contiguous leads of ECG **Exclusion criteria:** Previous MI Previous PCI Previous coronary artery bypass Left bundle branch block Bleeding diathesis Administration of fibrinolytic agents for the current episode Recent stoke Uncontrolled hypertension Recent surgery Oral anticoagulant therapy Known contraindications to therapy with abciximab, aspirin, clopidogrel or heparin Demographics and baseline characteristics see below	Early group (n = 27) All patients received abciximab (0.25 mg/kg as a bolus followed by a 12 hour infusion of 0.125 mcg/kg/min) in the emergency room After randomisation: all patients received heparin as a bolus of 70U/kg (maximum 7000U) together with 250mg aspirin intravenously in the emergency room If necessary additional boluses of heparin were administered to achieve an activated clotting time of 200s. Before angiography: Intravenous injection of 740 to 1110 MBq of technetium-99 m sestamibi. After PCI: 24 hour infusion of 7U/kg per hour of heparin was	Later group (n = 28) All patients received abciximab (0.25 mg/kg as a bolus followed by a 12 hour infusion of 0.125 mcg/kg/min) in the catheterisation lab after diagnostic angiography After randomisation: all patients received heparin as a bolus of 70U/kg (maximum 7000U) together with 250mg aspirin intravenously in the emergency room If necessary additional boluses of heparin were administered to achieve an activated clotting time of 200s. Before angiography: Intravenous injection of 740 to 1110 MBq of technetium-99 m sestamibi. After PCI: 24 hour infusion of 7U/kg per hour of heparin was performed. The target activated partical-	TIMI flow grade Stents Death Reinfarction Urgent TVR Major bleeding Intra-cranial bleeding **Length of follow-up** 7 days, 1 month	Not reported

			performed. The target activated partical-thromboplastin time was between 1.5 and 2.0 times the control value. Immediately after the procedure all patients received clopidogrel (300mg). patients were routinely treated with aspirin (100 mg/day indefinitely) and clopidogrel (75 mg/day for at least 1 month PCI and stenting performed in all patients.	thromboplastin time was between 1.5 and 2.0 times the control value. Immediately after the procedure all patients received clopidogrel (300mg). patients were routinely treated with aspirin (100 mg/day indefinitely) and clopidogrel (75 mg/day for at least 1 month PCI and stenting performed in all patients.		

Demographics and baseline characteristics		
	Early group (n = 27)	**Later group (n = 28)**
Age, years	62.7±11.5	63.8±11
Male gender	22 (81.5)	22 (78.6)
Diabetes	6 (22.2)	7 (25)
Hypertension	8 (29.6)	9 (32)
Hyperlipidimia	13 (48)	13 (46.4)
Current smoking	14 (51.8)	14 (50)
Kilip class ≥	5 (18.5)	8 (28.6)
Not-low-risk patients	15 (55.6)	15 (53.6)
Infarct artery Left anterior descending Right coronary artery Circumflex artery	 12 (44.4) 12 (44.4) 3 (11.2)	 13 (46.4) 13 (46.4) 2 (7.2)
Multivessel disease		

2 vessels 3 vessels	11 (40.7) 3 (11.2)	13 (46.4) 3 ()10.7
Symptom onset to admission (min)	129±63	122±95
Door to abciximab (min)	32±14	55±34
Door to balloon (min)	80±26	73±37
Start of abciximab to balloon (min)	49±14	19±9
Initial TIMI flow grade 0 1 2 3	 15 (55.6) 1 (3.7) 1 (3.7) 10 (37)	 19 (67.9) 2 (7.1) 4 (14.3) 3 (10.7)
Data are presented as mean±SD or n (%)		

Effect Size / Outcomes

Angiographic results	**Early group (n = 27)**	**Later group (n = 28)**	**p value**	**Details**
Final TIMI flow grade			0.37	
2	1 (3.7%)	4 (14.3%)		
3	26 (96.3%)	24 (85.7%)		
Direct stenting	8 (30%)	2 (7%)	0.07	
Multiple stents	4 (15%)	11 (39%)	0.08	
Number of stent	1.1±0.4	1.5±0.6	0.005	
1 month				
Death	1	1		Both cardiogenic shock
Reinfarction	0	0		
Urgent vessel revasculatisation	0	0		
Major bleeding (a decrease in haemoglobin >2g/dl with the need for transfusion	1	2		
Intra-cranial bleeding during treatment with abciximab	0	0		

Table 28: RELAX-AMI trial [79]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Outcome measures	Source of funding
M. Maioli, F. Bellandi, M. Leoncini, A. Toso, and R. P. Dabizzi. Randomized early versus late abciximab in acute myocardial infarction treated with primary coronary intervention (RELAx-AMI Trial). J Am Coll Cardiol 49 (14):1517-1524, 2007.	**Design:** RCT (prospective) **Enrolment:** June 2003 – March 2006 **Setting** Hospital (Italy). **Randomisation:** Yes. Open label randomisation. **Allocation concealment**: Unclear. **Blinding:** Unclear. Blinded envelopes after open label randomisation. **Sample size calculation:** The sample size to detect a difference between 10% and 20% increase in TIMI flow grade 3.	n = 210 Drop-outs: 9 patients died before 1 month follow-up (3 from early group, 6 from later group.	**Inclusion criteria:** Presenting within 12 hours of symptom onset with ST-segment elevation of more than 1 mm in at least 2 contiguous leads of ECG **Exclusion criteria:** Previous MI Previous PCI Previous coronary artery bypass surgery Left branch bundle block Bleeding diathesis administration of fibrinolytic agents for the current episode Recent stroke Uncontrolled hypertension Recent surgery Oral anticoagulant therapy Known contraindications to therapy with abciximab, aspirin, clopidogrel or heparin Previous AMI likely to have pre-existent asynergies Demographics and baseline characteristics see below	Early group (n = 105) All patients received abciximab (0.25 mg/kg as a bolus followed by a 12 hour infusion of 0.125 mcg/kg/min) in the emergency room After randomisation: all patients received heparin as a bolus of 70U/kg (maximum 7000U) together with 250mg aspirin intravenously in the emergency room If necessary additional boluses of heparin were administered to achieve an activated clotting time of 200s. After PCI: 24 hour infusion of 7U/kg per hour of heparin was performed. The target activated	Later group (n = 105) All patients received abciximab (0.25 mg/kg as a bolus followed by a 12 hour infusion of 0.125 mcg/kg/min) in the catheterisation lab after diagnostic angiography After randomisation: all patients received heparin as a bolus of 70U/kg (maximum 7000U) together with 250mg aspirin intravenously in the emergency room If necessary additional boluses of heparin were administered to achieve an activated clotting time of 200s. After PCI: 24 hour infusion of 7U/kg per hour of heparin was performed. The target activated partical-thromboplastin time	Mortality Recurrent MI Urgent PCI Coronary artery bypass grafting Bleeding complications Minor bleeding Major bleeding Intracranial bleeding TIMI flow rate **Length of follow-up** 1 month	Not reported

	With an α value of 0.05 and 80% power, was determined to be 95 per group. With regard to drop outs at least 105 patients were planned to be included in both groups. ITT analysis: No. Available case analysis		partical-thromboplastin time was between 1.5 and 2.0 times the control value. Patients routinely received aspirin (100 mg/day indefinitely) and clopidogrel (75 mg/day for at least 1 month PCI performed in all patients. Stent insertion in all patients.	was between 1.5 and 2.0 times the control value. Patients routinely received aspirin (100 mg/day indefinitely) and clopidogrel (75 mg/day for at least 1 month PCI performed in all patients. Stent insertion in all patients.		

	Early group (n = 105)	Later group (n = 105)
Age, years	60.4±10	66±12
Age ≥75 years	17 (16)	26 (25)
Female gender	25 (24)	27 (26)
Hypertension	51 (49)	48 (46)
Diabetes mellitus	31 (29)	31 (29)
History of smoking	45 (43)	54 (51)
Hyperlipidimia	43 (41)	41 (39)
Low risk patients	36 (34)	43 (41)
Killip class ≥2	20 (21)	25 (26)
Infarct artery		
Right coronary artery	44 (42)	40 (38)
Circumflex artery	9 (9)	12 (11)
Left anterior descending	52 (49)	52 (49)
Main vessel	0	1 (1)

Multivessel disease 2-vessel 3-vessel	 32 (30) 22 (21)	 40 (38) 25 (24)
Symptom onset to admission (min) (range)	85 (59–160)	105 (63–170)
Door to abciximab (min) (range)	23 (15–37)	60 (40–88)
Door to balloon (min) (range)	84 (67–107)	73 (59–104)
Start of abciximab to balloon (min) (range)	55 (46–72)	14 (11–18)
Initial TIMI flow grade 0–1 2 3	 63 (60) 17 (16) 25 (24)	 88 (84) 6 (6) 11 (10)
Data are presented as mean±SD or n (%)		

Effect Size / Outcomes

	Early group (n = 105)	Later group (n = 105)	p value	Details
1 Month				
Death	3	6		Early group: cardiogenic shock (1); sudden death (1); fatal repeat AMI (1) Later group: cardiogenic shock (4); free wall rupture (1); fatal repeat AMI (1)
Recurrent MI	2	4		
Repeated Urgent PCI	2	1	0.62	
Coronary artery bypass grafting	1	1		
Bleeding complications	9	6		
Minor bleeding	8	5		
Major bleeding	1	1		
Intracranial bleeding	0	0		
Final TIMI flow grade			NS	
0–1	4 (4)	5 (5)		
2	4 (4)	3 (3)		

3	97 (92)	97 (92)		

Table 29: Dudek et al. 2010[35]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Outcome measures	Source of funding
D Dudek, T Rakowski, S Bartus, D Giszterowicz, W Dobrowolski, K Zmudka et al. Impact of early abciximab administration on myocardial reperfusion in patients with ST-segment elevation myocardial infarction pretreated with 600 mg of clopidogrel before percutaneous coronary intervention. Journal of Thrombosis and Thrombolysi	**Design:** RCT (prospective) **Enrolment:** Not reported **Setting** PPCI centre (Poland). **Randomisation:** Yes. No details. **Allocation concealment:** Not mentioned / unclear. **Blinding:** No. The study was not double blinded. Sample size calculation: Not reported. The limitations of study stated the study was	n = 73 Drop-outs: None. Note: there was a third study group of 22 patients who received abciximab at the operator's discretion.	**Inclusion criteria:** > 18 years old Acute STEMI (chest pain > 30 minutes, ST-segment elevation >0.2mV in at least 2 contiguous leads) within 6 hours from chest pain onset **Exclusion criteria:** Previous MI contraindications to abciximab or clopidogrel Previous PCI or CABG Contraindications to PCI Killip class III or IV Left branch bundle block or pacemaker rhythm in the ECG Participation in another clinical study Neoplastic disease Pregnancy Previous treatment with fibrinolytic agents Demographics and baseline characteristics see below	Early group (n = 24) Patients received a bolus of abciximab (0.25 mg/kg) before transfer to the cathlab. Additionally they received an intravenous infusion of abciximab (0.125 microgram/kg/min) after arrival at the cathlab. All patients in community hospital received aspirin (300 mg), clopidogrel loading dose (600mg) and a bolus of heparin (70 U/kg) After the procedure all patients were given aspirin (75 mg/day) and clopidogrel (75 mg/day). the activated clotting time was monitored in all patients before PCI and unfractured heparin boluses were added if	Later group (n = 27) Patients received abciximab (bolus 0.25 mg/kg + infusion 0.125 microgram/kg/min) in the cathlab during PPCI All patients in community hospital received aspirin (300 mg), clopidogrel loading dose (600mg) and a bolus of heparin (70 U/kg) After the procedure all patients were given aspirin (75 mg/day) and clopidogrel (75 mg/day). the activated clotting time was monitored in all patients before PCI and unfractured heparin boluses were added if necessay to maintain an ACT	Mortality Reinfarction Repeated revascularisation Intracranial bleeding Major bleeding Minor bleeding Total bleeding complications TIMI flow **Length of follow-up:** 30 days	Grant from The State Committee for Scientific Research, Poland

s 30 (3):347-353, 2010.	underpowered. ITT analysis: Yes		necessay to maintain an ACT optimal level 200–250 seconds PCI performed in all patients. Stent insertion in 86.4% patients.	optimal level 200–250 seconds PCI performed in all patients. Stent insertion in 96.3% patients.		

	Early group (n = 24)	Later group (n = 27)
Age, years	62±9	61±9
Male sex %	75	81.5
BMI (kg/m^2)	27±3	27±4
Diabetes mellitus %	16.7	11.1
Arterial hypertension %	45.8	59.3
Hyperlipidimia %	41.7	33.3
Smoking %	45.8	40.1
SBP (mmHg)	143±27	138±25
DBP (mmHg)	86±16	85±14
Heart rate (beats per min)	79±21	76±18
Killip class I %	87.5	92.6
Killip class II %	12.5	7.4
Time from chest pain onset to clopidogrel administration (min)	165±88	189±99
Time from clopidogrel administration to first device/balloon inflation (min)	93±27	106±31
Time from chest pain onset to first device/balloon inflation (min)	252±95	285±98
Time from chest pain onset to abciximab administration (min)	173±104	262±97

Time from abciximab administration to first device/balloon inflation (min)	87±31	21±31
Data are presented as mean±SD or %		
Effect Size / Outcomes		
	Early group (n = 24)	**Later group (n = 27)**
30 days		
Death	1 (cardiac)	0
Reinfarction	0	0
Repeated revascularisation	0	0
Intracranial bleeding	0	0
Major bleeding	1	1
Minor bleeding	1	1
Total bleeding complications	12.5%	14.8%
TIMI flow 3 2 0 and 1	 91.7% 0% 8.3%	 88.9% 11.1% 0%
Hospital stay Not reported		

Table 30: ASSENT-4 [114]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Outcome measures	Source of funding
ASSENT 2006 / Van De Werf, 2006 ASSENT 4 ASSENT-4 PCI Investigators. Primary versus tenecteplase-facilitated percutaneous coronary intervention in patients with ST-segment elevation acute myocardial infarction (ASSENT-4 PCI): randomised trial. Lancet 367 (9510):569-578, 2006.	**Design:** RCT (prospective) **Enrolment:** November 10th 2003 – April 22nd 2005 **Setting** Hospital (3 tertiary care hospitals). **Randomisation:** Yes. Randomly via a central computerised telephone system. **Allocation concealment:** Unclear. **Blinding:** Unclear. **Sample size calculation:** The sample size to detect a 3.5% absolute difference for the	n = 1667 Drop-outs: 6 in the fPPCI group and 7 in the standard PPCI group.	**Inclusion criteria:** Over 18 years old <6 hours before randomisation Intention to undertake PPCI Total ST-segment elevations of 0.6 mV or more across multiple leads or for inferior infarction ST-segment deviations of 0.6mV or more provided ST-segment elevations of 0.4mV or more were present in leads II, III and aVF or new left branch bundle block with concordant ST-segment elevation of 0.1mV or more **Exclusion criteria:** Expected arrival at catherisation lab less than 1 hour or more than 3 hours after randomisation Anticipated problems with vascular access Previous enrolment to the study The usual contraindications to fibrinolytic therapy as described in ASSENT-3 Demographics and baseline	fPPCI (n = 829) PPCI preceded by the administration of a standard bodyweight adjusted bolus of tenecteplase as used in ASSENT-2 and ASSENT-3 All patients received 150–325 mg aspirin and a single intravenous bolus of unfractionated heparin (70 U/kg without a maximum does in the PPCI group and 60 U/kg with a maximum of 4000 U in the fPPCI group). Additional intravenous bolus could be administered to obtain an activated clotting time of 350–400 seconds in the PPCI group (or 250–300 seconds if glycoprotein IIb/IIIa inhibitor was used) or 300–350 seconds in the fPPCI group during	Standard PPCI (n = 838) Routine PPCI All patients received 150–325 mg aspirin and a single intravenous bolus of unfractionated heparin (70 U/kg without a maximum does in the PPCI group and 60 U/kg with a maximum of 4000 U in the fPPCI group). Additional intravenous bolus could be administered to obtain an activated clotting time of 350–400 seconds in the PPCI group (or 250–300 seconds if glycoprotein IIb/IIIa inhibitor was used) or 300–350 seconds in the fPPCI group during the intervention. Glycoprotein was not allowed in the facilitated group except for bailouts but was allowed at the discretion of the investigator in the PPCI group.	TIMI flow **Length of follow-up:** After PCI / in-hospital 90 days	Boehringer Ingelheim, Ingelheim, Germany and Genentech South San Francisco

	primary outcome, with a level of significance of 5% and 85% power using a χ2 test was determined to be 2000 per group. ITT analysis: No. Available case analysis	characteristics see below	the intervention. Glycoprotein was not allowed in the facilitated group except for bailouts but was allowed at the discretion of the investigator in the PPCI group. Instigators were encouraged to do coronary intervention on the culprit lesion but it was left to their decision. If stents were use a loading dose of 300mg clopidogrel was given followed by a maintenance dose of 75 mg PCI performed in 719 patients. Stent insertion in 667 patients.	Instigators were encouraged to do coronary intervention on the culprit lesion but it was left to their decision. If stents were use a loading dose of 300mg clopidogrel was given followed by a maintenance dose of 75 mg PCI performed in 762 patients. Stent insertion in 714 patients.		

	fPPCI (n = 829)	Standard PPCI (n = 838)
Age, years	61 ± 12.2	60 ± 12
Age >75 years	98/829 (12)	106/837 (13)
Women	193/829 (23)	189/838 (23)
Weight (kg)	77.9 ± 14.7	77.7 ± 14.9
Height (cm)	170.3 ± 8.2	169.8 ± 8.4

Killip class		
I	753/829 (91)	773/834 (93)
II/III	66/829 (8)	53/834 (6)
IV	10/829 (1)	8/834 (1)
Congestive heart failure at randomisation	42/806 (5)	41/814 (5)
Heart rate (bpm)	74.3 ± 16.9	76.1 ± 17.1
Systolic blood pressure	133.7 ± 24.2	133.7 ± 22.2
Infarct location		
Anterior	403/828 (49)	389/837 (46)
Inferior	418/828 (50)	429/837 (51)
Other	7/828 (1)	19/837 (2)
Previous infarction	108/822 (13)	90/834 (11)
Previous congestive heart failure	7/824 (1)	13/834 (2)
Previous PCI	70/819 (9)	68/829 (8)
Previous coronary artery bypass graft	18/825 (2)	16/833 (2)
Hypertension	391/829 (47)	391/837 (47)
Diabetes	144/828 (17)	131/836 (16)
TIMI		
0	196/812 (24)	512/821 (62)
1	83/812 (10)	70/821 (9)
2	172/812 (21)	107/821 (13)
3	353/812 (43)	124/821 (15)
Not assessable	8/812 (1)	8/821 (1)
Symptom onset to randomisation (min) (median, Q1, Q3)	140 (90, 210)	135 (91, 210)
Symptom onset to unfractionated heparin bolus (min) (median, Q1, Q3)	150 (101, 220)	145 (100, 215)
Symptom onset to tenecteplase (min) (median, Q1, Q3)	153 (105, 225)	--
Symptom onset to first balloon (min) (median, Q1, Q3)	263 (213, 339)	255 (200, 335)
Randomisation to first balloon (min) (median, Q1, Q3)	115 (94, 150)	107 (85, 140)
Tenecteplase to first balloon (min) (median, Q1, Q3)	104 (82, 135)	--

Effect Size / Outcomes			
After PCI / in hospital	**fPPCI (n = 829 before and n = 719 after PCI)**	**Standard PPCI (n = 838 before and n = 763 after PCI)**	**Details**
TIMI			
0	15/719 (2%)	13/763 (2%)	
1	15/719 (2%)	4/763 (1%)	
2	55/719 (8%)	68/763 (9%)	
3	631/719 (88%)	677/763 (89%)	
Not assessable	3/719 (<1%)	1/763 (<1%)	
Stroke			
Intracranial haemorrhage	8 (1%)	0	
Primary ischaemic stroke	5 (0.6%)	0	
Unclassified stroke	2 (0.2%)	0	
Total	15 (1.8%)	0	
In-hospital bleeding complications			
Major	46 (5.6%)	37 (4.4%)	
Minor	210 (25.3%)	159 (19%)	
Blood transufsions	48 (6.2%)	33 (4.2%)	
90 days			
Death	55/823 (7%)	41/831 (5%)	**fPPCI:** Reinfarction (4); cardiogenic shock (22); arrhythmia or sudden death (1); asystole or cardiac arrest (6); cardiac rupture or electromechanical dissociation (8); stroke of intracranial haemorrhage (8); other cardiac event (1); other non-cardiac event (5) **Standard PPCI:** Reinfarction (4); cardiogenic shock (17); arrhythmia or sudden death (3); asystole or cardiac arrest (5); cardiac rupture or electromechanical dissociation (5); other cardiac event (3); other non-cardiac event (3)
Congestive heart failure	97/807 (12%)	75/818 (9%)	
Shock	51/807 (6%)	39/817 (5%)	
Reinfarction	49/805 (6%)	30/820 (4%)	

Repeat target vessel revascularisation	53/805 (7%)	28/818 (3%)	
Rehospitalisation for congestive heart failure	15/807 (2%)	11/818 (1%)	
Rehospitalisation for shock	0/807 (0%)	1/817 (<1%)	
Rehospitalisation for other cardiac reasons	83/806 (10%)	90/819 (11%)	
Stroke			
Intracranial haemorrhage	1 /829 (0.1%)	1 /838 (0.1%)	
Primary ischaemic stroke	4 /829 (0.5%)	0/838	
Unclassified stroke	2 /829 (0.2%)	0/838	
Total	7/829	1/838	

Table 31: INTAMI-pilot trial [121]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Outcome measures	Source of funding
Zeymer, 2005 INTAMI pilot trial U Zeymer, R Zahn, Rudolf S, W Jansen, E Girth, A Gitt, K Seidl, R Schroder, S Schneider, and J Senges. Early eptifibatide improves TIMI 3 patency before primary percutaneous coronary intervention for acute ST elevation myocardial infarction: results of the randomized integrilin in	**Design:** RCT (prospective) **Enrolment:** October 2002-April 2004 **Setting** Hospital (3 Germany hospitals). **Randomisation:** Yes. Randomly stratified by centre in blocks of 10. **Allocation concealment:** Yes: randomisation done in blinded envelopes. **Blinding:** No. The trial was an open comparison. **Sample size**	n = 102 Drop-outs: 1 from the early group (1 DCM and 1 myocarditis). 2 from the later group (both myocarditis)	**Inclusion criteria:** >18 years old presented with an acute STEMI defined with angina or equivalent symptoms >30 minutes ST elevation >2 leads (>2 mm preccordial lead, < 1 mm limb lead) or ST depression > 1 mm precordial lead in posterior MI new or presumed new LBBB PCI planned **Exclusion criteria:** Fibrinolytic therapy with 24 hours before randomisation oral anticoagulation with an INR >2 platelets < 100000 or known haemorrhagic diathesis stroke or TIA within 30 days evidence of an active gastrointestinal or urogenital bleeding major surgery within 6 weeks history or allergic reaction to eptifibatide severe renal or hepatic insufficiency contraindications to coronary	Early group (n = 53) Early eptifibatide, heparin and aspirin All patients received aspirin 50 mg i.v. and heparin 5.000 U i.v. immediately followed but infusion 1.000 U/h – target aPTT 50–70 s. As early as possible patients received a double bolus of 180 microgram/kg (10 minute interval) followed by infusion of 2.0 microgram/kg/minute > 12–24 hours. Catheter evaluation and PCI with possible stent implantation were done according to the local guidelines but within 3 hours after administration. The continuation of unfractionated heparin post angiography or	Later group (n = 49) Heparin, aspirin and optional eptifibatide All patients received aspirin 50 mg i.v. and heparin 5.000 U i.v. immediately followed but infusion 1.000 U/h – target aPTT 50–70 s. Catheter evaluation and PCI with possible stent implantation were done according to the local guidelines but within 3 hours after administration. The continuation of unfractionated heparin post angiography or procedure was discouraged but left to the discretion of the investigator. Clopidogrel was started after PCI with stent, with a loading dose of 300 mg and	TIMI flow Death Reinfarction Repeat target vessel revascularisation PCI different vessel Coronary artery bypass Emergency CABG Stroke Severe bleeding complication Thrombocytopenia < 100.000 **Length of follow-up:** 60 minutes after PCI	Grant from ESSEX Pharma GbH, Munich, Germany

acute myocardial infarction (INTAMI) pilot trial. Eur.Heart J. 26 (19):1971-1977, 2005.	**calculation:** Not reported **ITT analysis:** No. Available case analysis	angiography severe concomitant disease with life expectancy <1 year Demographics and baseline characteristics see below	procedure was discouraged but left to the discretion of the investigator. Clopidogrel was started after PCI with stent, with a loading dose of 300 mg and maintained with a dose of 75 mg daily for at least 30 days. PCI performed in 46 (87%) patients. Stent insertion in 73% patients.	maintained with a dose of 75 mg daily for at least 30 days. PCI performed in 46 (94%) patients. Eptifibatide was given in 42 (86%) of patients immediately before PCI or during PCI (immediately before procedure in 30 patients and during procedure in 12 patients) Stent insertion in 74% patients.	30 days	

	Early (n = 53)	Later (n = 49)
Age, years	61±13	61±11
Male sex (%)	79	66
BMI	29±7	28±6
Pulse (b.p.m.)	80±21	74±17
Systolic blood pressure (mmHg)	133±22	136±26
Diastolic blood pressure (mmHg)	77±13	79±17
Anterior infarct location (%)	43	39
Troponin T positive on admission (%)	21	28
Killip class >1 (%)	16	14
Smoker (%)	51	41
Hyperlipidemia (%)	55	67
Diabetes mellitus (%)	15	22
Prior MI (%)	12	16

Prior PCI (%)	4	18	
Prior CABG (%)	0	2	
Prior angina (%)	19	25	
TIMI			
0/1 (%)	58.4	67.4	
2 (%)	7.6	22.4	
3 (%)	34	10.2	
60 minutes after procedure	**Early (n = 53)**	**Later (n = 49)**	**p value**
TIMI			
0/1 (%)	7.7	2.1	
2 (%)	5.8	14.9	
3 (%)	86.5	83	
Death (n, %)	2 (3.8)	2 (4.1)	0.9
Reinfarction (n, %)	3 (5.7)	0	0.09
Repeat target vessel revascularisation (n, %)	2 (3.8)	1 (2)	0.6
PCI different vessel (n, %)	4 (7.6)	4 (8)	0.9
Coronary artery bypass (n, %)	3 (5.7)	5 (10.2)	0.4
Emergency CABG (n, %)	1/3 (1.9)	2/5 (4)	
Stroke (n, %)	0	0	
Severe bleeding complication (n, %)	2 (3.8)	2 (4.1)	0.9
Thrombocytopenia < 100.000 (n, %)	1 (2)	1 (2)	0.3

Table 32: Lee et al. 2003[70]

Reference	Study type	Patient characteristics	Intervention	Comparison	Outcome measures	Source of funding
Lee. et al. 2003 Adjunctive platelet glycoprotein IIb/IIIa receptor inhibition with tirofiban before primary angioplasty improves angiographic outcomes. Results of the TIrofiban Given in the Emergency Room before Primary Angioplasty (TIGER-PA) pilot trial Circulation. 2003; 107:1497-	**Design:** RCT (prospective) **Enrolment:** July 1999 - December 2001 **Setting** Hospital **Randomisation:** Yes. Computerised randomisation **Allocation concealment:** Yes. Blinded envelopes. **Blinding:** No. open-label. **Sample size calculation:** study underpowered to show a significant difference in clinical end points. **ITT analysis:**	**Number of patients:** n = 100 Drop-outs: None **Inclusion criteria:** Clinical symptoms of AMI (acute myocardial infarction) with the initial onset of chest pain in the past 12 hours Deemed to be suitable candidates for percutaneous revascularisation An ECG that demonstrated ≥0.1mV ST-segment elevation in 2 or more contiguous leads or documented new left bundle-branch block. **Exclusion criteria:** Cardiogenic shock Use of an intra-aortic balloon pump (IABP) Known bleeding diathesis Demographics and baseline characteristics see below	Early tirofiban, in the ER, before primary angioplasty (n = 50) Notes: (3 patients underwent PPCI alone, 47received at least 1 stent after initial angioplasty) Tirofiban dose: bolus 10 microgram/kg over 3 minutes, followed by 0.15 microgram/kg/minute per 24 hours. Other medications: heparin bolus 70U/kg followed by 5 U/kg/h. If coronary stent was placed--> clopidrogel (300mg orally, following by 75 mg per day for at least 28 days) or Ticlopidine (500 mg orally followed by 250mg twice per day for at least 28 days)	Later tirofiban, in the cath lab, after diagnostic angioplasty, just before primary angioplasty (n = 50) Notes: (3 patients underwent PPCI alone, 47received at least 1 stent after initial angioplasty) Tirofiban dose: bolus 10 microgram/kg over 3 minutes, followed by 0.15 microgram/kg/minute per 24 hours. Other medications: heparin bolus 100U/kg with a maintenance dose of 10 U/kg/h. If coronary stent was placed--> clopidrogel (300mg orally, following by 75 mg per day for at least 28 days) or Ticlopidine (500 mg orally followed by 250mg twice per day for at least 28	1° Initial TIMI grade flow, corrected TIMI frame counts, TIMI grade myocardial perfusion. Other: 30-days major cardiac adverse events. **Length of follow-up** 30 days	Grant from Merck& Co.

1501.	Not mentioned / unclear.			days).		

Demographics and baseline characteristics

	Early tirofiban (n = 50)	Late tirofiban (n = 50)
Age, years	63.5±12.6	66.4±14.3
Male gender, %	60	64
Diabetes, %	24	24
Hypertension, %	36	40
Hyperlipidimia, %	32	32
Previous CAD (coronary artery disease), %	12	10
Duration of CP (chest pain), h	3.0±2.0	3.0±1.8
Door to tirofiban, min	55.7±18.0	81.8±18.0
Door to balloon, min	88.9±20.7	82.7±20.0

Data are presented as mean±SD or %

Definitions of end points

Bleeding: TIMI definition.

Effect Size / Outcomes

30 days	Early tirofiban (n = 50)	Later tirofiban (n = 50)	p value
TIMI-defined bleeding, %			
Minor	10	6	NS
Major	2	2	NS
30-day outcomes, %			
Death	2	2	NS
Re-MI (myocardial infarction)	0	2	NS
Re-hospitalisation	4	6	NS
Urgent TVR (target vessel revascularisation), %	0	2	NS

NS=not significant

Table 33: Emre 2006[43]

Reference	Study type	Patient characteristics	Intervention	Comparison	Outcome measures	Source of funding
Emre et al. 2006 Impact of early tirofiban administration on myocardial salvage in patients with acute myocardial infarction undergoing infarct-related artery stenting. Cardiology 2006; 106:264-269	**Design:** RCT **Enrolment:** Not stated **Setting** Hospital. Consecutive patients **Randomisation:** Yes, but details not given **Allocation concealment:** Not mentioned / unclear. **Blinding:** Not mentioned / unclear. **Sample size calculation:** the study was powered to detect a 20% difference in the myocardial salvage index (α 0.05 and β 0.80), with a minimum of 64 patients (32/arm). Study is underpowered to show a significant difference. ITT analysis: Not mentioned / unclear.	**Number of patients:** n = 66 Drop-outs: None **Inclusion criteria:** Chest pain > 30 minutes Presentation < 6 hours after the onset of symptoms ST-segment elevation of ≥1mm in ≥2 contiguous leads. **Exclusion criteria:** Previous administration of fibrinolytic agents Previous MI Previous percutaneous coronary intervention artery bypass graft surgery Known bleeding diathesis or allergy to study drugs Major surgery within 15 days Active bleeding Cardiogenic shock Demographics and baseline characteristics see below	Early tirofiban (emergency room) Stenting (n = 32) Tirofiban bolus (10 microgram/kg) followed by 0.15 microgram/kg for 24 hours) Note: All patients received bolus 5000 U unfractionated heparin during the procedure. And a loading dose of clopidogrel 300mg and aspirin 325mg. Procedural success achieved in all patients (and all patients given stents).	later tirofiban (cath lab) Stenting (n = 34) Tirofiban bolus (10 microgram/kg) followed by 0.15 microgram/kg for 24 hours)	1° Degree of MI salvage. Other: 30 day major adverse cardiac events. **Length of follow-up:** 30 days	Not stated

Demographics and baseline characteristics			
	Early tirofiban (n = 32)	**Later tirofiban (n = 34)**	**p value**
Age, years	58±10	59±12	ns
Male gender, %	81	82	ns
Anterior MI, %	13 (41)	15 (44)	ns
LVEF (Left ventricular ejection fraction)	48±11	49±11	ns
Symptom onset to presentation, min	118±52	122±48	ns
Smoking %	14 (44)	16 (47)	ns
Diabetes, %	7 (22)	8 (24)	ns
Hypercholesterolemia, %	15 (47)	15 (44)	ns
Systemic hypertension, %	15 (50)	17 (50)	ns
Door to tirofiban, min	18±4	52±10	0.004
Door to balloon, min	43±12	53±9	ns
Peak creatine kinase level, U/l, %	2,268±1,452	2,480±1,590	ns
Time to peak creating kinase level, h	8.6±5.6	8.8±4.4	ns
Initial TIMI, flow grade, %			
0	17 (53)	22 (64)	ns
1	2 (6)	3 (9)	ns
2	3 (10)	5 (15)	ns
3	10 (31)	4 (12)	0.04
30 day outcomes	**Early tirofiban (n = 32)**	**Later tirofiban (n = 34)**	**p value**
Death	0	0	ns
Recurrent MI	0	1 (3)	ns
Rehospitalisation	2 (6)	4 (12)	ns
TIMI-defined bleeding			
Minor	3 (10)	2 (6)	ns
Major	0	0	ns
Thrombocytopenia	1 (3)	0	ns

Table 34: Shen et al. 2008[100]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Outcome measures	Source of funding
Shen et al. 2008 Clinical benefits of adjunctive tirofiban therapy in patients with acute ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention. Coronary Artery Disease 2008, 19; 271-277	Design: RCT , prospective Enrolment: January 2005 – June 2006. Consecutive patients Setting Hospital. Randomisation: Yes, computer-generated random allocation system Allocation concealment: Not mentioned / unclear. Blinding: Not mentioned / unclear. Sample size calculation: Not mentioned / unclear.	n = 172 Drop-outs: none	INCLUSION CRITERIA Chest pain >30min Presented within 12 hours of symptoms New ST-segment elevation in at least 2 contiguous leads on electrocardiogram with the cut off points ≥0.2mV, with or without elevation of cardiac enzymes. EXCLUSION CRITERIA Cardiogenic shock Known bleeding diathesis Demographics and baseline characteristics see below	early tirofiban (emergency room, upstream group) PPCI (n = 57) Tirofiban bolus (10 microgram/kg) followed by 0.15 microgram/kg/minute for 36 hours) Note: All patients received before procedure: aspirin 300 mg; clopidogrel 450 mg; unfractionated heparin 100 U/kg through the femoral arterial access sheaths. All patients received after procedure: Clopidogrel (75 mg/day) for at least 9–12 months; aspirin (100 mg/day) infinitively; subcutaneous low molecular weight heparin for 7 days after the procedure. Procedural success achieved in all patients, and 99% stents - 1 person in control	later tirofiban (in cath lab, downstream group) PPCI (n = 57) Tirofiban bolus (10 microgram/kg) followed by 0.15 microgram/kg/minute for 36 hours) Control group: PPCI alone (n = 58)	1° Occurrence rate of major adverse cardiac events. **Length of follow-up** 30 days and 6 months	Grant from the Shanghai Science and Technology Committee.

	ITT analysis: Not mentioned / unclear.			group did not have stent (intra-aortic balloon counterpulsaion because of haemodynamic instability).			

Demographics and baseline characteristics

	Control (n = 58)	Early tirofiban upstream (n = 57)	Later tirofiban Downstream (n = 57)	p
Age, years	65.4±14.6	68.0±14.3	65.3±11.6	0.48
Male gender, %	86.2	75.4	82.5	0.32
Hypertension, %	65.5	73.3	68.4	0.63
Diabetes mellitus, %	27.2	31.6	21.1	0.44
Hypercholesterolemia, %	31.0	36.8	22.8	0.26
Current smoker, %	55.2	42.1	47.4	0.37
Previous PCI, %	5.2	5.3	7	0.89
Symptom-to-catheterisation time, h	6.5±2.7	6.7±3.6	5.6±2.9	0.17
Door-to-balloon time, min	75.3±25.9	79.9±26.7	68.9±24.3	0.08
Acute anterior MI, %	51.7	50.9	61.4	0.46
Acute inferior MI, %	43.1	40.4	33.3	0.54
Acute anterior+inferior MI, %	5.2	8.8	7.0	0.75
Sum of ST-segment elevation before procedure, mm	13.55±5.50	11.76±5.81	12.67±5.05	0.22
CK-MB before procedure, ng/ml	49.6±44.0	41.2±44.8	53.1±38.8	0.32
Tnl before procedure, ng/ml	10.8±9.2	9.8±8.5	10.8±16.9	0.89
Angiographic features				
No of implant stent	1.1±0.5	1.3±0.7	1.2±0.6	0.20
Effect Size				
Outcomes				
	Control (n = 58)	**Early tirofiban upstream (n = 57)**	**Later tirofiban Downstream (n = 57)**	**p**

Death, %	5.2	3.5	5.3	0.88
nonfatal MI, %	6.9	0	0	0.02
TVR, %	3.4	0	0	0.14
LVEF	0.47±0.08	0.51±0.07	0.50±0.07	0.0008
Death, %	5.2	3.5	5.3	0.88
nonfatal MI, %	6.9	1.8	1.8	0.22
TVR, %	5.2	1.8	1.8	0.45
LVEF	0.54±0.07	0.59±0.06	0.57±0.07	<0.001
Minor bleeding	1.7	3.5	1.8	-
Major bleeding	3.4	5.3	8.8	-
Hospital stay, mean days (SD)	14.5 (6.5)	10.6 (5.4)	12.6 (4.7)	-

LVEF: left ventricular ejection fraction. TVR: target vessel revascularisation

Table 35: El Khoury et al. 2010[38]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
El Khoury. et al. 2010 Prehospital high-dose tirofiban in patients undergoing primary percutaneous intervention. The AGIR-2 study. Archives of cardiovascular disease (2010) 103, 285-292	Design: RCT (multicentre, prospective) Enrolment: July 2007-July 2008. Out-of hospital patients managed by mobile intensive care units (MICU) staffed by a physicians. Setting MICU and Hospital Randomisation: Yes. Computer-generated random sequence. Allocation concealment: Yes. Scratch cards.	(n = 320) Drop-outs: 1	INCLUSION CRITERIA Presented within 12 hours after onset of symptoms of MI, ie: Characteristic pain lasting for at least 30 min Not responsive to nitrates Electrocardiographic ST-segment elevation ≥0.2mV in 2 or more contiguous precordial leads or 0.1mV for limb leads. EXCLUSION CRITERIA Haemorrhagic diathesis Pregnant Any allergy or contraindication to heparin, aspirin or tirofiban Suffered from severe renal or hepatic insufficiency Had major surgery within the past month Had any sign of cerebral ischaemic disease for <1 month or non-ischaemic disease whatever its date Received oral anticoagulant treatment, a fibrinolytic or a GP IIb/IIIa antagonist within the past 7 days Uncontrolled hypertension, severe conduction disorder or cardiogenic shock	Early tirofiban, in the ambulance (pre-hospital) PPCI (n = 164) Notes: Complete ST-segment resolution 60 minutes after the start of intervention: 52.6%. Stent placed in 112 (69.1%) of patients. Tirofiban dose: Bolus 25 microgram/kg in 3 min, followed by infusion of 0.15 microgram/kg per minute for	Later tirofiban, in the cath lab. PPCI (n = 156) Notes: Complete ST-segment resolution 60 minutes after the start of intervention: 55.4%. Stent placed in 113 (72.4%) of patients. Tirofiban dose: Bolus 25 microgram/kg in 3 min, followed by infusion of	In-hospital	In-hospital mortality Major bleeding In-stent thrombosis Stroke	Sponsor: Hospice Civil de Lyon, France. Merck Sharp Dhome and Iroko pharmaceuticals provided the tirofiban free of charge to the sponsor.

Blinding: No. open-label. Sample size calculation: the initial sample size calculation was 300 patients with a 5%alpha risk and a 80% power to detect a 16% difference in the primary end point. The higher than expected rate of patency in the later tirofiban group lowered the power of the study to detect a difference. ITT analysis: Yes	If duration to transfer to the hospital (entrance to the cath lab) exceeded 1 hour. Demographics and baseline characteristics see below	18–24 hours. Other medications: clopidogrel 600mg, 60 IU/kg IV heparin bolus (max 5000 IU), 250–500 mg aspirin	0.15 microgram/kg per minute for 18–24 hours. Other medications: clopidogrel 600mg			

	later tirofiban (cath lab) (n = 156)	early tirofiban (pre-hospital) (n = 164)	p
Male gender	124 (79.5)	123 (75.0)	0.34
Diabetes	17 (10.9)	18 (11.0)	0.98
Hypertension	62 (39.7)	74 (45.1)	0.33
Current smoker	56 (35.9)	61 (37.2)	0.81
Dyslipidaemia	67 (43.0)	55 (33.5)	0.08
Anterior MI	68 (43.6)	84 (51.2)	0.17

Previous MI	24 (15.4)	15 (9.1)	0.09
Previous coronary artery bypass graft	6 (3.8)	2 (1.2)	0.13
Previous percutaneous coronary intervention	23 (14.7)	13 (7.9)	0.05
Killip class ≥2	13 (8.3)	19 (11.6)	0.33
Heart rate (beats/min)	75.4 ± 16.2	77.2 ± 22.2	0.42
Systolic arterial pressure (mmHg)	139 ± 28	141 ± 25	0.80
Cumulative ST-deviation on diagnostic electrocardiogram (mm)	12 ± 9	13 ± 8	0.25
Treatment delay, median [25–75%] (min)			
Onset of chest pain to MICU	98 [50–200]	104 [56–233]	0.30
MICU to cath lab	54 [45–69]	61 [54–74]	0.0002
Cath lab to first angiography	26 [15–35]	21 [15–35]	0.007
MICU to first angiography	83 [70–96]	85 [72–100]	0.46
Data presented as mean±SD or number (%) of patients otherwise stated. MICU: mobile intensive care unit arrival on site of intervention; Cath lab: admission to the catheterisation laboratory. Definitions of end points TIMI flow grade 2–3 of the infarct-related vessel at initial angiography. ST-segment resolution 1 hour after percutaneous coronary intervention and peak serum troponin I concentration			
Effect Size / Outcomes			
	later tirofiban (cath lab) (n = 156)	**early tirofiban (pre-hospital) (n = 164)**	**p**
In-hospital mortality	5 (3.2)	9 (5.5)	0.26
Major bleeding	2 (1.3)	6 (3.7)	0.28
Stroke	1 (0.6)	2 (1.2)	Not reported
In-stent thrombosis	3 (1.9)	1 (0.6)	0.36
Data presented as number (%) of patients			

Table 36: Ohlmann et al. 2012 [88]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
P Ohlmann, P Reydel, L Jacquemin, F Adnet, O Wolf, J Claude Bartier, A Weiss,et al. Prehospital Abciximab in ST-Segment Elevation Myocardial Infarction. Circulation: Cardiovascular Interventions, 2012.	Design: RCT (11 centres in France serviced by 7 emergency ambulance services Enrolment: Jan 2005 – June 2009 Setting Ambulance to hospital Randomisation: Poor/unclear: stratified by centres, done according to manufacturer of treatment kits which had to be used consecutively Allocation concealment: Not mentioned Blinding:	n = 256 Drop-outs/missing patients/ineligible: For clinical outcomes: n = 5 (2%) at 1 month and another n = 5 (4% cumulative)at 6 months OVERALL acceptable losses (<20%)	INCLUSION CRITERIA: patients eligible for PPCI STEMI symptoms <6 hours ST-segment elevation 2 mm in V1 to V3 leads, or 1mm in remaining leads EXCLUSION CRITERIA Contraindications to anticoagulation increased risk of bleeding oral anticoagulation known hpersensitivity to study drugs pregnancy or breastfeeding presence of IV conduction abnormality (complete left or right bundle branch block) Demographics and baseline characteristics see below	EARLY abciximab (in ambulance) (n = 127) Abciximab – 0.25 mg/kg IV bolus additional bolus given if activated clotting time was < 150 seconds or 150–199 seconds NOTE: Before catheterisation – aspirin IV (250 mg) UFH (heparin) IV (40 IU/kg, maximum 3000 U) Post-PCI – 0.125 microgram/kg/minute abciximab infusion for 12 hours clopidogrel (300- or 600-mg loading dose) at discretion of physician	Placebo / later abciximab (in hospital cath lab) (n = 129) Placebo (pre-hospital) Abciximab (In-hospital, post-angiography and pre-PCI)– 0.25 mg/kg IV bolus	In-hospital 30 days / 1 month 6 months	Primary: STR. Secondary: composite MACEs; death; nonfatal MI; coronary revascularisation at 30 days and 6 months	Eli Lilly

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
	Double blind Sample size calculation: Powered study: 83% power using at least 240 patients for complete STR ITT analysis: Yes			Stent type used –BMS or DES at discretion of interventionalist. PCI – 93% (fPPCI) and 98% (PPCI) Stents used – 100% in both groups				

Demographics and baseline characteristics

%	EARLY abciximab (in ambulance) (n = 127)	Placebo / later abciximab (in hospital cath lab) (n = 129)	p value
Age, yrs; meean (SD)	56.0 (11.9)	57.7 (12.7)	0.27
Male gender	79	82	0.63
Diabetes	9	11	0.84
Hypertension	38	37	1.0
Current smoking	51	53	0.90
Hypercholesterolemia	38	39	0.90
Previous MI	5	5	1.0
Previous CABG	0	0	1.0
Previous PCI	4.7	4.7	1.0
Previous stroke	1	0	0.5
Killip Class			0.80
1	92	91	
2	6	7	
3	0	2	
4	2	1	
TIMI flow (%)			

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding

0	49/109 (45)	67/117 (57.3)	0.078
1	9/109 (8.3)	9/117 (7.7)	
2	26/109 (23.9)	20/117 (17.1)	
3	25/109 (53.2)	21/117 (17.9)	
0–1	58/109 (53.2)	76/117 (65)	0.08
2–3	51/109 (46.8)	41/117 (35)	
Critical time intervals, minutes; median (IQR)			
Symptom onset to balloon	190 (142–239)	198 (165–282)	0.87
Door (ambulance arrival) to balloon	105 (91–125)	103 (90–122)	0.91
Arrival to angiography	25 (16–35)	27 (20–35)	0.14
Bolus 1 to balloon	7 (60–86)	74 (64–89)	0.31
Bolus 2 to balloon	7 (4–12)	6 (3–14)	0.92

Effect Size

Angioplasty

Overall 91% and898% (early and later groups respectively) people had PCI and 100% in each arm had stents

Outcomes

	In-hospital (after procedure)		**p value**	**At 30 days**		**p value**	**At 6 months**		**p value**
N (%)	EARLY abciximab (in ambulance) (n = 127)	Placebo / later abciximab (in hospital cath lab) (n = 129)		EARLY abciximab (in ambulance) (n = 127)	Placebo / later abciximab (in hospital cath lab) (n = 129)		EARLY abciximab (in ambulance) (n = 127)	Placebo / later abciximab (in hospital cath lab) (n = 129)	
TIMI flow									
0	1/109 (0.9)	2/116 (1.7)	0.18	-	-	-	-	-	-
1	1/109 (0.9)	3/116 (2.6)		-	-	-	-	-	-

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding

2	7/109 (6.4)	11/116 (9.5)		-	-	-	-	-	-
3	100/109 (91.7)	100/116 (86.2)		-	-	-	-	-	-
0–1			0.45	-	-	-	-	-	-
2–3	2/109 (1.8)	5/116 (4.3)		-	-	-	-	-	-
	107/109 (98.2)	111/116 (95.7)							
Death	2 (2)	1 (1)	-	2 (2)	1 (1)	-	2 (2)	1 (1)	-
MI	2 (2)	2 (2)	-	3 (2)	2 (2)	-	3 (2)	2 (2)	-
TVR	2 (2)	4 (3)	-	2 (2)	4 (3)	-	9 (7)	11 (9)	-

Cardiac procedures

%	**EARLY abciximab (in ambulance) (n = 127)**	**Placebo / later abciximab (in hospital cath lab) (n = 129)**	**p value**
Coronary angiogram	100%	-	
PCI	91%	88%	-
Stents	100%		

Hospital stay

No details given

Table 37: LIU 2012B

Reference	Study type	Patient characteristics	Intervention	Comparison	Outcome measures	Source of funding
Liu J, Fu X-H, Xue L, Wu W-L, Gu X-S, Li S-Q. Equilibrium radionuclide angiography for evaluating the effect of facilitated percutaneous coronary intervention on ventricular synchrony in patients with acute myocardial infarction. Circulation Journal. 2012; 76(4):928-935.	Design RCT (1 hospital centre in China) Enrolment September 2006 to September 2009 **Randomisation** Not described **Allocation concealment** Not described **Blinding** Outcomes of interest not blinded. ERNA and ventricular phase analysis were carried out at 1 week and 6 months by 2 blinded independent observers. **Sample size calculation** Not described ITT analysis All randomised patients were included in ITT comparisons of outcome	**Number of patients:** n = 152 Drop-outs: n = 9 (fPPCI n=4, PCI n=5) **Inclusion criteria** Patients < 70 years with first AMI Onset within 6 hours ST elevation on contiguous ECG Transfer to PCI centre within 90 minutes Suitability for percutaneous revascularisation No prior use of t-PA Informed consent **Exclusion criteria** Cardiogenic shock or severe heart failure Bleeding diathesis or recent stroke within 4 weeks Recent surgery Previous inter-cranial or spinal surgery Neoplasm Severe hypertension Acute aortic dissection Contraindication for reperfusion therapy Serious arrhythmia or bundle branch block Demographics and baseline characteristics see below	fPPCI with 50 mg reteplase before PCI **Pre-PCI:** All patients received aspirin 300mg and clopidogrel 300 mg as they were enrolled. **Post-PCI:** If stents were used then clopidogrel (75 mg/day) and aspirin were given GPIs were given at discretion of attending physician. **PCI/STENTS:** 96% / 97% PCI and 94% / 96% STENTS IN PPCI and fPPCI groups respectively.	PPCI	Congestive heart failure; TVR; mortality, cardiac mortality; IC haemorrhage; bleeding Length of follow-up: 1 week and 6 months	Not stated

Demographics and baseline characteristics (data only reported in the patients analysed, not the complete number randomised)			
	PPCI n = 71	**fPPCI n = 72**	**p value**
Age (years)	55.91 ± 9.26	58.34 ± 11.58	0.262
Male sex	56	60	0.101
Medical history, n (%)			
• Smoking	26(36.62)	23(31.94)	0.822
• Diabetes mellitus	17 (23.94)	20 (27.78)	0.872
• Pre-MI angina	24 (33.08)	22 (30.56)	0.574
• Hypertension	40 (56.34)	44 (61.11)	0.608
• Hyperlipidemia	21 (29.58)	24 (33.33)	0.720
Number of diseased vessels n(%)			
• 1	11 (42.8)	11 (44)	
• 2	6 (26.1)	8 (32)	
• 3	6 (26.1)	6 (24.0)	
OUTCOMES Complications and Outcomes of the 2 PCI Groups; 6 months			
Parameter n (%)	**PPCI n = 71**	**fPPCI n = 72**	**p value**
New or worsening congestive heart failure	9 (12.68)	2 (2.78)	0.028
Recurrent ischaemia	7 (9.86)	2 (2.78)	0.043
Reinfarction	3 (4.23)	1 (1.39)	0.679
Urgent TVR	3 (4.23)	1 (1.39)	0.679
Cardiac death	4 (5.63)	1 (1.39)	0.161
Non-cardiac death	2 (2.82)	0	0.416
Intracranial haemorrhage	0	0	1.000
TIMI-defined bleeding			
• Minor	7 (9.86)	8 (11.11)	0.813
• Major	0	0	1.000
Access bleeding	1 (1.41)	1 (1.39)	1.000
Transfusion	0	1 (1.39)	1.000

Table 38: ZORMAN 2002

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Outcome measures	Source of funding
Simona Zorman, Darko Zorman, and Marko Noc. Effects of abciximab pretreatment in patients with acute myocardial infarction undergoing primary angioplasty. *Am.J.Cardiol.* 90 (5):533-536, 2002.	Design RCT (1 hospital centre in Slovenia) Enrollment: June 1998 to June 2001 **Randomisation:** Not described (just says randomised) **Allocation concealment:** Not described **Blinding:** Not mentioned. **Sample size calculation:** Not mentioned **ITT analysis:** Yes as not mentioned and no drop-outs mentioned	n = 163 Drop-outs: n = not mentioned	**Inclusion criteria** • STEMI • Admitted within 12 hours of symptom onset **Exclusion criteria** Not given Demographics and baseline characteristics see below	GROUP A: **fPPCI with abciximab / or early abciximab** (0.25 mg/kg) followed by 12 hours of 0.125 microgram/kg/mi. Given immediately after entering emergency department and the initial aspirin and heparin bolus; before PCI. GROUP B: **LATE abciximab** (0.25 mg/kg) followed by 12 hours of 0.125 microgram/kg/mi. Given after angiography and before the angioplasty attempt (thus not true faciliatation) **Pre-PCI:** All patients received aspirin 250–200 mg and IV heparin (70 U/kg) immediately as arrived in emergency department. **During/Post-PCI:** 12 hours infusion of abciximab (0.125 microgram/mg/kg). **PCI/STENTS:** 93% / 100% PCI and 59% / 69% STENTS IN fPPCI and PPCI groups respectively.	GROUP C: **PPCI (no abciximab)**	In-hospital: HF Bleeding Death 6 months: Death **Length of follow-up:** 6 months	Not stated

Demographics and baseline characteristics			
	fPPCI n = 56	**PPCI n = 51**	**Late abciximab n = 56**
Age, years (SD)	58 ± 13	63 ± 14	63 ± 11
Male sex, %	79	61	73
Medical history, n (%)			
• Smoking	20%	31%	22%
• Diabetes mellitus	18%	29%	23%
• MI	11%	14%	14%
• Systemic Hypertension	54%	61%	59%
• Hyperlipidemia	55%	43%	52%
Killip class, %			
• 1	86	69	75%
• 2	9	10	16%
• 3	2	6	2%
• 4	3	15	7%
Outcome, n (%)	**fPPCI n = 56**	**PPCI n = 51**	**Late abciximab n = 56**
In-hospital complicatons			
Heart Failure	4 (7%)	15 (29%)	10 (18%)
Bleeding	16 (29%)	6 (12%)	11 (20%)
Death	0 (0%)	5 (10%)	4 (7%)
6-month follow-up			
Cumulatiive death	0 (0%)	7 (14%)	5 (9%)

G.3 Radial versus femoral arterial access for PPCI

Table 39: Gan et al. 2009[48]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Gan L, Lib Q, Liuc R, Zhaoc Y, Qiuc J, Liao Y. Effectiveness and feasibility of transradial approaches for primary percutaneous coronary intervention in patients with acute myocardial infarction. Journal of Nanjing Medical University. 2009; 23(4):270-274.	Design RCT; 2 centres in China Enrolment June 2004 to July 2007 Randomisation Not detailed Allocation concealment Not detailed Blinding Patients and investigators were not masked to treatment allocation. All other outcomes were as reported by the investigators.	n = 195 PPCI done in all patients Drop outs (at 6 month follow-up) Radial n = 9 Femoral n = 14 Crossover 1 patient in radial group required crossover to femoral group due to un-successful puncture of radial artery Operator expertise Not stated	Inclusion criteria Patients with STEMI recruited within 12 h of symptom onset Typical chest pain lasting > 30 min and < 12 h, nitrate losing efficacy, ST-segment elevation > 0.1 mV in limb leads or > 0.2 mV in 2 or adjacent chest leads Exclusion for transradial group Negative Allen test (these patients were switched to femoral group) Demographics and baseline characteristics see below Drug therapy All patients received 300 mg aspirin, 300 mg clopidogrel on diagnosis. 30000 IU heparin administered after sheath insertion. Additional heparin during procedure dependent upon patients body mass (100 IU/kg). GP IIb/IIIa inhibitors were given dependent based on clinical need. After implantation of drug eluting	Radial access to perform coronary angiography and PPCI (if clinically indicated) (n = 90)	Femoral access to perform coronary angiography and PPCI (if clinically indicated) (n = 105)	In-hospital and 6 months	All-cause mortality Reinfarction Repeat revascularisation CABG Hospital stay Angiographic procedural success access site complications Fluproscopy time (see below for definitions)	Language support from; Editorial Dept of the Journal of Nanjing Medical University

	No		stents, patients were treated with 1000 IU/kg low molecular heparin twice a day for 5 to 7 days and 150 mg aspirin plus 75 mg aspirin plus 75 mg clopidogrel daily for 12 months					

Demographics and baseline characteristics

Characteristics	**Radial (n = 90)**	**Femoral (n = 105)**
Male/Female	73/17	84/21
Age(years), mean(SD)	56.6(12.5)*	52.3(11.9)
Smoking, n(%)	55(6.1)*	67(63.8)
Diabetes, n(%)	25(27.8)*	31(29.5)
Hypertension, n(%)	44(48.9)*	48(45.7)
Hyperlipidaemia, n(%)	33(36.7)*	37(35.2)
Prior MI, n(%)	8(8.9)*	11(10.5)
Onset of symptoms to arrival (h), mean(SD)	4.3(2.1)*	4.8(2.2)
Single vessel disease, n(%)	24(26.8)*	25(23.8)
Multivessel disease, n(%)	66(73.3)*	80(76.2)
Infarct related artery		
Left anterior descending artery, n(%)	47(52.2)*	57(54.3)
Left circumflex, n(%)	15(16.7)*	19(18.1)
Right coronary artery, n(%)	28(31.1)*	29(27.6)

Compared with femoral group, *p > 0.05

Definitions of operational data

Cannulation time: time from patient arrival at cath lab to effective placement of arterial sheath

Reperfusion time: time from cannulation to balloon inflation

Total procedural time: time from 1st attempt to puncture the artery to end of angioplasty

Comparison of operation data between radial versus femoral groups

Characteristics	**Radial (n = 90)**	**Femoral (n = 105)**
Success of puncture, n(%)	89(98.9)*	105(100)

Cannulation time (min), mean(SD)	3.15(1.56)*	2.86(0.97)
Cannulation-to-balloon-infusion time (min), mean(SD)	18.56(4.37)*	17.75(3.21)
Total procedural time (min), mean(SD)	29.75(4.38)**	27.89(3.95)
Glycoprotein II b/II a inhibitor, n(%)	28(31.1)*	36(34.3)
Final TIMI flow, n(%)		
TIMI 0	0	0
TIMI 1	1	1
TIMI 2	2	3
TIMI 3	87(97.7)*	101(96.2)
Angiographic procedural success, %	96.7*	96.2

TIMI; thrombolysis in myocardial infarction, Compared with femoral group, *p > 0.05, **p < 0.05

Definitions of outcomes

Angiographic procedural success: Residual obstruction < 20%, achieving TIMI flow of at least grade III and no major complications such as death, emergency surgical revascularisation or worsening of patients' clinical condition

Effect Size

Outcome	**Radial**	**Femoral**
6 month follow-up complete, n(%)	79(87.8)	88(83.8)
All-cause mortality at 6 months, n(%)	2(2.5)*	3(3.4)
All-cause mortality in-hospital, n(%)	2(2.2)*	3(2.9)
Reinfarction at 6 months, n(%)	1(1.3)*	0
Reinfarction in-hospital, n(%)	0	2(1.9)
CABD at 6 months, n(%)	0	0
CABD in-hospital, n(%)	0	0
Repeat revascularisation at 6 months, n(%)	2(13.3)*	2(9.5)
Access site complications in-hospital, n(%)	2(2.2)**	12(11.4)
Length of hospitalisation (days), mean(SD)	10.56(2.85)**	13.78(3.15)

Compared with femoral group, *p > 0.05, **p < 0.05

Table 40: Hou et al. 2010[56]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow - up	Outcome measures	Source of funding
Hou L, Wei YD, Li WM, Xu YW. Comparative study on transradial versus transfemoral approach for primary percutaneous coronary intervention in Chinese patients with acute myocardial infarction. Saudi Medical Journal. 2010; 31(2):158-162.	Design: RCT; 1 centre in China Enrolment: August 2005 to Sept 2008 Randomisation Not detailed Allocation concealment: Not detailed Blinding: Patients and investigator s were not masked to treatment allocation. All other outcomes were as reported by the investigators ITT analysis: Yes	n = 200 PPCI done in all patients Drop outs none Crossover 4 patients in radial group required crossover to femoral access (2 patients; severe subclavian artery tortuosity, 2 patients; radial artery tortuosity) Operator expertise 3 senior interventional cardiologists who had performed over 200 cases of radial PPCI	INCLUSION CRITERIA: Patients with Acute MI EXCLUSION Negative Allen test Non-palpable radial artery Cardiogenic shock Prior CABG Demographics and baseline characteristics see below Drug therapy Patients received 300 mg aspirin, 300 mg clopidogrel on diagnosis, and subcutaneous Fragmin (5000U) or FraxiParin (4100U) for all patients. Further 5000IU heparin given during procedure. GP IIb/IIIa inhibitors and stents were given during procedure dependent based on clinical need.	Radial access to perform coronary angiography and PPCI (if clinically indicated) (n =100)	Femoral access to perform coronary angiography and PPCI (if clinically indicated) (n = 100)	1 month	All-cause mortality Reinfarction Repeat revascularisatio n CABG Hospital stay Angiographic procedural success Access site complications Fluoroscopy time (see below for definitions)	None stated

Demographics and baseline characteristics			
Characteristics	**Radial (n = 100)**	**Femoral (n = 100)**	**p value**
Age(years), mean(SD)	64.9(8.4)	66.2(7.7)	0.23
Male, n(%)	72(72)	69(69)	0.64
Hypertension, n(%)	42(42)	50(50)	0.25
Diabetes, n(%)	22(22)	15(15)	0.20
Smoker, n(%)	50(50)	42(42)	0.27
Obesity, n(%)	23(23)	30(30)	0.26
Hypercholesterolaemia, n(%)	35(35)	40(40)	0.47
Three vessel disease, n(%)	22(22)	18(18)	0.48
Killip class	0.89		
Class I, n(%)	60(60)	58(58)	
Class II, n(%)	30(30)	33(33)	
Class II, n(%)	10(10)	9(9)	
Infarct related artery			
Left anterior descending artery, n	44	50	
Left circumflex, n	8	13	
Right coronary artery, n	44	37	
Initial TIMI flow, n	0.40		
TIMI 0 to 1	72	68	
TIMI 2	20	18	
TIMI 3	8	14	
TIMI; thrombolysis in mycocardial infarction			
Comparison of operation data between radial versus femoral groups			
Characteristics	**Radial (n = 100)**	**Femoral (n = 100)**	**p value**
Success of puncture, n	100	100	
Cannulation time (min), mean(SD) 95% CI	2.5(0.6) 2.2 to 2.4	2.4(0.6) 2.1 to 2.3	0.24
Reperfusion time (min), mean(SD)	16.4(1.7)	16.2(1.8)	0.42

95% CI	16 to 16.7	15.8 to 16.6	
Total procedural time (min), mean(SD) 95% CI	37.2(7.1) 35.8 to 38.6	35.7(8.1) 34 to 34.3	0.17
Fluoroscopy time (min), mean(SD)	11.2(2.0) 11.4 to 12.2	11.4(1.8) 11.1 to 11.8	0.14
Final TIMI flow, n	0.60		
TIMI 0 to 1	2	1	
TIMI 2	2	4	
TIMI 3	96	95	
Stents used, n	97	95	0.72
Tirofiban used, n	28	20	0.19
Angiographic procedural success*, n	96	97	1.00

TIMI; thrombolysis in myocardial infarction, Angiographic procedural success * = residual diameter stenosis < 30% with grade 3 coronary flow according to the classification of fibrinolysis in myocardial trial

Definitions of outcomes

Major access site bleeding: Haemoglobin loss ≥ 2 mmol/l, administration of blood transfusion, and needing vascular repair

Minor access site bleeding: Hematoma formation not requiring specific therapy

Effect Size – 1 month follow-up

Outcome	**Radial (n = 100)**	**Femoral (n = 100)**	**p value**
All-cause mortality, n	4	5	1.0
Reinfarction, n	0	0	
Repeat revascularisation, n	0	0	
Vascular complications, n	3	11	< 0.01
Major bleeding, n	0	3	2.4
Minor bleeding (haematoma), n	2	6	2.8
Pseudoaneurysm, n	0	2	0.16
Artery occlusion without ischaemia, n	1	0	
Hospital stay (day)			
Mean(SD) 95% CI	8.6(1.8) 8.3 to 9.0	12.7(3.0) 12.1 to 13.3	< 0.001

Table 41: Li 2007[73]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Li WM, Li Y, Zhao JY, Duan YN, Sheng L, Yang BF et al. Safety and feasibility of emergent percutaneous coronary intervention with the transradial access in patients with acute myocardial infarction. Chin Med J (Engl). 2007; 120(7):598-600.	Design RCT; 1 centre in China Enrolment June 2004 to July 2006 Randomisation Not detailed Allocation concealment Not detailed Blinding: Patients and investigators were not masked to treatment allocation. All other outcomes were as reported by the investigators. ITT analysis Yes	n = 370 PPCI done in all patients Drop outs None Crossover 3 patients in radial group required crossover to femoral and 2 patients in femoral group required crossover to radial group (reasons not given) Operator expertise Not stated	Inclusion criteria Acute MI within 12 h onset of chest pain (no further details given) Exclusion criteria for the transradial group Negative Allen test Aorto-arteritis Cardiogenic shock Non-palpable radial artery Severe tortuosity of radial arteries Body height > 150 cm Demographics and baseline characteristics see below Drug therapy All patients received aspirin and clopidogrel before PPCI, adjunctive bolus heparin was determined by body weight (70 to 100 IU/Kg).	Radial access to perform coronary angiography and PPCI (if clinically indicated) (n = 184)	Femoral access to perform coronary angiography and PPCI (if clinically indicated) (n = 186)	In-hospital	Angiographic procedural success	None stated

Baseline and clinical characteristics		
Baseline	**Radial (n = 184)**	**Femoral (n = 186)**
Male/Female	124/60	120/66
Age(years), mean(SD)	56.5(10.9)	55.4(12.8)
Body height (cm), mean(SD)	166(12.5)	165.8(13.1)
Diabetes, n(%)	37(20.1)	34(18.3)
Hypertension, n(%)	74(40.2)	78(41.9)
Hyperlipidaemia, n(%)	29(15.8)	31(16.7)
Smoker, n(%)	78(42.4)	80(43.0)
Clinical characteristics	**Radial (n = 184)**	**Femoral (n = 186)**
Anterior wall acute MI, n(%)	83(45.1)	80(43.0)
Inferior wall acute MI, n(%)	58(31.5)	63(33.9)
Lateral and posterior wall acute MI, n(%)	30(16.3)	32(17.8)
Right ventricular and inferior wall acute MI, n(%)	13(7.1)	11(5.9)
Culprit artery, n(%)		
• Left anterior descending artery, n(%)	82(44.6)	80(43.0)
• Left circumflex, n(%)	26(14.1)	29(15.6)
• Right coronary artery, n(%)	74(40.2)	77(41.4)
• Left anterior descending artery, n(%)	2(1.1)	0
Single vessel disease, n(%)	107(58.2)	107(57.5)
Multivessel disease, n(%)	77(41.8)	79(42.5)
Total occlusion, n(%)	76(41.3)	78(41.9)
Left ventricular ejection fracture, mean(SD)	48.42(8.48)	51.21(9.21)
No statistical difference between 2 groups for left ventricular ejection fracture and infarct location		
Procedural and angiographic details		
Angiographic procedural success: TIMI flow of at least grade III		
Variables	**Radial (n = 184)**	**Femoral (n = 186)**
Cannulation time (min), mean(SD)	27.1(5.8)	26.5(7.0)
Total procedural time (min), mean(SD)	56.2(12.1)	58.4(15.1)

Stent implantation, n	200	202
Successful rates of puncture, %	98.4	98.0
Final TIMI III flow	94.8	94.2

Table 42: RADIAMI 2009[26]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Chodór P, Krupa H, Kurek T, Sokal A, Swierad M, Was T et al. RADIal versus femoral approach for percutaneous coronary interventions in patients with Acute Myocardial Infarction (RADIAMI): A prospective, randomized, single-center clinical trial. Cardiology Journal. 2009; 16(4):332-340.	Design RCT; 1 centre in Poland Enrolment April 2005 to June 2006 Randomisation Based on year of birth (radial group; even years, femoral group; odd years) Allocation concealment Not detailed Blinding Patients and investigators were not masked to treatment	n = 100 PPCI not completed 1 patient in femoral group due to inability of balloon passage through occluded area of artery Drop outs 1 due to PPCI not completed Crossover 4 patients in radial group required crossover to femoral group, 3 abnormal Allen test, 1 excessive tortuous radial artery. 1 pateint in femoral	Inclusion criteria Presence of MI defined as retrosternal pain lasting > 20 min, but < 12 h, resistant to nitroglycerin, and ECG changes; ST elevation of at least 1 mV in two neighbouring leads or new left bundle branch block, found in the qualifying ECG Age between 18 and 75 years Participation consent Exclusion criteria Age over 75 years Killip class III or IV Necessity of an intra-aortic balloon pumpplacement before the PPCI Necessity of an endocavitary stimulating electrode placement before the PPCI Height < 150 cm History of CABG if the infarction may be due to a closed venous or arterial bypass graft Demographics and baseline characteristics	Radial access to perform coronary angiography and PPCI (if clinically indicated) (n = 50)	Femoral access to perform coronary angiography and PPCI (if clinically indicated) (n = 50)	In-hospital	All-cause mortality Reinfarction Stroke, CABD Repeat revascularisation Major bleeding, Fatal bleeding requiring operation, drop in Hb Intracranial haemorrhage Hospital stay Total radiographic contrast media used in	None stated

other outcomes were as reported by the investigators. ITT analysis Yes	crossed to radial due to athero-sclerosis obliterations of the lower limb Operator expertise Conducted by physicians with many years experience of performing femoral access PPCI (300 to 400 PPCIs per year), who had performed at least 50 to 100 radial access PPCIs	see below Drug therapy Verapamil (5mg) after puncture of radial artery; dose was repeated in the case of a spasm, until reaching a total dose of 15 mg. Dependent on activated clotting time result heparin (70 U/kg) was administered. Fibrinolytic drugs and platelet glycoprotein IIb/IIIa receptor blockers were administered during the intervention based on clinical need. Heparin administration was continued after the intervention only in the presence of clinical indications. Abciximab was administered to a similar percentage of patients in both groups (44% versus 42%, radial and femoral respectively). Stents were given to all the patients who underwent PPCI.		PPCI procedure Fluoroscopy time Hematoma

Characteristics	Entire study group (n = 100)	Radial (n = 90)	Femoral (n = 105)	p value
Age (years), mean(SD)	59.5(9.1)	59.9(9.4)	59.1(9.0)	NS
Height (cm), mean(SD)	169.1(8,4)	167.8(7,5)	169.5(9.2)	NS
Body weight (kg), mean(SD)	82.2(14.7)	79.5(11.7)	85.0(16.8)	NS
Men, n(%)	68(68)	35(51.5)	33(48.5)	NS
Diabetes, n(%)	15(15)	8(16)	7(14)	NS
Smoking, n(%)	64(64)	34(68)	30(60)	NS
Arterial hypertension, n(%)	47(47)	26(52)	21(42)	NS
Hyperlipidemia, n(%)	19(19)	11(22)	8(16)	NS
Past infarction, n(%)	11(11)	8(16)	3(6)	NS

Family history*, n(%)	32(32)	16(32)	16(32)	NS
Killip class 1, n(%)	99(99)	50(100)	49(98)	NS
Killip class 2, n(%)	1(1)	0(0)	1(2)	NS
HR at admission (beats/min), mean(SD)	78.2(15.0)	78.3(3.7)	78.2(6.4)	NS
SBP at admission (mmHg), mean(SD)	135.2(29.2)	138.8(33.2)	131.6(24.5)	NS
DBP at admission mmHg), mean(SD)	78.4(17.9)	80.1(18.6)	76.7(17.1)	NS
Infarction location				
Anterior wall, n(%)	42(42)	21(42%)	21(42)	NS
Inferior wall, n(%)	54(54)	27(54)	27(54)	NS
Left bundle branch block, n(%)	0(0)	0(0)	0(0)	NS
Other, n(%)	4(4)	1(4)	2(4%)	NS

*Family history of coronary heart disease; **Mann-Whitney U test; MIN; mean infarction duration; DBP; diastolic blood pressure; SBP; systolic blood pressure; HR; heart rate, NS; not significant

Angiographic data

Outcome	Total population (n =100)	Radial (n = 50)	Femoral (n = 50)	p value
No. of pathologic vessels, n(%)				
1	36(37.5)	21(42.9)	15(31.9)	NS
2	40(41.7)	19(38.8)	21(44.7)	NS
3	20(20.8)	9(18.4)	11(23.4)	NS
Infarct-related artery, n(%)				
LM	0(0%)	0(0)	0(0)	NS
LAD	43(44.3)	21(42.9)	22(45.8)	NS
Cx	12(12.4)	9(18.4)	3(6.2)	NS
Percutaneous coronary intervention, n(%)	50(100)	50(100)	50(100)	NS
Initial TIMI flow grade, n(%)				
0	53(54.5)	26(53.1)	27(56.3)	NS

1	9(9.3)	5(10.2)	4(8.3)	NS
2	19(19.6)	8(16.3)	11(22.9)	NS
3	16(16.5)	10(20.4)	6(12.5)	NS
Final TIMI flow grade, n(%)				
0	1(1)	0(0)	1(2)	NS
1	0(0)	0(0)	0(0)	NS
2	9(9)	6(12)	3(6)	NS
3	90(90)	44(88)	46(92)	NS
Residual stenosis after the intervention, n(%)	1.7(10.7)	0.8(4.0)	2.6(14.7)	NS*
Abciximab, n(%)	43(43)	22(44)	21(42)	NS
Exposure time (min), n(%)	11.1(6.3)	10.9(5.6)	11.2(7.0)	NS
Contrast amount (ml , n(%)	198.7(45.7)	198.7(45.7)	197.7(72.0)	NS*
No. of stents per patient, n(%)	1.27(0.47)	1.28(0.45)	1.26(0.49)	NS
Stenting percentage, n(%)	99(99)	50(100)	49 (98)	NS
*Mann-Whitney U test, LM; left mammary, LAD; left artery descending, Cx; circumflex artery, RCA; right coronary artery, TIMI; Thrombolysis In Myocardial Infarction, NS not significant				
Time intervals during coronary angiography and PPCI				
Time from admission to (door to), min (SD)	**Total population (n = 100)**	**Radial (n = 50)**	**Femoral (n = 50)**	**p value**
Arrival in the cath lab	35.7 (21.6)	37.8 (21.0)	33.7 (22.2)	NS
Sheath positioning	49.1 (22.9)	53.7 (21.9)	44.4 (23.1)	0.04
First contrast injection	56.0 (25.1)	50.2 (23.8)	62.3 (25.5)	0.02*
Balloon positioning	69.1 (27.9)	76.9 (25.9)	64.6 (26.9)	0.02*
Stent implantation (door to stent)	77.9 (27.2)	83.2 (26.3)	72.3 (27.3)	0.05
End of intervention	92.7 (28.7)	98.7 (26.8)	88.7 (30.1)	0.17
Arrival in the cath lab to sheath positioning time	13.6 (7.4)	15.7 (7.8)	11.4 (6.4)	0.0028
Sheath to injection time	6.6 (6.4)	8.6 (7.8)	4.5 (3.3)	0.008*
Injection to balloon time	15.1 (7.9)	15.6 (8.7)	14.6 (7.1)	NS

Balloon to stent time	8.0 (4.9)	7.3 (4.6)	8.7 (5.2)	0.21
Stent to end of intervention time	14.4 (10.6)	13.3 (8.6)	15.5 (12.4)	0.31
Procedure	56.8 (18.1)	58.3 (17.8)	55.1 (18.4)	0.38

*Mann-Whitney U test

Definitions of outcomes

Angiographic procedural success: TIMI grade 3 flow rate was obtained and residual stenosis was lower than 30%

Major bleeding: Fatal bleeding, bleeding requiring blood transfusion, operation or resulting in a drop of haemoglobin count of more than 3 g/dl as well as any intracranial haemorrhage

Minor bleeding: all non-major bleeding

Procedure time: Period from the patient's arrival in the cath lab to the removal of the vascular sheath for radial group , and to the removal of the catheter from the sheath for group femoral group.

Effect size

Outcome	**Entire study group**	**Radial (n = 50)**	**Femoral (n = 50)**	**p value**
All-cause mortality	1(1)	0(0)	1(2)	NS
Myocardial infarction	1(1)	1(2)	0(0)	NS
Stroke	1(1)	1(2)	0(0)	NS
Repeated revascularisation of the IRA	3(3)	1(2)	2(4)	NS
Coronary artery bypass grafting	0(0)	0(0)	0(0)	NS
Serious bleeding	10(9.3)	3(8.2)	17(14)	0.18
Fatal bleeding	0(0)	0(0)	0(0)	NS
Serious bleeding requiring transfusion	3(3%)	0(0)	3(6)	NS
Serious bleeding resulting in haemoglobin level decrease of > 3 g/dl	7(7%)	3(6%)	4(8%)	NS
Intracranial bleeding	0(0)	0(0)	0(0)	NS
Hematoma > 5 cm	13(13)	5(10)	8(16)	0.37

NS: not significant

Table 43: RADIAMI II 2011[27]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Chodór P, Kurek T, Kowalczuk A, Swierad M, Was T, Honisz G et al. Radial vs femoral approach with StarClose clip placement for primary percutaneous coronary intervention in patients with ST-elevation myocardial infarction. RADIAMI II: A prospective, randomised, single centre trial. Kardiologia Polska. 2011; 69(8):763-771.	Design RCT; 1 centres in Poland Enrolment Nov 2006 to Mar 2008 Randomisation Based on year of birth (radial group; even years, femoral group; odd years) Allocation concealment Not detailed Blinding Patients and investigator s were not masked to treatment allocation. All other outcomes were as reported by the investigators	n = 108 PPCI done in all patients Drop outs None Crossover 2 patients in radial group required crossover to femoral group, 1 patient in femoral group crossed over to radial (reasons not given) Operator expertise 3 physicians with 17 to 20 years of experience performed femoral	Inclusion criteria MI defined as retrosternal pain lasting between 20 min and 12 h and not relieved by nitroglycerine, accompanied by ECG changes in the form of ST elevation of at least 0.01 mV in two adjacent leads or new left bundle branch block Age between 18 and 75 years Participation consent Exclusion criteria Age over 75 years Killip class III or IV Necessity of an intra-aortic balloon pumping or temporary right ventricular pacing Placement before the PPCI Necessity of an endocavitary stimulating electrode Placement before the PPCI Height < 150 cm History of CABG Demographics and baseline characteristics see below Drug therapy	Radial access to perform coronary angiography and PPCI (if clinically indicated) (n = 49)	Femoral access and a StarClose device to perform coronary angiography and PPCI (if clinically indicated) (n = 59)	In-hospital	All-cause mortality Reinfarctio n Stroke CABD Repeat revasculari sation Serious bleeding Fatal bleeding Serious bleeding requiring transfusion Serious bleeding requiring surgery Serious bleeding giving drop in Hb of > 3 g/dl Intracrania l haemorrha ge Fluoroscop y time	None stated

	ITT analysis No	access PPCI, and several years experience in performing radial access PPCI	After placing the sheath, activated clotting time was determined and heparin was administered in doses that permitted the obtaining of activated clotting time of 350 to 450 s during procedures performed without the use of abciximab, and 250 to 350 s when abciximab was used. Whether to use abciximab was a decision left to the operator.				Total radiographic contrast media used in PPCI procedure hematoma > 5 cm	

Demographics and baseline characteristics

Characteristics	Entire study group (n = 108)	Radial (n = 49)	Femoral (n = 59)	p value
Age (years), mean(SD)	59.6(10.0)	62.1(9.3)	57.6(10.3)	0.02
Height (cm), mean(SD)	168.0(7.8)	168.5(7.7)	167.5(8.0)	NS
Body weight (kg), mean(SD)	79.1(13.0)	81.0(14.4)	77.5(11.6)	NS
Men, n(%)	69(64)	32(65)	37(63)	NS
Diabetes, n(%)	20(19)	10(21)	10(17)	NS
Smoking, n(%)	72(67)	29(60)	43(73)	NS
Arterial hypertension, n(%)	42(39)	22(46)	20(34)	NS
Hyperlipidemia, n(%)	22(21)	12(25)	10(17)	NS
Prior MI, n(%)	12(11)	4(8)	8(14)	NS
Family history of early CVD, n(%)	44(41)	22(46)	22(37)	NS
Circulatory status on admission				
Killip class 1, n(%)	90(83)	40(82)	50(85)	NS
Killip class 2, n(%)	18(17)	9(18)	9(15)	NS
Mean duration of symptoms (min), mean(SD)	271.8(168.5)	252.2(181.3)	288.2(156.6)	NS
HR at admission (beats/min), mean(SD)	81.4(18.4)	80.3(19.5)	82.3(17.5)	NS
SBP at admission (mmHg), mean(SD)	141.5(22.9)	139.9(21.6)	142.9(24.1)	NS

DBP at admission (mmHg), mean(SD)	90.7(14.6)	90.8(14.4)	90.7(14.9)	NS
MI location				
Anterior wall, n(%)	40(37)	21(43)	19(32)	NS
Inferior wall, n(%)	61(56)	24(49)	37(63)	NS
Left bundle branch block, n(%)	7(13)	4(8)	3(5)	NS
Other, n(%)	40(37)	21(43)	19(32)	NS
CVD; cardiovascular disease, diastolic blood pressure; SBP; systolic blood pressure; HR; heart rate, NS; not significant				
Comparison of angiographic and procedural data between radial versus femoral groups				
Characteristics	**Entire study group (n = 108)**	**Radial (n = 49)**	**Femoral (n = 59)**	**p value**
1-vessel disease, n(%)	50(47)	21(44)	29(49)	NS
2-vessel disease, n(%)	43(40)	21(44)	22(37)	NS
3-vessel disease, n(%)	14(13)	6(12)	8(14)	NS
Infarct related artery, n(%)				
Left main stem, n(%)	0(0)	0(0)	0(0)	NS
Left anterior descending artery, n(%)	38(35)	21(43)	17(29)	NS
Circumflex artery, n(%)	14(13)	4(8)	10(17)	NS
Right coronary artery, n(%)	55(51)	24(49)	31(53)	NS
Initial TIMI flow, n(%)				
0	57(53)	22(45)	35(59)	NS
1	8(7)	4(8)	4(7)	NS
2	18(17)	13(27)	5(8)	0.012
3	25(23)	10(20)	15(25)	NS
Final TIMI flow, n(%)				
0	0(0)	0(0)	0(0)	NS
1	0(0)	0(0)	0(0)	NS
2	1(1)	0(0)	1(2)	NS
3	107(99)	49(100)	58(98)	NS

RS post-procedure < 20%, n(%)	108(100)	49(100)	59(100)	NS
Maximum activated clotting time (sec), mean(SD)	322.8(68)	304.8(64.8)	336(68)	0.025
Abciximab administration, n(%)	57(53)	25(51)	32(54)	NS
Fluoroscopy time (min), mean(SD)	7.0(3.0)	7.5(3.0)	6.9(3.0)	NS
Contrast material (ml), mean(SD)	163.4(43.7)	165.0(41.4)	162.0(46.0)	NS
Number of stents implanted				
1 stent, n(%)	70(65)	34(69)	36(61)	NS
2 stents, n(%)	31(29)	13(27)	18(31)	NS
3 stents, n(%)	5(5)	2(4)	3(5)	NS
Stenting ratio, %	98.2	100	94.9	NS
Successful placement of StarClose clip n(%), or Terumo band, n(%)		48(98.0)	55(93.2)	
RS ; residual stenosis, NS; not significant				
Time intervals during coronary angiography and PPCI for radial and femoral groups				
Time interval	**Entire study group (n = 108)**	**Radial (n = 49)**	**Femoral (n = 59)**	**p value**
Interval from cath lab arrival to beginning of the procedure (min), mean(SD) (median; interquartile range)	10.3(5.6) (10.0; 5.0 to 13.0)	11.2(6.5) (10.0; 5.0 to 15.0)	9.6(4.7) (10.0; 6.0 to 10.0)	NS
Interval from beginning of procedure to vascular sheath introduction (min), mean(SD) (median; interquartile range)	4.7(5.16) (3.0; 2.0 to 5.0)	5.8(6.8) (4.0; 2.0 to 5.0)	3.8(3.0) (3.0; 2.0 to 5.0)	NS
Interval from vascular sheath introduction to first contrast injection (min), mean(SD) (median; interquartile range)	5.4 (5.5) (4.5; 3.0 to 5.0)	5.4(3.9) (5.0; 3.5 to 6.0)	5.4 (6.6) (4.0; 3.0 to 5.0)	NS
Interval from contrast injection	12.6(6.3)	11.9(4.9)	13.3(7.1)	NS

to balloon inflation (min), mean(SD) (median; interquartile range)	(11.0; 10.0 to 14.0)	(11.0; 10.0 to 13.0)	(11.5; 10.0 to 14.0)	
Interval from balloon inflation to stent implantation (min), mean(SD) (median; interquartile range)	7.3(5.7) (9.0; 6.0 to 9.0)	7.3(7.2) (5.5; 4.0 to 8.0)	7.3(4.2) (6.5; 5.0 to 10.0)	NS
Interval from stent implantation to end of procedure (min)*, mean(SD) (median; interquartile range)	11.0(7.2) (10.0; 6.0 to 15.0)	9.4(6.8) (7.0; 5.0 to 13.00)	12.6(7.3) (10.0; 8.0 to 16.0)	0.005
Total procedural time (from cath lab arrival to end of procedure) (min), mean(SD) (median; interquartile range)	50.2(20.2) (48.0; 40.0 to 58.0)	53.7 (20.6) (50.0; 41.5 to 60.0)	47.3(19.6) (45.0; 40.0 to 56.0)	NS

*in cases of implantation of more than one stent, this is the interval from final stent implantation to the end of the procedure, NS; not significant

Definitions of outcomes

Angiographic procedural success : TIMI grade 3 flow rate was obtained and residual stenosis < 20%

Major bleeding complications: Serious bleeding that resulted in death or a need for blood transfusion or surgical intervention, caused haemoglobin level decrease by > 3 g/dl, and central nervous system bleedings.

Minor bleeding: all non-major bleeding

Procedure time: Period from the patient's arrival in the cath lab to the removal of the vascular sheath and placement of Terumo band dressing for radial group , and to the removal of the catheter from the sheath and VCD implantation for group femoral group.

Effect size

Outcome	**Entire study population (n = 118)**	**Radial (n = 49)**	**Femoral (n = 59)**	**p value**
All-cause mortality, n(%)	0(0)	0(0)	0(0)	NS
MI, n(%)	0(0)	0(0)	0(0)	NS
Stroke, n(%)	1(0.9)	0(0)	1(1.7)	NS
Repeated revascularisation of the IRA, n(%)	1(0.9)	1(2.0)	0(0)	NS
Coronary artery bypass	0(0)	0(0)	0(0)	NS

grafting, n(%)				
PCI of a vessel other than the IRA , n(%)	2(1.9)	0(0)	2(3.4)	NS
Serious bleeding, n(%)	10(9.3)	4(8.2)	6(10.2)	NS
Serious bleeding resulting in death, n(%)	0(0)	0(0)	0(0)	NS
Serious bleeding requiring blood transfusion, n(%)		1(0)	1(0)	NS
Serious bleeding requiring surgery, n(%)	0(0)	0(0)	0(0)	NS
Serious bleeding resulting in haemoglobin level decrease of > 3 g/dl, n(%)	9(8.3)	3(6.1)	6(10.2)	NS
Intracranial bleeding, n(%)	0(0)	0(0)	0(0)	NS
Hematoma > 5 cm, n(%)	20(18.5)	8(16.3)	12(20.3)	NS
IRA: infarct-related artery, NS: not significant				

Table 44: RIFLE-STEACS[93]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Romagnoli E, Biondi-Zoccai G, Sciahbasi A, Politi L, Rigattieri S, Pendenza G, Summaria F, Patrizi R, Borghi A, Di RC, Moretti C, Agostoni P, Loschiavo P, Lioy E, Sheiban I, Sangiorgi G. Radial Versus Femoral Randomized Investigation in ST-Segment Elevation Acute Coronary Syndrome: The RIFLE-STEACS (Radial Versus Femoral Randomized Investigation in ST-Elevation Acute	Design: Multi-centre (4 centres) randomised, parallel group study Enrolment: 1,001 acute ST-segment elevation acute coronary syndrome patients undergoing primary/rescues percutaneous coronary intervention Randomisation: Based on a computer-generated random series and stratified by centre. Allocation concealment: Patients were randomised according to opaque, numbered, sealed envelopes Blinding: Patients and investigators were	n = 1001 Drop-outs: None Crossover: None	Inclusion criteria: Patients with acute ST-segment elevation acute coronary syndrome patients undergoing primary/rescues percutaneous coronary intervention Exclusion criteria: • Contraindication to either radial or femoral vascular access • Recent stroke (within 4 weeks) • Anti-coagulant therapy assumption with INR >2 • Other severe bleeding diathesis Demographics and baseline characteristics: See below Drug therapy: Procedural anticoagulation with administration of an un-fractionated heparin bolus at a dose of 70 UI/kg ; ASA	Radial approach for PPCI	Femoral approach for PCI	30 days	Cardiac death MI Stroke Target lesion revascularization CABG relater bleeding Hospital stay	No extramural funding

Coronary Syndrome) Study. *Journal of the American College of Cardiologists.* 2012	not blinded; end point adjudication was performed by a blinded central independent clinical event committee Sample size calculation: Assumptions for sample size analysis were based, for the control event rate, on NACE rates reported in the HORIZINS-AMI trial and pertinent meta-analyses. ITT analysis: 1001 patients included in ITT analysis. No loss to follow-up.		plus a loading dose of clopidogrel 300 -600 mg; use of pre-procedural antithrombotic agents was left to the operators' discretion.	

Demographics and baseline characteristics

Clinical characteristics n (%)	**Femoral (n = 501)**	**Radial (n = 500)**	**p value**
Age, yrs (median)	65 (55-77)	65 (56-75)	0.409
Female (%)	141 (28.1)	126 (25.2)	0.317
BMI, kg/m^2	26.6 (24-30)	27.2 (25-30)	0.140
LV ejection fraction	45.0 (40-50)	45.0 (40-52)	0.175
CK (GFR <60 ml/min/1.73m^2)	127 (25.3)	111 (22.2)	0.156
COPD	40 (8.0)	31 (6.2)	0.325
Peripheral arterial disease	68 (13.6)	75 (15.0)	0.529
Previous myocardial infarction	71 (14.2)	70 (14.0)	1.00

Previous CVA	22 (4.4)	19 (3.8)	0.750
Previous revascularisation	52 (10.4)	65 (13.0)	0.2.2
Previous PCI	45 (9.0)	60 (12.0)	0.123
Previous CABG	12 (2.4)	7(1.4)	0.356
Clinical characteristics n (%)	**Femoral (n = 501)**	**Radial (n = 500)**	**p value**
Hypertension	309 (61.7)	299 (59.8)	0.561
Hypercholesterolemia	199 (39.7)	218 (43.6)	0.223
Smoking	191 (38.1)	210 (42.0)	0.221
Family history of CAD	81 (16.2)	96 (19.2)	0.215
Diabetes	122 (24.4)	115 (23.0)	0.656
Single vessel disease	265 (52.9)	279 (55.8)	0.374
Double vessel disease	149 (29.7)	136 (27.2)	0.401
Triple vessel disease	80 (16.0)	79 (15.8)	1.00
Killip I	330 (65.9)	348 (69.6)	0.224
Killip II	108 (21.5)	102 (20.4)	0.670
Killip III	28 (5.6)	24 (4.8)	0.670
Killip IV	35.(7.0)	26 (5.2)	0.290
Results: 30 day outcome n (%)	**Femoral (n = 501)**	**Radial (n = 500)**	**p value**
NACE	105 (21.0)	68 (13.6)	0.003
MACE	57 (11.4)	36 (7.2)	0.029
Cardiac death	46 (9.2)	26 (5.2)	0.020
Stroke	3 (0.6)	4 (0.8)	0.725
MI	7 (1.4)	6 (1.2)	1.000
Target lesion revascularisation	9 (1.8)	6 (1.2)	0.604
Stent thrombosis	9 (1.8)	6 (1.2)	0.604
Non-CABG bleeding	61 (12.2)	39 (7.8)	0.026
Access site related bleeding	34 (6.8)	13 (2.6)	0.002
Non-access site related	27 (5.4)	26 (5.2)	1.000

Results: n (%)	Femoral (n = 501)	Radial (n = 500)	p value
Fatal bleeding	3 (0.6)	3 (0.6)	0.684
Hospital stay, days (range)			
Total hospital stay	6 (5-8)	5 (4-7)	0.0008
Intensive coronary care unit	4 (3-5)	3 (2-4)	<0.001
Cardiology ward	3 (1-4)	2 (1-4)	0.472

Table 45: RIVAL[59,60]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Jolly SS, Yusuf S, Cairns J, Niemela K, Xavier D, Widimsky P et al. Radial versus femoral access for coronary angiography and intervention in patients with acute coronary syndromes (RIVAL): a randomised, parallel group, multicentre trial. Lancet.	Design RCT (multicentre; 158 hospitals in 32 countries) Enrolment June 2006 to Nov 2010 Randomisation 1:1 randomisation, variable sizes (2, 4 and 6) stratified by centre Allocation concealment 24h computerised central automated voice response system (at the Population Health Research institute)	n = 7021 Drop-outs: n = 29 (radial) n = 47 (femoral) Crossover: n = 245 (7%) Radial to femoral after failed radial access due to; radial spasm (n = 80), radial artery loop (n = 20), subclavian tortuosity (n = 31), other data unavailable n = 32(2%) Femoral to radial	Inclusion criteria Patients with STEMI Patients with ACS with or without ST segment elevation Patients with UA or NSTEMI an invasive approach was planned intent to perform same-sitting coronary angiography and PPCI during index hospitalisation suitable candidate for either radial or femoral artery PPCI the interventional cardiologist was willing to proceed with either radial or femoral access (and had expertise for both, including at least 50 radial procedures for coronary angiography or intervention within the	Radial access to perform coronary angiography and PPCI (if clinically indicated) (n =3507) Note: For both groups, the use of an arterial vascular closure device is allowed at the discretion of the treating	Femoral access to perform coronary angiography and PPCI (if clinically indicated) (n =3514) Note: For both groups, the use of an arterial vascular closure device is allowed at the	48 h 30 days	All-cause mortality Reinfarction Stroke Repeat revascularisation Non-CABG-related major bleeding within 30 days Angiographic procedural success Major vascular access site complications at 48 h	Sanofi-Aventis, Population Health Researc Institute Canadian Network for Internati (CANNeCTIN)

2011; 377(9775):1 409-1420. RIVAL trial methods Jolly SS, Niemela K, Xavier D, Widimsky P, Budaj A, Valentin V et al. Design and rationale of the radial versus femoral access for coronary intervention (RIVAL) trial: a randomized comparison of radial versus femoral access for coronary angiography or intervention in patients with acute coronary syndromes. American Heart	Blinding Patients and investigators were not masked to treatment allocation, but a masked central committee adjudicated the primary outcome and its components and stent thrombosis. All other outcomes were as reported by the investigators. Sample size calculation Lower than expected overall event rate for the primary outcome, so sample size was increased from 4000 to 7000 (provide 80% power to detect 25% RR reduction with control event rate of 6% and 30% risk reduction with control event rate of 4.5%) ITT analysis All randomised patients were included in ITT comparisons of outcome (regardless of whether crossed over)	after failed femoral access due to iliac tortuosity (n = 10), peripheral vascular disease (n = 9), other data unavailable Operator expertise Each operator had performed ≥ 50 radial procedures within the previous year	previous year) dual circulation of the hand was intact as assessed by Allen test Exclusion criteria <18 years Active bleeding or significant increased risk of bleeding (severe hepatic insufficiency, current peptic ulceration, proliferative diabetic retinopathy) uncontrolled hypertension carcinogenic shock severe peripheral vascular disease precluding a femoral approach previous coronary bypass surgery with use of >1 internal mammary artery Previously entered in the study Investigational treatment (drug or drug device) within the previous 30 days Demographics and baseline characteristics see below Drug therapy Antithrombotic regimen (including glycoprotein IIb/IIIa inhibitors) used for	physician	discretion of the treating physician		(see below for definitions)	

Journal. 2011; 161(2):254.	PPCI was at the discretion of treating physician, (see Demographics and baseline characteristics). Stents were used in 95% of patients in both radial and femoral groups.	

Demographics and baseline characteristics		
	Radial (n = 3507)	**Femoral (= 3514)**
Age (years), mean (SD)	62 (2) (14.4% >75 years)	62 (12) (15.1% >75 years)
Male sex, n (%)	2599 (74.1)	2561 (72.9)
Diagnosis at admission, n (%)		
Unstable angina	1544 (44.3)	1606 (45.7)
NTSTEMI	998 (28.5)	905 (25.8)
STEMI	995 (27.2)	1003 (28.5)
Medical history, n (%)		
Present smoker	1083 (30.9)	1097 (31.2)
Diabetes mellitus	781 (22.3)	722 (20.5)
MI	658 (18.8)	622 (17.7)
PPCI	431 (12.3)	408 (11.6)
Hypertension	2118 (60.4)	2076 (59.1)
CABG	79 (2.3)	75 (2.1)
Peripheral vascular disease	91 (2.6)	82 (2.3)
Antithrombotic treatment in-hospital, n(%)		
Aspirin	3479 (99.2)	3489 (99.3)
Clopidogrel	3368 (96.0)	3358 (95.6)
Low Mwt heparin	1806 (51.5)	1819 (51.8)
IV unfractionated heparin	1168 (33.3)	1110 (31.6)
Fondaparinux	383 (10.9)	381 (10.8)

Bivalirudin		76 (2.2)		109 (3.1)	
Glyc IIb/IIIa inhibitor		887 (25.3)		844 (24.0)	
Other in-hospital medications, n(%)					
PPIs		1050 (29.9)		1097 (31.2)	
BBs		3104 (88.5)		3130 (89.1)	
ACEs		2546 (72.6)		2539 (72.3)	
ARBs		377 (10.7)		386 (11.0)	
Statins		3309 (94.4)		3289 (93.6)	
CCBs		655 (18.7)		623 (17.7)	
Procedural complications and outcomes and patient preference					
Outcome	**Radial (n = 3507)**	**Femoral (n = 3514)**	**HR**	**95% CI**	**p value**
Major vascular complications at 30 days					
Large haematoma, n(%)	42(1.2)	106(3.0)	0.40	0.28-0.57	< 0.0001
Pseudoaneurysm needing closure, n(%)	7(0.2)	23(0.6)	0.30	0.13-0.71	0.006
Arteriovenous fistual, n(%)	0(0)	5(0.1)			
Ischaemic limb needing closure, n(%)	1(0)*	0(0)			
PPCI complications#					
Abrupt closure, n(%)	12(0.5)	11(0.5)	1.11	0.49 to 2.51	0.81
No reflow, n(%)	21(0.9)	31(1.3)	0.69	0.40 to 1.20	0.19
Dissection with reduced flow, n(%)	30(1.3)	25(1.1)	1.22	0.72 to 2.07	0.46
Coronary perforation, n(%)	5(0.2)	4(0.2)	1.27	0.34 to 4.37	0.72
Catheter thrombus, n(%)	2(0.1)	2(0.1)	1.01	0.14 to 7.21	0.99
Stent thrombosis, n(%)‡	16(0.7)	26(1.2)	0.63	0.34 to 1.17	0.14
Definite, n(%)	8(0.4)	16(0.7)	0.51	0.22 to 1.19	0.12

Probable, n(%)	8(0.4)	11(0.5)	0.74	0.30 to 1.84	0.52
PPCI procedural time (min), median(IQR)	35(22,50)	34(22,50)			0.62
Fluoroscopy time (min), median(IQR)†	9.8(5.8,15.0)	8.0(04.5, 13.0)			< 0.0001
Length of stay in hospital (days), median(IQR)	4(3,7)	4(3,7)			0.18
Persistent pain at access site for > 2 weeks, n(%)	87/3378(2.6)	104/3392(3.1)	0.84	0.63 to 1.12¶	0.22
Patient prefers radial next procedure, n(%)	2962/3282(90.2)	1629/3210(50.7)	8.99	7.86 to 10.28¶	< 0.0001

*Related to iliac thrombosis secondary to intra-aortic balloon pump inserted via femoral site. ⍰ As a proportion of patients having PPCI; n =2311 in radial group and n = 2349 in femoral group. ‡As a proportion of patients receiving a stent; n = 2197 in femoral group and n = 2243 in femoral time. †Fluoroscopy times added to case reports and available for 2850 patients in the radial group and 2890 patients in the femoral group. ¶Odds ratio (95%CI)

Definitions of outcomes

Angiographic procedural success

- Failure: no success at dilating attempted lesion(s) and/or failure to cross/dilate/not attempted
- Partial success: one of ≥2 attempted lesions was successfully dilated and procedure performed but >50% residual or TIMI flow <3 or failure
- Full success: lesions(s) attempted was successfully dilated with <50% residual or TIMI 3 flow

Major bleeding: Bleeding that was: 1. fatal, 2. resulted in transfusion of 2 or more units of red blood cells or equivalent whole blood, 3. caused substantial hypotension or with the need for inotropes, 4. needed surgical intervention, 5. caused severely disabling sequelae, 6. was intracranial and symptomatic or intraocular and ked to significant visual loss, or 7. led to a drop in Hb of at least 50 g/l

Minor bleeding: Bleeding events that did not meet the criteria for major bleeding and required transfusion of 1 unit of blood or modification of the drug regiment (ie. cessation of antiplatelet or antithrombotic therapy)

Major vascular access site complications: Included pseudoaneurysms needing closure, large haematoma (as judged by investigator), arteriovenous fistula, or and ischaemic limb needing surgery; these complications were classed as a major bleeding event or a minor bleeding event only if they also met the above definitions of major or minor bleeding

Effect Size

Total combined populations; hazard ratios (log rank) and 95%CI

Outcome	Radial (n = 3507)	Femoral (n = 3514)	HR	95% CI	p value
Non-CABG major bleeding at 30 days, n(%)	24 (0.7)	33 (0.9)	0.73	0.43 to 1.23	0.23
Non-CABG major bleeding at 48 h, n(%)	11 (0.3)	18 (0.5)	0.61	0.29 to 1.30	0.20
All-cause mortality at 30 days, n(%)	44 (1.3)	51 (1.5)	0.86	0.58 to 1.29	0.47
All-cause mortality at 48 h, n(%)	9 (0.3)	15 (0.4)	0.60	0.26 to 1.37	0.23
Reinfarction at 30 days, n(%)	60 (1.7)	65 (1.9)	0.92	0.65 to 1.31	0.65
Reinfarction at 48 h, n(%)	29 (0.8)	31 (0.9)	0.94	0.56 to 1.56	0.80
Stroke at 30 days, n(%)	20 (0.6)	14 (0.4)	1.43	0.72 to 2.83	0.30
Stroke at 48 h, n(%)	7 (0.2)	6 (0.2)	1.17	0.39 to 3.48	0.78
Angiographic procedural success	2204 (95.4%)	2235 (95.2%)	1.01	0.95 to 1.07	0.83
Angiographic procedural success*					
Access site crossover	265 (7.6)	70 (2.0)	3.82	2.93 to 4.97	<0.0001
Major vascular complications	49 (1.4)	131 (3.7)	0.37	0.27 to 0.52	<0.0001
Minor bleeding	100 (2.9)	118 (3.4)	0.84	0.65 to 1.10	0.21
Non-CABG TIMI major bleeding	19 (0.5)	19 (0.5)	1.00	0.53 to 1.89	1.00
CABG related bleeding	48 (1.4)	48 (1.4)	1.00	0.67 to 1.49	1.00
Non-CABG-related blood transfusions	39 (1.1)	45 (1.3)	0.87	0.56 to 1.33	0.51
All blood transfusions	99 (2.8)	98 (2.8)	1.01	0.76 to 1.33	0.95
*As a proportion of patients who had PPCI: n = 2311 (radial group) and n = 2349 (femoral group)					
NSTE-ACS versus STEMI patients; hazard ratios (log rank) and 95%CI					

Outcome	Total	Radial (n/total population)	Femoral (n/total population)	HR	95% CI	p value
Non-CABG major bleeding at 30 days, n(%)						
NSTE-ACS	5063	16/2552(0.6)	24/2511(1.0)	0.66	0.35 to 1.23	0.19
STEMI	1958	8/955(0.8)	9/1003(0.9)	0.92	0.36 to 2.39	0.87
Overall	7021	24/3507(0.7)	33/3514(0.9)	0.73	0.43 to 1.23	0.23
All-cause mortality at 30 days, n(%)						
NSTE-ACS	5063	32/2552(1.2)	19/2511(0.8)	1.66	0.94 to 2.92	0.082
STEMI	1958	12/955(1.3)	32/1003(3.2)	0.39	0.20 to 0.76	0.006
Overall	7021	44/3507(1.3)	51/3514(1.5)	0.86	0.86 to 1.29	0.47
Major vascular complications at 30 days, n(%)						
NSTE-ACS	5063	37/2552(1.4)	96/2511(3.8)	0.38	0.26 to 0.55	< 0.0001
STEMI	1958	12/955(1.3)	35/1003(3.5)	0.36	0.19 to 0.70	0.002
Overall	7021	49/3507(1.4)	131/3514(3.7)	0.37	0.27 to 0.52	< 0.0001
Access site crossover, n(%)						
NSTE-ACS	5063	214/2552(8.4)	54/2511(2.2)	3.94	2.92 to 5.31	< 0.0001
STEMI	1958	51/955(5.3)	16/1003(1.6)	3.32	1.89 to 5.82	< 0.0001
Overall	7021	265/3507(7.6)	70/3514(2.0)	3.82	2.93 to 4.97	< 0.0001

STEMI patients

Outcome	**Radial** (n/population)	**Femoral** (n/population)	RR (95%CI)
Stroke	5/955	4/1003	1.31 (0.35 to 4.87)
Reinfartion	11/955	18/1003	0.64 (0.30 to 1.35)
Minor bleeding	33/955	22/1003	1.58 (0.93 to 2.38)

Table 46: TEMPURA 2003[95]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Saito S, Tanaka S, Hiroe Y, Miyashita Y, Takahashi S, Tanaka K, Satake S. Comparative study on transradial approach vs. transfemoral approach in primary stent imlplantation for patients with acute myocardial infarction: results of the test for myocardial infarction by prospective unicenter randomization for access sites (TEMPURA) trial. Catheterization and cardiovascular interventions.	Design RCT; 1 centre in Japan Enrolment July 1999 to Feb 2001 Randomisation Not detailed Allocation concealment Not detailed Blinding Open label ITT analysis: Yes	n = 149 PPCI done on all patients Drop-outs at 6 month angiogram follow-up; radial = 29, femoral = 24 at 9 month follow-up; none Crossover I patient from radial to femoral group due to inability to control and engage several types of guiding catheters into LAD due to tortuous	Inclusion criteria Acute MI within 12 h from onset into study, presence of both prolonged chest pain lasting ≥ 30 min unresponsiveness to nitroglycerin and ECG changes (ST elevation of ≥ 1 mm in ≥ 2 contiguous ECG leads) Informed consent before PPCI Onset and location of infarct clearly documented No fibrinolytic therapy given Age > 20 years Exclusion criteria Abnormal Allen test Severe cardiogenic shock with weak radial pulsation Poor background medical conditions Culprit vessel was previous CABG Culprit vessel not identified Culprit vessel too small by extreme tortuosity and /or	Radial access to perform coronary angiography and PPCI (if clinically indicated) (n = 77)	Femoral access to perform coronary angiography and PPCI (if clinically indicated) (n = 72)	In-hospital 6 months (angiogram results) 9 months	All-cause mortality MI Repeat n Angiographic procedural success Hospital stay Fluoroscopy time Total radiographic used in PPCI procedure (see below for definitions)	None stated

59:26-33 (2003)		iliac artery and enlarged aortic arch PCI Operator expertise Not stated	artery or of smaller vessel (< 2.5 mm diameter by visual estimate) Demographics and baseline characteristics see below Drug therapy Heparin given after arterial puncture (men; 6000 units, women; 5000 units). Any fibrinolytic agents were not given before or after PPCI. GP IIb/IIIa inhibitors were not given as not licensed in Japan. All patients received stents. Once daily aspirin (162 mg or more) and ticlopidine (200 mg) were started as soon as possible after stent implantation and continued for > 4 weeks					

Baseline characteristics

	Radial (n = 77)	Femoral (n = 72)	p value
Male, n(%)	62(80.5)	59(81.9)	0.824
Age, mean(SD)	66(12)	67(10)	0.872
Diabetes, n(%)	19(24.7)	19(26.4)	0.810
Hypertension, n(%)	38(49.4)	38(52.8)	0.676
Hyperlipidemia, n(%)	21(27.3)	17(23.6)	0.608
Smoking, n(%)	30(39.0)	39(54.2)	0.063

Prior MI, n(%)	5(6.5)	6(8.3)	0.668
Cerebrovascular disease, n(%)	2(2.6)	6(8.3)	0.121
Killip classification, n(%)			0.222
• 1	48(62.3)	44(61.1)	
• 2	16(20.8)	20(27.8)	
• 3	11(14.3)	4(5.6)	
• 4	2(2.6)	4(5.6)	
Symptom onset to arrival (hr), mean(%)	3.1(2.4)	3.3(2.8)	0.670
Number of diseased arteries, n(%)			0.538
• Single	57(74.0)	48(66.7)	
• Double	14(18.2)	15(20.8)	
• Triple	6(7.8)	9(12.5)	
Culprit artery, n(%)			0.918
• Left anterior descending artery	37(48.1)	37(51.4)	
• Left circumflex	9(11.7)	6(8.3)	
• Right coronary artery	29(37.7)	27(37.5)	
• Left anterior descending artery	2(2.6)	2(2.8)	
Initial TIMI flow			0.492
• 0	52(76.6)	56(77.8)	
• 1	4(5.2)	7(9.7)	
• 2	7(9.1)	6(8.3)	
• 3	7(9.1)	3(4.2)	
Absence of collateral	52(67.5)	50(69.4)	0.802
Left ventricular ejection fraction <0.40, n(%)	3(3.9)	6(8.3)	0.256
Left ventricular end-diastolic Pressure (mm Hg), mean (SD)	25(9)	21(9)	0.016
TIMI; thrombolysis in mycocardial			

infarction

Comparison of operation data between radial versus femoral groups

	Radial group (n = 77)	**Femoral group (n = 72)**	**p value**
IABP support, n(%)	7(9.1)	7(9.7)	0.895
Temporal pacing, n(%)	4(5.2)	6(8.3)	0.444
Guideline catheters used, n(SD)	1.1(0.4)	1.1(0.3)	0.307
Fluoroscopy time (min), mean(SD)	15.1(7.6)	16.1(7.9)	0.500
Total procedure time (min), mean (SD)	44(18)	51(21)	0.033
Onset of the end of PPCI (hr), mean(SD)	4.3(2.2)	4.7(3.0)	0.366
Total amount of radiographic contrast media used (ml), mean(SD)	180(61)	186(66)	0.579
Stent diameter (mm), mean(SD)	3.3(0.4)	3.2(0.4)	0.650
Stents given, n(%)	77(100)	72(100)	
Number of stents, n(SD)	1.4(0.6)	1.3(0.6)	0.760
Total stent length (mm), mean(SD)	19.8(8.0)	19.4(7.3)	0.763
Final TIMI flow, n(%)			0.624
• 0	1(1.3)	0	
• 1	0	0	
• 2	2(2.6)	2(2.8)	
• 3	74(96.1)	70(97.2)	
Reference vessel diameter (mm), mean(SD)			
• Pre	2.99(0.87)	3.10(0.74)	0.797
• Post	3.18(0.55)	3.25(0.55)	0.826
Minimum lumen diameter (mm), mean (SD) post	3.11(0.85)	3.10(0.50)	0.249
Post diameter stenosis, %(SD)	7.3(11.6)	6.6(9.1)	0.358
Peak CK (IU/l), mean (SD)	3170(2192)	3256(2123)	0.807

Peak CRP(mg/d), mean(SD)	3.6(4.0)	4.2(4.6)	0.448
Success of procedure, %	96.1	97.1	0.939
IABP; Intra-aortic balloon pump, CRP; C-reactive protein, CK; creatine kinase			

Definitions:

- Procedure times: Time from entry of patient into the catheterisation laboratory to arterial sheath removal within the laboratory in patients of the radial group and that to the removal of catheters from the arterial sheath in those of the femoral group
- Angiographic procedural success: Achievement of TIMI grade 3 flow at end of PPCI
- Restenosis: increase in % diameter stenosis to ≥ 50%
- Major bleeding: bleeding requiring blood transfusion and/or surgical repair or cerebral bleeding

Effect size

In-hospital

Outcome	**Radial**	**Femoral**	**p value**
N	77	72	
All-cause mortality, n(%)	4(5.2)	6(8.3)	0.444
Reinfarction, n	0	0	
Repeat revascularisation, n(%)	0	0	
Crossover to opposite arm, n(%)	0	1(1.5)	0.300
Major bleeding, n(%)	0	2(3.0)	0.141
Excluding patients with in-hospital death			
N	73	66	
Hospital stay, day(SD)	5.7(4.9)	7.4(0.95)	0.204
Success at day 3 discharge, n(%)	43(58.9)	32(48.5)	0.218
6 month follow-up angiogram			
N	44	43	
Reference vessel diameter (mm), mean(SD)	3.17(0.61)	3.08(0.53)	0.480
Minimum lumen diameter (mm), mean(SD)	2.19(0.76)	1.94(0.92)	0.189

Diameter stenosis, %(SD)	31(21)	39(27)	0.153
Binary restenosis, n(%)	13(29.5)	14(33.3)	0.705
9 month follow-up			
N	73	66	
All-cause mortality, n(%)	0	1(1.5)	0.629
MI, n(%)	2(2.7)	1(1.5)	0.291
Repeat revascularisation, n(%)	13(17.8)	15(22.7)	0.351

Table 47: Brasselet 2007[14]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Brasselet C, Tassan S, Nazeyrollas P, Hamon M, Metz D. Randomised comparison of femoral versus radial approach for percutaneous coronary intervention using abciximab in acute myocardial infarction: results of the FARMI trial. Heart. 2007; 93(12):1556-1561.	Design RCT; recruited either from the emergency unit of institution, mobile intensive care units, or referred from other hospitals to institution for emergent PCI, French study. Enrolment Jan 2004 to Sept 2005 Randomisation Not detailed Allocation	n = 114 PCI done in all patients Drop outs None Crossover Radial group; 7 (12%) required conversion to femoral access despite primary arterial cannulation success.	Inclusion criteria • Acute coronary syndrome with ST segment elevation associated with sustained chest pain • Recruited either from the emergency unit of institution, mobile intensive care units, or referred from other hospitals to institution for emergent PCI. • Emergent PCIs were defined as primary, rescue or facilitated PCI as follows: PPCI was defined as mechanical coronary recanalisation without previous thrombolysis or pretreatment by glycoprotein IIb/IIIa (GpIIb/IIIa) inhibitors; rescue PCI was defined as mechanical coronary recanalisation when thrombolytic treatment had failed; facilitated PCI was defined as mechanical coronary recanalisation after successful thrombolytic treatment, assessed by clinical and electrocardiographic criteria	Radial access to perform coronary angiography and PCI (if clinically indicated) (n = 57)	Femoral access to perform coronary angiography and PCI (if clinically indicated) (n = 57)	In-hospital	All-cause mortality Major bleeding Minor bleeding Angiographic procedural success, Fluoroscopy time n = 114	None stated

	concealment Not detailed Blinding Patients and investigator s were not masked to treatment allocation. All other outcomes were as reported by the investigators. ITT analysis Yes	Most radial approach failures resulted from technical difficulties (ie, inability to selectively catheterise the coronary ostia, anatomical variations of aortic roots, painful brachial artery loops Operator expertise Not stated	Exclusion criteria • Haemodynamic instability (ie, Killip state > 2 or cardiogenic shock) • Need for an intra-aortic balloon pump or temporary pacemaker • History of a coronary artery bypass graft • Intolerance to abciximab Demographics and baseline characteristics see below Drug therapy Before PCI, patients were pretreated by either an intravenous bolus of heparin as follows: unfractionated heparin 50 IU/kg with an upper limit of 4000 IU in patients > 75 years old, or low molecular weight heparin (enoxaparin) 30 mg intravenously and 1 mg/kg subcutaneously in patients aged > 75 years, and a bolus of aspirin (250 mg intravenously). This protocol was used irrespective of arterial access since it was started by emergency units, mobile intensive care units or hospitals referring patients to institution for emergent PCI. When complementary PCI was required, abciximab was conventionally given (ie, a 0.25 mg/kg bolus followed by a 0.125 mg/kg/min infusion during 12 hours). After completion of PCI, subcutaneous enoxaparin (100 IU/kg) was injected twice a day at the most during the first 72 hours, if necessary. All patients received oral clopidogrel (300 mg), followed by 75 mg daily for 1 year, plus 75–300 mg/day oral						

	aspirin.		
Demographics and baseline characteristics			
Characteristics	**Radial (n = 57)**	**Femoral (n = 57)**	**p value**
Age (years), mean(SD)	60(12)	58(13)	0.27
Men, n(%)	49(86.0)	47(82.5)	0.80
Diabetes, n(%)	12(21.1)	9(15.8)	0.48
Hypertension, n(%)	30(52.6)	17(29.8)	0.01
Current smoker, n(%)	42(73.7)	45(78.9)	0.66
Hypercholesterolaemia, n(%)	28(49.1)	22(38.6)	0.26
Systolic blood pressure (mm Hg), mean(SD)	123(21)	123(25)	0.93
Delay: pain onset-cath-lab (min), mean(SD)	409(305)	358(14)	0.33
LVEF (%), mean(SD)	46(9)	49(11)	0.18
Myocardial infarction topography, n(%)			
• Anterior	- 31(54.4)	26(45.6)	5.3
• Posterior	23(40.4)	27(47.4)	
• Lateral	3(5.3)	5(8.8)	
Angiographic and procedural characteristics			
Diffusion of the coronary artery disease			
• One-vessel disease, n(%)	27(47.4)	30(52.6)	
• Two-vessel disease, n(%)	16(28.1)	20(35.1)	0.22
• Three-vessel disease, n(%)	14(24.6)	7(12.3)	
Target lesion, n(%)			
• Left anterior descending coronary	29(50.9)	26(45.6)	
• Left circumflex	8(14.0)	8(14.0)	0.83
• Right coronary	20(35.1)	23(40.4)	
Pre-PCI TIMI flow grade, n(%)			
• 0	27(47.4)	31(54.4)	

• 1	5(8.8)	5(8.8)	0.87
• 2	11(19.3)	9(15.8)	
• 3	14(24.6)	12(21.1)	
Coronary angiography duration (min), mean(SD)	17(8)	13(6)	< 0.01
Crossover, n(%)	7(12.3)	1(1.8)	0.03
Indication of PCI, n(%)			
Primary PCI	26(45.6)	32(56.1)	
Rescue PCI	28(49.1)	20(35.1)	0.65
Facilitated PCI	3(5.3)	5(8.8)	
Stents (n), mean(SD)	1.15(0.36)	1.28(0.61)	0.22
Direct stent implantation, n(%)	29(50.9)	27(47.4)	0.87
Stent with predilatation, n (%)	25(43.9)	27(47.4)	
Angiographic success of PCI, n(%)	52(91.2)	55(96.5)	0.43
Duration of PCI (min), mean(SD)	28(14)	26(18)	0.72
Delay: pain onset to TIMI 3 flow (min), mean(SD)	450(46)	381(31)	0.22
Contrast medium for PCI (ml), mean(SD)	97(57)	91(47)	0.45
Overall fluoroscopy duration (min), mean(SD)	13(9)	8(6)	< 0.01
Definitions of outcomes Thrombolysis in myocardial infarction (TIMI) major bleeding; Heamoglobin drop of > 50 g/l, or intracranial haemorrhage or cardiac tamponade Thrombolysis in myocardial infarction (TIMI) major bleeding; Heamoglobin drop of > 30 g/l but < 50 g/l, with bleeding from a known sight or spontaneous gross haematuria, haemoptysis or haematemesis Groin haematoma: Local induration of > 4 cm diameter Ecchymosis: Cutaneous bruise or induration of > 4 cm diameter or both			
Effect size			
Outcome	**Radial (n = 57)**	**Femoral (n = 57)**	**p value**

In-hospital all-cause mortality, n(%)	3(5.3)	3(5.3)	NS
Ischaemic complication due to in-stent thrombosis, n(%)	4(7.0)	4(7.0)	NS
Duration of hospitalisation (days), mean(SD) 7.5(0.4) 0.59	7.2(0.5)	7.5(0.4)	NS
TIMI major bleeding, n(%)	3(5.3)	3(5.3)	NS
TIMI minor bleeding, n(%)	0(0)	1(1.8)	NS
Haematoma	2(3.5)	11(19.3)	0.05
Ecchymosis	6(10.5)	9(15.8)	NS
Transfusion, n(%)	1(1.8)	0(0)	NS
NS; not significant			

G.4 Thrombus extraction during PPCI

Table 48: AIMI 2006[2]

Reference	Study type	Number of patients	Intervention	Outcome measures	Source of funding
Ali, Cox, Dib.et al. Rheolytic thrombectomy with percutaneous coronary intervention for infarct size reduction in acute myocardial infarction. Journal of the American college of Cardiology. Vol. 48, No. 2. 2006	Prospective multicentre RCT US and Canada 2001–2004	n = 480 Timing of randomisation: after diagnostic angiography confirmed vessel size > 2.0 mm **Length of follow-up**: 30 days	Mechanical thrombus extraction; anjojet rheolytic thrombectomy as an adjunct to conventional PCI or to conventional PCI alone Inclusion: > 18 years of age; anterior MI (new ST-segment elevation of > 1 mm in at least 2 contiguous leads within V1 to V6) or large inferior MI (new ST-segment elevation of >1 mm in 2 contiguous leads of II, III, and a VF); presented within 12h symptoms onset; and reference coronary artery >2.0 mm in diameter Exclusion: known prior ejection fraction <35%, cardiogenic shock (systolic blood pressure <80 mmHg and requiring inotropic support), contraindication to treatment with GP IIb/IIIas, major surgery in preceding 6 weeks, or history of stroke within 30 days or any history of haemorrhagic stroke	Primary end point infarct size. 30-day MACE (death, new Q-wave MI, emergency CABG, target vessel revascularisation, stroke or stent thrombosis)	Millennium Pharmaceuticals (eptibatide)

Baseline characteristics:

Characteristic	Mechanical thrombus extraction (n = 240) (%)	No thrombectomy (n = 240) (%)	p value
Age (years), mean	60	59.9	0.92
Male, n (%)	182 (75.8)	178 (74.2)	0.75
Diabetes, n (%)s	40 (16.7)	28 (15.8)	0.81
Hypertension (requiring medication, n (%)	103 (42.9)	101 (42.1)	0.93
Dyslipidemia requiring medication, n (%)	53 (22.1)	61 (25.4)	0.52
Smoker in past year, n (%)	106 (44.2)	108 (45.0)	0.71

Prior coronary artery disease, n (%)	42 (17.5)	33 (13.8)	0.26
Prior stroke, n (%)	7 (2.9)	10 (4.2)	0.62
Rescue after failed fibrinolysis, n (%)	34 (14.2)	32 (13.3)	0.90
Prior percutaneous intervention in target vessel	10 (4.2)	8 (3.3)	0.81
Time from symptom onset to emergency departmentt (h), mean (SD)	2.4 (3.3)	2.5 (3.2)	0.76
Time from emergency department to randomisation (h), mean (SD)	2.7 (4.3)	2.5 (3.2)	0.61
Total time to procedure (min), mean (SD)	75.4 (30.9)	59.6 (26.8)	< 0.001
Before or during the procedure	228 (95.0)	226 (94.2)	0.84
Number of major coronary arteries with ≥50% stenosis, n (%)			
1	112 (46.7)	116 (48.3)	
2	86 (35.8)	78 (32.5)	
3	39 (16.3)	44 (18.3)	
Stents, n (%)			
None	16 (6.3)	13 (5.3)	
1	154 (64.5)	173 (72.1)	
2	57 (23.8)	45 (18.8)	
3 or more	13 (5.4)	9 (3.8)	
Crossover to RT treatment, n (%)		6 (0.25)	

Angiographic inclusion criteria: Did not require angiographically visible thrombus.

Concomitant therapy: All patients received 325 mg oral aspirin, clopidogrel 300 mg loading dose, clopidogrel 75 mg daily (cont. 4 weeks after) (ticlopidine 500mg loading dose and 250 mg twice a day dose given in event of intolerance to clopidogrel), unfractionated heparin during procedure to achieve activated clotting time >250 s. Use of beta-adrenergic blockers, nitroglycerine, and ACE-I before and after procedure at discretion of individual physician.

Results:	Mechanical thrombus extraction, n = 240	No thrombectomy, n = 240	p value
MACE, n (%)	16 (6.7)	4 (1.7)	0.01
All-cause mortality, n (%)	11 (4.6)	2 (0.8)	0.02
Q-wave MI, n (%)	0	0	-
Stroke, n (%)	4 (1.7)	2 (0.8)	0.69
Emergent CABG, n (%)	0	0	-

TLR/SAT, n (%)	5 (2.1)	1 (0.4)	0.22
Bleeding: requiring transfusion, n (%)	16 (6.7)	17 (7/1)	1.00
Bleeding: GI/GU, n (%)	11 (4.6)	15 (6.3)	0.55
Bleeding: retroperitoneal, n (%)	3 (1.3)	6 (2.5)	0.50
Bleeding: pericardial haemorrhage/tamponade, n (%)	2 (0.8)	0	0.50
Cardiogenic shock, post-procedure, n (%)	0	1 (0.4)	1.00
Ventricular fibrillation: pre-procedure, n (%)	12 (5.0)	5 (2.1)	0.34
Ventricular fibrillation: during/post-procedure, n (%)	7 (2.9)	3 (1.3)	
Ventricular tachycardia: non-sustained, n (%)	28 (11.7)	19 (7.9)	0.22
Ventricular tachycardia: sustained, n (%)	3 (1.3)	4 (1.7)	1.00

Table 49: Antoniucci 2004[3]

Reference	Study type	Number of patients	Intervention	Outcome measures	Source of funding
Antoniucci, Valenti, et al. Comparison of rheolytic thrombectomy before direct infart artery stenting versus direct stenting alone in patients undergoing Percutaneous coronary intervention for acute myocardial infarction. The American Journal of Cardiology. Vol. 93, 2004 15; 93(8):1033-5.	RCT Data collected November 2002 – June 2003 Italy	n = 100 Sample size calculation to detect 80% power and type 1 error of 0.05, 50 people in each group. Timing of randomisation: after angiography **Length of follow up:** 1 month	Mechanical thrombus extraction; anjojet rheolytic thrombectomy as an adjunct to conventional PCI or to conventional PCI alone. Inclusion Chest pain > 30 min and ST-segment elevation of ≥ 1 mm in at least 2 contiguous leads Exclusion Prior MI, administration of FT therapy, LBBB or ventricular pacing on baseline ECG preventing analysis of ST-segment changes, IRA diameter < 2.5 mm, inability to give informed consent	All-cause mortality Reinfarction Stroke Target vessel revascularisation Major bleeding	Not specified

Baseline characteristics:	Thrombectomy (n = 50)	No thrombectomy (n = 50)	p value
Age (years), mean (SD)	63 (13)	66 (12)	0.251
Men, n (%)	41 (82)	39 (78%)	0.617
Current smoker, n (%)	19 (38%)	14 (28)	0.288
Hypertension, n (%)	18 (36)	19 (38)	0.836
Cholesterolemia > 200 mg/dl, n (%)	23 (46)	24 (48)	0.841
Diabetes mellitus, n (%)	9 (18)	8 (16)	0.790
Angina pectoris, n (%)	10 (20)	4 (8)	0.084
Anterior wall acute myocardial infarction, n (%)	17 (34)	23 (46)	0.221
Cardiogenic shock, n (%)	3 (6)	6 (12)	0.295
Infarct coronary artery: left anterior descending, n (%)	17 (34)	23 (46)	
Infarct coronary artery: right, n (%)	26 (52)	21 (42)	
Infarct coronary artery: circumflex, n (%)	7 (14)	6 (12)	
Multivessel coronary disease, n (%)	15 (30)	20 (40)	0.295
Preprocedural TIMI grade flow 0–1, n (%)	38 (76)	40 (80)	0.629
Time-to-treatment, h, mean (SD)	3.9 (2)	4.4 (2.8)	0.295
Infarct artery stenting, n (%)	49 (98)	49 (98)	1.000
Direct stenting, n (%)	47 (94)	41 (82)	0.065
Multiple stents, n (%)	12 (24)	13 (26)	0.817
Stent length (mm), mean (SD)	20.7 (9.2)	21.1 (20.1)	0.848
Rheolytic thrombectomy, n (%)	48 (96)	4 (8)	< 0.001
Abciximab administration, n (%)	49 (98)	49 (98)	1.000
Intra-aortic balloon counterpulsation	3 (6)	5 (10)	0.461
Angiographic inclusion criteria:			

Concomitant therapy: All patients received abciximab if not contraindicated before the procedure to achieve activated clotting time of 200 to 300 seconds. Routine aspirin (325 mg/day indefinitely) and ticlopidine (500mg/day for 1 month) or clopidogrel (75 mg/day for 1 month).

Results:			
Outcome	**Mechanical thrombus extraction (n = 50)**	**No thrombectomy (n =50)**	**p Value**
All-cause mortality, n	0	0	
Reinfarction, n	0	0	
Target vessel revascularisation, n	0	0	
Major bleeding requiring blood transfusion, n	0	1	0.315
Disabling stroke, n	1 (2)	0	0.315

Table 50: Beran 2002[9]

Reference	Study	Number of patients	Patient characteristics	Intervention	Comparison	Outcomes	Source of funding
Beran G, Lang I, Schreiber W, Denk S, Stefenelli T, Syeda B, Maurer G, Glogar D, Siostrzonek P. Intracoronary thrombectomy with the X-sizer catheter system improves epicardial flow and accelerates ST-segment resolution in patients with acute coronary syndrome: a prospective, randomized,	RCT Austria **Randomisation** 1:1 ratio **Allocation concealment** Not stated **Blinding** Investigators blinded to outcome	n = 66 Initially 66 patients were randomised, and 5 were subsequently excluded Length of follow-up: 30 days.	**Inclusion criteria** Chest pain for > 30 minutes and ST-segment elevation > 1 mm in 2 or more contiguous leads on the 12-lead ECG, rescue PCI was defined as PCI within 12 hours after failed systemic fibrinolysis. patients with unstable angina included if presented with recurrent chest pain at rest associated with ischaemic ST-segment or T-wave changes **Exclusion criteria** Not stated Demographics and baseline characteristics see below **Drug therapy**	n = 30 Mechanical thrombus extraction; X-sizer catheter system (EndiCOR Medical Inc) consists of a dual-lumen catheter shaft connected to a handheld control module.3 Two catheter sizes, 1.5 mm (7F compatible) and 2-mm (8F compatible)	n = 31 Standard PPCI	All-cause mortality Target vessel revascularisation	Not stated

controlled study. Circulation. 2002 May 21; 105(20):2355-60.	Patients with STEMI received unfractionated heparin, acetylsalicylic acid (ASA), beta blockers, and analgesics unless contraindicated, at operators discretion; patients with unstable angina were pretreated with low-molecular-weight heparin, ASA, and nitroglycerin		
Baseline characteristics	**No thrombectomy (n = 31)**	**Mechanical thrombus extraction (n = 30)**	**p value**
Age (years), mean (SD)	53.9 (10.0)	55.0 (9.9)	NS
Male, n (%)	24 (77)	22 (73)	NS
STEMI, %	74	77	NS
Risk factors, %			
• Diabetes	13	17	NS
• Hypertension	36	53	
• Rescue PCI	10	23	
• Current smoking	55	57	
Baseline angiographic and procedural data			
Target vessel, %			
• Left anterior descending coronary artery	10	9	NS
• Left circumflex coronary artery	9	3	
• Right coronary artery	12	18	
Results			
One month	**No thrombectomy (n = 31)**	**Mechanical thrombus extraction (n = 30)**	
All-cause mortality, n	1	2	
Target vessel revascularisation, n	1	0	

Table 51: Bulum 2012[17]

Reference	Study	Number of patients	Patient characteristics	Intervention	Comparison	Length of outcome	Outcomes	Source
Bulum J, Ernst A, Strozzi M. The impact of successful manual thrombus aspiration on in-stent restenosis after primary PCI: angiographic and clinical follow-up. Coronary Artery Disease. 2012; 23:487-491.	RCT Croatia **Randomisation** 1:1 ratio; no other details were reported **Allocation concealment** Not reported **Blinding** Not reported **Intention to treat** Yes	n = 60	Inclusion criteria Symptoms suggesting acute myocardial ischaemia >20 minutes, the onset of symptoms <12 hours previously, and ST-segment elevation of > 0.1 mV in 2 or more contiguous ECG leads. Exclusion criteria Rescue PCI after failed fibrinolysis, cardiogenic shock, triple-vessel disease, significant left main stem stenosis, previous PCI of an infarct-related artery, previous coronary artery bypass grafting, and known existence of a concomitant disease with life expectancy less than 6 months. Demographics and baseline characteristics see below Drug therapy Before PPCI Aspirin (300 mg) and clopidogrel (600 mg), weight adjusted dose of unfractionated heparin, and glycoprotein IIb/IIIa inhibitor (eptifibatide) at the discretion of the operator. After PPCI Beta-blockers, high-dose lipid-lowering agents, angiostensin- converting enzyme inhibitors or angiostensin-II receptor	Thrombus aspiration with Export Aspiration catheter	Standard PPCI	6 months	Primary Referent vessel diameter, minimal lumen diameter (MLD), lesion length, and perentage diameter stenosis (acute gain, and late lumen loss) Secondary Incidence of major adverse cardiocerebro vascular events (death, reinfarction, stroke, and the need for TLR)	None stated

		antagonists, and w-3-acid ethyl esters.	
Demographics and baseline characteristics:			
Characteristics	**Thrombus aspiration PPCI (n = 30)**	**Standard PPCI (n = 30)**	
Age (years), mean (SD)	54.3 (8.6)	58.5 (9.7)	
Men, n (%)	25 (83)	22 (73.3)	
Hypertension, n (%)	12 (40)	13 (43.3)	
Diabetes, n (%)	3 (10)	3 (10)	
Current smoker, n (%)	16 (53.3)	15 (50)	
Hyperlipdaemia, n (%)	25 (83.3)	26 (86.7)	
Family history of CAD, n (%)	14 (46.7)	11 (36.7)	
Angiographic data and procedural results			
Number of stents			
1, n (%)	19(63.6)	18(60.0)	
2, n (%)	9(30.0)	9(30.0)	
3, n (%)	1(3.9)	3(10.0)	
4, n (%)	1(3.9)	0	
Left anterior descending, n (%)	14 (46.7)	11 (36.7)	
Left circumflex, n (%)	4 (13.3)	8 (26.7)	
Right coronary, n (%)	12 (40.0)	11 (36.7)	
Results at 6 month follow-up			
	Thrombus aspiration PPCI (n = 30)	**Standard PPCI (n = 30)**	**p value**
All-cause mortality, n	0	0	1
Reinfarction, n	0	0	1
Target vessel revascularisation, n	8	5	0.347

Table 52: EXPORT 2008[25]

Reference	Study type	Number of patients	Intervention	Length of follow-up	Outcome measures	Source of funding
Chevalier B, Gilard M, et al. Systematic primary aspiration in acute myocardial Percutaneous intervention: a multicentre randomised controlled trial of the export aspiration catheter. EuroIntervention. 2008: 222-228.	RCT France, Austria, Italy, India Randomised using computerised telephone system.	n = 249 Inclusion Consecutive patients > 18 years old, with 2\mm or more of ST-segment elevation in 2 or more contiguous leads, with visual reference vessel diameter ≥\2.5 mm, and TIMI flow 0 or 1 before placing the wire in the infarct-related artery Exclusion Cardiogenic shock, cardiac arrest at any time before the intervention, pre-catheterisation with lytic agents, with GPI IIb/IIIa, or with pacemakers; a current medical condition with expected survival less than a year, and current participation in other investigations Data collected May 2005 – April 2007	Thrombus aspiration using export aspiration catheter by stenting versus conventional stenting without thrombectomy	30 days	All-cause mortality Myocardial reinfarction	Not stated

Baseline characteristics:

	No thrombectomy (n = 129)	Thrombus aspiration PPCI (n = 120)	p value
Age (years), (SD)	61.2 (12.9)	59.2 (12.8)	0.18
Male (%)	81.4	80.8	0.91
Prior Q-wave MI (% patients)	8.5	9.2	0.86
Prior non-Q-wave MI (%)	2.3	1.7	1.00
Prior CABG (%)	0.0	0.8	0.48
Prior non-target vessel PCI (%)	2.3	3.3	0.71
Prior target vessel PCI (%)	3.1	5.0	0.53
Smoking (%)	35.7	42.5	0.18
Diabetes (%)	13.2	16.7	0.44

NIDDM	94.1	65.0	0.05
IDDM	5.9	35.0	
Hypertension (%)	44.2	41.7	0.69
Hypercholesterolaemia (%)	41.9	36.7	0.40
Family history of cardiovascular disease (%)	25.6	32.5	0.23
Killip class ≥ 2 (% patients)	10.9	11.6	0.69
Symptom onset to randomisation, min Mean Median (range)	 271.4 (197.6 219 (145–362.5)	 321.7 (413.5 225 (149–333)	 0.53

Angiographic inclusion criteria: The choice of PCI including stent treatment was at the investigator's discretion, with permissible options including predilatation followed by stention, direct stenting, and stenting with postdilatation.

Concomitant therapy: Aspirin, heparin, clopidogrel, and GPI IIb/IIIa inhibitors at investigator's discretion, and administered according to standard hospital procedure.

Results

	No thrombectomy (n = 129)	**Thrombus aspiration PPCI (n = 120)**	**p value**
Predilatation performed (%)	55.8	28.3	< 0.001
Postdilatation performed (%)	18.6	8.3	0.02
Number of stents used, mean (SD)	1.17 (0.58)	1.28 (0.58)	0.08
Procedure time, mean (SD)	34.5 (21.5)	36.7 (18.0)	0.08
Median (IQR)	30 (20–45)	32 (25–45)	
Bailout performed (% patients)	14.7	5.8	0.02
No thrombectomy (n = 129)	**Thrombus aspiration PPCI (n = 120)**	57.1 (4)	
Rescue distal protection	0	0	
Rescue aspirations, , % (n)	42.1 (8)	42.9 (3)	
30-day cardiac mortality, n	5	3	
Myocardial reinfarction, n	1	2	

Table 53: De Luca 2006[30]

Reference	Study type	Number of patients	Intervention	Length of follow-up	Outcome measures	Source of funding
De Luca L, Sardella G, Davidson C, et al. Impact of intracoronary aspiration thrombectomy during primary angioplasty on left ventricular remodelling in patients with anterior ST-elevation myocardial infarction. Heart. 2006, 92: 951-957	RCT Italy	n = 76 Inclusion >18 years with anterior STEMI and identifiable thrombus on IRA at coronary angiography. Exclusion Coronary bypass grafting, 3 vessel coronary artery disease, severe valvar heart disease, TIMI grade 2 or 3 flow at time of initial angiography, or unsuccessful PCI defined as no anterograde flow or >50% residual stenosis in the IRA.	Thrombus aspiration with Diver CE aspiration thrombectomy catheter (Invatex, Brescia, Italy).	6 months	All-cause mortality Chronic heart failure Myocardial infarction	Not stated

Baseline characteristics:

	No thrombectomy (n = 38)	Thrombus aspiration PPCI (n = 38)
Age (years)	64.6 (12.5)	66.7 (14.1)
Men, n (%)	21 (55.3)	27 (71)
Hypertension, n (%)	19 (50)	15 (39.5)
Diabetes, n (%)	7 (18.4)	9 (23.7)
Smoking, n (%)	10 (26.3)	7 (18.4)
Obesity, n (%)	1 (2.6)	3 (7.9)

Family history of CAD, n (%)	14 (36.8)	5 (13.1)*
Cholesterol (mmol/l), n (%)	4.32 (0.39)	4.17 (0.28)*
Triglycerides (mmol/l), n (%)	1.41 (0.29)	1.37 (0.44)
Renal failure, n (%)	3 (7.9)	5 (13.1)
Killip class III, n (%)	11 (28.9)	8 (21)
Previous PCI, n (%)	4 (10.5)	7 (18.4)
Symptoms to balloon (h), n (%)	7.6 (1.8)	7.2 (1.9)
Medication at follow-up: ACE inhibitors/ARBs, n (%) Aldosterone blockers, n (%) Beta-blockers, n (%) Statins, n (%) Aspirin, n (%)	 31 (81.6) 22 (57.9) 27 (71) 36 (94.7) 37 (97.4)	 36 (94.7) 19 (50) 31 (81.6) 32 (84.2) 37 (97.4)
Data are mean (SD) or number (%) *p < 0.05 between conventional and thrombectomy groups		

Angiographic inclusion criteria:

Concomitant therapy: Aspirin 300 mg orally and heparin 8000 IU intravenously before the procedure and with abciximab as a 0.25 mg/kg bolus and 0.125 ug/kg/min intravenous infusion immediately before the revascularisation and continued for 12 hours. Heparin for 48 hours, aspirin 100mg/day, and ticlopidine (250 mg orally twice a day for at least 4 weeks) or clopidogrel (loading does of 300 mg followed by 75 mg/day for at least 4 weeks. Other adjunctive pharmacotherapy was administered at the discretion of the operator.

Results:

6 months	**No thrombectomy (n = 38)**	**Thrombus aspiration PPCI (n = 38)**	
Mortality, n	2	0	
New onset MI, n	0	1	
Hospitalisation for chronic heart failure, n	3	2	
MACE, n	4	3	

Table 54: DEAR-MI 2006[102]

Reference	Study type	Number of patients	Intervention	Length of follow-up	Outcome measures	Source of funding
Silva-Orrego P, Colombo P, Bigi R, Thrombus aspiration before primary angioplasty improves myocardial reperfusion in acute myocardial infarction. The DEAR-MI (Dethrombosis to enhance acute reperfusion in myocardial infarction) study. Journal of the American College of Cardiology, Vol. 48, No. 8, 2006.	RCT Italy Data collected March 2004 to June 2005 12% dropout due to protocol exclusions	n = 148 Inclusion: continuous chest pain ≥ 30 min, ST-segment elevation > 0.1mV (0.2 mV in case of anterior leads) in ≥3 contiguous leads on 12-lead ECG, and technical feasibility for primary angioplasty independently of initial TIMI flow or angiographic evidence of intraluminal thrombus in the culprit artery. Exclusion: cardiogenic shock, previous myocardial infarction or CABG, bundle branch block or pacemaker induced rhythm on admission ECG, and contraindication to GP IIb/IIIa inhibitors.	Standard PPCI with stenting and abciximab versus thrombus aspiration using Pronto extraction catheter (Vasc.solutions, Minneapolis, Minnesota) plus standard PPCI.	30-days	Mortality, myocardial reinfarction, left ventricular failure, Target vessel revascularisation.	Not stated

Baseline characteristics:

	Thrombus aspiration PPCI (n = 74)	No thrombectomy (n = 74)	p Value
Age, years (SD)	57.3 (13)	58.9 (14)	0.472
Male, n (%)	62 (84)	56 (76)	0.314
Diabetes, n (%)	16 (21)	11 (15)	0.465
Hypertension, n (%)	28 (37)	32 (46)	0.349
Dyslipidemia, n (%)	26 (34)	18 (25)	0.309
Smoking, n (%)	38 (54)	43 (60)	0.571
Killip class >1, n (%)	8 (11)	4 (5)	0.297
Anterior infarction, n (%)	32 (42)	38 (51)	0.355

Ejection fraction, n (%)	53 (7)	51 (9)	0.133
Ischaemic time, min (SD)	206 (115)	199 (124)	0.722
Target vessel			
Left anterior descending coronary artery, n (%)	32 (43)	38 (51)	0.420
Left circumflex coronary artery, n (%)	7 (10)	10 (14)	0.623
Right coronary artery, n (%)	35 (47)	26 (35)	0.191
CAD extension			
1 vessel, n (%)	36 (49)	36 (49)	0.876
2 vessels, n (%)	23 (31)	24 (32)	0.965
3 vessels, n (%)	15 (20)	14 (19)	0.958
TIMI flow			
0/1, n (%)	60 (81)	54 (73)	0.657
2, n (%)	12 (16)	16 (22)	0.646
3, n (%)	2 (3)	4 (5)	0.822
Glycoprotein IIb/IIIa inhibitors, n (%)	100	100	
Stenting, n (%)	73 (99)	72 (97)	
Direct stenting, n (%)	52 (70)	18 (24)	< 0.0001
Procedural time (min), mean (SD)	57 (19)	53 (21)	0.363

Results:

	Thrombus aspiration, n = 74	**No thrombus aspiration, n = 74**
In-hospital mortality, n	0	0
In-hospital myocardial reinfarction, n	0	0
In-hospital left ventricular failure, n	0	1
In-hospital target vessel revascularisation, n	1	0

Table 55: EXPIRA 2010[96]

Reference	Study	Number of patients and Patient characteristics	Intervention	Comparison	Length of outcome	Outcomes	Source of funding
Sardella G, Mancone M, Canali E, Di RA, Benedetti G, Stio R et al. Impact of thrombectomy with EXPort Catheter in Infarct-Related Artery during Primary Percutaneous Coronary Intervention (EXPIRA Trial) on cardiac death. American Journal of Cardiology. 2010; 106(5):624-629.	RCT Italy **Randomisation** 1:1 manner **Allocation concealment** Not stated **Blinding** Single blind **Intention to treat** Unclear	n = 175 Inclusion criteria First STEMI within 9 h from symptoms onset ischaemic chest pain > 30 min and ST-segment elevation ≥ 2mm in ≥ 2 contiguous electrocardiographic leads, infarct-related artery 2.5 mm diameter, identifiable lesion, thrombus score ≥ 3, TIMI flow grade O to 1, and age > 18 years Exclusion criteria Previous PCI on infarct-related artery, previous CABG, cardiogenic shock, 3-vessel disease, left main disease, severe valvular heart disease, fibrinolysis, fPPCI, contraindication to glycoprotein IIb/IIIa inhibitors administration Demographics and baseline characteristics see below Drug therapy Before PPCI Patients treated with 300 mg aspirin, heparin to maintain clotting time > 250 seconds, abciximab (0.25 mg/kg followed by intravenous infusion at 0.125 microgram/kg/minute) Subsequently patients received heparin for 48 h, aspirin 100 mg/day, clopidogrel (300 mg loading dose, followed by 75 mg/day for ≥ 12 months) Adjunctive therapy at operator discretion; standard therapies after PPCI; beta blockers, lipid lowering drugs, ACE or ARB inhibitors	Thrombus aspiration with Export Medronic PCI (EM-PCI)	Standard PPCI	2 years	All-cause mortality, Myocardial reinfarction, Target vessel revascularisation	None stated

Demographics and baseline characteristics:			
Characteristics	**No thrombectomy (n = 88)**	**Thrombus extraction (n = 87)**	**p value**
Age (years), mean (SD)	64.6 (12.5)	66.7 (14.1)	0.298
Men, n (%)	48.0 (51.1)	57 (64.7)	0.218
Hypertension, n (%)	43 (41.4)	59.0 (67.2)	0.021
Diabetes, n (%)	16.0 (18.4)	21 (23.8)	0.459
Smoking, n (%)	23.0 (26.4)	43.0 (48.8)	0.003
Cholesterol mg/dl), mean (SD)	167 (15)	161 (11)	0.002
Renal failure, n (%)	7 (8.0)	7 (7.9)	1
Killip class III, n (%)	25.0 (28.7)	17.0 (19.3)	0.160
Symptom to balloon (h), mean (SD)	6.1 (1.8)	6.2 (0.9)	0.642
LVEF, n (%)	40.7 (9.3)	42.0 (10.5)	0.192
MV coronary disease, n (%)	16.0 (18.4)	21.0 (23.8)	0.459
Direct stenting, n (%)	2.0 (2.3)	67.0 (76.2)	0.0001
Drug eluting stent, n (%)	53.0 (60.9)	49.0 (55.7)	0.540
Location of infarct –related coronary artery			
Left anterior descending, n (%)	38.0 (43.7)	38.0 (43.2)	1
Left circumflex, n (%)	20.0 (23.0)	22.0 (25.0)	0.859
Right coronary, n (%)	29.0 (33.3)	28.0 (31.8)	0.872
Results at 2 year follow-up			
	Thrombus aspiration PPCI (n = 88)	**No thrombectomy (n = 87)**	**p value**
All-cause mortality, n	0	6	0.0001
Reinfarction , n	0	1	0.999
Target vessel revascularisation, n	4	5	0.651

Table 56: INFUSE-AMI 2012[106]

Reference	Study type	Number of patients	Intervention	Length of follow-up	Outcome measures	Source of funding
Stone G, Maehara A, Witzenbichler R, et al. Intracoronary abciximab and aspiration thrombectomy in patients with large anterior myocardial infarction. The INFUSE-AMI randomised trial. JAMA. 2012; 307 (17): 1817-1826.	RCT USA Multicentre, single-blind Data collected November 2009-December 2011 Powered for infarct size at 30-days	n = 452 Inclusion: >18 years, symptoms consistent with STEMI longer than 30 minutes' duration and 1 mm or greater of ST-segment elevation in 2 or more contiguous leads in V1-V4, or new LBBB, with anticipated symptom onset to device time of 5 hours of less Exclusion: contraindications to study medications or contrast; prior MI, bypass graft surgery or LAD stenting; planned surgery necessitating antiplatelet agent interruption, contraindication to cMRI; known creatine clearance less than 30 mL/min/1.73 m2, dialysis, platelet count less than 100000 or > 7000000 cells/mm3, or haemoglobin level less than 10 g/dL; recent major bleeding, bleeding diathesis, or current warfarin use; history of intracranial disease; ischaemic stroke or transient ischaemic attack within 6 months or any permanent neurologic defect; pre-randomisation cardiogenic shock or cardiopulmonary resuscitation; prior fibrinolysis or IIb/IIIa inhibitor for the present admission; and any comorbid conditions likely to interfere with protocol compliance or associated with less than 1-year survival.	Thrombus aspiration performed with 6 F Export Catheter (Medtronic),PPCI for anterior STEMI, PCI performed using standard techniques with bare metal or drug-eluting stent implantation at operator discretion Patient randomised to either: a) thrombus aspiration followed by intracoronary bolus abciximab, (b) thrombus aspiration without abciximab, (c) intracoronary plus abciximab without aspiration, or (d) no abciximab and no aspiration	30 day	MACE: All-cause mortality Myocardial reinfarction New onset severe heart failure, or rehospitalisation for heart failure. MACCE: all-cause mortality, reinfarction, stroke, or clinically driven Target vessel revascularisation.	Atrium medical

Baseline characteristics:		
	Thrombus aspiration PPCI + no abciximab (n = 111)	**No aspiration PPCI + no abciximab (n = 112)**
Age, median (IQR), years	62.0 (53.0–73.0)	62.5 (52.5–71.0)
Male, n/total (IQR)	85/111 (76.6)	81/112 (72.3)
Body mass index, median (IQR)[a]	26.8 (24.3–30.5)	26.6 (24.0–28.7)
Killip class, n/total (%) I II III	 82/110 (74.5) 13/110 (11.8) 0/110	 90/112 (80.4) 13/112 (11.6) 2/111 (1.8)
Hypertension n/total (%)	39/111 (35.1)	36/112 (32.1)
Hyperlipidemia n/total (%)	18/111 (1632)	14/112 (12.5)
Diabetes mellitus n/total (%)	19/110 (17.3)	8/112 (7.1)
Prior myocardial infarction n/total (%)	1/110 (0.9)	0/112
Prior Percutaneous coronary intervention n/total (%)	3/111 (2.7)	3/112 (2.7)
Cigarette smoking, current n/total (%)	46/109 (42.2)	55/112 (49.1)
Symptom to hospital arrival, median (IQR), min	107.0 (66.5–152.5)	98.0 (67.0–136.0)
Hospital arrival to first device, median (IQR), min [b]	42.0 (30.0–61.0)	46.5 (34.0–70.5)
Symptom onset to first device, median (IQR)	151 (117–205)	160 (126–217)
Infarct artery lesion location[c]: Proximal left anterior descending n/total (%) Mid left anterior descending n/total (%)	 68/111 (61.3) 47/111 (39.6)	 74/112 (66.1) 48/112 (42.9)
Left ventricular ejection fraction, median (IQR), %[d]	40.0 (38.0–50.0)	40.0 (31.0–50.0)
[a] calculated as weight in kilograms divided by height in meters squared [b] Balloon angioplasty, local drug delivery, or aspiration [c] Some patients had both proximal and mid left anterior descending lesions [d] From contrast left venticulography during the index procedure		
Angiographic inclusion criteria: infarct lesion to be located in the proximal or mid LAD with visually assessed TIMI 0–2 flow, and absence of excessive tortuosity, diffuse disease, heavy calcification, or significant left main disease.		
Concomitant therapy: 324 [sic] aspirin orally, or 250 to 500 mg intravenously; clopidogrel, 600 mg, or prasugrel, 60 mg. Patients undergoing PCI received procedural anticoagulation with bivalirudin (intravenous bolus 0.75 mg/kg plus infusion of 1.75 mg/kg per hour, discontinued at procedure end. Following procedure, all patients		

were treated with aspirin indefinitely and with clopidogrel or prasugrel for at least 1 year. Discharge medicines included aspirin in 99% of patients, clopidogrel in 66.4%, prasugrel in 31.8%, statins in 97.7%, beta-blockers in 96.6% and angiotensin-converting enzyme inhibitors or receptor blockers in 94.1%, with no significant differences between the groups.

Results:

30-day outcomes[a]	**Aspiration thrombectomy[c] (n = 229)**	**No thrombectomy[c] (n = 223)**	**p value**
All-cause mortality, n (%)	7 (3.1)	6 (2.7)	0.81
Reinfarction, n (%)	1 (0.5)	2 (0.9)	0.55
New-onset severe heart failure, n (%)	8 (3.5)	9 (4.1)	0.77
Rehospitalisation for heart failure, n (%)	0	2 (0.9)	0.15
Stroke, n (%)	0	1 (0.5)	0.31
Clinically driven total vascular revascularisation, n (%)	1 (0.5)	4 (1.8)	0.17
HORIZONS-AMI major bleeding, n (%)	9 (4.0)	10 (4.6)	0.79
TIMI major bleeding, n (%)	2 (0.9)	4 (1.8)	.40
TIMI minor bleeding, n (%)	1 (0.5)	2 (0.9)	0.55
GUSTO severe bleeding, n (%)	9 (4.0)	10 (4.5)	0.77
GUSTO moderate, n (%)	2 (0.9)	1 (0.5)	0.58
GUSTO mild bleeding, n (%)	1 (0.4)	4 (1.8)	0.17
Any blood product transfusion	2 (0.9)	3 (1.4)	0.64
Thrombocytopenia, in-hospital[d], n/total (%)	1/186 (0.5)	3/189 (1.6)	0.62

[a]Data are Kaplan-Meier estimates

[c]Pooled, either with or without intracoronary abciximab

[d]<100 000 cells/mm3 in patients with a baseline platelet count > 150 000 cells/mm^3 (n = 384)

Table 57: ITTI 2012[75]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Liu CP, Lin MS, Chiu YW, Lee JK, Hsu CN, Hung CS, Kao HL. Additive benefit of glycoprotein IIb/IIIa inhibition and adjunctive thrombus aspiration during primary coronary intervention: results of the Initial Thrombosuction and Tirofiban Infusion (ITTI) trial. International Journal of Cardiology. 2012; 156(2):174-179.	Design RCT (5 hospital centres in Taiwan) Enrolment Not stated Randomisation 2 x 2 factorial design Allocation concealment Not stated Blinding Not stated Sample size calculation Based on previous studies a sample size of 22 patients in each group ware required to achieve the power of 0.80 for the primary end point of MBC 3 rate ITT analysis All randomised patients were included in ITT comparisons of outcome (regardless of whether crossed over)	n = 100 2 x 2 factorial study and 2 2 arms relevant to the review (47 patients) Drop-outs: n = 0 Crossover: n = 2	Inclusion criteria Patients > 18years with STEMI undergoing PPCI within 12 hours of symptom onset Exclusion criteria <18 years cardiogenic shock history of bleeding tendency hepatic or renal insufficiency major operation within 6 weeks contraindication to tirofiban use Demographics and baseline characteristics see below Drug therapy All patients received aspirin (300 mg loading followed by 100 mg daily), and clopidogrel (300 mg loading followed by 75 mg daily) and unfractionated heparin 100 IU /kg before the procedure	Thrombus aspiration with thrombuster device	Standard PPCI	6 months	MACE All-cause mortality Reinfarction Target lesion revascularisation Stroke	Not stated
Demographics and baseline characteristics:								

Characteristics	No thrombectomy (n = 23)	Thrombus extraction (n = 24)
Age, year (SD)	57 (13)	62 (9)
Male, n (%)	20 (87)	21 (87.5)
Smoker, n (%)	13 (56.5)	10 (40)
Hypertension, n (%)	13 (56.5)	14 (58.3)
Diabetes mellitus, n (%)	5 (21.7)	7 (29.2)
Hypercholesteremia, n (%)	7 (30.4)	4 (16.7)
Previous PCI, n (%)	0 (0)	1 (4.2)
Body-mass index, n (%)	25 (2)	25 (3)
Cardiogenic shock, n (%)	2 (8.7)	0 (0)
Killip class III or IV, n (%)	2 (8.7)	0 (0)
Systolic blood pressure (mmHg)	144 (31)	148 (26)
Diatolic blood pressure (mmHg)	82 (18)	83 (18)
Heart rate (bpm), n (%)	85 (24)	80 (13)
Number of disease vessels 1 2 3	 11 (47.8) 6 (26.1) 6 (26.1)	 8 (33.3) 10 (41.7) 6 (25.0)
Infarct related vessel Left anterior descending artery	 12 (52.2)	 15 (62.5)
Results	**No thrombectomy (n = 23)**	**Thrombus extraction (n = 24)**
All-cause mortality (6 months) , n	0	1
Reinfarction (6 months) , n	3	0
Target lesion revascularisation (6 months) , n	3	1
Stroke (6 months) , n	0	1

Table 58: JETSTENT 2010[83]

Reference	Study	Number of patients and Patient characteristics	Intervention	Comparison	Length of outcome	Outcomes	Source of funding
Migliorini, Stabile, Rodriguez et al. Comparison of angioJet rheolytic thrombectomy before direct infarct artery stenting with direct stenting alone in patients with acute myocardial infarction. The JETSTENT Trial. Journal of the American College of Cardiology. 2010: 56(16) 1298-306	RCT (multicentre, international trial) Italy, Germany Poland, Argentina, **Randomisation** Randomised to thrombectomy before direct stenting or direct stenting alone was performed after coronary angiograpy and wiring of the infarct artery. The TIMI study thrombus score was used for the assessment of thrombus dimensions. Patients with angiographic evidence of TIMI thrombus grade 3–5 after infarct artery wiring could be randomised if the reference diameter of the infarct artery was ≥ 2.5mm on visual assessment. Angiographic criteria for exclusion from randomisation included: 1)TIMI thrombus grade < 3; infarct artery reference diameter < 2.5 mm on visual assessment; previous stenting of the infarct artery; and inability to identify the infarct artery Randomisation was carried	n = 501 **Inclusion criteria** Patients with ST-segment elevation AMI were considered eligible for the study without restriction based on age or clinical status on presentation, patients with cardiogenic shock were eligible Acute MI diagnosed according minutes and M 12 hours and 2) at least 2 contiguous leads or branch block **Exclusion criteria** 1) Thombolysis for current AMI; 2) Major surgery <6 weeks; 3) Stroke <30 days or any history of haemorrhagic stroke; 4) Comorbidities with expected survival <1 year; and participation in another study Demographics and baseline characteristics see below	Mechanical thrombus aspiration; angioJet rheolytic thrombectomy system consists of a drive unit console, a disposable pump set and a 4-F disposable catheter. The single-pass anterograde thrombectomy technique was used. Multivessel intervention was allowed only in patients with cardiogenic shock; otherwise, procedures in noninfarct arteries were performed after the 1-month scintigraphy	In both arms, direct stenting was attempted in all cases using bare-metal stents. The stent type choice was at the operator's discretion. If the stent failed to directly cross the lesion, pre-dilation was performed using an balloon to risk of before stent . Pressure and were at the	1, 6 and 12 months Baseline and 30-min post procedur e electroc a rdiogram undertak en	All-cause mortality Myocardial infarction Target vessel revascularisation Stroke	Medrad Intervention al/Possis (Minneapoli s, Minnesota). Provided financial support and thrombecto my devices only (not involved in the managemen t, collection or analysis of data

	out by computer-generated sequence and assignments were provided by a centralised telephone system **Allocation concealment** **Blinding** All clinical events were adjudicated by an independent clinical event committee blinded to treatment allocation after review of original source documentation	**Drug therapy** Patients received 325mg of aspirin orally, or 250mg intravenously at the emergency room, and a loading dose of 600mg of clopidogrel before or immediately after the procedure. All patients received abciximab unless contraindicated. Abciximab was administered immediately before or during the procedure as a bolus of 0.25 mg/kg body weight followed by a 12 hour infusion at a rate of 0.125 microgram/kg/minute. Heparin was given as an initial bolus of 70U/kg and additional boluses were administered during the procedure to achieve an activated clotting time of 200 to 250 seconds. After the procedure, patients were treated with aspirin (100 to 325 mg daily indefinitely) and clopidogrel (75 mg daily for 6 months). Other drugs such as beta blockers, angiotensin-converting enzyme inhibitors and statins were used in accordance with standard and recommended practice.		the operator according to the characteristi c of the stent and lesion			

Baseline characteristics			
	Mechanical thrombus aspiration (n = 256)	**No thrombectomy (n = 245)**	**p value**
Age, years (range)	63 (12.3 (24–94)	64.3 (11.5 (34–91)	0.208
Male, n (%)	195 (76)	199 (81)	0.168
Hypertension, n (%)	120 (47)	116 (47)	0.916
Dyslipidemia, n (%)	77 (30)	85 (35)	0.270
Diabetes mellitus, n (%)	36 (14)	37 (15)	0.742
Previous myocardial infarction, n (%)	10 (3.9)	12 (4.9)	0.588
Anterior myocardial infarction, n (%)	101 (39)	91 (37)	0.595
Cardiogenic shock, n (%)	7 (2.7)	13 (5.3)	0.142
Previous PCI, n (%)	11 (4.3)	10 (4.1)	0.904
Previous CABG, n (%)	1 (0.4)	1 (0.4)	0.975
Symptoms to admission (min), median (interquartile ranges)	125 (85–221)	135 (86–227)	0.853
ST-segment elevation (mm), mean (SD)	3.98 (2.49)	4.02 (2.69)	0.886
Baseline angiographic characteristics			
Infarct artery			
• Left anterior descending artery, n (%)	107 (42)	91 (37)	0.483
• Right coronary artery, n (%)	112 (44)	120 (49)	
• Circumflex artery, n (%)	37 (14)	34 (14)	
Reference vessel diameter (mm), median (interquartile ranges)	29.4 (2.67–3.24)	2.91 (2.62–3.25)	0.67
Multivessel disease, n (%)	114 (44)	95 (39)	0.192
Pre-wiring TIMI flow grade 0–1, n (%)	212/254 (83.5)	203/242 (83.9)	0.899
Post-wiring TIMI flow grade 0–1, n (%)	142/231 (61.5)	129/222 (58.1)	0.465
TIMI thrombus grade post-wiring			
• 1–2, n (%)	3 (1.4)	3 (1.4)	0.64
• 3, n (%)	73 (32.5)	80 (37.4)	

• 4, n (%)	83 (37.4)	79 (36.9)	
• 5, n (%)	63 (28.4)	52 (24.3)	
Procedural characteristics (values are median (interquartile range), n (%) or mean (SD).			
Procedural time (minutes, median (interquartile range)	59.5 (44.7–70)	46 (35–60)	< 0.001
Stent per patient, mean (SD)	1.26 (0.54)	1.40 (0.73)	0.022
Multiple stenting, n (%)	58 (23)	72 (30)	0.079
Abciximab, n (%)	249 (97)	239 (98)	0.841
Procedural success *, n (%)	237 (92.6)	229 (93.6)	0.696
* Residual stenosis < 30% and TIMI flow grade 3 by operator's assessment.			
Results			
1 month	**Mechanical thrombus aspiration (n = 256)**	**No thrombectomy (n = 245)**	
All-cause mortality, n (%)	4 (1.6)	7 (2.9)	
Myocardial infarction, n (%)	2 (0.8)	3 (1.2)	
Target vessel revascularisation, n (%)	2 (0.8)	6 (2.5)	
Stroke, n (%)	0 (0)	1 (0.4)	
6 months			
All-cause mortality, n (%)	7 (2.8)	11 (4.5)	
Myocardial infarction, n (%)	2 (0.8)	3 (1.2)	
Target vessel revascularisation, n (%)	18 (7.2)	32 (13.2)	
Stroke, n (%)	1 (0.4)	1 (0.4)	

TIMI: thrombolysis in myocardial infarction

Table 59: Kaltoft et al. 2006[61]

Reference	Study type	Number of patients	Intervention	Length of follow-up	Outcome measures	Source of funding
Kaltoft A, Bottcher M, Nielsen S, et al. Routine thrombectomy in Percutaneous coronary intervention for acute ST-segment elevation myocardial infarction: a randomised, controlled trial. Circulation 2006, 114:40-47	RCT Denmark Data collected 2004–2005 Randomisation using varying block sizes stratified by sex and diabetes.	n = 215 Inclusion: symptoms lasting > 30 min but < 12 h and cumulative ST-segment elevation ≥2 mV in ≥2 contiguous leads Exclusion criteria were left bundle-branch block, acute myocardial infarction within the previous 30 days, fibrinolytics treatment, previous coronary bypass surgery, left main stem stenosis, need for mechanical ventilation, and sever heart failure treated with intra-aortic balloon pump	Thrombus aspiration versus no thrombectomy	30 days	All-cause mortality Reinfarction Stroke.	Boston Scientific, Denmark.

Baseline characteristics:

	Thrombectomy (n = 108)	No thrombectomy (n = 107)
Age, y, mean (SD)	65 (11)	63 (13)
Male, n (%)	82 (76)	86 (80)
Diabetes mellitus, n (%)	9 (8)	6 (6)
Current smoker, n (%)	59 (55)	69 (64)
Hypertension*, n (%)	33 (31)	22 (21)
Hypercholesterolemia*	10 (9)	10 (9)
Prior myocardial infarction, n (%)	14 (13)	11 (10)
Symptom onset to first balloon inflation (minutes) mean (IQR)	242 (171–321)	208 (155–329)
ST-segment elevation immediately before PCI, mV, n (%)	0.65 (0.35–1.3)	0.7 (0.3–1.1)
Systolic blood pressure before PCI, mmHg, n (%)	133 (114–150)	130 (117–155)
Killip class ≥	7 (6)	(4)
* Requiring medication, n (%)		

Abciximab administered, n (%)	104 (96)	100 (93)	0.37
Stent implanted, n (%)	103 (95)	104 (97)	1.0
Device success, n (%)	96 (89)	-	

Concomitant therapy: Before intervention: aspirin 300 mg orally or intravenously, clopidogrel 300 mg orally, and unfractionated heparin 100000 IE intravenously. During the intervention, all treated with abciximab. Post intervention: infusion of abciximab for 12 hours and aspirin 75 mg/d and clopidogrel 75 mg/day for 12 months.

Results:

	Thrombectomy (n = 108)	No thrombectomy (n = 107)	p value
Total procedure time (min), mean (IQR)	39 (29–48)	29 (23–38)	< 0.0001
All-cause mortality, n	0	1	
Reinfarction, n	0	1	
Disabling stroke, n	2	0	

Table 60: Liistro 2009[74]

Reference	Study	Number of patients and Patient characteristics	Intervention	Comparison	Length of outcome	Outcomes	Source
Liistro F, Grotti S, Angioli P, Falsini G, Ducci K, Baldassarre S et al. Impact of thrombus aspiration on myocardial tissue reperfusion and left ventricular functional recovery and remodeling after primary	RCT Italy **Randomisation** 1:1 manner, computer generated random series of numbers. And block randomisation (blocks of 10 patients) **Allocation** concealment	n = 111 Inclusion criteria Symptoms suggesting acute myocardial ischaemia lasting > 30 minutes, the onset of symptoms < 12 hours previously, and ST-segment elevation of > 0.1 mV in 2 or more leads on the ECG, patients without contraindication to the use of platelet glycoprotein IIb/IIIa inhibitors. Exclusion criteria Rescue PCI after fibrinolysis, previous MI, the absence of an optimal echocardiographic apical view, the known existence of a disease resulting in a life expectancy of < 6 months, and the lack of	Thrombus aspiration with Export Aspiration catheter; 6 F catheter	Standard PPCI	6 months	Cardiac mortality Target vessel revascularisation Heart failure	None stated

angioplasty. Circulation Cardiovascular Interventions. 2009; 2(5):376-383.	Physicians unaware of block randomisation **Blinding** Single bind, outcomes blinded to operator **Intention to treat** Yes	informed consent, patients with poor images Demographics and baseline characteristics see below Drug therapy Before PPCI Aspirin (a loading dose of 500 mg), heparin (70 IU/kg), clopidogrel (a loading dose of 600 mg), glycoprotein IIb/IIIa inhibitor abciximab with an intravenous procedural bolus of 0.25 mg/kg followed by a continuous intravenous infusion of 0.125 microgram/kg/minute for 12 hours and postprocedural infusion without heparin					

Demographics and baseline characteristics:

Characteristics	No thrombectomy (n = 88)	Thrombus extraction (n = 87)
Age (years), mean (SD)	65 (11)	64 (11)
Men, n (%)	43 (77)	43 (64.7)
Hypertension, n (%)	43 (41.4)	59.0 (67.2)
Diabetes, n (%)	16.0 (18.4)	21 (23.8)
Current smoker, n (%)	23.0 (26.4)	43.0 (48.8)
Hyperlipdaemia, n (%)	167 (15)	161 (11)
History of CAD, n (%)	7 (8.0)	7 (7.9)
Killip class ≥ III, n (%)	25.0 (28.7)	17.0 (19.3)
Symptom to balloon (min), mean (SD)	6.1 (1.8)	6.2 (0.9)
Symptom to door (min), mean (SD)		
Door to balloon (min), mean (SD)		
MV coronary disease, n (%)	16.0 (18.4)	21.0 (23.8)
Direct stenting, n (%)	2.0 (2.3)	67.0 (76.2)
Stented patients, n (%)	53.0 (60.9)	49.0 (55.7)

Location of infarct–related coronary artery			
Left anterior descending, n (%)	38.0 (43.7)	38.0 (43.2)	1
Left circumflex, n (%)	20.0 (23.0)	22.0 (25.0)	0.859
Right coronary, n (%)	29.0 (33.3)	28.0 (31.8)	0.872
Results at 2 year follow-up			
	Thrombus aspiration PPCI (n = 88)	**No thrombectomy (n = 87)**	**p value**
All-cause mortality, n	0	6	0.0001
Reinfarction, n	0	1	0.999
Target vessel revascularisation, n	4	5	0.651

Table 61: Napodano 2003[85]

Reference	Study type	Number of patients	Intervention	Length of follow-up	Outcome measures	Source of funding
Napodano M, Pasquetto G, Sacca S. Intracoronary thrombectomy improves myocardial reperfusion in patients undergoing direct angioplasty for acute myocardial infarction. Journal of the American College of Cardiology. Vol. 42. No. 8. 2003.	RCT Italy **Randomisation** 1:1 manner	N = 92 Inclusion: continuous chest pain for at least 30 minutes and within 12 hours of onset of pain, and ST-segment elevation ≥1 mm (0.1 mV) in 2 or more contiguous leads, angiographic evidence of intraluminal thrombus in the IRA, TIMI flow ≤2, or ≥70% diameter stenosis. Exclusion: presence of LBBB or pacemaker-induced rhythm at admission ECG, left main stem lesions, IRA diameter <2.5 mm.	Mechanical thrombus extraction with X-sizer catheter	30-days	All-cause mortality Chronic heart failure, Nonfatal reinfarction Stroke Severe bleeding Target vessel revascularisation	Not reported

Baseline characteristics:			
	Mechanical thrombus extraction (n = 46)	**No thrombectomy (n = 46)**	**p value**
Age (years), mean (SD)	61.3 (10.8)	63.6 (11.7)	0.33
Male, mean	82.6	71.7	0.32
Smokers			

Current, %	45.6	34.8	0.39
Former, %	20.5	30.4	0.34
Hypertension, %	60.9	65.2	0.38
Dyslipidemia, %	50.0	52.1	1.0
Diabetes, %	13.0	13.0	1.0
Previous MI, %	17.4	6.5	0.19[¥]
Anterior MI, %	39.1	43.5	0.83
Time from onset of symptoms to hospital presentation (min), mean (SD)	202.9 (204.9)	165.7 (134.7)	0.54*
Time from hospital presentation to angioplasty (min), mean (SD)	35 (12)	38 (15)	0.82
Multivessel disease, %	52.2	41.3	0.46
Killip class, mean (SD)	1.5 (1.0)	1.5 (0.9)	0.83*
Killip class IV, %	8.7	8.7	1.0
HR > 100 beats/min, %	19.6	13.0	0.57
BP < 100 mm Hg, %	15.2	15.2	1.0
*Wilcoxon rand-sum test, ^ categorical data are presented as frequency values and were compared by chi-square, [¥] Fisher exact test			
Stents, %	**93.5**	**91.3**	**1.0**
Intraaortic balloon pump, %	**10.9**	**10.9**	**1.0**
Baseline TIMI flow, mean(SD)	**1.46(1.24)**	**1.48(1.31)**	**0.93**
TIMI flow final, mean(SD)	**2.91(0.35)**	**2.89(0.53)**	**0.82**
Concomitant therapy			
GP IIIb/IIa inhibitors, %	**43.4**	**41.3**	**1.0**
In-hospital	**Mechanical thrombus extraction (n = 46)**	**No thrombectomy (n = 46)**	**p value**
All-cause mortality, %	6.5	6.5	1.0*
Chronic heart failure, %	10.9	21.7	0.17^
Nonfatal reinfarction, %	2.2	2.2	1.0*
Stroke, %	0	0	1.0*
Severe bleeding, %	2.2	2.2	1.0*

Target vessel revascularisation, %	0	0	1.0*
30 days			
All-cause mortality, %	6.5	6.5	1.0*
Reinfarction, %	4.3	4.3	0.2*
Stroke, %	0	0	0*
Target vessel revascularisation, %	0	0	1.0*
* Data compared using Fischer exact test, or ^ chi-square			

Table 62: PIHRATE 2010[34]

Reference	Study	Number of patients and Patient characteristics	Intervention	Comparison	Length of outcome	Outcomes	Source of funding
Dudek D, Mielecki W, Burzotta F, Gasior M, Witkowski A, Horvath IG et al. Thrombus aspiration followed by direct stenting: a novel strategy of primary percutaneous coronary intervention in ST-segment elevation myocardial infarction. Results of the Polish-Italian-Hungarian RAndomized ThrombEctomy Trial (PIHRATE Trial). American Heart Journal. 2010; 160(5):966-972.	RCT Poland Hungary Italy **Randomisation** 1:1 ratio **Allocation concealment** Not stated **Blinding** Investigators blinded to outcome	n = 196 **Inclusion criteria** Patients with first STEMI with 6 hours from chest pain onset, ≥ 2 mm ST elevation in at least 2 contiguous leads and , ≥ 3 mm ST elevation in a lead, occluded infarct related artery **Exclusion criteria** Prior MI, CABG, cardiogenic shock, treated with fibrinolysis before admission to cath lab Demographics and baseline characteristics see below **Drug therapy**	n = 100 Thrombus aspiration with DIVER 6 F compatible catheter	n = 96 Standard PPCI	In-hospital: All-cause mortality Reinfarction Target vessel revascularisation Heart failure 6 months All-cause mortality Reinfarction	In-hospital: All-cause mortality Reinfarction Target vessel revascularisation Heart failure 6 months All-cause mortality Reinfarction	Not stated

	Patients received aspirin (325 mg), clopidogrel loading dose, unfractionated heparin (70 U/kg), GPPI IIIb/IIa inhibitors at operators discretion		
Baseline characteristics			
	No thrombectomy (n = 96)	**Thrombus aspiration PPCI (n = 100)**	**p value**
Age (years), mean (SD)	58.8 (10.3)	58.8 (10.3)	NS
Male, %	80	81.7	NS
Risk factors, %			
• Diabetes	13	9.6	NS
• Hypertension	58.0	53.7	NS
• Current smoking	63.7	62.0	NS
• Prior angina	4.3	13.0	0.033
Baseline angiographic and procedural data			
Target vessel, %			
• Left anterior descending coronary artery	39.6	39.0	NS
• Left circumflex coronary artery	12.5	11.0	
• Right coronary artery	47.9	50.0	
Results			
In-hospital	**No thrombectomy (n = 96)**	**Thrombus aspiration PPCI (n = 100)**	
All-cause mortality, n	3	3	
Reinfarction, n	1	0	
Target vessel revascularisation, n	1	2	
Heart failure, n	6	10	
6 months			
All-cause mortality, n	3	3	
Reinfaction, n	1	0	

Table 63: REMEDIA 2005[19]

Reference	Study	Number of patients and Patient characteristics	Intervention	Comparison	Length of outcome	Outcomes	Source of funding
Burzotta F, Trani C, Romagnoli E, Mazzari MA, Rebuzzi AG, De VM et al. Manual thrombus-aspiration improves myocardial reperfusion: the randomized evaluation of the effect of mechanical reduction of distal embolization by thrombus-aspiration in primary and rescue angioplasty (REMEDIA) trial. Journal of the American College of Cardiology. 2005; 46(2):371-376.	RCT (single centre) Italy Randomisation Undertaken after enrolment and before coronary angiography 1:1 randomisation using a computer generated random series of numbers **Allocation concealment** Not stated **Blinding** Cardiologist analysing ECG was blinded to procedural and clinical data. Otherwise not stated ITT analysis used	n = 99 Inclusion criteria All patients within 12 hours of onset of STEMI referred for primary or rescue PCI to a catheterisation laboratory were entered for the study. Exclusion criteria No angiographic exclusion criteria. Demographics and baseline characteristics see below Drug therapy All patients were treated by heparin (initial weight adjusted intravenous bolus then further boluses administered with the aim of obtaining an activated clotting time of 250 to 300s in patients treated with abciximab and >300s in the remaining subjects) and with double antiplatelet therapy with aspirin and clopidogrel (loading dose of 300mg followed by 75 mg/day) for at least 4 weeks. Unless contraindicated, abciximab (0.25 mg/kg bolus plus infusion of	PCI with thrombus-aspiration n = 50, 1 had no significant culprit lesion, 1 had surgical coronary anatomy, therefore 48 eligible for procedure 1 failure to cross the lesion with the guidelines, 1 death during PCI 2 protocol violations (crossover to standard PCI because of low thrombus burden) Thrombus-	Standard PPCI n = 49, all eligible for standard PCI 1 failure to cross the lesion with guidewire, 2 died during PCI. 4 protocol violations (crossover to thrombus-aspiration because of high thrombus burden/distal embolism) After crossing of the target lesion with the guidewire, direct stent implantation was	30 day	All-cause mortality Reinfarction, Stroke Target vessel revascularisation	None stated

	0.125 microgram/kg/minute for 12 hours) was intravenously administered in all patients undergoing PPCI, whereas in those with failed fibrinolysis, abciximab use was left to the operator's discretion.	aspirating device: Diver CE (Invated, Brescia, Italy). A rapid exchange, 6-F compatible thrombus-aspirating catheter	attempted if judged possible by the operator, in the remaining cases, pre-dilation with an undersized balloon was used before stent implantatio	

NB. Patients who died during the procedure and had non-crossable target lesions were considered to have no reperfusion in the analyses. Data of the patients whose treatment crossed over were included in the assigned group and analysed according to ITT principle.

Baseline characteristics

No differences reported between groups for clinical or angiographic characteristics.

	Thrombus aspiration PPCI (n = 50)	No thrombectomy (n = 49)	p value
Age (years) (mean (SD)	61 (13	60 (13	0.76
Gender: males (%) / females (%)	45 (90) / 5 (10)	38 (77.6) / 11 (22.4)	0.09
Risk factors, n (%)			
• Smokers	31 (62)	26 (53.1)	0.37
• Hyperchloesterolemia	27 (54)	17 (34.7)	0.06
• Hypertension	31 (62)	28 (57.1)	0.62
• Diabetes mellitus	11 (22)	9 (18.4)	0.65
• Positive family history	15 (30)	11 (22.4)	0.96
Previous history of ischaemic heart disease, n (%)	10 (20)	10 (20.4)	0.96
Pre-infarction angina, n (%)	14 (28)	16 (32.7)	0.61
Anterior myocardial infarction, n (%)	20 (40)	25 (51)	0.27
Symptoms to angiography time (min)	274 (137)	300 (202)	0.28

Referred after failure of fibrinolysis	16 (32)	12 (24.5)	0.41
Use of abciximab, n (%)	34 (68)	31 (63.3)	0.53
Renal failure (creatine ≥ 1.2mg/dl)	6 (12)	8 (16.3)	0.53
Killip class III or IV, n (%)	15 (30)	14 (28.6)	0.88
Cardiogenic shock, n (%)	4 (8)	5 (10.2)	0.74
Multivessel disease, n (%)	17 (34)	21 (42.9)	0.36
LAD as culprit vesse, n (%)	20 40)	25 (51)	0.15
Culprit lesion with proximal location, n (%)	26 (52)	21 (42.9)	0.27
Pre-intervention TMI flow grade, n (%)			
• 0	32 (64)	34 (69.4)	0.48
• 1	11 (22)	10 (20.4)	
• 2	2 (4)	3 (6.1)	
• 3	5 (6.3)	2 (4.1)	

Results (at 30 days)

	Thrombus aspiration PPCI (n = 48)	No thrombectomy (n = 48)
All-cause mortality, n (%)		
• In the cath lab	1 (2)	2 (4.1)
• After PCI	2 (4)	1 (2.1)
Reinfarction, n (%)	2 (4)	2 (4.1)
Stroke, n (%)	1 (2)	1 (2.1)
Target lesion revascularisation, n (%)	1 (2)	1 (2.1)

Table 64: TAPAS 2008[109,118]

Reference	Study type	Number of patients	Intervention	Length of follow-up	Outcome measures	Source of funding
Vlaar P, Svilaas T, van der Horst, Diercks G, et al. Cardiac death and reinfarction after 1 year in the thrombus aspiration during Percutaneous coronary intervention in acute myocardial infarction study (TAPAS): a 1-year follow-up study. Lancet. 2008; 371(9628):1915-1920 Svilaas T, Vlaar PJ, van der Horst IC, Diercks GF, de Smet BJ, van den Heuvel AF et al. Thrombus aspiration during primary percutaneous coronary intervention. New England Journal of Medicine. 2008; 358(6):557-567.	RCT Netherlands Single centre Data collected January 2005 to December 2006 Patients randomised BEFORE coronary angiography	n = 1071 Inclusion criteria: symptoms suggesting acute myocardial ischaemia >30 minutes, time from symptoms onset <12 h, ST-segment elevation > 0.1 mV in 2 or more lead on the ECG Exclusion: rescue PCI after fibrinolysis and known existence of concomitant disease with life expectancy less than 6 months	Thrombus aspiration with Export aspiration catheter versus conventional PPCI.	30 days and 1 year	All-cause mortality Myocardial reinfarction Target vessel revascularisation	Medtronic

Baseline characteristics:

	Thrombus aspiration PPCI (n = 535)	Conventional PCI (n = 536)
Age, mean (SD)	63 (13)	63 (13)
Men, n (%)	363 (67.9%)	392 (73.1%)
Diabetes, n/total (%)	56/530 (10.6%)	67/532 (12.6%)
Hypertension, n/total (%)	171/517 (33.1%)	195/526 (37.1%)
Hypercholesteroleamia, n/total (%)	115/485 (23.7%)	130/480 (27.1%)
Previous myocardial infarction, n/total (%)	50/528 (9.5%)	57/533 (10.7%)

Previous PCI, n/total (%)	39/526 (7.4%)	38/531 (7.2%)
Previous CABG, n/total (%)	17/529 (3.2%)	22/533 (4.1%)
Family history, n/total (%)	235/509 (46.2%)	229/514 (44.6%)
Body mass index, mean (SD)	27 (4)	27 (4)
Current smoking, n/total (%)	213/463 (46.0%)	225/469 (48.0%)
Total ischaemic time (min), median (IQR)	190 (110–270)	185 (107–263)
Infarct –related vessel, n/total (%)		
Left anterior descending artery	221/515 (42.9%)	223/517 (43.1%)
Left circumflex artery	93/515 (18.1%)	79/517 (15.3%)
Right coronary artery	180/515 (36.7%)	204/517 (39.5%)
Other	12/515 (2.3%)	11/517 (2.1%)
Initial TIMI flow, n/total (%)		
0/1	288/526 (54.7%)	316/531 (59.5%)
2	102/526 (19.4%)	85/531 (16.0%)
3	136/526 (25.9%)	130/531 (24.5%)

Concomitant therapy: All patients pre-treated with aspirin (500 mg followed by 80–100 mg per day), heparin (5000 IU), and clopidogrel (loading dose 600 mg followed by 75 mg per day). Unless contraindicated, abciximab given during procedure and additional heparin guided by activated clotting time. Standard therapies after PCI included beta-blockers, lipid-lowering agents, and angiotensin-converting-enzyme inhibitors, or angiotensin-II receptor antagonists, according to current guidelines.

Results:

30 day follow-up	**Thrombus aspiration, n = 529**	**No thrombectomy, n = 531**	**Risk ratio (95% CI)**	**p value**
All-cause mortality, n (%)	11 (2.1)	21 (4.0)	0.52 (0.26-1.07)	0.07
Reinfarction, n (%)	4 (0.8)	10 (1.9)	0.40 (0.13-1.27)	0.11
Target vessel revascularisation, n (%)	24 (4.5)	31 (5.8)	0.77 (0.46-1.30)	0.34
Major bleeding, n (%)	20 (3.8)	18 (3.4)	1.11 (0.60-2.08)	0.11
1 year follow-up	**Thrombus aspiration, n = 535**	**No thrombectomy, n = 536**	**Hazard ratio (95% CI)**	**p value**
All-cause mortality, n (%)	25 (4.7)	41 (7.6)	1.67 (1.02–2.75)	0.042
Cardiac death, n (%)	19 (3.6)	36 (6.7)	1.93 (1.11–3.37)	0.020
Reinfarction, n (%)	12 (2.2)	23 (4.3)	1.97 (0.98–3.96)	0.05
Target vessel revascularisation, n (%)	60 (12.9)	69 (11.2)	1.19 (0.84–1.68)	0.34
Second PCCI target vessel, n (%)	37 (6.9)	51 (9.5)		

CABG target vessel, n (%)	25 (4.7)	20 (3.7)		
Cardiac death or non-fatal reinfarction, n (%)	30 (5.6)	53 (9.9)	1.81 (1.16–2.84)	0.009
Major adverse cardiac events, n (%)	89 (16.6)	109 (20.3)	1.26 (0.95–1.67)	0.10

Table 65: VAMPIRE 2008[57]

Reference	Study type	Number of patients	Intervention	Length of follow-up	Outcome measures	Source of funding
Ikari Y, Sakurada et al. Upfront thrombus aspiration in primary coronary intervention for patients with ST-segment elevation acute myocardial infarction: report of the VAMPIRE (VAcuuM asPIration thrombus REmoval) trial. JACC: cardiovascular inventions. Vol. 1, No. 4, 2008.	RCT Japan Patients enrolled 2003–2005 ITT analysis	n = 355 Inclusion: 21 years with AMI presenting 30 min but 24 h after symptom onset, with 2 mm or more of ST-segment elevation in 2 or more contiguous leads or with a presumably new left bundle-branch block Exclusion: presence of primary fibrinolysis prior to randomisation, cardiogenic shock, history of cardiac arrest, history or coronary bypass surgery, chronic renal failure (Cr >2.0 mg/dl) or haemodialysis, left main disease, or target vessel <2.5 mm or >5 mm in diameter	PPCI with or without thrombus aspiration using Nipros's TransVascular Aspiration Catheter.	In-hospital 8 months	All-cause mortality, MACE (composite death, recurrence of myocardial infarction, and target lesion revascularisation)	Not stated

Baseline characteristics:

	Thrombus aspiration PPCI (n = 180)	No thrombectomy (n = 175)	p Value
Age, (years), mean (SD)	63.2 (10.6)	63.5 (9.9)	0.81
Male, %	80.6	77.7	0.51
Body mass index, (kg/m^2)	24.1	24.3	0.53
Hypertension, %	54.8	59.0	0.45

Hyperlipidemia, %	50.0	48.5	0.78
Diabetes, %	23.3	29.9	0.16
Insulin use, %	3.6	3.1	
Smoking			
Current smoking, %	56.6	50.9	0.26
Ex-smoker, %	12.1	9.3	
Family history of CAD, %	13.9	14.4	0.89
Previous PCI, %	3.4	5.2	0.42
Killip class > 1, %	11.2	8.4	0.17
Onset to hospital (h), mean (SD)	4.5 (5.0)	5.2 (5.5)	0.13
Stent use, %	94.1	93.4	0.79
IABP or percutaneous cardiopulmonary support, %	9.4	13.4	0.25
Transfemoral approach, %	94.8	92.4	0.34
Glycoprotein IIb/IIIa inhibitors, %	0	0	1
Procedural success, %	98.9	98.3	0.64
Vascular access complication, %	2.9	4.1	0.54

Concomitant therapy: Aspirin and intravenous heparin boluses were administered during he procedure to maintain an activated clotting time ≥300 s. No drug eluting stents were allowed. Use of fibrinolytic agents or GPI IIb/IIIa inhibitors was not allowed.

Results:

	Thrombus aspiration PPCI (n = 180)	**No thrombectomy (n = 175)**	**p value**
In-hospital mortality (composite death, recurrence of myocardial infarction, and target lesion revascularisation) , n	1	1	NS
MACE (in-hospital) , n	1 (0.6)	2 (1.2)	NS
Myocardial Infarction (in-hospital), n	0	1 (subacute thrombus)	NS
Target lesion revascularisation (in-hospital) , n	0	1	NS
8-month MACE (composite death, recurrence of myocardial infarction, and target lesion revascularisation) , n	12.9%	21.0%	< 0.05
All-cause mortality (8 months) , n	2	1	NS

Myocardial infarction (8 months) , n	0	1	NS
Target lesion revascularisation (8 months) , n	20	31	0.05

Table 66: X AMINE ST 2005[72]

Reference	Study	Number of patients and Patient characteristics	Intervention	Comparison	Length of outcome	Outcomes	Source of funding
Lefevre, Garcia, Reimers, Lang et al. X-sizer for thrombectomy in acute myocardial infarction improves ST-segment resolution. Results of the X-sizer in AMI for negligible embolization and optimal ST resolution (X AMINE ST) trial. Journal of the American College of Cardiology. 2005: 46 (2) 246-52	RCT (14 European centres) France, Spain, Italy, Austria, Germany, UK **Randomisation** 1:1 ratio **Allocation concealment** **Blinding** Coronary angiograms were analysed by an independent core laboratory that was blinded to other data. ITT analysis used	n = 201 **Inclusion criteria** Patients suffering an AMI who were amenable to PIC were included. AMI < 12 hours (that is, evidence of ischaemic chest pain for > 30 minutes and new ST-segment elevation for ≥ 2mm in 2 or more contiguous electrocardiographic leads, de novo lesion, single vessel treatment in a native vessel ≥ 2.5mm in diameter and occluded, thrombus-containing, TIMI flow grade 0 to 1 infarct related artery. **Exclusion criteria** Previous PCI in IRA, rescue PCI, Killip class ≥3, left or right bundle branch block, IRA with excessive proximal tortuosity or severe calcification, left ventricular ejection fraction <30%, contraindication to emergency coronary artery bypass grafting and current participation in another study protocol	n = 100 Mechanical thrombus extraction X-sizer catheter system used. A 2-lumen over the wire system (diameters 1.5 and 2 mm) with a helical shape cutter at its distal tip. 2 or more passages across the lesion from proximal to distal were performed by slowly advancing the activated catheter. Subsequently, additional balloon angioplasty or coronary stenting was performed Before the intervention, all patients received aspirin. Heparin (70 U/kg) was given to maintain an activated	n = 101 PCI (excluding anything but balloon angioplasty and stent)	1 and 6 months ECG recorded 60 min after the procedure	All-cause mortality Stroke MI Target vessel revascularisation	Not stated

	Demographics and baseline characteristics see below **Drug therapy** Glycoprotein IIb/IIIa inhibitors were used according to the operator's judgement	clotting time of > 250s	
Baseline characteristics			
	No thrombectomy (n = 101)	**Mechanical thrombus extraction (n = 100)**	**p value**
Age (years), mean (SD)	62 (11)	61 (13)	NS
Female, %	27	24	NS
Risk factors, % • Diabetes • Hypertension • Dyslipidemia • Current smoking	 18 50 61 51	 25 54 58 52	 NS
Previous MI, %	6	10	NS
Baseline angiographic and procedural data			
Target vessel, % • Left anterior descending coronary artery • Left circumflex coronary artery • Right coronary artery	 48 5 43	 55 7 37	 NS
TIMI flow grade pre-PCI, %	0.18 (0.52	0.15 (0.46	NS
Glycoprotein IIb/IIIa inhibitors, %	65	55	NS
Coronary stenting, %	99	100	NS
Postprocedural angiographic data			
TIMI flow, % grade 3	89	95.9	0.105
Procedural success, %	75	84.5	0.112

Results			
One month	**No thrombectomy**	**Thrombectomy**	**p value**
All-cause mortality, n	4	4	NS
Stroke, n	0	2	NS
Reinfarction	3	1	NS
Target vessel revascularisation, n	0	2	NS
6 months			
All-cause mortality, n	4	6	NS
Stroke, n	0	2	NS
Reinfarction, n	4	2	NS
Target vessel revascularisation, n	5	3	NS

G.5 Culprit versus complete revascularisation **Updated, see the 2020 evidence review**

Table 67: APEX-AMI [113]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Toma M, Buller CE, Westerhout CM, Fu Y, O'Neill WW, Holmes DR, Jr. et al. Non-culprit coronary artery percutaneous coronary intervention during acute ST-segment elevation myocardial infarction: insights from the APEX-AMI trial. European Heart Journal. 2010; 31(14):1701-1707.	Post hoc analysis of RCT (APEX-AMI), subgroup population assessed as cohort	n = 2201	Inclusion criteria presentation within 6 hours high risk electrographic characteristics; 2 mm ST-elevation in 2 anterior lateral leads or at least 2 mm ST-elevation in 2 inferior leads couples with ST-depression in 2 contiguous anterior leads for a total of 8 mm or more or left bundle branch block Presence of maximum percent stenosis of 70% or greater in more than major epicardial coronary artery or a non-infarct-related vessel requiring intervention by PCI operators Exclusion criteria Rescue PCI Isolated inferior MI Pregnant or breastfeeding Complement deficiency Serious infection Serious medical condition that would likely alter recovery	Culprit only revascularisation (COR); the infarct related artery only was treated and the other arteries were left untreated n = 1984	Multivessel revascularisation(MVR); the infarct related artery and the non-infarct related artery within the same procedure n = 217	90 days	All-cause mortality	Proctor & Gamble Pharmaceuticals Alexion Pharmaceuticals

			Demographics and baseline characteristics See below Drug therapy After stent implantation all patients received clopidogrel 75 mg per day for at least 4 weeks, other adjunctive treatments were administered at the discretion of the operator					

Baseline characteristics

	COR (n = 1984)	MVD (n = 217)	p value	
Male, %	79.2	79.4	77.4	0.498
Age, median (25th and 75th percentile)	64 (55, 73)	64 (55, 73)	64 (53, 74)	0.937
Heart rate, BPM, median (25th and 75th percentile)	75 (65, 87)	75 (64, 87)	77 (67, 88)	0.106
SBP, mmHg, median (25th and 75th percentile)	134 (116, 150)	134 (117, 150)	130 (112, 148)	0.069
Killip class >1, %	11.6	11.4	13.8	0.288
Inferior MI, %	44.7	45.5	37.0	0.017
Hypertension, %	54.8	55.6	47.5	0.022
Prior MI, %	15.5	15.9	12.4	0.185
Prior PCI, %	11.5	11.7	9.7	0.366
Prior CABG, %	3.6	4.0	0.5	0.009
Prior congestive heart failure,%	4.0	3.9	4.6	0.602
Diabetes mellitus, %	19.2	20.0	11.5	0.003
Current smoker, %	39.7	39.9	38.2	0.635
Prior MI, %	15.5	15.9	12.4	0.185

Creatine clearance, ml/min, median (25th and 75th percentile)	77.9 (59.8, 100.8)	78.4 (59.9, 100.7)	74.0 (58.6, 101.1)	0.632
IRA, %				
LAD	49.0	48.3	55.8	< 0.001
LCX	12.3	11.4	19.8	
RCA	38.5	40.0	24.4	
Extent of multivessel disease, %				
2-vessel disease	37.7	68.2	63.4	0.534
3-vessel disease	31.2	31.8	25.9	
Time from symptom onset to PCI, hours, median (25th and 75th percentile)	3.4 (2.6, 4.7)	3.4 (2.6, 4.7)	3.5 (2.7, 4.9)	0.436
In-hospital GPI use, %	72.6	71.9	78.8	0.030
Stent, %	94.7	94.6	95.9	0.436
Target vessel revascularisation, n (%)	28 (7.9)	1 (3.8)	8 (6.3)	0.66
Length of hospital stay, days, median (25t, 75th percentile)	6 (4,9)	6 (4,9)	6 (4,9.5)	0.203
Results				
90 day mortality				
	COR (n = 1984)	MVD (n = 214)	p value	
All-cause mortality, n (%)	119 (5.6)	27 (12.5)	< 0.001	
Procedure time, min	42	56	< 0.001	
GUSTO severe bleeding	0.6	1.8	p = 0.065	

Table 68: Corpus 2004 [29]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Corpus RA, House JA, Marso SP, Grantham JA, Huber KCJ, Laster SB et al. Multivessel xtfpercutaneous coronary intervention in patients with multivessel disease and acute myocardial infarction. American Heart Journal . 2004; 148(3):493-500.	Design Retrospective cohort study, 1998 to 2002, USA	n = 1982	Inclusion criteria clinical evidence of acute MI, defined as symptoms consistent with ongoing myocardial ischaemia, ECG evidence of acute MI (≥ 1mm ST elevation in ≥ 2 contiguous leads), new left bundle branch block, or true posterior infarction), or both presentation ≤ 12 hours before symptom onset procedure generally begun within 30 to 60 min of patients arrival at hospital Exclusion criteria patients undergoing PPCI of vein graft or left main coronary artery lesions patients undergoing PPCI for acute occlusion after coronary angioplasty or arteriography patients with multivessel disease undergoing stage revascularisation procedures of the non-infarct related artery after discharge from hospital Demographics and baseline	Culprit only revascularisation (COR); the infarct related artery only was treated and the other arteries were left untreated n = 354	Multivessel revascularisation(MVR); the infarct related artery and the non-infarct related artery within the same procedure n = 26 Staged revascularisation (SR); the infarct related artery was treated immediately and the non-infarct related artery was staged within the indexed hospitalisation n = 126	In-hospital ≤ 30 days 1 year	All-cause mortality Reinfarction Target vessel revascularisation CABG Major bleed	None stated

			characteristics see below Drug therapy After stent implantation all patients received clopidogrel 75 mg per day for at least 4 weeks, other adjunctive treatments were administered at the discretion of the operator					

Baseline characteristics

	COR (n = 354)	**MVR and SR combined (n = 152)**	**p value**
Age, years, mean (SD)	63 (14)	64 (13)	0.27
Diabetes, n (%)	60 (17)	29 (19)	0.56
Male, n (%)	245 (69)	109 (72)	0 .57
Hypertension, n (%)	194 (55)	74 (49)	0.21
Creatine > 1.5mg /dl, n (%)	12 (3.4)	5 (3.3)	0.87
Ejection fraction, %	35 (18)	35 (19)	0.96
Killip class IV on admission, n (%)	12 (3.4)	5 (3.3)	0.95
Glycoprotein IIb/IIIa inhibitors	139 (39)	44 (29)	0.03
Stent, n (%)	307 (87)	148 (97)	< 0.001

	COR (n = 354)	MVR (n = 26)	SR (n = 126)	p value
In-hospital				
Major bleeding, n (%)	26 (7.3)	1 (3.8)	6 (4.7)	0.51
All-cause mortality, n (%)	20 (5.6)	5 (19)	3 (2.4)	0.003
≤ 30 days	**COR (n = 354)**	**MVR (n = 26)**	**SR (n = 126)**	**p value**

Mortality, n (%)	23 (6.5)	5 (19)	10 (7.9)	0.06
Reinfarction, n (%)	2 (0.6)	0 (0)	14 (11)	< 0.001
Target vessel revascularisation, n (%)	28 (7.9)	1 (3.8)	8 (6.3)	0.66
CABG, n (%)	28 (8.0)	1 (3.8)	2 (2.4)	0.07
1 year	**COR (n = 354)**	**MVR (n = 26)**	**SR (n = 126)**	**p value**
Mortality, n (%)	42 (12)	5 (19)	12 (9.5)	0.36
Reinfarction, n (%)	10 (2.8)	1(3.8)	19 (15)	< 0.001
Target vessel revascularisation, n (%)	53 (15)	3 (12)	35 (28)	0.004
CABG, n (%)	41 (12)	2 (67.7)	8 (6.3)	0.21

Table 69: EUROTRANSFER Reg 2010[37]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Dziewierz A, Siudak Z, Rakowski T, Mielecki W, Dubiel JS, Dudek D. Impact of multivessel coronary artery disease and non-infarct related artery revascularisation on outcome of patients with ST-segment elevation myocardial	Retrospective cohort study, 15 STEMI hospital networks from 17 European hospitals, Nov 2005 to Jan 2007	n = 777	Inclusion criteria STEMI ≥ 1 significantly stenosed epicardial coronary artery, without previous CABG Exclusion criteria None stated Demographics and baseline Not reported for cohort population comparing culprit-only PPCI versus multivessel PCI	Culprit only revascularisation (COR); the infarct related artery only was treated and the other arteries were left untreated n = 707	Multivessel revascularisation(MVR); the infarct related artery and the non-infarct related artery within the same procedure n = 77	≤ 30 days 12 months	All-cause mortality Reinfarction Repeat revascularisation, Major bleeding,	Eli Lilly and Company, Critical Care Europe, Geneva, Switzerland

infarction transferred for primary percutaneous coronary intervention. EuroInterventi on. 2010; 20100525(201 00528).			Drug therapy Not reported for cohort population comparing culprit-only PPCI versus multivessel PCI					

Results					
≤ 30 days	**COR (n = 707)**	**MVR (n = 70)**	**p value**	**Adjusted OR (95% CI)**	**Adjusted p value**
Death	42 (5.9%)	9 (12.9%)	0.039	2.42 (0.96, 6.06)	0.06
Major bleeding requiring transfusion	12 (1.7%)	2 (2.9%)	0.36	1.81 (0.35, 9.27)	0.48
Reinfarction	13 (7.5%)	0 (5.7%)	Not reported	Not reported	Not reported
All bleeding	62 (8.8%)	11 (15.7%)	0.08	1.97 (0.90, 4.29)	0.09
12 months					
Death					

Table 70: HELP-AMI 2004[33]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Outcome measures	Source of funding
Di Mario C, Mara S, Flavio A, Imad S, Antonio M, Anna P et al. Single vs multivessel treatment during primary angioplasty: results of the multicentre randomised HEpacoat for cuLPrit or multivessel stenting for Acute Myocardial Infarction (HELP AMI) Study. International Journal of Cardiovascular Interventions. 2004; 6(3-4):128-133.	Design RCT; multicentre Enrolment Dates not reported Randomisation Not detailed Allocation concealment Not detailed Blinding Open label Sample size calculation For primary outcome of repeat revascularisation; as 75% of the patients in the culprit lesion group were expected to need a second procedure at 1-year follow-up (mainly because of elective treatment	n = 69 **Length of follow-up:** 12 months	Inclusion criteria presence of ischaemic chest pain started less than 12 hours before hospital admission and / or ST segment elevation of at least 1 mm in 2 or more contiguous electrocardiographic leads (peripheral leads) or 2 mm in the pre-cordial leads multivessel CAD (defined as < 70% diameter stenosis of 2 or more epicardial coronary arteries or their major branches by visual estimation multivessel disease with the technical possibility of coronary and revascularisation with stents of at least 2 lesions (infarct related artery and 1 or more, to a maximum of 3 lesions in a major non-culprit related artery) Exclusion criteria presence of significant lesions in vein grafts or arterial conduits or in segments previously treated with angioplasty or stent implantation. recent fibrinolysis (less than 1 week) cardiogenic shock, defined as hypertension with systolic blood pressure less than 90 mmHg and	Culprit lesion only revascularisation (COR) n = 17 Stent implantation in the culprit artery using 1 or more heparin coated Bx Velocity stents, and subsequent interventions on the non-culprit lesions performed at the investigator's discretion; need and timing of the subsequent interventions were decided according to clinical status (persistent or recurrent angina), evidence of ischaemia in non-invasive tests (perfusion scintigraphy or stress echocardiogram), angiographic severity of non-culprit lesions and clinical relevance of the affected vessels, as well as organisation standards at participating centres	Multivessel revascularisation (MVR) n = 52 Revascularisation of all suitable lesions, using coated Bx Velocity stents in these lesions	Primary; 12 month incidence of repeat revascularisation (any revascularisation, infarct related artery as well as non-infarct related artery) Secondary; In-hospital repeat revascularisation, reinfarction All-cause mortality	None stated

	of other lesions), a total of 70 patients were randomised in a 3:1 ratio (53 patients assigned to MVR treatment group and 17 patients assigned to COR group); this was required in order to test for a 55% difference in the incidence of new revascularisation with a power of 0.80 and a 2-sided alpha error equal to 0.05, this unbalanced enrolment strategy was adopted in order to increase the reliability of the main secondary end point (the incidence of adverse in-hospital events in the 2 groups) ITT analysis Not done		tachycardia greater than 100 BPM, not due to hypovolemia or requiring inotropic support or balloon counter pulsation single vessel disease the presence of left main stenosis of 50% or more intention to treat more than 1 totally occluded major epicardial vessel diffuse calcification or severe tortuosity in the culprit and the non-culprit arteries preventing the implantation of the study stents a side branch larger than 2.0 mm which was required to be covered by the stent, unless the operator was willing and technically able to maintain patency of this side branch with either further balloon angioplasty or stent replacement Demographics and baseline characteristics see below Drug therapy All patients received aspirin ≥ 100mg and clopidogrel 75 mg or ticlopidine 500 mg for at least 1 month after the procedure					

Baseline characteristics			
	COR (n = 17)	**MVR (n = 52)**	**p value**
Age (years), n (%)	65.3 (7.4)	63.5 (12.4)	0.575
Male, (%)	84.6	88.2	0.531
Pre-PCI, (%)	2.0	0	0.796
Pre-CABG, (%)	9.6	23.5	0.144
LVEF, (%)	48.9 (8.6)	48.4 (9.9)	0.883
Diabetes, (%)	41.2	11.5	0.012
Hypercholesterolemia, (%)	52.9	41.2	0.285
Smoke, (%)	81.0	66.6	0.514
Hypertension, (%)	58.8	36.5	0.092
Clinical presentation of acute MI			
	COR (n = 17)	**MVR (n = 52)**	**p value**
Time onset of symptoms-hospital (min)	167 (180)	122 (97)	0.247
Time hospital to cath lab (min), mean (SD)	69 (54)	88 (90)	0.423
Q wave infarction, (%)	75.0	80.4	0.445
r-tPA (%)	5.9	7.7	0.641
Glycoprotein IIb/IIIa	82.4	75.0	0.397
Anterior infarction (%)	58.8	51.9	0.491
Killip 2 – 3 (%)	18.8	20.0	0.318
Systolic BP (mmHg), mean (SD)	141 (24)	136 (25)	0.474
Diastolic BP (mmHg), mean (SD)	85 (18)	83 (15)	0.528
Heart rate (BPM), mean (SD)	78 (18)	76 (19)	0.651
Two vessel disease, (%)	52.9	69.2	0.432
Three-vessel disease, (%)	47.1	30.8	
Procedural characteristics (all lesions)			
	COR (n = 17)	**MVR (n = 52)**	**p value**
Treated lesion/patient, mean (SD)	1.00 (0)	2.36 (0.64)	0.001

Stent/lesion, mean (SD)	1.29 (0.61)	1.12 (0.33)	0.008
Stent/patient, mean (SD)	1.29 (0.61)	2.73 (0.78)	0.001
Mean stent length, (mm), mean (SD)	19.9 (8.4)	16.4 (5.0)	0.088
Maximum balloon pressure, (atm), mean (SD)	13.6 (2.6)	14.1 (2.5)	0.561
Procedure duration (min), mean (SD)	53 (24)	69 (38)	0.032
Contrast used, (ml) , mean (SD)	242 (106)	341 (163)	0.025
Results			
In-hospital	**COR (n = 17)**	**MVR (n = 52)**	**p value**
Death, (%)	0	1 (1.9)	0.754
Reinfarction, (%)		0	0
PPCI, (%)	0	1 (1.9)	0.675
CABG, (%)	0	0	-
12 months	**COR (n = 17)**	**MVR (n = 52)**	**p value**
Death (%)	0	1 (1.9)	0.754
Reinfarction, (%)	1 (5.9)	1 (1.9)	0.435
PPCI or CABG, (%)	6 (35.3)	9 (17.3)	0.174

Table 71: KAMIR 2012[71]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Lee HW, Hong TJ, Yang MJ, An SG, Oh J-H, Choi JH, Lee HC, Cha KS, Hong JY. Comparison of infarct-related artery vs multivessel revascularization in ST-segment elevation myocardial infarction with multivessel disease: Analysis from Korea acute myocardial infarction registry. Cardiology Journal. 2012; 19(3):256-266.	Design Prospective cohort study, Korea Acute Myocardial Infarction Registry carried out in about 50 tertiary hospitals Enrolment 2005-2007; STEMI patients with MVD who had had PPCI Patients divided into 2 groups: patients with IRA (infarct related revascularisation) and patients with multivessel revascularisation. Confounders taken into account in the covariates analysis	n = 1,644	Inclusion criteria patients with STEMI with multivessel disease who had PPCI Exclusion criteria not specifically stated Demographics and baseline characteristics see below Drug therapy see below	IRA revascularisation n = 1106, 67.3%	Multivessel revascularisation n = 538, 32.7%	In hospital One month 12 months	In hospital: Cardiac death Non-cardiac death IABP Cerebrovascular accident Acute renal failure Defib/cardioversion due to VT or VFib Major bleeding New onset HF Short- and long-term follow-up: Primary: MACE at	2 year research grand of Pusan National University

							short and long-term follow-up All-cause mortality Reinfarction Repeat revascularisation CABG Stent thrombosis	

Baseline characteristics			
%	**IRA revascularisation (n = 1106, 67.3%)**	**Multivessel revascularisation (n = 538, 32.7%**	**p value**
Male,	800 (72.3%)	413 (76.8%)	0.055
Age, mean (SD)	63.6 (12.0)	62.1 (11.1)	0.014
Hypertension	604 (55.2%)	256 (47.9%)	0.005
Dyslipidemia	103 (10.8%)	40 (8.1%)	0.106
Diabetes	323 (29.6%)	161 (30.3%)	0.769
Current smoker	484 (44.0%)	263 (49.1%)	0.055
Familial history IHD	81 (8.1%)	54 (10.6%)	0.103
Previous PCI	59 (5.3%)	17 (3.2%)	0.049
Previous CABG	7 (0.6%)	1 (0.2%)	0.286
Previous MI	29 (2.6%)	13 (2.4%)	0.804
Previous cerebrovascular accident	73 (6.6%)	26 (4.8%)	0.157
Discharge medication:			
Aspirin	1081 (97.7%)	526 (97.8%)	0.969
Clopidogrel	1070 (94.7%)	523 (97.2%)	0.608
Cilostazol	308 (27.8%)	285 (53.0%)	< 0.0001

Beta-blocker	818 (74.0%)	417(77.5%)	0.118
ACE-1	749 (67.7%)	381 (70.8%)	0.0204
Statin	838 (75.8%)	423 (87.6%)	0.199
Follow-up duration (days)	370.5 (356.0 – 394.8)	358.5 (329.3 – 374.5)	0.017
N – cumulative incidences	**IRA revascularisation (n = 1106, 67.3%)**	**Multivessel revascularisation (n = 538, 32.7%)**	**p value**
In-hospital outcomes			
Cardiac death	6 (0.5%)	2 (0.4%)	NS
Non-cardiac death	0	0	NS
IABP	51 (4.6%)	27 (5.0%)	0.715
Stroke	7 (0.6%)	0	0.104
Acute renal failure	3 (0.3%)	1 (0.2%)	NS
Defib/cardioversion	50 (4.5%)	13 (2.4%)	0.037
Major bleeding	2 (0.2%)	1 (0.2%)	NS
New onset HF	10 (0.9%)	1 (0.2%)	0.115
Events at 1-month follow-up			
Cardiac Death	7 (0.6%)	5 (0.9%)	0.0.543
Non-cardiac death	0	0	0
Re-MI	4 (0.4%)	3 (0.6%)	0.689
re-PCI	22 (2.0%)	4 (0.7%)	0.057
CABG	0	2 (0.4%)	0.107
MACE (hierarchical)	35(3.2%)	14 (2.6%)	0.529
Events at 12 month follow-up			
Cardiac Death	15 (1.4%)	8 (1.5%)	0.836
Non-cardiac Death	10 (0.9%)	1 (0.2%)	0.115
Re-MI	7 (0.6%)	4 (0.7%)	0.799
re-PCI	129 (11.7%)	66 (12.3%)	0.732
CABG	4 (0.4%)	2 (0.4%)	0.976
MACE (hierarchical)	165 (14.9%)	81 (15.1%)	0.953
Definite / probable stent thrombosis	4 (0.9%)	6 (2.6%)	0.097

Table 72: Meliga 2011[82]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Meliga E, Fiorina C, Valgimigli M, Belli R, Gagnor A, Sheiban I et al. Early angio-guided complete revascularization versus culprit vessel pci followed by ischemia-guided staged PCI in STEMI patients with multivessel disease. Journal of Interventional Cardiology. 2011; 24(6):535-541.	Design Retrospective cohort study, multicentre (6 tertiary care centres), consecutive patients treated between 2004 to 2008, Italy	n = 800 Decision to address patients to a multivessel PCI or culprit-only PPCI approach was dependent on the policy of the single institution. Incomplete was the default strategy in 3/6 institutions	Inclusion criteria patients with STEMI with multivessel disease who had PPCI at the centres Exclusion criteria patients who did not survive to PPCI or who underwent multivessel PCI during the index procedure patients with extensive CAD in whom bypass surgery was likely to be required within ≤ 30 days patients in whom the non-IRA was a chronic total occlusion or a vessel < 2mm diameter Demographics and baseline characteristics see below Drug therapy not detailed	Culprit only revascularisation (COR) n = 383	Staged revascularisation during index stay (SR) n = 417	In-hospital Mean follow-up 642 (545) days	All-cause mortality Reinfarction Repeat revascularisation	None stated

Baseline characteristics				
	COR (n = 383)	**MVR (n = 417)**	**p value**	
Male, mean (SD)	78.3	74.6	0.63	

Age, mean (SD)	64.5 (11.3)	66.9 (12.4)	0.21
Hypertension	42.8	49.2	0.2
Dyslipidemia	35.5	44.4	0.05
Diabetes	19.3	12.0	0.22
Active smokers	33.4	34.5	0.13
Extracardiac arteriopathy	7.8	1.9	0.08
Familial history	13.8	17.7	0.82
Previous PCI	9.9	10.1	0.94
Previous CABG	1.8	1.9	0.81
Previous acute MI	13.6	8.4	0.31
Number of diseased vessels			
2	61.6	64.8	0.32
3	38.6	35.2	0.11
Culprit lesion site			
LAD	42.2	39.7	0.35
Cx	19.2	23.5	0.29
RCA	38.6	36.8	0.38
Culprit lesion site			
LAD	42.2	39.7	0.01
Cx	19.2	23.5	0.01
RCA	38.6	36.8	0.01
stenosis (nonculprit lesion)	84	81	0.13
RVD	3.22 (0.67)	3.04 (0.34)	0.14
Bare metal stent for culprit lesion	96.2	91.1	0.58
Bare metal stent for nonculprit lesion	65.5	33.9	0.01
Time to PCI on non-IRAs	7 (4.2)	41 (23)	0.01
patients having PCI on non-IRAs	100	68.4	0.01
LVEF	54.8 (13.6)	55.1 (12.9)	0.64

Glycoprotein IIIb/IIa used	89.4	87.5	0.38
Results			
In-hospital events	**SR (n = 417)**	**COR (n = 383)**	**p value**
Death	10	17	0.11
Reinfarction	58	12	0.01
Repeat revascularisation	15	6	0.08
21 months events	**SR (n = 417)**	**COR (n = 383)**	**p value**
Death	19	28	0.13
Reinfarction	20	26	0.22
Revascularisation	72	34	0.012

Table 73: Nat'l CV Data Reg 2009[24]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Outcome measures	Source of funding
Cavender MA, Milford-Beland S, Roe MT, Peterson ED, Weintraub WS, Rao SV. Prevalence, predictors, and in-hospital outcomes of non-infarct artery intervention during primary percutaneous coronary intervention for ST-	Design Retrospective cohort study; National Cardiovascular Data registry, data from > 600 sites across USA, April 2004 to March 2007	n = 28936 **Length of follow-up:** 'In-hospital'	Inclusion criteria patients presenting with STEMI coronary artery disease in >1 major artery STEMI is defined as: Indicate whether the patient was hospitalised for an ST Elevation Myocardial Infarction (STEMI) documented in the medical record. At least one of the following biochemical indicators for detecting myocardial necrosis must be present (see below for a definition of Reference Control Limits): 1) Troponin T or I: a) Maximal concentration of troponin T or I > the MI decision limit on at least 1 occasion during the first 24	Culprit only revascularisation (COR); the infarct related artery only was treated and the other arteries were left untreated n = 25802	Multivessel revascularisation (MVR) n = 3134	All-cause mortality Cerebrovascular accident / Stroke Bleeding complications Renal failure	American College of Cardiology, Washington DC and Society for Cardiac Angiography and Interventions, Washington, DC

segment elevation myocardial infarction (from the National Cardiovascular Data Registry). American Journal of Cardiology. 2009; 104(4):507-513.			hours after the index clinical event. 2) CK-MB: a) Maximal value of CK-MB > 2× the upper limit of normal on 1 occasion during the first hours after the index clinical event; OR b) Maximal value of CK-MB, preferable CK-MB mass, > upper limit of normal on 2 successive samples. 3) Total CK a) In the absence of availability of a troponin or CK-MB assay, total CK > 2× the upper limit of normal, or the B fraction of CK may be employed, but these last 2 biomarkers are considerably less satisfactory than CK-MB; and one of the following ECG changes: 1) ST-segment elevation: New or presumed new ST-segment elevation at the J point in 2 or more contiguous leads with the cut-off points ≥ 0.2 mV in leads V1, V2, or V3, or ≥ 0.1 mV in other leads; OR 2) Development of any Q wave in leads V1 through V3, or the development of a Q-wave ≥ 30 ms (0.03 seconds) in leads I, II, aVL, aVF, V4, V5, or V6. (Q wave changes must be present in any 2 continguous leads, and be ≥ 1 mm in depth.) in patients with multivessel PCI, the infarct-related artery was considered the artery with the greatest preoperative stenosis (in percentages), in the event of a tie, the artery with				

			the worst pre-PCI TIMI flow was considered the infarct-related artery patients with cardiogenic shock included; patients with the systolic blood pressure < 80 mmHg, or a cardiac index < 1.8 despite maximal treatment or requiring intravenous ion tropes, or an intra-aortic balloon pump to maintain the systolic blood pressure at > 80 mmHg and or cardiac index > 1.8 litres/minute/m^2 were classified as being in cardiogenic shock Exclusion criteria Patients receiving PPCI of the left main coronary artery Patients receiving staged PCI (multiple PCI procedures before hospital discharge) Patients receiving fibrinolytics Demographics and baseline characteristics see below Drug therapy Not detailed				

Baseline characteristics				
	COR (n = 25,802)	**MVR (n = 3134)**	**p value**	
Age (years) median (IQR)	62 (53–73)	60 (52–72)	< 0.01	
Male gender, (%)	72.1	71.5	0.32	
Previous MI, (%)	19.3	17.4	< 0.01	
Previous PCI, (%)	17.4	15.1	< 0.01	

Previous CABG, (%)	9.9	5.1	< 0.01	
Cerebrovascular disease, (%)	7.7	8.2	0.37	
Congestive heart disease, (%)	9.8	13.2	< 0.01	
Diabetes, (%)	23.4	24.7	0.06	
Hypertension, (%)	63.2	60.4	< 0.01	
Hypercholesterolemia, (%)	58.6	56.5	0.05	
Renal failure, (%)			> 0.99	
Interval from symptom onset to admission				
≤ 6 hours, (%)	78.8	74.4		
> 6 and ≤ 12 hours, (%)	10.1	10.6		
> 12 and ≤ 24 hours (%)	5.3	6.7		
> 24 and ≤ 48 hours, (%)	2.6	3.8		
> 48 hours and ≤ 7 days, (%)	2.6	4.1		
No time / silent MI, (%)	0.5	0.6		
LVEF, (%)	7.0	10.0		
Cardiogenic shock on presentation, (%)	10.3	13.8		
Emergent or salvage PCI status, (%)	91.3	87.3		
Intra-aortic balloon pump use, (%)	11.1	16.0		
Culprit coronary lesion, (%)		< 0.01		
Proximal LAD artery	16.9	19.8		
Proximal right, mid LAD, proximal circumflex artery	35.5	32.2		
Other	47.2	47.6		
Contrast volume (ml)		< 0.01		
Median	200	255		
Quartile 1, quartile 3 150, 262	200, 336			
Fluoroscopy time (min)		< 0.01		

Median	11.5	16.2	
Quartile 1, quartile 3	7.6, 17.9	11.3, 24.0	
	COR (n = 605)	MVR (n = 193)	p value
Results			
All patients with STEMI	**n = 25802**	**n = 3134**	**p value**
In-hospital all-cause mortality, n (%)	1321 (5.12)	246 (7.85)	< 0.01
Cerebrovascular accident/stroke, n (%)	144 (0.56)	22 (0.72)	0.31
Bleeding complications, n (%)	1368 (5.30)	210 (6.71)	< 0.01
Renal failure, n (%)	467 (1.81)	72 (2.31)	0.09
Patients with STEMI without	n = 23,146	n = 2701	p value
In-hospital all-cause mortality, n (%)	585 (2.53)	88 (3.26)	0.09
Cerebrovascular accident/stroke, n (%)	106 (0.46)	12 (0.45)	0.90
Bleeding complications, n (%)	1049 (4.53)	151 (5.67)	0.02
Renal failure, n (%)	280 (1.21)	23 (1.23)	0.96
Patients with STEMI with	n = 2654	n = 433	p value
In-hospital all-cause mortality, n (%)	737 (27.77)	158 (36.49)	≤ 0.01
Cerebrovascular accident/stroke, n (%)	40 (1.49)	11 (2.56)	0.18
Bleeding complications, n (%)	331 (12.48)	60 (13.81)	0.44
Renal failure, n (%)	197 (7.41)	42 (9.72)	0.03

Table 74: NYS Angioplasty Reg 2006[64]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Kong JA, Chou ET, Minutello RM, Wong SC, Hong MK. Safety of single versus multi-vessel angioplasty for patients with acute myocardial infarction and multi-vessel coronary artery disease: report from the New York State Angioplasty Registry. Coronary Artery Disease. 2006; 17(1):71-75.	Design Retrospective cohort study; New York State Angioplasty Registry database 2000 – 2001	n = 1982	Inclusion criteria acute MI multivessel disease >70% stenosis in at least 2 major coronary arteries PCI within 24 hours of acute MI Exclusion criteria cardiogenic shock haemodynamic instability cardio pulmonary resuscitation left main stenosis >50% Haemodynamic instability (ie, Killip state > 2 or cardiogenic shock) history of prior MI, PCI, or coronary artery bypass surgery Demographics and baseline characteristics see below Drug therapy see below	Culprit only revascularisation (COR); the infarct related artery only was treated and the other arteries were left untreated n = 1350	Multivessel revascularisation (MVR) n = 632	In-hospital	All-cause mortality Confounders taken into account in the propensity analysis (stepwise multiple logistic regression analysis for independent predictors); age, sex, hypertension, diabetes, tobacco use, prior stroke, chronic renal failure, peripheral vascular disease, congestive heart failure, ejection fraction, GP IIb/III a inhibitor therapy, fibrinolytic therapy, PCI total occlusion, proximal LAD lesion present, proximal LAD lesion present, no PCI, stent	None stated

Baseline characteristics				
	COR (n = 1350)	**MVR (n = 632)**	**p value**	
Age (years), n (%)	62.0 (13.0)	60.0 (12.3)	0.002	
Female (%)	27.9	22.8	0.016	
Hypertension (%)	61.3	31.9	NS	
Diabetes (%)	20.5	16.8	0 .051	
Tobacco use (%)	36.7	37.2	NS	
Prior stroke (%)	3.9	1.3	0.001	
Chronic renal failure (%)	1.0	0.6	NS	
Peripheral vascular disease (%)	8.9	4.7	0.001	
Clinical and procedural characteristics				
	COR (n = 1350)	**MVR (n = 632)**	**p value**	
Congestive heart failure on admission (%)	7.9	6.6	NS	
Ejection fraction mean (SD)	46.5 (11.2)% (n = 1125)	48.3 (10.5) % (n = 582)	0.002	
GP IIb/IIIa inhibitor therapy (%)	20.0	21.2	NS	
PCI total occlusion (%)	52.0	41.8	< 0.001	
Proximal LAD lesion present (%)	26.1	25.6	NS	
Proximal LAD lesion present, no PCI (%)	7.0	0.9	< 0.001	
Stent(%)	91.3	98.9	< 0.001	
Congestive heart failure on admission (%)	7.9	6.6	NS	
Length of stay (days) mean (SD)	5.4 (6.7)	5.3 (8.1)	NS	
Angiographic characteristics				
	COR (n = 1350)	MVR (n = 632)	p value	
Number of lesions >70%, per patient	3.2	3.5	< 0.001	

A	12.0	8.4	< 0.001	
B	60.6	67.5	< 0.001	
C	27.5	24.1	0.004	
Lesions treated / lesions present (%)				
A	209/511 (40.9)	175/186 (94.1)	< 0.001	
B	1362/2584 (52.7)	1403/1488 (94.3)	< 0.001	
C	757/1172 (64.6)	496/531 (93.4)	< 0 .001	
Total lesions treated/present (%)	2328/4267 (54.5)	2074/2205 (94.1)	< 0.001	
Results				
	COR (n = 1350)	**MVR (n = 632)**	**p value**	
All-cause mortality (%)	2.3	0.8	0.018	
Emergent bypass surgery (%)	0.7	0.5	NS	
Acute occlusion or stent thrombosis (%)	0.7	0.9	NS	
Stroke (%)	1.0	0.8	NS	
Renal failure requiring dialysis (%)	0.2	0.3	NS	
Length of stay (days) mean (SD)	5.4 (6.7)	5.3 (8.1)	NS	

Table 75: NYS PCIRS 2010[51]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Outcome measures	Source of funding
Hannan EL, Samadashvili Z, Walford G, Holmes DR, Jr., Jacobs AK, Stamato NJ et al. Culprit vessel percutaneous coronary intervention versus multivessel and staged percutaneous coronary intervention for ST-segment elevation myocardial infarction patients with multivessel disease. JACC Cardiovascular Interventions. 2010; 3(1):22-31.	Design Retrospective cohort study obtained from New York State's Percutaneous Coronary Interventions Reporting System (PCIRS), January 2003 to June 2006, USA	n = 4024, outcome data available for 1006 patients. **Length of follow-up:** In-hospital 12, 24, and 42 months	Inclusion criteria all multivessel disease patients (New York State residents) who experienced a STEMI within 24 hours before undergoing PCI Exclusion criteria patients with missing ejection fraction left main disease previous open-heart surgery cardiogenic shock fibrinolytic therapy before PCI Demographics and baseline characteristics see below Drug therapy not detailed	Culprit only revascularisation (COR); the infarct related artery only was treated and the other arteries were left untreated n = 538, propensity matched with MVR group n = 259, propensity matched with SR group Patients preprocedural characteristics that were potentially related to whether patients underwent single vessel or multivessel PCI were identified, patients matched on the basis of those characteristics with propensity matched samples Matching characteristics included demographic data, left ventricular function, haemodynamic status, the number and location (left anterior descending coronary artery/no left anterior descending artery) of disease coronary vessels, congestive heart failure, TIMI flow, several co morbidities and device used	Multivessel revascularisation(MVR); revascularisation of infarct related artery and other diseased vessels n = 259 Staged multivessel revascularisation (In-hospital SR); revascularisation of index infarct related artery and other vessels during index visit n = 259 Staged multivessel revascularisation (within 60 days SR); revascularisation of index infarct related artery and other vessels within 60 days n =538	All-cause mortality	None stated

Baseline characteristics

Demographic factors for COR PPCI versus MVR PCI population

Risk factor	Percent with culprit vessel revascularisation at time of PPCI, n = 503	Percent with multivessel revascularisation at time of PCI, n = 503	Standard difference (%)	

Age				
59 or less	55.47	54.67	1.60	
60 to 69	20.68	21.67	2.43	
70 to 79	15.7	14.12	4.47	
80 or more	8.15	9.54	4.90	
Female	21.27	25.05	8.96	
Cardiac factors				
Number of diseased vessels				
2 no proximal LAD	49.30	50.30	1.99	
2 with proximal LAD	24.25	24.06	0.46	
3 no proximal LAD	15.71	17.10	3.76	
Ejection fracture				
19% or less	2.39	3.38	5.94	
20% to 29%	6.16	7.55	5.51	
30% to 39%	16.30	16.30	0.07	
40% to 49%	28.63	28.23	0.88	
50% or more	46.52	44.53	3.99	
Haenodynamic status				
Unstable	2.98	4.77	9.28	
Chronic heart failure history				
Chronic total occlusion	5.57	5.37	0.87	
TIMI flow grade ≤ 2	40.16	43.54	6.86	
Comorbidities				
Cerebrovascular	3.38	3.78	2.14	
Peripheral vascular	3.58	4.17	3.09	
Ventricular arrhythmia	1.79	1.79	0.07	

COPD	4.97	5.37	1.80	
Renal failure	0.80	1.60	7.33	
Type of PCI				
Only drug eluting stent	57.85	57.06	1.61	
Bare metal stent	40.95	41.35	0.81	
No stents	1.19	1.59	3.39	
Baseline characteristics for COR PPCI and SR PCI populations				
Demographic factors				
Age, years				
Risk factor	**Percent with culprit vessel revascularisation at time of PPCI, n = 503**	**Percent with staged revascularisation at time of PPCI, n = 503**	**Standard difference (%)**	
59 or less	47.88	49.03	2.32	
60 to 69	28.96	28.96	0.00	
70 to 79	16.60	16.99	1.03	
80 or more	6.56	5.02	6.62	
Female	18.90	15.83	8.16	
Cardiac factors				
Number of diseased vessels				
2 no proximal LAD	40.15	42.08	3.92	
2 with proximal LAD	18.15	15.83	6.17	
3 no proximal LAD	26.64	27.80	2.60	
Ejection fracture				
19% or less	1.16	1.16	0.00	
20% to 29%	7.34	5.79	6.24	

30% to 39%	18.53	19.31	1.97	
40% to 49%	31.66	29.34	5.03	
50% or more	41.31	44.40	6.24	
Haemodynamic status				
Unstable	3.47	3.09	2.17	
Chronic heart failure history				
This admission	4.10	2.32	9.08	
Chronic total occlusion	6.56	7.72	4.50	
TIMI flow grade ≤ 2	50.58	53.28	5.41	
Comorbidities				
Cerebrovascular	3.86	4.63	3.83	
Peripheral vascular	2.70	2.32	2.47	
Ventricular arrhythmia	0.39	1.16	8.83	
COPD	6.56	6.95	1.54	
Renal failure	0.39	0.39	0.00	
Type of PCI				
Only drug eluting stent	65.64	66.80	2.45	
Bare metal stent	31.27	30.5	1.67	
No stents	3.09	2.70	2.30	
Results				
Mortality rates for propensity matched STEMI patients; COR versus in-hospital MVR, n (%)				
	COR	**In-hospital SR**	**percentage difference**	**p value**
In-hospital	10 (2.0)	17 (3.4)	1.4	0.14
12 months	28 (5.5)	35 (7.1)	1.6	0.23
24 months	33 (6.6)	43 (8.6)	2.0	0.17
42 months	54 (10.8)	60 (11.8)	1.0	0.23
In-hospital	10 (2.0)	17 (3.4)	1.4	0.14
Mortality rates for propensity matched STEMI patients; COR versus in-hospital SR, n (%)				
	COR	In-hospital SR	percentage difference	p value

In-hospital	5 (1.9)	3 (1.2)	0.7	0.48
12 months	14 (5.5)	10 (3.9)	1.6	0.53
24 months	19 (7.4)	16 (6.3)	1.1	0.71
42 months	22 (8.4)	16 (6.3)	2.1	0.72

Table 76: Politi 2010[92]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Outcome measures	Source of funding
Politi L, Sgura F, Rossi R, Monopoli D, Guerri E, Leuzzi C et al. A randomised trial of target-vessel versus multi-vessel revascularisation in ST-elevation myocardial infarction: major adverse cardiac events during long-term follow-up. Heart (British Cardiac Society). 2010; 96(9):662-667.	Design RCT single centre Italy Enrolment Jan 2003 to Dec 2007 Randomisation Before the angioplasty, dedicated software generated a number (1 for the COR group, 2 for the capital SR group and 3 for the MVR group) Allocation concealment Not detailed Blinding Open label Sample size	n = 214 Excluded patients: n = 4 patients with unsuccessful procedure included in randomisation but not in final analysis **Length of follow-up:** In-hospital Mean (SD) 2.5(1.4) years	Inclusion criteria presence of prolonged (more than 30 min) chest pain started less than 12 hours before hospital arrival and ST segment elevation of at least 1 mm in 2 or more contiguous electrocardiographic leads (peripheral leads) or 2 mm in the pre-cordial leads multivessel coronary artery disease (defined as greater than 70% diameter stenosis of 2 or more epicardial coronary arteries, or their major branches by visual estimation Exclusion criteria <18 years Active bleeding or significant increased risk of bleeding (severe hepatic insufficiency, current peptic ulceration, proliferative diabetic retinopathy) uncontrolled hypertension carcinogenic shock	Culprit only revascularisation (COR); the infarct related artery only was treated and the other arteries were left untreated n = 84	1. Multivessel revascularisation(MVR); the infarct related artery was opened followed by dilation of other significantly narrowed arteries during the same procedure n = 65 2. Stage revascularisation (SR); the infarct related artery only was treated during the primary intervention while the complete revascularisation was planned in the second procedure n = 65	In-hospital All-cause mortality Long-term All-cause mortality Reinfarction Repeat revascularisation Cardiac death	None stated

	calculation Sample size was calculated on the primary end point (major adverse cardiac event (MACE) defined as cardiac or non-cardiac death, in-hospital death, reinfarction, re-hospitalisation for acute coronary syndrome and repeat coronary revascularisation). Note MACE is not outcome of interest for clinical question. In an expected rate of MACE of 17% full groups undergoing multivessel revascularisation (both simultaneous and staged) versus 50% for the culprit-only group, aiming for a 0.05 alpha and 0.90 power, the total of 123 patients needed to be enrolled (41 patients per group). ITT analysis Yes		severe peripheral vascular disease precluding a femoral approach previous coronary bypass surgery with use of >1 internal mammary artery Previously entered in the study Investigational treatment (drug or drug device) within the previous ≤ 30 days Demographics and baseline characteristics see below Drug therapy Before procedure patients were treated with aspirin, unfractionated heparin, and abciximab bolus followed by 12 hour infusion. In addition, the bolus of N- acetylcysteine 1200 mg and hydration was saline for 12 hours after contrast exposure as infusion rate of 1 ml/kg per hour. Iodixamol was used as a contrast media in all patients. Post PPCI medical oral treatment included aspirin, statins and clopidogrel, unless contraindicated, which was recommended for ≤ 30 days in case of bare metal stent implantation and 12 months in case of drug eluting stents. See below for further information.				

Baseline characteristics				
	COR (n = 84)	**SR (n = 65)**	**MVR (n = 65)**	**p value**
Age (years)	66.9 (13.2)	64.1 (11.1)	64.5 (11.7)	0.413
Male gender, n (%)	64 (76.2)	52 (80.0)	50 (76.9)	0.849
Diabetes, n (%)	20 (23.8)	12 (18.5)	9 (13.8)	0.305
Hypertension, n (%)	50 (59.5)	42 (64.6)	32 (49.2)	0.192
Systolic blood pressure before PPCI, mm Hg, mean (SD)	136.2 (30.2)	136.2 (31.4)	136.0 (24.3)	0.999
Anterior location of STEMI, n (%)	35 (41.7)	28 (43.8)	31 (47.7)	0.761
Killip class that admission, mean (SD)	1.48 (0.61)	1.40 (0.70)	1.24 (0.53)	0.083
Three-vessel disease, n (%)	21 (25.0)	29 (44.6)	19 (29.2)	0.033
TIMI flow grade before PPCI, mean (SD)	0.76 (1.21)	0.89 (1.21)	1.11 (1.32)	0.244
Door to balloon time, min mean (SD)	63.1 (27.2)	65.7 (19.4)	60.1 (22.6)	0.824
Drug eluting stent, n (%)	10 (11.9)	6 (9.2)	5 (7.7)	0.722
Chronic renal failure, n (%)	24 (29.3)	16 (24.6)	17 (26.6)	0.816
Plasma creatine before PPCI mg/dl, mean (SD)	1.14(0.69)	1.13 (0.99)	0.98 (0.27)	0.369
Contrast induced neuropathy n (%)	3 (3.6)	2 (3.1)	1 (1.5)	0.748
Therapy at discharge	n = 77	n = 65	n = 63	
aspirin, n (%)	74 (96.1)	65 (100)	62 (98.4)	0.239
clopidogrel, n (%)	71 (92.2)	65 (100)	61 (96.8)	0.054
beta-blockers, n (%)	62 (80.5)	52 (80.0)	52 (82.5)	0.927
nitrates, n (%)	16 (20.8)	4 (6.2)	4 (6.3)	0.007
ACE inhibitors, n (%)	48 (62.3)	38 (58.5)	35 (55.6)	0.594
Results				

In-hospital outcomes			
	COR (n = 84)	**SR (n = 65)**	**MVR (n = 65)**
In-hospital all-cause mortality, n (%)	7 (8.3)	0 (0)	2 (3.1)
Length of hospital stay, days, n (%)	5.3 (2.5)	5.4 (3.1)	4.8 (2.6)
Rehospitalisation, n (%)	30 (35.7)	9 (13.8)	8 (12.3)
Length of hospital stay, days, n (%)	5.3 (2.5)	5.4 (3.1)	4.8 (2.6)
Follow-up (mean(SD)) 2.5(1.4) years			
	COR (n = 84)	SR (n = 65)	MVR (n = 65)
Repeat revascularisation, n (%)	28 (33.3)	8 (12.3)	6 (9.2)
All-cause mortality, n (%)	13 (15.5)	4 (6.2)	6 (9.2)
Cardiac death, n (%)	10 (11.9)	2 (3.1)	4 (6.3)
Reinfarction, n (%)	7 (8.3)	4 (6.2)	2 (3.1)

G.6 Cardiogenic shock

Table 77: SHOCK

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
30 DAYS and 6 MONTHS Hochman JS et al. 1999 [53] 1 YEAR DATA Hochman JS et al. 2001 SHOCK Investigators 2001 [54] 6- YEAR DATA Hochman JS et al. 2006 SHOCK Investigators [55] QUALITY OF LIFE and HEART FAILURE Sleeper LA et al. 2005 SHOCK Investigators [103] ADVERSE EVENTS Hochman J.	**Design:** RCT **Enrolment:** April 1993 to November 1998. **Setting** 30 sites in USA and Canada and 20% in other countries. **Randomisation** Patients were enrolled by means of computerised telephone randomisation, with randomisation at each site performed according to a permuted-block design. **Allocation concealment:** Yes. Central telephone system.	n = 302 Drop-outs (lost to follow-up): Hospital survivors n = 143 6 MONTHS 2 patients were lost (n = 1 ERV and n = 1 IMS) 1 YEAR n = 1 (IMS patient was omitted from survival analysis) 6 YEARS (April 2005)	**Inclusion criteria** ST-segment elevation, Q-wave infarction, a new left bundle-branch block or a posterior infarction with anterior ST-segment depression, complicated by shock due to left ventricular dysfunction Onset of shock <36 hours of infarction and randomisation no more than 12 hours after diagnosis of shock. **Exclusion criteria** Severe systemic illness Mechanical or other cause of shock Sever vulgar disease Dilated cardiomyopathy Inability to gain catheterisation Unsuitable for revascularisation Demographics and baseline characteristics see below	(n = 152) Early Revascularisation (ERV) Intra-aortic balloon pump (IABP/Pharmacological support Possible prior fibrinolysis Emergency early PCI/CABG Hospital survivors (n = 77) Notes: Had to be performed of randomisation Intra-aortic balloon counterpulsation was recommended.	(n = 150) Initial medical stabilisation (IMS) IABP/Pharmacological support Fibrinolysis unless absolute contraindication Delayed revascularisation at a minimum of 54 hours Hospital survivors (n = 66) **Notes:** Intra-aortic balloon counterpulsation and fibrinolytic therapy recommended.	30 days, 6 months 1 year 6 years MILQ, NYHA 2 weeks after discharge, 6 and 12 months Notes: Hospital survivors, median follow-up was 5.9 (up to 11 years) An updated vital status was obtained for all	1° All-cause mortality 2° Multidimensional Index of Life Quality (MILQ) – instrumen t point questions, Andrew's life'. New York Heart Associatio congestive failure	National Heart, Lung and Blood Institute. & American Heart foundation.

1999 (SHOCK)[52] SUBGROUP ANALYSIS DIABETES Farkouh ME, et al. 2006 SHOCK Trial Investigators[45] Shindler DM et al. 2000[101] AGE Dzavik V et al. 2005 (SHOCK)[36] Jeger RV et al. 2011	**Blinding:** Angiograms and echocardiograms were viewed by readers blind to enrolling site and treatment group. **Sample size calculation:** 328 patients would give the study 90 percent power, with an overall type I error rate of 0.05 to detect 20% absolute difference. 30 DAYS, 6 MONTHS **ITT analysis**: Yes 1 YEAR ITT analysis: Yes 6 YEARS ITT analysis: Yes AGE SUBGROUPS: ITT analysis: Yes DIABETES ITT analysis: Yes	ERV n = 70 (24 dead, 46 alive) IMS n = 51 (20 dead, 31 alive)	Definitions Used Index MI- Prolonged (> 30 minutes) chest pain or equivalent symptoms ECG criteria at time of MI diagnosis: ≥ 2 leads with ST elevation or ≥ 1 mm precordial ST depression known to reflect posterior STEMI OR new left bundle branch black (known not to be old) OR new pathologic Q waves in ≥ 2 related leads or posterior Q waves manifested by R/S ration V1 or V2 > 1 Cardiogenic shock – Clinical criteria were hypotension (SBP < 90 mm Hg for at least 30 minutes or supportive measure to maintain SBP ≥ 90 mm Hg) and end-organ hypoperfusion (cool extremities or a urine output of < 30ml per hour and heart rate of ≥ 60 beats per minute). Haversusemodynamic criteria were a cardiac index of no more than 2.2 litres/minute/m^2 body-surface area and pulmonary-capillary wedge pressure of at least		Delayed revascularisation at minimum of 54 hours after randomisation.	patients in 1999–2000 regardless of randomisation date. Follow-up visits were conducted annually from until April 2005.	class – using 4 standard questions Renal failure Major/minor bleeding Intracranial bleeding IABP – intra-aortic balloon pump	

	QUALITY OF LIFE ITT analysis: No. PPA		15mm Hg.					

End point definitions:
Acute renal failure – serum creatine level above of 3.0mg per decilitre
NYHA Congestive Heart Failure -
Class I: no limitation is experienced in any activities; there are no symptoms from ordinary activities.
Class II: slight, mild limitation of activity; the patient is comfortable at rest or with mild exertion.
Class III: marked limitation of any activity; the patient is comfortable only at rest.
Class IV: any physical activity brings on discomfort and symptoms occur at rest.

Baseline characteristics. Patients in 2 groups were similar except that more patients in IMS had previously undergone bypass surgery

	Early Revascularisation (n =152)	**Initial Medical Stabilisation (n =150)**
Mean age, years (SD)	65.5 ± 10.0	66.2 ± 10.9
Men (%)	63.2	72.7
Hypertension (%)	49.0	43.5
White race, non-Hispanic	72.4	78.7
Previous MI (%)	29.6	35.3
Hypertension (%)	49.0	43.5
Diabetes mellitus (%)	34.2	27.9
Congestive heart failure (%)	4.0	8.2
Renal insufficiency (%)	4.6	6.9
Prior coronary artery by-pass grafting (%)	2.0	10.0
Cigarette smoking (%)	52.6	56.8
Eligible for fibrinolytic therapy (%)	94.1	94.6
Transfer admission (%)	55.3	55.3
Anterior index MI (%)	63.6	57.4
Highest total creatine kinase (IU/L)	3068 (1322–6350)	3464 (1543–5411)
Median time from MI to shock (hr)	5.0 (2.2–12.0)	6.2 (2.4–15.5)

Median time from MI to randomisation (hr)	11.0 (5.9–19.4)	12.0 (6.3–21.8)
<6 hr from MI to randomisation (%)	25.0	23.7
Lowest systolic blood pressure (mm Hg)	66.4 ± 14.3	69.8 ± 11.3
Systolic blood pressure (mm Hg)	89.0 ± 22.8	86.5 ± 17.4
Diastolic blood pressure (mm Hg)	53.9 ± 16.8	55.1 ± 13.6
Heart rate (beats/minute)	103.3 ± 22.0	100.1 ± 22.7
Pulmonary-capillary wedge pressure (mm Hg)	24.2 ± 7.1	24.3 ± 7.7
Cardiac index (litres/minute/m^2)	1.8 ± 0.7	1.7 ± 0.5
Left ventricular ejection fraction (%)	29.1 ± 10.6	32.5 ± 13.9
Number of diseased vessels (%)		
≤ 1	14	11.5
2	21.7	24
3	64.3	64.6
Left main coronary artery disease (%)	23.4	17.5

Treatment (includes treatment recommended or required according to the protocol i.e fibrinolytic therapy & revascularisation)

	Early Revascularisation n = 152 n (%)	**Initial Medical Stabilisation n = 150 n (%)**
Cardiopulmonary resuscitation, VT, or VF before randomisation N/total (%)	37/113 (32.7%)	27/113 (23.9%)
Fibrinolytic therapy, N (%)	75 (49.3%)	95 (63.3%)
Inotropes or vasopressors, N (%)	151 (99.3%)	148 (98.6%)
Intraaortic balloon counterpulsation, N (%)	131 (86.2%)	129 (86.0%)
Pulmonary-artery catheterisation, N (%)	142 (93.4%)	144 (96.0%)
Left ventricular assist device, N (%)	4/111 (3.6%)	1/110 (0.9%)
Heart transplantation, N (%)	3 (2.0%)	1 (0.7%)
Coronary angiography, N (%)	147 (96.7%)	100 (66.7%)
Angioplasty or coronary-artery bypass grafting, N (%)	132 (86.8%)	38 (25.3%)
Angioplasty, N (%)	83 (54.6%)	21 (14.0%)

• Stent placed	35.7	52.3
• Platelet glycoprotein IIb/IIIa receptor antagonist: N/total (%)	25/60 (41.7%)	5/20 (25.0%)
Coronary-artery bypass grafting, N (%)	57 (37.5%)	17 (11.3%)
Median time from randomisation to revascularisation (hr) (interquartile rage)	1.4(0.6–2.8)	102.8 (79.0–162.0)
Revascularisation more than 6 hours after revascularisation	10 (6.6%)	
VT: sustained ventricular tachycardia, VF: sustained ventricular fibrillation		

Treatment post randomisation

	Early Revascularisation (n = 152)	Initial Medical Stabilsation (n = 150)
No Revascularisation attempt	20	112
• Died prior to	5	?
IABP	86%	86%
Early Revascularisation attempt	125	3 (Performed less than 54 hours after randomisation (protocol violation))
• PCI	83	1
• CABG	42	2
Late Revascularisation attempt	7 (Performed more than 6 hours after randomisation (protocol violation))	35 (Protocol for this group: Performed at a minimum of 54 hours after randomisation (if clinically appropriate))
• PCI	1	20
• CABG	6	15

Results: Mortality at 30 days, 6 months, 1 year and 6 years

	Early Revascularisation (ERV) n = 152	Initial Medical Stabilisation (IMS) n = 150	RR 95% CI ERV versus IMS	Odds Ratio 95% CI ERV versus IMS	HR 95% CI ERV versus IMS
30-day mortality N/Total (%)					
Total[53]	71/152 (46.7%)	84/150 (56%)	0.83 (0.67 to 1.04)		
• Age < 75 years	53/128 (41.4%)	67/118 (56.8%)	0.73 (0.56 to 0.95)		

• Age > 75 years	18/24 (75.0%)	17/32 (53.1%)	1.41 (0.95 to 2.11)		
• Age > 75 years[58]			0.93 (0.39 to 2.25)		
• Age ≤ 75 years			0.83 (0.62 to 1.11)		
• Age 71–75			0.83 (0.48 to 1.43)		
• Age 68–70			0.82 (0.51 to 1.32)		
• Age 56–65			0.81 (0.52 to 1.26)		
• Age ≤ 55			0.86 (0.32 to 2.26)		
• Diabetes[45]				0.73 (0.42 to 1.27)	
• Non-diabetes[45]				0.54 (0.23 to 1.24)	
6 month mortality N/Total (%)[53] 2 patients (1 EVR and 1 IMS) were lost to follow-up					
Total	76/151 (50.3%)	94/149 (63.1%)	0.80 (0.65 to 0.98)		
• Age < 75 years	57/127 (44.9%)	76/117(65.0%)	0.70 (0.56 to 0.89)		
• Age > 75 years	19/24 (79.2%)	18/32 (56.3%)	1.41 (0.97 to 2.03)		
• Diabetes, N/total (%)[101]	23/51 (45%)	26/41 (63%)	0.71 (0.49 to 1.04)		
• Without diabetes, N/total (%) [101]	49/98 (50%)	66/106 (62%)	0.80 (0.63 to 1.03)		
1 year mortality, N/total (%)					
Total[54,55]	83/151 (55%)	109/150 (72.7%)	0.72 (0.54 to 0.95)		
Total[58]			0.83 (0.70 to 0.96)		
• Age > 75 years[58]			0.93 (0.56 to 1.53)		
• Age > 75 years[36]	19/24 (79.2%)	21/32 (65.6%)			
• Age < 75 years[36]	62/127 (48.4%)	78/117 (66.7%)			
• Age ≤ 75 years[58]			0.79 (0.63 to 0.99)		
• Age 71–75			0.86 (0.60 to 1.23)		
• Age 68–70			0.72 (0.48 to 1.09)		
• Age 56–65			0.78 (0.52 to 1.17)		
• Age ≤ 55			0.82 (0.30 to 2.26)		
6 year mortality, N/total					

(%)					
Total[55]	107/151 (71%)	119/150 (79.3%)			0.74 (0.57 to 0.97)

Renal Failure 30 days and Intracranial bleeding[52]

	Revascularisation	Medical therapy
Acute renal failure **n/Total (%)**	20/152 (13%)	36/150 (24%)
Intracranial bleeding **n/Total (%)**	0/152	2/150 (0.7%)

Multidimensional Index of Life Quality (MILQ) Physical Domain Scores of One-Year survivors by Treatment Modality and Time[103]. 35 questions, scoring from 1 to 7 each. Scores can range from 35 to 245, with a better quality of life showing a higher score.

	Revascularisation Max n = 41	Medical therapy Max n = 23
2 weeks after discharge	17.1 ± 5.2	15.9 ± 7.9
6 months post MI	19.9 ± 6.4	17.3 ± 5.7
1 year post MI	19.1 ± 6.2	19.3 ± 4.4

NYHA Congestive Heart Failure Class of 126 SHOCK trial hospital survivors

	Revascularisation	Medical therapy
2 weeks after discharge	**n = 58**	**n = 48**
Class I	n = 27 (46.6%)	n = 18 (37.5%)
Class II	n = 17 (29.3%)	n = 12 (25.0%)
Class III	n = 6 (10.3%)	n = 6 (12.5%)
Class IV	n = 8 (13.8%)	n = 12 (25.0%)
6 months post MI	**n = 55**	**n = 37**
Class I	n = 30 (54.6%)	n = 20 (54.1%)
Class II	n = 9 (16.4%)	n = 6 (16.2%)
Class III	n = 7 (12.7%)	n = 3 (8.1%)
Class IV	n = 9 (16.4%)	n = 8 (21.6%)
1 year post MI	**n = 54**	**n = 35**
Class I	n = 31 (57.4%)	n = 20 (57.1%)

Class II	n = 15 (27.8%)	n = 8 (22.9%)
Class III	n = 1 (1.9%)	n = 1(2.9%)
Class IV	n = 7 (13.0%)	n = 6 (17.1%)

Further analysis:

30 days: Adverse events including stroke and haemorrhage were similar in both groups[52] NB Abstract, no numbers provided.

1 year: No significant difference between treatment effect and gender or diabetes mellitus[54]

6 years: Long-term survival analysis of the entire cohort identified no interactions between treatment assignment and any subgroup factor, including age (≤75 versus ≥75 years), sex, diabetes.[55]

Figure 1: Study flow

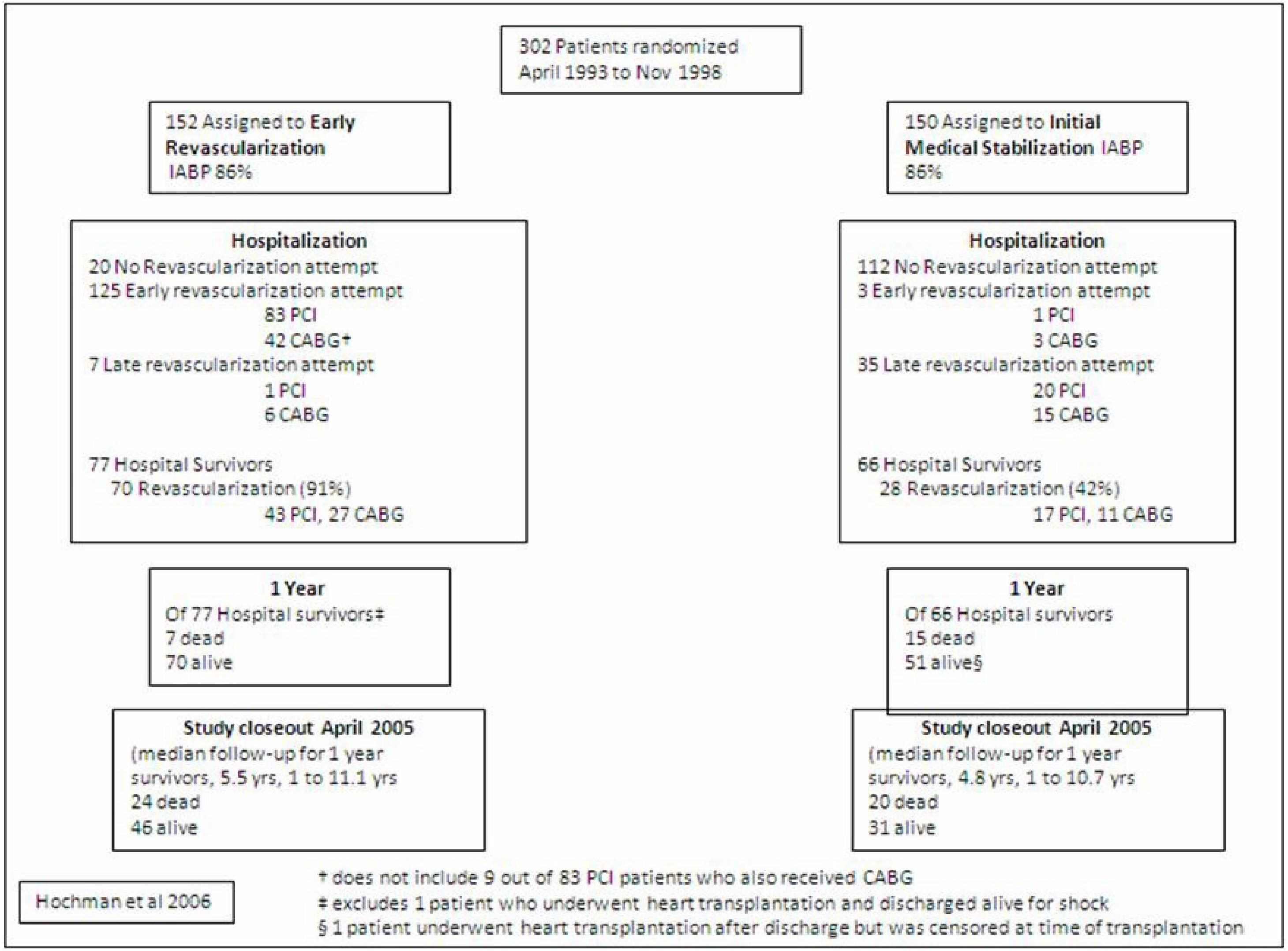


Table 78: SMASH

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Urban P et al. 1999 Shock-(S)MASH	**Design:** RCT (conducted with 2 parallel centres) **Enrolment:** Jan 1992 to May 1996 **Setting** 9 settings in 3 European countries **Randomisation** carried out by contacting a central 24/24 hours randomisation service by telephone. It was stratified for each individual centre. **Allocation concealment** Yes. Central telephone system **Power calculation:** Accepting a probability of a type I error of 0·05, and	n = 55	**Inclusion criteria** cardiogenic shock present for 30 minutes or more, with a systolic blood pressure of 90 mmHg or less for at least 30 minutes despite inotropic and intravenous volume administration as needed acute myocardial infarction onset <48 h prior to randomisation; the diagnosis was made if at least 2 of the following 3 elements were present: chest pain; ST segment elevation of at least 0·1 mV in limb leads or 0·2 mV in precordial leads or left bundle branch block; serum creatine-phosphokinase MB isoenzyme elevation above twice the upper limit of normal. if measured, capillary wedge pressure >15 mmHg and thermodilution cardiac index <2·2 l. min^{-1}. m^{-2}; coronary angiography technically feasible (vascular access and catheterisation laboratory available); informed consent given if requested. Exclusion criteria ongoing manual cardiopulmonary resuscitation; prior cardiac arrest with presumed severe cerebral damage; shock not primarily cardiogenic in origin, evidence of ventricular rupture (free wall or septum), acute severe mitral regurgitation, or pericardial tamponade;	Emergency Coronary Angiography n = 32 Notes: Patients were taken to the catheterisation laboratory as soon as possible, coronary angiography was completed, and PCI or CABG were attempted if considered feasible. Revascularisation procedures were performed with as little delay as possible.	Initial medical management n = 23 Notes: patients did not undergo immediate coronary angiography, but were admitted to the intensive care unit. Late coronary angiography, with or without subsequent revascularisation, was not considered a protocol violation.	30 days & after 1 year.	1° mortality from all-causes (cardiac and non-cardiac) 30 days after randomisation 2° need for non-emergency PCI or CABG during hospital stay; New York Heart Association (NYHA) heart failure class at discharge from hospital mortality, cardiac	Swiss Cardiology Foundation, Bristol-Myers Squibb AG, Switzerland, Schneider-Worldwide, Arteromed SA, Medtronic Europe, Cook (Switzerland) AG.

	desiring a 0·9 probability of detecting a true difference, 57 patients were required in each arm to demonstrate a significant difference between the 2 treatment strategies using a chi-square test. Bc recruitment was slow, the study was terminated when the presence of a 2-sided p value of < 0.029 was detected between 2 treatment arms. ITT analysis: Yes.		serious non-cardiac illness contraindicating an invasive approach; decision to perform angiography taken before the onset of shock 'need for PCI' (specific individual circumstances made immediate PCI indispensable in the opinion of the attending physicians). Investigators were encouraged to use this last exclusion criterion as seldom as possible Demographics and baseline characteristics see below				events and functional status at 1 year.	

End point definitions

Success of percutaneous revascularisation: the intervention was deemed a technical success by the operator if he/she estimated the residual diameter stenosis as < 50%
and the flow in the culprit vessel after the procedure as TIMI grade 2 or 3.

Reinfarction: No definition provided

Unplanned revascularisation: Counted as patients, post-hospital discharge, who required late percutaneous transluminal coronary angioplasty and late cardiac surgery

Stroke: No definition provided

Baseline characteristics at randomisation.

	Invasive (n = 32)	Conservative (n = 23)
Age (years, mean ± SD)	66 ± 10	64 ± 8
Age >65	19 (59%)	11 (48%)
Male sex	23 (72%)	14 (61%)
Hypertension 1	11 (34%)	6 (26%)
Diabetes	6 (19%)	4 (18%)
Smoking 3	19 (59%)	15 (65%)
Hypercholesterolaemia	6 (19%)	3 (14%)
Previous acute myocardial infarction	9 (28%)	10 (43%)
Previous PCI or CABG	3 (9%)	4 (17%)
Prior heart failure (NYHA >I)	9 (28%)	5 (22%)
Prior angina (CCS >I)	12 (38%)	10 (45%)
Median (range) time from acute myocardial infarction to shock (h)	2·5 (0–27)	5 (0–47)
Median (Range) time from shock to randomisation (h)	3 (0–33)	2 (1–7)
Heart rate (beats . min^{-1})	101 ± 30	105 ± 30
Systolic blood pressure	77 ± 10	78 ± 13
Cardiac index (l . min^{-1} . m^{-2})	1·7 ± 0·3 (n = 7)	1·8 (n = 1)
Pulmonary capillary wedge pressure	21 ± 4 (n = 8)	29 ± 6 (n = 4)
Anterior or lateral acute myocardial infarction	15 (47%)	10 (43%)
ST segment elevation	26 (81%)	18 (78%)
Right ventricular acute myocardial infarction	5 (16%)	4 (17%)
VF or sustained VT since acute myocardial infarction onset	9 (28%)	9 (39%)
Cardiopulmonary resuscitation required	9 (28%)	8 (35%)
Intravenous inotropes	30 (94%)	23 (100%)
Fibrinolysis	11 (34%)	9 (39%)
IABP	3 (9%)	1 (4%)
Temporary RV pacing	5 (16%)	4 (17%)
Tracheal intubation	15 (47%)	14 (61%)
Creatine phosphokinase > 2× upper limit of normal	15 (47%)	14 (61%)

Arterial pH	7·3 ± 0·1 (n = 20)	7·3 ± 0·1 (n = 13)
Lactates (mmol . l^{-1})	7.5 ± 4.8 (n = 11)	7.8 ± 6.0 (n = 8)

CCS: Canadian Cardiology Society (classification); IABP: intra-aortic balloon pump; VT: sustained ventricular tachycardia; VF: sustained ventricular fibrillation; RV: right ventricle

Outcomes

NYHA

- Class I: no limitation is experienced in any activities; there are no symptoms from ordinary activities.
- Class II: slight, mild limitation of activity; the patient is comfortable at rest or with mild exertion.
- Class III: marked limitation of any activity; the patient is comfortable only at rest.
- Class IV: any physical activity brings on discomfort and symptoms occur at rest.

Treatments

	Invasive	**Conservative**
30 days	**n = 32**	**n = 23** Subsequent revascularisation was not considered a protocol violation.
No Revascularisation attempt	4 (2 died before coronary angiography, 1 died after angiography before revascularisation, and 1 other patient was not revascularised because the residual lesion was considered non-significant)	
Early Revascularisation attempt		
• PCI	27	
• CABG	1	
Intra-aortic counterpulsation balloon (IABP) during hospital study, either prior to or following hospitalisation	21 (66%)	7 (30%)

Main outcomes at 30 days and 30 days to 1 year

	Invasive	**Conservative**
30 days	**n = 32**	**n = 23**
All-cause mortality	22 (69%)	18 (78%)
Reinfarction	1 (3%)	1 (4%)

Stroke	0	2 (13%)
Late PCI	0	1 (4%)
Late cardiac surgery	2 (6%)	0
Median Heart Failure, NYHA	II (I-III)	II (I-IV)
30 days to 1 year	**n = 10**	**n = 5**
Mortality	1 (10%)	1 (20%)
Reinfarction	0	0
Late PCI	0	0
Late cardiac surgery	1 (10%)	0

G.7 People who remain unconscious after a cardiac arrest

Table 79: Bulut 2000[18]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Effect sizes	Source of funding
Bulut S, Aengevaeren WRM, Luijten HJE, Verheugt FWA. Successful out-of-hospital cardiopulmonary resuscitation: What is the optimal in-hospital treatment strategy? Resuscitation. 2000; 47(2):155-161.	Retrospective cohort study, single centre, Netherlands	n = 30	Inclusion criteria • Out-of-hospital cardiac arrest • Electrographic and enzymatic evidence of acute MI Exclusion criteria • None given Baseline characteristics • None given for usual care • Mean (SD) age PPCI group, years: 53(13) • Mean (SD) cardiopulmonary resuscitation time PPCI group, minutes: 26 (12) Stents • Not reported GP 11b/111a inhibitor • Not reported	PPCI n = 10 Note 6/10 patients conscious prior to PPCI	Usual care n = 20 Note No data given for number of patients that were conscious after resuscitation	In-hospital	All-cause mortality Successful procedure, not defined (PPCI group only) Neurological recovery, not defined; (PPCI group only)	PPCI; 6/10 (60%) patients (4/6 patients due to neurological cause and 2/6 due to cardiac cause) Usual care; 13/20 (65%) patients (9/13 patients due to neurological cause) PPCI; 8/10 patients PPCI; 3/4 patients	None stated

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Effect sizes	Source of funding
Univariate (Pearson's Spearman rho and Kendall's tau model) Out of 21 possible predictive factors, the following items associated with in-hospital all-cause mortality; • Glasgow coma scale at admission (GSC), r = −0.77 • Need for ventilation in emergency department, r = −0.61 • Tracheal intubation on admission, r = −0.56 • Need for inotropic drugs at hospital, r = −0.54 • Need for inotropic drugs during transportation to hospital, r = −0.51 • Ventilation at admission, r = −0.51 • Duration of cardiopulmonary resuscitation, r = −0.46 • Cardiac rhythm on admission, r = −0.38 • Initial cardiac rhythm on admission, r = −0.37 • Presence of witness during collapse, r = −0.34 • Duration of stay in intensive care unit, r = −0.24 Multivariable stepwise regression analysis of 11 univariate factors associated with in-hospital all-cause mortality • GCS most important predictor, r = −0.76 (p < 0.001) Excluding GCS, following were predictive factors for in-hospital all-cause mortality • Initial cardiac rhythm on admission, r = −0.65 (p < 0.001) Ventilation at admission r = −0.60 (p < 0.001)									

Table 80: Liu 2012[76]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Outcome measures	Source of funding
Liu Hw, Pan W, Wang Lf, Sun Ym, Li Zq, Wang Zh. Impact of emergency percutaneous coronary intervention on outcomes of ST-segment elevation myocardial infarction patients complicated by out-of-hospital cardiac arrest. *Chinese Medical Journal.* 2012; 125(8):1405-1409.	Retrospective cohort study, China	n = 81 **Length of follow-up:** In hospital	Inclusion criteria • Out-of-hospital coronary arrest • Typical chest pain with ST-segment elevation ≥ 1 mm in at least 2 consecutive precordial or inferior limbs, or chest pain with new onset of complete bundle branch block Exclusion criteria: Not stated Demographics and baseline characteristics: See below Drug therapy: All patients received aspirin, clopidogrel, atorvastatin and subcutaneous low molecular weight heparin for 2–3 days. Beta blockers, ACEIs or ARBs and aldosterone receptor antagonists were administered early according to heart rate and blood pressure.	PCI n = 49	Usual care TH, restricted to comatose patients n = 32	All-cause mortality Stroke Acute renal failure Confounders taken into account in the covariates analysis	None stated

Baseline characteristics of the OHCA patients with and without PCI

	Without PCI (n = 32)	With PCI (n = 49)	p value
Male, n (%)	23 (71.9)	40 (81.6)	0.4477
Age (years), mean(SD)	59 (16)	54 (13)	0.1267
History of MI, n (%)	1 (3.1)	2 (4.1)	0.7048
Hypertension, n (%)	14 (43.8)	20 (40.8)	0.9751
Diabetes mellitus, n (%)	4 (12.5)	6 (12.2)	0.7555

Renal insufficiency, n (%)	2 (6.3)	2 (4.1)	0.9329
Smokers, n (%)	17 (53.1)	26 (53.1)	0.8242
Onset to admission time (minutes), mean (SD)	138 (42)	122 (38)	0.0794
On admission			
Systolic blood pressure (mmHg), mean (SD)			
Heart rate (beats/minutes), mean (SD)	101 (23)	96 (19)	0.2903
Killip IV, n (%)	15 (46.9)	19 (38.8)	0.6229
GCS ≤ 7, n (%)	10 (31.27)	14 (28.6)	0.9926
Results: During hospitalisation n, (%)			
Stroke			
Acute renal failure	3 (9.3)	1 (2.0)	0.3346
All-cause mortality	27 (84.3)	18 (36.7)	0.0001

Table 81: Pleskot 2008[91]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Effect sizes	Source of funding
Pleskot M, Babu A, Hazukova R, Stritecky J, Bis J, Matejka J et al. Out-of-hospital cardiac arrests in patients with acute ST	Retrospective cohort study, multi-centre April 2002 to Aug 2004, Czech Republic	n = 26	Inclusion criteria • Out-of-hospital cardiac arrest • Acute STEMI defined as dynamic ST segment elevations on the ECG along with a typical rise (a minimum 3 times above the upper border of normal values) and	n = 20 underwent urgent coronary angiography, and n = 19 underwent PPCI Note	Usual care n = 6 Note No patients conscious at admission	In-hospital 1 year	All-cause mortality; in-hospital; All-cause mortality; 12 months	PPCI; 6/19 patients Usual care; 5/6 patients PPCI; 0/14 patients Usual care; 0/1 patients	None stated

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Effect sizes	Source of funding
elevation myocardial infarctions in the East Bohemian region over the period 2002-2004. Cardiology. 2008; 109(1):41-51.			fall in biochemical markers of myocardial necrosis (serum creatine kinase and its MB fraction) with the consequent development of a pathologic Q wave on the ECG • Due to disputable interpretation of biochemical markers of myocardial necrosis following a cardiopulmonary resuscitation as a diagnostic indicator, the coronary angiogram was taken into consideration prior to direct PCI, myocardial wall kinetics (ultrasound) and in some cases the autopsy report	2/20 patients conscious at admission			Good cerebral performance using Glasgow-Pittsburgh Outcome Categorisation (CPC) of brain injury; discharged from hospital (defined as CPC = 1); in-hospital	PPCI; 11/14 patients Usual care; 0/1 patients	
							Good cerebral performance using Glasgow-Pittsburgh Outcome Categorisation (CPC) of brain injury (defined as CPC = 1); 12 months follow-up	PPCI; 13/14 patients Usual care; 0/1 patients	

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Effect sizes	Source of funding
			Exclusion criteria • Individuals with cardiac arrest occurring in the presence of emergency medical services • Toxic, traumatic, suicidal etiologies for unconsciousness including drowning and terminal illness Demographics and baseline characteristics See below Drug therapy PPCI arm Prior to transport to the cardiac catheterisation laboratory (mostly from intensive care units) patients in this subgroup received 500 mg aspirin and 5,000–10,000 units of unfractionated heparin intravenously Usual care Patients in this subgroup were treated with intravenous unfractionated heparin				Successful procedure; optimal angiographic results after direct P were considered to be achieved when < 30% of residual luminal stenosis remained in the target vessel, that is, fibrinolysis in MI (TIMI) flow grade II and III	PPCI; 17/19 patients	

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Effect sizes	Source of funding
			without fibrinolysis. Stents • PPCI group; 17/19 (85%) GP 11b/111a inhibitor • Not reported All patients; beta-blockers, nitroglycerine, sedatives, analgesia, angiotensin-converting enzyme inhibitors, statins (similar in both groups) Ticlopidine/clopidogrel given in cases of stent implantation						

Clinical, pre-hospital and hospital characteristics of hospitalised individuals		
	With coronary angiography (n = 20)	**Without coronary angiography (n = 6)**
Age, years		
Median	55.5	61.5
Range	35–79	43–69
Mean (SD)	56.38 (10)	56.78 (8.2)
> 70 years	2 (10)	0
Males, n (%)	18 (90)	4 (67)
Risk factors for coronary artery disease, n (%)		
0	10 (50)	0
1	7 (35)	3 (50)

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Effect sizes	Source of funding

2	3 (15)	3 (50)
Hypertension (diastolic pressure, >90 mm Hg), n (%)	6 (30)	2 (33)
Diabetes mellitus, n (%)	0	2 (33)
Hypercholesterolemia (cholesterol >5.7 mmol/l), n (%)	2 (10)	2 (33)
Smoking, n (%)	7 (35)	3 (50)
Previous IHD, n (%)	10 (50)	3 (50)
Initial cardiac rhythm, n (%)		
Ventricular fibrillation, n (%)	20 (100)	3 (50)
Asystole, n (%)	0	1 (17)
Pulseless electrical activity, n (%)	0	1 (17)
Atrioventricular block, n (%)	0	1 (17)
Distance from the location of cardiac arrest to cardiac catheterisation laboratory, n (%)		
≤ 20 km, n (%)	16 (80)	3 (50)
> 20 km, n (%)	4 (20)	3 (50)
Infarct location (ECG) on admission, n (%)		
Anterior	10 (50)	4 (67)
Inferior	9 (45)	0
Lateral	1 (5)	0
Others (combination)	0	2 (33)
GCS at admission, n (%)		
3–5	17 (85)	6 (100)
6–10	1 (5)	0
11–15	2 (10)	0
Cardiogenic shock, n (%)	8 (40)	4 (67)
Postanoxic encephalopathy, n (%)	7 (35)	4 (67)
Artificial pulmonary ventilation, n (%)	17 (85)	6 (100)
Left ventricular ejection fraction ≤ 35% (Echo), n (%)	8 (40)	4 (67)

G.8 Hospital volumes of PPCI

Table 82: Kumbhani et al. 2009[66]

Reference	Study type	Number of patients	Intervention	Length of follow-up	Outcome measures	Source of funding
Kumbhani D, Cannon C, Fonarow G, Liang L, Askari A, Peacock W, Peterson E, Bhatt D. Association of hospital primary angioplasty volume in ST-segment elevation myocardial infarction with quality and outcomes. 2009. JAMA. Vol. 302, No. 20: p. 2007 - 2213	Retrospective observational analysis of American Heart Association's get with the guidelines – coronary artery disease national database, July 2001 to December 2007.	n = 29,513 Inclusion: ECG evidence of new ST-segment elevation or new left bundle branch block. Cardiac diagnosis of STEMI. Exclusion: People without STEMI, no PPCI, patients receiving fibrinolytic therapy, patients with 25% or more missing data, patients treated at hospitals that submitted less than 30 PPCI cases over 6-year duration of study.	PPCI, divided into tertiles of PPCI volume as low (< 36 procedures per year), medium (36–70 procedures per year), and high (>70 procedures per year). Total angioplasty volume divided into tertiles of low (< 200 procedures per year), medium (200–400 procedures per year) and high (> 400 procedures per year).	In-hospital	In-hospital mortality	Merck/Schering Plough Parmaceutical.

Baseline characteristics:

	Hospital Primary Angioplasty Volume			
Characteristic	**Low (n = 3900)**	**Medium (n = 9008)**	**High (n = 16,605)**	**p value**
Age	60.5 (13.0)	60.5 (12.9)	61.1 (13.3)	0.002
Female sex	1089 (27.9)	2480 (27.5)	4875 (29.4)	0.01
BMI, mean (SD)	28.6 (5.9)	28.8 (6.0)	28.9 (6.0)	0.02
White	2502 (64.2)	6874 (76.3)	13,887 (83.6)	
Black	211 (5.4)	605 (6.7)	793 (4.8)	0.001
Hispanic	483 (12.4)	651 (7.2)	821 (4.9)	
Diabetes	893 (22.9)	2003 (22.2)	3537 (21.3)	0.01
Hyperlipidemia	1495 (38.3)	4016 (44.6)	7070 (42.6)	0.01
Hypertension	2074 (53.2)	4824 (53.6)	9064 (54.6)	0.06

Peripheral vascular disease	140 (3.6)	346 (3.8)	798 (4.8)	< 0.001
Prior myocardial infarction	503 (12.9)	1155 (12.8)	2506 (15.1)	< 0.001
History of heart failure	172 (4.4)	365 (4.1)	953 (5.7)	< 0.001
Stroke or TIA	149 (3.8)	317 (3.5)	690 (4.2)	0.07
Chronic or recurrent AF	120 (3.1)	259 (2.9)	587 (3.5)	0.02
COPD or asthma	268 (6.9)	664 (7.4)	1500 (9.0)	< 0.001
Smoking history	1671 (42.9)	4015 (44.6)	7099 (42.8)	< 0.001
Chronic renal insufficiency	113 (2.9)	262 (2.9)	533 (3.2)	0.17
Renal dialysis	33 (0.9)	55 (0.6)	112 (0.7)	0.47
Anaemia	12 (0.3)	27 (0.3)	51 (0.3)	0.98
Depression	23 (0.6)	127 (1.4)	143 (0.9)	0.63
Alcohol misuse	200 (5.1)	433 (4.8)	594 (3.6)	< 0.001

Data are shown as no. (%) unit. Low volume indicates less than 36 primary angioplasty procedures performed per year; medium volume, 36 to 70 primary angioplasty procedures per year; and high volume, more than 70 primary angioplasty procedures per year.

Results:

	Odds ratio (95% confidence interval)					
Model	**Low versus high volume hospital (< 36 versus 36–70 PPCI/year)**	**p value**	**Medium versus high volume hospitals (36–70 versus > 70 PPCI/year)**	**p value**	**Volume as a continuous variable[b]**	**p value**
Unadjusted	1.21 (0.87–1.69)	0.26	1.00 (0.77–1.31)	0.99	1.08 (0.93–1.26)	0.32
Adjusted for demographics and hospital characteristics	1.23 (0.87–1.74)	0.24	1.04 (0.79–1.38)	0.77	1.11 (0.93–1.32)	0.23
Adjusted for demographics, hospital characteristics, and past medical history	1.30 (0.91–1.87)	0.15	1.09 (0.81–1.47)	0.56	1.13 (0.95–1.36)	0.17
Adjusted for demographics,	1.22 (0.78–1.91)	0.38	1.14 (0.78–1.66)	0.49	1.13 (0.93–1.37)	0.23

hospital characteristics, past medical history, and acute use of aspirin and beta blockers						

[a] crude in-hospital mortality rates were 3.9% for low-volume hospitals, 3.2% for medium-volume hospitals, and 3.0% for high-volume hospitals.
[b] For every decrease in 50 procedures per year

Table 83: Magid et al. 2000[78]

Reference	Study type	Number of patients	Intervention	Outcome measures	Source of funding
Magid D, Calonge B, Rumsfeld J, Canto J, Frederick P, Every N, Barron H. relation between hospital primary angioplasty volume and mortality for patients with acute MI treated with primary angioplasty vs thrombolytic therapy. Journal of American Medical Association. 2000. Vol. 284, No. 24, 3131-3138.	Retrospective cohort National registry of myocardial infarction (NRMI) (voluntary, database). United States. Data collected June 1 1994 to July 31 1999.	n = 62,299 Inclusion: arrival at hospital within 12 hours of AMI onset; initial ECG ST-segment elevation or left bundle branch block; absence of cardiogenic shock; no contraindications to fibrinolytic therapy. Exclusions: hospital that did not regularly report data to the NRMI registry and those who had participated <6 months; patients who did not complete their hospital stay at a single hospital.	PPCI	In-hospital mortality	Emergency Medicine Foundation and Genetech

Baseline characteristics:

Characteristic	**Low volume** (≤ 16 PPCI procedures per year) (n = 1423)	**Intermediate volume** (≤ 16 PPCI procedures per year) (n = 8817)	**High volume**(≤ 49 PPCI procedures per year) (n = 11,733)
Time from onset of MI symptoms to hospital arrival, hours			
< 2	59.6	59.7	59.8
2–6	30.4	30.3	31.1
7–12	10.1	10.0	9.0

Time of hospital arrival			
Day (8am–4pm)	59.4	55.5	49.8
Evening (4pm–midnight)	20.6	24.3	27.7
Night (midnight–8am)	20.0	20.2	22.5
Chest pain at presentation	92.9	94.6	96.2
Pulse ≥ 100 beats/minute	11.9	11.0	9.6
Systolic blood pressure, mm Hg			
< 90	4.9	4.1	3.8
90–120	23.6	22.9	23.2
> 120	71.6	73.0	73.1
Killip class			
I (no heart failure)	89.0	89.0	89.8
II (heart failure)	8.6	8.6	8.3
III (pulmonary edema)	2.4	2.4	1.9
ST-segment elevation	98.6	98.6	98.9
ST-segment depression	38.3	44.4	46.3
Nonsp. ST-segment or T-wave changes	6.1	4.6	3.2
Q waves	14.9	16.1	14.0
LBBB	2.6	2.8	2.1
RBBB	3.6	3.4	3.4
Anterior location of infarct	40.2	40.4	37.2
Admission diagnosis			
MI or rule-out MI	94.6	95.8	96.2
Unstable angina	3.2	2.8	2.5
Other	2.2	1.4	1.3
Medication within 24 h			
Aspirin	89.2	91.7	92.9
b-blocker	49.6	49.3	52.6
ACE inhibitor	16.4	15.3	16.6

- Values are percentages unless otherwise indicated.

- MI – myocardial infarction; ECG – electrocardiogram; LBBB – left bundle branch block; RBBB – right bundle branch block; ACE – angiotensin-converting enzyme.

Results:

	Low volume (≤16 PPCI procedures per year)	**Intermediate volume** (≤16 PPCI procedures per year)	**High volume** (≤49 PPCI procedures per year)
In-hospital death (%)	6.2	4.5	3.4

Table 84: Srinivas et al. 2009[104]

Reference	Study type	Number of patients	Intervention Comparison	Outcome measures	Source of funding
Srinivas VS, Hailpern S, Koss E, Monrad ES, Alderman M. Effect of physicians volume on the relationship between hospital volume and mortality during primary angioplasty. Journal of the American College of Cardiology. Vol. 53. No. 7. 2009	Retrospective cohort Data collected 2000 State PCI reporting	n = 7321 Inclusion: AMI presenting within 12h of fibrinolytics.	PPCI for acute myocardial infarction	In-hospital mortality	

Baseline characteristics:	**Hospital volume (PPCI/year) ≤ 50 (n = 18)**	**Hospital volume (PPCI/year) ≥ 50 (n = 18)**
Patients	1148	6173
Age, mean (SD)	61.1 (13.0)	61.2 (13.0)
Female	30.3	28.3
Hispanic ethnicity	13.0	6.7‡
Black race	9.4	5.2
Hypertension	62	60
Diabetes	22.4	18.2¥
Current smoker	29.4	32
Previous MI	15.2	16.5
Previous PCI	16.7	17.2
Previous cardiac surgery	5.8	7.7†

Renal failure	1.1	1.2
Need for dialysis	1.3	0.65
Current heart failure	8.9	9.2
Previous heart failure	2.8	2.3
Chronic lung disease	5.3	5.7
Vascular disease	4.2	6.6
Prior stroke	4.3	3.9
Malignant arrhythmia	4.3	3.4
Haemodynamic unstable	7.4	5.8†
Cardiogenic shock	2.5	2.1
Cardiopulmonary resuscitation	0.7	1.5
Balloon pump	6.3	6.3
Stent thrombosis	2.2	3.0
Myocardial infarction ≤ 6 hours	72	75.4†
Ejection fraction		
< 20%	1.9	1.2
20% to 29%	7.6	6.8
Single vessel disease	53.3	56.4
Left main disease	1.2	1.9
Stent used	91.1	90.9
PCI risk score, mean (SD)	10.4 (4.1)	10.2 (3.8)
Hospital mortality	5.4	3.4¥
†p < 0.05; ‡p < 0.0001; ¥p < 0.001		

Risk adjusted in-hospital mortality			
Annual hospital volume threshold for PPCI	**N**	**Mortality (%)**	**OR (95% CI)**
≤ 25 years	410	5.37	Reference

> 25 years	6911	3.62	0.61 (0.34–1.10)
≤ 50 years	1148	5.40	Reference
> 50 years	6173	3.40	0.58 (0.38–0.88)
≤ 75 years	3159	4.24	Reference
> 75 years	4162	3.32	0.82 (0.57–1.17)

^Risk adjusted mortality was calculated as the rate of observed mortality to predicted mortality multiplied by the statewide mortality rate of 3.75%

Table 85: Canto et al. 2000[20]

Reference	Study type	Number of patients	Intervention	Outcome measures	Source of funding
Canto J, Every N, Magid D, Rogers W, Malmgren J, Frederick P, French W, Tiefenbrunn A, Misra V, Kiefe C, Barron H. The volume of primary and survival after acute New England Journal of 21: 1573 – 1580.	Retrospective cohort Data collected June 1994 and March 1998 Myocardial Infarction patients hospitalised with	n = 36,535	PPCI patients divided into 4 quartiles according to volume of PPCI procedures the hospital performs each year.	In-hospital mortality	Genetech and the Agency for Health Care policy and research

Baseline characteristics:	Quartile 1 (5–11 PPCI/year)	Quartile 2 (12–20 PPCI/year)	Quartile 3 (21–33 PPCI/year)	Quartile 4 (> 33 PPCI/year)	p value
Number of patients	2825	5245	9303	19162	
Age (years) mean	61.7	61.6	61.7	62.0	
Female	30.5	31.0	30.4	30.4	
White race	82.5	84.1	87.3	90.5	≤ 0.01
Diabetes mellitus	20.7	20.2	20.3	18.5	≤ 0.01
Hypertension	45.4	48.4	46.6	45.4	≤ 0.01
Current smoking	34.0	34.9	33.9	35.4	
Family history of	31.5	33.4	33.3	32.6	

Reference	Study type	Number of patients	Intervention	Outcome measures	Source of funding
coronary disease					
High serum cholesterol	27.2	29.3	30.9	31.6	≤ 0.01
Angina	16.9	14.3	14.6	13.8	≤ 0.01
Myocardial infarction	19.7	19.9	19.3	18.4	
Heart failure	4.0	4.4	4.3	3.7	
PCI	13.3	13.4	13.7	13.5	≤ 0.01
CABG	7.4	7.3	8.6	8.3	≤ 0.01
Stroke	5.4	5.7	5.8	4.8	≤ 0.01
Median interval between onset of symptoms and arrival at hospital (minutes)	109.8	111.0	108.0	105.0	
Mean systolic blood pressure	136.8	137.6	138.8	139.0	≤ 0.01
Mean pulse (beats/minute)	78.2	78.1	78.3	77.9	
Killip class (% of patients)					
I	84.9	83.8	84.9	85.7	≤ 0.01
II	9.0	9.0	8.6	8.8	
III	2.1	3.2	2.9	2.4	≤ 0.01
IV	4.0	4.0	3.5	3.0	≤ 0.01
Type of myocardial infarction (% of patients)					
Q wave	72.1	75.8	75.3	76.2	≤ 0.01
Anterior	36.5	39.1	36.5	36.1	≤ 0.01
Length of stay	6.1	6.0	5.9	5.8	
Mean	7.5	7.6	7.5	7.3	
Crude death rate (%)	7.7	7.5	7.0	5.7	≤ 0.01

Reference	Study type	Number of patients	Intervention	Outcome measures	Source of funding

Adjunctive pharmacological treatments and arrival to angioplasty:

	Quartile 1 (n = 2825)	Quartile 2 (n = 5245)	Quartile 3 (n = 9303)	Quartile 4 (n = 19,162)	p value
Aspirin or an antiplatelet agent (%)	88.1	88.6	89.4	90.9	< 0.01
Beta-blocker	43.8	46.9	44.5	46.4	< 0.01
Heparin	91.8	93.1	92.7	94.7	< 0.01
Arrival to angioplasty, mean (minutes)	198.6	196.8	189.6	170.4	
Arrival to angioplasty, median (minutes)	129.0	135.0	129.0	118.8	

Unadjusted and adjusted relative risk of death among patients who underwent PPCI

Model*	Quartile 2 (12–20 PPCI/year)	Quartile 3 (21–33 PPCI/year)	Quartile 4 (> 33 PPCI/year)
Unadjusted	0.96 (0.81–1.14)	0.89 (0.76–1.04)	0.72 (0.62–0.84)
Adjusted for demographic characteristics	0.92 (0.76–1.10)	0.84 (0.71–1.00)	0.71 (0.61–0.83)
Adjusted for demographic characteristics and medical history	0.92 (0.77–1.10)	0.84 (0.71–1.00)	0.72 (0.61 – 0.84)
Adjusted for demographic characteristics, medical history, clinical presentation, and medication within 24 hours	0.87 (0.71–1.07)	0.84 (0.70–1.02)	0.74 (0.62 – 0.89)
Adjusted for demographic characteristics, medical history, clinical presentation, medications within 24 hours, year, and volume of patients with MI	0.87 (0.71–1.07)	0.83 (0.69–1.01)	0.72 (0.60 – 0.87)

*The relative risk is for the comparisons with the first quartile.

Table 86: Every et al. 2000[44]

Reference	Study type	Number of patients	Intervention	Outcome measures	Source of funding
Every N, Maynard C, Schulman K, Ritchie J. The association between angioplasty procedure elderly Americans. Journal 2000. Vol. 12, no. 6: 303 -	Retrospective cohort Cardiovascular database – improvement United States	n = 2623 (STEMI subgroup) n = 6124 (total AMI population) and July 1995. years) with confirmed AMI who within 12 hours of hospital admission. Exclusion: Patients admitted with cardiogenic shock or who received fibrinolytic therapy prior to the performance of angioplasty; patients without data for the first 12 hours of treatment.	PPCI in patients with STEMI Volume quartiles based on angioplasty procedures observation period. Total Medicare patients and PCI all Stent usage not reported.	30-day and 1 year mortality	None stated.

Baseline characteristics:	25th quartile (~4.4 PPCI/year – medicare patients) (~10.2 PPCI/year – all patients)	50th quartile (~13.5 PPCI/year - medicare patients) (~31.4 PPCI/year – all patients)	75th quartile (~24.3 PPCI/year - medicare patients) (~56.5 PPCI/year – all patients)	100th quartile (~47.2 PPCI/year - medicare patients) (~109.8 PPCI/year – all patients)	p value
Age	71.2 ± 8.2	71.5 ± 8.1	71.2 ± 8.2	71.6 ± 7.6	0.46
Male (%)	61.2	57.9	60.7	59.7	0.26
White race (%)	89.6	92.3	93.3	94.7	< 0.001
Diabetes	26.3	22.8	22.6	23.2	0.069
Myocardial infarction	25.2	22.7	23.8	24.2	0.451
Heart failure	6.6	7.5	7.6	6.2	0.34
Apache score (mean ±)	7.8 ± 3.6	7.6 ± 3.5	7.5 ± 3.4	7.4 ± 3.4	0.008
Time to PCI (mean hours	3.2 ± 2.4	2.9 ± 2.2	3.0 ± 2.4	2.0 ± 2.4	0.002

Reference	Study type	Number of patients	Intervention	Outcome measures	Source of funding
±)					
Heart failure during hospitalisation (%)	27.6	27.5	27.8	25.3	0.163
Recurrent myocardial infarction (%)	4.9	5.0	3.0	3.9	0.038
Bypass surgery during hospitalisation (%)	9.7	9.8	8.3	8.5	0.328
Results (STEMI subgroup):					
Time to treatment in lowest volume centre 2.7 ± 1.9h versus highest volume centre 2.4 ± 1.8h; p < 0.0001					
Multivariate adjustment for baseline differences by hospital 30-day mortality, OR = 0.95 per quartile, 95% CI 0.91 – 1.00, NS (30 day and 1-year mortality % presented by quartiles graphically in paper. None of the results were statistically significant but patients admitted to higher volume primary angioplasty trended toward lower 30-day and 1-year mortality).					

G.9 Pre-hospital versus in-hospital fibrinolysis

Table 87: BARBASH1990A[6]; ROTH1990A[94]

Reference	Study type	Number of patients	Patient Characteristics	Intervention	Comparison	Outcome	Funding source
Barbash , G., Roth, A., Hod, H., Miller, H., et al., Improved survival but not left ventricular function with early and pre-hospital treatment with tissue plasminogen activator in acute myocardial infarction. The Journal of Cardiology. 1990. 66: 261-266 Roth, A., Barbash, G., Hanoch, H., Miller, H., et al. Should thombolytic therapy be administered in the mobile intensive care unit in patients with evolving myocardial infarction? JACC, Vol 15, No. 5 April 1990:932-6	Design: RCT Enrolment: via the emergency ward and the mobile intensive care units which were staffed by a physician and paramedic. October 1986 to December 1987. Randomisation: 'by month' into pre-hospital or in-hospital treatment Allocation concealment: no Blinding: no ITT analysis	n = 191 Male: n = 161; 56 ± 9.4 years old Female: n = 29; 62 ± 7.1 years old; p < 0.001 Except for age there was no significant difference between men and women in either baseline characteristic or clinical outcome. 165 (87%) with first MI: 76 (40%) had anterior wall and 89 (47%) inferior wall infarctions. An additional 25 patients (13%) had a previous MI. 8 patients in whom initial clinical diagnosis of AMI was not confirmed.	Inclusion: < 72 years old, had severe chest pain for > 30 minutes, but not > 4 hours; had ST-segment elevation of 0.1 mV in at least 2 contiguous ECG leads Exclusion: LBBB on ECG; history of congestive heart failure, terminal illness or bleeding predisposition; prior cardiac surgery, SBP > 120 mmHg. Diagnosis: the team radioed senior physician on call to describe patient's history and ECG.	Rt-PA infusion initiated at home. .	Same drug therapy as intervention but patients treated as soon as possible after admission with recombinant tissue plasminogen activator (rt-PA) infusion initiated in emergency room or on admission to intensive coronary care unit.	Mortality, bleeding, reinfarction, length of stay, heart failure **Length of follow-up** 24 months	Not stated

Reference	Study type	Number of patients	Patient Characteristics	Intervention	Comparison	Outcome	Funding source

End point definitions:

Infarction – confirmed by occurrence of ischaemic chest pain lasting > 30 minutes and accompanied by ST-segment elevation of at least 0.1 mV in 2 contiguous ECG leads, followed by either an increase of creatine kinas-MB fraction to values >5% of total creatine kinase, or appearance of a Q wave not present on entry ECG.
Patency – TIMI grade 2 or 3 was defined as patent. Occluded infarct-artery was accordingly defined as TIMI grade 0 or 1.

Treatment:

- 120 mg recombinant tissue plasminogen activator (rt-PA) during 6-hour infusion starting with 10mg bolus followed by continuous infusion of 50 mg during first hour, 20 mg in second hour and 10 mg during following 4 hours.
- Heparin bolus 5000IU continuing with 25000 IU/24 hours. 1.5 to 2 times each patient's baseline value. Continued 5 days. 250 mg aspirin daily.
- Antianginal and anticongestive therapy administered as needed. 2g/day intravenous lidocaine for first 24 hours.
- All patients underwent coronary angiography 72 hours after treatment unless their clinical situation necessitated earlier catheterisation. Decision to proceed to angioplasty was based on coronary anatomy.

Baseline characteristics:

	Enrolment by mobile coronary unit			Enrolment by time to treatment	
	Pre-hospital (n = 43)	**In-hospital (n = 44)**	**Emergency ward (n = 103)**	**< 120 minutes (n = 96)**	**≥ 120 minutes (n = 94)**
Age (yrs)	59 ± 7	58 ± 8	56 ± 10.0	57 ± 8	57 ± 10
Sex (%male)	79.1	81.8	88.3	81.0	88.0
Clinical prognostic groups					
Anterior AMI (%)	37.2	31.8	44.6	54.1	39.4*
Inferior AMI (%)	46.5	47.7	46.7	32.4	47.8
Previous AMI (%)	16.3	20.5	8.7	13.5	12.8
Angina pectoria (% patients)					
Absent	46.5	52.3	54.3	49.0	55.0
< 6 months	27.9	36.4	34.9	32.3	35.1
> 6 months	25.6	11.4	10.6	18.7	9.5
Functional classification (% patients)					

Reference	Study type	Number of patients	Patient Characteristics	Intervention	Comparison	Outcome	Funding source
0 to 1	81.0	84.1	87.3	81.3		89.3	
2 to 3	19.0	15.9	12.6	18.7		10.8	
Rates over 1/3 lung fields (% patients)	19.0	9.3	10.6	15.6		8.5^	
% patients with 2- and 3-vessel CAD	48.8	60.5	56.4	53.1		57.7	
Time to treatment (minutes)	1.6 ± 0.6[&]	2.2 ± 0.7	2.0 ± 0.8	1.3 ± 0.4		2.7 ± 0.5	

*statistical difference between the prevalence of anterior wall infarction in the early (< 120 minutes) versus late (≥ 120 minutes) treatment groups, p = 0.06

^ by Canadian classification

[&]p < 0.0001

Results:

Mortality by enrolment groups and time to treatment

	Mobile coronary unit		**Emergency**		
Time to treatment	Pre-hospital	Hospital	Ward	Total	
< 120 minutes	n = 33	n = 14	n = 51	n = 96	
≥ 120 minutes	n = 10	n = 10	n = 52	n = 94	
All patients	n = 43	n = 44	n = 103	n = 190	p value*
Mortality at 60 days					
< 120 minutes	0	0	0	0	
≥ 120 minutes	1	3	2	6	0.01
Mortality at 24 months (all)					
< 120 minutes	0	0	1	1	
≥ 120 minutes	3	3	3	9	0.01
Mortality at 24 months (cardiac only)					
< 120 minutes	0	0	1	1	
≥ 120 minutes	1	3	3	7	0.03

Reference	Study type	Number of patients	Patient Characteristics	Intervention	Comparison	Outcome	Funding source
*statistically significant different in mortality between the total early and late treatment groups. Examined by Fisher's exact test for 2x2 tables.							

In-hospital outcomes	Group A (MICU, n =72)	Group B (CCU, n =44)	p value
Bleeding (%)	14	9	NS
PCI (%)	42 (65*)	56 (43*)	NS
CABG (%)	7	5	NS
Reinfarction (%)	13.9	13.6	NS
Mortality (%)	5.5^	6.8[$]	NS
Length of stay (days)	11	14	NS
Congestive heart failure (at discharge %)	5 (7)	7 (16)	NS

*No. of patients catheterised. CABG=coronary artery bypass graft
^ 2 x electromechanical dissociation, 1 x cardiogenic shock, 1 x rupture of left ventricular free wall, 1 x after coronary bypass operation.
$ 2 x cardiogenic shock, 1 x rupture of left ventricular wall.

Table 88: Castaigne et al. 1989[23]

Reference	Study type	Number of patients	Patient Characteristics	Intervention	Comparison	Length of follow-up	Outcome	Funding source
Castaigne, A., Herve, C., et al. Prehospital use of APSAC: results of a placebo-controlled study. The American Journal of Cardiology. Vol.	Design: RCT Enrolment: Val de Marne district of Paris. Randomisation: yes Allocation concealment: coded injections.	n = 100 (91 male; 9 female) Mean age 55 years for men [range 35 to 75] and 63 years for women [range 45 to 75]	Inclusion: < 75 years who had typical ischaemic chest pain for > 30 minutes and < 3 hours that did not respond to nitrates. ST-segment elevation ≥ 0.2mV in at least 2 standard leads (posterior infarction) or 3 precordial leads	n = 57^ 30U of APSAC injected > 4 minutes before arriving at the hospital.	n = 36* On arrival at hospital the code was broken and if the patient received placebo at home the physician decided	In-hospital	All-cause mortality	Not stated .

Reference	Study type	Number of patients	Patient Characteristics	Intervention	Comparison	Length of follow-up	Outcome	Funding source
62: 30A-33A	Blinding: Mobile care unit physician was blinded to the treatment given but could break the code if he or she thought it necessary, or if a cardiologist was present when the ambulance reached the patient's home. Sample size calculation: not stated ITT analysis	Loss to follow-up:	(anterior infarction). Exclusion: history of severe hypertension or any other 'classic contraindication' to fibrinolytic therapy. Diagnosis: Diagnosis made by anesthesiologist in mobile care unit.		whether fibrinolytic treatment was appropriate.			

Treatment: 30U of APSAC injected > 4 minutes.

Coronary angiography was confirmed as soon as possible after admission. Angioplasty was indicated if the infarct-related artery was patent and if there were no other severe coronary stenoses. Coronary artery bypass graft was indicated if the infarct-related artery was patent and if there was 1 or more other coronary stenoses.

^7 patients transferred from the placebo to the active treatment group.

*7 patients did not receive fibrinolytic treatment in the home or hospital.

30 patients underwent angioplasty 1 to 10 days after MI. 18 patients underwent coronary artery bypass grafting 1 to 15 days after MI.

Results:	Pre-hospital (n = 57)	In-hospital (n = 36)
All-cause mortality; pre-hospital	1	1
All-cause mortality; in-hospital	2	1

Table 89: McAleer et al. 2006[80]

Reference	Study type	Number of patients	Patient Characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
McAleer, B., Feasibility and long term outcome of home vs hospital initiated thrombolysis. Irish journal of medical science, 2006, Volume 175, number 4.	Design: RCT Enrolment: Northern Ireland district hospital, 1988-1992 Randomisation: on call rota (SHO) Allocation concealment: no Blinding: no Sample size calculation: no No ITT analysis	n = 248	Inclusion criteria: Patients whose major symptoms were less than 6 hours; ECG evidence of MI: ST-segment elevation of at least 1 mm in 2 or more standard leads or at least 2 mm in 2 or more praecordial leads. Exclusion criteria: bleeding disorder, concurrent anticoagulant therapy, active peptic ulceration, recent stroke (< 3 months), recent surgery (< 4 weeks), severe HT (BP > 220/120 mmHg) and any patient whose life expectancy is less than 2 years.	All patients assessed by MCCU staff (physician at SHO level) then randomly allocated to receive fibrinolysis at home.	All patients assessed by MCCU staff then randomly allocated to wait to receive fibrinolysis at the hospital coronary care unit.	5 years	Mortality, time to treatment, adverse events.	Not reported

Treatment:

All patients received 1.5 million units of streptokinase in 100ml of N saline over 30 minute period. Immediately followed by IV infusion of heparin in dosage of 1000–1500U/hour such that PTTK ration was maintained at 1.5–3 times the baseline value. After 5 days of heparin therapy oral anticoagulation was substituted and continued for at least 3 months in the vast majority of cases. Ancilliary therapy (such as aspirin, beta-blockers, ACE inhibitors) was prescribed along standard post-infarct guidelines.

End point definitions:

Reperfusion:

- Rapid relief of chest pain and improvement in haemodynamic parameters
- Regression of ST-segment elevation (50% reduction in ST elevation)
- Early CK and CK-MB peak
- Occurrence of specific reperfusion arrhythmias: idioventricular rhythm, ventricular fibrillation, ventricular ectopic beats

Reference	Study type	Number of patients	Patient Characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Baseline characteristics:			**MCCU**	**Hospital**				
Male (%)			76.8	76.5				
Age (mean, years)			61.0	60.5				
Age (range, years)			37–78	37–95				
Previous infarction			17.1	22.3				
Anterior infarct (%)			40.2	41.6				
Angina (%)			43.9	41.0				
VF prior to treatment (%)			6.1	7.2				
Results:								
Mortality*			**MCCU**	**Hospital**			**p value**	
• 30 days			4/82 (4.9%)	26/166 (15.7%)			0.014	
• 1 year			8/82 (9.8%)	39/166 (23.5%)			0.009	
• 2 years			9/82 (11.0%)	46/166 (27.7%)			0.003	
• 5 years			14/81 (17.3%)	58/165 (35.2%)			0.005	
Minor bleeding (bleeding at venepuncture, haematuria)			16%	15%				
Major bleeding events			0%	0%				
• 1 patient lost to follow-up in each group								

Table 90: Schofer et al.[98]

Reference	Study type	Number of patients	Patient Characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Schofer, J., Butter, J., Geng., Gutschmidt. K., Herden, H., Mathey, D.,	Design: RCT Enrolment: Setting: Randomisation: assigned	n = 78 (66 male, 12 female, mean age ± standard	Inclusion criteria: severe chest pain typical for myocardial ischaemia lasting > 30 minutes, arrival of	n = 40 Mobile care unit staffed by a physician and 2	n = 38 After hospital admission a 12 lead ECG performed and	In-hospital	Mortality in-hospital, bleeding, myocardial reinfarctio	Not stated.

Reference	Study type	Number of patients	Patient Characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Moecke, H., Polster, P., Raftopoulo, A., Sheehan, F., Voelz, P. Prehospital thrombolysis in acute myocardial infarction. The American Journal of Cardiology. 1990	to the next in the series of ampule pairs of either urokinase in ampule A and placebo in ampule B, or vice versa. Allocation concealment: Blinding: double-blind Sample size calculation: ITT analysis? No (the diagnosis of an AMI could not be confirmed at hospital admission – he had pulmonary embolism)	deviation 55 ± 8 years)	ambulance doctor within 4 hours of onset of symptoms, ≥ 2 mm ST-elevation in ≥ 2 ECG leads for inferior AMI and ≥ 3 mm ST elevation in ≥ 2 precordial leads for anterior AMI, age ≤ 70 years, no prior AMI, and no contrindications against fibrinolysis. Exclusion criteria: prior AMI, contraindications to fibrinolysis; age > 70 years.	emergency technicians.1st injection given at home before hospital admission.	if patient still meets inclusion criteria and had no contraindications to fibrinolytic therapy received an IV injection of ampule B followed by heparin (1000U/hour). Patient then transferred to ICU.		n	

Definitions:

Reinfarction – new onset of symptoms combined with typical ECG changes or a secondary peak of creatine kinase to more than twice the upper limit of normal, or both.

Coronary patency – complete filling of the suspected infarct artery with a delayed or normal runoff of the contrast medium (TIMI perfusion grade 2 or 3).

Treatment:

All patients who were given fibrinolytic therapy received urokinase (2 million units IV). Administration of ampule B was followed by heparin (1000 U/hour). Coronary angiography was performed before hospital discharge unless clinical instability necessitated earlier catheterisation.

Angiography was performed before hospital discharge in 31 of 40 patients in group A and in 30 of 38 patients in group B. Angiography was not performed in 17 patients because of death before discharge (n =3), refusal by the patient (n =4), a wrong diagnosis (n =1), and logistic difficulties in studying patients from other cities (n =9).

Baseline characteristics:	Pre-hospital (Group A)	In-hospital (Group B)
Number of patients	40	38

Reference	Study type	Number of patients	Patient Characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Age, years (mean ± SD)		57 ± 7			55 ± 8			
Anterior AMI (%)		47			32			
Number of narrowed coronary arteries (%)*								
1		53 (31)^			38 (30)			
2		40 (31)			41 (30)			
3		7 (31)			21 (30)			
Initial clinical status								
Blood pressure (mmHg)								
Systolic (mean ± SD)		141 ± 23 (39)			137 ± 32			
Diastolic (mean ± SD)		86 ± 14 (39)			82 ± 17			
Cardiogenic shock (%)		6			6			
Pulmonary congestion (%)		17			14			
Resuscitation (%)		5			3			
*Disease ≥ 50% diameter stenosis								
^Where data are incomplete, the number of observations is indicated in parentheses								
Results:		**Pre-hospital (Group A)**			**In-hospital (Group B)**			
Pre-hospital								
Bleeding		0			0			
Wrong diagnosis		1			1			
Death		0			0			
In-hospital								
Bleeding complications								
• Puncture site		1			1			
• Haematuria		0			0			
• Gastrointestinal		0			1			
• Cerebral		0			0			

Reference	Study type	Number of patients	Patient Characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Reinfarction		4			5			
Death		1			2			
PCI / CABG		4/1			1/0			
CABG = coronary artery bypass surgery								

Table 91: Weaver et. Al. & Brouwer et al.[16,120]

Reference	Study type	Number of patients	Patient Characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Weaver, W., Cerqeuira, M., Hallstrom, A., Litwin, P., et al. Pre-hospital initiated vs hospital initiated thrombolytic therapy, JAMA, 1993, Volume 270, No. 10.[120] Brouwer, M., Martin, J., Maynard, C., et al. Influence of early pre-hospital thrombolysis on mortality and event free	Design: RCT Enrolment: Paramedics obtained directed history and physical examination, then transmit an ECG to a base station emergency physician for all potentially suitable candidates for fibrinolytic therapy. Findings discussed by phone or radio with this physician before decision is made to proceed with therapy. Setting: 19 hospitals and 5 paramedic systems in the city of Seattle and	Total n = 360 (from n = 1973 who met history criteria and had ECG done) 353 (98%) of the 360 patient enrolled had subsequent evidence of acute myocardial infarction, as determined by serial enzyme tests and ECGs. 5 had no enzyme elevation and diagnosed as UA/NSTEMI; most had residual ST elevation from a prior infarction. 1 had pericarditis; 1 had peptic ulcer disease. ECG evidence of anterior injury in 39% of patients, inferior wall injury in 58%,	Inclusion criteria: <75 years who were alert, orientated and had on going chest discomfort for ≥ 15 minutes and 6 hours. SBP > 80 and < 180 mmHg, DBP < 120 mmHg and systolic BP difference between arms < 20 mmHg. 2 or more contiguous leads in a group location displayed ST-segment elevation ≥ 1 mm. Exclusion criteria: any known	Active kit containing aspirin (325 mg) and alteplase (100 mg) were administered immediately, the latter infused in open-label manner over 3 hours using special infusion pump)	No placebo was given pre-hospital, but the active treatment kit (identical to pre-hospital) was available in the emergency department.	5 years	Mortality, heart failure	Not stated

survival (The myocardial infarction triage and intervention [MITI] randomised trial. American journal of cardiology 1996; 78; 497-502[16]	surrounding area Randomisation: kits were identical for weight and balance Allocation concealment: for patients allocated to treatment in-hospital, no treatment was given in the field. Sample size calculation: 360 patients would provide 90% power to detect a 5% difference in infarct size in the composite end point with an α level of 0.05. ITT analysis	and lateral wall infarction in 1% of patients. 2% had non-diagnostic abnormalities on the initial ECG. Drop outs: pre-hospital n = 1 Hospital n = 23 Reasons given were death before treatment initiated (n = 4), direct coronary angioplasty after initial physician assessment in-hospital (n = 6), not treated due to spontaneous improvement in ECG abnormality by time of admission (n = 4), or because of admitting physician's decision (n = 10; all have evidence of acute infarction)	bleeding condition, a history of stroke, seizures or transient cerebral ischaemic attacks, major surgery in preceding 2 months, gastrointestinal bleeding in past year, cancer or other terminal illness, known liver disease or jaundice, renal insufficiency or insulin-dependent diabetes, a history of active colitis, recent trauma or central line placement and warfarin therapy

Treatment:

All patients received basic medical care (oxygen, intravenous cannulation, and rhythm monitoring) during pre-hospital period. Morphine sulphate was used for pain relief, lidocaine and atropine for arrhythmias and vasopressors and diuretics for treatment of hypotension or pulmonary oedema if prescribed by remote physicians. All patients received sodium heparin at time of hospital arrival and continued for at least 48 hours.

Baseline characteristics:

	Pre-hospital treatment group (n = 175)	**Hospital treatment group (n = 185)**	**p value**
Age, years ± SD	57 ± 10	59 ± 10	0.04
Male (%)	82	82	0.99
Prior cardiac histories			
• angina (%)	33	28	0.30
• myocardial infarction (%)	21	20	0.69

• congestive failure (%)	2	4	0.60
• coronary bypass surgery (%)	4	9	0.11
ECG findings			
• anterior ST elevation* (%)	39	39	0.99
• inferior ST elevation (%)	58	58	0.99
• no ST elevation (%)	2	2	0.99
Haemodynamic findings			
• heart rate, beats/minute ± SD	76 ± 17	73 ± 18	0.11
• systolic pressure, mmHg ± SD	133 ± 23	131 ± 23	0.29
• heart rate >100 beats/min, no.	6	4	0.72
• systolic pressure <100mmHg (%)	8	9	0.83
Onset of symptoms to calling 911, minutes, median time (25th percentile–75th percentile)	27 (30–60)	28 (11–58)	0.31
Calling 911 to randomisation, minutes, mean ± SD	30 ± 9	28 ± 10	0.007
Randomisation to treatment, minutes, mean ± SD	15 ± 11	53 ± 21	< 0.001
Randomisation to hospital arrival, mean ± SD	38 ± 12	23 ± 9	< 0.001

*atypical (V_{4i} V_{5i} V_6) and lateral (I, aVL) changes were grouped with anterior (V_{1i} V_{2i} V_3) or inferior (II, II, aVF) if both abnormalities were present.

Results:

Up to discharge	**Pre-hospital treatment group**	**Hospital treatment group**	**p value**
All patients, mortality^, %	5.7 (2.3–9.1)	8.1 (4.2–12.0)	0.49
Anterior infarct, mortality, %	5.9	12.3	0.30
Inferior infarct, mortality, %	5.9	5.6	0.99
First infarction, mortality, %	4.4	7.5	0.40
First anterior infarction, mortality %	5.3	11.9	0.35

'Serious' bleeding, %	6	6	
Stroke	4	2	95% CI: 0.3% to 3.0%

*first infarction excludes patients with known prior infarction

^6 due to stroke; 1 to arrhythmia; 11 to myocardial failure; 2 to cardiac rupture; 1 to pulmonary embolism; 2 to cardiac surgery; 2 associated with multisystem disease from complications following acute myocardial infarction.

Observed cardiac-related events for patients treated very early and those treated later (2 years follow-up):

	Number of events		Number of events/100 patients/year		p value
	< 70 minutes (n = 82)	≥ 70 minutes (n = 254)	< 70 minutes (n = 82)	≥ 70 minutes (n = 254)	
Angiography	27	89	11.0	13.1	0.45
Angioplasty	22	46	9.0	6.8	0.35
Bypass surgery	9	29	3.7	4.3	0.69
Congestive heart failure	4	19	1.6	2.8	0.38
Myocardial infarction	8	35	3.3	5.1	0.18
Recurrent ischaemia	11	49	4.5	7.2	0.18

5 year cumulative and event-free survival curves available for those treated very early (< 70 minutes) versus those treated later (70 minutes to 3 hours)

Table 92: Kuhn et al.[13,65]

Reference	Study type	Number of patients	Patient Characteristics	Intervention	Comparison	Outcome measures	Source of funding
Kuhn et al. Pre-hospital thrombolytic therapy in patients with suspected acute myocardial infarction (The European myocardial infarction project group). The New England Journal of Medicine. Vol 329. No 6. 383-389 Boissel, J. P. The European Myocardial Infarction Project: an assessment of pre-hospital thrombolysis. of Cardiology 49 Suppl, S29-S37. 1995.	Design: Enrolment: October 1988 to January 1992 by 163 centres in 15 European countries and Canada Randomisation: stratified on whether ST-segment elevation was present in ECG; and Allocation concealment: Double-blinded. Sample size calculation: sample reduction in mortality, with a power of 90 percent and an ITT analysis	n = 5469; n = 2750 pre-hospital; n = 2719 in-hospital Drop outs: n = 73 didn't receive any study treatments (39 pre-hospital, 34 in-hospital – main reasons broken problems with computer). 343 received only first injection, but 89 died before the second injection could be **Length of follow** 30 days	Inclusion criteria: pain characteristic of MI and ≥ 30 minutes duration, or pain < 30 minutes but not responsive to nitrates and who underwent 12-lead ECG. Exclusion criteria: those receiving oral (but aspirin, dipyridamole, or any other antiplatelet was allowed, known to have haemorrhagic diathesis or recently active peptic ulcer, stroke, surgery or major trauma in >200mmHg or DBP >120 mmHg; known or or PCI in previous 2 weeks.	30 units of anistreplase when first seen by emergency medical personnel (physician) outside the hospital, placebo after hospital admission.	Placebo when first seen outside hospital, then anistreplase after hospital admission.	Mortality at 30 days	Smith Kline Beecham

Treatment: Other treatments were given at the discretion of the attending physician.

Baseline characteristics:

	Pre-hospital group (n = 2750)	Hospital group (n = 2719)
Male sex (%)	76.8	77.0
Age (years)	61.1 ± 12.2	61.2 ± 12.1
Previous myocardial infarction (%)	19.0	19.2

Previous angina pectoris (%)	44.0	45.3
Previous atherosclerotic diseases (%)	15.3	16.3
Ventricular fibrillation (%)	1.5	1.3
Shock (%)	7.3	8.1
Systolic blood pressure (mmHg)	131 ± 29	131 ± 28
Diastolic blood pressure (mmHg)	79 ± 21	79 ± 15
Heart rate (beats/minute)	77 ± 19	76 ± 20
ST-segment elevation (%)	87.0	87.3
Final diagnosis		
Myocardial infarction	2408 (87.6)	2396 (88.1)
Probable myocardial infarction*	46 (1.7)	42 (1.5)
Acute coronary syndrome	206 (7.5)	184 (6.8)
Pericarditis	9 (0.3)	12 (0.4)
Aortic dissection	6 (0.2)	3 (0.1)
Other cardiac disease	25 (0.9)	32 (1.2)
Noncardiac disease	50 (1.8)	50 (1.8)
Compliance		
Both injections received	2499 (90.9)	2462 (90.5)
Pre-hospital injection only received	164 (6.0)	179 (6.6)
Hospital injection only received	0	1 (< 0.1)
No study injection received	39 (1.4)	34 (1.3)
Incomplete information	48 (1.7)	43 (1.6)
Died before hospital injection	49 (1.8)	40 (1.5)
± values are means ± SD * these patients died before a diagnosis could be made		
Results:		
	Pre-hospital group (n = 2750)	**Hospital group (n = 2719)**
Pre-hospital mortality	36	24
Total mortality at 30 days	266	303

G.10 Use of antithrombin as an adjunct to fibrinolysis

None.

G.11 Rescue PCI

Table 93: REACT 2005[22,49]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Protocol outcome measures	Source of funding
Gershlick AH, et al. Rescue angioplasty after failed thrombolytic therapy for acute myocardial infarction. N Engl J Med. 2005; 353(26):2758-68. Carver A, et al. Longer-term follow-up of patients recruited to the REACT	Design: RCT (Multicentre – 35 sites in UK) Enrolment Dec 1999 – Mar 2004. Terminated prematurely due to declining recruitment and funding issues Randomisation/ allocation concealment: 24-hour computer generated allocation system Blinding: Open-label. Investigators blinded	n = 427 Drop-outs: 0 Crossover 18 (see below)	Inclusion criteria Acute myocardial infarction with ST-segment elevation of > 0.1 mV in at least 2 contiguous leads, excluding V1 Aspirin and fibrinolysis administered within 6 hours of onset of symptoms Age 21 to 85 years Ability to give informed consent At 90 minutes (± 15 minutes) after the beginning of initial fibrinolytic therapy, electrocardiogram shows failed fibrinolytic therapy – less than 50% resolution of the ST segment in the lead showing the greatest ST-segment elevation measured from the baseline (isoelectric line) to 80ms beyond the J point, with or without chest pain Rescue angioplasty, if assigned, can be performed within 12 hours of the onset of pain	Rescue PCI (n = 144) Coronary angiography, followed by angioplasty if required (< TIMI grade 3 flow and >50% stenosis in the infarct-related artery). Adjunctive strategies (stenting or GPIs) were used at the discretion of the interventionist. Notes:	Repeated fibrinolysis (n = 142) Alteplase or reteplase and IV heparin - LMWH was not used in the first 24 hours Conservative therapy (n = 141) Standard medical therapy for MI without	30 days; 6, 12 months; and mortality at a median of 4.4 years	1° Composite of death, recurrent MI, cerebrovascular event, and severe heart failure at 6 months 2° Components of the primary end point Bleeding Revascularisation	British Heart Foundation; Roche Pharmaceuticals provided reteplase for repeated fibrinolysis (its use was optional)

(Rescue Angioplasty Versus Conservative Treatment or Repeat Thrombolysis) trial. J Am Coll Cardiol. 2009; 54(2):118-26.	to outcomes. Sample size calculation: During study design (1998), it was estimated that the primary end point rate in the conservative group would approach 20%. To detect a 40% relative reduction in the rescue-PCI group 1200 patients would be required (80% power, α = 0.05). In December 2001, on the basis of new published evidence, it was determined that a sample size of 156 patients in each group would provide 80% power (α = 0.05) to detect the same 40% relative reduction. ITT analysis: Yes. At 6 months all components of the primary end point were recorded for 406/427 subjects.		Exclusion criteria Probable inability to gain femoral access for intervention (for example, severe peripheral vascular disease) Left bundle-branch block Life expectancy <6 months owing to noncardiac cause Previous inclusion in this trial at any time, or in any other clinical trial during the previous month Contraindication to fibrinolysis (for example, cardiopulmonary resuscitation after first fibrinolytic treatment) Haemoglobin greater than 1.5 g/dl below normal range within previous 6 hours Platelet count below normal range within previous 6 hours For patients ≥75 years: SBP >200 mm Hg, DBP >100 mm Hg, or both at any time during the current episode of pain, even if successfully reduced by therapy For patients <75 years of age: after prescription of first fibrinolytic therapy, SBP >200 mm Hg, DBP >100 mm Hg, or both on more than 1 occasion Estimated body weight <65 kg Cardiogenic shock, either in the opinion of the investigator or defined as persistent (lasting >30 minutes) systolic hypotension (<90 mm Hg) with oliguria and autonomic	Crossover between treatment groups was discouraged but allowed if a patient had on going or further chest pain associated with ST-segment re-elevation or new elevation in at least 2 contiguous leads or had cardiogenic shock.	fibrinolysis or PCI. To ensure a standardised group, conservative therapy included intravenous heparin for 24 hours, irrespective of the first fibrinolytic agent. Notes: Heparin administration in the repeated-fibrinolysis and conservative-therapy groups was titrated to an activated partial-thromboplas tin time ratio of 1.5 to 2.5.		(See below for definitions)	

	Mortality status was confirmed for the remainder (R-PCI = 9; RT = 6; CT = 6). At 12 months complete clinical follow-up was available for 388/427 patients. At a median of 4.4 years, mortality was obtained for 416/427 (missing: R-PCI = 1; RT = 3; CT = 7). Data on missing subjects was censored at time of last follow-up		activation, with or without pulmonary oedema despite appropriate volume replacement, and considered to be due to ventricular dysfunction rather than to any other cause Administration of low-molecular-weight heparin within the previous 12 hours Demographics and baseline characteristics see below					

Crossover				
	Rescue PCI → conservative therapy	**Rescue PCI → repeated fibrinolysis**	**Repeated fibrinolysis → conservative therapy**	**Repeated fibrinolysis → rescue PCI**
Patients who did not receive their randomly assigned treatment	14	2	1	1

Demographics and baseline characteristics			
	Repeated fibrinolysis (n = 142)	Conservative therapy (n = 141)	Rescue PCI (n = 144)
Mean age±SD (range) – years	61.3±10.3 (40–85)	61.0±10.7 (37–85)	61.1±11.9 (34–85)
Male sex – no. (%)	114 (80.3)	111 (78.7)	113 (78.5)
Medical history – no. (%)			
Angina	32 (22.5)	29 (20.6)	32 (22.2)

Acute MI	23 (16.2)	17 (12.1)	14 (9.8)*
PCI	6 (4.2)	4 (2.8)	6 (4.2)
CABG	7 (4.9)	4 (2.8)	7 (4.9)
Diabetes	23 (16.2)	16 (11.3)	21 (14.6)
Hypertension	60 (42.3)	53 (37.6)	47 (32.6)
Smoking history			
Currently smoked	70 (49.6)*	65 (46.1)	68 (47.2)
Formerly smoked	41 (29.1)*	42 (29.8)	40 (27.8)
Never smoked	30 (21.3)*	34 (24.1)	36 (25.0)
Anterior infarct – no. (%)	54 (38.0)	66 (46.8)	61 (42.7)*
First fibrinolytic therapy – no. (%)			
Reteplase	43 (30.3)	28 (19.9)	42 (29.2)
Streptokinase	82 (57.7)	88 (62.4)	84 (58.3)
Tenecteplase	2 (1.4)	5 (3.5)	3 (2.1)
Tissue plasminogen activator	15 (10.6)	20 (14.2)	15 (10.4)
Time to first fibrinolytic therapy (min)			
Median	135	150	140
Interquartile range	94–217	100–210	95–240

* Data were missing for 1 patient

Definitions of end points

Reinfarction

During index admission: further chest pain lasting more than 30 minutes and accompanied by new electrocardiographic changes (new Q waves above 0.04 second or ST-segment elevation above 0.1 mV in 2 leads for more than 30 minutes), further enzyme rise, or both

Late chest pain lasting more than 30 minutes and accompanied by new electrocardiographic changes, enzyme rise, or both

Cerebrovascular event

A new focal neurologic deficit of presumed vascular cause persisting for more than 24 hours and without evidence of a nonvascular cause according to a neurologic imaging study

Severe heart failure

Early heart failure: any new-onset cardiogenic shock or heart failure with pulmonary oedema that is resistant to medical therapy and that occurs during the index admission and after randomisation

Late heart failure: admission to hospital for treatment of heart failure (New York Heart Association class III or IV)

Bleeding

Major bleeding: decrease in haemoglobin of at least 5 g/dl during index admission, severe bleeding event (for example, intracranial haemorrhage, haemopericardium, or haemodynamic compromise, with or without transfusion), or both

Minor bleeding: observed bleeding during index admission, with or without a decrease in haemoglobin of at least 5 g/dl, with or without transfusion

Effect Size

Rescue PCI

Of the 144 patients assigned to rescue PCI, 88 (61.1%) were recruited from hospitals with interventional capabilities

The median transfer time for patients from hospitals without interventional capabilities was 85 minutes (IQR 55 to 120). At 6 months, among patients assigned to rescue PCI, there was no significant difference in event rates between those who were transferred for intervention (16.4 %) and those who were recruited in hospitals with on-site facilities for intervention (14.6%, p = 0.80)

16 patients in this group crossed from their assigned therapy, and 128 proceeded to angiography, 13 of whom did not require angioplasty because of patent vessels

Of the remaining 115 patients, only 9 were deemed to have had an unsuccessful rescue-PCI procedure; in 6 of these patients the artery was deemed not amenable to PCI, in 1 instance affecting 1 patient there was a technical failure of x-ray equipment, and in 2 patients the attempts to open the artery were unsuccessful

Rescue PCI was commenced (the wire crossed the lesion) a median of 414 minutes after the onset of pain (IQR 350 to 505). At 6 months, logistic-regression analysis indicated that the time to repeated PCI (up to 12 hours) had no significant effect on outcome

Stents were deployed in 68.5% of patients, and a glycoprotein IIb/IIIa receptor inhibitor (abciximab) was administered in 43.4%

For patients assigned to rescue PCI rather than repeated fibrinolysis, the median additional delay in the time to the assigned treatment was 84 minutes (4.6 hours for rescue PCI versus 3.2 hours for repeated fibrinolysis)

Outcomes

	0 – 30 days§			**0 – 6 months**				**0 – 12 months**		
	RT (n = 142)	**CT (n = 141)**	**R-PCI (n = 144)**	**RT (n = 142)**	**CT (n = 141)**	**R-PCI (n = 144)**	**Overall p value**	**RT (n = 142)**	**CT (n = 141)**	**R-PCI (n = 144)**
Primary end point	Not reported									
Death from any cause (%)		15 (11)	7 (4.9)	18 (12.7)	18 (12.8)	9 (6.2)	0.12	20 (14.1)	21 (14.9)	11 (7.6)
Death from cardiac		Not reported		15 (10.6)	14 (9.9)	8 (5.6)	0.26	Not reported		

causes (%)									
Recurrent acute MI (%)	9 (6.4)	1 (0.7)	15 (10.6)	12 (8.5)	3 (2.1)	<0.01			
Cerebrovascular event (%)	1 (0.7)	2 (1.4)	1 (0.7)	1 (0.7)	3 (2.1)	0.63	1 (0.7)	1 (0.7)	3 (2.1)
Severe heart failure (%)	10 (7.1)	6 (4.2)	10 (7.0)	11 (7.8)	7 (4.9)	0.58	13 (9.2)	13 (9.2)	8 (5.6)
Secondary end point									
Major bleeding (no. deaths)	Not reported		7 (5)	5 (3)	4 (0)	0.65	Not reported		
Minor bleeding (no. sheath-related)			10 (3)	8 (0)	33 (28)	<0.001			
Revascularisation – PCI or CABG (%)			33 (23.2)	29 (20.6)	19 (13.2)	0.08†	41 (28.9)	40 (28.4)	25 (17.4)

§ Data reported in Kunadian B, et al. Am Heart J. 2007; 153(5):763-71.[67]

† p = 0.05 by the log-rank test.

Mortality at median 4.4 years

	Repeat fibrinolysis (n = 139)	Conservative therapy (n = 134)	Rescue PCI (n = 143)
All-cause mortality	31	30	16
Cardiovascular deaths*	28	23	13

*Defined as cardiac or cerebrovascular death

Hazard ratios

	At 6 months			At 12 months			Median 4.4 years		
	HR	95% CI	p value	HR	95% CI	p value	HR	95% CI	p value
All-cause mortality*									

Rescue PCI versus repeat fibrinolysis	0.42	0.19–0.94	<0.04	Not reported			0.41	0.22–0.75	0.004
Rescue PCI versus conservative therapy	0.42	0.19–0.94	<0.04				0.43	0.23–0.79	0.006
Repeat fibrinolysis versus conservative therapy	Not reported						1.04	0.63–1.72	0.89
Cardiovascular mortality									
Rescue PCI versus repeat fibrinolysis	Not reported						0.43	0.22–0.83	0.0116
Rescue PCI versus conservative therapy							0.52	0.27–1.04	0.06280
Repeat fibrinolysis versus conservative therapy							0.82	0.47–1.42	0.4746
Recurrent MI									
Rescue PCI versus repeat fibrinolysis	0.23	0.09–0.62	0.004	Not reported			Not reported		
Rescue PCI versus conservative therapy	0.33	0.12–0.93	0.04						
Repeat fibrinolysis versus conservative therapy	Not reported								
Revascularisation									
Rescue PCI versus repeat fibrinolysis	0.5	0.29–0.88	<0.02	0.53[§]	0.32–0.86	0.011	Not reported		
Rescue PCI versus conservative therapy	0.58	0.33–1.04	<0.07	0.50[§]	0.30–0.83	0.007			

Repeat fibrinolysis versus conservative therapy	1.17	0.71–1.92	0.56	1.05[§]	0.68–1.62	0.84	
* Adjusted for age and diabetes at 6 months and age, previous history of angina, and diabetes at 4.4 years – the only baseline characteristics that were identified as predictors of mortality by multivariate analysis §Adjusted for first fibrinolytic treatment and previous PCI							

Table 94: MERLIN 2004[67,107,108]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Protocol outcome measures	Source of funding
Sutton AG, et al. A randomized trial of rescue angioplasty versus a conservative approach for failed fibrinolysis in ST-segment elevation myocardial infarction: the Middlesbrough Early Revascularization to Limit Infarction (MERLIN) trial. J Am	Design: RCT (Multicentre – 3 sites in UK) Enrolment Feb 1999 – June 2002 Randomisation: Standard random number charts and was a block randomisation process (block size 4) Allocation concealment: Telephone/sealed envelope Blinding: Open-label	n = 307 Drop-outs: 100% follow-up at 3 years Crossover: Not stated	INCLUSION CRITERIA Patients with STEMI and evidence of failure to respond to the administration of fibrinolytic therapy Presentation to the hospital within 10 h of the onset of major symptoms was required Myocardial infarction was defined by the presence of ischaemic chest pain lasting more than 30 min, unrelieved by sublingual nitrate and associated with typical ST segment elevation on the 12-lead electrocardiogram (ECG; at least 2 mm of ST-segment elevation in 2 or more contiguous chest leads and at least 1 mm in 2 or more contiguous limb leads) Failure to respond to fibrinolytic therapy was defined by a second 12-lead ECG obtained 60 minutes after the onset of fibrinolytic therapy, showing failure of the ST-segment elevation in the worst lead (the lead with maximal ST-segment elevation) to have resolved by 50%, as compared with the pre-treatment ECG (ST-segment measured 80 ms after the J	Rescue PCI (n = 153) Coronary followed by required. Unfractionated administered who had a activated clotting time of 300 s at the time of intervention. Stents, IABP, other mechanical devices, and	Conservative therapy (n = 154) Standard medical treatment after the administration of fibrinolytic therapy. Note: The use of repeat fibrinolytic therapy was discouraged but allowed during the trial if this was standard local policy. The use of heparin and other	30 days, 6 months, 1 and 3 years	1° All-cause mortality at 30 days 2° Composite of death, reinfarction, stroke, heart failure, and clinically driven subsequent revascularisation within 30 days Length of stay	Guidant, Boston-Scientific, Jomed, and Datascope

Coll Cardiol. 2004; 44(2):287-96. Sutton AG, et al. One year results of the Middlesbrough early revascularisation to limit infarction (MERLIN) trial. Heart. 2005; 91(10):1330-7. Kunadian B, et al. Early invasive versus conservative treatment in patients with failed fibrinolysis--no late survival benefit: the final analysis of the Middlesbrough Early Revascularis	Sample size calculation: Based on available data, 150 patients would be required in each arm to detect a mortality difference between 18% in the conservative group and 6% in the salvage group, with 90% power and a p value of 0.05. ITT analysis: Yes (100% follow-up at 3 years)		point), as well as the absence of an accelerated idioventricular rhythm at the time of the 60-minute ECG EXCLUSION CRITERIA Cardiogenic shock (defined by SBP ≤90 mm Hg, oliguria, and poor peripheral perfusion with or without clinical or radiologic evidence of pulmonary edema) Confounding features on the pre-fibrinolytic ECG, preventing ST-segment reduction analysis Reinfarction in the same ECG territory within 2 months of an original infarction Absent femoral pulses Pregnancy Presence of significant coexisting pathology likely to affect the prognosis during the follow-up period Demographics and baseline characteristics see below	adjunctive pharmacologic therapy were used at the discretion of the attending cardiologist Note: In both arms electrocardiography was performed every 3 h after the initiation of therapy for 24 hours and all patients were treated initially with 300 mg aspirin and thereafter ≥75 mg/day aspirin; use of mechanical devices and additional pharmacotherapy was discretionary (see below for in-hospital treatment) If ≥1 stents were used, ticlopidine 250	treatments was at the discretion of the attending physician. Early crossover to the rescue angioplasty arm was not allowed, except for cardiogenic shock Angiography and revascularisation were permitted for reinfarction (defined subsequently) or for recurrent ischaemia or a positive exercise test during the hospital admission.		Minor bleeding (See below for definitions)

ation to Limit Infarctio (MERLIN) randomized trial. Am Heart J. 2007; 153(5):763-71.		mg twice daily following an initial immediate dose of 500 mg, or clopidogrel 75 mg/day following an initial dose of 300 mg, was administered.	

Demographics and baseline characteristics

	Conservative arm (n = 154)	Rescue angioplasty arm (n = 153)
Male (%)	114 (74)	108 (71)
Age (yrs)	62.7 ± 10.9	63.0 ± 11.2
History of hypertension (%)	47 (30.5)	62 (40.5)
History of diabetes (%)	23 (14.9)	18 (11.8)
Insulin therapy (%)	7 (4.5)	4 (2.6)
Known hyperlipidemia (%)	24 (15.6)	29 (19.0)
Total cholesterol on admission (mmol/l)	5.54 ± 1.17	5.82 ± 1.32
Blood glucose on admission (mmol/l)	8.9 ± 3.0	9.0 ± 3.3
Current smoker (%)	57 (37.0)	64 (41.8)
Ex-smoker (%)	51 (33.1)	45 (29.4)
Previous MI (%)	20 (13.0)	17 (11.1)
Anterior MI (%)	62 (40.3)	74 (48.4)
Fibrinolytic therapy		
Streptokinase (%)	149 (96.8)	147 (96.1)
rt-PA (%)	5 (3.2)	6 (3.9)
Pain to lysis time (min)	170 ± 96	180 ± 120
Lysis to laboratory time (min)	–	146 ± 37

Pain to laboratory time (min)	–	327 ± 121
ECG to laboratory time (min)	–	85 ± 36
In-hospital treatment		
	Conservative arm (n = 154)	**Rescue angioplasty arm (n = 153)**
Immediate coronary angiography (%)	0	149 (97.4)
Immediate coronary angioplasty (%)	0	100 (65.4)
Stent(s) deployment (%)	0	77 (50.3)
Glycoprotein IIb/IIIa inhibitor (%)	0	5 (3.3)
IABP (%)	0	19 (12.4)
Additional fibrinolytic therapy (%)	18 (11.7)	0
Transfusion (%)	2 (1.3)	17 (11.1)
Discharge medication*		
Aspirin (%)	135 (97.1)	136 (97.8)
Thienopyridine (%)	21 (15.1)	84 (60.4)
Warfarin (%)	4 (2.9)	6 (4.3)
Beta-blocker (%)	114 (82.0)	110 (79.1)
Lipid-lowering medication (%)	101 (72.7)	98 (70.5)
ACE inhibitor (%)	97 (69.8)	109 (78.4)
*In each arm, 139 patients were discharged from the hospital. Medication use was comparable at 3 years		

Definitions of end points

Reinfarction

Repeat episode of ischaemic chest pain after recovery from the initial event, associated with typical ST-segment re-elevation on the ECG and lasting for >30 minutes despite opiate and nitrate therapy.

Stroke

Any new neurologic deficit lasting >24 hours; computed axial tomography was performed when possible

Heart failure

Requirement for diuretic treatment in the presence of typical chest X-ray characteristics, or auscultatory crackles extending at least one-third of the way up the lung fields without a previous history of chronic pulmonary disease, or

A third heart sound with persistent tachycardia

Subsequent revascularisation

Any catheter-based or surgical intervention in the conservative group and any additional revascularisation procedure in the rescue group that was not planned after the initial coronary angiogram

Minor bleeding

Transfusion was reserved for those with a fall in haemoglobin of ≥2 g/dl, and only if this took the total haemoglobin to <10 g/dl.

Effect Size*

	at 30 days			**at 6 months***		**at 1 year**			**at 3 year**		
	CT (n = 154)	**R-PCI (n = 153)**	**p value**	**CT (n = 154)**	**R-PCI (n = 153)**	**CT (n = 154)**	**R-PCI (n = 153)**	**p value**	**CT (n = 154)**	**R-PCI (n = 153)**	**p value**
All-cause death (%)	17 (11.0)	15 (9.8)	0.7	19 (12.3)	17 (11.1)	20 (13.0)	22 (14.4)	0.7	26 (16.9)	27 (17.6)	0.9
CAD death (%)	17 (11.0)	13 (8.5)	0.4	Not reported		Not reported			Not reported		
Unplanned revascularisation (%)	31 (20.1)¥	10 (6.5)€	<0.01	40 (25.8)	19 (12.4)	46 (29.9)†	19 (12.4)§	<0.001	52 (33.8)	22 (14.4)	<0.01
Stroke (%)	1 (0.6)	7 (4.6)	0.03	2 (1.3)	7 (4.6)	2 (1.3)	8 (5.2)	0.06	4 (2.6)	10 (6.5)	0.1
Reinfarction (%)	16 (10.4)	11 (7.2)	0.3	20 (12.6)	12 (7.9)	22 (14.3)	16 (10.5)	0.3	23 (15)	17 (11.1)	0.3
Heart failure (%)	46 (29.9)	37 (24.2)	0.3	48 (31.3)	39 (25.3)	48 (31.2)	40 (26.1)	0.3	50 (32.5)	44 (28.8)	0.5
Minor bleeding	2 (1.3)	17 (11.1)	<0.001	NA							
Median hospital stay, days (range)	7 (2–23)	7 (2–46)	0.95	NA							

*p value not reported at 6 months

¥16 patients underwent emergency revascularisation (PCI 15, 1 CABG); 1 urgent CABG for unstable angina and severe triple vessel disease; 14 unscheduled PCI for post infarction angina with ECG changes (8) or positive exercise treadmill test (6)

€7 patients underwent emergency revascularisation (5 PCI, 2 CABG); 1 urgent CABG after readmission for unstable angina; 2 patients who did not undergo rescue PCI

underwent unplanned PCI for post infarction angina (1) or positive exercise treadmill test (1)
†In addition to 30 days: 6 CABG; 9 PCI
§ In addition to 30 days: 5 CABG; 4 PCI
HR for all-cause mortality was calculated at 3 years from Kaplan-Meier curve 0.97 [0.57–1.65]

Table 95: RESCUE I 1994[39]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Protocol outcome measures	Source of funding
Ellis SG, et al. Randomized comparison of rescue angioplasty with conservative management of patients with early failure of thrombolysis for acute anterior myocardial infarction. Circulation. 1994; 90(5):2280-4	Design: RCT (Multicentre – 20 sites in Brazil, USA, Europe, Japan) Enrolment Jan 1990 – Mar 1993 Randomisation: Permuted block design, stratifying for site and time from onset to randomisation (≥ 4 hours or < 4 hours). Allocation concealment: Closed envelopes Blinding: Open label.	n = 151 Drop-outs: 0 Crossover: conservative therapy → rescue angioplasty within 72 hours (n = 2)	INCLUSION CRITERIA Anterior myocardial infarction with ST-segment elevation ≥ 2 mV in at least 2 of 6 precordial leads with cardiac catheterisation within 6 hours of chest pain onset; with severe ongoing chest pain, the time window could be extended to within 8 hours at the discretion of the investigator. Treatment with any acceptable intravenous fibrinolytic regimen (including but not limited to streptokinase [1.5 million U], tissue-type plasminogen activator [TPA; 100 to 125 mg], and urokinase [3 million U]) Aged 21–79 years TIMI flow grade 0–1 in the left anterior descending coronary artery (LAD) after intracoronary nitrate administration and at least 90 minutes after initiation of fibrinolytic therapy Ability to give informed consent EXCLUSION CRITERIA Cardiogenic shock (SBP <90 mm Hg after fluid resuscitation and treatment of	Rescue angioplasty (n = 78) Before catheterisation patients received aspirin (325 mg chewed) and sedation. Angioplasty was performed by experts (≥50 procedures with≥80% success); it was recommended that non-infarct artery stenosis not be dilated. Additional streptokinase (500 000 U) or	Conservative therapy (n = 73) Note: Angioplasty or bypass surgery was proscribed for 72 hours.	30 days	Death Severe heart failure (New York Heart Association functional class III or IV)	None stated

	Investigators remained blinded to study outcome at all times. Sample size calculation: 138 patients required to detect a 4±12% difference in ejection fraction (1° end point) with 2-sided p = 0.05 and β = 0.80. ITT analysis: Yes		bradycardia <60 beats per minute) Prior myocardial infarction Left main stenosis ≥50% in diameter Demographics and baseline characteristics see below	urokinase (1 million U) was given to patients who had received fibrin-specific agents Use of IABP was discretionary Notes: Patients in both arms received aspirin (80 to 325 mg/d), IV nitrates for ≥24 hours, and IV or high-dose (> 10 000 U BID) sc heparin for ≥3 days, as tolerated.				

Demographics and baseline characteristics

	Angioplasty (n = 78)	**Conservative (n = 73)**
Age,y	59±11	59±11
Sex, % male	79	85
Diabetes, %	16	11
Smoking, %	44	56
Time from MI, h	4.5±1.9	4.5±1.9
Systolic BP, mm Hg	126±23	135±26

Heart rate, bpm	84±15	83±17
Killip class ≥2, %	21	26
Multivessel disease, %	34	40
Ongoing angina at the time of catheterisation, %	81	67
Proximal occlusion site, %	46	51
TIMI 1 flow, %	36	46
Angiographic collaterals, %	32	37

Effect Size

Procedures and outcomes

	Angioplasty (n = 78)	**Conservative (n = 73)**	**p value**
PCI success† (%)	72 (92.3)	1* (50.0)	–
IABP use (%)	7 (9.0)	4 (5.6)	0.42
30-day outcomes (%)			

†Final TIMI flow ≥ 2 and stenosis ≤ 50%

*2 patients 'crossed over' to urgent PCI

Table 96: RESCUE II 2000[40]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Protocol outcome measures	Source of funding
Ellis SG, et al. Review of immediate angioplasty after fibrinolytic therapy for acute myocardial infarction: insights from the RESCUE I, RESCUE II, and other contemporary clinical experiences. Am Heart J. 2000; 139(6):1046-53.	Design: RCT (no further details) Enrolment Sep 1995 – Jan 1998. Terminated prematurely due to funding issues and concern that randomising patients with TIMI 2 flow to CT was inappropriate Randomisation: Permuted block design stratified by site and time from infarct onset (≤5 hours, >5 hours) Allocation concealment: Closed envelope Blinding: Open-label Sample size calculation:	n = 29 Drop-outs: Not stated Crossover: Not stated	INCLUSION CRITERIA Acute MI with ST-segment elevation ≥2.0 mV in ≥ 4 leads of a standard 12-lead electrocardiogram Aged ≥ 21 years Receipt of any accepted IV fibrinolytic regimen Cardiac catheterisation within 12 hours of infarct onset (usually precipitated by suspected incomplete fibrinolysis) TIMI 2 flow and diameter stenosis ≥ 60% after intracoronary nitroglycerin ≥ 90 minutes after onset of fibrinolytic therapy Suitability for PCI by local standards Capacity to sign informed consent EXCLUSION CRITERIA None stated Demographics and baseline characteristics see below	Rescue PCI (n = 14) Note: Stents were suggested when PCI failed to achieve a <40% stenosis or TIMI 3 flow All patients received aspirin and heparin (titrated to achieved clotting time ≥350 seconds during coronary intervention and to an activated partial thromboplastin time 60–80 seconds for ≥ 48 hours thereafter Use of β-blockers, ACEi	Conservative therapy (n = 15) No further details	30 days, 1 year	All-cause mortality Reintervention during index admission Reinfarction Length of stay	No details

	No details ITT analysis: Yes			and IABP was discretionary				

Demographics and baseline characteristics		
	R-PCI (n = 14)	**CT (n = 15)**
Age (y)	66 ± 10	59 ± 9
Men (%)	93	93
Hours to		
Fibrinolytic therapy	3.5 ± 2.6	2.9 ± 2.1
Catheterisation	4.9 ± 4.2	5.4 ± 2.5
Anterior MI	79†	40
Cardiogenic shock (%)	0	0
Infarct artery		
Left anterior descending (%)	79†	40
Left circumflex (%)	0†	40
Right coronary (%)	21	20
LVEF (%)	44 ± 10	45 ± 9
Treatment		
Stent (%)	29	0
Abciximab (%)	7	0
Technical success (%)*	100 (21% TIMI 2)	–
†p ≤ 0.05 versus CT *Defined as diameter stenosis <50% and TIMI flow ≥2		
Effect Size		
	R-PCI (n = 14)	CT (n = 15)
In hospital		
Reintervention	0	5*

Reinfarction	0	0
Length of stay (d)	7.6 ± 3.0	6.4 ± 1.6
30 days		
All-cause mortality	1	0
1 year		
All-cause mortality	1	1
Reintervention	4 (3 PCI, 1 CABG)	7 (all PCI)

Table 97: Belenkie 1992[7]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Protocol outcome measures	Source of funding
Belenkie I, et al. Rescue angioplasty during myocardial infarction has a beneficial effect on mortality: a tenable hypothesis. Can J Cardiol. 1992; 8(4):357-62	Design: RCT (4 sites, Canada) Enrolment: Aug 1986 – Oct 1988 Randomisation: Method not stated Allocation concealment: Not stated Blinding: Open label Sample size	n = 28 Drop-outs: 0 Crossover: Not stated	INCLUSION CRITERIA Aged <76 Chest pain characteristic of myocardial ischaemia present for >30 minutes unrelieved by sublingual nitroglycerin ST segment elevation >0.1 mV in ≥2 limb leads or >0.2 mV in ≥2 precordial leads Treatment with a fibrinolytic agent feasible within 3 h of symptom onset Persistently occluded IRA >3 hours after the onset of infarction EXCLUSION CRITERIA Fibrinolytic therapy contraindicated Demographics and baseline characteristics see below	Rescue PCI (n = 16) Note: All patients received fibrinolytic therapy (streptokinase or rt-PA), heparin and indefinite aspirin. Cardiac catheterisation performed immediately after initiation of fibrinolytic therapy	Conservative therapy (n = 12)	In-hospital	Mortality Bleeding	Foothills Hospital Research and Development the Heart Stroke on of Calgary

	calculation: Not stated ITT analysis: Yes							

Demographics and baseline characteristics		
	Rescue PCI (n = 16)	Conservative (n = 12)
Age (years)	58 ± 8	61 ± 13
Male (%)	7 (44)	6 (50)
Study myocardial infarction:		
Anterior (%)	9 (56)	6 (50)
Inferior (%)	7 (44)	6 (50)
1 vessel disease (%)	7 (44)	5 (42)
2 vessel disease (%)	6 (37)	4 (33)
3 vessel disease (%)	3 (19)	3 (25)
Previous myocardial infarction	2 (12)	1 (8)
Time to PCI (minutes)	257 ± 57	–
Mortality (total)	1/16 (6.3)	4/12 (33.3)*
Mortality (successful PCI)	0 (13)	–
*p = 0.13 versus patients randomised to rescue PCI		
Effect Size **Outcomes – In-hospital**		
	Rescue PCI (n = 16)	**Conservative (n = 12)**
All-cause mortality	1	4
Complications	1: gastrointestinal bleeding 1: groin hematoma requiring transfusion	1: severe groin hematoma
PCI was successful in 13 of 16 patients		

Table 98: Mounsey 1995[84]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Protocol outcome measures	Source of funding
Mounsey JP, et al. Rescue thrombolysis: alteplase as adjuvant treatment after streptokinase in acute myocardial infarction. Br Heart J. 1995; 74(4):348-53.	Design: RCT (UK) Enrolment: Not stated Randomisation: Minimisation programme Allocation concealment: Not stated Blinding: Double-blind Sample size calculation: >32 randomly allocated patients – calculated to detect an improvement in left ventricular ejection fraction of 10%, assuming σ = 10%, α = 0.05 and β = 0.2 ITT analysis: Yes	n = 37 Drop-outs: 0 Cross-over: Not stated	INCLUSION CRITERIA Presented within 6 hours of the onset of a first acute myocardial infarction, defined as chest pain of more than 30 minutes' duration unresponsive to glyceryl trinitrate; electrocardiographic ST segment elevation, either ≥2 mm in ≥2 contiguous leads V1-V6 or ≥1 mm in ≥2 contiguous limb leads; or ST depression of ≥2 mm with tall R waves in leads V1-V3 suggesting true posterior infarction Evidence of failed reperfusion (<25% reduction of ST elevation in the electrocardiographic lead with maximum ST shift on a pre-treatment electrocardiogram) 30 minutes after 1.5 MU iv streptokinase over 60 minutes EXCLUSION CRITERIA Previous Q wave myocardial infarction Previous coronary surgery Pre-existing right or left bundle branch block or fascicular block Left ventricular hypertrophy Any of the general contraindications to fibrinolysis There was no upper age limit Demographics and baseline characteristics see below	Repeat fibrinolysis (n = 19) Alteplase (rtPA) 100 mg over 3 hours Notes: All patients received heparin following initial fibrinolysis for ≥ 24 hours, and aspirin; all other treatments were discretionary	Placebo (n = 18)	6 weeks	Mortality Bleeding	Boehringer Ingelheim provided alteplase and identical placebo

Demographics and baseline characteristics			
	Streptokinase + rtPA (n = 19)	**Streptokinase + placebo (n = 18)**	**p value***
Age (years)	63 (10)	63 (10)	0.9
No (%) of men	11 (58)	13 (72)	0.4
No (%) with infarct site:			
Anterior	10 (53)	10 (56)	
Inferior	8 (42)	6 (33)	
other	1 (5)	2 (11)	0.7
Time to streptokinase (h)	3.4 (1.9)	4.3 (2.1)	0.2
Time to rt-PA (h)	5.6 (1.9)	6.5 (2.2)	0.3
*For difference between rt-PA and placebo assessed by t or χ2 test.			

Effect Size		
Outcomes		
	Streptokinase + rtPA (n = 19)	**Streptokinase + placebo (n = 18)**
Mortality	1	1
There were 5 episodes of bleeding. Only 1, a gastrointestinal haemorrhage in a patient randomly allocated placebo, required transfusion. Minor bleeding included 2 haemoptyses, 1 epistaxis, and 1 rectal bleed; it was not specified which arm these patients were allocated to. There were no cerebral haemorrhages		

Table 99: Sarullo 2000[97]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Protocol outcome measures	Source of funding
Sarullo FM, et al. Efficacy of rescue thrombolysis in patients with acute myocardial infarction: preliminary findings. Cardiovasc Drugs Ther. 2000; 14(1):83-9	Design: RCT (3 sites – Italy) Enrolment: Jan 1995–Dec 1997 Randomisation: Sequentially numbered boxes Allocation concealment: Not stated Blinding: Double-blind Sample size calculation: Not stated ITT analysis: Yes	n = 90 Drop-outs: 0 Cross-over: Not stated	INCLUSION CRITERIA First episode of AMI Aged <70 years Admitted to hospital and given fibrinolysis within 4 hours of onset of pain Killip class I-II plus acceptable echocardiographic window to allow electrocardiographic images of adequate technical quality ST elevation of >1 mm in the peripheral leads or 2 mm in the pericardial leads, involving >4 leads, with concomitant alterations of the segmentary kinetics in the ECG performed at entry Basal creatine kinase within normal range Pain and ST segment elevation showed lack of response 120 minutes after starting treatment (<50% ST segment resolution) EXCLUSION CRITERIA Patients unsuitable for fibrinolysis or who had LBBB on the admission ECG History of cardiomyopathy or heart failure Patients receiving β-blockers Patients who showed no enzymatic alterations after fibrinolysis (classified as having unstable angina)	Repeat fibrinolysis (n = 45) rTPA 50 mg (10 mg bolus, 40 mg in 60 minutes) Note: All patients received nitrates, aspirin, metoprolol where possible and heparin. A continuously adjusted maintenance infusion of heparin was administered to keep the aPTT at 1.5–2.5 times laboratory control values (45s). aPTT was determined within 4 hours after heparinisation on the first day and every 12 hours the next 4 days	Placebo (n = 45)	In-hospital	Death Reinfarction Major bleeding Minor bleeding Urgent revascularsation	None stated

			Demographics and baseline characteristics see below					

Demographics and baseline characteristics		
	Repeat fibrinolysis (n = 45)	**Placebo (n = 45)**
Sex F/M	10/35	11/34
Age, years	56±9	57±8
Onset of symptoms (min)	107±53	116±54
Anterior AMI	26	24
Lateral + inferior AMI	10	11
Anterior + inferior AMI	9	10
Beta-blockers	18	20
Hypertension	30	23
Diabetes	15	13
Hypercholesterol	18	13
Smokers	30	24
Effect Size		
Outcomes – In-hospital	**Repeat fibrinolysis (n = 45)**	**Placebo (n = 45)**
All-cause mortality (%)	3 (6.6)	13 (28.8)
Non-fatal reinfarction (%)	7* (15.5)	0
Major bleeding (%)	1 (2.2)	0
Minor bleeding (%)	20 (44.4)	7 (15.5)
Urgent revascularisation (PCI or CABG) (%)	14 (31)	1 (2.2)
*2/7 received a further administration of fibrinolytic drug 35 (77.7%) patients receiving additional rTPA (50 mg) showed a rapid reduction of pain and ST elevation 10–50 minutes after the start of additional rTPA administration Only 12 (26.6%) patients receiving placebo showed successful reperfusion 35–85 minutes (mean 55 minutes) after standard fibrinolysis		

G.12 Routine early angiography following fibrinolysis

Table 100: GRACIA-1[46]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Fernandez-Avilés F, et al. Routine invasive strategy within 24 hours of thrombolysis versus ischaemia-guided conservative approach for acute myocardial infarction with ST-segment elevation (GRACIA-1): a randomised controlled trial. Lancet. 2004; 364(9439):1045-53.	Design: RCT (22 sites – Spain, Portugal) Enrolment: Mar 2000 – Nov 2001 Setting 15/22 sites had onsite interventional facilities. When required patients were transferred to an interventional centre Randomisation Computerised block (6, 8 or 10 patients) randomisation Allocation concealmisedent: Central telephone system Blinding: Open label. Outcome	n = 500 Drop-outs: 10 (invasive strategy: 4 lost to 12 month follow-up; conservative: 1 withdrew consent; 5 lost to 12 month follow-up)	Low risk patients Inclusion criteria Patients aged >18 years Chest pain lasting 30 minutes – 12 hours unresponsive to nitroglycerin with ST-segment elevation ≥ 1 mm in ≥ 2 contiguous leads or a non-diagnostic ECG due to LBBB or paced rhythm Received fibrinolytic treatment with accelerated dose of alteplase within 12 hours of pain onset Exclusion criteria Cardiogenic shock (sustained SBP < 90 mm Hg, with no response to fluids, or SBP > 100 mm Hg with vasopressors (in absence of bradycardia) Suspicion or evidence of mechanical complication Non-cardiac condition with expected survival < 1 year Women with positive pregnancy test	Routine invasive (n = 248) Routine angiography and revascularisation if indicated within 6–24 hours of fibrinolysis (direct stenting of culprit artery attempted if morphologically suitable; non-culprit lesions only stented if a large amount of myocardium was threatened by stenosis. Surgery was done if stenting not feasible or when: continued ischaemia secondary to failure of culprit artery stenting; any other lesion with continuing ischaemia of a functionally important territory unsuitable for stenting; ≥ 70% left main artery stenosis Notes:	Ischaemia-guided (n = 252) Predischarge angiography and revascularisation were only done in cases with spontaneous recurrent ischaemia with ECG changes or a non-invasive stress test, under β-blockade which identified ischaemia with a heart-rate of < 100 bpm or functional capacity <5 METS, hypotension	In-hospital, 30 days, 12 months	1° Combined death, non-fatal reinfarction or ischaemi-induced revascularisation at 1 year 2° Mortality Reinfarction Ischaemia-induced revascularisation Major bleeding Intracranial bleeding	Spanish Ministry of Health, Spanish Network for Cardiovascular Research, Spanish Society of Cardiology, Guidant, Lilly

	reviewers (all events) blinded to treatment assignment Sample size calculation: 250 patients in each group based on ≥ 11% difference in primary end point (80% power; β error = 0.2) ITT analysis: Yes, 1 patient from ischaemia-guided strategy who withdrew consent excluded from analysis		Current use of warfarin or other anticoagulant drug Active bleeding or major surgery within past 2 weeks prohibiting use of heparin or antiplatelet therapy Aspirin, ticlopidine, clopidogrel or heparin contraindication Known renal failure (creatine > 221 micromol/L Any kind of stroke in the past year or haemorrhagic stroke ever Inclusion in other clinical trial Known multivessel coronary artery disease not suitable for revascularisation Major surgery pending in coming year Peripheral vascular disease prohibiting catheterisation Demographics and baseline characteristics see below	Given oral ticlopidine (500 mg) or clopidogrel (300 mg). Abciximab was strongly recommended in patients with clear evidence of thrombus. Heparin was interrupted at time of stent implantation.	on effort or ventricular tachycardia on effort Patients in both arms were given chewable aspirin (200–500 mg), IV fibrinolysis, β-blockers and ACEI. Secondary prevention measures were explained and strongly encouraged Heparinisation maintained ≤ 48 hours after fibrinolysis in stable patients assigned to conservative treatment		Length of hospital stay Recurrent ischaemia (see below for definitions)	

Baseline characteristics and medication at discharge and at 1 year		
	Invasive (n = 248)	**Conservative (n = 251)**
Mean age, years (SD)	60 (12)	61 (12)

Men (%)	215 (87)	214 (85)
Hypertension (%)	82 (33)	86 (34)
Cholesterol (>5.5 mmol/L) (%)	93 (38)	105 (42)
Diabetes mellitus (%)	31 (13)	34 (14)
Family history (%)	48 (19)	53 (21)
Current smoker (%)	141 (57)	141 (56)
Previous MI (%)	17 (7)	22 (9)
Previous angina (%)	40 (16)	35 (14)
Previous treatment (%)		
Antianginal medication (%)	32 (13)	30 (12)
Aspirin (%)	32 (13)	28 (11)
Statin (%)	57 (23)	48 (19)
Anterior MI (%)	107 (43)	93 (37)
Time from onset to fibrinolysis (h)	3.04 (1.88)	3.12 (2.01)
Time from onset to randomisation (h)	14.8 (4.4)	14.2 (4.6)
Time from onset to angiography (h)*	19.6 (5.5)	NA
Medication at discharge		
Aspirin (%)	233 (94)	233 (93)
β blockade (%)	205 (83)	206 (82)
Statins (%)	178 (72)	163 (65)
ACEI (%)	119 (48)	136 (54)
Calcium antagonist (%)	15 (6)	22 (9)
Medication at 1 year	n = 244	n = 246
Aspirin (%)	228 (92)	226 (90)
β blockade (%)	201 (81)	203 (81)
ACEI (%)	126 (51)	128 (51)
Calcium antagonist (%)	32 (13)	35 (14)

*The time between fibrinolysis and angiography was longer for the 61 patients who were transferred from a non-interventional centre to an interventional hospital (17.7 [SD 7.5] hours versus 14.6 [8.9] hours, p = 0.01)

Definitions of end points

Reinfarction

Typical chest pain lasting > 30 minutes with a new increment of creatine kinase MB isoenzyme with or without new ECG abnormalities

Myocardial ischaemia

Spontaneous (at rest) or stress-induced recurrence of typical angina pectoris (or anginal equivalent) that had to coincide with new ECG abnormalities, or abnormal stress test

Ischaemia-driven revascularisation

- Any revascularisation procedure (percutaneous or surgical) involving any diseased coronary artery after identification of severe myocardial ischaemia that had to meet at least 1 of the following criteria: (a) spontaneous typical angina (at rest) with ECG changes; (b) grade III or IV effort angina (Canadian classification); and (c) stress test under β-blockade showing unequivocal ECG changes, perfusion defects, or regional contractility abnormalities along with 1 feature of poor prognosis (appearance of ischaemia before 100 bpm or 5 METS are reached); functional capacity under 5 METS; hypotension on effort; or ventricular tachycardia on effort
- Revascularisation of patients assigned to the conservative group after spontaneous ischaemia in hospital, or after detecting high-risk ischaemia in a predischarge non-invasive test, was regarded as part of this strategy. Consequently, predischarge revascularisation in the conservative group was analysed as a secondary end point, but not included as part of the primary end point. Instead, post-discharge revascularisation was regarded as part of the primary end point.

Major bleeding or vascular complication

Any complication causing death, need for surgery or transfusion, or extended time in hospital

Angiographic profile and results

	Invasive (n = 248)
One-vessel disease (%)	146 (59)
Multivessel disease (%)	86 (35)
Angiographically non-significant CAD or normal coronary arteries (%)	16 (6)
Angioplasty with stenting of the culprit artery	199
Angioplasty of an additional artery	51
Pre/post PCI TIMI flow 0 (%)	16 (6)/ 0 (0)
Pre/post PCI TIMI flow 1 (%)	9 (4)/ 0 (0)
Pre/post PCI TIMI flow 2 (%)	22 (9)/ 4 (2)

Pre/post PCI TIMI flow 3 (%)	201 (81)/ 164 (98)	
Abciximab	64	
Not eligible for culprit artery stenting	49	
Medical treatment	40	
Non-culprit stenting	3	
CABG	2	
	Conservative (n = 251)	
Cardiac catheterisation before discharge (%)	52 (21)	
Predischarge ischaemia-driven revascularisation (stenting in all cases)	51*	
Unsuitable for any type of revascularisation (%)	1	
*successfully achieved in all cases		

Outcomes

	Invasive (n = 248)	Conservative (n = 251)
Deaths, n (%)		
Index hospital stay	5 (2)	6 (2)
By 30 days	6 (2)	6 (2)
By 1 year	9 (4)	16 (6)
Non-fatal reinfarction, n (%)		
Index hospital stay	3 (1)	2 (1)
By 30 days	3 (1)	4 (2)
By 1 year	9 (4)	15 (6)
Revascularisation, n (%)		
Index hospital stay		
Induced by spontaneous ischaemia	6 (2)	30 (12)
Induced by noninvasive stress tests	0	21 (8)
By 1 year after discharge	9* (4)	30† (12)
Readmission due to ischaemia by 1 year	37 (15)	62 (25)
Major bleeding, n (%)	4 (1.6)	4 (1.6)

Intracranial haemorrhage, n (%)	0 (0)	1 (0.4)
Mean index hospital duration (days)	7.1 ± 5.6	10.5 ± 5.7
*PCI in 8 and CABG in 1. †PCI in 25 and CABG in 5		
Transfer		
Patients who were transported and those who were not, did not differ with respect to the frequency of minor or major cardiac events between fibrinolysis and angiography, and no patient died during this period. Only 1 event (angina) took place during transportation (1.6%); it was not reported what group this patient was allocated to.		

Table 101: SIAM III[28]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures
Scheller B, et al. Beneficial effects of immediate stenting after thrombolysis in acute myocardial infarction. J Am Coll Cardiol. 2003; 42(4):634-41. Clever Y, et al. Long-term follow-up of early versus delayed invasive approach after fibrinolysis in acute	Design: RCT (5 sites – Germany) Enrolment: July 1998 – April 2001 Setting Patients were recruited from community hospitals without cathlab facilities located within 35 km of an interventional centre Randomisation: Computer algorithm Allocation concealment: Not stated	n = 163 Drop-outs: 0	No details on whether high or low risk patients INCLUSION CRITERIA Age >18 yrs Patients presenting with symptoms of MI present for <12 hours and having, on the basis of 12-lead electrocardiography, ST-segment elevation of ≥1 mm in ≥2 limb leads, ST-segment elevation of ≥2 mm in the precordial leads, or new LBBB Patients eligible for fibrinolysis No secondary or iatrogenic infarction No chronic renal insufficiency requiring dialysis Secondary angiographic inclusion criteria Indication for angioplasty independent of the study Infarct-related lesion in a native coronary artery >2.5 mm	Immediate stenting (n = 82) Transferred within 6 hours after fibrinolysis for coronary angiography, including stenting of the infarct-related artery (IRA) Note: Reteplase was administered in 2 boluses of 10 MU 30 minutes apart. Patients received 250 mg of aspirin intravenously and a bolus of 5,000 IU heparin. GPIs use was discretionary.	Elective stenting (n = 81) Elective coronary angiography 2 weeks after fibrinolysis with stenting of the IRA or earlier in case of ongoing ischaemia	In-hospital, 30 days, 6 months	1° Death, reinfarction, ischaemic events, and target lesion revas-cularisation at 6 months 2° Each component of primary end point Major bleeding Cerebral bleeding

myocardial infarction. Circ. Cardiovascula r interventions. 2011; 4:342-348.	Blinding: Open-label. Unclear whether outcome assessors were blinded to treatment allocation Sample size calculation: 163 patients, with a 2-sided type I error rate of 0.05, yielded 90% power to detect a decrease in the incidence of the primary end point from 50% – 25% by immediate stenting. ITT analysis: Yes	Diameter stenosis of ≥70% or TIMI flow <grade 3 Secondary angiographic exclusion criteria Coronary anatomy unsuitable for stent placement Anticipated indication for surgical coronary revascularisation within 6 months Previous MI in the area of the infarct-related vessel Infarct-related lesion not clearly defined Demographics and baseline characteristics see below	Heparin was continued by an infusion of 1,000 IU/h. The initial rate of heparin infusion was reduced to 800 weighing <80 kg and was adjusted to maintain an activated partial thromboplastin time of 50–70 s in all patients. Additional heparin was given in the cathlab (target activating clotting time was 250 seconds). Aspirin and clopidogrel were continued for 4 weeks.	(see below for definitions)

Demographics and baseline characteristics

	Immediate stenting (n = 82)	Delayed stenting (n = 81)
Male gender	76.8%	80.2%
Age	62.4 ± 11.2 years	63.4 ± 9.9 years
Time from symptom onset to fibrinolysis	3.2 ± 2.2 hours	3.6 ± 2.6 hours
CK	945 ± 874 IU/l	969 ± 684 IU/l
CK-MB	125 ± 101 IU/l	116 ± 95 IU/l
Cardiogenic shock at randomisation	3.7%	1.2%
Anterior wall infarction	43.9%	40.7%
Diabetes mellitus	29.3%	34.6%
Smoker	42.7%	38.3%

Hypertension	62.2%	63.0%
Hyperlipidemia	51.2%	60.5%
In-hospital medical treatment		
β-blocker	77.3%	76.2%
Nitrates	57.6%	77.8%
ACE inhibitors	93.9%	93.7%
AT antagonists	1.5%	1.6%
Statins	62.1%	57.1%
Time from symptom onset to first angiography	6.7 ± 2.9 h	11.7 ± 6.8 days
Time from fibrinolysis to angiography	3.5 ± 2.3 h	11.7 ± 6.8 days
Unplanned premature angiography	0	23.5%
Abciximab	9.8%	16.0%
Stents	100%*	100%*
*Based on methods section (no further details were reported in the results section)		
Angiographic profile and results	**Immediate stenting (n = 82)**	**Delayed stenting (n = 81)**
Three-vessel disease (%)	28	25.9
TIMI flow before intervention (%)		
0/ 1	21 (5.8 with collaterals)	24.3 (11.1 with collaterals)
2	18.5	16.2
3	60.5	59.5
TIMI 3 flow post intervention	97.5	91.9
TIMI 3 flow after 6 months	95.5	91.2

Definitions of end points

Reinfarction:

Two or more of the following: (1) chest pain lasting for more than 30 minutes; (2) a new significant ST-elevation; (3) rise in the serum creatine kinase level to >3X ULN

Target lesion revascularisation:

Any reintervention or CABG involving the infarct-related vessel

Ischaemic events

Unplanned hospitalisation or unplanned angiography due to postinfarction angina, recurrent angina pectoris lasting >15 m despite the administration of nitrates or being accompanied by ECG changes, pulmonary oedema, or hypotension

Major bleeding

Defined as need for transfusion, bleeding requiring surgical intervention with a timely connection with the coronary intervention, bleeding documented by computed tomography or ultrasound, intracerebral as well as ocular, retroperitoneal, abdominal, intestinal, or urogenital, or a decrease in haemoglobin >4g% within 72 hours with a timely connection with the coronary intervention

Effect Size

Outcomes

Acute phase	**Early PCI (n = 82)**	**Delayed PCI (n = 81)**	**p value**
Cardiogenic shock at randomisation	3 (3.7%)	1 (1.2%)	0.315
Cardiogenic shock at follow-up	5 (6.1%) (new 2)	7 (8.6%) (new 6)	0.374
Major bleeding	8 (9.8%)	6 (7.4%)	0.400
Cerebral bleeding	1 (1.2%)	2 (2.5%)	
Stroke after fibrinolysis	2 (2.4%)	2 (2.5%)	0.685
30 days			
CABG	0	0	1.000
Target lesion reintervention	2 (2.4%)	2 (2.5%)	0.685
Ischaemic events	3 (3.7%)	20 (24.7%)	0.001
Reinfarction	2 (2.4%)	2 (2.5%)	0.685
Death	4 (4.9%)	8 (9.9%)	0.179
6-months follow-up			
Follow-up	272.4 ± 191.0 days	302.0 ± 255.8 days	0.404
CABG	6 (7.3%)	6 (7.4%)	0.609
Target lesion reintervention	16 (19.5%)	19 (23.5%)	0.336
Ischaemic events	4 (4.9%)	23 (28.4%)	0.001
Reinfarction	2 (2.4%)	2 (2.5%)	0.685
Death	4 (4.9%)	9 (11.1%)	0.119

Transfer No details

Longer-term follow-up	Early PCI (n = 82)	Delayed PCI (n = 81)	Hazard ratio (95% CI)	p
Follow-up time, years (SD)	8.1 (3.1)	7.9 (3.6)		0.603
Death	16	26	0.59 (0.32–1.11)	0.101
Ischaemic events	4	23	0.18 (0.06–0.51)	0.001
Target lesion revascularisation	23	24	0.87 (0.49–1.55)	0.646
Stroke	5	9	0.55 (0.19–1.65)	0.287
Reinfarction	6	6	0.96 (0.31–2.98)	0.944

Table 102: CAPITAL-AMI[68]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Outcome measures	Source of funding
Le May MR, et al. Combined angioplasty and gical versus s alone in acute myocardial infarction (CAPITAL AMI study). J Am Coll Cardiol. 46(3):417-	Design: RCT (4 sites – Canada) Enrolment: 2004 When required patients were transferred to interventional centre Randomisation: Not stated concealment: Not stated	n = 170 Drop-outs: 2 from TNK alone group. 1 lost to follow-up at 30 days; 1 lost to follow-up at 6 months	High risk patients INCLUSION CRITERIA Patients presenting ≤6 hours of the onset of chest discomfort of ≥ 30 minutes duration and having ≥1 mm ST-segment elevation in 2 or more contiguous leads or left bundle branch block on a 12-lead electrocardiogram were eligible if they had 1 of the following high-risk criteria: 1) anterior infarction with ST-segment elevation ≥2 mm in each of 2 contiguous precordial leads; 2) extensive non-anterior infarction: 8 or more leads with ≥ 1 mm ST-segment elevation or depression or both, or the sum of ST-segment elevation >20 mm; 3) Killip class 3; or 4) systolic blood pressure <100 mm Hg EXCLUSION CRITERIA	Tenecteplase-facilitated angioplasty (n = 86) Fibrinolysis followed by immediate transfer to interventional facility. Heparin was stopped upon arrival at the cath lab and coronary angiography performed as soon as possible. Angioplasty was performed unless angiography identified diffuse disease not amenable to revascularisation or the IRA had TIMI flow grade 3 and <70% stenosis at the culprit site. Coronary stenting was performed unless the IRA was small	TNK alone (n = 84) Indications for acute angiography were persistent chest pain and ST-segment elevation ≥90 minutes after initiation of fibrinolysis or deteriorating haemodynamic status.	1° Composite of death, reinfarction, recurrent unstable ischaemia, or stroke at 6 months 2° Bleeding Heart failure Length of stay (index hospitalisation) Unplanned revascularisatio n	Canadian Institutes of Health Research (CIHR) and a CIHR Industry-Partnered with La-Roche Limited, Canada, and Corporatio

	Blinding: Open-label. Outcome assessors were blinded to all possible events related to the primary outcome and heart failure Sample size calculation: A primary end point rate of 40% and 20% in the tenecteplase and tenecteplase facilitated PCI groups respectively at 6 months required 85 patients per group (2-sided alpha of 5%, a power of 80%, and a non-adherence rate of 2%). ITT analysis: Yes		Active bleeding History of stroke, or central nervous system damage Major surgery or trauma within 3 months Uncontrolled hypertension (systolic blood pressure ≥ 200 mm Hg or diastolic blood pressure ≥ 120 mm Hg) Prolonged (> 10 minutes) cardiopulmonary resuscitation A blood coagulation disorder Current warfarin treatment Previous CABG, PCI within 6 months Glycoprotein IIb/IIIa inhibitors within 7 days ≥ 5,000 IU of unfractionated heparin within 6 hours A therapeutic dose of any low molecular weight heparin within 6 hours Intolerance to aspirin Other illness likely to result in death within 12 months Pregnancy A creatine > 300 micromol/litre (3.40 mg/dl) Cardiogenic shock Severe contrast allergy Demographics and baseline characteristics see below	or technical difficulties prevented it. GPIs were not routinely used. Bolus doses of heparin were used, targeting an activated clotting time (ACT) of 250 s. Heparin was not routinely reinitiated after the procedure. Patients received clopidogrel 300 mg as a single dose and 75 mg daily for ≥1 month. The femoral arterial approach without any closure device was used; femoral sheaths were removed 8 to 12 hours after the tenecteplase bolus. Note: All patients received: 160 mg of chewable aspirin immediately, (then aspirin 325 mg daily), weight-adjusted tenecteplase and weight adjusted unfractionated heparin.		(see below for definitions) **Length of follow-up:** In-hospital, 30 days, 6 months	

Demographics and baseline characteristics*			
	Tenecteplase-alone (n = 84)	**Tenecteplase-facilitated angioplasty (n = 86)**	**p value**
Age, yrs	58 (51, 66)	57 (50, 67)	0.82
Age ≥75 yrs	10.7	18.6	0.19
Male gender	76.1	75.6	1.00
Hypertension	44.0	44.2	1.00
Diabetes	11.9	20.9	0.15
Current smoking	63.1	54.7	0.28
Previous angina	16.7	23.2	0.34
Previous myocardial infarction	10.7	16.3	0.37
Previous angioplasty	3.6	5.8	0.72
Anterior index myocardial infarction	47.6	52.3	0.65
Critical time intervals, minutes			
• Onset of symptoms to hospital arrival	64 (48, 141)	68 (45, 115)	0.68
• Hospital arrival to randomisation	37 (25, 54)	34 (22, 50)	0.48
• Randomisation to tenecteplase bolus	5 (5, 6)	5 (5, 10)	0.12
• Hospital arrival to tenecteplase bolus	45 (34, 61)	43 (32, 55)	0.40
• Onset of symptoms to tenecteplase	120 (90, 208)	120 (90, 153)	0.61
• Randomisation to first balloon inflation		95 (73, 106)	
• Randomisation to first balloon inflation in • transferred patients, n = 39		104 (95, 111)	
• Randomisation to first balloon inflation in • non-transferred patients, n = 46		88 (63, 102)	

• Hospital arrival to first balloon inflation		132 (113, 150)	
• Onset of symptoms to first balloon inflation		204 (172, 250)	
Cardiac medication at discharge (at 6 months)			
• clopidogrel	57%	91%	<0.001
• Aspirin	96% (96%)		
• Beta-blockers	93% (84%)		
• ACEI	90% (84%)		
• Lipid-lowering drugs	92% (91%)		

*Values are given as percentages or medians (25th, 75th percentiles)

Definitions of end points

Reinfarction

Recurrent ischaemic symptoms at rest lasting ≥30 minutes and accompanied by: 1) new or recurrent ST-segment elevation of ≥1 mm in any contiguous leads; 2) new left bundle branch block; or 3) re-elevation in serum creatine kinase level to greater than twice the upper limit of normal and ≥50% above the lowest level measured after infarction. If reinfarction occurred within 18 h, enzyme criteria were not used.

Recurrent unstable ischaemia

Recurrent symptoms of ischaemia at rest associated with new ST-segment or T-wave changes, hypotension, or pulmonary oedema.

Stroke

Focal neurological deficit, compatible with damage in the territory of a major cerebral artery with signs or symptoms persisting for >24 hours and was classified as haemorrhagic or non-haemorrhagic according to computerised tomography.

Congestive heart failure

When any 2 of the following were present: 1) dyspnea; 2) pulmonary venous congestion with interstitial or alveolar oedema on chest radiograph; 3) crackles greater than or equal to one-third of the way up the lung fields; and 4) third heart sound associated with tachycardia.

Bleeding : Classified as minor or major according to the TIMI criteria

Effect Size

Angioplasty

- Among the 86 patients assigned to tenecteplase-facilitated PCI, 40 required ambulance transfer, and 85 (99%) had coronary angiography within 3 hours from the time of randomisation. Of the latter, 79 patients (91%) underwent PCI. Stents were implanted in 77 patients (89%), and PCI with balloon alone was performed in 2 patients (2.3%)
- Platelet glycoprotein IIb/IIIa inhibitors were prescribed in 12 patients (14%) and used only when the angiographic result was suboptimal
- Angiographic success (stenosis of<50% and TIMI flow grade 3) was observed in 92% of the 79 patients who underwent facilitated PCI.

Outcomes†

	In-hospital		**At 30 days**		**At 6 months**	
	Tenecteplase alone (n = 84)	**Angioplasty (n = 86)**	**Tenecteplase alone (n = 84)**	**Angioplasty (n = 86)**	**Tenecteplase alone (n = 84)**	**Angioplasty (n = 86)**
Death	3 (3.6)	2 (2.3)	3 (3.6)	Death	3 (3.6)	2 (2.3)
Reinfarction	11 (13.1)	3 (3.5)	11 (13.3)	Reinfarction	11 (13.1)	3 (3.5)
Recurrent unstable ischaemia*	15 (17.9)	5 (5.8)	15 (18.1)	Recurrent unstable ischaemia*	15 (17.9)	5 (5.8)
Stroke (due to intracranial haemorrhage)	1 (1.2)	1 (1.2)	1 (1.2)	Stroke (due to intracranial haemorrhage)	1 (1.2)	1 (1.2)
Congestive heart failure**			10 (12.1)	Congestive heart failure**		
Major bleeding	6 (7.1)	7 (8.1)		Major bleeding	6 (7.1)	7 (8.1)
Minor bleeding	11 (13.1)	20 (23.3)		Minor bleeding	11 (13.1)	20 (23.3)
Length of stay	6.0 (5.5, 8.0)	5.0 (4.0, 7.0)		Length of stay	6.0 (5.5, 8.0)	5.0 (4.0, 7.0)

†Values are given as number (percentages) or medians (25th, 75th percentiles). *Includes patients with reinfarction. **Includes patients with cardiogenic shock

Unscheduled cardiac procedures†

	In-hospital		**At 30 days**		**At 6 months**	
	Tenecteplase alone (n = 84)	**Angioplasty (n = 86)**	**Tenecteplase alone (n = 84)**	**Angioplasty (n = 86)**	**Tenecteplase alone (n = 84)**	**Angioplasty (n = 86)**
Coronary angiogram	56 (66.6)	12 (14.0)	56 (67.5)	Coronary angiogram	56 (66.6)	12 (14.0)
• Time to angiography (days)	2.5 (0, 6.0)	3.5 (1.5, 6.0)		Time to angiography (days)	2.5 (0, 6.0)	3.5 (1.5, 6.0)

• Indication				Indication		
• Recurrent ischaemia	33 (39.3)	5 (5.8)		Recurrent ischaemia	33 (39.3)	5 (5.8)
• Failed fibrinolysis	8 (9.5)	–		Failed fibrinolysis	8 (9.5)	–
• Other	15 (17.8)	7 (8.1)		Other	15 (17.8)	7 (8.1)
PCI	42 (50.0)	12 (14.0)*	42 (50.6)	PCI	42 (50.0)	12 (14.0)*
CABG	2 (2.4)	0 (0.0)	2 (2.4)	CABG	2 (2.4)	0 (0.0)

†Values are given as number (percentages)

*In 7 patients this involved a coronary artery other than the IRA

Transfer No details

Table 103: WEST[4]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Armstrong PW, et al. A comparison of pharmacologic therapy with/without timely coronary intervention vs. primary percutaneous intervention early after ST-elevation myocardial infarction: the WEST (Which Early ST-elevation myocardial	Design: RCT (4 sites – Canada) Enrolment: Not stated Setting The protocol emphasised pre-hospital randomisation and treatment where possible Randomisation:	n = 204 Drop-outs: not stated	High risk patients INCLUSION CRITERIA Eligible patients were male or non-pregnant females (≥18 years) with symptoms presumed secondary to STEMI lasting at least 20 minutes accompanied by ECG evidence of high risk. These included: ≥2 mm of ST-elevation in 2 or more contiguous precordial leads or limb leads; or ≥1 mm ST-elevation in 2 or more limb leads coupled with ≥1 mm ST-depression in 2 or more contiguous precordial leads (total ST-deviation ≥4 mm) or presumed new left bundle branch block Reperfusion therapy (PPCI, fibrinolysis or transfer for rescue PCI) was feasible within 3 hours of randomisation	Invasive strategy (n = 104) Weight-adjusted tenecteplase and mandatory invasive management within 24 hours of enrolment including protocol-specified rescue PCI, if the admission ST-	TNK only (n = 100) Weight-adjusted TNK followed by the usual standard of care	In-hospital, 30 days	1° Composite of 30-day death, reinfarction, refractory ischaemia, congestive heart failure, cardiogenic shock, and major ventricular arrhythmia 2°	Hoffmann-LaRoche Limited, Aventis Pharma, and Eli-Lilly.

infarction Therapy) study. Eur Heart J. 2006; 27(13):1530-8	No details. Pre-specified subgroup analyses included pre-hospital versus in-hospital randomisation and time from symptom onset to randomisation (≤ 2 hours versus > 2 hours) Allocation concealment: No details Blinding: Open-label. Outcome assessors blinded to treatment allocation for reinfarction, recurrent ischaemia, and the indications for rescue PCI Sample size calculation: Feasibility		EXCLUSION CRITERIA PPCI was deemed to be available within 1 hour of diagnosis Contraindications to fibrinolysis Prior CABG Glycoprotein IIb/IIIa antagonist use within 7 days Demographics and baseline characteristics see below	elevation failed to decrease by ≥ 50% at 90 minutes after tenecteplase therapy or if haemodynamic or electrical instability occurred Note: All patients received aspirin (160–325 mg) and sc enoxaparin (1 mg/kg) at randomisation with subsequent use recommended every 12 hours for ≥ 72 hours; additional iv enoxaparin (0.3–0.5 mg/kg) was permitted during PCI, post-PCI use was discretionary. Abciximab was recommended for all PCI			Individual components of primary outcome Intracranial haemorrhage Disabling stroke Major systemic bleeding (see below for definitions)	

	study to test non-inferiority of fibrinolytic arms (as discussed here) with PPCI arm (not discussed here); 15% difference in the primary end point is evidence of the non-inferiority of pharmacologic therapy relative to PPCI ITT analysis: Yes			procedures unless performed within 3 hours of fibrinolytic therapy. Clopidogrel use was according to ACC/AHA PCI guidelines.				

Demographics and baseline characteristics		
	Tenecteplase only (n = 100)	**Invasive strategy (n = 104)**
Age, median (IQR) (years)	58 (51–69)	57 (50–67)
Gender (female)	25 (25.0)	19 (18.3)
Hypertension (yes)	37 (37.0)	56 (53.8)
Diabetes mellitus, yes (total)	18 (18.0)	8 (7.7)
Family history of early CAD (yes)	39 (39.0)	44 (42.3)
History of angina (yes)	25 (25.0)	31 (29.8)
Previous MI (yes)	14 (14.0)	12 (11.5)
Previous PCI (yes)	9 (9.0)	8 (7.7)
Smoking status (current smoker)	45 (45.0)	53 (51.0)
MI location on Q-ECG (anterior)	42 (42.0)	37 (35.6)

Killip class		
• I	93 (93.9)	99 (97.1)
• II	6 (6.1)	3 (2.9)

Definitions of end points

Refractory ischaemia

Symptoms of ischaemia with ST-deviation or definite T-wave inversion persisting for at least 10 minutes despite medical management while in hospital.

Recurrent MI:

- In the first 18 hours after randomisation: (a) Recurrent signs and symptoms of ischaemia at rest accompanied by new or recurrent ST-segment elevations of ≥0.1 mV in at least 2 contiguous leads lasting ≥ 30 minutes.
- After 18 h: (a) New Q-waves (by Minnesota Code Criteria) in 2 or more leads or enzyme evidence of reinfarction: re-evaluation of CK-MB or troponin to above the upper limit of normal and increased by >50% over the previous value. (b) The total CK must either be re-elevated to 2 times or more the upper limit of normal and increased by >25% or be re-elevated to >200 U/mL over the previous value. (1) If re-evaluated to less than 2 times the upper limit of normal, the total CK must exceed the upper limit of normal by >50% and exceed the previous value by 2-fold or be re-elevated to > 200 U/mL.
- Reinfarction after PCI (+/-stenting): (a) CK greater than 3 times the upper limit of normal and 50% greater than the previous value, or new Q-waves (Minnesota Code) in 2 or more contiguous leads.
- Reinfarction after CABG surgery: (a) CK greater than 5 times the upper limit of normal and ≥ 50% greater than the previous value, or new Q-waves (Minnesota Code) in 2 or more contiguous leads.

Congestive heart failure:

(i) Physician’s decision to treat congestive heart failure with a diuretic, intravenous inotropic agent or intravenous vasodilator and either (a) the presence of pulmonary oedema or pulmonary vascular congestion on chest X-ray believed to be of cardiac cause or (b) at least 2 of the following: (1) rales greater than one-third up the lung fields believed to be due to congestive heart failure. (2) PCWP >18 mm Hg (3) Dyspnoea, with documented pO2 less than 80 mm Hg on room air or O2 saturation <90% on room air, without significant lung disease.

Major bleeding:

Bleeding that causes haemodynamic compromise requiring blood or fluid replacement, inotropic support, ventricular assist devices, surgical intervention, or cardiopulmonary resuscitation to maintain a sufficient cardiac output.

Median (IQR) minutes from symptom onset to treatment

	Tenecteplase only (n = 100)	Invasive strategy (n = 104)
Symptom onset to randomisation	105 (63–158)	114 (67–172)

Symptom onset to Tenecteplase	113 (74–179)	130 (75–185)
Symptom onset to PCI	395 (294–3711), n = 58	425 (288–1331), n = 81†
Symptom onset to rescue PCI	299 (270–325), n = 14	277 (213–381), n = 29
Symptom onset to non-rescue PCI	1498 (341–5465), n = 44	926 (398–1454), n = 52
First medical contact* to Tenecteplase	51 (37–75)	54 (38–77)
First medical contact* to PCI	350 (245–3561)	324 (218–1216)

†Protocol-mandated procedure.

*First medical contact refers to ambulance arrival or hospital arrival.

Effect Size

Outcomes

At 30 days	**Tenecteplase only (n = 100)**	**Invasive strategy (n = 104)**
• Death	4 (4.0)	1 (1.0)
• Re-MI	9 (9.0)	6 (5.8)
• Heart failure	15 (15.0)	15 (14.4)
• Refractory ischaemia	0	3 (2.9)
In-hospital		
• Intracranial haemorrhage	0	0
• Non-haemorrhagic stroke	0	1 (1.0)
• Major systemic bleeding	1 (1.0)	2 (1.9)

Cardiac procedures	**In-hospital**		**At 30 days**	
	Tenecteplase only (n = 100)	**Invasive strategy (n = 104)**		**Tenecteplase only (n = 100)**
Cardiac catheterisation	Not reported	102 (within 24 hours)	Cardiac catheterisation	Not reported
Revascularisation	60	89*	Revascularisation	60
Rescue PCI	14, at a median of 197 minutes after randomisation (IQR 172–280 minutes).	38 (29 protocol-mandated; 6 ECG criteria)	Rescue PCI	14, at a median of 197 minutes after randomisation (IQR 172–280 minutes).

* Of these, 8 patients received CABG

- 48% of the 91 patients undergoing PCI within 24 hours of randomisation in the invasive strategy arm received abciximab; 81% of these patients had TIMI 3 and 12% had TIMI 2 flow at the end of the procedure
- Coronary stents were used in over 97% of all patients undergoing PCI

Transfer

There were no significant differences (in the primary end point) across the treatment groups in either setting (pre-hospital or in-hospital)

Table 104: TRANSFER-AMI[21]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Cantor WJ, et al. Routine early angioplasty after fibrinolysis for acute myocardial infarction. N Engl J Med. 2009; 360(26):2705-18.	Design: RCT (52 sites – Canada) Enrolment: July 2004 – Dec 2007. Terminated prematurely due to slowing enrolment, lack of additional funding, and loss to follow-up that was lower than anticipated Setting Enrolment was at centres that did not have the capability of performing PCI Randomisation: Performed by the	n = 1059 Drop-outs: At 30 days: 1 patient in the early-PCI group At 6 months: 9 in the early PCI group, 11 in the standard treatment group	High risk patients INCLUSION CRITERIA Patients with myocardial infarction with ST-segment elevation who presented within 12 hours of symptom onset and were treated with tenecteplase ST-segment elevation of 2 mm or more in 2 anterior leads or if they had ST-segment elevation of 1 mm or more in 2 inferior leads and at least 1 of the following high-risk characteristics: systolic blood pressure of less than 100 mm Hg, heart rate of > 100 bpm, Killip class II or III, ST-segment depression of 2 mm or more in the anterior leads, or ST-segment elevation of 1 mm or more in right-sided lead V4 (V4R), which is indicative of right ventricular involvement. EXCLUSION CRITERIA Cardiogenic shock before randomisation PCI within the previous month Previous coronary-artery bypass surgery Availability of PPCI with an anticipated	Routine early PCI (n = 537) Patients were transferred to a PCI centre for angiography and PCI 6 hours after fibrinolysis. PCI was performed when persistent occlusion or substantial stenosis of IRA (stenosis of ≥70% or stenosis of 50 to 70% with thrombus, ulceration, or spontaneous	Standard treatment (n = 522) 12-lead electrocardiography was repeated 60 to 90 minutes after randomisation; patients with persistent ST-segment elevation (a decrease in ST-segment elevation of less than 50%) and chest pain or with haemodynamic instability were transferred to	In-hospital, 30 days, 6 months	1° Combined incidence of death, reinfarction, recurrent ischaemia, new or worsening heart failure, or cardiogenic shock at 30 days. 2° Death or reinfarction at 6 months Bleeding complications	Canadian Institutes of Health Research, Roche Canada, and Abbott Vascular Canada

	coordinating centre or physician delegated by centre and was stratified by site and patient's age (> 75 versus ≤ 75 years) Allocation concealment: No details Blinding: Open label. All non-fatal components of the primary end point were adjudicated by assessors blinded to treatment allocation Sample size calculation: A sample size of 1200 patients (80% power to show a relative risk reduction of 30% with the early-PCI strategy, at an alpha level of 0.05) assuming an		door-to-balloon time of less than 60 minutes Demographics and baseline characteristics see below	dissection) was present. Stents were used whenever technically possible. Use of GPIs during PCI and for 12 hours (for abciximab) or 18 hours (for eptifibatide) after PCI was discretionary Note: All patients received tenecteplase, aspirin, and unfractionated heparin or enoxaparin in the emergency department. After April 2005 concomitant treatment with clopidogrel at the time of fibrinolysis (at an initial dose of either 300 mg for participants aged ≤75 years or 75 mg for	another hospital for rescue PCI. All other patients remained at their presenting hospital for at least 24 hours. Patients underwent cardiac catheterisation within 2 weeks after randomisation.		(see below for definitions)	

	event rate for the primary end point of 21% with the standard-treatment strategy and a 5% loss to follow-up. ITT analysis: Yes	participants aged >75 years) was recommended. Patients aged >75 years did not receive enoxaparin.

Demographics and baseline characteristics

	Standard treatment (n = 522)	Routine early PCI (n = 537)	p value
Age — yr			
• Median	56	57	0.45
• Interquartile range	50–66	51–66	
Age >75 yr — no. (%)	46 (8.8)	52 (9.7)	0.62
Female sex — no. (%)	105 (20.1)	111 (20.7)	0.82
Prior congestive heart failure — no. (%)	11 (2.1)	3 (0.6)	0.03
Prior myocardial infarction — no. (%)	51 (9.8)	59 (11.0)	0.52
Prior PCI — no. (%)	22 (4.2)	34 (6.3)	0.12
Prior stroke or transient ischaemic attack — no. (%)	5 (1.0)	16 (3.0)	0.02
History of smoking — no./total no. (%)	316/519 (60.9)	332/533 (62.3)	0.64
Hypertension — no. (%)	178 (34.1)	173 (32.2)	0.52
Dyslipidemia — no. (%)	149 (28.5)	147 (27.4)	0.67
Diabetes — no. (%)	80 (15.3)	79 (14.7)	0.78
Killip class — no./total no. (%)			0.39
• I	480/522 (92.0)	488/535 (91.2)	
• II	37/522 (7.1)	36/535 (6.7)	
• III	4/522 (0.8)	6/535 (1.1)	
• IV	1/522 (0.2)	5/535 (0.9)	
ST-segment elevation — no. (%)			

• Anterior	271 (51.9)	302 (56.2)	0.16
• Inferior¶	250 (47.9)	236 (43.9)	0.20
• With systolic BP <100 mm Hg	48 (9.2)	52 (9.7)	0.79
• With heart rate >100 bpm	29 (5.6)	28 (5.2)	0.81
• With Killip class II or III	17 (3.3)	13 (2.4)	0.41
• With ≥2-mm ST depression in the anterior leads	162 (31.0)	157 (29.2)	0.52
• With ≥1-mm ST elevation in lead V_4R	101 (19.3)	96 (17.9)	0.54
Time from symptom onset to administration of tenecteplase — min‖			
• Median	115	113	0.72
• Interquartile range	75–191	74–182	
Time from hospital presentation to administration of tenecteplase — min‡			
• Median	25	27	0.07
• Interquartile range	16–41	17–44	

¶ To qualify for participation in the trial, patients presenting with inferior ST-segment elevation were required to have at least 1 of the following high-risk characteristics: systolic blood pressure less than 100 mm Hg, heart rate more than 100 bpm, Killip class II or III, ST-segment depression of 2 mm or more in the anterior leads, or ST-segment elevation of 1 mm or more in lead V4R.

‖ Data were calculated on the basis of 522 patients in the standard-treatment group and 535 in the early-PCI group
‡ Data were calculated on the basis of 522 patients in the standard-treatment group and 536 in the early-PCI group.

Interventions used in the 2 study groups

	Standard treatment (n = 522)	**Routine early PCI (n = 537)**	**p value**
Drug therapy			
Before admission or within the first 6 hours – no. (%)			
• Aspirin	509 (97.5)	525 (97.8)	0.79
• Clopidogrel	359 (68.8)	475 (88.5)	<0.001

• With fibrinolysis – no. (%)			
• Unfractionated heparin	239 (45.8)	266 (49.5)	0.22
• Enoxaparin	282 (54.0)	269 (50.1)	0.20
• At discharge – no./total no. (%)†			
• Aspirin	468/506 (92.5)	487/513 (94.9)	0.11
• Clopidogrel	412/506 (81.4)	463/513 (90.3)	<0.001
• Beta-blocker	432/506 (85.4)	462/513 (90.1)	0.02
• ACE inhibitor or angiotensin-receptor blocker	409/506 (80.8)	425/513 (82.8)	0.40
• Statin	453/506 (89.5)	463/513 (90.3)	0.70
Cardiac catheterisation			
• Total – no. (%)	463 (88.7)	529 (98.5)	<0.001
• Time from randomisation to insertion of arterial sheath – hours‡			
• Median	32.5	2.8	<0.001
• Interquartile range	4.0–69.1	2.2–3.8	
• Single-vessel coronary artery disease – no./total no. (%)	216/463 (46.7)	227/529 (42.9)	0.24
• Baseline TIMI flow – no./total no. (%)			
• 0	83/405 (20.5)	88/511 (17.2)	
• 1	37/405 (9.1)	68/511 (13.3)	
• 2	56/405 (13.8)	89/511 (17.4)	
• 3	229/405 (56.5)	266/511 (52.1)	
PCI			
• Total – no. (%)	352 (67.4)	456 (84.9)	<0.001
• Time from randomisation to first balloon inflation – hours§			
• Median	21.9	3.2	<0.001
• Interquartile range	3.9–73.8	2.5–4.2	

• Time from tenecteplase administration to first balloon inflation – hours¶			
• Median	22.7	3.9	<0.001
• Interquartile range	4.5–74.3	3.1–4.9	
• Access – no./total no. (%)			
• Femoral	285/349 (81.7)	382/455 (84.0)	0.39
• Thrombectomy – no./total no. (%)	11/352 (3.1)	19/456 (4.2)	0.44
• Stent implanted – no./total no. (%)	349/352 (99.1)	445/456 (97.6)	0.09
• Glycoprotein IIb/IIIa inhibitor use – no. (%)	286/352 (81.2)	381/456 (83.6)	0.39
Coronary-artery bypass grafting – no. (%)	45 (8.6)	38 (7.1)	0.35

† The total number represents the number of patients who were discharged alive.

‡ Data were from 449 patients in the standard-treatment group and 528 in the early-PCI group.

§ Data were from 348 patients in the standard-treatment group and 455 in the early-PCI group.

¶ Data were from 348 patients in the standard-treatment group and 454 in the early-PCI group.

Definitions of end points

Reinfarction

- During the first 18 hours after enrolment, reinfarction was diagnosed on the basis of recurrent ST-segment elevation and recurrent chest pain lasting at least 30 minutes
- After 18 hours, the diagnosis of reinfarction required that there be an elevation in the MB fraction of creatine kinase to higher than the upper limit of the normal range (more than 3 times the upper limit of normal after PCI and more than 5 times the upper limit of normal after coronary-artery bypass surgery) or new Q waves

Recurrent ischaemia

- Chest pain lasting 5 minutes or longer associated with ST-segment or T-wave changes.

New or worsening heart failure

- Heart failure that required treatment 6 hours or more after enrolment and either pulmonary oedema on a chest radiograph, rales, or a pulmonary-capillary wedge pressure greater than 18 mm Hg

Bleeding complications

- Classified according to TIMI and GUSTO severity scales

Effect Size

Outcomes

	Standard treatment (n = 522)	Routine early PCI (n = 536)†	p value
Efficacy end points at 30 days – no. (%)			
• Death	18 (3.4)	24 (4.5)	0.39
• Reinfarction	30 (5.7)	18 (3.4)	0.06
• Recurrent ischaemia	11 (2.1)	1 (0.2)	0.003
• New or worsening congestive heart failure	29 (5.6)	16 (3.0)	0.04
Efficacy end points at 6 mo – no./total no. (%)			
• Death	23/511 (4.5)	30/528 (5.7)	0.39
• Reinfarction	33/511 (6.5)	21/528 (4.0)	0.07
Safety end points during index hospitalisation – no. (%)			
• Intracranial haemorrhage	6 (1.1)	3 (0.6)	0.34
• TIMI bleeding			
• Minor	17 (3.3)	26 (4.8)	0.19
• Major	47 (9.0)	40 (7.4)	0.36
• Major, non–CABG-related	25 (4.8)	18 (3.4)	0.24
• GUSTO bleeding			
• Mild	47 (9.0)	70 (13.0)	0.04
• Moderate	29 (5.6)	34 (6.3)	0.59
• Severe	8 (1.5)	6 (1.1)	0.55
• Severe, non–CABG-related	7 (1.3)	5 (0.9)	0.53
Final TIMI flow – no./total no. (%)			0.58
• 0	3/339 (0.9)	2/451 (0.4)	

• 1	3/339 (0.9)	4/451 (0.9)	
• 2	12/339 (3.5)	24/451 (5.3)	
• 3	321/339 (94.7)	421/451 (93.3)	

†In this group, the efficacy end points were calculated on the basis of 536 patients because 1 patient was lost to follow-up at 30 days. The safety end points were calculated on the basis of all 537 patients in the group.

Transfer

Complications requiring treatment developed during transfer in 3.0% of the patients in the standard treatment group who were transferred to a PCI facility and in 2.4% of the patients in the early-PCI group (all of whom were transferred to a PCI facility). The most common complication was hypotension. The only death that occurred during transfer was of a patient in the standard treatment group who was being transferred for rescue PCI

Table 105: NORDISTEMI[11,12]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Bøhmer E, et al. Efficacy and safety of immediate angioplasty versus ischaemia-guided managemen t after thrombolysi s in acute myocardial infarction in areas with very long transfer distances results of the	Design: RCT (5 sites – Norway) Enrolment: Feb 2005 – April 2008 Settings: Community hospitals in rural area with long transfer distances (100–400 km) to PCI and well established systems for pre-hospital fibrinolysis Randomisation: Permuted block	n = 266 Drop-outs: 0 for clinical outcomes 7 patients were unwilling to register the 15D questionna ire and were excluded from QoL analysis; 2 patients surviving	Low risk patients INCLUSION CRITERIA Age 18–75 yrs Symptoms of myocardial infarction present for <6 h ECG indicative of an acute STEMI: ≥2 mm ST-segment elevation in 2 contiguous precordial leads or ≥1 mm ST-segment elevation in 2 contiguous extremity leads or new left bundle branch block Expected time delay from first medical contact to PCI >90 min Receiving fibrinolytic treatment with tenecteplase	Early invasive group (n = 134) Patients were transferred to a PCI center as soon as possible after fibrinolysis, for immediate angiography and angioplasty of the IRA if indicated (≥50% diameter stenosis). Choice of stent type and use of GPIs were discretionary. As was referral for surgery in case of left main coronary artery disease or serious 3-	Conservative group (n = 132) Patients were admitted to (in case of pre-hospital fibrinolysis) or kept in community hospitals for continued care, with referral for urgent angiography if persistent chest pain and <50% reduction of ST-segment elevation 60 minutes after initiation of fibrinolysis (rescue indication) or haemodynamic	In-hospital, 30 days, 12 months	1° Composite of death, reinfarctio n, stroke, or new myocar-dial ischaemia at 12 months 2° Composite stroke, or n at 12 months	Scientifi c Board of the Eastern Norway Regional Health Authorit y, Hamar, Norway; Ada and Hagbart h Waage's Humanit ære og Veldedi ge Stiftelse, Oslo,

NORDISTEMI (Norwegian study on District treatment of ST-elevation myocardial infarction). J Am Coll Cardiol. 2010; 55(2):102-10. Bøhmer E, et al. Health and cost consequences of early versus late invasive strategy after thrombolysis for acute myocardial infarction. Eur J Cardiovasc Prev Rehabil. 2011; 18(5):717-23	randomisation stratified by site. The random allocation sequence was generated at Oslo University Hospital Allocation concealment: Sealed envelopes Blinding: Open-label. A blinded, independent committee adju-dicated all possible events related to the primary outcome. Sample size calculation: Total of 266 patients required (2-sided alpha of 5% and a power of 80%) based on a 30% and 15% occurrence of the primary end point in the conservative group and early invasive group respectively. ITT analysis: Yes	cerebral haemorrhage were unable to report QoL for the first 3 months. Here, missing data were replaced by age- and sex-adjusted data from an unpublished Finnish study of stroke patients	EXCLUSION CRITERIA Standard exclusion criteria for tenecteplase Cardiogenic shock or serious arrhythmias at randomisation Pregnancy Known serious renal failure (serum creatine > 250 mmol/l) Other diseases with life expectancy <12 months Psychiatric disease, mental retardation, dementia, drug abuse, alcoholism, or conditions that can severely reduce compliance Demographics and baseline characteristics see below	vessel disease. Note: All patients received standard weight-adjusted dose tenecteplase, aspirin 300 mg orally, and iv enoxaparin 30 mg followed by a sc dose of 1 mg/kg repeated every 12 hours up to hospital discharge or revascularisation for a maximum of 7 days. All patients also received clopidogrel 300 mg on the first day. Beta-blockers and statins were given unless contraindicated, ACE inhibitors when indicated. Patients receiving stents were recommended clopidogrel 75 mg daily for 9 months. Other patients were recommended clopidogrel until angiography or for 9 months	instability. Referral for early angiography was recommended if the patient had spontaneous recurrent ischaemia with or without ECG changes, or if signs of ischaemia (chest pain, significant ST-segment changes, hypotension, or ventricular tachycardia) occurred in the exercise ECG recommended before hospital discharge. Angiography was encouraged in all other patients as a routine assessment after successful fibrinolysis within 2 to 4 weeks after discharge.		health quality of life (HRQoL) Bleeding at 30 days Hospital stay (see below for definitions)	Norway; and the Innland et Hospital Trust, Hamar, Norway

Demographics and baseline characteristics			
	Early invasive group (n = 134)	**Conservative group (n = 132)**	**p value**
Age (yrs)	60 (55, 67)	61 (53, 68)	0.98
Men	107 (80%)	94 (71%)	0.13
Treated hypertension	33 (25%)	50 (38%)	0.03
Diabetes mellitus	8 (6%)	10 (8%)	0.78
Current or previous smoker	106 (79%)	104 (79%)	0.93
Family history of coronary heart disease	77 (58%)	78 (59%)	0.88
Previous angina	17 (13%)	17 (13%)	0.89
Previous myocardial infarction	15 (11%)	14 (11%)	0.97
Previous coronary bypass graft	4 (3%)	3 (2%)	1.0
Previous angioplasty	9 (7%)	12 (9%)	0.62
Infarct location on ECG			
• Anterior	59 (44%)	51 (39%)	0.44
• New left bundle branch block	4 (3%)	0 (0%)	0.12
• Nonanterior	71 (53%)	81 (61%)	0.21
Time intervals (minutes)			
• Symptom onset to first medical contact	67 (34, 122)	65 (40, 135)	0.68
• Symptom onset to tenecteplase	117 (80, 195)	126 (80, 195)	0.72
Pre-hospital tenecteplase	80 (60%)	71 (54%)	0.40

- At discharge, 98% of patients were prescribed aspirin, 92% clopidogrel, 90% beta-blockers, and 99% statins, with no difference between groups
- At 1 year, medication was unchanged except for clopidogrel, which was used in only 21% of patients (no difference between groups)

Invasive procedures			
	Early invasive group (n = 134)	**Conservative group (n = 132)**	**p value**
Coronary angiography performed	133 (99%)	125 (95%)	0.04
Time from tenecteplase to arrival at catheterisation laboratory	130 (105, 155) min	5.5 (0, 17.5) days	<0.001

PCI performed	119 (89%)	94 (71%)	0.001
Time from tenecteplase to first balloon	163 (137, 191) min	3.0 (0, 13) days	<0.001
Radial access	111 (83%)	118 (89%)	0.17
Stents implanted	115 (86%)	90 (68%)	0.001
Abciximab	16 (14%)	8 (6%)	0.14
Thrombectomy	0 (0%)	1 (0.8%)	0.5
Intra-aortic balloon pump	2 (1.5%)	2 (1.5%)	1.0
CABG performed	9 (7%)	16 (12%)	0.19
Repeat angiography during follow-up	23 (17%)	17 (13%)	0.42
Repeat PCI during follow-up	15 (11%)	9 (7%)	0.30
Data are n (%) or median (25th, 75th percentiles).			
• In the conservative group, 36 patients (27%) were transferred for rescue coronary intervention, and 32 patients underwent rescue PCI			
Angiographic characteristics of the early invasive group and the rescue population of the conservative group			
	Early invasive group (n = 134)	**Conservative/ rescue group (n = 36)**	**p value**
Time from tenecteplase to arrival at catheterisation laboratory (minutes)	130 (105, 155)	187 (149, 240)	<0.001
Immediate/rescue PCI performed	118 (88%)	32 (89%)	1.0
Time from tenecteplase to first balloon (minutes)	162 (137, 189)	20 (193, 247)	<0.001
Symptom onset to first balloon (minutes)	302 (236, 380)	340 (279, 400)	0.04
TIMI flow grade pre-PCI	n = 133	n = 36	
• 0	17 (13%)	9 (25%)	0.12
• 1	10 (8%)	2 (6%)	1.0
• 2	39 (29%)	8 (22%)	0.54
• 3	67 (50%)	17 (47%)	0.91
TIMI flow grade post-PCI	n = 118	n = 32	
• 0	2 (2%)	1 (3%)	0.52
• 1	2 (2%)	0 (0%)	1.0

• 2	11 (9%)	3 (9%)	1.0
• 3	103 (87%)	28 (88%)	1.0

Data are n (%) or median (25th, 75th percentiles).

Definitions of end points

Reinfarction

- In the first 18 hours was defined as recurrent symptoms of ischaemia at rest accompanied by new ST-segment elevation of ≥0.1 mV in at least 2 contiguous leads, lasting ≥30 min.
- After 18 h, the definition was: new Q waves in 2 or more leads, or new increase in concentrations of creatine kinase-MB or troponins above the upper limit of normal (>3X upper limit of normal after PCI and >5X upper limit of normal after coronary artery bypass graft), and >50% higher than the previous value.

Stroke

- A new focal, neurological deficit of vascular origin lasting more than 24 h.

New myocardial ischaemia

- Unstable angina (chest pain at rest suspicious for coronary disease with or without ECG changes), recurrent angina grade II to IV (Canadian Cardiovascular Society classification) or serious arrhythmias (ventricular tachycardia/ventricular fibrillation) that appeared more than 12 hours after randomisation.

HRQoL

Health-related quality of life (HRQoL) was assessed using the 15D instrument. This is a generic, multidimensional, standardised, self-administered evaluative tool with 15 dimensions and 5 levels for each dimension (no problems to severe problems). The 15D scores were translated into a single index score with values from zero (dead) to 1.0 (perfect health) using a simple algorithm.

Bleeding

Classified according to the GUSTO severity scale

Effect Size

Clinical outcomes

	Early invasive group (n = 134)	**Conservative group (n = 132)**
Hospital stay (index admission)	5 days (IQR 4–6)	5 days (IQR 4–7)
At 30 days		
• Death	3 (2.2%)	3 (2.3%)
• Reinfarction	2 (1.5%)	7 (5.3%)

• Stroke	3 (2.2%)	5 (3.8%)
• Recurrent ischaemia	8 (6.0%)	16 (12.1%)
• Severe bleeding, including intracranial haemorrhage (All severe bleedings were caused by intracranial haemorrhage)	2	3
• Moderate bleeding	0	3
• Minor bleeding	14	13
At 12 months		
• Death	3 (2.2%)	4 (3.0%)
• Reinfarction	4 (3.0%)	12 (9.1%)
• Stroke	3 (2.2%)	7 (5.3%)
• Recurrent ischaemia	20 (15.0%)	20 (15.2%)
Health-related quality of life (15D scores)		
	Early invasive group*	**Conservative group***
0 (baseline)†	0.913±0.092	0.902±0.089
At 1 month	0.873±0.156	0.856±0.167
At 3 months	0.882±0.162	0.873±0.163
At 7 months	0.889±0.160	0.872±0.182
At 12 months	0.889±0.164	0.866±0.186
Values are mean±SD		
†4 days before STEMI		
*7 patients were unwilling to register the 15D questionnaire and were excluded from the analysis. The study did not report which group these patients were originally allocated to.		
Transfer		
One patient (0.7%) died during transfer, and 4 (3%) were successfully defibrillated in the early invasive group. In the conservative group, 2 patients had ventricular tachycardia treated with intravenous drugs		

Table 106: AGATI et al[1]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Agati L, et al. Does coronary angioplasty after timely thrombolysis improve microvascular perfusion and left ventricular function after acute myocardial infarction? Am Heart J. 2007; 154(1):151-7.	Design: RCT (Multicentre – 3 sites in Italy) Enrolment: Dec 2004 – Nov 2005 Randomisation: No details Allocation concealment: No details Blinding: Open label. No details on whether outcome assessors were blinded Sample size calculation: No details ITT analysis: Yes	N = 96 in 3 arms. For fibrinolysis alone versus fibrinolysis within 24 hours followed by PCI, N = 60 Drop-outs: None stated	No details on whether high or low risk patients INCLUSION CRITERIA Patients with STEMI who presented within 3 hours of symptom onset EXCLUSION CRITERIA Patients who underwent revascularisation procedure as a result of failed fibrinolysis, early reinfarction, or ischaemia after the initial treatment (lysis or PCI) Patients aged ≥80 years History of previous MI, cardiomyopathy or CABG surgery Contraindications to glycoprotein IIb/IIIa receptor antagonists, PPCI, or lysis Patients in cardiogenic shock Demographics and baseline characteristics see below	Fibrinolysis alone (n = 30) Enoxaparin was repeated every 12 hours up to 7 days after lysis and 100 mg aspirin once a day was given indefinitely Note: All patients received a full dose of tenecteplase, aspirin and sc enoxaparin (1 mg/kg) at randomisation. All patients were maintained on ACE inhibitors and beta-blockers throughout hospital stay and at discharge.	Fibrinolysis followed within 24 hours by PCI (n = 30) Patients received abciximab immediately before the interventional procedure (0.25 mg/kg body weight) followed by a 12-hour infusion (0.125 microgram/kgminutes) and loading dose of clopidogrel 300 mg. After the procedure, 75 mg clopidogrel was prescribed for 6 months and 100 mg aspirin once a day indefinitely. Patients received IRA stenting using a standard procedure	In-hospital	Major bleeding Minor bleeding	No details

Demographics and baseline characteristics		
	Fibrinolysis plus PCI (n = 30)	Fibrinolysis alone (n = 30)

Mean age (y)	59±7	57±7
Male	25 (83)	26 (86)
Hypertension	26 (86)	24 (80)
Current smoker	17 (56)	19 (63)
Diabetes	6 (20)	5 (16)
Time to fibrinolysis (minutes)	118 (72–170)	129 (74–167)
PCI time after fibrinolysis	20±2 hours	–
Killip class >1	11 (36)	11 (36)
Multivessel disease	11 (36)	10 (33)
Anterior MI	24 (80)	22 (73)
TIMI 3 flow before PCI	20 (66)	–
TIMI 3 flow after PCI	26 (86)	–
Data presented are mean value ±SD or number (%)		
Effect Size		
	Fibrinolysis plus PCI (n = 30)	Fibrinolysis alone (n = 30)
Major bleeding	0	0
Minor bleeding (at access site)	4	0

Appendix H: Economic evidence tables

H.1 Time to reperfusion

Table 107: BRAVO VERGEL 2007[15]

Bravo Vergel Y, Palmer S, Asseburg C, Fenwick E, de Belder M, Abrams K et al. Is primary angioplasty cost effective in the UK? Results of a comprehensive decision analysis. Heart 93(10): 1238-1243, 2007.

Study details	Population & interventions	Costs	Health outcomes	Cost effectiveness
Economic analysis: CUA (health outcome = QALYs) **Study design:** Probabilistic decision analytic model. **Approach to analysis:** Short-term decision tree that captures differential outcomes up to 6 months (IHD death, new non-fatal MI; non-fatal stroke or no further event [alive with IHD]). Followed by Markov model to extrapolate to lifetime costs and QALYs. Markov model with 1 year cycles and 8 states (no further event [IHD] year 1, no further event [IHD]	**Population:** Acute STEMI patients **Cohort settings:** Start age = 61 Male = NR **Intervention 1:** Fibrinolysis **Intervention 2:** PPCI with PPCI-related time delay of 54 minutes (Average delay from trials) ~~Sensitivity analyses by time delay:~~ • 30 minutes • 60 minutes • 90 minutes	**Total costs (mean per patient):** ~~Average (PPCI-related time delay 54 minutes)~~ Intervention 1: £10,080 Intervention 2: £12,760 Incremental (2−1): £2680 (CI NR; p = NR) **Sensitivity analyses by PPCI-related time delay:** ~~30 minutes~~ Intervention 1: £10,080 Intervention 2: £12,820 Incremental (2−1): £2740 (CI NR; p = NR) ~~60 minutes~~ Intervention 1: £10,080 Intervention 2: £12,750 Incremental (2−1): £2670 (CI NR; p = NR) ~~90 minutes~~ Intervention 1: £10,080	**QALYs (mean per patient):** ~~Average (PPCI-related time delay 54 minutes)~~ Intervention 1: 6.83 Intervention 2: 7.12 Incremental (2−1): 0.29 (CI NR; p = NR) **Sensitivity analyses by PPCI-related time delay:** ~~30 minutes~~ Intervention 1: 6.83 Intervention 2: 7.23 Incremental (2−1): 0.40 (CI NR; p = NR) ~~60 minutes~~ Intervention 1: 6.83 Intervention 2: 7.09 Incremental (2−1): 0.26 (CI NR; p = NR) ~~90 minutes~~ Intervention 1: 6.83 Intervention 2: 6.87	**ICER (Intervention 2 versus Intervention 1):** ~~Average (PPCI-related time delay 54 minutes)~~ £9241 per QALY gained (pa) CI: NR Probability cost effective (£20K/30K threshold): 90%/95% **Sensitivity analyses by PPCI-related time delay:** ~~30 minutes~~ £6850 per QALY gained (pa) CI: NR Probability cost effective (£20K/30K threshold): 98%/99% ~~60 minutes~~ £10,269 per QALY gained (pa) CI: NR Probability cost effective (£20K/30K threshold): 83%/91% ~~90 minutes~~ £64,750 per QALY gained (pa) CI: NR Probability cost effective (£20K/30K threshold): 36%/45%

year 2+, new non-fatal MI, post-MI, new non-fatal stroke, post-stroke, IHD death, other death. The possibility of needing further revascularisation was also modelled in short-term model. **Perspective:** UK NHS and PSS **Time horizon:** lifetime **Treatment effect duration:** 6 months **Discounting:** Costs = 3.5%; Outcomes = 3.5%		Intervention 2: £12,670 Incremental (2−1): £2590 (CI NR; p = NR) **Currency & cost year:** 2003/4 UK pounds **Cost components incorporated:** Short-term model: initial interventions (drug acquisition costs, procedure costs and associated hospital length of stay), further revascularisations, repeat MIs and stroke. Long-term model: management of non-fatal MI and stroke year1 and year 2+.	Incremental (2−1): 0.04 (CI NR; p = NR)	**Analysis of uncertainty:** Probabilistic analysis results and time delay SA results are reported in main table. In a threshold analysis the time-delay up to which PPCI remained cost effective (at a £20K CE threshold) was 79 minutes (84.5 minutes at a £30K threshold). With a reduced length of stay with PPCI compared to fibrinolysis (assumed the same in base case) ICERs were reduced to £5448, £4087, £6038 and £37,250 respectively. The probability PPCI cost effective also increased. Only using fibrin-specific trials to estimate effectiveness reduced the cost effectiveness of PPCI. ICERs were £9833, £7284 and £11,500 for average, 30-minute and 60-minute delays. And PPCI was dominated by fibrinolysis with a 90-minute delay. With both a reduced length of stay with PPCI and only using t-Pa trials ICERS were £5788, £4324 and £6739 for average, 30-minute and 60-minute delays. And PPCI was dominated by fibrinolysis with a 90-minute delay.
Data sources				
Health outcomes: Initial 6-month decision tree: Baseline risks with fibrinolysis and relative risk with PPCI for clinical outcomes (non-fatal MI, non-fatal stroke, death) at 6 months were based on a systematic review and Bayesian meta-regression of 22 RCTs with the impact of PPCI-related time delay analysed using the mean additional time delay compared to fibrinolytic administration as a covariate in a random effects model – parallel clinical paper included in clinical review (Asseburg et al. 2007[5]). Post-6-month Markov model: Non-IHD death by 10 year age bands: Office of National Statistics data (does not appear to take account of gender split). Probabilities of transitioning between other health states based on Nottingham Heart Attack Registry (NHAR) data analysis. **Quality-of-life weights:** published EQ-5D estimates for health states, tariff not stated, who completed questionnaire not stated. **Resource use and cost sources:** Initial intervention: Assumed all PPCI patients required angiogram, GPIs and stent and all fibrinolysis patients did not require angiogram and received alteplase (most expensive agent). Initial length of hospital stay: assumed equal in base case based on average from Hospital Episode Statistics; in SA 5.76 days for PPCI and 12.12 days for fibrinolysis based on personal communication of estimates from a sample of 80 patients from a London hospital. Further revascularisation rates: based on analysis of same studies as health outcomes. Long-term costs associated with Markov model health states: MI resource use was based on analysis of NHAR hospitalisation data combined with national estimates of length of stay and published data to take account outpatient/day case care of costs outside the hospital setting. Stroke resource use was based on probability of being disabled, severity and discharge location from published literature. IHD death based on probability of dying in hospital from published literature. Unit costs: UK national sources (BNF, NHS reference costs) or published sources, inflated where appropriate.				
Comments				
Source of funding: Study funded by unrestricted educational grant to University of York from Cordis Ltd (manufacturer of medical devices used in PCI). Some authors				

also declared having received previous research funding or consultancy fees from various manufacturers of medical devices such as stents. **Limitations:** More recent estimates of initial resource use that better reflect current healthcare system are used in Wailoo 2010 update to analysis. Some uncertainly about measurement and valuation methods of health-related quality of life due to unclear reporting but considered minor limitation (EQ-5D used). Relative effectiveness of PPCI compared with fibrinolysis and the impact of time from study-level meta-regression based on systematic review of literature (Asseburg 2007[5]). This found no mortality benefit at 90 minutes with PPCI; however, an IPD analysis (Boersma 2006[10]) found benefit for 1-month mortality in patents 79–120 minutes and so there is uncertainty that relative treatment effects are from best available source. Three new RCTs that meet inclusion criteria have been published since Asseburg but considered likely to have small impact on effect estimates as low patient numbers relative to meta-analysis total. Ambulance costs not incorporated – may be higher with PPCI due to more transfers or longer journeys, although other PPCI cost assumptions generally conservative. **Other:** None.
Overall applicability*: minor limitations **Overall quality**:** partially applicable

Abbreviations: CI = confidence interval; CUA = cost–utility analysis; EQ-5D = EuroQol 5 dimension utility instrument, scale 0.0 (death) to 1.0 (full health), negative scores indicate a state worse than death; ICER = incremental cost-effectiveness ratio; IHD = ischaemic heart disease; MI = myocardial infarction; NR = not reported; pa = probabilistic analysis; QALYs = quality-adjusted life years

** Directly applicable / Partially applicable / Not applicable; ** Minor limitations /Potentially serious Limitations / Very serious limitations*

Table 108: WAILOO 2010,[119] GOODACRE 2008[50]

Wailoo A, Goodacre S, Sampson F, Alava MH, Asseburg C, Palmer S et al. Primary angioplasty versus thrombolysis for acute ST-elevation myocardial infarction: An economic analysis of the National Infarct Angioplasty project. Heart 96(9): 668-672, 2010.

Goodacre S, Sampson F, Carter A, Wailoo A, O'Cathain A, Wood S et al. Evaluation of the National Infarct Angioplasty Project. Report for the National Co-ordinating Centre for NHS Service Delivery and Organisation R&D (NCCSDO). National Coordinating Centre for the Service Delivery and Organisation (NCCSDO), 2008.

Study details	Population & interventions	Costs†	Health outcomes†	Cost effectiveness†
Economic analysis: CUA (health outcome = QALYs) **Study design:** Probabilistic decision analytic model incorporating cost analysis of UK observational data. **Approach to analysis:** Development of Bravo Vergel model: 1) updated with 'real-life' NIAP cost data; 2)	**Population:** Acute STEMI patients **Cohort settings:** Start age = 64.3 years Male = NR **Intervention 1:** Fibrinolysis-based service • Fibrinolysis: 72.6% (median CTN 67 min) • PPCI: 15.8%; with PPCI-related time delay 52 minutes (median CTB 119 minutes)	**Total costs (mean per patient):** Average (time delay 64 minutes) Intervention 1: £10,700 Intervention 2: £11,600 Incremental (2–1): £829 (CI £130, £1440; p = NR) **Sensitivity analyses by time delay:** Transferred patients (delay 100 minutes) Intervention 1: £10,700 Intervention 2: £11,400 Incremental (2–1): £664 (CI –£324, £1390; p = NR) Non-transferred patients (delay	**QALYs (mean per patient):** Average (time delay 64 minutes) Intervention 1: 6.40 Intervention 2: 6.58 Incremental (2–1): 0.183 (CI –0.0764, 0.415; p = NR) **Sensitivity analyses by time delay:** Transferred patients (delay 100 minutes) Intervention 1: 6.40 Intervention 2: 6.32 Incremental (2–1): –0.0848	**Primary ICER (Intervention 2 versus Intervention 1):** Average (time delay 64 minutes) £4520 per QALY gained (pa) CI: NR Probability cost effective (£20K/30K threshold): 90%/95% **Sensitivity analyses by time delay:** Transferred patients (delay 100 minutes) Intervention 1 dominates CI: NR Probability cost effective (£20K/30K threshold): 38%/NR Non-transferred patients (delay 53 minutes)

updated with 'real-life' treatment NIAP delay estimates; 3) took system level perspective where some patients receive fibrinolysis in PPCI service, and vice versa; 4) adjusted baseline mortality rates with fibrinolysis to reflect the effectiveness of fibrinolysis as a function of the observed patient presentation delay in these patients. **Perspective:** UK NHS and PSS **Time horizon:** lifetime **Treatment effect duration:**6 months **Discounting:** Costs = 3.5%; Outcomes =3.5%	Note that untreated patients were excluded from model. **Intervention 2:** PPCI-based service • Fibrinolysis: 4.3% (median CTB 67 minutes) • PPCI: 67.1%; with PPCI-related time delay 64 minutes (median CTB 131 minutes) (Average delay from NIAP) Sensitivity analyses by time delay: • Transferred patients: delay 100 minutes (median CTB 167 minutes) • Non-transferred patients: delay 53 minutes (median CTB 120) • Direct to cath lab: delay 56 minutes (median CTB 123 minutes) • Not direct to cath lab: delay 73 minutes (median CTB 140 minutes)	53 minutes) Intervention 1: £10,700 Intervention 2: £11,600 Incremental (2−1): ~£900 (CI NR; p = NR) Direct to cath lab (delay 56 minutes) Intervention 1: £10,700 Intervention 2: £11,600 Incremental (2−1): ~£900 (CI NR; p = NR) Not direct to cath lab (delay 73 minutes) Intervention 1: £10,700 Intervention 2: £11,500 Incremental (2−1):~£800 (CI NR; p = NR) **Currency & cost year:** 2006/7 UK pounds **Cost components incorporated:** Short-term model: initial interventions (drug acquisition costs, procedure costs and associated hospital length of stay), further revascularisations, repeat MIs and stroke. Long-term model: management of non-fatal MI and stroke year 1 and year 2+. Real-world initial costs did not account for potential additional ambulance time for PPCI centres operating a 'bypass' system.	(CI −0.831, 0.343; p = NR) Non-transferred patients (delay 53 minutes) Intervention 1: 6.40 Intervention 2: 6.64 Incremental (2−1):0.24 (CI NR; p = NR) Direct to cath lab (delay 56 minutes) Intervention 1: 6.40 Intervention 2: 6.63 Incremental (2−1): 0.23 (CI 0.135, 0.597; p = NR) Arrive via emergency department or CCU (delay 73 minutes) Intervention 1: 6.40 Intervention 2: 6.53 Incremental (2−1): 0.13 (CI NR; p = NR)	£3635 per QALY gained (pa) CI:NR Probability cost effective (£20K/30K threshold): 95%/NR Direct to cath lab (delay 56 minutes) £3817 per QALY gained (pa) CI: NR Probability cost effective (£20K/30K threshold): 95%/NR Arrive via emergency department or CCU (delay 73 minutes) £6112 per QALY gained (pa) CI: NR Probability cost effective (£20K/30K threshold): 75%/NR **Analysis of uncertainty:** Probabilistic analysis results and time delay SA results are above. Replacing the post-acute revascularisation rates from the evidence synthesis in the York model with those observed in NIAP increased the ICER to £7070 due to reduced benefit of PPCI in terms of repeat PCI. Probability cost effective (£20K threshold) was 85%.

Data sources
Health outcomes: The distribution of patient presentation delays was used to estimate baseline mortality for fibrinolysis-treated patients. Baseline event rates were modified by presentation time (call to arrival in hospital) and treatment times (arrival in hospital to reperfusion treatment) based on analysis of 10 NIAP sites implementing PPCI (n = 2083) and 5 other sites routinely providing fibrinolysis (n = 919). Relative effectiveness was not updated from Bravo-Vergel model (see evidence table). **Quality-of-life weights:** Not updated from Bravo Vergel model –published EQ-5D estimates for health states, tariff not stated, who completed questionnaire not stated. **Resource use and cost sources:** Initial intervention: Costs calculated using patient-level NIAP resource use and length of stay data for control site fibrinolysis (£3509), NIAP site fibrinolysis (£4361) and NIAP site PPCI (£5176). Control site PPCI had insufficient information and was assumed to be the same as in NIAP sites. Resource use was based on analysis of 10 NIAP sites implementing PPCI (n = 2083) and 5 other sites routinely providing fibrinolysis (n = 919) supplemented by data from questionnaire (n = 50) where necessary. Further revascularisation rates: not updated from Bravo Vergel model in base case – based on analysis of same studies as health outcomes. Long-term costs associated with Markov model health states: not updated from Bravo Vergel model – MI resource use was based on analysis of NHAR hospitalisation data combined with national estimates of length of stay and published data to take account outpatient/day case care of costs outside the hospital setting. Stroke resource use was based on probability of being disabled, severity and discharge location from published literature. IHD death based on probability of dying in hospital from published literature. Unit costs: UK national sources (BNF, NHS reference costs, PSSRU) and NIAP site costs. **Other:** None.
Comments
Source of funding: National Co-ordinating Centre for NHS Service Delivery and Organisation R&D. **Limitations:** Some uncertainly about measurement and valuation methods of health-related quality of life due to unclear reporting but considered minor limitation (EQ-5D used). Relative effectiveness of PPCI compared with fibrinolysis and the impact of time from study-level meta-regression based on systematic review of literature (Asseburg 2007[5]). This found no mortality benefit at 90 minutes with PPCI; however, an IPD analysis (Boersma 2006[10]) found benefit for 1-month mortality in patients at 79–120 minutes and so there is uncertainty that relative treatment effects are from the best available source. Three new RCTs that meet inclusion criteria have been published since Asseburg but considered likely to have small impact on effect estimates as low patient numbers relative to meta-analysis total. Ambulance costs to first hospital not incorporated – may be higher with PPCI due to longer journeys. **Other:** 'Real-world' data collection (NIAP) took place 2005–06. Data analyses were adjusted for case-mix.
Overall applicability*: minor limitations **Overall quality**:** directly applicable

Abbreviations: CI = confidence interval; CUA = cost–utility analysis; EQ-5D = EuroQol 5 dimension utility instrument, scale 0.0 (death) to 1.0 (full health), negative scores indicate a state worse than death; ICER = incremental cost-effectiveness ratio; IHD = ischaemic heart disease; MI = myocardial infarction; NR = not reported; pa = probabilistic analysis; QALYs = quality-adjusted life years

†Total costs were reported in paper rounded to nearest hundred whereas incremental costs were reported to nearest whole pound therefore resulting in some discrepancies between total and incremental costs reported here; where incremental cost was not reported an approximate incremental cost is calculated from the rounded total costs. Total QALYs were reported in paper rounded to 2 decimal places and incremental QALYs rounded to 3 significant figures resulting in some discrepancies between total and incremental QALYs reported here; where incremental QALYs were not reported they were calculated from the totals and so are reported to 2 decimal places here. Cost effectiveness ratios are as reported in the paper.

** Directly applicable / Partially applicable / Not applicable; ** Minor limitations /Potentially serious Limitations / Very serious limitations*

H.2 Facilitated PPCI

None.

H.3 Radial versus femoral arterial access for PPCI

None.

H.4 Thrombus extraction during PPCI

None.

H.5 Culprit versus complete revascularisation **Updated, see the 2020 evidence review**

Table 109: HELP-AMI[33]

Di Mario C, Mara S, Flavio A, Imad S, Antonio M, Anna P et al. Single vs multivessel treatment during primary angioplasty: results of the multicentre randomised HEpacoat for cuLPrit or multivessel stenting for Acute Myocardial Infarction (HELP AMI) Study. International Journal of Cardiovascular Interventions 6(3-4): 128-133, 2004.				
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: CCA (various health outcomes) **Study design:** Within-trial analysis (RCT: HELP-AMI study - same paper) **Approach to analysis:** Analysis of individual-level data for health outcomes. Initial procedure costs: exact costing methodology unclear, probably individual-level costs, unit cost source unclear. Downstream costs: trial event rates with standard unit costs used. **Perspective:** Italy health service† **Time horizon:** 12 months	**Population:** Patients admitted to hospital with ischaemic chest pain or STEMI with arteriography showing lesions in multiple coronary arteries **Patient characteristics:** n = 69 Mean age = 63.9 Male = 87.3 (see Tables 1–3 in chapter 9 for further details) **Intervention 1:** PCI using heparin-coated stents to recanalise all suitable lesions. n = 52	**Total costs (mean per patient):** Intervention 1: £14,771 Intervention 2: £16,183 Incremental (2−1): £1,412 (CI = NR; p = 0.323) **Cost breakdown:** Initial procedure costs: Intervention 1: £9,659 Intervention 2: £9,141 Incremental (2−1): −£518 (CI = NR; p = 0.263) Downstream costs: Intervention 1: £5,112 Intervention 2: £7,042 Incremental (2−1): £1,930	**12 month outcomes:** From clinical review - same paper (2 versus 1) • Mortality: RR 0.98 (CI: 0.04, 23.03); ARD 19 fewer per 1000 • Reinfarction: RR 3.06 (CI: 0.20, 46.30); ARD 40 more per 1000 • Repeat revascularisation: RR 2.04 (CI: 0.85, 4.90); ARD 180 more per 1000	Not applicable **Analysis of uncertainty:** No sensitivity analysis performed

Treatment effect duration: 12 months **Discounting:** Costs = n/a; Outcomes = n/a	Diabetes = 11.5% **Intervention 2:** PPCI using heparin-coated stents to recanalise culprit lesion only n = 17 Diabetes = 41.2%	(CI = NR; p = 0.185) **Currency & cost year:** 2004†† Euros (presented here as 2004 UK pounds‡) **Cost components incorporated:** Initial procedure: all materials, stay in hospital including intensive care and cardiology wards. Downstream costs: additional revascularisation procedures (PCI or CABG)		
Data sources				
Health outcomes: Within trial analysis. **Quality-of-life weights:** N/a. **Cost sources:** Time in hospital and materials used for initial procedures from within RCT patient-level analysis, source of unit costs not reported. Downstream event numbers for later revascularisation procedures from within RCT, costs based on Disease Related Group price (primary/complex angioplasty) for Lombardy region of Italy.				
Comments				
Source of funding: NR; 1 author was from Cordis Italia who manufacture the heparin-coated stents used in the trial. **Limitations:** Intervention used heparin-coated stents which are not routinely used in current practice. Contradictory definitions of study population - not certain whether all patients had STEMI. Study arms had unbalanced proportions of patients with diabetes. Some uncertainty about the applicability of unit costs and resource use from Italy pre-2004 (exact year not stated). Quality of life difference was not measured; QALYs not used. One-year time horizon may not fully capture differences in costs and health outcomes. Quality of life difference was not measured. Within-trial analysis, therefore by definition does not reflect all evidence available (see clinical review for comparison with other studies). Unclear if all relevant costs are included, and some unit cost sources are unclear. The costs of the initial procedures do not appear to account for the additional stents used in multivessel procedures – this would make the multivessel strategy appear cheaper and therefore more likely to be cost effective than it would otherwise have been. No sensitivity analysis undertaken. Funding not reported but 1 author worked for Cordis. **Other:** None.				
Overall applicability*: Partially applicable **Overall quality**:** Very serious limitations				

Abbreviations: ARD = absolute risk difference; CABG = coronary artery bypass graft; CCA = Cost-consequence analysis; CI = confidence interval; ICER = incremental cost-effectiveness ratio; MI = myocardial infarction; n/a = not applicable; NR = not reported; PCI = percutaneous coronary intervention; RCT = randomised controlled trial; RR = relative risk

†Perspective not reported, but assumed to be Italy as 1 Italian cost is cited. Health service assumed as only direct medical costs included.

††Cost year not reported, assumed to be the same as publication year.

‡ Converted using 2004 purchasing power parities [89]

** Directly applicable / Partially applicable / Not applicable; ** Minor limitations /Potentially serious limitations / Very serious limitations*

H.6 Cardiogenic shock

None.

H.7 People who remain unconscious after a cardiac arrest

None.

H.8 Hospital volumes of PPCI

None.

H.9 Pre-hospital versus in-hospital fibrinolysis

None.

H.10 Use of antithrombin as an adjunct to fibrinolysis

None.

H.11 Rescue PCI

None.

H.12 Routine early angiography following fibrinolysis

Table 110: NORDISTEMI 2011[12]

Bohmer E, Kristiansen IS, Arnesen H, and Halvorsen S. Health and cost consequences of early versus late invasive strategy after thrombolysis for acute myocardial infarction. European Journal of Cardiovascular Prevention Rehabilitation 18(5): 717-723, 2011.				
Study details	**Population & interventions**	**Costs§**	**Health outcomes**	**Cost effectiveness§**
Economic analysis: CUA (health outcome = QALYs) **Study design:** within-trial analysis (RCT – NORDISTEMI) with probabilistic analysis **Approach to analysis:** QALYs were calculated based on patient-level utility data recorded over 12 months (see clinical review) and adjusted for baseline utility. Missing data was imputed. Bootstrapping was used to test for differences. **Perspective:** Norway healthcare system† **Time horizon:** 1 year **Treatment effect duration:** 1 year **Discounting:** Costs =	*See clinical review for more details* – NORDISTEMI[12] **Population:** ST-elevation MI < 6 hour duration and > 90 minutes expected delay to PPCI, received full dose tenecteplase (57% pre-hospital) **Patient characteristics:** • n = 259 (n = 266 in main study; 7 people who were unwilling to register the 15D were excluded from the cost-effectiveness analysis) • Mean age (total population) = 61 (SD: 10) • Male (total population) = 76% **Intervention 1:** Deferred/selective angiography – admission to community hospital, with referral for urgent angiography (27%) if rescue indication or haemodynamic	**Total costs (mean per patient):** Intervention 1: £8888 Intervention 2: £9768 Incremental (2−1): £868 (CI −£777, £2545; p = NR) Total cost difference breakdown (2−1): • In-hospital care: £272 (CI −£1142, £1725) • Out-patient care: £65 (CI −£379, £473) • Transportation: £575 (CI £381, £769) • Pharmaceuticals: −£27 (CI −£69, £14) **Total costs excluding those assumed to be unrelated (mean per patient) (used in base case ICER calculation):** Intervention 1: £8756 Intervention 2: £9257 Incremental (2−1): £501 (CI NR; p = NR) Total cost difference breakdown (2−1): • As above except in-hospital care: −£182 (CI NR; p = NR) Hospitalisations assumed to be unrelated were mostly orthopaedic, cancer-related and hernia surgery). **Currency & cost year:** 2008 Norwegian Kroner	**Key outcome measure:** QALYs – unadjusted / adjusted (mean per patient) Intervention 1: 0.885 / NR Intervention 2: 0.870 / NR Incremental (2−1): 0.016 (CI −0.023, 0.055; p = NR) / NR 0.008 (CI −0.027, 0.043; p = NR) / NR Adjusted QALYs used to calculate cost effectiveness.	**ICER – total costs excluding unrelated (Intervention 2 versus Intervention 1):** £62,648 per QALY gained (pa) CI: NR at a threshold of £41,061 intervention 2 was cost effective in 49% of bootstrap iterations.§§ **Subgroup analyses:** none **Analysis of uncertainty:** When unrelated hospitalisation costs were included the ICER rose to £108,463. When intra-cardiac defibrillator costs were excluded as well as unrelated hospitalisation costs the ICER reduced to £20,077.

n/a; Outcomes = n/a	instability; early angiography was recommended if recurrent ischaemia occurred spontaneously or in a pre-discharge exercise test. Otherwise angiography was recommended within 2 weeks of discharge. (86% had angiography with 30 days) **Intervention 2:** Routine early angiography – immediate transfer for angiography with PCI if indicated.	(presented here as 2008 UK pounds‡) **Cost components incorporated:** In-hospital care (length of stay of index hospitalisation including the number of hours in the coronary care unit and days in the cardiology ward, number of subsequent hospital admissions, investigations or interventions including coronary angiography, PCI, CABG and implantation of intra-cardiac defibrillator), out-patient care (including GP visits, emergency department, clinic visits, home visits, household task assistance, hotel and rehabilitation) transportation (including ground ambulance, escorting nurse, helicopter ambulance, taxi, train, bus, private car) and pharmaceuticals. Sick leave was costed but is not presented in the results reported here.		
Data sources				
Health outcomes: within-RCT analysis. **Quality-of-life weights:** within-RCT analysis (measured at baseline (4 days before ST-elevation MI) and at 1, 3, 7 and 12 months) – 15D instrument, Finnish visual analogue scale valuation set. Study reports an imbalance in 15D at baseline (mean difference 0.011) and therefore adjusts for baseline score in QALY calculations. **Cost sources:** resource use collected prospectively in RCT from hospital databases, records and patients' self-reporting; for the index hospitalisation and later visits at the invasive centre direct costing using hospital accounts was used, while diagnosis-related group costs were used for other hospital admissions. Healthcare resources were costed using national fees, municipality and institutional accounts; transportation was costed according to type and distance.				
Comments				
Source of funding: Eastern Norway Regional Health Authority, A and H Waage's Veldedige stiftelse, Oslo Norway and Innlandet Hospital Trust, Brumunddal, Norway. **Limitations:** Some uncertainty about the applicability of Norway resource use and unit costs. Utility instrument used in QALY estimation does not meet NICE reference case (15D instrument with Finnish VAS-based valuation set). One-year time horizon may not fully capture differences in costs and health outcomes. Within-trial analysis therefore by definition does not reflect all evidence available (see clinical review tables for comparison with other studies) – judged to be one of the more relevant clinical trials, although patients were considered to be fairly low risk. Limited sensitivity analysis. **Other:** None.				
Overall applicability*: partially applicable **Overall quality**:** potentially serious limitations				

Abbreviations: CI = confidence interval; CUA = cost–utility analysis; ICER = incremental cost-effectiveness ratio; n/a = not applicable; NR = not reported; pa = probabilistic analysis;
† Study used societal perspective but results are presented disaggregated and so results have been recalculated to only include healthcare system costs in line with NICE reference case
‡ Converted from Euros to Norwegian Kroner using exchange rate reported in paper of €1.00 = NOK8.22 and from NOK to UK pounds using 2008 Purchasing Power Parities[89]
§ Results have been recalculated to exclude sick leave costs in line with the NICE reference case
§§ It was not possible to recalculate the probability cost effective, and so this result includes sick leave costs. Since sick leave costs were higher for early than deferred strategy, if this had been excluded it is likely that the probability of the early strategy being cost effective would have been higher.
** Directly applicable / Partially applicable / Not applicable; ** Minor limitations /Potentially serious Limitations / Very serious limitations*

National Clinical Guideline Centre

Myocardial infarction with ST-segment elevation

The acute management of myocardial infarction with ST-segment elevation

Clinical guideline 167

Appendices I - P

July 2013

November 2020: NICE's original guidance on Myocardial infarction with ST-segment elevation was published in 2013. See the NICE website for the guideline recommendations and for the 2020 Acute coronary syndromes update. This document preserves evidence reviews and committee discussions from the 2013 guideline.

Commissioned by the National Institute for Health and Care Excellence

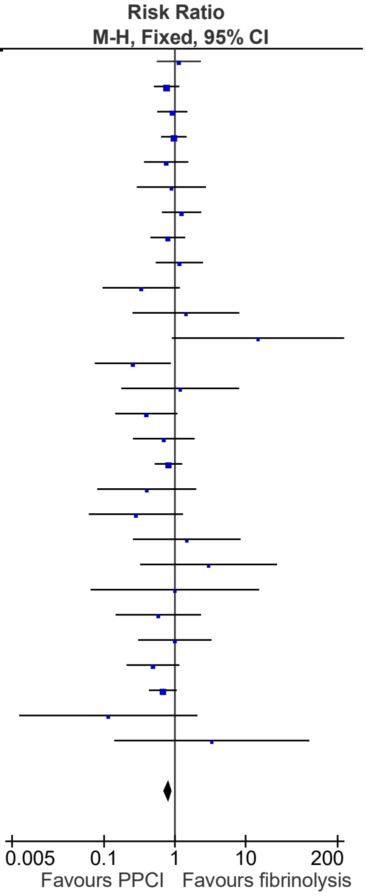
Appendix I: Forest plots

I.1 Time to reperfusion

Figure 2: PPCI versus fibrinolysis for the outcome of short-term all-cause mortality

Study or Subgroup	PPCI Events	PPCI Total	Fibrinolysis Events	Fibrinolysis Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Andersen invasive 2003	15	223	13	220	3.5%	1.14 [0.55, 2.34]
Anderson referral 2003	37	567	48	562	12.9%	0.76 [0.51, 1.15]
Armstrong 2006	23	100	25	100	6.7%	0.92 [0.56, 1.51]
Armstrong 2013	42	946	43	939	11.5%	0.97 [0.64, 1.47]
Aversano 2002	12	225	16	226	4.3%	0.75 [0.36, 1.56]
Berrocal 2003	5	54	6	58	1.5%	0.90 [0.29, 2.76]
Bonnefoy 2002	20	421	16	419	4.3%	1.24 [0.65, 2.37]
Bueno 2011	18	132	23	134	6.1%	0.79 [0.45, 1.40]
de Boer 1994	13	152	11	149	3.0%	1.16 [0.54, 2.50]
de Boer 2002	3	46	8	41	2.3%	0.33 [0.09, 1.18]
DeWood 1992	3	46	2	44	0.5%	1.43 [0.25, 8.18]
Gao 2010	15	210	0	101	0.2%	14.99 [0.91, 247.97]
Garcia 1999	3	109	12	111	3.2%	0.25 [0.07, 0.88]
Gibbons 1993	2	47	2	56	0.5%	1.19 [0.17, 8.14]
Grines 1993	5	195	13	200	3.4%	0.39 [0.14, 1.09]
Grines 2002	6	71	8	66	2.2%	0.70 [0.26, 1.90]
GUSTO IIb 1997	32	565	40	573	10.6%	0.81 [0.52, 1.27]
Kastrati 2002	2	81	5	81	1.3%	0.40 [0.08, 2.00]
Kedev 1997	2	68	7	67	1.9%	0.28 [0.06, 1.31]
Le May 2001	3	62	2	61	0.5%	1.48 [0.26, 8.53]
Ribeiro 1993	3	50	1	50	0.3%	3.00 [0.32, 27.87]
Ribichini 1998	1	55	1	55	0.3%	1.00 [0.06, 15.59]
Schomig 2000	3	71	5	69	1.4%	0.58 [0.14, 2.35]
Vermeer 1999	5	75	5	75	1.3%	1.00 [0.30, 3.31]
Widimsky 2000	7	101	14	99	3.8%	0.49 [0.21, 1.16]
Widimsky 2003	29	429	42	421	11.3%	0.68 [0.43, 1.07]
Zijlstra 1993	0	70	4	72	1.2%	0.11 [0.01, 2.08]
Zijlstra 1997	1	45	0	50	0.1%	3.33 [0.14, 79.64]
Total (95% CI)		**5216**		**5099**	**100.0%**	**0.82 [0.71, 0.94]**
Total events	310		372			

Heterogeneity: Chi² = 25.63, df = 27 (P = 0.54); I² = 0%
Test for overall effect: Z = 2.75 (P = 0.006)



I.2 Facilitated PPCI

I.2.1 GPIs: fPPCI versus PPCI – all GPIs

Figure 3: All-cause mortality (in-hospital)

Study or Subgroup	fPPCI (GPIs) Events	fPPCI (GPIs) Total	PPCI (placebo / no drug) Events	PPCI (placebo / no drug) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Zorman 2002	0	56	5	51	100.0%	0.08 [0.00, 1.46]
Total (95% CI)		**56**		**51**	**100.0%**	**0.08 [0.00, 1.46]**
Total events	0		5			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.70 (P = 0.09)

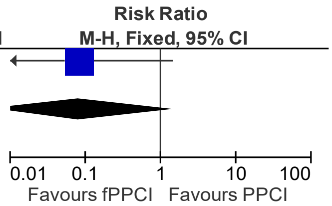


Figure 4: All-cause mortality (short-term)

Study or Subgroup	fPPCI (GPIs) Events	fPPCI (GPIs) Total	PPCI (placebo / no drug) Events	PPCI (placebo / no drug) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ASSIST 2009	7	201	4	199	12.2%	1.73 [0.52, 5.83]
BRAVE-3 2009	13	401	10	399	30.4%	1.29 [0.57, 2.92]
ON-TIME2 2008	11	473	19	477	57.4%	0.58 [0.28, 1.21]
Total (95% CI)		**1075**		**1075**	**100.0%**	**0.94 [0.58, 1.52]**
Total events	31		33			

Heterogeneity: Chi² = 3.20, df = 2 (P = 0.20); I² = 37%
Test for overall effect: Z = 0.25 (P = 0.80)

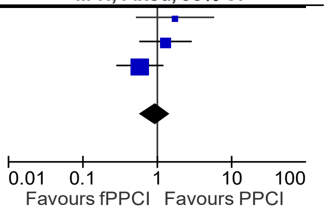


Figure 5: All-cause mortality (longer-term)

Study or Subgroup	fPPCI (GPIs) Events	fPPCI (GPIs) Total	PPCI (placebo / no drug) Events	PPCI (placebo / no drug) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ASSIST 2009	9	201	6	199	11.0%	1.49 [0.54, 4.09]
BRAVE-3 2010	27	401	16	399	29.3%	1.68 [0.92, 3.07]
ON-TIME2 2010	16	467	25	470	45.4%	0.64 [0.35, 1.19]
Zorman 2002	0	56	7	51	14.3%	0.06 [0.00, 1.04]
Total (95% CI)		**1125**		**1119**	**100.0%**	**0.96 [0.66, 1.38]**
Total events	52		54			

Heterogeneity: Chi² = 9.29, df = 3 (P = 0.03); I² = 68%
Test for overall effect: Z = 0.24 (P = 0.81)

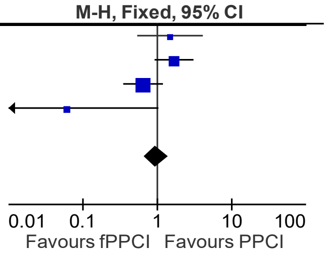


Figure 6: All-cause stroke (short-term)

Study or Subgroup	fPPCI (GPIs) Events	fPPCI (GPIs) Total	PPCI (placebo / no drug) Events	PPCI (placebo / no drug) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ASSIST 2009	0	201	1	199	8.6%	0.33 [0.01, 8.05]
BRAVE-3 2009	1	401	1	399	5.7%	1.00 [0.06, 15.85]
FINESSE 2008	9	814	8	795	46.1%	1.10 [0.43, 2.83]
ON-TIME2 2008	1	473	7	477	39.7%	0.14 [0.02, 1.17]
Total (95% CI)		**1889**		**1870**	**100.0%**	**0.65 [0.31, 1.36]**
Total events	11		17			

Heterogeneity: Chi² = 3.44, df = 3 (P = 0.33); I² = 13%
Test for overall effect: Z = 1.14 (P = 0.25)

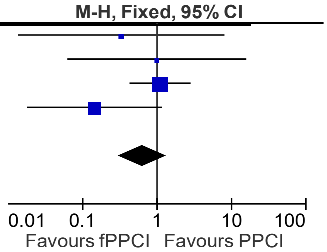


Figure 7: All-cause stroke (longer-term)

Study or Subgroup	fPPCI (GPIs) Events	fPPCI (GPIs) Total	PPCI (placebo / no drug) Events	PPCI (placebo / no drug) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ASSIST 2009	0	201	4	199	81.9%	0.11 [0.01, 2.03]
BRAVE-3 2010	3	401	1	399	18.1%	2.99 [0.31, 28.58]
Total (95% CI)		**602**		**598**	**100.0%**	**0.63 [0.17, 2.40]**
Total events	3		5			

Heterogeneity: Chi² = 3.20, df = 1 (P = 0.07); I² = 69%
Test for overall effect: Z = 0.67 (P = 0.50)

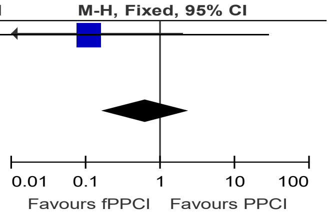


Figure 8: Fatal stroke (short-term)

Study or Subgroup	fPPCI (GPIs) Events	fPPCI (GPIs) Total	PPCI (placebo / no drug) Events	PPCI (placebo / no drug) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
FINESSE 2008	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Total (95% CI)		**814**		**795**	**100.0%**	**6.84 [0.35, 132.14]**
Total events	3		0			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.27 (P = 0.20)

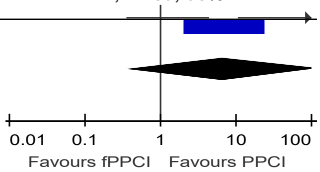


Figure 9: Reinfarction or non-fatal reinfarction or recurrent MI (short-term)

Study or Subgroup	fPPCI (GPIs) Events	fPPCI (GPIs) Total	PPCI (placebo / no drug) Events	PPCI (placebo / no drug) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ASSIST 2009	3	201	1	199	3.0%	2.97 [0.31, 28.31]
BRAVE-3 2009	3	401	4	399	11.8%	0.75 [0.17, 3.31]
FINESSE 2008	16	818	15	806	44.4%	1.05 [0.52, 2.11]
ON-TIME2 2008	13	473	14	477	40.9%	0.94 [0.44, 1.97]
Total (95% CI)		**1893**		**1881**	**100.0%**	**1.02 [0.64, 1.64]**
Total events	35		34			

Heterogeneity: Chi² = 1.09, df = 3 (P = 0.78); I² = 0%
Test for overall effect: Z = 0.10 (P = 0.92)

Risk Ratio
M-H, Fixed, 95% CI

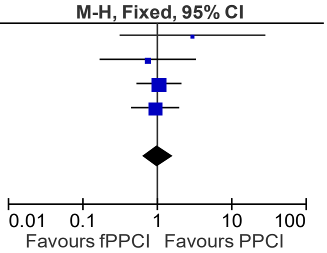


Figure 10: Reinfarction or non-fatal reinfarction or recurrent MI (longer-term)

Study or Subgroup	fPPCI (GPIs) Events	fPPCI (GPIs) Total	PPCI (placebo / no drug) Events	PPCI (placebo / no drug) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ASSIST 2009	4	201	2	199	15.4%	1.98 [0.37, 10.69]
BRAVE-3 2010	12	401	11	399	84.6%	1.09 [0.48, 2.43]
Total (95% CI)		**602**		**598**	**100.0%**	**1.22 [0.59, 2.52]**
Total events	16		13			

Heterogeneity: Chi² = 0.40, df = 1 (P = 0.53); I² = 0%
Test for overall effect: Z = 0.55 (P = 0.58)

Risk Ratio
M-H, Fixed, 95% CI

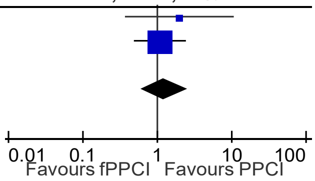


Figure 11: Major bleeding (in-hospital)

Study or Subgroup	fPPCI (GPIs) Events	fPPCI (GPIs) Total	PPCI (placebo / no drug) Events	PPCI (placebo / no drug) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Zorman 2002	16	56	6	51	100.0%	2.43 [1.03, 5.73]
Total (95% CI)		**56**		**51**	**100.0%**	**2.43 [1.03, 5.73]**
Total events	16		6			

Heterogeneity: Not applicable
Test for overall effect: Z = 2.03 (P = 0.04)

Risk Ratio
M-H, Fixed, 95% CI

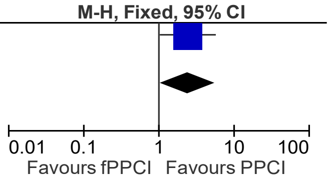


Figure 12: Major bleeding (short-term)

Study or Subgroup	fPPCI (GPIs) Events	fPPCI (GPIs) Total	PPCI (placebo / no drug) Events	PPCI (placebo / no drug) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
BRAVE-3 2009	7	401	7	399	16.6%	1.00 [0.35, 2.81]
FINESSE 2008	39	814	21	795	50.3%	1.81 [1.08, 3.06]
ON-TIME2 2008	19	473	14	477	33.0%	1.37 [0.69, 2.70]
Total (95% CI)		1688		1671	100.0%	1.53 [1.04, 2.24]
Total events	65		42			

Heterogeneity: Chi² = 1.17, df = 2 (P = 0.56); I² = 0%
Test for overall effect: Z = 2.18 (P = 0.03)

Risk Ratio
M-H, Fixed, 95% CI

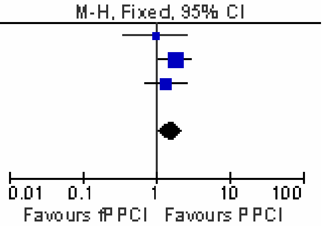


Figure 13: Heart failure (in-hospital)

Study or Subgroup	fPPCI (GPIs) Events	fPPCI (GPIs) Total	PPCI (placebo / no drug) Events	PPCI (placebo / no drug) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Zorman 2002	4	56	15	51	100.0%	0.24 [0.09, 0.68]
Total (95% CI)		**56**		**51**	**100.0%**	**0.24 [0.09, 0.68]**
Total events	4		15			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.68 (P = 0.007)						

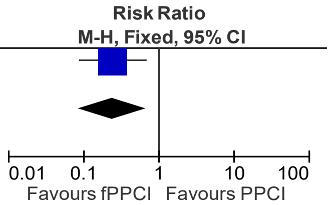


Figure 14: Heart failure (short-term)

Study or Subgroup	Eptifibatide fPPCI Events	Eptifibatide fPPCI Total	PPCI Events	PPCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ASSIST 2009	15	201	22	199	100.0%	0.68 [0.36, 1.26]
Total (95% CI)		**201**		**199**	**100.0%**	**0.68 [0.36, 1.26]**
Total events	15		22			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.23 (P = 0.22)						

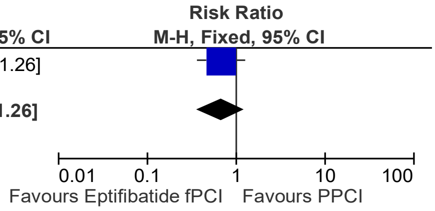


Figure 15: Heart failure (longer-term)

Study or Subgroup	Eptifibatide fPPCI Events	Eptifibatide fPPCI Total	PPCI Events	PPCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ASSIST 2009	15	201	24	199	100.0%	0.62 [0.33, 1.14]
Total (95% CI)		**201**		**199**	**100.0%**	**0.62 [0.33, 1.14]**
Total events	15		24			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.53 (P = 0.13)						

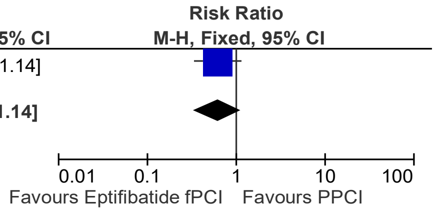


Figure 16: Repeat revascularisation – repeat or urgent (short-term)

Study or Subgroup	Eptifibatide fPPCI Events	Eptifibatide fPPCI Total	PPCI Events	PPCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ASSIST 2009	8	201	4	199	100.0%	1.98 [0.61, 6.47]
Total (95% CI)		**201**		**199**	**100.0%**	**1.98 [0.61, 6.47]**
Total events	8		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.13 (P = 0.26)						

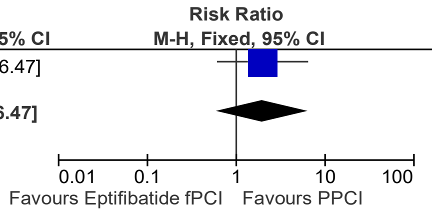
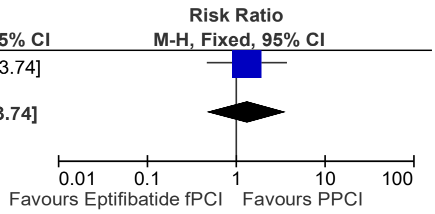


Figure 17: Repeat revascularisation – repeat or urgent (longer-term)

Study or Subgroup	Eptifibatide fPPCI Events	Eptifibatide fPPCI Total	PPCI Events	PPCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ASSIST 2009	8	201	6	199	100.0%	1.32 [0.47, 3.74]
Total (95% CI)		**201**		**199**	**100.0%**	**1.32 [0.47, 3.74]**
Total events	8		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.52 (P = 0.60)						



I.2.2 GPIs: fPPCI versus PPCI – all GPIs: subgroup analysis of trials using background of clopidogrel + aspirin or aspirin

Figure 18: All-cause mortality (in-hospital)

Study or Subgroup	fPPCI (GPIs) Events	fPPCI (GPIs) Total	PPCI (placebo / no drug) Events	PPCI (placebo / no drug) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.1.1 Aspirin (background Tx)						
Zorman 2002	0	56	5	51	100.0%	0.08 [0.00, 1.46]
Subtotal (95% CI)		56		51	100.0%	0.08 [0.00, 1.46]
Total events	0		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.70 (P = 0.09)						
Total (95% CI)		56		51	100.0%	0.08 [0.00, 1.46]
Total events	0		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.70 (P = 0.09)						
Test for subgroup differences: Not applicable						

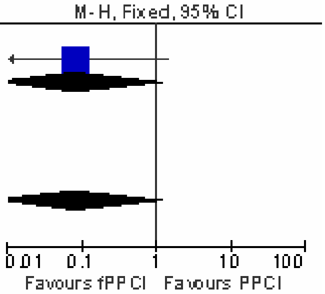


Figure 19: All-cause mortality (short-term)

Study or Subgroup	fPPCI (GPIs) Events	fPPCI (GPIs) Total	PPCI (placebo / no drug) Events	PPCI (placebo / no drug) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.2.1 Clopidogrel + aspirin (background Tx)						
ASSIST 2009	7	201	4	199	12.2%	1.73 [0.52, 5.83]
BRAVE-3 2009	13	401	10	399	30.4%	1.29 [0.57, 2.92]
ON-TIME2 2008	11	473	19	477	57.4%	0.58 [0.28, 1.21]
Subtotal (95% CI)		**1075**		**1075**	**100.0%**	**0.94 [0.58, 1.52]**
Total events	31		33			
Heterogeneity: Chi² = 3.20, df = 2 (P = 0.20); I² = 37%						
Test for overall effect: Z = 0.25 (P = 0.80)						
7.2.2 Aspirin (background Tx)						
Subtotal (95% CI)		**0**		**0**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**1075**		**1075**	**100.0%**	**0.94 [0.58, 1.52]**
Total events	31		33			
Heterogeneity: Chi² = 3.20, df = 2 (P = 0.20); I² = 37%						
Test for overall effect: Z = 0.25 (P = 0.80)						
Test for subgroup differences: Not applicable						

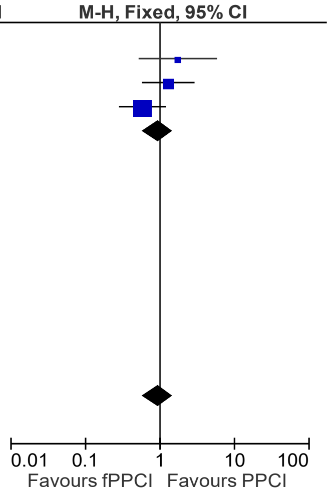


Figure 20: All-cause mortality (longer-term)

Study or Subgroup	fPPCI (GPIs) Events	fPPCI (GPIs) Total	PPCI (placebo / no drug) Events	PPCI (placebo / no drug) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.3.1 Clopidogrel + aspirin (background Tx)						
ASSIST 2009	9	201	6	199	11.0%	1.49 [0.54, 4.09]
BRAVE-3 2010	27	401	16	399	29.3%	1.68 [0.92, 3.07]
ON-TIME2 2010	16	467	25	470	45.4%	0.64 [0.35, 1.19]
Subtotal (95% CI)		**1069**		**1068**	**85.7%**	**1.11 [0.75, 1.63]**
Total events	52		47			
Heterogeneity: Chi² = 5.14, df = 2 (P = 0.08); I² = 61%						
Test for overall effect: Z = 0.51 (P = 0.61)						
7.3.2 Aspirin (background Tx)						
Zorman 2002	0	56	7	51	14.3%	0.06 [0.00, 1.04]
Subtotal (95% CI)		**56**		**51**	**14.3%**	**0.06 [0.00, 1.04]**
Total events	0		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.93 (P = 0.05)						
Total (95% CI)		**1125**		**1119**	**100.0%**	**0.96 [0.66, 1.38]**
Total events	52		54			
Heterogeneity: Chi² = 9.29, df = 3 (P = 0.03); I² = 68%						
Test for overall effect: Z = 0.24 (P = 0.81)						
Test for subgroup differences: Chi² = 3.94, df = 1 (P = 0.05), I² = 74.6%						

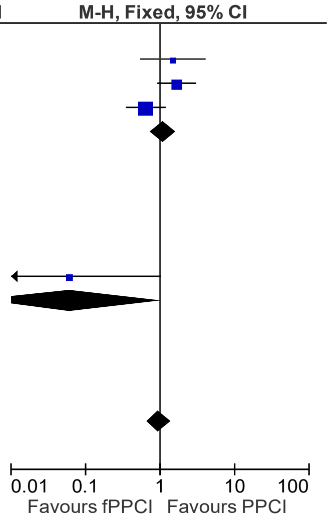


Figure 21: All-cause stroke (short-term)

Study or Subgroup	fPPCI (GPIs) Events	fPPCI (GPIs) Total	PPCI (placebo / no drug) Events	PPCI (placebo / no drug) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.4.1 Clopidogrel + aspirin (background Tx)						
ASSIST 2009	0	201	1	199	8.6%	0.33 [0.01, 8.05]
BRAVE-3 2009	1	401	1	399	5.7%	1.00 [0.06, 15.85]
ON-TIME2 2008	1	473	7	477	39.7%	0.14 [0.02, 1.17]
Subtotal (95% CI)		**1075**		**1075**	**53.9%**	**0.26 [0.07, 1.06]**
Total events	2		9			
Heterogeneity: Chi² = 1.22, df = 2 (P = 0.54); I² = 0%						
Test for overall effect: Z = 1.88 (P = 0.06)						
7.4.2 Aspirin (background Tx)						
FINESSE 2008	9	814	8	795	46.1%	1.10 [0.43, 2.83]
Subtotal (95% CI)		**814**		**795**	**46.1%**	**1.10 [0.43, 2.83]**
Total events	9		8			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.19 (P = 0.85)						
Total (95% CI)		**1889**		**1870**	**100.0%**	**0.65 [0.31, 1.36]**
Total events	11		17			
Heterogeneity: Chi² = 3.44, df = 3 (P = 0.33); I² = 13%						
Test for overall effect: Z = 1.14 (P = 0.25)						
Test for subgroup differences: Chi² = 2.76, df = 1 (P = 0.10), I² = 63.8%						

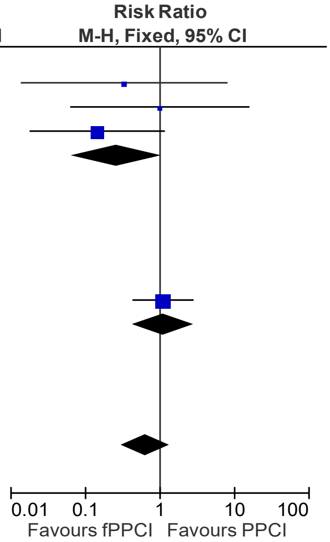


Figure 22: All-cause stroke (longer-term)

Study or Subgroup	fPPCI (GPIs) Events	fPPCI (GPIs) Total	PPCI (placebo / no drug) Events	PPCI (placebo / no drug) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
11.4.1 Clopidogrel + aspirin (background Tx)						
ASSIST 2009	0	201	4	199	81.9%	0.11 [0.01, 2.03]
BRAVE-3 2010	3	401	1	399	18.1%	2.99 [0.31, 28.58]
Subtotal (95% CI)		**602**		**598**	**100.0%**	**0.63 [0.17, 2.40]**
Total events	3		5			
Heterogeneity: Chi² = 3.20, df = 1 (P = 0.07); I² = 69%						
Test for overall effect: Z = 0.67 (P = 0.50)						
11.4.2 Aspirin (background Tx)						
Subtotal (95% CI)		**0**		**0**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**602**		**598**	**100.0%**	**0.63 [0.17, 2.40]**
Total events	3		5			
Heterogeneity: Chi² = 3.20, df = 1 (P = 0.07); I² = 69%						
Test for overall effect: Z = 0.67 (P = 0.50)						
Test for subgroup differences: Not applicable						

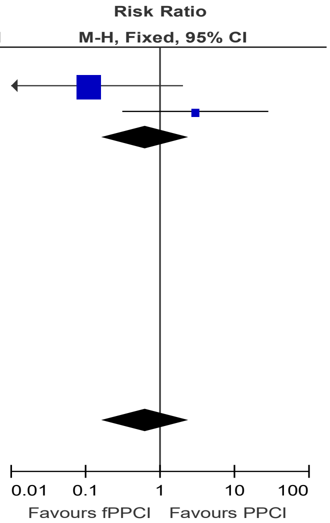


Figure 23: Reinfarction or non-fatal reinfarction or recurrent MI (short-term)

Study or Subgroup	fPPCI (GPIs) Events	fPPCI (GPIs) Total	PPCI (placebo / no drug) Events	PPCI (placebo / no drug) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.7.1 Clopidogrel + aspirin (background Tx)						
ASSIST 2009	3	201	1	199	3.0%	2.97 [0.31, 28.31]
BRAVE-3 2009	3	401	4	399	11.8%	0.75 [0.17, 3.31]
ON-TIME2 2008	13	473	14	477	40.9%	0.94 [0.44, 1.97]
Subtotal (95% CI)		**1075**		**1075**	**55.6%**	**1.00 [0.54, 1.88]**
Total events	19		19			
Heterogeneity: Chi² = 1.07, df = 2 (P = 0.58); I² = 0%						
Test for overall effect: Z = 0.01 (P = 0.99)						
7.7.2 Aspirin (background Tx)						
FINESSE 2008	16	818	15	806	44.4%	1.05 [0.52, 2.11]
Subtotal (95% CI)		**818**		**806**	**44.4%**	**1.05 [0.52, 2.11]**
Total events	16		15			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.14 (P = 0.89)						
Total (95% CI)		**1893**		**1881**	**100.0%**	**1.02 [0.64, 1.64]**
Total events	35		34			
Heterogeneity: Chi² = 1.09, df = 3 (P = 0.78); I² = 0%						
Test for overall effect: Z = 0.10 (P = 0.92)						
Test for subgroup differences: Chi² = 0.01, df = 1 (P = 0.92), I² = 0%						

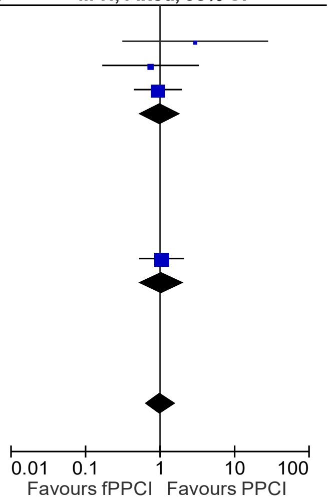


Figure 24: Reinfarction or non-fatal reinfarction or recurrent MI (longer-term)

Study or Subgroup	fPPCI (GPIs) Events	fPPCI (GPIs) Total	PPCI (placebo / no drug) Events	PPCI (placebo / no drug) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.8.1 Clopidogrel + aspirin (background Tx)						
ASSIST 2009	4	201	2	199	15.4%	1.98 [0.37, 10.69]
BRAVE-3 2010	12	401	11	399	84.6%	1.09 [0.48, 2.43]
Subtotal (95% CI)		**602**		**598**	**100.0%**	**1.22 [0.59, 2.52]**
Total events	16		13			
Heterogeneity: Chi² = 0.40, df = 1 (P = 0.53); I² = 0%						
Test for overall effect: Z = 0.55 (P = 0.58)						
7.8.2 Aspirin (background Tx)						
Subtotal (95% CI)		**0**		**0**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**602**		**598**	**100.0%**	**1.22 [0.59, 2.52]**
Total events	16		13			
Heterogeneity: Chi² = 0.40, df = 1 (P = 0.53); I² = 0%						
Test for overall effect: Z = 0.55 (P = 0.58)						
Test for subgroup differences: Not applicable						

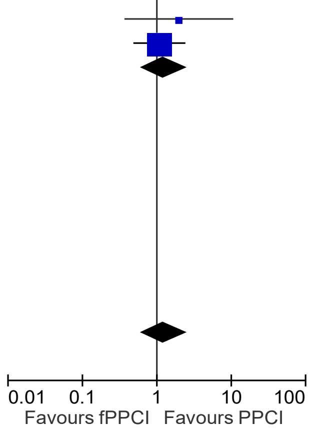


Figure 25: Major bleeding (in-hospital)

Study or Subgroup	fPPCI (GPIs) Events	fPPCI (GPIs) Total	PPCI (placebo / no drug) Events	PPCI (placebo / no drug) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.9.1 Aspirin + clopidogrel						
Subtotal (95% CI)		**0**		**0**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
7.9.2 Aspirin						
Zorman 2002	16	56	6	51	100.0%	2.43 [1.03, 5.73]
Subtotal (95% CI)		**56**		**51**	**100.0%**	**2.43 [1.03, 5.73]**
Total events	16		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.03 (P = 0.04)						
Total (95% CI)		**56**		**51**	**100.0%**	**2.43 [1.03, 5.73]**
Total events	16		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.03 (P = 0.04)						
Test for subgroup differences: Not applicable						

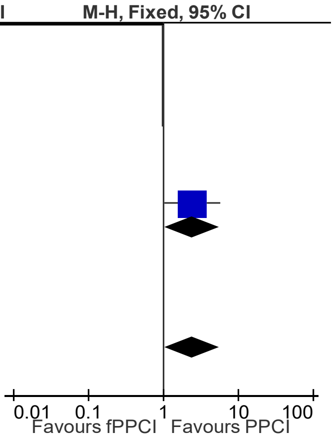


Figure 26: Major bleeding (short-term)

Study or Subgroup	fPPCI (GPIs) Events	fPPCI (GPIs) Total	PPCI (placebo / no drug) Events	PPCI (placebo / no drug) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.9.1 Clopidogrel + aspirin (background Tx)						
BRAVE-3 2009	7	401	7	399	16.6%	1.00 [0.35, 2.81]
ON-TIME2 2008	19	473	14	477	33.0%	1.37 [0.69, 2.70]
Subtotal (95% CI)		874		876	49.7%	1.24 [0.71, 2.19]
Total events	26		21			
Heterogeneity: Chi² = 0.25, df = 1 (P = 0.61); I² = 0%						
Test for overall effect: Z = 0.75 (P = 0.45)						
7.9.2 Aspirin (background Tx)						
FINESSE 2008	39	814	21	795	50.3%	1.81 [1.08, 3.06]
Subtotal (95% CI)		814		795	50.3%	1.81 [1.08, 3.06]
Total events	39		21			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.24 (P = 0.03)						
Total (95% CI)		1688		1671	100.0%	1.53 [1.04, 2.24]
Total events	65		42			
Heterogeneity: Chi² = 1.17, df = 2 (P = 0.56); I² = 0%						
Test for overall effect: Z = 2.18 (P = 0.03)						
Test for subgroup differences: Chi² = 0.92, df = 1 (P = 0.34), I² = 0%						

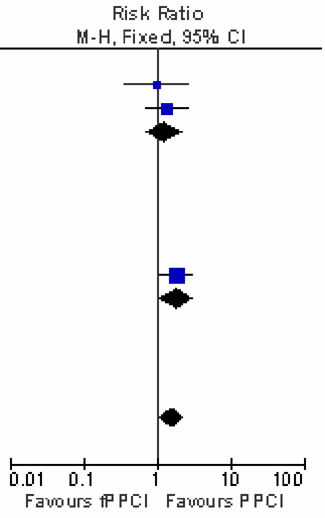
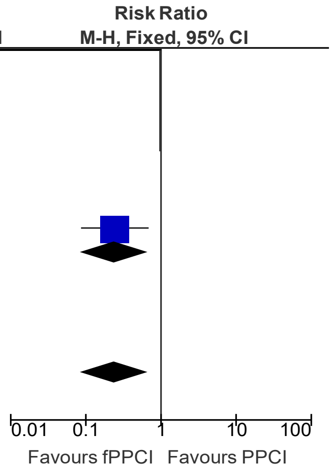


Figure 27: Heart failure (in-hospital)

Study or Subgroup	fPPCI (GPIs) Events	fPPCI (GPIs) Total	PPCI (placebo / no drug) Events	PPCI (placebo / no drug) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.12.1 Aspirin + clopidogrel						
Subtotal (95% CI)		**0**		**0**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
7.12.2 Aspirin						
Zorman 2002	4	56	15	51	100.0%	0.24 [0.09, 0.68]
Subtotal (95% CI)		**56**		**51**	**100.0%**	**0.24 [0.09, 0.68]**
Total events	4		15			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.68 (P = 0.007)						
Total (95% CI)		**56**		**51**	**100.0%**	**0.24 [0.09, 0.68]**
Total events	4		15			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.68 (P = 0.007)						
Test for subgroup differences: Not applicable						



I.2.3 GPIs: fPPCI versus PPCI – abciximab

Figure 28: All-cause mortality (in-hospital)

Study or Subgroup	fPPCI (GPIs) Events	fPPCI (GPIs) Total	PPCI (placebo / no drug) Events	PPCI (placebo / no drug) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Zorman 2002	0	56	5	51	100.0%	0.08 [0.00, 1.46]
Total (95% CI)		**56**		**51**	**100.0%**	**0.08 [0.00, 1.46]**
Total events	0		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.70 (P = 0.09)						

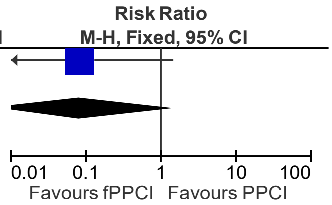


Figure 29: All-cause mortality (short-term)

Study or Subgroup	Abciximab fPPCI Events	Abciximab fPPCI Total	PPCI (placebo) Events	PPCI (placebo) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
BRAVE-3 2009	13	401	10	399	100.0%	1.29 [0.57, 2.92]
Total (95% CI)		**401**		**399**	**100.0%**	**1.29 [0.57, 2.92]**
Total events	13		10			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.62 (P = 0.53)						

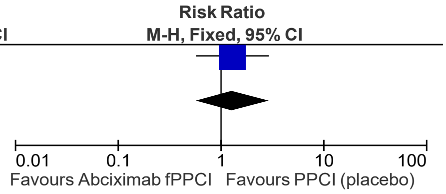


Figure 30: All-cause mortality (longer-term)

Study or Subgroup	Abciximab fPPCI Events	Abciximab fPPCI Total	PPCI (placebo) Events	PPCI (placebo) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
BRAVE-3 2010	27	401	16	399	67.2%	1.68 [0.92, 3.07]
Zorman 2002	0	56	7	51	32.8%	0.06 [0.00, 1.04]
Total (95% CI)		**457**		**450**	**100.0%**	**1.15 [0.67, 1.96]**
Total events	27		23			
Heterogeneity: Chi² = 5.65, df = 1 (P = 0.02); I² = 82%						
Test for overall effect: Z = 0.50 (P = 0.61)						

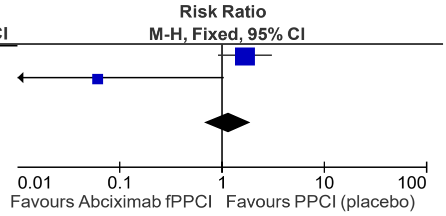


Figure 31: All-cause stroke (short-term)

Study or Subgroup	Abciximab fPPCI Events	Abciximab fPPCI Total	PPCI (placebo) Events	PPCI (placebo) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
BRAVE-3 2009	1	401	1	399	11.0%	1.00 [0.06, 15.85]
FINESSE 2008	9	814	8	795	89.0%	1.10 [0.43, 2.83]
Total (95% CI)		**1215**		**1194**	**100.0%**	**1.09 [0.44, 2.66]**
Total events	10		9			
Heterogeneity: Chi² = 0.00, df = 1 (P = 0.95); I² = 0%						
Test for overall effect: Z = 0.18 (P = 0.85)						

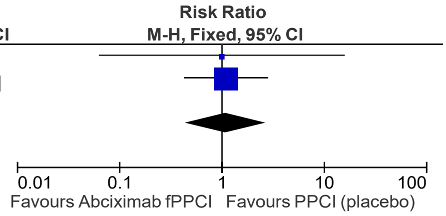


Figure 32: All-cause stroke (longer-term)

Study or Subgroup	Abciximab fPPCI Events	Abciximab fPPCI Total	PPCI (placebo) Events	PPCI (placebo) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
BRAVE-3 2010	3	401	1	399	100.0%	2.99 [0.31, 28.58]
Total (95% CI)		**401**		**399**	**100.0%**	**2.99 [0.31, 28.58]**
Total events	3		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.95 (P = 0.34)						

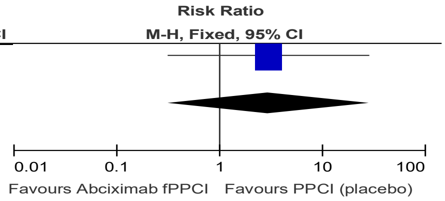


Figure 33: Fatal stroke (short-term)

Study or Subgroup	Abciximab fPPCI Events	Abciximab fPPCI Total	PPCI (placebo) Events	PPCI (placebo) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
FINESSE 2008	3	814	0	795	100.0%	6.84 [0.35, 132.14]
Total (95% CI)		**814**		**795**	**100.0%**	**6.84 [0.35, 132.14]**
Total events	3		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.27 (P = 0.20)						

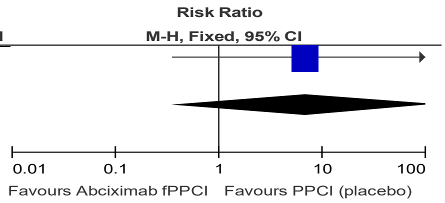


Figure 34: Reinfarction or non-fatal reinfarction or recurrent MI (short-term)

Study or Subgroup	Abciximab fPPCI Events	Abciximab fPPCI Total	PPCI (placebo) Events	PPCI (placebo) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
BRAVE-3 2009	3	401	4	399	21.0%	0.75 [0.17, 3.31]
FINESSE 2008	16	818	15	806	79.0%	1.05 [0.52, 2.11]
Total (95% CI)		**1219**		**1205**	**100.0%**	**0.99 [0.53, 1.85]**
Total events	19		19			

Heterogeneity: Chi² = 0.17, df = 1 (P = 0.68); I² = 0%
Test for overall effect: Z = 0.04 (P = 0.97)

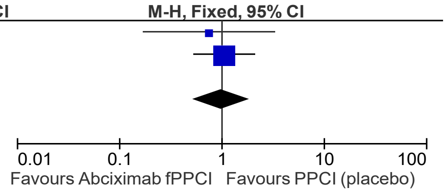


Figure 35: Reinfarction or non-fatal reinfarction or recurrent MI (longer-term)

Study or Subgroup	Abciximab fPPCI Events	Abciximab fPPCI Total	PPCI (placebo) Events	PPCI (placebo) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
BRAVE-3 2010	12	401	11	399	100.0%	1.09 [0.48, 2.43]
Total (95% CI)		**401**		**399**	**100.0%**	**1.09 [0.48, 2.43]**
Total events	12		11			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.20 (P = 0.84)

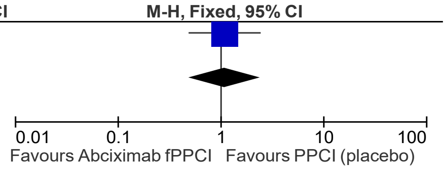


Figure 36: Intracranial bleeding or intracranial haemorrhage (short-term)

Study or Subgroup	Abciximab fPPCI Events	Abciximab fPPCI Total	PPCI (placebo) Events	PPCI (placebo) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
FINESSE 2008	5	814	1	795	100.0%	4.88 [0.57, 41.71]
Total (95% CI)		**814**		**795**	**100.0%**	**4.88 [0.57, 41.71]**
Total events	5		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.45 (P = 0.15)

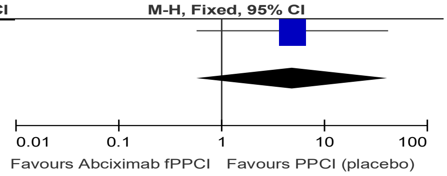


Figure 37: Major bleeding (short-term)

Study or Subgroup	Abciximab fPPCI Events	Abciximab fPPCI Total	PPCI (placebo) Events	PPCI (placebo) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
BRAVE-3 2009	7	401	7	399	24.8%	1.00 [0.35, 2.81]
FINESSE 2008	39	814	21	795	75.2%	1.81 [1.08, 3.06]
Total (95% CI)		**1215**		**1194**	**100.0%**	**1.61 [1.01, 2.56]**
Total events	46		28			

Heterogeneity: Chi² = 1.03, df = 1 (P = 0.31); I² = 3%
Test for overall effect: Z = 2.02 (P = 0.04)

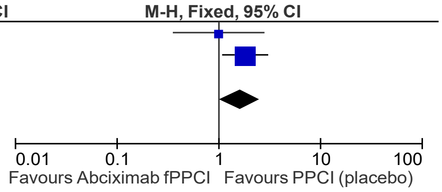


Figure 38: Major bleeding (in-hospital)

Study or Subgroup	fPPCI (GPIs) Events	fPPCI (GPIs) Total	PPCI (placebo / no drug) Events	PPCI (placebo / no drug) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Zorman 2002	16	56	6	51	100.0%	2.43 [1.03, 5.73]
Total (95% CI)		**56**		**51**	**100.0%**	**2.43 [1.03, 5.73]**
Total events	16		6			

Heterogeneity: Not applicable
Test for overall effect: Z = 2.03 (P = 0.04)

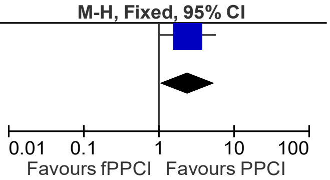


Figure 39: Minor bleeding (short-term)

Study or Subgroup	Abciximab fPPCI Events	Abciximab fPPCI Total	PPCI (placebo) Events	PPCI (placebo) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
BRAVE-3 2009	7	401	7	399	24.8%	1.00 [0.35, 2.81]
FINESSE 2008	39	814	21	795	75.2%	1.81 [1.08, 3.06]
Total (95% CI)		**1215**		**1194**	**100.0%**	**1.61 [1.01, 2.56]**
Total events	46		28			

Heterogeneity: Chi² = 1.03, df = 1 (P = 0.31); I² = 3%
Test for overall effect: Z = 2.02 (P = 0.04)

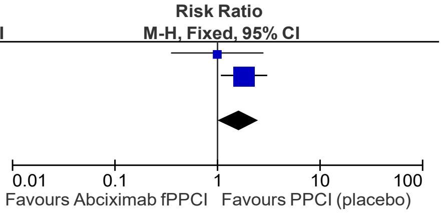


Figure 40: Heart failure or fatal heart failure (short-term)

Study or Subgroup	Abciximab fPPCI Events	Abciximab fPPCI Total	PPCI (placebo) Events	PPCI (placebo) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
FINESSE 2008	45	818	52	806	100.0%	0.85 [0.58, 1.26]
Total (95% CI)		**818**		**806**	**100.0%**	**0.85 [0.58, 1.26]**
Total events	45		52			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.81 (P = 0.42)

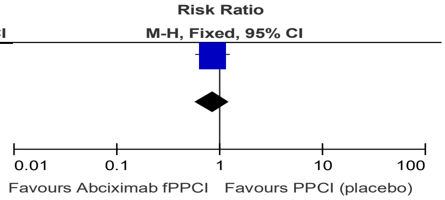


Figure 41: Repeat revascularisation or reintervention (short-term)

Study or Subgroup	Abciximab fPPCI Events	Abciximab fPPCI Total	PPCI (placebo) Events	PPCI (placebo) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
FINESSE 2008	111	818	111	806	100.0%	0.99 [0.77, 1.26]
Total (95% CI)		**818**		**806**	**100.0%**	**0.99 [0.77, 1.26]**
Total events	111		111			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.12 (P = 0.91)

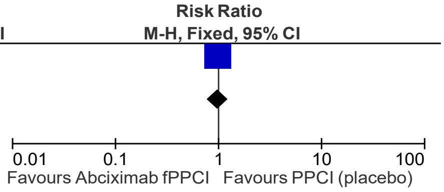
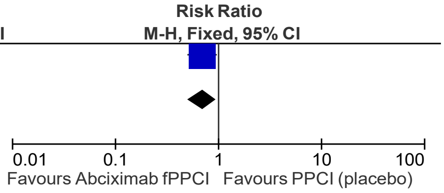


Figure 42: Repeat revascularisation or reintervention (longer-term)

Study or Subgroup	Abciximab fPPCI Events	Abciximab fPPCI Total	PPCI (placebo) Events	PPCI (placebo) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
BRAVE-3 2010	53	401	76	399	100.0%	0.69 [0.50, 0.96]
Total (95% CI)		**401**		**399**	**100.0%**	**0.69 [0.50, 0.96]**
Total events	53		76			

Heterogeneity: Not applicable
Test for overall effect: Z = 2.22 (P = 0.03)



I.2.4 GPIs: fPPCI versus PPCI – tirofiban

Figure 43: All-cause mortality (short-term)

Study or Subgroup	Tirofiban fPPCI Events	Tirofiban fPPCI Total	PPCI (placebo) Events	PPCI (placebo) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ON-TIME2 2008	11	473	19	477	100.0%	0.58 [0.28, 1.21]
Total (95% CI)		**473**		**477**	**100.0%**	**0.58 [0.28, 1.21]**
Total events	11		19			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.44 (P = 0.15)

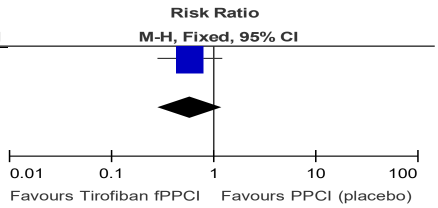


Figure 44: All-cause mortality (longer-term)

Study or Subgroup	Tirofiban fPPCI Events	Tirofiban fPPCI Total	PPCI (placebo) Events	PPCI (placebo) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ON-TIME2 2010	16	467	25	470	100.0%	0.64 [0.35, 1.19]
Total (95% CI)		**467**		**470**	**100.0%**	**0.64 [0.35, 1.19]**
Total events	16		25			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.40 (P = 0.16)						

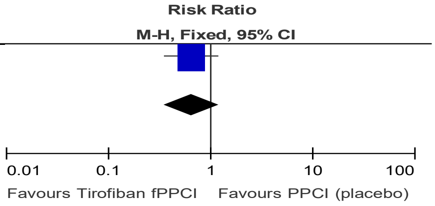


Figure 45: All-cause stroke (short-term)

Study or Subgroup	Tirofiban fPPCI Events	Tirofiban fPPCI Total	PPCI (placebo) Events	PPCI (placebo) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ON-TIME2 2008	1	473	7	477	100.0%	0.14 [0.02, 1.17]
Total (95% CI)		**473**		**477**	**100.0%**	**0.14 [0.02, 1.17]**
Total events	1		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.82 (P = 0.07)						

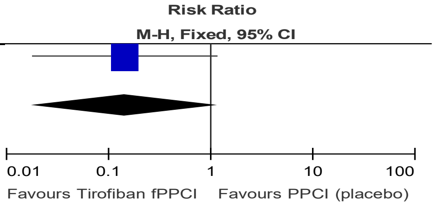


Figure 46: Reinfarction or non-fatal reinfarction or recurrent MI (short-term)

Study or Subgroup	Tirofiban fPPCI Events	Tirofiban fPPCI Total	PPCI (placebo) Events	PPCI (placebo) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ON-TIME2 2008	13	473	14	477	100.0%	0.94 [0.44, 1.97]
Total (95% CI)		**473**		**477**	**100.0%**	**0.94 [0.44, 1.97]**
Total events	13		14			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.17 (P = 0.86)						

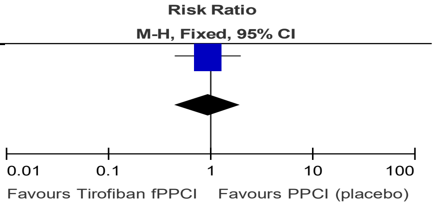


Figure 47: Major bleeding (short-term)

Study or Subgroup	Tirofiban fPPCI Events	Tirofiban fPPCI Total	PPCI (placebo) Events	PPCI (placebo) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ON-TIME2 2008	19	473	14	477	100.0%	1.37 [0.69, 2.70]
Total (95% CI)		**473**		**477**	**100.0%**	**1.37 [0.69, 2.70]**
Total events	19		14			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.91 (P = 0.36)						

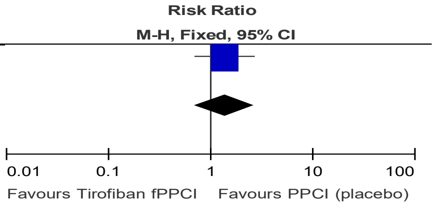


Figure 48: Minor bleeding (short-term)

Study or Subgroup	Tirofiban fPPCI Events	Tirofiban fPPCI Total	PPCI (placebo) Events	PPCI (placebo) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ON-TIME2 2008	29	473	21	477	100.0%	1.39 [0.81, 2.41]
Total (95% CI)		**473**		**477**	**100.0%**	**1.39 [0.81, 2.41]**
Total events	29		21			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.19 (P = 0.24)						

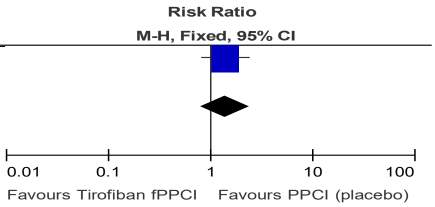
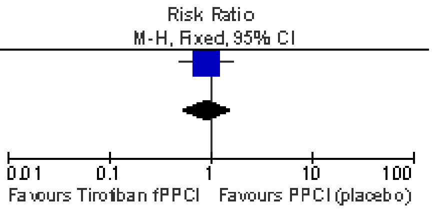


Figure 49: Repeat revascularisation – repeat or urgent (short-term)

Study or Subgroup	Tirofiban fPPCI Events	Tirofiban fPPCI Total	PPCI (placebo) Events	PPCI (placebo) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ON-TIME2 2008	18	473	20	477	100.0%	0.91 [0.49, 1.69]
Total (95% CI)		473		477	100.0%	0.91 [0.49, 1.69]
Total events	18		20			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.30 (P = 0.76)						



I.2.5 GPIs: fPPCI versus PPCI – eptifibatide

Figure 50: All-cause mortality (short-term)

Study or Subgroup	Eptifibatide fPPCI Events	Eptifibatide fPPCI Total	PPCI Events	PPCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ASSIST 2009	7	201	4	199	100.0%	1.73 [0.52, 5.83]
Total (95% CI)		**201**		**199**	**100.0%**	**1.73 [0.52, 5.83]**
Total events	7		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.89 (P = 0.37)						

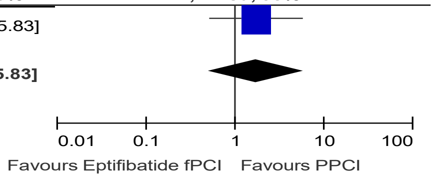


Figure 51: All-cause mortality (longer-term)

Study or Subgroup	Eptifibatide fPPCI Events	Eptifibatide fPPCI Total	PPCI Events	PPCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ASSIST 2009	9	201	6	199	100.0%	1.49 [0.54, 4.09]
Total (95% CI)		**201**		**199**	**100.0%**	**1.49 [0.54, 4.09]**
Total events	9		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.76 (P = 0.44)						

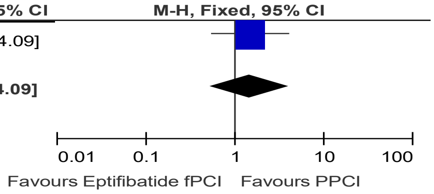


Figure 52: All-cause stroke (short-term)

Study or Subgroup	Eptifibatide fPPCI Events	Eptifibatide fPPCI Total	PPCI Events	PPCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ASSIST 2009	0	201	1	199	100.0%	0.33 [0.01, 8.05]
Total (95% CI)		**201**		**199**	**100.0%**	**0.33 [0.01, 8.05]**
Total events	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.68 (P = 0.50)						

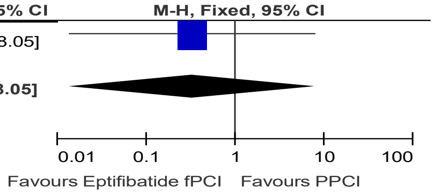


Figure 53: All-cause stroke (longer-term)

Study or Subgroup	Eptifibatide fPPCI Events	Eptifibatide fPPCI Total	PPCI Events	PPCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ASSIST 2009	0	201	4	199	100.0%	0.11 [0.01, 2.03]
Total (95% CI)		**201**		**199**	**100.0%**	**0.11 [0.01, 2.03]**
Total events	0		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.48 (P = 0.14)						

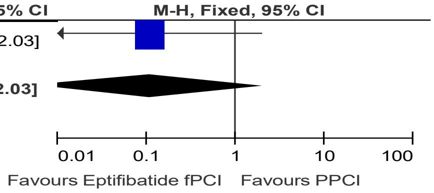


Figure 54: Reinfarction or non-fatal reinfarction or recurrent MI (short-term)

Study or Subgroup	Eptifibatide fPPCI Events	Eptifibatide fPPCI Total	PPCI Events	PPCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ASSIST 2009	3	201	1	199	100.0%	2.97 [0.31, 28.31]
Total (95% CI)		**201**		**199**	**100.0%**	**2.97 [0.31, 28.31]**
Total events	3		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.95 (P = 0.34)						

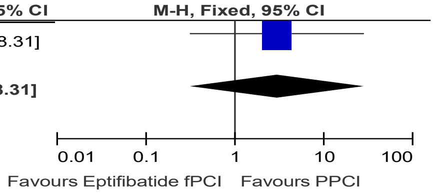


Figure 55: Reinfarction or non-fatal reinfarction or recurrent MI (longer-term)

	Eptifibatide fPCI		PPCI			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
ASSIST 2009	4	201	2	199	100.0%	1.98 [0.37, 10.69]
Total (95% CI)		**201**		**199**	**100.0%**	**1.98 [0.37, 10.69]**
Total events	4		2			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.79 (P = 0.43)

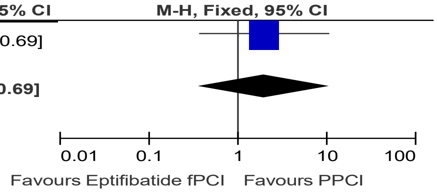


Figure 56: Heart failure or fatal heart failure (short-term)

	Eptifibatide fPCI		PPCI			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
ASSIST 2009	15	201	22	199	100.0%	0.68 [0.36, 1.26]
Total (95% CI)		**201**		**199**	**100.0%**	**0.68 [0.36, 1.26]**
Total events	15		22			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.23 (P = 0.22)

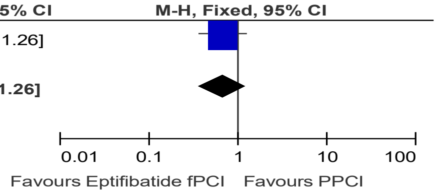


Figure 57: Heart failure or fatal heart failure (longer-term)

	Eptifibatide fPCI		PPCI			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
ASSIST 2009	15	201	24	199	100.0%	0.62 [0.33, 1.14]
Total (95% CI)		**201**		**199**	**100.0%**	**0.62 [0.33, 1.14]**
Total events	15		24			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.53 (P = 0.13)

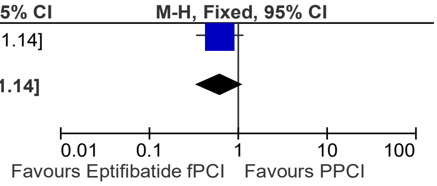


Figure 58: Repeat revascularisation or urgent revascularisation (short-term)

	Eptifibatide fPCI		PPCI			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
ASSIST 2009	8	201	4	199	100.0%	1.98 [0.61, 6.47]
Total (95% CI)		**201**		**199**	**100.0%**	**1.98 [0.61, 6.47]**
Total events	8		4			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.13 (P = 0.26)

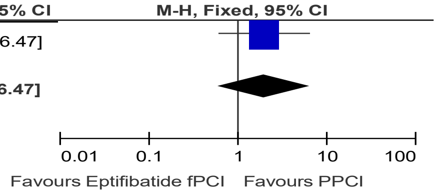
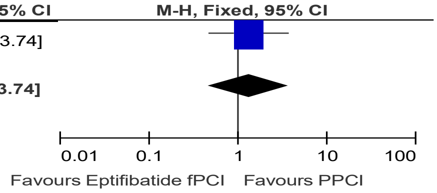


Figure 59: Repeat revascularisation or urgent revascularisation (longer-term)

	Eptifibatide fPCI		PPCI			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
ASSIST 2009	8	201	6	199	100.0%	1.32 [0.47, 3.74]
Total (95% CI)		**201**		**199**	**100.0%**	**1.32 [0.47, 3.74]**
Total events	8		6			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.52 (P = 0.60)



I.2.6 GPIs: Pre-catheter laboratory versus in-catheter laboratory administration – all GPIs

Figure 60: All-cause mortality (in-hospital)

	GPI fPPCI (early)		GPI fPPCI (later)			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
AGIR-2 2010	5	156	9	164	61.5%	0.58 [0.20, 1.70]
MISTRAL	2	127	1	129	7.0%	2.03 [0.19, 22.12]
Zorman 2002	0	56	4	56	31.5%	0.11 [0.01, 2.02]
Total (95% CI)		**339**		**349**	**100.0%**	**0.54 [0.23, 1.27]**
Total events	7		14			

Heterogeneity: Chi² = 2.35, df = 2 (P = 0.31); I² = 15%
Test for overall effect: Z = 1.41 (P = 0.16)

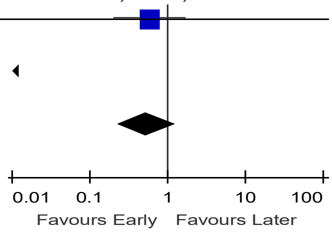


Figure 61: All-cause mortality (short-term)

	GPI fPPCI (early)		GPI fPPCI (later)			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
Bellandi 2006	1	27	1	28	8.6%	1.04 [0.07, 15.76]
Dudek 2010	1	24	0	27	4.1%	3.36 [0.14, 78.79]
Emre 2006	0	32	0	34		Not estimable
ERAMI 2006	4	36	5	38	42.7%	0.84 [0.25, 2.90]
INTAMI-pilot 2005	2	53	2	49	18.3%	0.92 [0.14, 6.31]
MISTRAL	2	127	1	129	8.7%	2.03 [0.19, 22.12]
ON-TIME 2004	9	245	2	247	17.5%	4.54 [0.99, 20.78]
Total (95% CI)		**544**		**552**	**100.0%**	**1.73 [0.85, 3.52]**
Total events	19		11			

Heterogeneity: Chi² = 3.57, df = 5 (P = 0.61); I² = 0%
Test for overall effect: Z = 1.51 (P = 0.13)

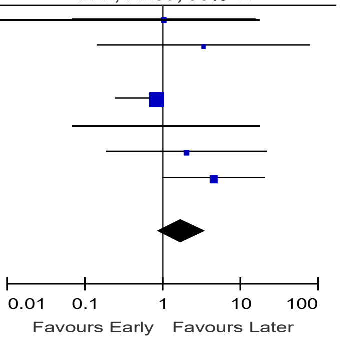


Figure 62: All-cause mortality (longer-term)

	GPI fPPCI (early)		GPI fPPCI (later)			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
MISTRAL	2	127	1	129	6.4%	2.03 [0.19, 22.12]
ON-TIME 2004	11	245	9	244	58.1%	1.22 [0.51, 2.88]
Zorman 2002	0	56	5	56	35.5%	0.09 [0.01, 1.61]
Total (95% CI)		**428**		**429**	**100.0%**	**0.87 [0.42, 1.78]**
Total events	13		15			

Heterogeneity: Chi² = 3.44, df = 2 (P = 0.18); I² = 42%
Test for overall effect: Z = 0.38 (P = 0.70)

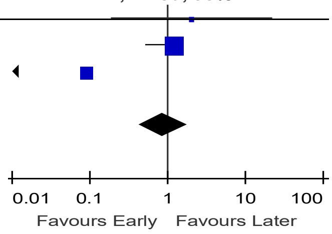


Figure 63: All-cause stroke (in-hospital)

	GPI fPPCI (early)		GPI fPPCI (later)			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Total (95% CI)		**156**		**164**	**100.0%**	**0.53 [0.05, 5.74]**
Total events	1		2			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.53 (P = 0.60)

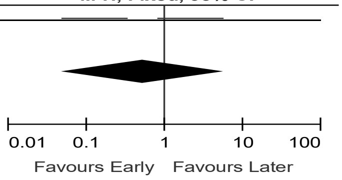


Figure 64: All-cause stroke (short-term)

Study or Subgroup	GPI fPPCI (early) Events	GPI fPPCI (early) Total	GPI fPPCI (later) Events	GPI fPPCI (later) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
INTAMI-pilot 2005	0	53	0	49		Not estimable
ON-TIME 2004	0	245	1	256	100.0%	0.35 [0.01, 8.51]
Total (95% CI)		**298**		**305**	**100.0%**	**0.35 [0.01, 8.51]**
Total events	0		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.65 (P = 0.52)

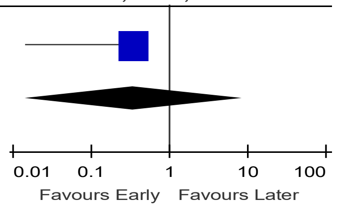


Figure 65: Reinfarction or non-fatal reinfarction or recurrent MI (in-hospital)

Study or Subgroup	GPI fPPCI (early) Events	GPI fPPCI (early) Total	GPI fPPCI (later) Events	GPI fPPCI (later) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Total (95% CI)		**127**		**129**	**100.0%**	**1.02 [0.15, 7.10]**
Total events	2		2			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.02 (P = 0.99)

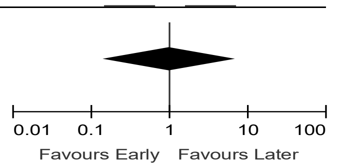


Figure 66: Reinfarction or non-fatal reinfarction or recurrent MI (short-term)

Study or Subgroup	GPI fPPCI (early) Events	GPI fPPCI (early) Total	GPI fPPCI (later) Events	GPI fPPCI (later) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Bellandi 2006	0	27	0	28		Not estimable
Dudek 2010	0	24	0	27		Not estimable
Emre 2006	0	32	1	34	12.8%	0.35 [0.01, 8.38]
ERAMI 2006	0	36	1	38	12.8%	0.35 [0.01, 8.36]
INTAMI-pilot 2005	3	53	0	49	4.5%	6.48 [0.34, 122.37]
MISTRAL	3	127	2	129	17.4%	1.52 [0.26, 8.97]
ON-TIME 2004	3	245	2	247	17.5%	1.51 [0.25, 8.97]
RELAX-AMI 2007	2	105	4	105	35.1%	0.50 [0.09, 2.67]
Total (95% CI)		**649**		**657**	**100.0%**	**1.09 [0.49, 2.42]**
Total events	11		10			

Heterogeneity: Chi² = 3.49, df = 5 (P = 0.63); I² = 0%
Test for overall effect: Z = 0.21 (P = 0.83)

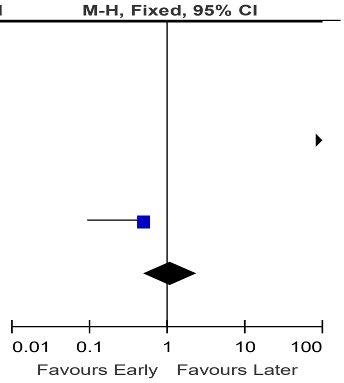


Figure 67: Reinfarction or non-fatal reinfarction or recurrent MI (longer-term)

Study or Subgroup	GPI fPPCI (early) Events	GPI fPPCI (early) Total	GPI fPPCI (later) Events	GPI fPPCI (later) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
MISTRAL	3	127	2	129	18.0%	1.52 [0.26, 8.97]
ON-TIME 2004	6	245	9	244	82.0%	0.66 [0.24, 1.84]
Total (95% CI)		**372**		**373**	**100.0%**	**0.82 [0.34, 1.95]**
Total events	9		11			

Heterogeneity: Chi² = 0.63, df = 1 (P = 0.43); I² = 0%
Test for overall effect: Z = 0.45 (P = 0.65)

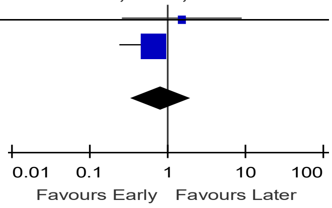


Figure 68: Bleeding (in-hospital)

Study or Subgroup	GPI fPPCI (early) Events	GPI fPPCI (early) Total	GPI fPPCI (later) Events	GPI fPPCI (later) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Zorman 2002	16	56	11	56	100.0%	1.45 [0.74, 2.85]
Total (95% CI)		**56**		**56**	**100.0%**	**1.45 [0.74, 2.85]**
Total events	16		11			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.09 (P = 0.27)						

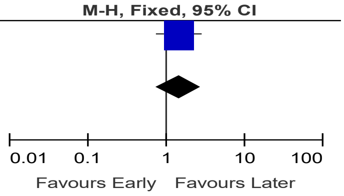


Figure 69: Major bleeding (in-hospital)

Study or Subgroup	GPI fPPCI (early) Events	GPI fPPCI (early) Total	GPI fPPCI (later) Events	GPI fPPCI (later) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Total (95% CI)		**156**		**164**	**100.0%**	**0.35 [0.07, 1.71]**
Total events	2		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.30 (P = 0.19)						

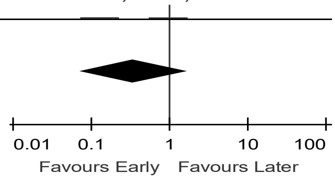


Figure 70: Major bleeding (short-term)

Study or Subgroup	GPI fPPCI (early) Events	GPI fPPCI (early) Total	GPI fPPCI (later) Events	GPI fPPCI (later) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Bellandi 2006	1	27	2	28	13.7%	0.52 [0.05, 5.39]
Dudek 2010	1	24	1	27	6.6%	1.13 [0.07, 17.02]
Emre 2006	0	32	0	34		Not estimable
ERAMI 2006	1	36	0	38	3.4%	3.16 [0.13, 75.20]
INTAMI-pilot 2005	2	53	2	49	14.5%	0.92 [0.14, 6.31]
ON-TIME 2004	11	245	8	256	54.7%	1.44 [0.59, 3.51]
RELAX-AMI 2007	1	105	1	105	7.0%	1.00 [0.06, 15.78]
Total (95% CI)		**522**		**537**	**100.0%**	**1.24 [0.63, 2.46]**
Total events	17		14			
Heterogeneity: Chi² = 1.09, df = 5 (P = 0.95); I² = 0%						
Test for overall effect: Z = 0.63 (P = 0.53)						

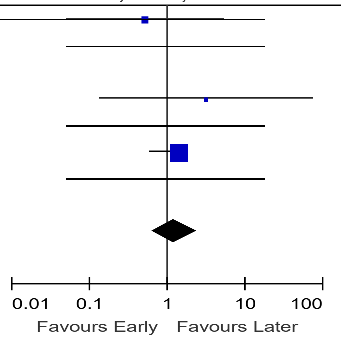
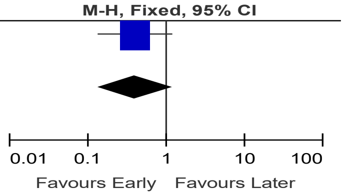


Figure 71: Heart failure (in-hospital)

Study or Subgroup	GPI fPPCI (early) Events	GPI fPPCI (early) Total	GPI fPPCI (later) Events	GPI fPPCI (later) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Zorman 2002	4	56	10	56	100.0%	0.40 [0.13, 1.20]
Total (95% CI)		**56**		**56**	**100.0%**	**0.40 [0.13, 1.20]**
Total events	4		10			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.63 (P = 0.10)						



I.2.7 GPIs: Pre-catheter laboratory versus in-catheter laboratory administration – abciximab

Figure 72: All-cause mortality (in-hospital)

Study or Subgroup	Early abciximab (fPCI) Events	Early abciximab (fPCI) Total	Later abciximab (fPCI) Events	Later abciximab (fPCI) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
MISTRAL	2	127	1	129	18.1%	2.03 [0.19, 22.12]
Zorman 2002	0	56	4	56	81.9%	0.11 [0.01, 2.02]
Total (95% CI)		**183**		**185**	**100.0%**	**0.46 [0.10, 2.01]**
Total events	2		5			

Heterogeneity: Chi² = 2.41, df = 1 (P = 0.12); I² = 59%
Test for overall effect: Z = 1.03 (P = 0.30)

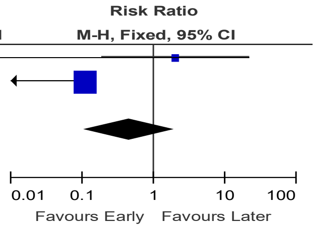


Figure 73: All-cause mortality (short-term)

Study or Subgroup	Early abciximab (fPCI) Events	Early abciximab (fPCI) Total	Later abciximab (fPCI) Events	Later abciximab (fPCI) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Bellandi 2006	1	27	1	28	13.4%	1.04 [0.07, 15.76]
Dudek 2010	1	24	0	27	6.5%	3.36 [0.14, 78.79]
ERAMI 2006	4	36	5	38	66.5%	0.84 [0.25, 2.90]
MISTRAL	2	127	1	129	13.6%	2.03 [0.19, 22.12]
Total (95% CI)		**214**		**222**	**100.0%**	**1.19 [0.47, 3.06]**
Total events	8		7			

Heterogeneity: Chi² = 0.92, df = 3 (P = 0.82); I² = 0%
Test for overall effect: Z = 0.37 (P = 0.71)

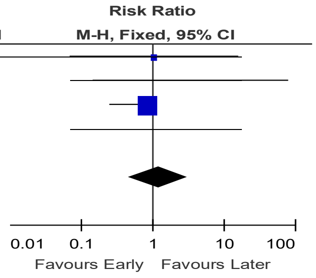


Figure 74: All-cause mortality (longer-term)

Study or Subgroup	Early abciximab (fPCI) Events	Early abciximab (fPCI) Total	Later abciximab (fPCI) Events	Later abciximab (fPCI) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
MISTRAL	2	127	1	129	15.3%	2.03 [0.19, 22.12]
Zorman 2002	0	56	5	56	84.7%	0.09 [0.01, 1.61]
Total (95% CI)		**183**		**185**	**100.0%**	**0.39 [0.09, 1.64]**
Total events	2		6			

Heterogeneity: Chi² = 2.83, df = 1 (P = 0.09); I² = 65%
Test for overall effect: Z = 1.29 (P = 0.20)

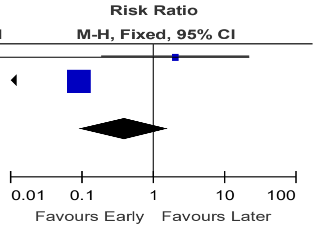


Figure 75: Intracranial bleeding or intracranial haemorrhage (in-hospital)

Study or Subgroup	Early abciximab (fPCI) Events	Early abciximab (fPCI) Total	Later abciximab (fPCI) Events	Later abciximab (fPCI) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Bellandi 2006	0	27	0	28		Not estimable
Total (95% CI)		**27**		**28**		**Not estimable**
Total events	0		0			

Heterogeneity: Not applicable
Test for overall effect: Not applicable

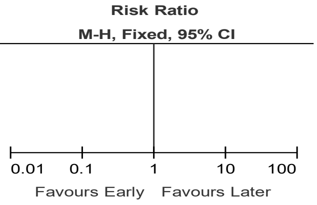


Figure 76: Intracranial bleeding or intracranial haemorrhage (short-term)

Study or Subgroup	Early abciximab (fPCI) Events	Early abciximab (fPCI) Total	Later abciximab (fPCI) Events	Later abciximab (fPCI) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Dudek 2010	0	24	0	27		Not estimable
RELAX-AMI 2007	0	105	0	105		Not estimable
Total (95% CI)		**129**		**132**		**Not estimable**
Total events	0		0			

Heterogeneity: Not applicable
Test for overall effect: Not applicable

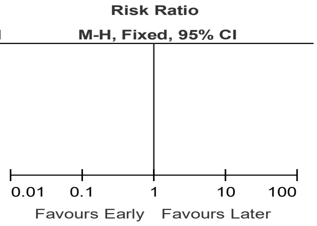


Figure 77: Reinfarction or non-fatal reinfarction or recurrent MI (in-hospital):

Study or Subgroup	Early abciximab (fPCI) Events	Early abciximab (fPCI) Total	Later abciximab (fPCI) Events	Later abciximab (fPCI) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Total (95% CI)		**127**		**129**	**100.0%**	**1.02 [0.15, 7.10]**
Total events	2		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.02 (P = 0.99)						

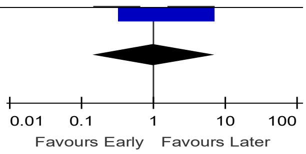


Figure 78: Reinfarction or non-fatal reinfarction or recurrent MI (short-term)

Study or Subgroup	Early abciximab (fPCI) Events	Early abciximab (fPCI) Total	Later abciximab (fPCI) Events	Later abciximab (fPCI) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Bellandi 2006	0	27	0	28		Not estimable
Dudek 2010	0	24	0	27		Not estimable
ERAMI 2006	0	36	1	38	19.6%	0.35 [0.01, 8.36]
MISTRAL	3	127	2	129	26.7%	1.52 [0.26, 8.97]
RELAX-AMI 2007	2	105	4	105	53.7%	0.50 [0.09, 2.67]
Total (95% CI)		**319**		**327**	**100.0%**	**0.74 [0.25, 2.21]**
Total events	5		7			
Heterogeneity: Chi² = 1.06, df = 2 (P = 0.59); I² = 0%						
Test for overall effect: Z = 0.53 (P = 0.59)						

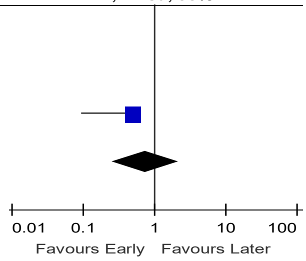


Figure 79: Reinfarction or non-fatal reinfarction or recurrent MI (longer-term)

Study or Subgroup	Early abciximab (fPCI) Events	Early abciximab (fPCI) Total	Later abciximab (fPCI) Events	Later abciximab (fPCI) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Total (95% CI)		**127**		**129**	**100.0%**	**1.52 [0.26, 8.97]**
Total events	3		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.47 (P = 0.64)						

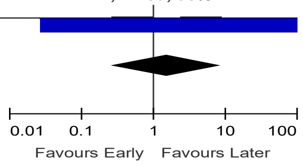


Figure 80: Bleeding (in-hospital)

Study or Subgroup	Early abciximab (fPCI) Events	Early abciximab (fPCI) Total	Later abciximab (fPCI) Events	Later abciximab (fPCI) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Zorman 2002	16	56	11	56	100.0%	1.45 [0.74, 2.85]
Total (95% CI)		**56**		**56**	**100.0%**	**1.45 [0.74, 2.85]**
Total events	16		11			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.09 (P = 0.27)						

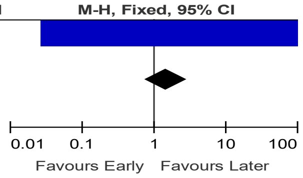


Figure 81: Major bleeding (short-term)

Study or Subgroup	Early abciximab (fPCI) Events	Early abciximab (fPCI) Total	Later abciximab (fPCI) Events	Later abciximab (fPCI) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Bellandi 2006	1	27	2	28	44.7%	0.52 [0.05, 5.39]
Dudek 2010	1	24	1	27	21.4%	1.13 [0.07, 17.02]
ERAMI 2006	1	36	0	38	11.1%	3.16 [0.13, 75.20]
RELAX-AMI 2007	1	105	1	105	22.8%	1.00 [0.06, 15.78]
Total (95% CI)		**192**		**198**	**100.0%**	**1.05 [0.29, 3.80]**
Total events	4		4			
Heterogeneity: Chi² = 0.82, df = 3 (P = 0.85); I² = 0%						
Test for overall effect: Z = 0.08 (P = 0.94)						

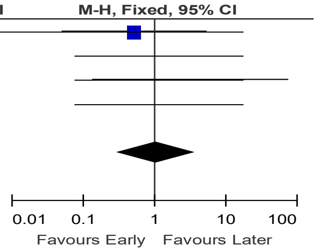


Figure 82: Minor bleeding (short-term)

Study or Subgroup	Early abciximab (fPCI) Events	Total	Later abciximab (fPCI) Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Dudek 2010	1	24	1	27	11.9%	1.13 [0.07, 17.02]
ERAMI 2006	3	36	2	38	24.7%	1.58 [0.28, 8.93]
RELAX-AMI 2007	8	105	5	105	63.4%	1.60 [0.54, 4.73]
Total (95% CI)		**165**		**170**	**100.0%**	**1.54 [0.65, 3.67]**
Total events	12		8			
Heterogeneity: Chi² = 0.06, df = 2 (P = 0.97); I² = 0%						
Test for overall effect: Z = 0.97 (P = 0.33)						

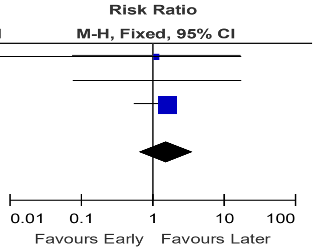


Figure 83: Repeat revascularisation – repeat or urgent (short-term)

Study or Subgroup	Early abciximab (fPCI) Events	Total	Later abciximab (fPCI) Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Bellandi 2006	0	27	0	28		Not estimable
Dudek 2010	0	24	0	27		Not estimable
ERAMI 2006	1	36	0	38	32.7%	3.16 [0.13, 75.20]
RELAX-AMI 2007	2	105	1	105	67.3%	2.00 [0.18, 21.72]
Total (95% CI)		**192**		**198**	**100.0%**	**2.38 [0.36, 15.84]**
Total events	3		1			
Heterogeneity: Chi² = 0.05, df = 1 (P = 0.82); I² = 0%						
Test for overall effect: Z = 0.90 (P = 0.37)						

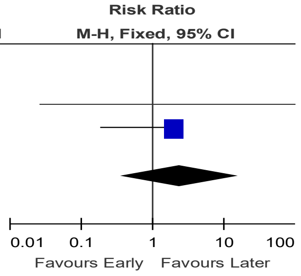
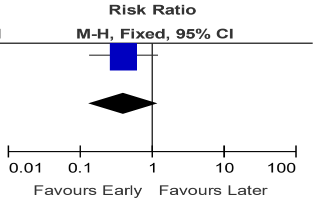


Figure 84: Heart failure (in-hospital)

Study or Subgroup	Early abciximab (fPCI) Events	Total	Later abciximab (fPCI) Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Zorman 2002	4	56	10	56	100.0%	0.40 [0.13, 1.20]
Total (95% CI)		**56**		**56**	**100.0%**	**0.40 [0.13, 1.20]**
Total events	4		10			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.63 (P = 0.10)						



I.2.8 GPIs: Pre-catheter laboratory versus in-catheter laboratory administration – tirofiban

Figure 85: All-cause mortality (in-hospital)

Study or Subgroup	Early tirofiban (fPCI) Events	Total	Later tirofiban (fPCI) Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
AGIR-2 2010	5	156	9	164	100.0%	0.58 [0.20, 1.70]
Total (95% CI)		**156**		**164**	**100.0%**	**0.58 [0.20, 1.70]**
Total events	5		9			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.98 (P = 0.33)						

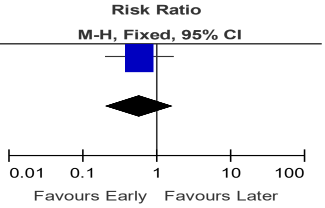


Figure 86: All-cause mortality (short-term)

Study or Subgroup	Early tirofiban (fPCI) Events	Total	Later tirofiban (fPCI) Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Emre 2006	0	32	0	34		Not estimable
ON-TIME 2004	9	245	2	247	100.0%	4.54 [0.99, 20.78]
Total (95% CI)		**277**		**281**	**100.0%**	**4.54 [0.99, 20.78]**
Total events	9		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.95 (P = 0.05)						

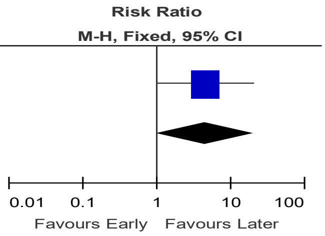


Figure 87: All-cause mortality (longer-term)

Study or Subgroup	Early tirofiban (fPCI) Events	Early tirofiban (fPCI) Total	Later tirofiban (fPCI) Events	Later tirofiban (fPCI) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ON-TIME 2004	11	245	9	244	100.0%	1.22 [0.51, 2.88]
Total (95% CI)		**245**		**244**	**100.0%**	**1.22 [0.51, 2.88]**
Total events	11		9			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.45 (P = 0.66)						

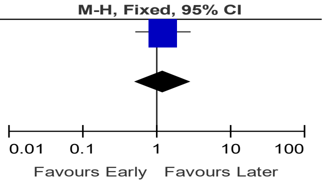


Figure 88: All-cause stroke (in-hospital)

Study or Subgroup	Early tirofiban (fPCI) Events	Early tirofiban (fPCI) Total	Later tirofiban (fPCI) Events	Later tirofiban (fPCI) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Total (95% CI)		**156**		**164**	**100.0%**	**0.53 [0.05, 5.74]**
Total events	1		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.53 (P = 0.60)						

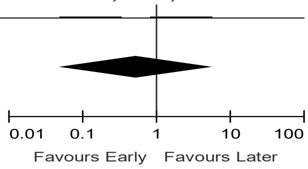


Figure 89: All-cause stroke (short-term)

Study or Subgroup	Early tirofiban (fPCI) Events	Early tirofiban (fPCI) Total	Later tirofiban (fPCI) Events	Later tirofiban (fPCI) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ON-TIME 2004	0	245	1	256	100.0%	0.35 [0.01, 8.51]
Total (95% CI)		**245**		**256**	**100.0%**	**0.35 [0.01, 8.51]**
Total events	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.65 (P = 0.52)						

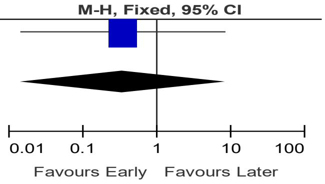


Figure 90: Reinfarction or non-fatal reinfarction or recurrent MI (short-term)

Study or Subgroup	Early tirofiban (fPCI) Events	Early tirofiban (fPCI) Total	Later tirofiban (fPCI) Events	Later tirofiban (fPCI) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Emre 2006	0	32	1	34	42.2%	0.35 [0.01, 8.38]
ON-TIME 2004	3	245	2	247	57.8%	1.51 [0.25, 8.97]
Total (95% CI)		**277**		**281**	**100.0%**	**1.02 [0.23, 4.48]**
Total events	3		3			
Heterogeneity: Chi² = 0.62, df = 1 (P = 0.43); I² = 0%						
Test for overall effect: Z = 0.03 (P = 0.98)						

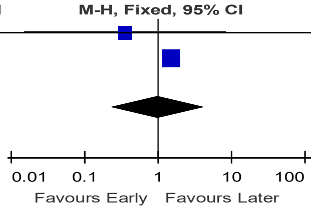


Figure 91: Reinfarction or non-fatal reinfarction or recurrent MI (longer-term)

Study or Subgroup	Early tirofiban (fPCI) Events	Early tirofiban (fPCI) Total	Later tirofiban (fPCI) Events	Later tirofiban (fPCI) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ON-TIME 2004	6	245	9	244	100.0%	0.66 [0.24, 1.84]
Total (95% CI)		**245**		**244**	**100.0%**	**0.66 [0.24, 1.84]**
Total events	6		9			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.79 (P = 0.43)						

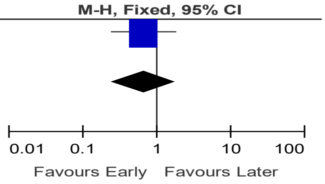


Figure 92: Major bleeding (in-hospital)

Study or Subgroup	Early tirofiban (fPCI) Events	Early tirofiban (fPCI) Total	Later tirofiban (fPCI) Events	Later tirofiban (fPCI) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
AGIR-2 2010	2	156	6	164	100.0%	0.35 [0.07, 1.71]
Total (95% CI)		**156**		**164**	**100.0%**	**0.35 [0.07, 1.71]**
Total events	2		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.30 (P = 0.19)						

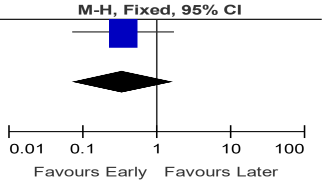


Figure 93: Major bleeding (short-term)

Study or Subgroup	Early tirofiban (fPCI) Events	Early tirofiban (fPCI) Total	Later tirofiban (fPCI) Events	Later tirofiban (fPCI) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Emre 2006	0	32	0	34		Not estimable
ON-TIME 2004	11	245	8	256	100.0%	1.44 [0.59, 3.51]
Total (95% CI)		**277**		**290**	**100.0%**	**1.44 [0.59, 3.51]**
Total events	11		8			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.79 (P = 0.43)						

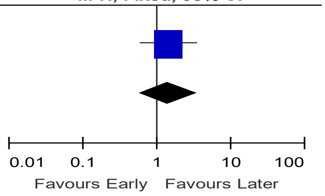


Figure 94: Minor bleeding (short-term)

Study or Subgroup	Early tirofiban (fPCI) Events	Early tirofiban (fPCI) Total	Later tirofiban (fPCI) Events	Later tirofiban (fPCI) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Total (95% CI)		**32**		**34**	**100.0%**	**1.59 [0.28, 8.93]**
Total events	3		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.53 (P = 0.60)						

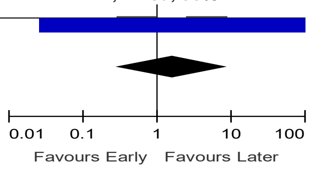
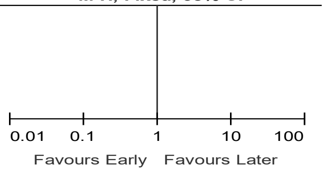


Figure 95: Intracranial bleeding or intracranial haemorrhage (short-term)

Study or Subgroup	Early tirofiban (fPCI) Events	Early tirofiban (fPCI) Total	Later tirofiban (fPCI) Events	Later tirofiban (fPCI) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ON-TIME 2004	0	245	0	256		Not estimable
Total (95% CI)		**245**		**256**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						



I.2.9 GPIs: Pre-catheter laboratory versus in-catheter laboratory administration – eptifibatide

Figure 96: All-cause mortality (short-term)

Study or Subgroup	Early tirofiban (fPCI) Events	Early tirofiban (fPCI) Total	Later tirofiban (fPCI) Events	Later tirofiban (fPCI) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
INTAMI-pilot 2005	2	53	2	49	100.0%	0.92 [0.14, 6.31]
Total (95% CI)		**53**		**49**	**100.0%**	**0.92 [0.14, 6.31]**
Total events	2		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.08 (P = 0.94)						

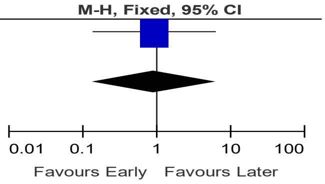


Figure 97: All-cause stroke (short-term)

Study or Subgroup	Early tirofiban (fPCI) Events	Early tirofiban (fPCI) Total	Later tirofiban (fPCI) Events	Later tirofiban (fPCI) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
INTAMI-pilot 2005	0	53	0	49		Not estimable
Total (95% CI)		**53**		**49**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						

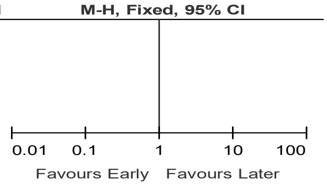


Figure 98: Reinfarction or non-fatal reinfarction or recurrent MI (short-term)

Study or Subgroup	Early tirofiban (fPCI) Events	Early tirofiban (fPCI) Total	Later tirofiban (fPCI) Events	Later tirofiban (fPCI) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Total (95% CI)		**53**		**49**	**100.0%**	**6.48 [0.34, 122.37]**
Total events	3		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.25 (P = 0.21)						

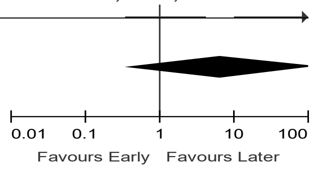


Figure 99: Major bleeding (short-term)

Study or Subgroup	Early tirofiban (fPCI) Events	Early tirofiban (fPCI) Total	Later tirofiban (fPCI) Events	Later tirofiban (fPCI) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Total (95% CI)		**53**		**49**	**100.0%**	**0.92 [0.14, 6.31]**
Total events	2		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.08 (P = 0.94)						

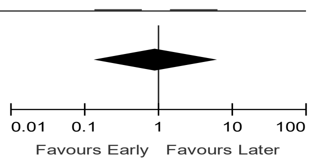
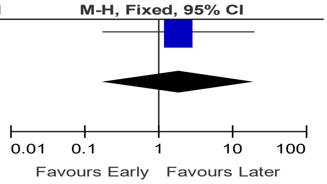


Figure 100: Repeat revascularisation (short-term)

Study or Subgroup	Early tirofiban (fPCI) Events	Early tirofiban (fPCI) Total	Later tirofiban (fPCI) Events	Later tirofiban (fPCI) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
INTAMI-pilot 2005	2	53	1	49	100.0%	1.85 [0.17, 19.76]
Total (95% CI)		**53**		**49**	**100.0%**	**1.85 [0.17, 19.76]**
Total events	2		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.51 (P = 0.61)						



I.2.10 Fibrinolytics: fPPCI versus PPCI – all fibrinolytics

Figure 101: All-cause mortality (in-hospital)

Study or Subgroup	Tenecteplase (fPPCI) Events	Tenecteplase (fPPCI) Total	PPCI Events	PPCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ASSENT-4	15	719	0	763	8.8%	32.89 [1.97, 548.74]
ATHENS PCI 2009	8	143	5	141	91.2%	1.58 [0.53, 4.71]
Total (95% CI)		**862**		**904**	**100.0%**	**4.33 [1.74, 10.75]**
Total events	23		5			
Heterogeneity: Chi² = 5.27, df = 1 (P = 0.02); I² = 81%						
Test for overall effect: Z = 3.16 (P = 0.002)						

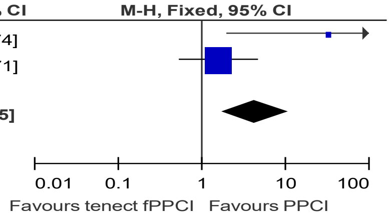


Figure 102: All-cause mortality (short-term)

Study or Subgroup	Tenecteplase (fPPCI) Events	Tenecteplase (fPPCI) Total	PPCI Events	PPCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ASSENT-4	55	823	41	831	91.0%	1.35 [0.91, 2.01]
LIPSIA-STEMI 2011	5	80	4	78	9.0%	1.22 [0.34, 4.37]
Total (95% CI)		**903**		**909**	**100.0%**	**1.34 [0.92, 1.95]**
Total events	60		45			

Heterogeneity: Chi² = 0.02, df = 1 (P = 0.88); I² = 0%
Test for overall effect: Z = 1.54 (P = 0.12)

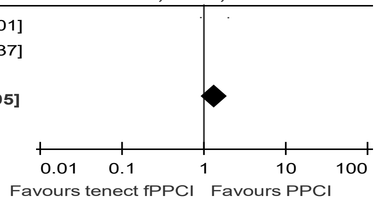


Figure 103: All-cause mortality (longer-term)

Study or Subgroup	Reteplase (fPPCI) Events	Reteplase (fPPCI) Total	PPCI Events	PPCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Liu 2012	1	72	6	71	100.0%	0.16 [0.02, 1.33]
Total (95% CI)		**72**		**71**	**100.0%**	**0.16 [0.02, 1.33]**
Total events	1		6			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.69 (P = 0.09)

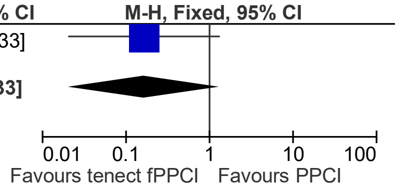


Figure 104: All-cause stroke (in-hospital)

Study or Subgroup	Tenecteplase (fPPCI) Events	Tenecteplase (fPPCI) Total	PPCI Events	PPCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ASSENT-4	15	829	0	838	49.7%	31.34 [1.88, 522.85]
ATHENS PCI 2009	1	143	0	141	50.3%	2.96 [0.12, 72.01]
Total (95% CI)		**972**		**979**	**100.0%**	**17.06 [2.29, 127.32]**
Total events	16		0			

Heterogeneity: Chi² = 1.34, df = 1 (P = 0.25); I² = 25%
Test for overall effect: Z = 2.77 (P = 0.006)

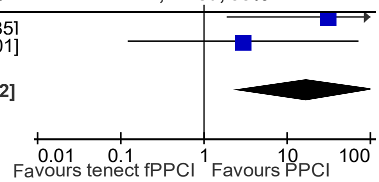


Figure 105: All-cause stroke (short-term)

Study or Subgroup	Tenecteplase (fPPCI) Events	Tenecteplase (fPPCI) Total	PPCI Events	PPCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ASSENT-4	7	829	1	838	49.6%	7.08 [0.87, 57.39]
LIPSIA-STEMI 2011	1	80	1	78	50.4%	0.97 [0.06, 15.32]
Total (95% CI)		**909**		**916**	**100.0%**	**4.00 [0.86, 18.67]**
Total events	8		2			

Heterogeneity: Chi² = 1.29, df = 1 (P = 0.26); I² = 23%
Test for overall effect: Z = 1.76 (P = 0.08)

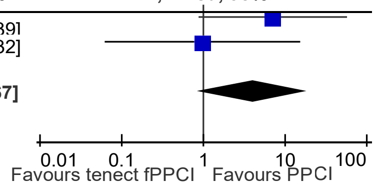


Figure 106: Non-fatal stroke (in-hospital)

Study or Subgroup	Tenecteplase (fPPCI) Events	Tenecteplase (fPPCI) Total	PPCI Events	PPCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ATHENS PCI 2009	1	143	0	141	100.0%	2.96 [0.12, 72.01]
Total (95% CI)		**143**		**141**	**100.0%**	**2.96 [0.12, 72.01]**
Total events	1		0			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.67 (P = 0.51)

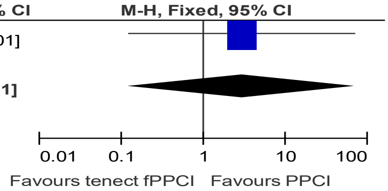


Figure 107: Reinfarction or non-fatal reinfarction or recurrent MI (short-term)

Study or Subgroup	Tenecteplase (fPPCI) Events	Total	PPCI Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ASSENT-4	49	805	30	820	80.8%	1.66 [1.07, 2.59]
LIPSIA-STEMI 2011	5	80	4	78	11.0%	1.22 [0.34, 4.37]
Liu 2012	1	72	3	71	8.2%	0.33 [0.04, 3.09]
Total (95% CI)		**957**		**969**	**100.0%**	**1.51 [1.00, 2.26]**
Total events	55		37			
Heterogeneity: Chi² = 2.07, df = 2 (P = 0.35); I² = 4%						
Test for overall effect: Z = 1.97 (P = 0.05)						

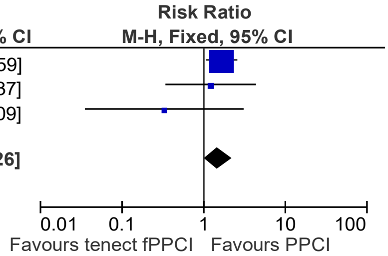


Figure 108: Intracranial bleeding or intracranial haemorrhage (in-hospital)

Study or Subgroup	Tenecteplase (fPPCI) Events	Total	PPCI Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ASSENT-4	8	719	0	763	100.0%	18.04 [1.04, 311.96]
ATHENS PCI 2009	0	143	0	141		Not estimable
Total (95% CI)		**862**		**904**	**100.0%**	**18.04 [1.04, 311.96]**
Total events	8		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.99 (P = 0.05)						

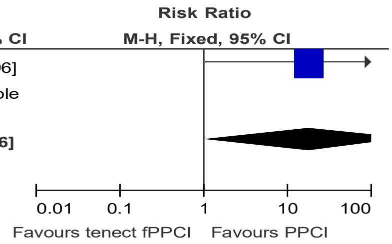


Figure 109: Intracranial bleeding or intracranial haemorrhage (short-term)

Study or Subgroup	Tenecteplase (fPPCI) Events	Total	PPCI Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Total (95% CI)		**829**		**838**	**100.0%**	**1.01 [0.06, 16.13]**
Total events	1		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.01 (P = 0.99)						

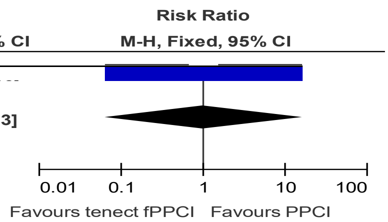


Figure 110: Intracranial bleeding or intracranial haemorrhage (longer-term)

Study or Subgroup	Reteplase (fPPCI) Events	Total	PPCI Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Liu 2012	0	72	0	71		Not estimable
Total (95% CI)		**72**		**71**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						

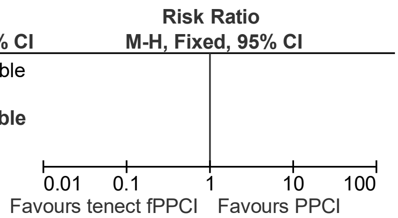


Figure 111: Major bleeding (in-hospital)

Study or Subgroup	Tenecteplase (fPPCI) Events	Total	PPCI Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ASSENT-4	46	719	37	763	87.7%	1.32 [0.87, 2.01]
ATHENS PCI 2009	8	143	5	141	12.3%	1.58 [0.53, 4.71]
Total (95% CI)		**862**		**904**	**100.0%**	**1.35 [0.91, 2.00]**
Total events	54		42			
Heterogeneity: Chi² = 0.09, df = 1 (P = 0.76); I² = 0%						
Test for overall effect: Z = 1.50 (P = 0.13)						

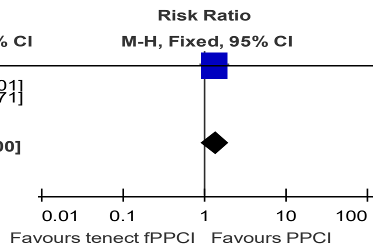


Figure 112: Major bleeding (longer-term)

Study or Subgroup	Reteplase (fPPCI) Events	Total	PPCI Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Liu 2012	0	72	0	71		Not estimable
Total (95% CI)		**72**		**71**		**Not estimable**
Total events	0		0			

Heterogeneity: Not applicable
Test for overall effect: Not applicable

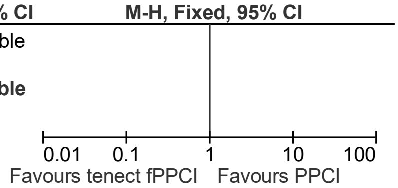


Figure 113: Minor bleeding (in-hospital)

Study or Subgroup	Tenecteplase (fPPCI) Events	Total	PPCI Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ASSENT-4	210	719	159	763	100.0%	1.40 [1.17, 1.68]
Total (95% CI)		**719**		**763**	**100.0%**	**1.40 [1.17, 1.68]**
Total events	210		159			

Heterogeneity: Not applicable
Test for overall effect: Z = 3.69 (P = 0.0002)

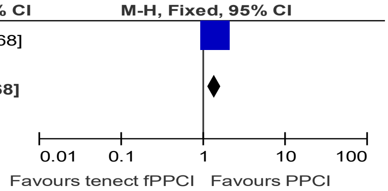


Figure 114: Minor bleeding (longer-term)

Study or Subgroup	Tenecteplase (fPPCI) Events	Total	PPCI Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Liu 2012	8	72	7	71	100.0%	1.13 [0.43, 2.94]
Total (95% CI)		**72**		**71**	**100.0%**	**1.13 [0.43, 2.94]**
Total events	8		7			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.24 (P = 0.81)

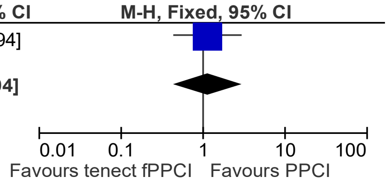


Figure 115: Heart failure (in-hospital)

Study or Subgroup	Tenecteplase (fPPCI) Events	Total	PPCI Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ATHENS PCI 2009	24	143	5	141	100.0%	4.73 [1.86, 12.06]
Total (95% CI)		**143**		**141**	**100.0%**	**4.73 [1.86, 12.06]**
Total events	24		5			

Heterogeneity: Not applicable
Test for overall effect: Z = 3.26 (P = 0.001)

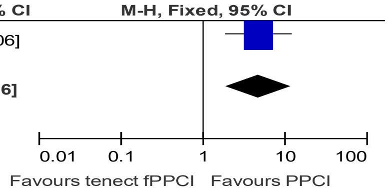


Figure 116: Heart failure (short-term)

Study or Subgroup	Tenecteplase (fPPCI) Events	Total	PPCI Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ASSENT-4	97	807	75	818	96.1%	1.31 [0.99, 1.74]
LIPSIA-STEMI 2011	6	80	3	78	3.9%	1.95 [0.51, 7.52]
Total (95% CI)		**887**		**896**	**100.0%**	**1.34 [1.01, 1.77]**
Total events	103		78			

Heterogeneity: $Chi^2 = 0.32$, df = 1 (P = (.57); $I^2 = 0\%$
Test for overall effect: Z = 2.04 (P = 0.04)

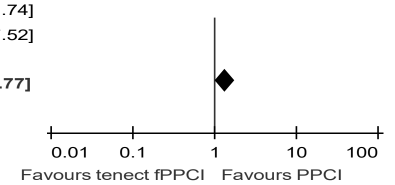


Figure 117: Heart failure (longer-term)

Study or Subgroup	Reteplase (fPPCI) Events	Reteplase (fPPCI) Total	PPCI Events	PPCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Liu 2012	2	72	9	71	100.0%	0.22 [0.05, 0.98]
Total (95% CI)		**72**		**71**	**100.0%**	**0.22 [0.05, 0.98]**
Total events	2		9			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.99 (P = 0.05)

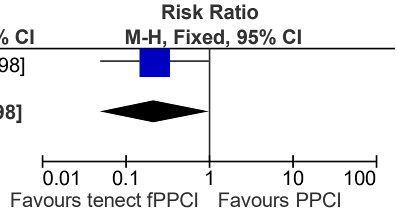
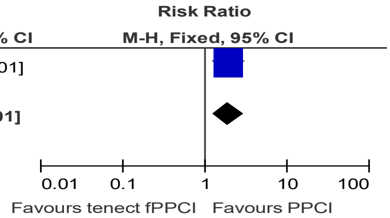


Figure 118: Repeat revascularisation – repeat or urgent (short-term)

Study or Subgroup	Tenecteplase (fPPCI) Events	Tenecteplase (fPPCI) Total	PPCI Events	PPCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ASSENT-4	53	805	28	818	100.0%	1.92 [1.23, 3.01]
Total (95% CI)		**805**		**818**	**100.0%**	**1.92 [1.23, 3.01]**
Total events	53		28			

Heterogeneity: Not applicable
Test for overall effect: Z = 2.87 (P = 0.004)



I.2.11 Fibrinolytics: fPPCI versus PPCI - tenecteplase

Figure 119: All-cause mortality (in-hospital)

Study or Subgroup	Tenecteplase (fPPCI) Events	Tenecteplase (fPPCI) Total	PPCI Events	PPCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ASSENT-4	15	719	0	763	8.8%	32.89 [1.97, 548.74]
ATHENS PCI 2009	8	143	5	141	91.2%	1.58 [0.53, 4.71]
Total (95% CI)		**862**		**904**	**100.0%**	**4.33 [1.74, 10.75]**
Total events	23		5			

Heterogeneity: Chi² = 5.27, df = 1 (P = 0.02); I² = 81%
Test for overall effect: Z = 3.16 (P = 0.002)

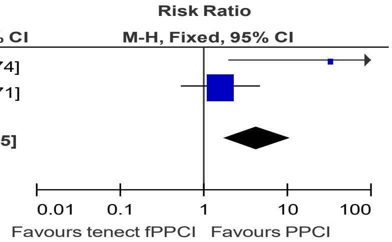


Figure 120: All-cause mortality (short-term)

Study or Subgroup	Tenecteplase (fPPCI) Events	Tenecteplase (fPPCI) Total	PPCI Events	PPCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ASSENT-4	55	823	41	831	91.0%	1.35 [0.91, 2.01]
LIPSIA-STEMI 2011	5	80	4	78	9.0%	1.22 [0.34, 4.37]
Total (95% CI)		**903**		**909**	**100.0%**	**1.34 [0.92, 1.95]**
Total events	60		45			

Heterogeneity: Chi² = 0.02, df = 1 (P = 0.88); I² = 0%
Test for overall effect: Z = 1.54 (P = 0.12)

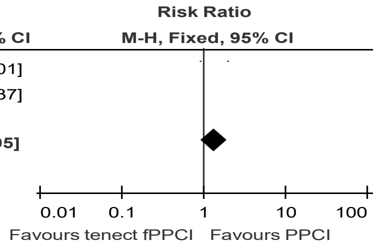


Figure 121: All-cause stroke (in-hospital)

Study or Subgroup	Tenecteplase (fPPCI) Events	Tenecteplase (fPPCI) Total	PPCI Events	PPCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ASSENT-4	15	829	0	838	49.7%	31.34 [1.88, 522.85]
ATHENS PCI 2009	1	143	0	141	50.3%	2.96 [0.12, 72.01]
Total (95% CI)		**972**		**979**	**100.0%**	**17.06 [2.29, 127.32]**
Total events	16		0			

Heterogeneity: Chi² = 1.34, df = 1 (P = 0.25); I² = 25%
Test for overall effect: Z = 2.77 (P = 0.006)

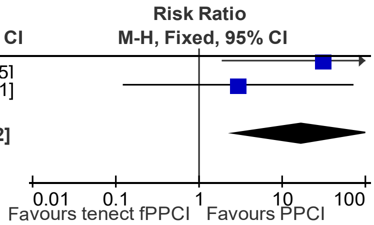


Figure 122: All-cause stroke (short-term)

Study or Subgroup	Tenecteplase (fPPCI) Events	Tenecteplase (fPPCI) Total	PPCI Events	PPCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ASSENT-4	7	829	1	838	49.6%	7.08 [0.87, 57.39]
LIPSIA-STEMI 2011	1	80	1	78	50.4%	0.97 [0.06, 15.32]
Total (95% CI)		**909**		**916**	**100.0%**	**4.00 [0.86, 18.67]**
Total events	8		2			

Heterogeneity: Chi² = 1.29, df = 1 (P = 0.26); I² = 23%
Test for overall effect: Z = 1.76 (P = 0.08)

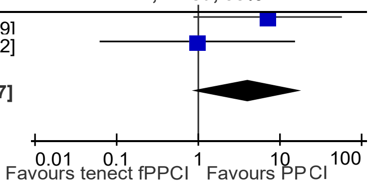


Figure 123: Non-fatal stroke (in-hospital)

Study or Subgroup	Tenecteplase (fPPCI) Events	Tenecteplase (fPPCI) Total	PPCI Events	PPCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ATHENS PCI 2009	1	143	0	141	100.0%	2.96 [0.12, 72.01]
Total (95% CI)		**143**		**141**	**100.0%**	**2.96 [0.12, 72.01]**
Total events	1		0			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.67 (P = 0.51)

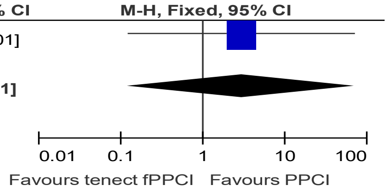


Figure 124: Reinfarction or non-fatal reinfarction or recurrent MI (short-term)

Study or Subgroup	Tenecteplase (fPPCI) Events	Tenecteplase (fPPCI) Total	PPCI Events	PPCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ASSENT-4	49	805	30	820	88.0%	1.66 [1.07, 2.59]
LIPSIA-STEMI 2011	5	80	4	78	12.0%	1.22 [0.34, 4.37]
Total (95% CI)		**885**		**898**	**100.0%**	**1.61 [1.06, 2.45]**
Total events	54		34			

Heterogeneity: Chi² = 0.20, df = 1 (P = 0.65); I² = 0%
Test for overall effect: Z = 2.23 (P = 0.03)

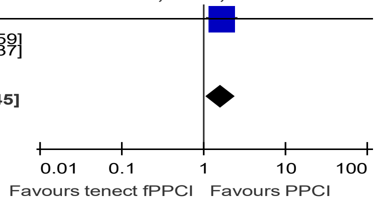


Figure 125: Intracranial bleeding or intracranial haemorrhage (in-hospital)

Study or Subgroup	Tenecteplase (fPPCI) Events	Tenecteplase (fPPCI) Total	PPCI Events	PPCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ASSENT-4	8	719	0	763	100.0%	18.04 [1.04, 311.96]
ATHENS PCI 2009	0	143	0	141		Not estimable
Total (95% CI)		**862**		**904**	**100.0%**	**18.04 [1.04, 311.96]**
Total events	8		0			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.99 (P = 0.05)

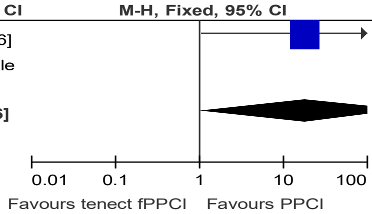


Figure 126: Intracranial bleeding or intracranial haemorrhage (short-term)

Study or Subgroup	Tenecteplase (fPPCI) Events	Tenecteplase (fPPCI) Total	PPCI Events	PPCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ASSENT-4	1	829	1	838	100.0%	1.01 [0.06, 16.13]
Total (95% CI)		**829**		**838**	**100.0%**	**1.01 [0.06, 16.13]**
Total events	1		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.01 (P = 0.99)

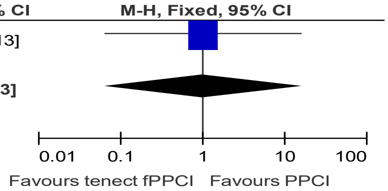


Figure 127: Major bleeding (in-hospital)

Study or Subgroup	Tenecteplase (fPPCI) Events	Tenecteplase (fPPCI) Total	PPCI Events	PPCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ASSENT-4	46	719	37	763	87.7%	1.32 [0.87, 2.01]
ATHENS PCI 2009	8	143	5	141	12.3%	1.58 [0.53, 4.71]
Total (95% CI)		**862**		**904**	**100.0%**	**1.35 [0.91, 2.00]**
Total events	54		42			

Heterogeneity: Chi² = 0.09, df = 1 (P = (.76); I² = 0%
Test for overall effect: Z = 1.50 (P = 0.13)

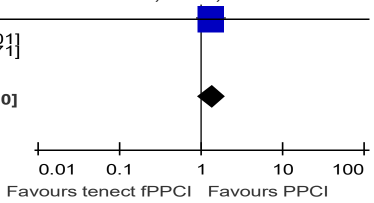
Risk Ratio M-H, Fixed, 95% CI


Figure 128: Minor bleeding (in-hospital)

Study or Subgroup	Tenecteplase (fPPCI) Events	Tenecteplase (fPPCI) Total	PPCI Events	PPCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ASSENT-4	210	719	159	763	100.0%	1.40 [1.17, 1.68]
Total (95% CI)		**719**		**763**	**100.0%**	**1.40 [1.17, 1.68]**
Total events	210		159			

Heterogeneity: Not applicable
Test for overall effect: Z = 3.69 (P = 0.0002)

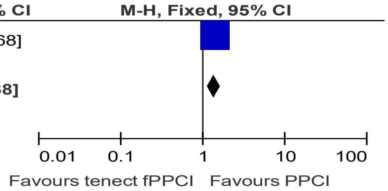
Risk Ratio M-H, Fixed, 95% CI


Figure 129: Heart failure (in-hospital)

Study or Subgroup	Tenecteplase (fPPCI) Events	Tenecteplase (fPPCI) Total	PPCI Events	PPCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ATHENS PCI 2009	24	143	5	141	100.0%	4.73 [1.86, 12.06]
Total (95% CI)		**143**		**141**	**100.0%**	**4.73 [1.86, 12.06]**
Total events	24		5			

Heterogeneity: Not applicable
Test for overall effect: Z = 3.26 (P = 0.001)

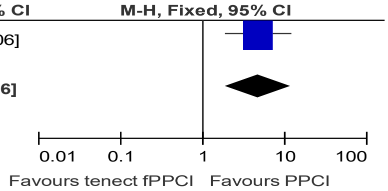
Risk Ratio M-H, Fixed, 95% CI


Figure 130: Heart failure (short-term)

Study or Subgroup	Tenecteplase (fPPCI) Events	Tenecteplase (fPPCI) Total	PPCI Events	PPCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ASSENT-4	97	807	75	818	96.1%	1.31 [0.99, 1.74]
LIPSIA-STEMI 2011	6	80	3	78	3.9%	1.95 [0.51, 7.52]
Total (95% CI)		**887**		**896**	**100.0%**	**1.34 [1.01, 1.77]**
Total events	103		78			

Heterogeneity: Chi² = 0.32, df = 1 (P = (.57); I² = 0%
Test for overall effect: Z = 2.04 (P = 0.04)

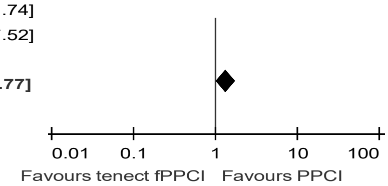
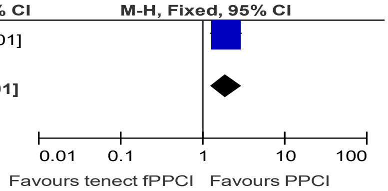
Risk Ratio M-H, Fixed, 95% CI


Figure 131: Repeat revascularisation – repeat or urgent (short-term)

Study or Subgroup	Tenecteplase (fPPCI) Events	Tenecteplase (fPPCI) Total	PPCI Events	PPCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ASSENT-4	53	805	28	818	100.0%	1.92 [1.23, 3.01]
Total (95% CI)		**805**		**818**	**100.0%**	**1.92 [1.23, 3.01]**
Total events	53		28			

Heterogeneity: Not applicable
Test for overall effect: Z = 2.87 (P = 0.004)

Risk Ratio M-H, Fixed, 95% CI


I.2.12 Fibrinolytics: fPPCI versus PPCI - reteplase

Figure 132: All-cause mortality (longer-term)

Study or Subgroup	Reteplase (fPPCI) Events	Reteplase (fPPCI) Total	PPCI Events	PPCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Liu 2012	1	72	6	71	100.0%	0.16 [0.02, 1.33]
Total (95% CI)		**72**		**71**	**100.0%**	**0.16 [0.02, 1.33]**
Total events	1		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.69 (P = 0.09)						

Risk Ratio
M-H, Fixed, 95% CI

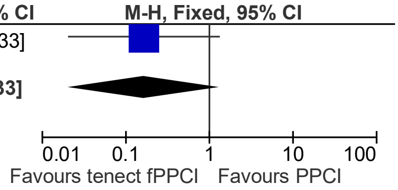


Figure 133: Reinfarction or non-fatal reinfarction or recurrent MI (short-term)

Study or Subgroup	Reteplase (fPPCI) Events	Reteplase (fPPCI) Total	PPCI Events	PPCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Liu 2012	1	72	3	71	100.0%	0.33 [0.04, 3.09]
Total (95% CI)		**72**		**71**	**100.0%**	**0.33 [0.04, 3.09]**
Total events	1		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.97 (P = 0.33)						

Risk Ratio
M-H, Fixed, 95% CI

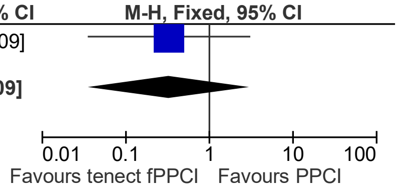


Figure 134: Intracranial bleeding or intracranial haemorhage (longer-term)

Study or Subgroup	Reteplase (fPPCI) Events	Reteplase (fPPCI) Total	PPCI Events	PPCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Liu 2012	0	72	0	71		Not estimable
Total (95% CI)		**72**		**71**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						

Risk Ratio
M-H, Fixed, 95% CI

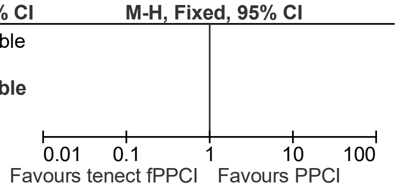


Figure 135: Major bleeding (longer-term)

Study or Subgroup	Reteplase (fPPCI) Events	Reteplase (fPPCI) Total	PPCI Events	PPCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Liu 2012	0	72	0	71		Not estimable
Total (95% CI)		**72**		**71**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						

Risk Ratio
M-H, Fixed, 95% CI

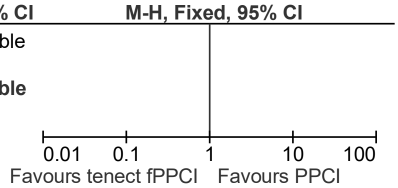


Figure 136: Minor bleeding (longer-term)

Study or Subgroup	Tenecteplase (fPPCI) Events	Tenecteplase (fPPCI) Total	PPCI Events	PPCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Liu 2012	8	72	7	71	100.0%	1.13 [0.43, 2.94]
Total (95% CI)		**72**		**71**	**100.0%**	**1.13 [0.43, 2.94]**
Total events	8		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.24 (P = 0.81)						

Risk Ratio
M-H, Fixed, 95% CI

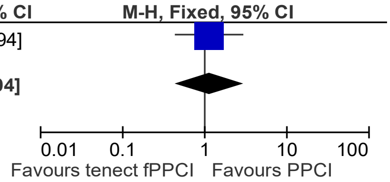
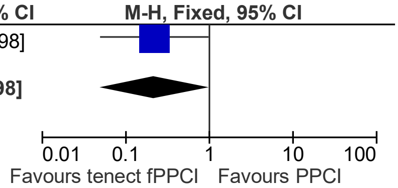


Figure 137: Heart failure (longer-term)

Study or Subgroup	Reteplase (fPPCI) Events	Reteplase (fPPCI) Total	PPCI Events	PPCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Liu 2012	2	72	9	71	100.0%	0.22 [0.05, 0.98]
Total (95% CI)		**72**		**71**	**100.0%**	**0.22 [0.05, 0.98]**
Total events	2		9			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.99 (P = 0.05)



I.2.13 Combination: fPPCI (GPI + fibrinolytic) versus PPCI

Figure 138: All-cause stroke (short-term)

Study or Subgroup	Abcix + rete fPPCI Events	Abcix + rete fPPCI Total	PPCI(placebo) Events	PPCI(placebo) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
FINESSE 2008	4	805	8	795	100.0%	0.49 [0.15, 1.63]
Total (95% CI)		805		795	100.0%	0.49 [0.15, 1.63]
Total events	4		8			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.16 (P = 0.25)

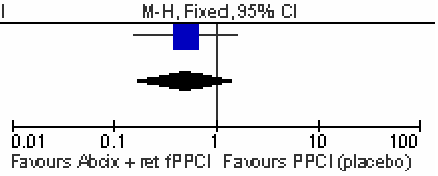


Figure 139: Fatal stroke (short-term)

Study or Subgroup	Abcix + rete fPPCI Events	Abcix + rete fPPCI Total	PPCI (placebo) Events	PPCI (placebo) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
FINESSE 2008	0	805	0	795		Not estimable
Total (95% CI)		**805**		**795**		**Not estimable**
Total events	0		0			

Heterogeneity: Not applicable
Test for overall effect: Not applicable

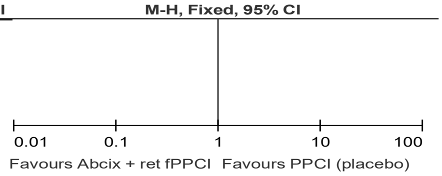


Figure 140: Recurrent MI (short-term)

Study or Subgroup	Abcix + rete fPPCI Events	Abcix + rete fPPCI Total	PPCI (placebo) Events	PPCI (placebo) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
FINESSE 2008	17	828	15	806	100.0%	1.10 [0.55, 2.19]
Total (95% CI)		**828**		**806**	**100.0%**	**1.10 [0.55, 2.19]**
Total events	17		15			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.28 (P = 0.78)

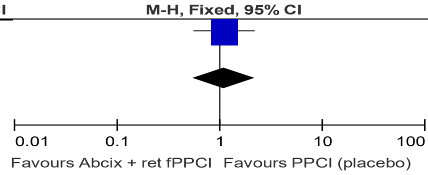


Figure 141: Intracranial bleeding or intracranial haemorrhage (short-term)

Study or Subgroup	Abcix + rete fPPCI Events	Abcix + rete fPPCI Total	PPCI (placebo) Events	PPCI (placebo) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
FINESSE 2008	0	805	1	795	100.0%	0.33 [0.01, 8.07]
Total (95% CI)		**805**		**795**	**100.0%**	**0.33 [0.01, 8.07]**
Total events	0		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.68 (P = 0.50)

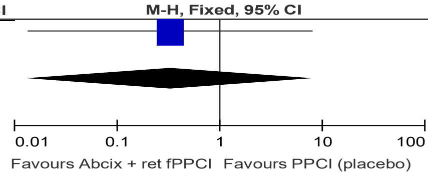


Figure 142: Major bleeding (short-term)

Study or Subgroup	Abcix + rete fPPCI Events	Abcix + rete fPPCI Total	PPCI (placebo) Events	PPCI (placebo) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
FINESSE 2008	33	805	21	795	100.0%	1.55 [0.91, 2.66]
Total (95% CI)		**805**		**795**	**100.0%**	**1.55 [0.91, 2.66]**
Total events	33		21			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.60 (P = 0.11)

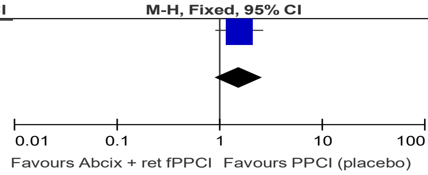


Figure 143: Minor bleeding (short-term)

Study or Subgroup	Abcix + rete fPPCI Events	Abcix + rete fPPCI Total	PPCI (placebo) Events	PPCI (placebo) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
FINESSE 2008	48	805	34	795	100.0%	1.39 [0.91, 2.14]
Total (95% CI)		**805**		**795**	**100.0%**	**1.39 [0.91, 2.14]**
Total events	48		34			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.52 (P = 0.13)

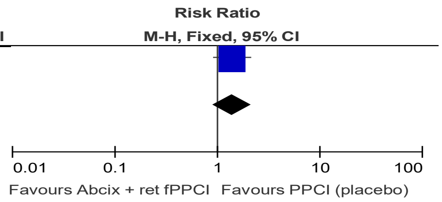


Figure 144: Heart failure (short-term)

Study or Subgroup	Abcix + rete fPPCI Events	Abcix + rete fPPCI Total	PPCI (placebo) Events	PPCI (placebo) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
FINESSE 2008	54	828	52	806	100.0%	1.01 [0.70, 1.46]
Total (95% CI)		**828**		**806**	**100.0%**	**1.01 [0.70, 1.46]**
Total events	54		52			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.06 (P = 0.95)

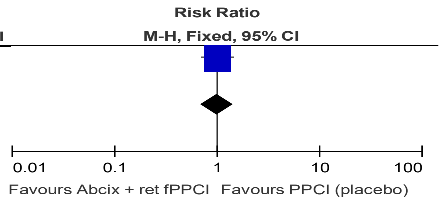
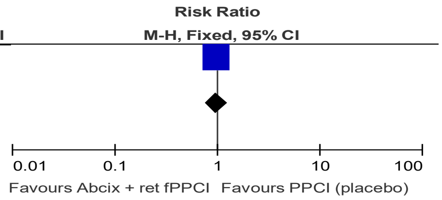


Figure 145: Repeat revascularisation (short-term)

Study or Subgroup	Abcix + rete fPPCI Events	Abcix + rete fPPCI Total	PPCI (placebo) Events	PPCI (placebo) Total	Weight	Risk Ratio M-H, Fixed, 95% CI
FINESSE 2008	111	828	111	806	100.0%	0.97 [0.76, 1.24]
Total (95% CI)		**828**		**806**	**100.0%**	**0.97 [0.76, 1.24]**
Total events	111		111			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.22 (P = 0.83)



I.3 Radial versus femoral arterial access for PPCI

Figure 146: All-cause mortality (≤ 30 days)

Study or Subgroup	Radial access Events	Radial access Total	Femoral access Events	Femoral access Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Brasselet 2007	3	57	3	57	3.1%	1.00 [0.21, 4.75]
GAN 2009	2	90	3	105	2.9%	0.78 [0.13, 4.55]
HOU 2010	4	100	5	100	5.2%	0.80 [0.22, 2.89]
RADIAMI 2009	0	50	1	50	1.6%	0.33 [0.01, 7.99]
RADIAMI II 2011	0	49	0	59		Not estimable
RIFLE-STEACS 2012	26	500	46	501	48.0%	0.57 [0.36, 0.90]
RIVAL 2011	12	955	32	1003	32.6%	0.39 [0.20, 0.76]
TEMPURA 2003	4	77	6	72	6.5%	0.62 [0.18, 2.12]
Total (95% CI)		**1878**		**1947**	**100.0%**	**0.54 [0.39, 0.75]**
Total events	51		96			

Heterogeneity: $Chi^2 = 2.19$, df = 6 (P = 0.90); $I^2 = 0\%$
Test for overall effect: Z = 3.63 (P = 0.0003)

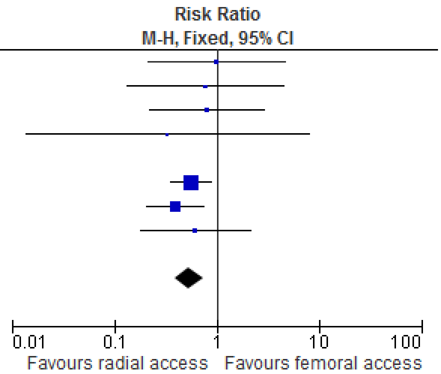
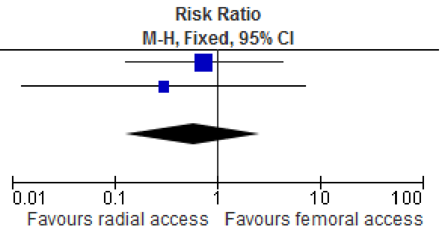


Figure 147: All-cause mortality (longer-term)

Study or Subgroup	Radial access Events	Radial access Total	Femoral access Events	Femoral access Total	Weight	Risk Ratio M-H, Fixed, 95% CI
GAN 2009	2	79	3	88	64.3%	0.74 [0.13, 4.33]
TEMPURA 2003	0	73	1	66	35.7%	0.30 [0.01, 7.28]
Total (95% CI)		**152**		**154**	**100.0%**	**0.59 [0.13, 2.66]**
Total events	2		4			

Heterogeneity: $Chi^2 = 0.24$, df = 1 (P = 0.63); $I^2 = 0\%$
Test for overall effect: Z = 0.69 (P = 0.49)



6 months TEMPURA 2003, 9 months; GAN 2009

Figure 148: Reinfarction (≤ 30 days)

Study or Subgroup	Radial access Events	Radial access Total	Femoral access Events	Femoral access Total	Weight	Risk Ratio M-H, Fixed, 95% CI
GAN 2009	0	90	2	105	8.4%	0.23 [0.01, 4.79]
HOU 2010	0	100	0	100		Not estimable
RADIAMI 2009	1	25	0	25	1.8%	3.00 [0.13, 70.30]
RADIAMI II 2011	0	49	0	59		Not estimable
RIFLE-STEACS 2012	6	500	7	501	25.6%	0.86 [0.29, 2.54]
RIVAL 2011	11	955	18	1003	64.2%	0.64 [0.30, 1.35]
TEMPURA 2003	0	77	0	72		Not estimable
Total (95% CI)		**1796**		**1865**	**100.0%**	**0.71 [0.40, 1.26]**
Total events	18		27			

Heterogeneity: Chi² = 1.51, df = 3 (P = 0.68); I² = 0%
Test for overall effect: Z = 1.18 (P = 0.24)

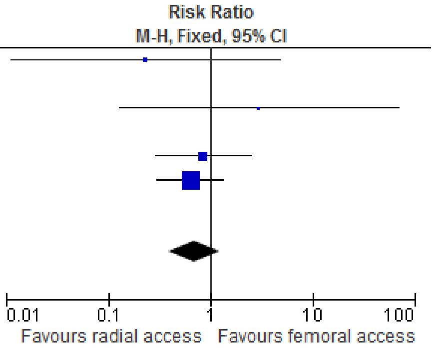
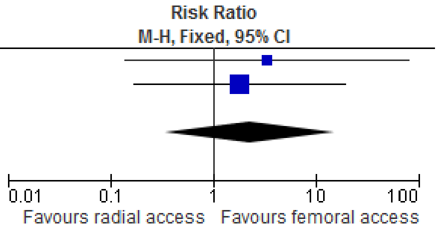


Figure 149: Reinfarction (longer-term)

Study or Subgroup	Radial access Events	Radial access Total	Femoral access Events	Femoral access Total	Weight	Risk Ratio M-H, Fixed, 95% CI
GAN 2009	1	79	0	88	31.1%	3.34 [0.14, 80.77]
TEMPURA 2003	2	73	1	66	68.9%	1.81 [0.17, 19.48]
Total (95% CI)		**152**		**154**	**100.0%**	**2.28 [0.35, 15.06]**
Total events	3		1			

Heterogeneity: Chi² = 0.09, df = 1 (P = 0.76); I² = 0%
Test for overall effect: Z = 0.86 (P = 0.39)



6 months TEMPURA 2003, 9 months; GAN 2009

Figure 150: Major bleeding (≤ 30 days)

Study or Subgroup	Radial access Events	Radial access Total	Femoral access Events	Femoral access Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Brasselet 2007	3	57	3	57	6.9%	1.00 [0.21, 4.75]
GAN 2009	0	90	2	105	5.3%	0.23 [0.01, 4.79]
HOU 2010	0	100	3	100	8.0%	0.14 [0.01, 2.73]
RADIAMI 2009	3	50	7	50	16.0%	0.43 [0.12, 1.56]
RADIAMI II 2011	4	49	6	59	12.5%	0.80 [0.24, 2.68]
RIFLE-STEACS 2012	9	500	14	501	32.0%	0.64 [0.28, 1.47]
RIVAL 2011	8	955	6	1003	13.4%	1.40 [0.49, 4.02]
TEMPURA 2003	0	77	2	72	5.9%	0.19 [0.01, 3.83]
Total (95% CI)		**1878**		**1947**	**100.0%**	**0.67 [0.42, 1.06]**
Total events	27		43			

Heterogeneity: Chi² = 4.90, df = 7 (P = 0.67); I² = 0%
Test for overall effect: Z = 1.73 (P = 0.08)

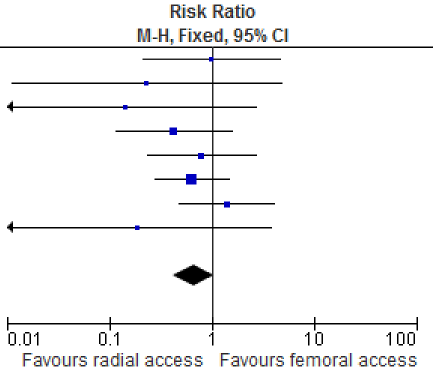


Figure 151: Minor bleeding (≤ 30 days)

Study or Subgroup	Radial access Events	Radial access Total	Femoral access Events	Femoral access Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Brasselet 2007	0	57	1	57	1.6%	0.33 [0.01, 8.01]
GAN 2009	1	90	0	105	0.5%	3.49 [0.14, 84.73]
HOU 2010	2	100	6	100	6.6%	0.33 [0.07, 1.61]
Li 2007	2	184	7	186	7.6%	0.29 [0.06, 1.37]
RADIAMI 2009	5	50	8	50	8.8%	0.63 [0.22, 1.78]
RADIAMI II 2011	8	49	12	59	11.9%	0.80 [0.36, 1.81]
RIFLE-STEACS 2012	20	500	36	501	39.4%	0.56 [0.33, 0.95]
RIVAL 2011	33	955	22	1003	23.5%	1.58 [0.93, 2.68]
Total (95% CI)		**1985**		**2061**	**100.0%**	**0.81 [0.60, 1.09]**
Total events	71		92			

Heterogeneity: Chi² = 12.16, df = 7 (P = 0.10); I² = 42%
Test for overall effect: Z = 1.41 (P = 0.16)

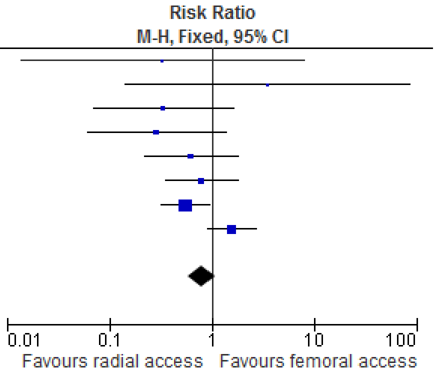


Figure 152: Repeat revascularisation (≤ 30 days)

Study or Subgroup	Radial access Events	Radial access Total	Femoral access Events	Femoral access Total	Weight	Risk Ratio M-H, Fixed, 95% CI
HOU 2010	0	100	0	100		Not estimable
RADIAMI 2009	1	50	2	50	21.2%	0.50 [0.05, 5.34]
RADIAMI II 2011	1	49	0	59	4.8%	3.60 [0.15, 86.44]
RIFLE-STEACS 2012	6	500	7	501	74.0%	0.86 [0.29, 2.54]
TEMPURA 2003	0	77	0	72		Not estimable
Total (95% CI)		**776**		**782**	**100.0%**	**0.91 [0.37, 2.28]**
Total events	8		9			

Heterogeneity: Chi² = 0.98, df = 2 (P = 0.61); I² = 0%
Test for overall effect: Z = 0.19 (P = 0.85)

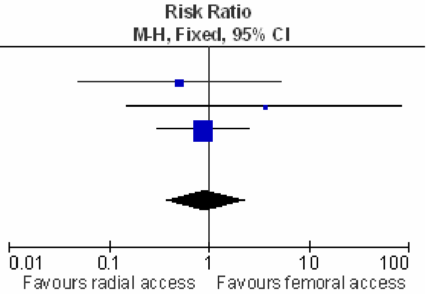
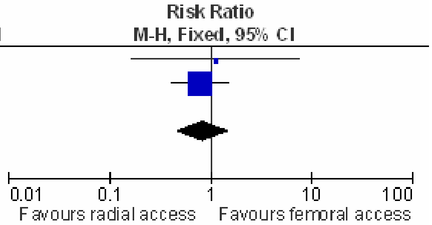


Figure 153: Repeat revascularisation (longer-term)

Study or Subgroup	Radial access Events	Radial access Total	Femoral access Events	Femoral access Total	Weight	Risk Ratio M-H, Fixed, 95% CI
GAN 2009	2	79	2	88	10.7%	1.11 [0.16, 7.72]
TEMPURA 2003	13	73	15	66	89.3%	0.78 [0.40, 1.52]
Total (95% CI)		**152**		**154**	**100.0%**	**0.82 [0.44, 1.54]**
Total events	15		17			

Heterogeneity: Chi² = 0.11, df = 1 (P = 0.74); I² = 0%
Test for overall effect: Z = 0.62 (P = 0.53)



6 months TEMPURA 2003, 9 months; GAN 2009

Figure 154: CABG (≤ 30 days)

Study or Subgroup	Radial access Events	Radial access Total	Femoral access Events	Femoral access Total	Weight	Risk Ratio M-H, Fixed, 95% CI
GAN 2009	0	90	0	105		Not estimable
RADIAMI 2009	0	50	0	50		Not estimable
RADIAMI II 2011	0	49	0	59		Not estimable
Total (95% CI)		**189**		**214**		**Not estimable**
Total events	0		0			

Heterogeneity: Not applicable
Test for overall effect: Not applicable

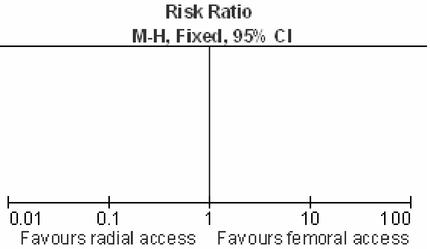
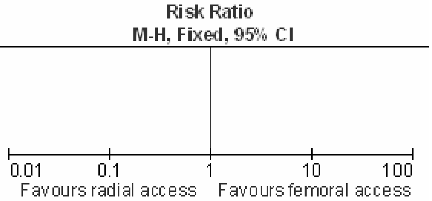


Figure 155: CABG (longer-term)

Study or Subgroup	Radial access Events	Radial access Total	Femoral access Events	Femoral access Total	Weight	Risk Ratio M-H, Fixed, 95% CI
GAN 2009	0	79	0	88		Not estimable
Total (95% CI)		**79**		**88**		**Not estimable**
Total events	0		0			

Heterogeneity: Not applicable
Test for overall effect: Not applicable



9 months GAN 2009

Figure 156: Stroke (short-term)

Study or Subgroup	Radial access Events	Radial access Total	Femoral access Events	Femoral access Total	Weight	Risk Ratio M-H, Fixed, 95% CI
RADIAMI 2009	0	50	1	50	17.9%	0.33 [0.01, 7.99]
RIFLE-STEACS 2012	4	500	3	501	35.7%	1.34 [0.30, 5.94]
RIVAL 2011	5	955	4	1003	46.5%	1.31 [0.35, 4.87]
Total (95% CI)		**1505**		**1554**	**100.0%**	**1.15 [0.46, 2.88]**
Total events	9		8			

Heterogeneity: Chi² = 0.66, df = 2 (P = 0.72); I² = 0%
Test for overall effect: Z = 0.29 (P = 0.77)

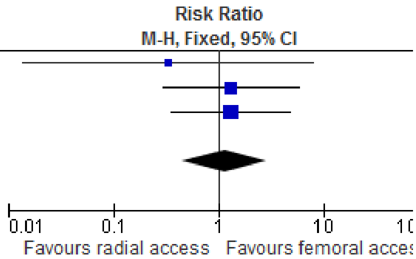


Figure 157: Access site crossover

Study or Subgroup	Radial access Events	Radial access Total	Femoral access Events	Femoral access Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Brasselet 2007	7	57	1	57	2.8%	7.00 [0.89, 55.08]
GAN 2009	1	90	0	105	1.3%	3.49 [0.14, 84.73]
HOU 2010	4	100	0	100	1.4%	9.00 [0.49, 165.00]
Li 2007	3	184	2	186	5.5%	1.52 [0.26, 8.97]
RADIAMI 2009	4	50	1	50	2.8%	4.00 [0.46, 34.54]
RADIAMI II 2011	2	49	1	59	2.5%	2.41 [0.23, 25.77]
RIFLE-STEACS 2012	47	500	14	501	38.9%	3.36 [1.88, 6.03]
RIVAL 2011	51	955	16	1003	43.4%	3.35 [1.92, 5.83]
TEMPURA 2003	1	77	0	72	1.4%	2.81 [0.12, 67.83]
Total (95% CI)		**2062**		**2133**	**100.0%**	**3.42 [2.38, 4.93]**
Total events	120		35			

Heterogeneity: Chi² = 1.82, df = 8 (P = 0.99); I² = 0%
Test for overall effect: Z = 6.62 (P < 0.00001)

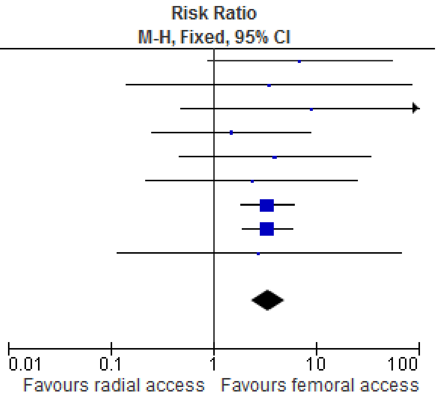


Figure 158: Angiographic procedural success

Study or Subgroup	Radial access Events	Radial access Total	Femoral access Events	Femoral access Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Brasselet 2007	52	57	55	57	3.0%	0.95 [0.86, 1.04]
GAN 2009	87	90	101	105	5.1%	1.00 [0.95, 1.06]
HOU 2010	96	100	95	100	5.2%	1.01 [0.95, 1.07]
Li 2007	174	184	175	185	9.6%	1.00 [0.95, 1.05]
RADIAMI 2009	44	50	46	50	2.5%	0.96 [0.84, 1.09]
RADIAMI II 2011	49	49	58	59	2.9%	1.02 [0.97, 1.07]
RIFLE-STEACS 2012	435	500	436	501	23.9%	1.00 [0.95, 1.05]
RIVAL 2011	789	825	806	842	43.8%	1.00 [0.98, 1.02]
TEMPURA 2003	74	77	70	72	4.0%	0.99 [0.93, 1.05]
Total (95% CI)		**1932**		**1971**	**100.0%**	**1.00 [0.98, 1.01]**
Total events	1800		1842			

Heterogeneity: Chi² = 2.51, df = 8 (P = 0.96); I² = 0%
Test for overall effect: Z = 0.29 (P = 0.77)

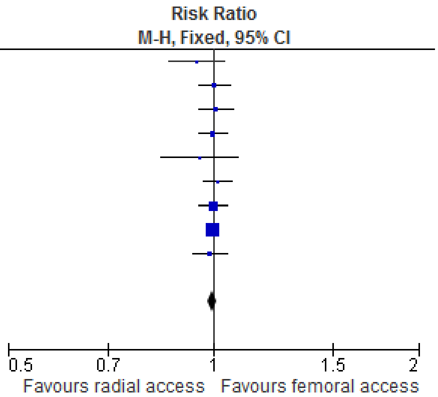


Figure 159: Fluoroscopy time

Study or Subgroup	Radial access Mean [min]	Radial access SD [min]	Radial access Total	Femoral access Mean [min]	Femoral access SD [min]	Femoral access Total	Weight	Mean Difference IV, Fixed, 95% CI [min]
Brasselet 2007	28	14	57	26	18	57	0.6%	2.00 [-3.92, 7.92]
HOU 2010	11.2	2	100	11.4	1.8	100	76.2%	-0.20 [-0.73, 0.33]
RADIAMI 2009	10.9	5.6	50	11.2	7	50	3.4%	-0.30 [-2.78, 2.18]
RADIAMI II 2011	7	3	49	7.5	3	59	16.4%	-0.50 [-1.64, 0.64]
TEMPURA 2003	15.1	7.6	77	16.1	7.9	72	3.4%	-1.00 [-3.49, 1.49]
Total (95% CI)			**333**			**338**	**100.0%**	**-0.27 [-0.73, 0.19]**

Heterogeneity: Chi² = 1.12, df = 4 (P = 0.89); I² = 0%
Test for overall effect: Z = 1.14 (P = 0.26)

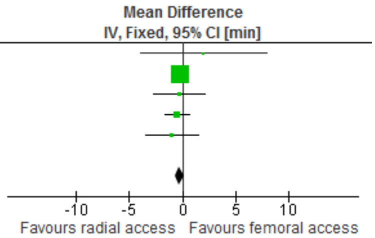


Figure 160: Total radiographic contrast media used in PPCI procedure

Study or Subgroup	Radial access Mean [ml]	Radial access SD [ml]	Radial access Total	Femoral access Mean [ml]	Femoral access SD [ml]	Femoral access Total	Weight	Mean Difference IV, Fixed, 95% CI [ml]
Brasselet 2007	97	57	57	91	47	57	25.4%	6.00 [-13.18, 25.18]
RADIAMI 2009	198.7	45.7	50	197.7	50	59	28.9%	1.00 [-16.98, 18.98]
RADIAMI II 2011	165	41.4	49	162	59	50	23.3%	3.00 [-17.05, 23.05]
TEMPURA 2003	180	61	77	186	66	72	22.4%	-6.00 [-26.45, 14.45]
Total (95% CI)			**233**			**238**	**100.0%**	**1.17 [-8.50, 10.84]**

Heterogeneity: Chi² = 0.75, df = 3 (P = 0.86); I² = 0%
Test for overall effect: Z = 0.24 (P = 0.81)

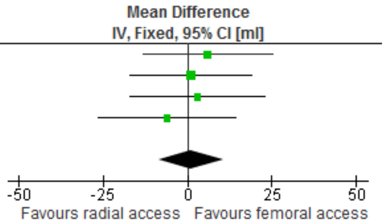


Figure 161: Vascular access site complications

Study or Subgroup	Radial access Events	Radial access Total	Femoral access Events	Femoral access Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Brasselet 2007	0	57	0	0		Not estimable
GAN 2009	1	100	10	100	21.9%	0.10 [0.01, 0.77]
HOU 2010	0	100	2	100	5.5%	0.20 [0.01, 4.11]
RIVAL 2011	12	955	34	1003	72.6%	0.37 [0.19, 0.71]
Total (95% CI)		**1212**		**1203**	**100.0%**	**0.30 [0.17, 0.55]**
Total events	13		46			

Heterogeneity: Chi² = 1.58, df = 2 (P = 0.45); I² = 0%
Test for overall effect: Z = 3.91 (P < 0.0001)

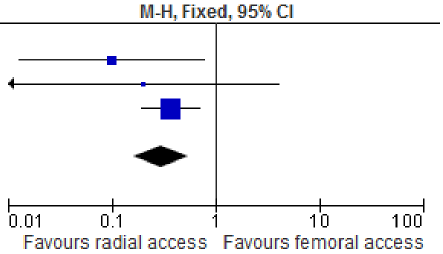


Figure 162: Length of hospital stay

Study or Subgroup	Radial access Mean [days]	Radial access SD [days]	Radial access Total	Femoral access Mean [days]	Femoral access SD [days]	Femoral access Total	Weight	Mean Difference IV, Fixed, 95% CI [days]
Brasselet 2007	7.2	0.5	57	7.5	0.4	57	88.4%	-0.30 [-0.47, -0.13]
GAN 2009	10.56	2.85	90	13.78	3.15	105	3.4%	-3.22 [-4.06, -2.38]
HOU 2010	8.6	1.8	100	12.7	3	100	5.2%	-4.10 [-4.79, -3.41]
RADIAMI 2009	6.26	3.86	50	6.75	4.02	50	1.0%	-0.49 [-2.03, 1.05]
TEMPURA 2003	5.7	4.9	77	7.4	0.95	72	2.0%	-1.70 [-2.82, -0.58]
Total (95% CI)			374			384	100.0%	-0.63 [-0.78, -0.47]

Heterogeneity: Chi² = 153.38, df = 4 (P < 0.00001); I² = 97%
Test for overall effect: Z = 7.87 (P < 0.00001)

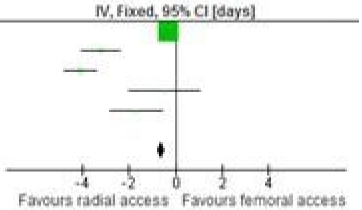
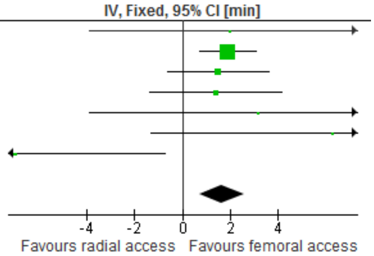


Figure 163: Procedure length

Study or Subgroup	Radial access Mean [min]	Radial access SD [min]	Radial access Total	Femoral access Mean [min]	Femoral access SD [min]	Femoral access Total	Weight	Mean Difference IV, Fixed, 95% CI [min]
Brasselet 2007	28	14	57	26	18	57	2.5%	2.00 [-3.92, 7.92]
GAN 2009	29.8	4.4	90	27.9	4	105	61.5%	1.90 [0.71, 3.09]
HOU 2010	37.2	7.1	100	35.7	8.1	100	19.5%	1.50 [-0.61, 3.61]
Li 2007	56.2	12.1	184	54.8	15.1	185	11.1%	1.40 [-1.39, 4.19]
RADIAMI 2009	58.3	17.8	50	55.1	18.4	50	1.7%	3.20 [-3.90, 10.30]
RADIAMI II 2011	53.7	20.6	49	47.4	19.6	59	1.5%	6.30 [-1.33, 13.93]
TEMPURA 2003	44	18	77	51	21	72	2.2%	-7.00 [-13.30, -0.70]
Total (95% CI)			**607**			**628**	**100.0%**	**1.66 [0.73, 2.59]**

Heterogeneity: Chi² = 9.08, df = 6 (P = 0.17); I² = 34%
Test for overall effect: Z = 3.50 (P = 0.0005)



I.3.1 Economic analysis forest plots

Figure 164: Bleeding requiring transfusion

Study or Subgroup	Radial access Events	Radial access Total	Femoral access Events	Femoral access Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Brasselet 2007	1	57	0	57	1.2%	3.00 [0.12, 72.13]
HOU 2010	0	100	3	100	8.5%	0.14 [0.01, 2.73]
RADIAMI 2009	0	50	3	50	8.5%	0.14 [0.01, 2.70]
RADIAMI II 2011	1	49	0	59	1.1%	3.60 [0.15, 86.44]
RIFLE-STEACS 2012	5	500	16	501	38.8%	0.31 [0.12, 0.85]
RIVAL 2011	11	955	15	1003	35.6%	0.77 [0.36, 1.67]
TEMPURA 2003	0	77	2	72	6.3%	0.19 [0.01, 3.83]
Total (95% CI)		**1788**		**1842**	**100.0%**	**0.51 [0.30, 0.86]**
Total events	18		39			

Heterogeneity: Chi² = 6.52, df = 6 (P = 0.37); I² = 8%
Test for overall effect: Z = 2.54 (P = 0.01)

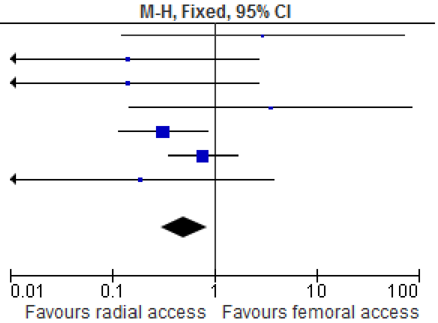
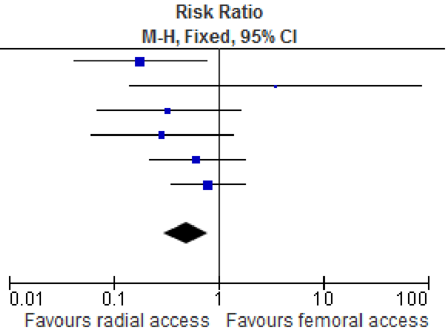


Figure 165: Haematomas

Study or Subgroup	Radial access Events	Radial access Total	Femoral access Events	Femoral access Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Brasselet 2007	2	57	11	57	25.4%	0.18 [0.04, 0.78]
GAN 2009	1	90	0	105	1.1%	3.49 [0.14, 84.73]
HOU 2010	2	100	6	100	13.9%	0.33 [0.07, 1.61]
Li 2007	2	184	7	186	16.1%	0.29 [0.06, 1.37]
RADIAMI 2009	5	50	8	50	18.5%	0.63 [0.22, 1.78]
RADIAMI II 2011	8	49	12	59	25.1%	0.80 [0.36, 1.81]
Total (95% CI)		**530**		**557**	**100.0%**	**0.49 [0.30, 0.81]**
Total events	20		44			

Heterogeneity: Chi² = 5.51, df = 5 (P = 0.36); I² = 9%
Test for overall effect: Z = 2.81 (P = 0.005)



I.4 Thrombus extraction during PPCI

Figure 166: All-cause mortality (≤ 30 days)

Study or Subgroup	Thrombus device Events	Thrombus device Total	No thrombus device Events	No thrombus device Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.1.1 Thrombus aspiration						
DEAR-MI 2006	0	74	0	74		Not estimable
INFUSE-AMI 2012	7	229	6	223	11.5%	1.14 [0.39, 3.33]
Kaltoft 2006	0	108	1	107	2.9%	0.33 [0.01, 8.02]
PIHRATE 2010	3	100	3	96	5.8%	0.96 [0.20, 4.64]
REMEDIA 2005	3	48	3	48	5.7%	1.00 [0.21, 4.71]
TAPAS 2008	11	529	21	531	39.7%	0.53 [0.26, 1.08]
VAMPIRE 2008	1	178	1	171	1.9%	0.96 [0.06, 15.24]
Subtotal (95% CI)		**1266**		**1250**	**67.5%**	**0.71 [0.43, 1.17]**
Total events	25		35			
Heterogeneity: Chi² = 2.00, df = 5 (P = 0.85); I² = 0%						
Test for overall effect: Z = 1.33 (P = 0.18)						
1.1.2 Mechanical thrombus extraction						
AIMI 2006	11	240	2	240	3.8%	5.50 [1.23, 24.55]
Antoniucci 2004	0	50	0	50		Not estimable
Beran 2002	2	33	1	33	1.9%	2.00 [0.19, 21.00]
JETSTENT 2010	4	256	7	245	13.6%	0.55 [0.16, 1.84]
Napadano 2003	3	46	3	46	5.7%	1.00 [0.21, 4.70]
X AMINE ST 2005	4	100	4	100	7.6%	1.00 [0.26, 3.89]
Subtotal (95% CI)		**725**		**714**	**32.5%**	**1.39 [0.76, 2.57]**
Total events	24		17			
Heterogeneity: Chi² = 6.01, df = 4 (P = 0.20); I² = 33%						
Test for overall effect: Z = 1.07 (P = 0.29)						
Total (95% CI)		**1991**		**1964**	**100.0%**	**0.93 [0.64, 1.37]**
Total events	49		52			

Heterogeneity: Chi² = 9.55, df = 10 (P = 0.48); I² = 0%
Test for overall effect: Z = 0.35 (P = 0.72)
Test for subgroup differences: Chi² = 2.79, df = 1 (P = 0.10), I² = 64.1%

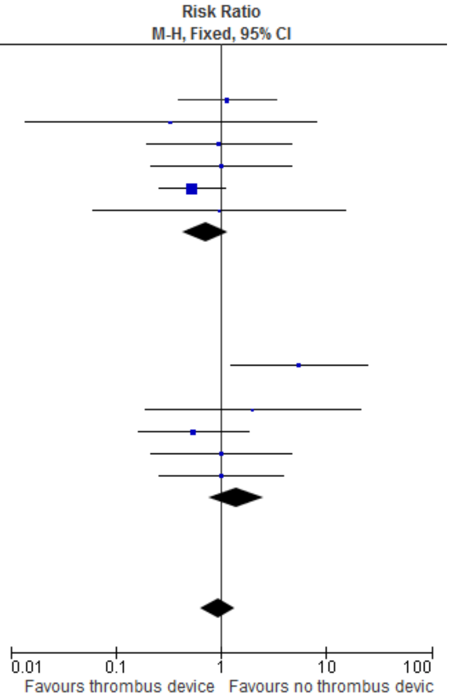
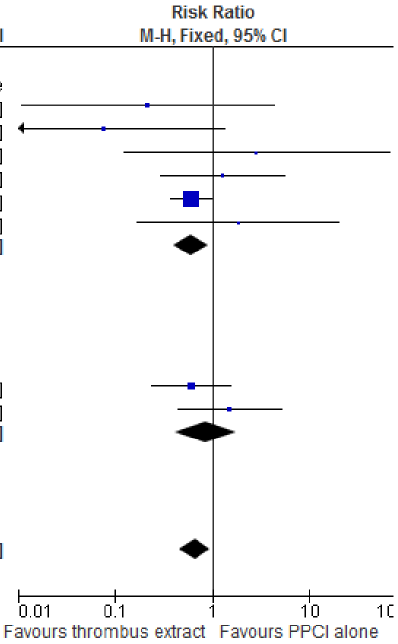


Figure 167: All-cause mortality (longer-term)

Study or Subgroup	Thrombus device Events	Thrombus device Total	No thrombus device Events	No thrombus device Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.2.1 Thrombus aspiration						
Bulum 2012	0	30	0	30		Not estimable
De Luca 2006	0	35	2	38	3.4%	0.22 [0.01, 4.36]
EXPIRA 2009	0	88	6	87	9.4%	0.08 [0.00, 1.33]
ITTI 2012	1	24	0	23	0.7%	2.88 [0.12, 67.29]
PIHRATE 2010	4	100	3	96	4.4%	1.28 [0.29, 5.57]
TAPAS 2008	25	535	41	536	58.7%	0.61 [0.38, 0.99]
VAMPIRE 2008	2	170	1	158	1.5%	1.86 [0.17, 20.30]
Subtotal (95% CI)		**982**		**968**	**78.1%**	**0.61 [0.40, 0.93]**
Total events	32		53			
Heterogeneity: Chi² = 5.22, df = 5 (P = 0.39); I² = 4%						
Test for overall effect: Z = 2.29 (P = 0.02)						
1.2.2 Mechanical thrombus extraction						
JETSTENT 2010	7	256	11	245	16.1%	0.61 [0.24, 1.55]
X AMINE ST 2005	6	100	4	100	5.7%	1.50 [0.44, 5.15]
Subtotal (95% CI)		**356**		**345**	**21.9%**	**0.84 [0.41, 1.74]**
Total events	13		15			
Heterogeneity: Chi² = 1.31, df = 1 (P = 0.25); I² = 23%						
Test for overall effect: Z = 0.46 (P = 0.64)						
Total (95% CI)		**1338**		**1313**	**100.0%**	**0.66 [0.46, 0.95]**
Total events	45		68			
Heterogeneity: Chi² = 6.88, df = 7 (P = 0.44); I² = 0%						
Test for overall effect: Z = 2.22 (P = 0.03)						
Test for subgroup differences: Chi² = 0.56, df = 1 (P = 0.45), I² = 0%						



Follow-up: Bulum 2012; 6 months, De Luca 2006; 6 months, EXPIRA 2009; 2 years, ITTI 2012; 6 months, PIHRATE 2010; 6 months, TAPAS 2008; 1 year, VAMPIRE 2008; 8 months, JETSTENT 2010; 6 months, X AMINE ST 2005; 6 months

Figure 168: Myocardial reinfarction (≤ 30 days)

Study or Subgroup	Thrombus device Events	Thrombus device Total	No thrombus device Events	No thrombus device Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.3.1 Thrombus aspiration						
EXPORT 2008	2	120	1	129	3.5%	2.15 [0.20, 23.41]
INFUSE-AMI 2012	1	229	2	223	7.3%	0.49 [0.04, 5.33]
Kaltoft 2006	0	108	1	107	5.5%	0.33 [0.01, 8.02]
PIHRATE 2010	0	100	1	96	5.5%	0.32 [0.01, 7.76]
REMEDIA 2005	2	48	2	48	7.2%	1.00 [0.15, 6.81]
TAPAS 2008	4	529	10	531	36.2%	0.40 [0.13, 1.27]
VAMPIRE 2008	0	178	1	171	5.5%	0.32 [0.01, 7.81]
Subtotal (95% CI)		**1312**		**1305**	**70.8%**	**0.54 [0.26, 1.13]**
Total events	9		18			
Heterogeneity: Chi² = 2.24, df = 6 (P = 0.90); I² = 0%						
Test for overall effect: Z = 1.63 (P = 0.10)						
1.3.2 Mechanical thrombus extraction						
Antoniucci 2004	0	50	0	50		Not estimable
JETSTENT 2010	2	256	3	245	11.1%	0.64 [0.11, 3.79]
Napadano 2003	2	46	2	46	7.2%	1.00 [0.15, 6.80]
X AMINE ST 2005	1	100	3	100	10.9%	0.33 [0.04, 3.15]
Subtotal (95% CI)		**452**		**441**	**29.2%**	**0.61 [0.20, 1.86]**
Total events	5		8			
Heterogeneity: Chi² = 0.53, df = 2 (P = 0.77); I² = 0%						
Test for overall effect: Z = 0.86 (P = 0.39)						
Total (95% CI)		**1764**		**1746**	**100.0%**	**0.56 [0.30, 1.04]**
Total events	14		26			
Heterogeneity: Chi² = 2.82, df = 9 (P = 0.97); I² = 0%						
Test for overall effect: Z = 1.84 (P = 0.07)						
Test for subgroup differences: Chi² = 0.04, df = 1 (P = 0.85), I² = 0%						

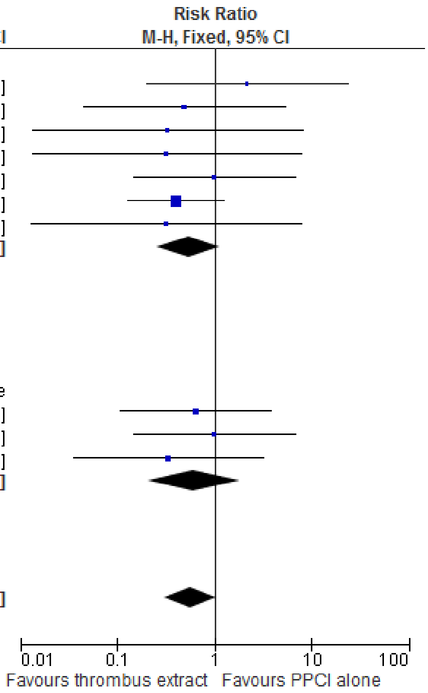
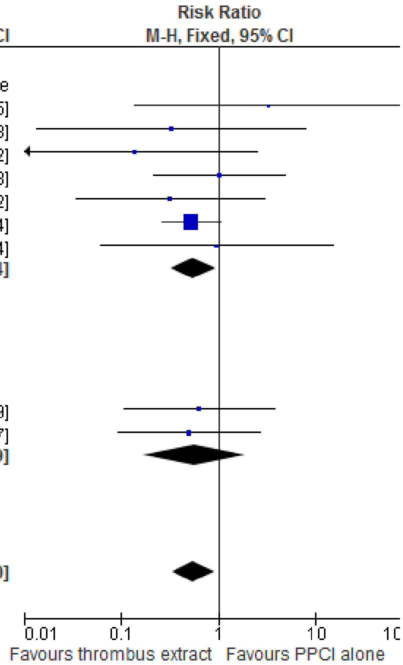


Figure 169: Myocardial reinfarction (longer-term)

Study or Subgroup	Thrombus device Events	Thrombus device Total	No thrombus device Events	No thrombus device Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.4.1 Thrombus aspiration						
Bulum 2012	0	30	0	30		Not estimable
De Luca 2006	1	35	0	38	1.1%	3.25 [0.14, 77.25]
EXPIRA 2009	0	88	1	87	3.5%	0.33 [0.01, 7.98]
ITTI 2012	0	24	3	23	8.4%	0.14 [0.01, 2.52]
Liistro 2009	3	55	3	56	7.0%	1.02 [0.21, 4.83]
PIHRATE 2010	1	100	3	96	7.2%	0.32 [0.03, 3.02]
TAPAS 2008	12	535	23	536	53.9%	0.52 [0.26, 1.04]
VAMPIRE 2008	1	178	1	171	2.4%	0.96 [0.06, 15.24]
Subtotal (95% CI)		**1045**		**1037**	**83.4%**	**0.55 [0.32, 0.94]**
Total events	18		34			
Heterogeneity: Chi² = 3.19, df = 6 (P = 0.79); I² = 0%						
Test for overall effect: Z = 2.16 (P = 0.03)						
1.4.2 Mechanical thrombus extraction						
JETSTENT 2010	2	256	3	245	7.2%	0.64 [0.11, 3.79]
X AMINE ST 2005	2	100	4	100	9.4%	0.50 [0.09, 2.67]
Subtotal (95% CI)		**356**		**345**	**16.6%**	**0.56 [0.17, 1.89]**
Total events	4		7			
Heterogeneity: Chi² = 0.04, df = 1 (P = 0.85); I² = 0%						
Test for overall effect: Z = 0.93 (P = 0.35)						
Total (95% CI)		**1401**		**1382**	**100.0%**	**0.55 [0.34, 0.90]**
Total events	22		41			
Heterogeneity: Chi² = 3.22, df = 8 (P = 0.92); I² = 0%						
Test for overall effect: Z = 2.36 (P = 0.02)						
Test for subgroup differences: Chi² = 0.00, df = 1 (P = 0.98), I² = 0%						



Follow-up: Bulum 2012; 6 months, De Luca 2006; 6 months, EXPIRA 2009; 2 years, ITTI 2012; 6 months, Liistro 2012; 6 month, PIHRATE 2010; 6 months, TAPAS 2008; 1 year, VAMPIRE 2008; 8 months, JETSTENT 2010; 6 months, X AMINE ST 2005; 6 months

Figure 170: Stroke (≤ 30 days)

Study or Subgroup	Thrombus device Events	Thrombus device Total	No thrombus device Events	No thrombus device Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.5.1 Thrombus aspiration						
INFUSE-AMI 2012	0	229	1	223	21.5%	0.32 [0.01, 7.93]
REMEDIA 2005	1	48	1	48	14.2%	1.00 [0.06, 15.53]
Subtotal (95% CI)		**277**		**271**	**35.7%**	**0.59 [0.08, 4.42]**
Total events	1		2			
Heterogeneity: Chi² = 0.28, df = 1 (P = 0.60); I² = 0%						
Test for overall effect: Z = 0.51 (P = 0.61)						
1.5.2 Mechanical thrombus extraction						
AIMI 2006	4	240	2	240	28.4%	2.00 [0.37, 10.82]
ANTONIUCCI 2004	1	50	0	50	7.1%	3.00 [0.13, 71.92]
JETSTENT 2010	0	256	1	245	21.7%	0.32 [0.01, 7.79]
NAPADANO 2003	0	46	0	46		Not estimable
X AMINE ST 2005	2	100	0	100	7.1%	5.00 [0.24, 102.85]
Subtotal (95% CI)		**692**		**681**	**64.3%**	**1.87 [0.60, 5.82]**
Total events	7		3			
Heterogeneity: Chi² = 1.67, df = 3 (P = 0.64); I² = 0%						
Test for overall effect: Z = 1.08 (P = 0.28)						
Total (95% CI)		**969**		**952**	**100.0%**	**1.42 [0.54, 3.69]**
Total events	8		5			
Heterogeneity: Chi² = 2.76, df = 5 (P = 0.74); I² = 0%						
Test for overall effect: Z = 0.71 (P = 0.48)						
Test for subgroup differences: Chi² = 0.96, df = 1 (P = 0.33), I² = 0%						

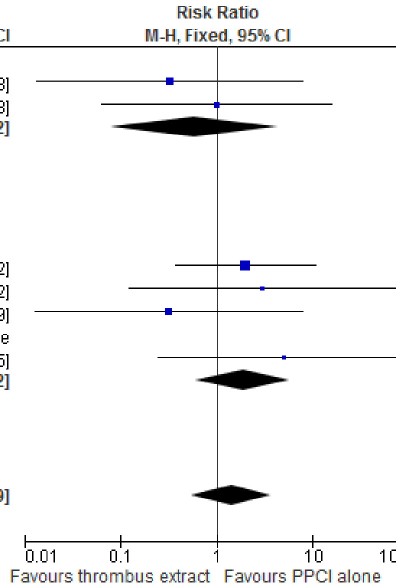
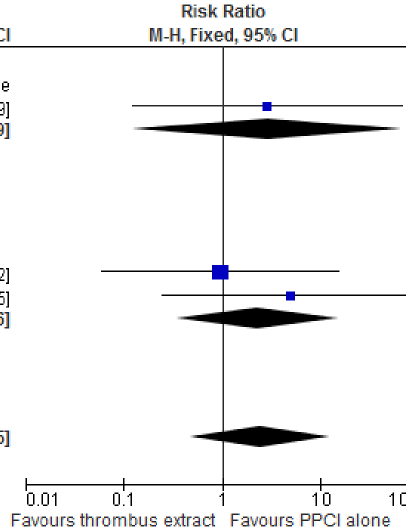


Figure 171: Stroke (longer-term)

Study or Subgroup	Thrombus device Events	Thrombus device Total	No thrombus device Events	No thrombus device Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.6.1 Thrombus aspiration						
Bulum 2012	0	30	0	30		Not estimable
ITTI 2012	1	24	0	23	25.1%	2.88 [0.12, 67.29]
Subtotal (95% CI)		**54**		**53**	**25.1%**	**2.88 [0.12, 67.29]**
Total events	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.66 (P = 0.51)						
1.6.2 Mechanical thrombus extraction						
JETSTENT 2010	1	256	1	245	50.3%	0.96 [0.06, 15.22]
X AMINE ST 2005	2	100	0	100	24.6%	5.00 [0.24, 102.85]
Subtotal (95% CI)		**356**		**345**	**74.9%**	**2.29 [0.34, 15.26]**
Total events	3		1			
Heterogeneity: Chi² = 0.64, df = 1 (P = 0.42); I² = 0%						
Test for overall effect: Z = 0.85 (P = 0.39)						
Total (95% CI)		**410**		**398**	**100.0%**	**2.43 [0.48, 12.35]**
Total events	4		1			
Heterogeneity: Chi² = 0.67, df = 2 (P = 0.72); I² = 0%						
Test for overall effect: Z = 1.07 (P = 0.28)						
Test for subgroup differences: Chi² = 0.02, df = 1 (P = 0.90), I² = 0%						



Follow-up: Bulum 2012; 6 months, ITTI 2012; 6 months, JETSTENT 2010; 6 months, X AMINE ST 2005; 6 months

Figure 172: Heart failure (≤ 30 days)

Study or Subgroup	Thrombus device Events	Thrombus device Total	No thrombus device Events	No thrombus device Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.7.1 Thrombus aspiration						
INFUSE-AMI 2012	8	229	11	223	35.6%	0.71 [0.29, 1.73]
PIHRATE 2010	6	100	10	96	32.5%	0.58 [0.22, 1.52]
Subtotal (95% CI)		**329**		**319**	**68.1%**	**0.65 [0.33, 1.24]**
Total events	14		21			
Heterogeneity: Chi² = 0.09, df = 1 (P = 0.76); I² = 0%						
Test for overall effect: Z = 1.31 (P = 0.19)						
1.7.2 Mechanical thrombus extraction						
NAPADANO 2003	5	46	10	46	31.9%	0.50 [0.19, 1.35]
Subtotal (95% CI)		**46**		**46**	**31.9%**	**0.50 [0.19, 1.35]**
Total events	5		10			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.37 (P = 0.17)						
Total (95% CI)		**375**		**365**	**100.0%**	**0.60 [0.35, 1.03]**
Total events	19		31			
Heterogeneity: Chi² = 0.27, df = 2 (P = 0.87); I² = 0%						
Test for overall effect: Z = 1.84 (P = 0.07)						
Test for subgroup differences: Chi² = 0.18, df = 1 (P = 0.67), I² = 0%						

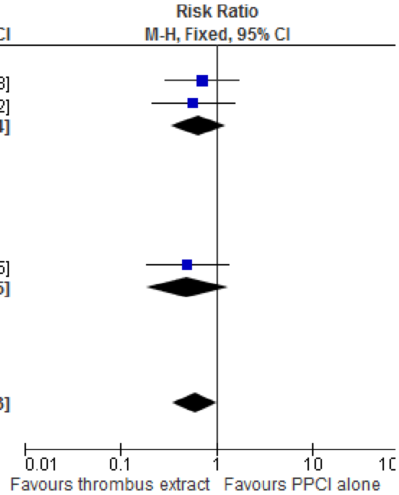
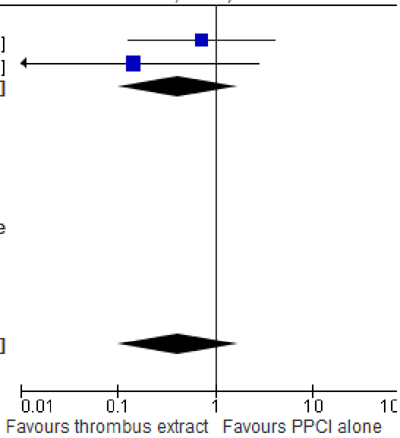


Figure 173: Heart failure (longer-term)

Study or Subgroup	Thrombus device Events	Thrombus device Total	No thrombus device Events	No thrombus device Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.8.1 Thrombus aspiration						
DE LUCA 2006A	2	35	3	38	45.3%	0.72 [0.13, 4.08]
Liistro 2009	0	55	3	56	54.7%	0.15 [0.01, 2.75]
Subtotal (95% CI)		**90**		**94**	**100.0%**	**0.41 [0.10, 1.68]**
Total events	2		6			
Heterogeneity: Chi² = 0.90, df = 1 (P = 0.34); I² = 0%						
Test for overall effect: Z = 1.24 (P = 0.22)						
1.8.2 Mechanical thrombus extraction						
Subtotal (95% CI)		**0**		**0**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**90**		**94**	**100.0%**	**0.41 [0.10, 1.68]**
Total events	2		6			
Heterogeneity: Chi² = 0.90, df = 1 (P = 0.34); I² = 0%						
Test for overall effect: Z = 1.24 (P = 0.22)						
Test for subgroup differences: Not applicable						



Follow-up: De Luca 2006; 6 months, Liistro 2012; 6 month

Figure 174: Target vessel revascularisation (≤ 30 days)

Study or Subgroup	Thrombus device Events	Thrombus device Total	No thrombus device Events	No thrombus device Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.9.1 Thrombus aspiration						
DEAR-MI 2006	1	74	0	74	1.2%	3.00 [0.12, 72.47]
PIHRATE 2010	2	100	1	96	2.4%	1.92 [0.18, 20.83]
REMEDIA 2005	1	48	1	48	2.3%	1.00 [0.06, 15.53]
TAPAS 2008	24	529	31	531	71.8%	0.78 [0.46, 1.31]
VAMPIRE 2008	0	178	1	171	3.5%	0.32 [0.01, 7.81]
Subtotal (95% CI)		**929**		**920**	**81.1%**	**0.83 [0.51, 1.34]**
Total events	28		34			
Heterogeneity: Chi² = 1.52, df = 4 (P = 0.82); I² = 0%						
Test for overall effect: Z = 0.77 (P = 0.44)						
1.9.2 Mechanical thrombus extraction						
Antoniucci 2004	0	50	0	50		Not estimable
Beran 2002	0	33	1	33	3.5%	0.33 [0.01, 7.90]
JETSTENT 2010	2	256	6	245	14.2%	0.32 [0.07, 1.57]
Napadano 2003	0	46	0	46		Not estimable
X AMINE ST 2005	2	100	0	100	1.2%	5.00 [0.24, 102.85]
Subtotal (95% CI)		**485**		**474**	**18.9%**	**0.61 [0.20, 1.84]**
Total events	4		7			
Heterogeneity: Chi² = 2.64, df = 2 (P = 0.27); I² = 24%						
Test for overall effect: Z = 0.88 (P = 0.38)						
Total (95% CI)		**1414**		**1394**	**100.0%**	**0.79 [0.51, 1.22]**
Total events	32		41			
Heterogeneity: Chi² = 4.51, df = 7 (P = 0.72); I² = 0%						
Test for overall effect: Z = 1.06 (P = 0.29)						
Test for subgroup differences: Chi² = 0.25, df = 1 (P = 0.62), I² = 0%						

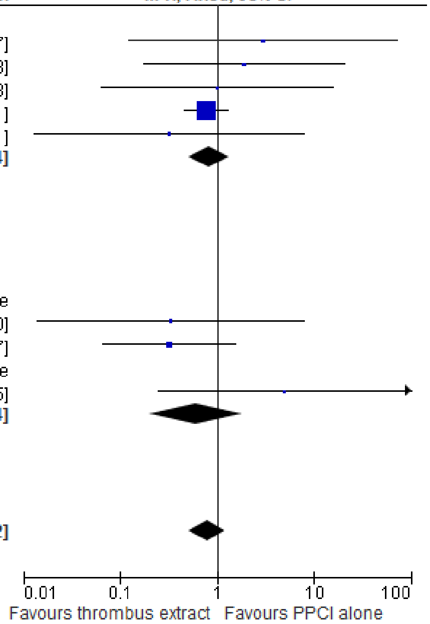
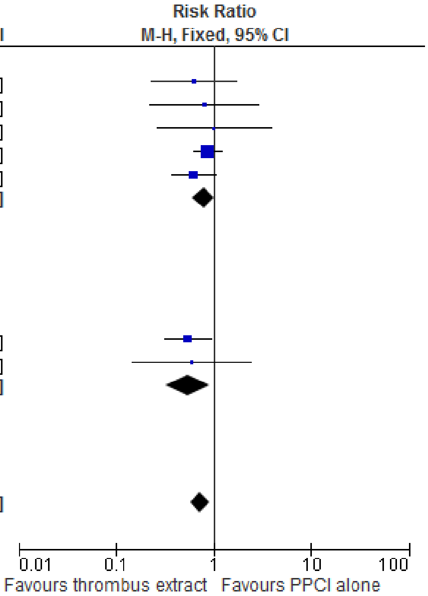


Figure 175: Target vessel revascularisation (longer-term)

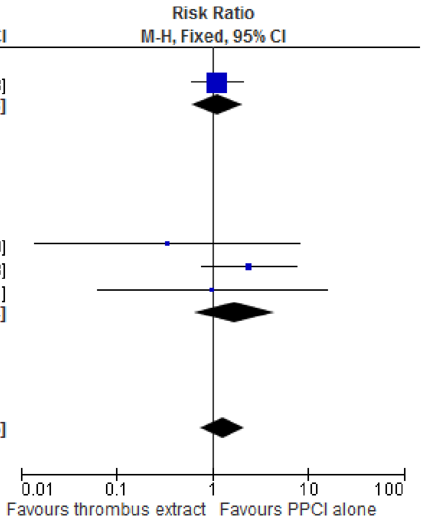
Study or Subgroup	Thrombus device Events	Thrombus device Total	No thrombus device Events	No thrombus device Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.10.1 Thrombus aspiration						
Bulum 2012	5	30	8	30	5.2%	0.63 [0.23, 1.69]
EXPIRA 2009	4	88	5	88	3.2%	0.80 [0.22, 2.88]
Liistro 2009	4	55	4	56	2.6%	1.02 [0.27, 3.87]
TAPAS 2008	60	535	69	536	44.4%	0.87 [0.63, 1.21]
VAMPIRE 2008	20	178	31	171	20.4%	0.62 [0.37, 1.04]
Subtotal (95% CI)		**886**		**881**	**75.7%**	**0.79 [0.61, 1.02]**
Total events	93		117			
Heterogeneity: Chi² = 1.53, df = 4 (P = 0.82); I² = 0%						
Test for overall effect: Z = 1.83 (P = 0.07)						
1.10.2 Mechanical thrombus extraction						
JETSTENT 2010	18	256	32	245	21.1%	0.54 [0.31, 0.93]
X AMINE ST 2005	3	100	5	100	3.2%	0.60 [0.15, 2.44]
Subtotal (95% CI)		**356**		**345**	**24.3%**	**0.55 [0.33, 0.91]**
Total events	21		37			
Heterogeneity: Chi² = 0.02, df = 1 (P = 0.89); I² = 0%						
Test for overall effect: Z = 2.31 (P = 0.02)						
Total (95% CI)		**1242**		**1226**	**100.0%**	**0.73 [0.58, 0.92]**
Total events	114		154			
Heterogeneity: Chi² = 3.12, df = 6 (P = 0.79); I² = 0%						
Test for overall effect: Z = 2.71 (P = 0.007)						
Test for subgroup differences: Chi² = 1.58, df = 1 (P = 0.21), I² = 36.7%						



Follow-up: Bulum 2012; 6 months, EXPIRA 2009; 2 years, Liistro 2012; 6 months, TAPAS 2008; 1 year, VAMPIRE 2008; 8 months, JETSTENT 2010; 6 months, X AMINE ST 2005

Figure 176: Major bleeding (≤ 30 days)

Study or Subgroup	Thrombus device Events	Thrombus device Total	No thrombus device Events	No thrombus device Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.11.1 Thrombus aspiration						
TAPAS 2008	20	529	18	531	73.2%	1.12 [0.60, 2.08]
Subtotal (95% CI)		**529**		**531**	**73.2%**	**1.12 [0.60, 2.08]**
Total events	20		18			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.34 (P = 0.73)						
1.11.2 Mechanical thrombus extraction						
Antoniucci 2004	0	50	1	50	6.1%	0.33 [0.01, 7.99]
JETSTENT 2010	10	256	4	245	16.6%	2.39 [0.76, 7.53]
Napadano 2003	1	46	1	46	4.1%	1.00 [0.06, 15.51]
Subtotal (95% CI)		**352**		**341**	**26.8%**	**1.71 [0.66, 4.44]**
Total events	11		6			
Heterogeneity: Chi² = 1.49, df = 2 (P = 0.47); I² = 0%						
Test for overall effect: Z = 1.11 (P = 0.27)						
Total (95% CI)		**881**		**872**	**100.0%**	**1.28 [0.76, 2.15]**
Total events	31		24			
Heterogeneity: Chi² = 2.05, df = 3 (P = 0.56); I² = 0%						
Test for overall effect: Z = 0.92 (P = 0.36)						
Test for subgroup differences: Chi² = 0.54, df = 1 (P = 0.46), I² = 0%						



I.4.1 Economic analysis forest plots

Figure 177: Stent usage

Study or Subgroup	Thrombus device Events	Thrombus device Total	No thrombus device Events	No thrombus device Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.8.1 Thrombus aspiration						
Bulum 2012	30	30	30	30	2.0%	1.00 [0.94, 1.07]
De Luca 2006	38	38	38	38	2.5%	1.00 [0.95, 1.05]
DEAR-MI 2006	73	74	72	74	4.7%	1.01 [0.97, 1.06]
EXPIRA 2009	88	88	87	87	5.8%	1.00 [0.98, 1.02]
INFUSE-AMI 2012	170	229	158	223	10.5%	1.05 [0.94, 1.17]
Kaltoft 2006	103	108	104	107	6.8%	0.98 [0.93, 1.03]
Liistro 2009	55	55	56	56	3.7%	1.00 [0.97, 1.04]
PIHRATE 2010	99	100	93	96	6.2%	1.02 [0.98, 1.06]
TAPAS 2008	448	448	485	485	30.5%	1.00 [1.00, 1.00]
VAMPIRE 2008	0	0	0	0		Not estimable
Subtotal (95% CI)		**1170**		**1196**	**72.7%**	**1.01 [0.99, 1.03]**
Total events	1104		1123			
Heterogeneity: Chi² = 16.20, df = 8 (P = 0.04); I² = 51%						
Test for overall effect: Z = 0.84 (P = 0.40)						
1.8.2 Mechanical thrombus extraction						
AIMI 2006	224	240	227	240	14.9%	0.99 [0.94, 1.03]
Antoniucci 2004	49	50	49	50	3.2%	1.00 [0.95, 1.06]
Napadano 2003	43	46	42	46	2.7%	1.02 [0.91, 1.15]
X AMINE ST 2005	100	100	99	101	6.5%	1.02 [0.99, 1.06]
Subtotal (95% CI)		**436**		**437**	**27.3%**	**1.00 [0.97, 1.03]**
Total events	416		417			
Heterogeneity: Chi² = 1.82, df = 3 (P = 0.61); I² = 0%						
Test for overall effect: Z = 0.00 (P = 1.00)						
Total (95% CI)		**1606**		**1633**	**100.0%**	**1.01 [0.99, 1.02]**
Total events	1520		1540			
Heterogeneity: Chi² = 11.05, df = 12 (P = 0.52); I² = 0%						
Test for overall effect: Z = 0.72 (P = 0.47)						
Test for subgroup differences: Chi² = 0.20, df = 1 (P = 0.65), I² = 0%						

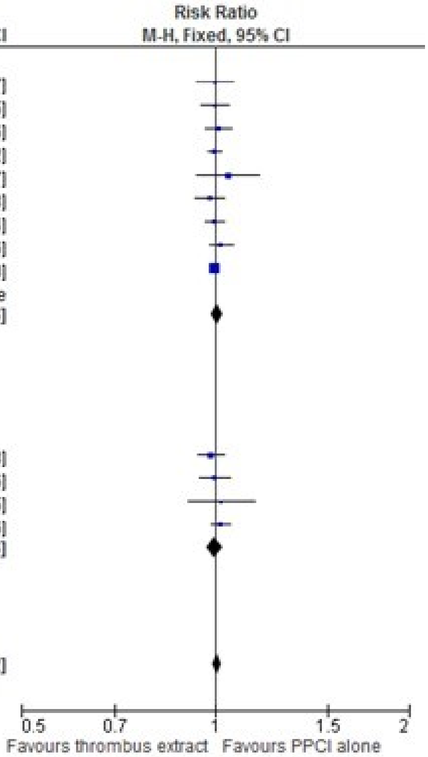


Figure 178: Balloon catheter usage

Study or Subgroup	Thrombus device Events	Thrombus device Total	No thrombus device Events	No thrombus device Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.15.1 Thrombus aspiration						
De Luca 2006	3	38	36	38	3.9%	0.08 [0.03, 0.25]
DEAR-MI 2006	21	74	54	74	5.9%	0.39 [0.26, 0.57]
EXPIRA 2009	21	88	85	87	9.3%	0.24 [0.17, 0.36]
Liistro 2009	43	55	51	56	5.5%	0.86 [0.73, 1.01]
PIHRATE 2010	24	100	88	96	9.8%	0.26 [0.18, 0.37]
TAPAS 2008	153	448	485	485	50.8%	0.34 [0.30, 0.39]
Subtotal (95% CI)		**803**		**836**	**85.1%**	**0.35 [0.31, 0.38]**
Total events	265		799			
Heterogeneity: Chi² = 133.04, df = 5 (P < 0.00001); I² = 96%						
Test for overall effect: Z = 20.87 (P < 0.00001)						
1.15.2 Mechanical thrombus extraction						
Antoniucci 2004	2	50	8	50	0.9%	0.25 [0.06, 1.12]
JETSTENT 2010	25	256	34	245	3.8%	0.70 [0.43, 1.14]
Napadano 2003	15	46	29	46	3.2%	0.52 [0.32, 0.83]
X AMINE ST 2005	40	100	65	101	7.0%	0.62 [0.47, 0.82]
Subtotal (95% CI)		**452**		**442**	**14.9%**	**0.60 [0.48, 0.75]**
Total events	82		136			
Heterogeneity: Chi² = 2.17, df = 3 (P = 0.54); I² = 0%						
Test for overall effect: Z = 4.58 (P < 0.00001)						
Total (95% CI)		**1255**		**1278**	**100.0%**	**0.38 [0.35, 0.42]**
Total events	347		935			
Heterogeneity: Chi² = 134.59, df = 9 (P < 0.00001); I² = 93%						
Test for overall effect: Z = 20.79 (P < 0.00001)						
Test for subgroup differences: Chi² = 19.65, df = 1 (P < 0.00001), I² = 94.9%						

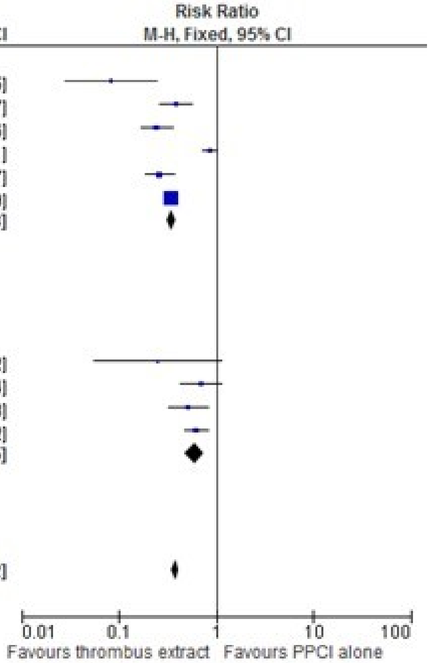
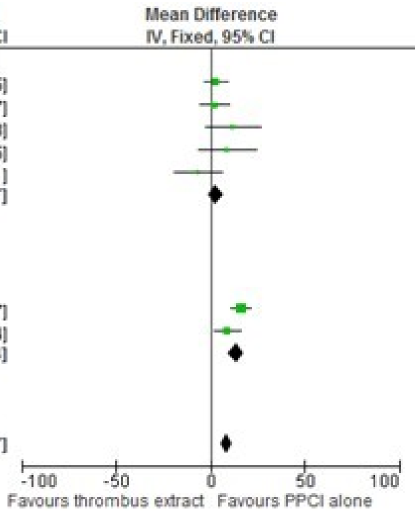


Figure 179: Procedure length

Study or Subgroup	Thrombus device Mean	SD	Total	No thrombus device Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
1.16.1 Thrombus aspiration								
DEAR-MI 2006	57	19	74	54	21	74	21.5%	3.00 [-3.45, 9.45]
EXPORT 2008	36.7	18	50	34.5	21.5	50	14.8%	2.20 [-5.57, 9.97]
ITTI 2012	53	32	24	41	16	23	4.3%	12.00 [-2.38, 26.38]
REMEDIA 2005	81	43	50	72	34	49	3.8%	9.00 [-6.25, 24.25]
VAMPIRE 2008	87	32.4	178	93.6	78.6	171	5.5%	-6.60 [-19.31, 6.11]
Subtotal (95% CI)			376			367	50.0%	2.94 [-1.29, 7.17]
Heterogeneity: Chi² = 4.33, df = 4 (P = 0.36); I² = 8%								
Test for overall effect: Z = 1.36 (P = 0.17)								
1.16.2 Mechanical thrombus extraction								
AIMI 2006	75.4	30.9	240	59.2	26.8	240	33.4%	16.20 [11.03, 21.37]
X AMINE ST 2005	54	28	100	45	25	101	16.6%	9.00 [1.66, 16.34]
Subtotal (95% CI)			340			341	50.0%	13.81 [9.58, 18.04]
Heterogeneity: Chi² = 2.47, df = 1 (P = 0.12); I² = 59%								
Test for overall effect: Z = 6.40 (P < 0.00001)								
Total (95% CI)			716			708	100.0%	8.37 [5.38, 11.37]
Heterogeneity: Chi² = 19.49, df = 6 (P = 0.003); I² = 69%								
Test for overall effect: Z = 5.49 (P < 0.00001)								
Test for subgroup differences: Chi² = 12.69, df = 1 (P = 0.0004), I² = 92.1%								



I.5 Culprit versus complete revascularisation

****Updated, see the 2020 evidence review****

I.5.1 Culprit-only PPCI versus immediate multivessel PCI

Figure 180: RCTs: all-cause mortality (≤ 30 days)

Study or Subgroup	Culprit only PPCI Events	Total	Multivessel PCI Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
HELP-AMI 2004	0	17	1	52	25.2%	0.98 [0.04, 23.03]
Politi 2010	7	84	2	65	74.8%	2.71 [0.58, 12.60]
Total (95% CI)		101		117	100.0%	2.27 [0.58, 8.85]
Total events	7		3			
Heterogeneity: Chi² = 0.32, df = 1 (P = 0.57); I² = 0%						
Test for overall effect: Z = 1.18 (P = 0.24)						

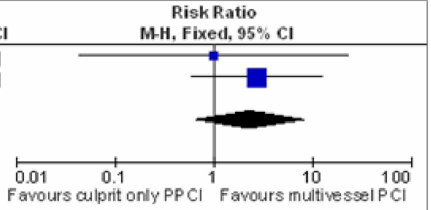


Figure 181: Cohort studies: all-cause mortality (≤ 30 days)

Study or Subgroup	Culprit only PPCI Events	Total	Multivessel PCI Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Corpus 2004	23	354	5	26		0.34 [0.14, 0.82]
EUROTRANSFER Reg 2010	42	707	9	70		0.46 [0.23, 0.91]
KAMIR 2012	7	1106	5	538		0.68 [0.22, 2.14]
Meliga 2011	17	383	10	417		1.85 [0.86, 3.99]
Nat'l CV Data Reg 2009	585	23146	88	2701		0.78 [0.62, 0.97]
NYS Angioplasty Reg 2006	31	1350	5	632		2.90 [1.13, 7.43]
NYS PCIRS 2010	10	503	17	503		0.59 [0.27, 1.27]

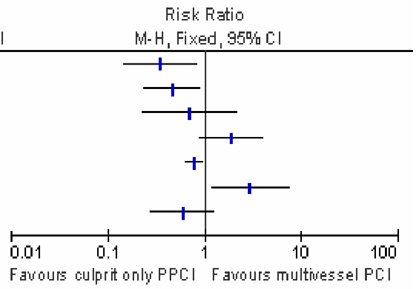
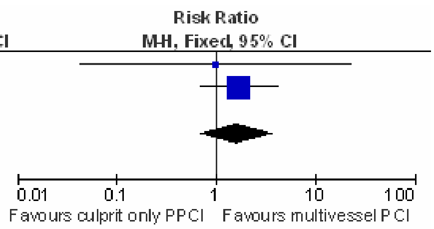


Figure 182: RCTs: all-cause mortality (longer-term)

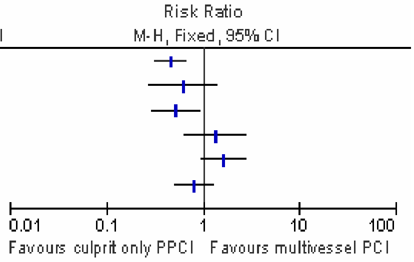
Study or Subgroup	Culprit only PPCI Events	Total	Multivessel PCI Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
HELP-AMI 2004	0	17	1	52	10.1%	0.98 [0.04, 23.03]
Politi 2010	13	84	6	65	89.9%	1.68 [0.67, 4.17]
Total (95% CI)		101		117	100.0%	1.61 [0.67, 3.85]
Total events	13		7			
Heterogeneity: Chi² = 0.10, df = 1 (P = 0.75); I² = 0%						
Test for overall effect: Z = 1.06 (P = 0.29)						



Follow-up: HELP-AMI 2004; 12 months, Politi 2010; 2.5 years

Figure 183: Cohort studies: all-cause mortality (longer-term)

Study or Subgroup	Culprit only PPCI Events	Culprit only PPCI Total	Multivessel PCI Events	Multivessel PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
APEX-AMI cohort2010	116	1984	28	217		0.45 [0.31, 0.67]
Corpus 2004	42	354	5	26		0.62 [0.27, 1.43]
EUROTRANSFER Reg 2010	57	707	11	70		0.51 [0.28, 0.93]
KAMIR 2012	25	1106	9	538		1.35 [0.64, 2.87]
Meliga 2011	28	383	19	417		1.60 [0.91, 2.83]
NYS PCIRS 2010	28	503	35	503		0.80 [0.49, 1.29]



Follow-up: Corpus 2004, EUROTRANSFER Reg 2012, KAMIR 2012, NYS PCIRS 2010; 12months, Meliga 2011; mean (SD) = 642 (545) days

Figure 184: RCTs: reinfarction (≤ 30 days)

Study or Subgroup	Culprit only PPCI Events	Culprit only PPCI Total	Multivessel PCI Events	Multivessel PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
HELP-AMI 2004	0	17	0	52		Not estimable
Total (95% CI)		**17**		**52**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						

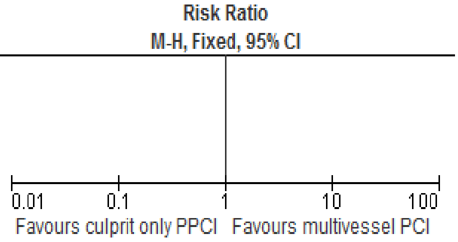


Figure 185: Cohort studies: reinfarction (≤ 30 days)

Study or Subgroup	Culprit only PPCI Events	Culprit only PPCI Total	Multivessel PCI Events	Multivessel PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Corpus 2004	2	354	0	26		0.38 [0.02, 7.72]
EUROTRANSFER Reg 2010	13	707	0	28		1.11 [0.07, 18.15]
KAMIR 2012	4	1106	3	538		0.65 [0.15, 2.89]
Meliga 2011	12	383	58	417		0.23 [0.12, 0.41]

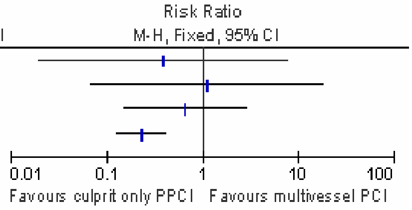
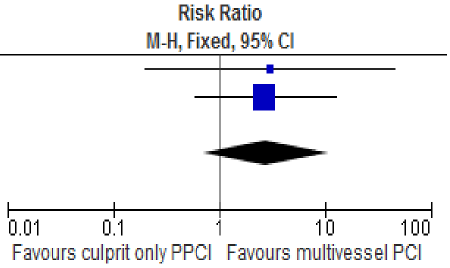


Figure 186: RCTs: reinfarction (longer-term)

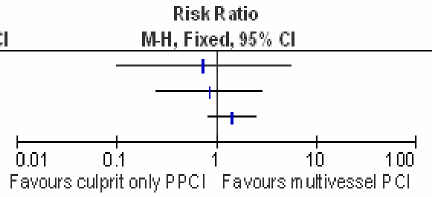
Study or Subgroup	Culprit only PPCI Events	Culprit only PPCI Total	Multivessel PCI Events	Multivessel PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
HELP-AMI 2004	1	17	1	52	17.9%	3.06 [0.20, 46.30]
Politi 2010	7	84	2	65	82.1%	2.71 [0.58, 12.60]
Total (95% CI)		**101**		**117**	**100.0%**	**2.77 [0.72, 10.67]**
Total events	8		3			
Heterogeneity: $Chi^2 = 0.01$, df = 1 (P = 0.94); $I^2 = 0\%$						
Test for overall effect: Z = 1.48 (P = 0.14)						



Follow-up: HELP-AMI 2004; 12 months, Politi 2010; 2.5 years

Figure 187: Cohort studies: reinfarction (longer-term)

Study or Subgroup	Culprit only PPCI Events	Culprit only PPCI Total	Multivessel PCI Events	Multivessel PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Corpus 2004	10	354	1	26		0.73 [0.10, 5.52]
KAMIR 2012	7	1106	4	538		0.85 [0.25, 2.90]
Meliga 2011	26	383	20	417		1.42 [0.80, 2.49]



Follow-up: Corpus 2004, KAMIR 2012; 12months, Meliga 2011; mean (SD) = 642 (545) days

Figure 188: RCTs: repeat revascularisation (≤ 30 days)

Study or Subgroup	Culprit only PPCI Events	Culprit only PPCI Total	Multivessel PCI Events	Multivessel PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
HELP-AMI 2004	0	17	0	52		Not estimable
Total (95% CI)		**17**		**52**		**Not estimable**
Total events	0		0			

Heterogeneity: Not applicable
Test for overall effect: Not applicable

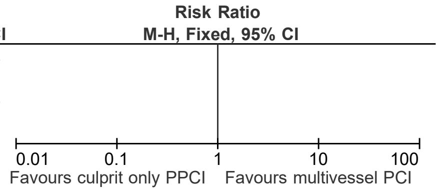


Figure 189: Cohort studies: repeat revascularisation (≤ 30 days)

Study or Subgroup	Culprit only PPCI Events	Culprit only PPCI Total	Multivessel PCI Events	Multivessel PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
EUROTRANSFER Reg 2010	10	707	0	70		2.11 [0.12, 35.56]
KAMIR 2012	22	1106	6	538		1.78 [0.73, 4.37]

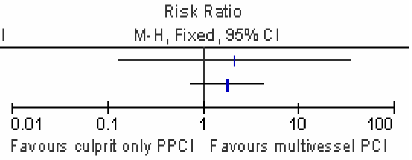
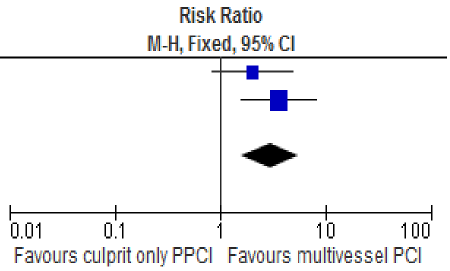


Figure 190: RCTs: repeat revascularisation (longer-term)

Study or Subgroup	Culprit only PPCI Events	Culprit only PPCI Total	Multivessel PCI Events	Multivessel PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
HELP-AMI 2004	6	17	9	52	39.6%	2.04 [0.85, 4.90]
Politi 2010	28	84	6	65	60.4%	3.61 [1.59, 8.20]
Total (95% CI)		**101**		**117**	**100.0%**	**2.99 [1.62, 5.53]**
Total events	34		15			

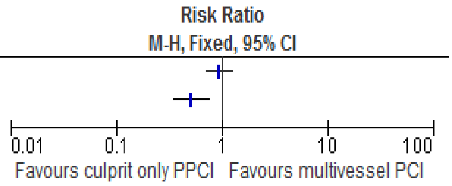
Heterogeneity: $Chi^2 = 0.94$, df = 1 (P = 0.33); $I^2 = 0\%$
Test for overall effect: Z = 3.49 (P = 0.0005)



Follow-up: HELP-AMI 2004; 12 months, Politi 2010; 2.5 years

Figure 191: Cohort studies: repeat revascularisation (longer-term)

Study or Subgroup	Culprit only PPCI Events	Culprit only PPCI Total	Multivessel PCI Events	Multivessel PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
KAMIR 2012	129	1106	66	538		0.95 [0.72, 1.26]
Meliga 2011	34	383	72	417		0.51 [0.35, 0.75]



Follow-up: KAMIR 2012; 12months, Meliga 2011; mean (SD) = 642 (545) days

Figure 192: Cohort studies: CABG (≤ 30 days)

Study or Subgroup	Culprit only PPCI Events	Culprit only PPCI Total	Multivessel PCI Events	Multivessel PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Corpus 2004	28	354	1	26		2.06 [0.29, 14.52]
KAMIR 2012	0	1106	2	538		0.10 [0.00, 2.02]
NYS Angioplasty Reg 2006	5	1350	3	632		0.78 [0.19, 3.25]

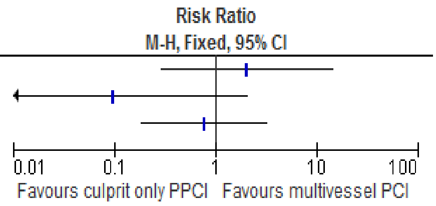
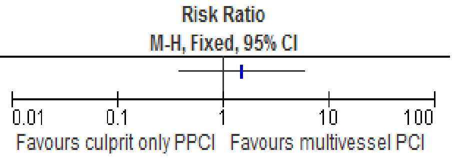


Figure 193: Cohort studies: CABG (longer-term)

Study or Subgroup	Culprit only PPCI Events	Culprit only PPCI Total	Multivessel PCI Events	Multivessel PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Corpus 2004	41	354	2	26		1.51 [0.39, 5.88]



Follow-up: Corpus 2004; 12 months

Figure 194: Cohort studies: target vessel revascularisation (≤ 30 days)

Study or Subgroup	Culprit only PPCI Events	Culprit only PPCI Total	Multivessel PCI Events	Multivessel PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Corpus 2004	28	354	1	26		2.06 [0.29, 14.52]
KAMIR 2012	1	1106	2	538		0.24 [0.02, 2.68]

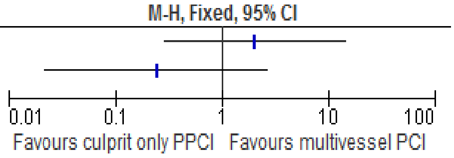
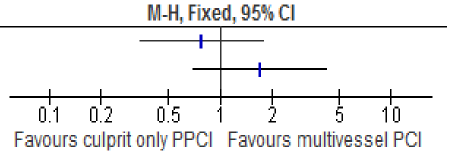


Figure 195: Cohort studies: target vessel revascularisation (longer-term)

Study or Subgroup	Culprit only PPCI Events	Culprit only PPCI Total	Multivessel PCI Events	Multivessel PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Corpus 2004	53	354	5	26		0.78 [0.34, 1.78]
KAMIR 2012	21	1106	6	538		1.70 [0.69, 4.19]



Follow-up: Corpus 2004, KAMIR 2012; 12months

Figure 196: Cohort studies: stroke (≤ 30 days)

Study or Subgroup	Culprit only PPCI Events	Culprit only PPCI Total	Multivessel PCI Events	Multivessel PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Nat'l CV Data Reg 2009	106	23146	12	2701		1.03 [0.57, 1.87]
NYS Angioplasty Reg 2006	13	1350	5	632		1.22 [0.44, 3.40]

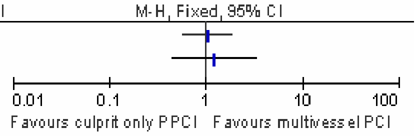


Figure 197: Cohort studies: renal failure(≤ 30 days)

Study or Subgroup	Culprit only PPCI Events	Culprit only PPCI Total	Multivessel PCI Events	Multivessel PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
KAMIR 2012	3	1106	1	538		1.46 [0.15, 14.00]
Nat'l CV Data Reg 2009	280	23146	23	2701		1.42 [0.93, 2.17]
NYS Angioplasty Reg 2006	3	1350	2	632		0.70 [0.12, 4.19]

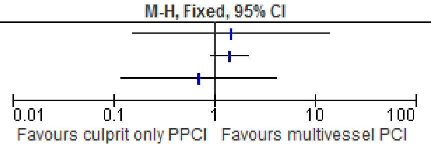


Figure 198: Cohort studies: major bleeding (≤ 30 days)

Study or Subgroup	Culprit only PPCI Events	Culprit only PPCI Total	Multivessel PCI Events	Multivessel PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
APEX-AMI cohort 2010	36	1984	3	214		1.29 [0.40, 4.17]
Corpus 2004	26	354	1	26		1.91 [0.27, 13.52]
EUROTRANSFER Reg 2010	12	707	2	70		0.59 [0.14, 2.60]
KAMIR 2012	2	1106	1	538		0.97 [0.09, 10.71]
Nat'l CV Data Reg 2009	1049	23146	151	2701		0.81 [0.69, 0.96]

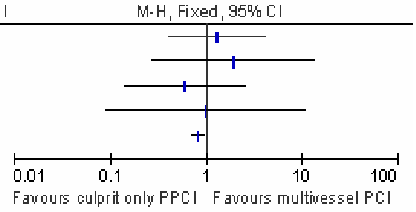


Figure 199: RCTs: procedure time

Study or Subgroup	Culprit only PPCI Mean [min]	Culprit only PPCI SD [min]	Culprit only PPCI Total	Multivessel PCI Mean [min]	Multivessel PCI SD [min]	Multivessel PCI Total	Weight	Mean Difference IV, Fixed, 95% CI [min]
HELP-AMI 2004	53	24	17	69	39	52	100.0%	-16.00 [-31.57, -0.43]
Total (95% CI)			17			52	100.0%	-16.00 [-31.57, -0.43]

Heterogeneity: Not applicable
Test for overall effect: Z = 2.01 (P = 0.04)

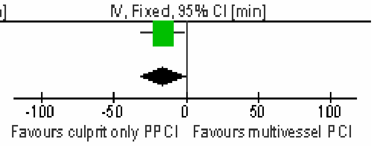


Figure 200: RCTs: length of hospital stay

Study or Subgroup	Culprit only PPCI Mean [days]	Culprit only PPCI SD [days]	Culprit only PPCI Total	Multivessel PCI Mean [days]	Multivessel PCI SD [days]	Multivessel PCI Total	Weight	Mean Difference IV, Fixed, 95% CI [days]
Politi 2010	5.3	2.5	84	4.8	2.6	65	100.0%	0.50 [-0.33, 1.33]
Total (95% CI)			84			65	100.0%	0.50 [-0.33, 1.33]

Heterogeneity: Not applicable
Test for overall effect: Z = 1.18 (P = 0.24)

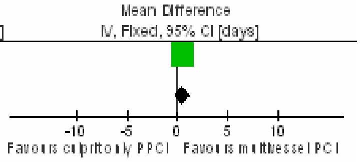
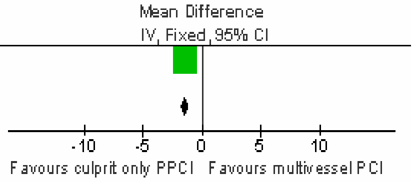


Figure 201: RCTs: stents per person

Study or Subgroup	Culprit only PPCI Mean	Culprit only PPCI SD	Culprit only PPCI Total	Multivessel PCI Mean	Multivessel PCI SD	Multivessel PCI Total	Weight	Mean Difference IV, Fixed, 95% CI	Year
HELP-AMI 2004	1.29	0.61	17	2.73	0.78	52	100.0%	-1.44 [-1.80, -1.08]	2004
Total (95% CI)			17			52	100.0%	-1.44 [-1.80, -1.08]	

Heterogeneity: Not applicable
Test for overall effect: Z = 7.86 (P < 0.00001)



I.5.2 Culprit-only PPCI versus staged PCI

Figure 202: RCTs: all-cause mortality (≤ 30 days)

Study or Subgroup	Culprit only PPCI Events	Culprit only PPCI Total	Multivessel PCI Events	Multivessel PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Politi 2010	7	84	0	65	100.0%	11.65 [0.68, 200.27]
Total (95% CI)		**84**		**65**	**100.0%**	**11.65 [0.68, 200.27]**
Total events	7		0			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.69 (P = 0.09)

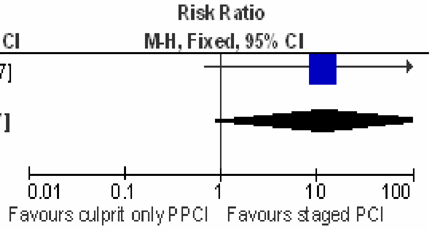


Figure 203: Cohort studies: all-cause mortality (≤ 30 days)

Study or Subgroup	Culprit only PPCI Events	Culprit only PPCI Total	Multivessel PCI Events	Multivessel PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Corpus 2004	23	354	10	126		0.82 [0.40, 1.67]
NYS PCIRS 2010	5	259	3	259		1.67 [0.40, 6.90]

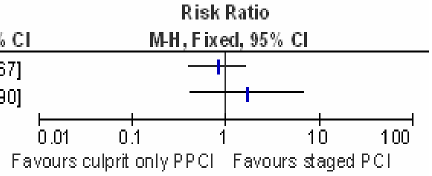
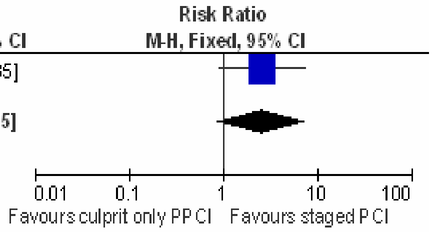


Figure 204: RCTs: all-cause mortality (longer-term)

Study or Subgroup	Culprit only PPCI Events	Culprit only PPCI Total	Multivessel PCI Events	Multivessel PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Politi 2010	13	84	4	65	100.0%	2.51 [0.86, 7.35]
Total (95% CI)		**84**		**65**	**100.0%**	**2.51 [0.86, 7.35]**
Total events	13		4			

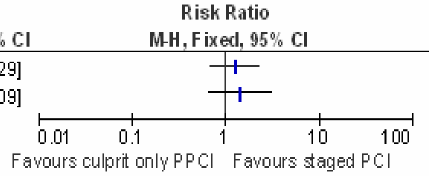
Heterogeneity: Not applicable
Test for overall effect: Z = 1.68 (P = 0.09)



Follow-up: Politi 2010; 2.5 years

Figure 205: Cohort studies: all-cause mortality (longer-term)

Study or Subgroup	Culprit only PPCI Events	Culprit only PPCI Total	Multivessel PCI Events	Multivessel PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Corpus 2004	42	354	12	126		1.25 [0.68, 2.29]
NYS PCIRS 2010	14	259	10	259		1.40 [0.63, 3.09]



Follow-up: Corpus 2004, NYS PCIRS; 12 months

Figure 206: Cohort studies: reinfarction (≤ 30 days)

Study or Subgroup	Culprit only PPCI Events	Culprit only PPCI Total	Multivessel PCI Events	Multivessel PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Corpus 2004	2	354	14	126		0.05 [0.01, 0.22]

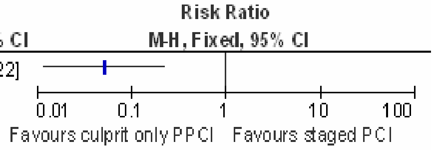
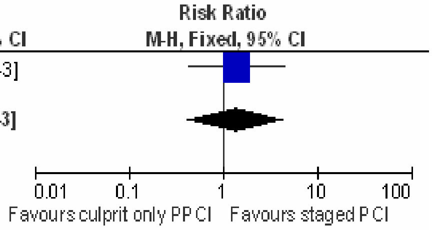


Figure 207: RCTs: reinfarction (longer-term)

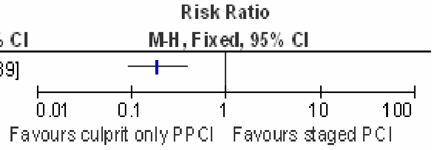
Study or Subgroup	Culprit only PPCI Events	Culprit only PPCI Total	Multivessel PCI Events	Multivessel PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Politi 2010	7	84	4	65	100.0%	1.35 [0.41, 4.43]
Total (95% CI)		**84**		**65**	**100.0%**	**1.35 [0.41, 4.43]**
Total events	7		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.50 (P = 0.62)						



Follow-up: Politi 2010; 2.5 years

Figure 208: Cohort studies: reinfarction (longer-term)

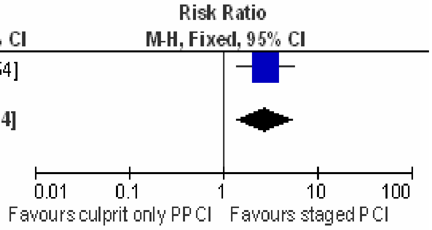
Study or Subgroup	Culprit only PPCI Events	Culprit only PPCI Total	Multivessel PCI Events	Multivessel PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Corpus 2004	10	354	19	126		0.19 [0.09, 0.39]



Follow-up: Corpus 2004; 12 months

Figure 209: RCTs: repeat revascularisation (longer-term)

Study or Subgroup	Culprit only PPCI Events	Culprit only PPCI Total	Multivessel PCI Events	Multivessel PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Politi 2010	28	84	8	65	100.0%	2.71 [1.32, 5.54]
Total (95% CI)		**84**		**65**	**100.0%**	**2.71 [1.32, 5.54]**
Total events	28		8			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.73 (P = 0.006)						



Follow-up: Politi 2010; 2.5 years

Figure 210: Cohort studies: CABG (≤ 30 days)

Study or Subgroup	Culprit only PPCI Events	Culprit only PPCI Total	Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Year
Corpus 2004	28	354	2	126		4.98 [1.20, 20.62]	2004

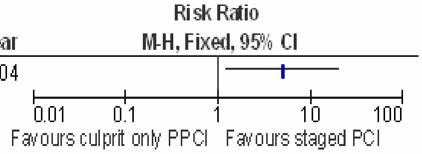
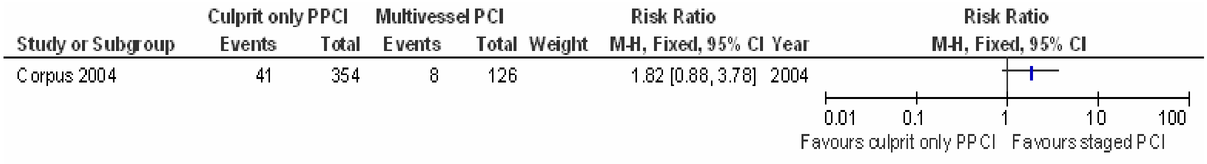


Figure 211: Cohort studies: CABG (longer-term)



Follow-up: Corpus 2004, NYS PCIRS; 12 months

Figure 212: Cohort studies: target vessel revascularisation (≤ 30 days)

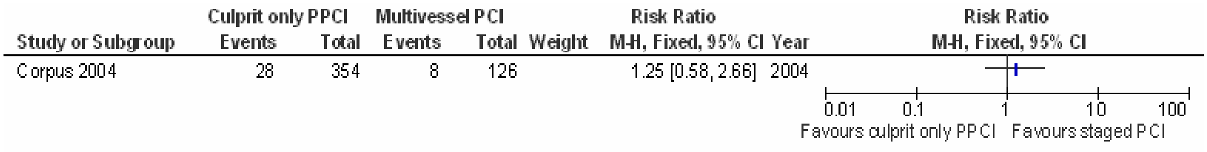
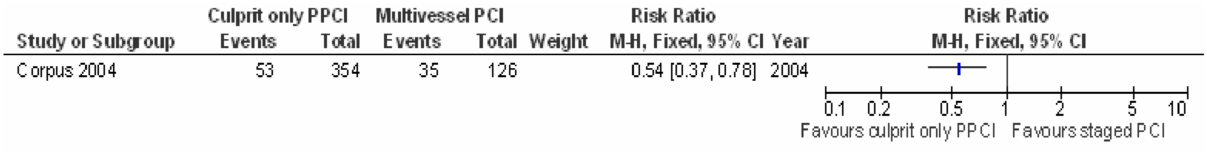
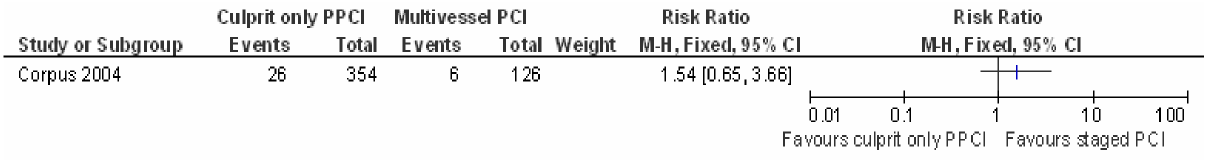


Figure 213: Cohort studies: target vessel revascularisation (longer-term)



Corpus 2004, NYS PCIRS; 12 months

Figure 214: Cohort studies: major bleeding (≤ 30 days)



Follow-up: Corpus 2004, NYS PCIRS; 12 months

I.6 Cardiogenic shock

Figure 215: All-cause mortality – hazard ratio (time to event: 6 years)

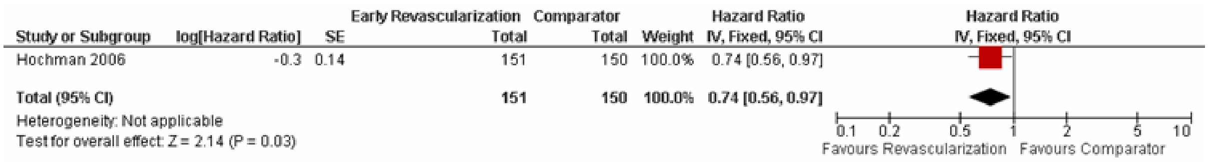


Figure 216: All-cause mortality (short-term: 30 days)

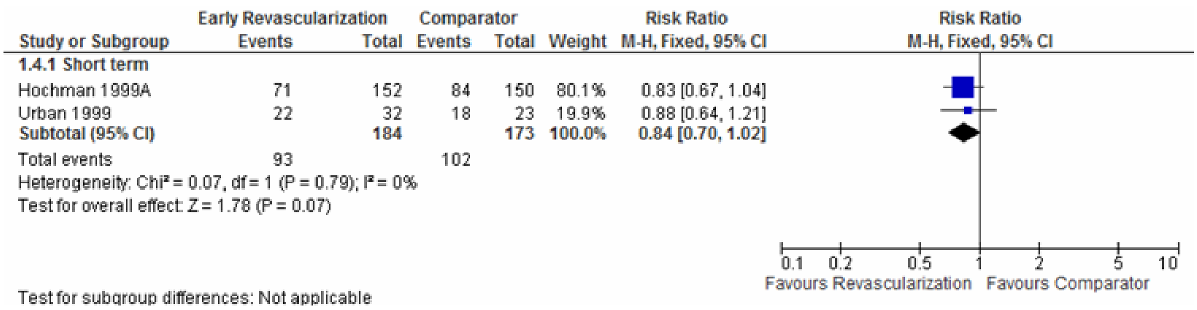


Figure 217: All-cause mortality (short-term: 30 days) – >75 years and <75 years

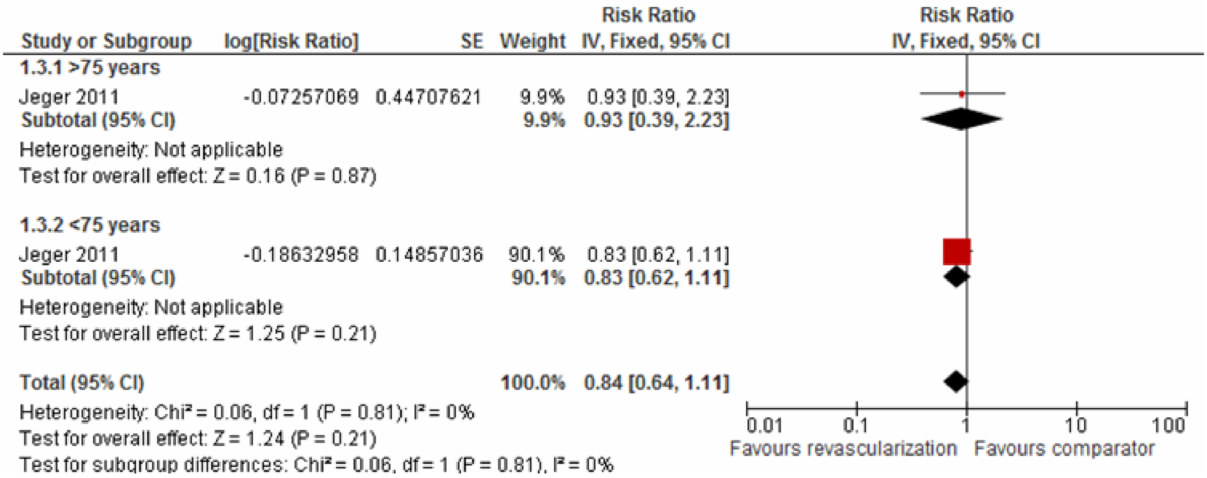


Figure 218: All-cause mortality (longer-term: 1 year) – >75 years and < 75 years

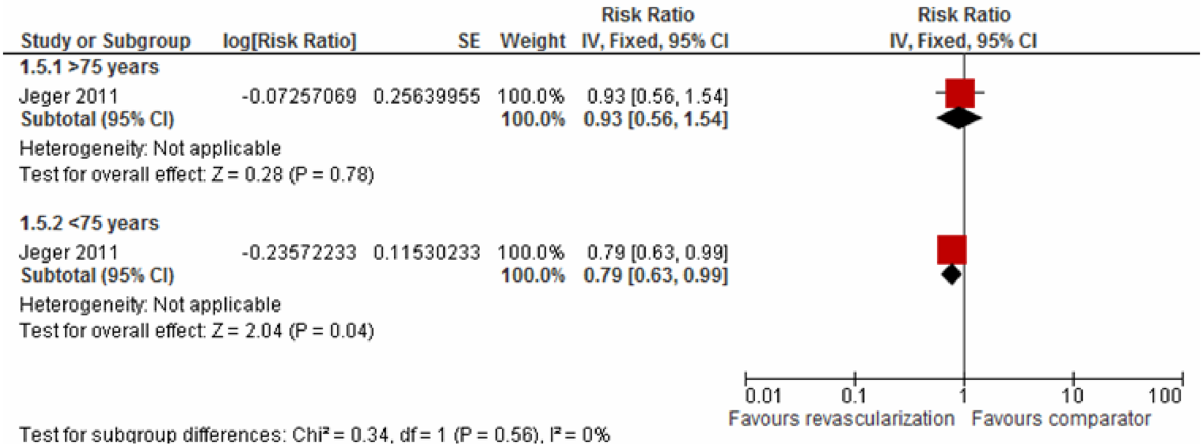


Figure 219: Survival (longer-term: 1 year)

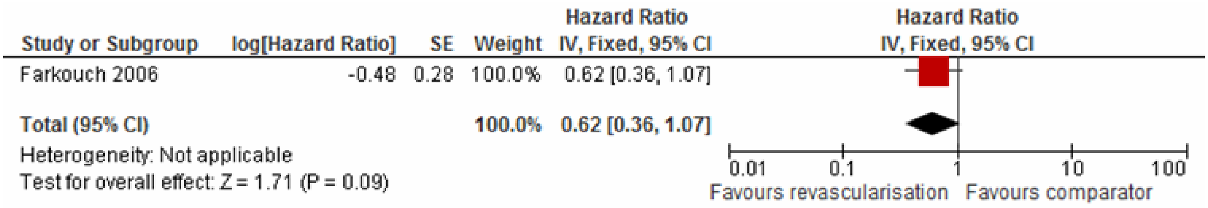


Figure 220: Survival for people without diabetes

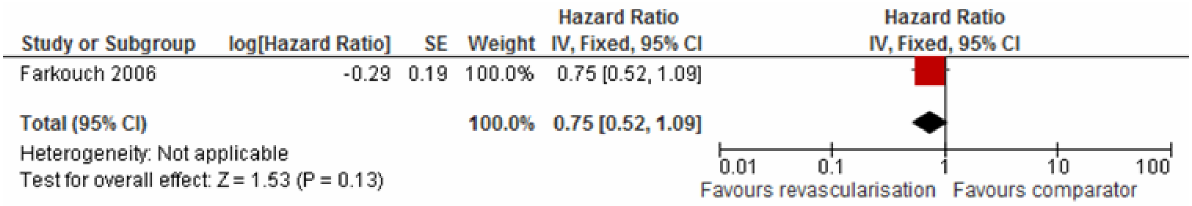


Figure 221: Quality of life (short-term: 14 days and longer-term: 6 months)

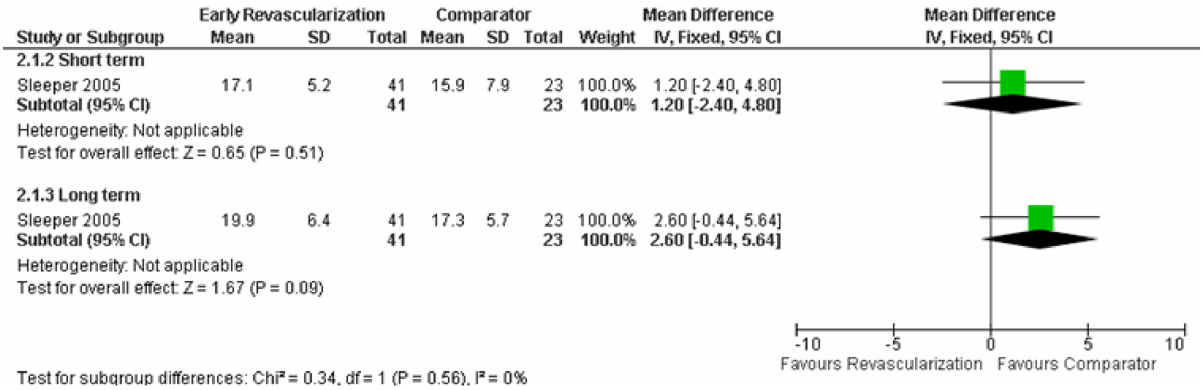


Figure 222: Stroke (short-term: 30 days)

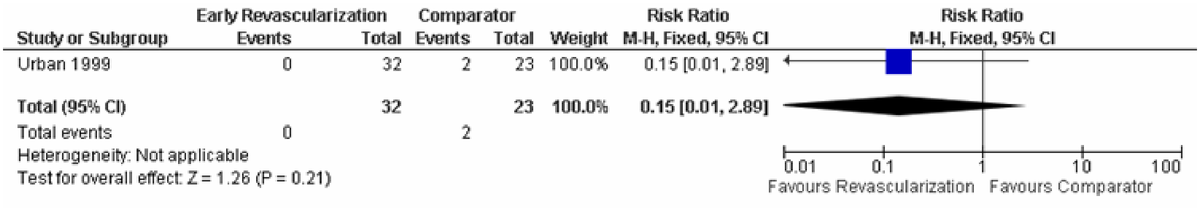


Figure 223: Renal failure (short-term: 30 days)

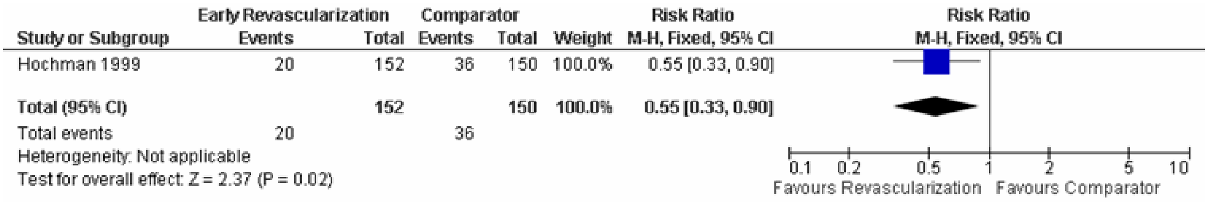


Figure 224: Reinfarction (short-term: 30 days and longer-term: 30 days to 1 year)

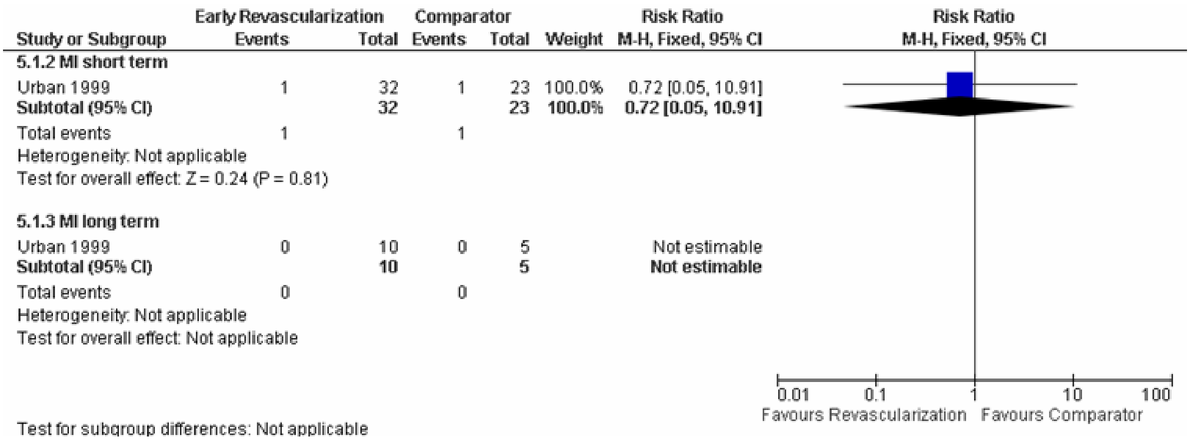


Figure 225: Unplanned revascularisation (short-term: 30 days and longer-term: 30 days to 1 year)

Study or Subgroup	Favours Revascularization Events	Favours Revascularization Total	Favours Comparator Events	Favours Comparator Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.1.2 Short term						
Urban 1999	2	32	1	23	100.0%	1.44 [0.14, 14.92]
Subtotal (95% CI)		**32**		**23**	**100.0%**	**1.44 [0.14, 14.92]**
Total events	2		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.30 (P = 0.76)						
7.1.3 Long term						
Urban 1999	1	10	0	5	100.0%	1.64 [0.08, 34.28]
Subtotal (95% CI)		**10**		**5**	**100.0%**	**1.64 [0.08, 34.28]**
Total events	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.32 (P = 0.75)						

Test for subgroup differences: Chi² = 0.00, df = 1 (P = 0.95), I² = 0%

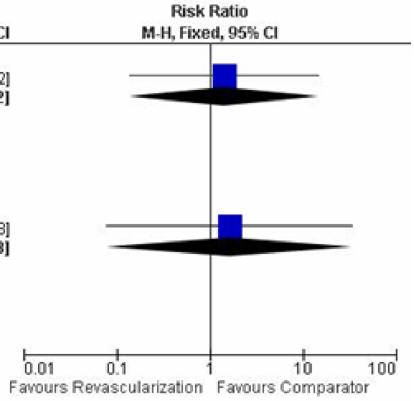


Figure 226: Intracranial bleeding (longer-term: 6 months)

Study or Subgroup	Early revascularization Events	Early revascularization Total	Comparator Events	Comparator Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hochman 1999A	0	152	2	150	100.0%	0.20 [0.01, 4.08]
Total (95% CI)		**152**		**150**	**100.0%**	**0.20 [0.01, 4.08]**
Total events	0		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.05 (P = 0.29)						

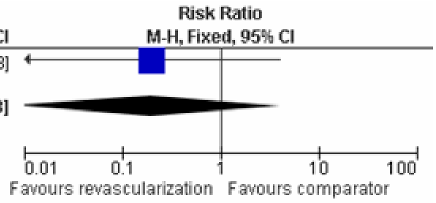


Figure 227: Heart failure Class I (short-term: 2 weeks and longer-term: 6 months)

Study or Subgroup	Revascularization Events	Revascularization Total	Comparator Events	Comparator Total	Weight	Risk Ratio M-H, Fixed, 95% CI
6.1.1 2 weeks						
Sleeper 2005	27	58	18	48	100.0%	1.24 [0.79, 1.96]
Subtotal (95% CI)		**58**		**48**	**100.0%**	**1.24 [0.79, 1.96]**
Total events	27		18			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.93 (P = 0.35)						
6.1.2 6 months						
Sleeper 2005	30	55	20	37	100.0%	1.01 [0.69, 1.48]
Subtotal (95% CI)		**55**		**37**	**100.0%**	**1.01 [0.69, 1.48]**
Total events	30		20			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.05 (P = 0.96)						

Test for subgroup differences: Chi² = 0.46, df = 1 (P = 0.50), I² = 0%

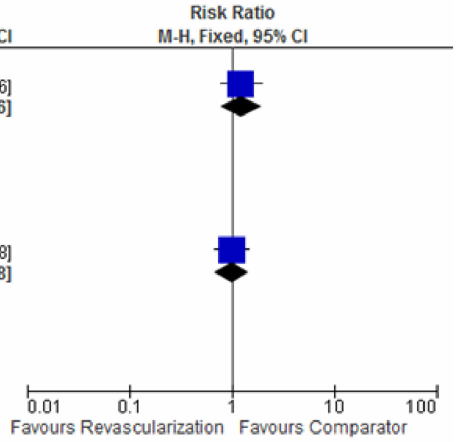


Figure 228: Heart failure Class II (short-term: 2 weeks and longer-term: 6 months)

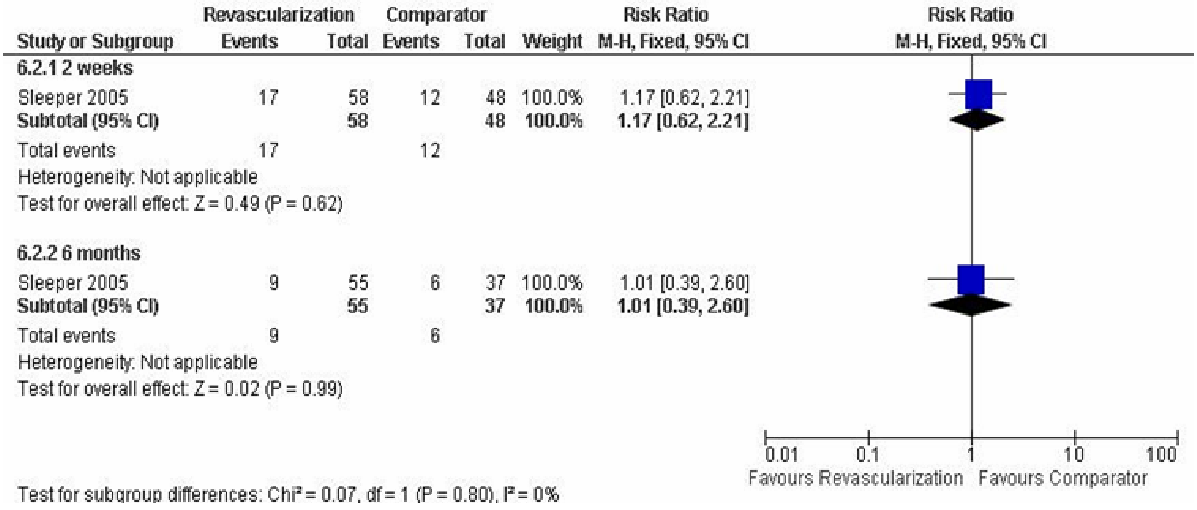


Figure 229: Heart failure Class III (short-term: 2 weeks and longer-term: 6 months)

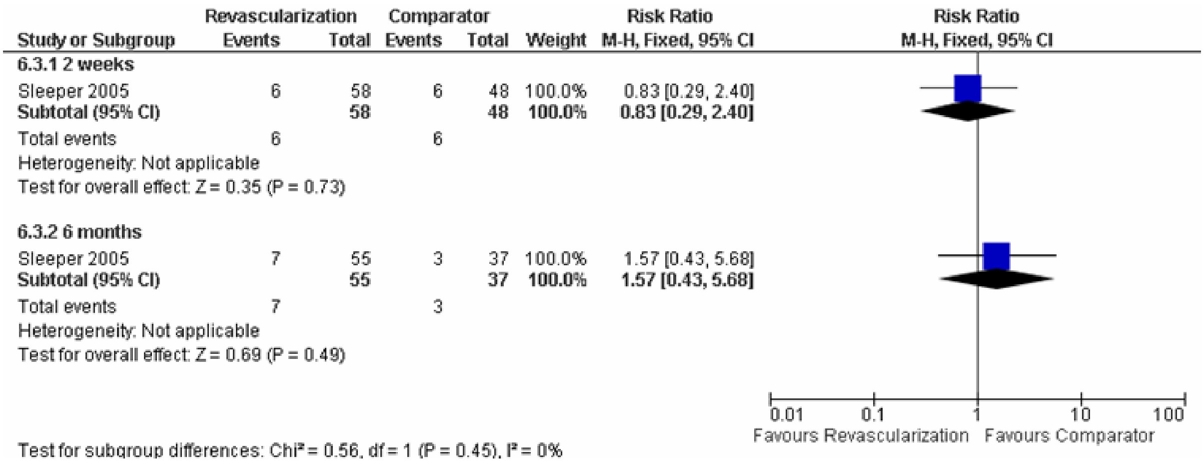
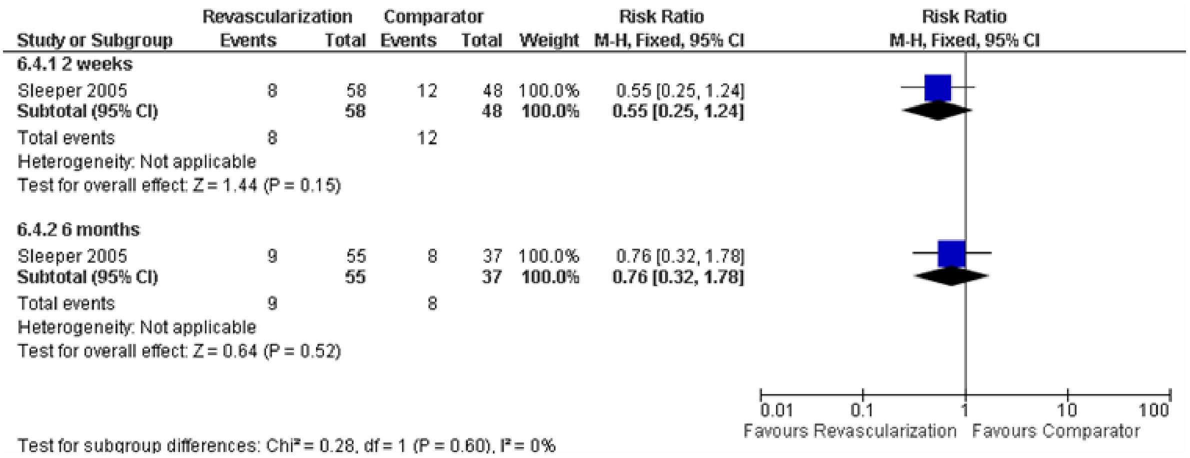


Figure 230: Heart failure Class IV (short-term: 2 weeks and longer-term: 6 months)



I.7 People who remain unconscious after a cardiac arrest

Figure 231: All-cause mortality (≤ 30 days)

	PPCI		Usual care		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	M-H, Fixed, 95% CI
Bulut 2000	6	10	13	20	0.92 [0.51, 1.68]
Liu 2012	18	49	27	32	0.44 [0.29, 0.65]
Pleskot 2008	6	19	5	6	0.38 [0.18, 0.80]

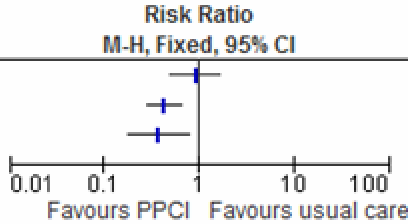


Figure 232: All-cause mortality (longer-term)

Study or Subgroup	log[Hazard Ratio]	SE	Hazard Ratio IV, Fixed, 95% CI
Pleskot 2008	-1.13	0.52	0.32 [0.12, 0.90]

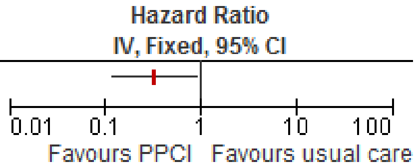


Figure 233: Good performance on CPC ≤ 30 days

	PPCI		Usual care		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	M-H, Fixed, 95% CI
Pleskot 2008	11	14	0	1	3.07 [0.27, 34.37]

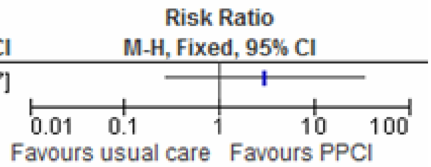


Figure 234: Good performance on CPC longer-term

	PPCI		Usual care		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	M-H, Fixed, 95% CI
Pleskot 2008	13	14	0	1	3.60 [0.32, 39.94]

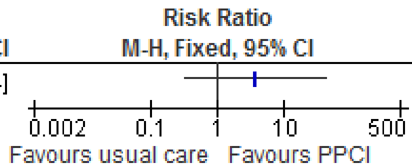


Figure 235: Stroke ≤ 30 days

	PPCI		Usual care		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	M-H, Fixed, 95% CI
Liu 2012	13	49	17	32	0.50 [0.28, 0.88]

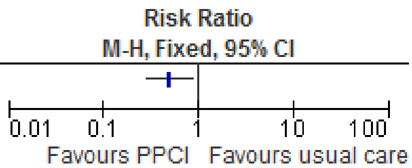
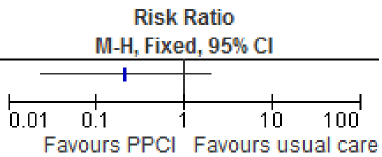


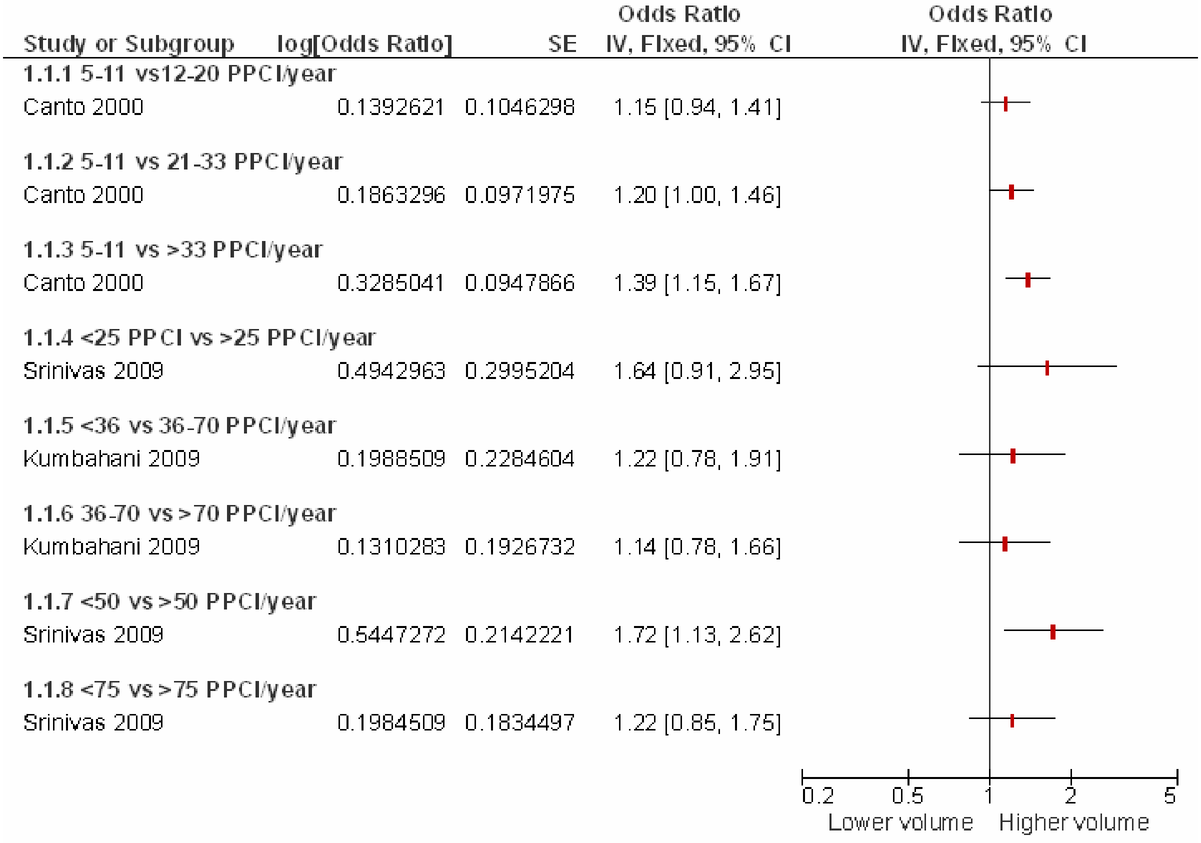
Figure 236: Renal failure stroke ≤ 30 days

	PPCI		Usual care			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
Liu 2012	1	49	3	32		0.22 [0.02, 2.00]



I.8 Hospital volumes of PPCI

Figure 237: Odds ratios of in-hospital mortality as a function of hospital PPCI volume



Srinvas 2009 and Canto 2000 results are presented as inverse log odds ratios.

Adjustment factors – Canto 2000 adjusted for demographic characteristics, medical history, clinical presentation, medications within 24 hours, year, and volume of patients with MI; Srinivas 2009 adjusted for New York State PCI risk score (age, sex, haemodynamic status, ejection fraction, pre-procedural myocardial infarction status, peripheral arterial disease, congestive heart failure, renal failure, and left main coronary disease; Kumbhani 2009 adjusted for demographics, hospital characteristics, past medical history, acute use of aspirin and beta-blockers.

I.9 Pre-hospital versus in-hospital fibrinolysis

Figure 238: All-cause mortality (pre-hospital)

Study or Subgroup	Pre-hospital Events	Pre-hospital Total	In-hospital Events	In-hospital Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Year
Castaigne 1989	1	57	1	36	4.8%	0.63 [0.04, 9.78]	1989
Schofer 1990	0	40	0	38		Not estimable	1990
Kuhn 1993/Boissel 1995	36	2750	24	2719	95.2%	1.48 [0.89, 2.48]	1995
Total (95% CI)		**2847**		**2793**	**100.0%**	**1.44 [0.87, 2.39]**	
Total events	37		25				

Heterogeneity: Chi² = 0.36, df = 1 (P = 0.55); I² = 0%
Test for overall effect: Z = 1.42 (P = 0.15)

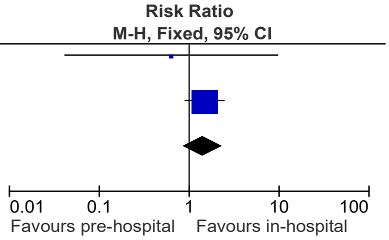
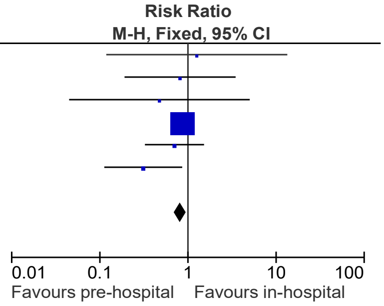


Figure 239: All-cause mortality (short-term: ≤ 30 days)

Study or Subgroup	Pre-hospital Events	Pre-hospital Total	In-hospital Events	In-hospital Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Year
Castaigne 1989	2	57	1	36	0.4%	1.26 [0.12, 13.43]	1989
Barbash 1990 / Roth 1990	4	72	3	44	1.1%	0.81 [0.19, 3.47]	1990
Schofer 1990	1	40	2	38	0.6%	0.47 [0.04, 5.03]	1990
Kuhn 1993/Boissel 1995	266	2750	303	2719	88.7%	0.87 [0.74, 1.01]	1995
Weaver 1993/Brouer1996	10	175	15	185	4.2%	0.70 [0.33, 1.53]	1996
McAleer 2006	4	82	26	166	5.0%	0.31 [0.11, 0.86]	2006
Total (95% CI)		**3176**		**3188**	**100.0%**	**0.83 [0.72, 0.97]**	
Total events	287		350				

Heterogeneity: Chi² = 4.37, df = 5 (P = 0.50); I² = 0%
Test for overall effect: Z = 2.42 (P = 0.02)



McAleer 2006 % converted to patient numbers

Figure 240: All-cause mortality (longer-term: ≥30 days)

Study or Subgroup	Pre-hospital Events	Pre-hospital Total	In-hospital Events	In-hospital Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Year
Weaver 1993/Brouer1996	10	175	15	185	36.1%	0.70 [0.33, 1.53]	1996
McAleer 2006	8	82	39	166	63.9%	0.42 [0.20, 0.85]	2006
Total (95% CI)		**257**		**351**	**100.0%**	**0.52 [0.31, 0.88]**	
Total events	18		54				

Heterogeneity: Chi² = 0.98, df = 1 (P = 0.32); I² = 0%
Test for overall effect: Z = 2.46 (P = 0.01)

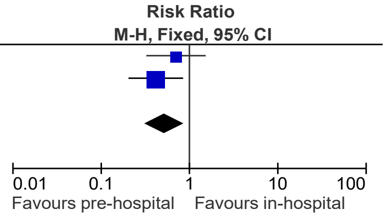


Figure 241: Cardiac mortality (short-term: ≤30 days)

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Year
Kuhn 1993/Boissel 1995	228	2750	267	2719	100.0%	0.84 [0.71, 1.00]	1995
Total (95% CI)		**2750**		**2719**	**100.0%**	**0.84 [0.71, 1.00]**	
Total events	228		267				

Heterogeneity: Not applicable
Test for overall effect: Z = 1.97 (P = 0.05)

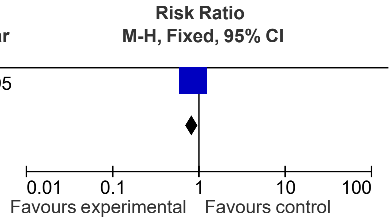


Figure 242: Myocardial reinfarction (short-term: ≤30 days)

Study or Subgroup	Pre-hospital Events	Pre-hospital Total	In-hospital Events	In-hospital Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Year
Barbash 1990 / Roth 1990	10	72	6	44	59.2%	1.02 [0.40, 2.61]	1990
Schofer 1990	4	40	5	38	40.8%	0.76 [0.22, 2.62]	1990
Total (95% CI)		**112**		**82**	**100.0%**	**0.91 [0.43, 1.93]**	
Total events	14		11				

Heterogeneity: Chi² = 0.14, df = 1 (P = 0.71); I² = 0
Test for overall effect: Z = 0.24 (P = 0.81)

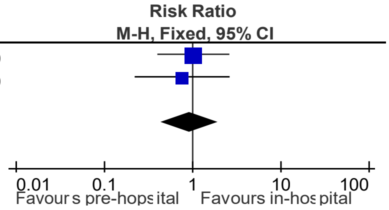


Figure 243: Heart failure (short-term: ≤30 days)

Study or Subgroup	Pre-hospital Events	Pre-hospital Total	In-hospital Events	In-hospital Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Year
Barbash 1990 / Roth 1990	5	72	7	44	40.7%	0.44 [0.15, 1.29]	1990
Weaver 1993/Brouer1996	12	175	13	185	59.3%	0.98 [0.46, 2.08]	1996
Total (95% CI)		**247**		**229**	**100.0%**	**0.76 [0.41, 1.39]**	
Total events	17		20				

Heterogeneity: Chi² = 1.42, df = 1 (P = 0.23); I² = 30%
Test for overall effect: Z = 0.90 (P = 0.37)

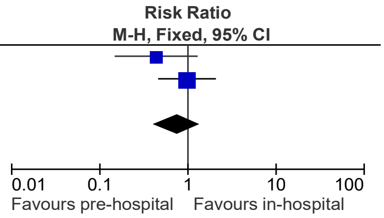


Figure 244: Stroke (short-term: ≤30 days)

Study or Subgroup	Pre-hospital Events	Pre-hospital Total	In-hospital Events	In-hospital Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Year
Kuhn 1993/Boissel 1995	86	2750	84	2719	97.8%	1.01 [0.75, 1.36]	1995
Weaver 1993/Brouer1996	4	175	2	185	2.2%	2.11 [0.39, 11.40]	1996
Total (95% CI)		**2925**		**2904**	**100.0%**	**1.04 [0.78, 1.39]**	
Total events	90		86				

Heterogeneity: Chi² = 0.71, df = 1 (P = 0.40); I² = 0%
Test for overall effect: Z = 0.25 (P = 0.81)

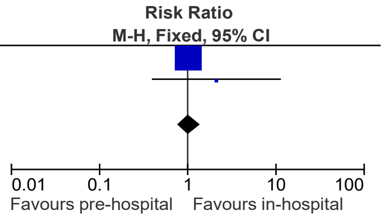
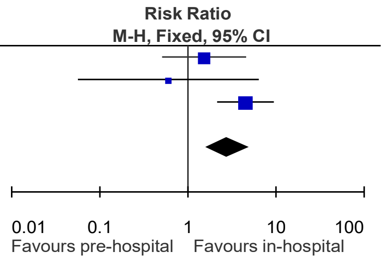


Figure 245: Major and minor bleeding (short-term: ≤30 days)

Study or Subgroup	Pre-hospital Events	Pre-hospital Total	In-hospital Events	In-hospital Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Year
Barbash 1990 / Roth 1990	10	72	4	44	39.0%	1.53 [0.51, 4.58]	1990
Schofer 1990	1	40	2	48	14.3%	0.60 [0.06, 6.38]	1990
McAleer 2006	20	82	9	166	46.7%	4.50 [2.14, 9.44]	2006
Total (95% CI)		**194**		**258**	**100.0%**	**2.78 [1.58, 4.90]**	
Total events	31		15				

Heterogeneity: Chi² = 4.38, df = 2 (P = 0.11); I² = 54%
Test for overall effect: Z = 3.55 (P = 0.0004)



Definitions:

Barbash/Roth: not specified

Schofer: bleeding at puncture site, haematuria, gastrointestinal bleeding, cerebral bleeding

McAleer: minor – bleeding at venepuncture and haematuria

Weaver/Brouer: 'serious' bleeding

I.10 Use of antithrombin as an adjunct to fibrinolysis

None.

I.11 Rescue PCI

I.11.1 Rescue PCI versus conservative therapy

Figure 246: All-cause mortality (short-term: 30 days unless specified)

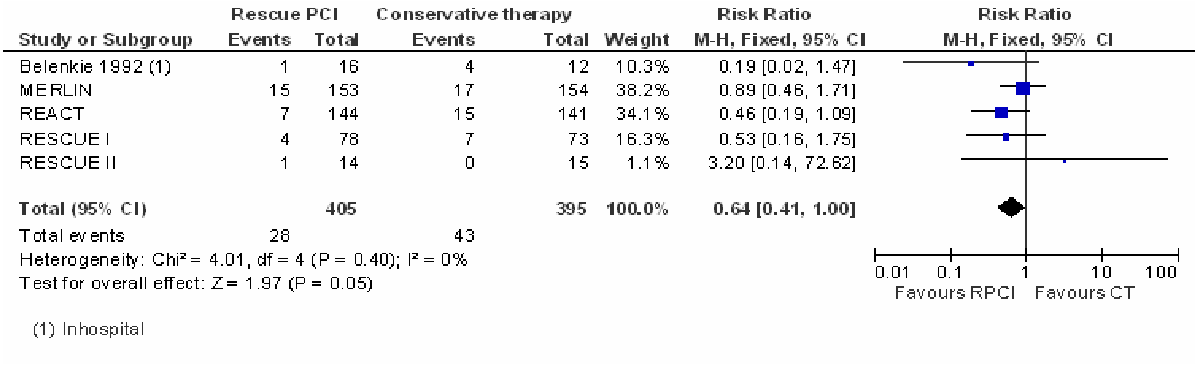


Figure 247: All-cause mortality (longer-term)

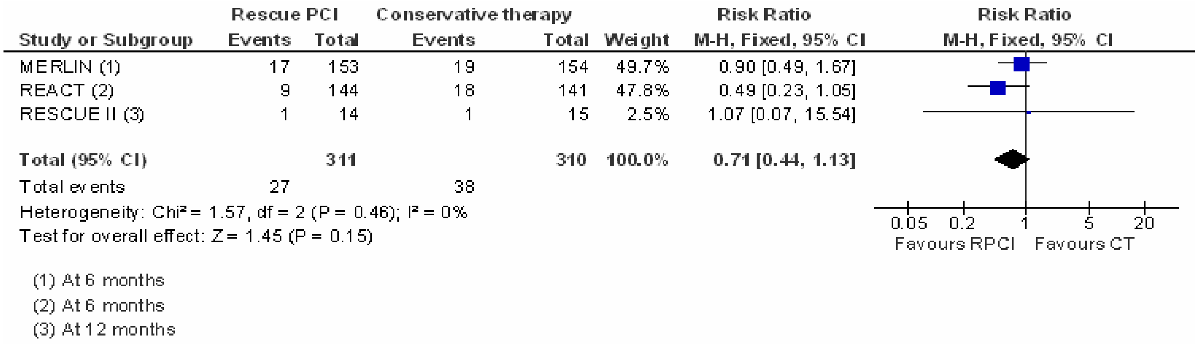


Figure 248: All-cause mortality – time to event

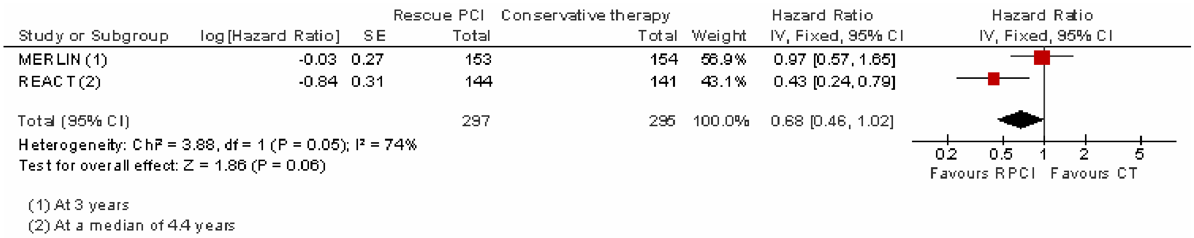


Figure 249: Cardiovascular mortality (short-term: 30 days unless specified)

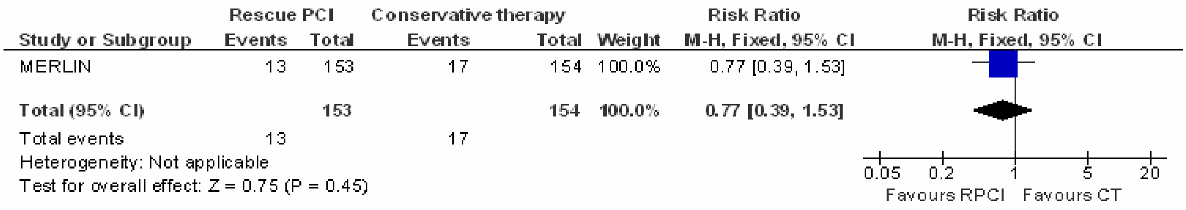


Figure 250: Cardiovascular mortality – time to event

Study or Subgroup	log[Hazard Ratio]	SE	Rescue PCI Total	Conservative therapy Total	Weight	Hazard Ratio IV, Fixed, 95% CI
REACT (1)	-0.65	0.34	144	141	100.0%	0.52 [0.27, 1.02]
Total (95% CI)			144	141	100.0%	0.52 [0.27, 1.02]

Heterogeneity: Not applicable
Test for overall effect: Z = 1.91 (P = 0.06)

(1) At a median of 4.4 years

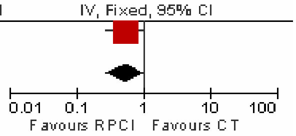


Figure 251: Reinfarction (short-term: 30 days unless specified)

Study or Subgroup	Rescue PCI Events	Rescue PCI Total	Conservative therapy Events	Conservative therapy Total	Weight	Risk Ratio M-H, Fixed, 95% CI
MERLIN	11	153	16	154	63.7%	0.69 [0.33, 1.44]
REACT	1	144	9	141	36.3%	0.11 [0.01, 0.85]
RESCUE II (1)	0	14	0	15		Not estimable
Total (95% CI)		**311**		**310**	**100.0%**	**0.48 [0.25, 0.93]**
Total events	12		25			

Heterogeneity: Chi² = 2.96, df = 1 (P = 0.09); I² = 66%
Test for overall effect: Z = 2.16 (P = 0.03)

(1) Inhospital

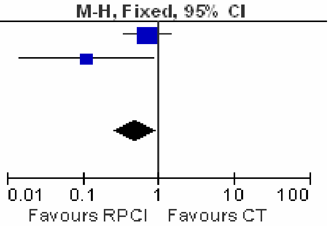


Figure 252: Reinfarction (longer-term)

Study or Subgroup	Rescue PCI Events	Rescue PCI Total	Conservative therapy Events	Conservative therapy Total	Weight	Risk Ratio M-H, Fixed, 95% CI
MERLIN (1)	12	153	20	154	62.2%	0.60 [0.31, 1.19]
REACT (2)	3	144	12	141	37.8%	0.24 [0.07, 0.85]
Total (95% CI)		**297**		**295**	**100.0%**	**0.47 [0.26, 0.84]**
Total events	15		32			

Heterogeneity: Chi² = 1.58, df = 1 (P = 0.21); I² = 37%
Test for overall effect: Z = 2.53 (P = 0.01)

(1) At 6 months
(2) At 6 months

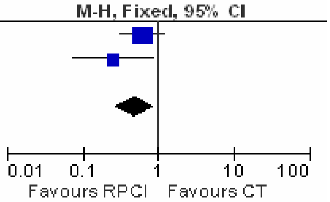


Figure 253: Reinfarction – time to event

Study or Subgroup	log[Hazard Ratio]	SE	Rescue PCI Total	Conservative therapy Total	Weight	Hazard Ratio IV, Fixed, 95% CI
REACT (1)	-1.11	0.52	144	141	100.0%	0.33 [0.12, 0.91]
Total (95% CI)			144	141	100.0%	0.33 [0.12, 0.91]

Heterogeneity: Not applicable
Test for overall effect: Z = 2.13 (P = 0.03)

(1) At 6 months

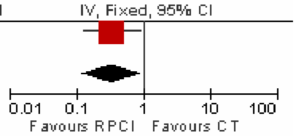


Figure 254: Heart failure (short-term: 30 days unless specified)

Study or Subgroup	Rescue PCI Events	Rescue PCI Total	Conservative therapy Events	Conservative therapy Total	Weight	Risk Ratio M-H, Fixed, 95% CI
MERLIN	37	153	46	154	75.0%	0.81 [0.56, 1.17]
REACT	6	144	10	141	16.5%	0.59 [0.22, 1.57]
RESCUE I	1	78	5	73	8.5%	0.19 [0.02, 1.56]
Total (95% CI)		**375**		**368**	**100.0%**	**0.72 [0.51, 1.01]**
Total events	44		61			

Heterogeneity: Chi² = 2.09, df = 2 (P = 0.35); I² = 5%
Test for overall effect: Z = 1.88 (P = 0.06)

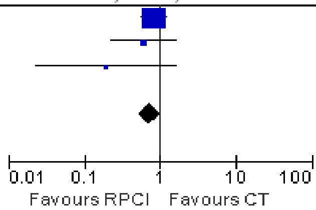


Figure 255: Heart failure – Longer-term

	Rescue PCI		Conservative therapy			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
MERLIN (1)	39	153	48	154	81.1%	0.82 [0.57, 1.17]
REACT (2)	7	144	11	141	18.9%	0.62 [0.25, 1.56]
Total (95% CI)		**297**		**295**	**100.0%**	**0.78 [0.56, 1.09]**
Total events	46		59			

Heterogeneity: Chi² = 0.30, df = 1 (P = 0.59); I² = 0%
Test for overall effect: Z = 1.44 (P = 0.15)

(1) At 6 months
(2) At 6 months

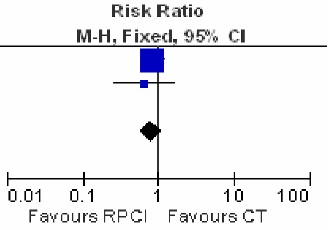


Figure 256: Stroke – Short-term (30 day data unless specified)

	Rescue PCI		Conservative therapy			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
MERLIN	7	153	1	154	49.7%	7.05 [0.88, 56.58]
REACT	2	144	1	141	50.3%	1.96 [0.18, 21.36]
Total (95% CI)		**297**		**295**	**100.0%**	**4.48 [0.98, 20.52]**
Total events	9		2			

Heterogeneity: Chi² = 0.64, df = 1 (P = 0.42); I² = 0%
Test for overall effect: Z = 1.93 (P = 0.05)

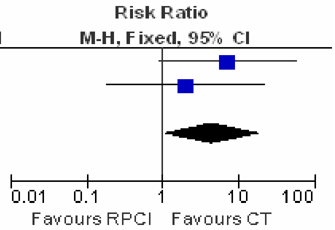


Figure 257: Stroke (longer-term)

	Rescue PCI		Conservative therapy			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
MERLIN (1)	7	153	2	154	66.4%	3.52 [0.74, 16.69]
REACT (2)	3	144	1	141	33.6%	2.94 [0.31, 27.90]
Total (95% CI)		**297**		**295**	**100.0%**	**3.33 [0.93, 11.95]**
Total events	10		3			

Heterogeneity: Chi² = 0.02, df = 1 (P = 0.90); I² = 0%
Test for overall effect: Z = 1.84 (P = 0.07)

(1) At 6 months
(2) At 6 months

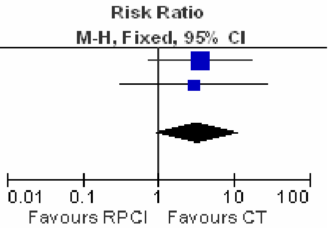


Figure 258: Unplanned revascularisation (short-term: 30 days unless specified)

	Rescue PCI		Conservative therapy			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
MERLIN	10	153	31	154	85.3%	0.32 [0.17, 0.64]
RESCUE II (1)	0	14	5	15	14.7%	0.10 [0.01, 1.61]
Total (95% CI)		**167**		**169**	**100.0%**	**0.29 [0.15, 0.56]**
Total events	10		36			

Heterogeneity: Chi² = 0.69, df = 1 (P = 0.41); I² = 0%
Test for overall effect: Z = 3.69 (P = 0.0002)

(1) Inhospital

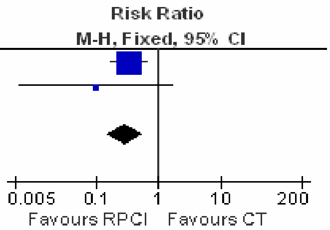
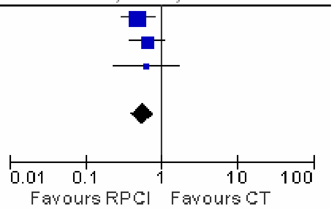


Figure 259: Unplanned revascularisation (longer-term)

Study or Subgroup	Rescue PCI Events	Rescue PCI Total	Conservative therapy Events	Conservative therapy Total	Weight	Risk Ratio M-H, Fixed, 95% CI
MERLIN (1)	19	153	40	154	52.5%	0.48 [0.29, 0.79]
REACT (2)	19	144	29	141	38.6%	0.64 [0.38, 1.09]
RESCUE II (3)	4	14	7	15	8.9%	0.61 [0.23, 1.65]
Total (95% CI)		**311**		**310**	**100.0%**	**0.55 [0.39, 0.78]**
Total events	42		76			

Heterogeneity: Chi² = 0.67, df = 2 (P = 0.72); I² = 0%
Test for overall effect: Z = 3.40 (P = 0.0007)

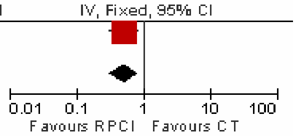


(1) At 6 months
(2) At 6 months
(3) At 12 months

Figure 260: Unplanned revascularisation – time to event

Study or Subgroup	log [Hazard Ratio]	SE	Rescue PCI Total	Conservative therapy Total	Weight	Hazard Ratio IV, Fixed, 95% CI
REACT (1)	-0.69	0.26	144	141	100.0%	0.50 [0.30, 0.83]
Total (95% CI)			144	141	100.0%	0.50 [0.30, 0.83]

Heterogeneity: Not applicable
Test for overall effect: Z = 2.65 (P = 0.008)

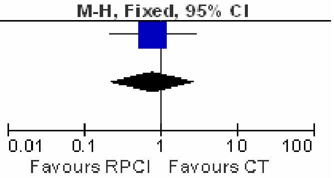


(1) At 12 months

Figure 261: Major bleeding (short-term: 30 days unless specified)

Study or Subgroup	Rescue PCI Events	Rescue PCI Total	Conservative therapy Events	Conservative therapy Total	Weight	Risk Ratio M-H, Fixed, 95% CI
REACT (1)	4	144	5	141	100.0%	0.78 [0.21, 2.86]
Total (95% CI)		**144**		**141**	**100.0%**	**0.78 [0.21, 2.86]**
Total events	4		5			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.37 (P = 0.71)

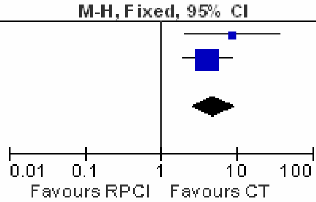


(1) Inhospital

Figure 262: Minor bleeding (short-term: 30 days unless specified)

Study or Subgroup	Rescue PCI Events	Rescue PCI Total	Conservative therapy Events	Conservative therapy Total	Weight	Risk Ratio M-H, Fixed, 95% CI
MERLIN (1)	17	153	2	154	19.8%	8.56 [2.01, 36.40]
REACT (2)	33	144	8	141	80.2%	4.04 [1.93, 8.44]
Total (95% CI)		**297**		**295**	**100.0%**	**4.93 [2.56, 9.49]**
Total events	50		10			

Heterogeneity: Chi² = 0.84, df = 1 (P = 0.36); I² = 0%
Test for overall effect: Z = 4.78 (P < 0.00001)

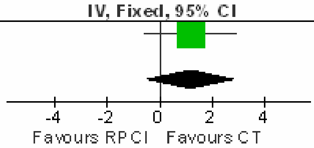


(1) Inhospital
(2) Inhospital

Figure 263: Length of hospital stay – index admission

Study or Subgroup	Rescue PCI Mean	Rescue PCI SD	Rescue PCI Total	Conservative therapy Mean	Conservative therapy SD	Conservative therapy Total	Weight	Mean Difference IV, Fixed, 95% CI
RESCUE II	7.6	3	14	6.4	1.6	15	100.0%	1.20 [-0.57, 2.97]
Total (95% CI)			**14**			**15**	**100.0%**	**1.20 [-0.57, 2.97]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.33 (P = 0.18)



I.11.2 Repeated fibrinolysis versus conservative therapy

Figure 264: All-cause mortality (short-term)

Study or Subgroup	Repeated fibrinolysis Events	Repeated fibrinolysis Total	Conservative therapy Events	Conservative therapy Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Mounsey 1995 (1)	1	19	1	18	7.3%	0.95 [0.06, 14.04]
Sarullo 2000 (2)	3	45	13	45	92.7%	0.23 [0.07, 0.76]
Total (95% CI)		**64**		**63**	**100.0%**	**0.28 [0.10, 0.81]**
Total events	4		14			

Heterogeneity: Chi² = 0.89, df = 1 (P = 0.35); I² = 0%
Test for overall effect: Z = 2.34 (P = 0.02)

(1) At 6 weeks
(2) Inhospital

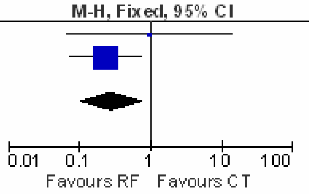


Figure 265: All-cause mortality – time to event

Study or Subgroup	log[Hazard Ratio]	SE	Repeated fibrinolysis Total	Conservative therapy Total	Weight	Hazard Ratio IV, Fixed, 95% CI
REACT (1)	0.04	0.26	142	141	100.0%	1.04 [0.63, 1.73]
Total (95% CI)			142	141	100.0%	1.04 [0.63, 1.73]

Heterogeneity: Not applicable
Test for overall effect: Z = 0.15 (P = 0.88)

(1) At a median of 4.4 years

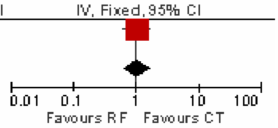


Figure 266: Cardiovascular mortality – time to event

Study or Subgroup	log[Hazard Ratio]	SE	Repeated fibrinolysis Total	Conservative therapy Total	Weight	Hazard Ratio IV, Fixed, 95% CI
REACT (1)	-0.2	0.28	142	141	100.0%	0.82 [0.47, 1.42]
Total (95% CI)			142	141	100.0%	0.82 [0.47, 1.42]

Heterogeneity: Not applicable
Test for overall effect: Z = 0.71 (P = 0.48)

(1) At a median of 4.4 years

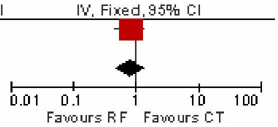


Figure 267: Reinfarction (short-term)

Study or Subgroup	Repeated fibrinolysis Events	Repeated fibrinolysis Total	Conservative therapy Events	Conservative therapy Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Sarullo 2000 (1)	7	45	0	45	100.0%	15.00 [0.88, 255.04]
Total (95% CI)		**45**		**45**	**100.0%**	**15.00 [0.88, 255.04]**
Total events	7		0			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.87 (P = 0.06)

(1) Inhospital

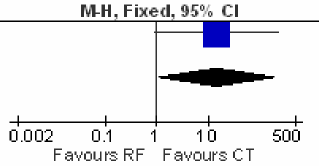


Figure 268: Reinfarction (longer-term)

Study or Subgroup	Repeated fibrinolysis Events	Repeated fibrinolysis Total	Conservative therapy Events	Conservative therapy Total	Weight	Risk Ratio M-H, Fixed, 95% CI
REACT (1)	15	142	12	141	100.0%	1.24 [0.60, 2.56]
Total (95% CI)		**142**		**141**	**100.0%**	**1.24 [0.60, 2.56]**
Total events	15		12			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.59 (P = 0.56)

(1) At 6 months

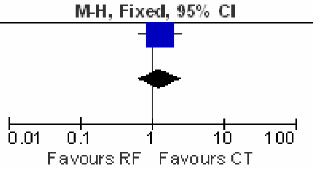


Figure 269: Heart failure (longer-term)

Study or Subgroup	Repeated fibrinolysis Events	Repeated fibrinolysis Total	Conservative therapy Events	Conservative therapy Total	Weight	Risk Ratio M-H, Fixed, 95% CI
REACT (1)	10	142	11	141	100.0%	0.90 [0.40, 2.06]
Total (95% CI)		**142**		**141**	**100.0%**	**0.90 [0.40, 2.06]**
Total events	10		11			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.24 (P = 0.81)

(1) At 6 months

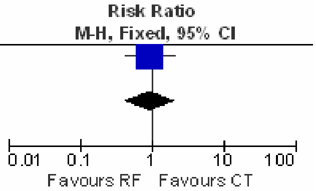


Figure 270: Stroke (longer-term)

Study or Subgroup	Repeated fibrinolysis Events	Repeated fibrinolysis Total	Conservative therapy Events	Conservative therapy Total	Weight	Risk Ratio M-H, Fixed, 95% CI
REACT (1)	1	142	1	141	100.0%	0.99 [0.06, 15.72]
Total (95% CI)		**142**		**141**	**100.0%**	**0.99 [0.06, 15.72]**
Total events	1		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.01 (P = 1.00)

(1) At 6 months

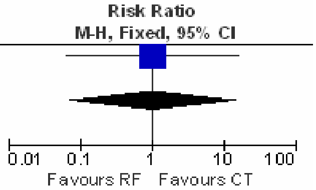


Figure 271: Unplanned revascularisation (short-term)

Study or Subgroup	Repeated fibrinolysis Events	Repeated fibrinolysis Total	Conservative therapy Events	Conservative therapy Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Sarullo 2000 (1)	14	45	1	45	100.0%	14.00 [1.92, 102.03]
Total (95% CI)		**45**		**45**	**100.0%**	**14.00 [1.92, 102.03]**
Total events	14		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 2.60 (P = 0.009)

(1) Inhospital

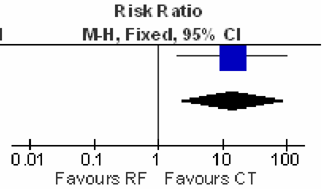


Figure 272: Unplanned revascularisation – time to event

Study or Subgroup	log[Hazard Ratio]	SE	Repeated fibrinolysis Total	Conservative therapy Total	Weight	Hazard Ratio IV, Fixed, 95% CI
REACT (1)	0.05	0.22	142	141	100.0%	1.05 [0.68, 1.62]
Total (95% CI)			142	141	100.0%	1.05 [0.68, 1.62]

Heterogeneity: Not applicable
Test for overall effect: Z = 0.23 (P = 0.82)

(1) At 12 months

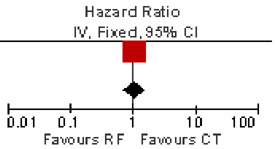


Figure 273: Major bleeding (short-term)

Study or Subgroup	Repeated fibrinolysis Events	Repeated fibrinolysis Total	Conservative therapy Events	Conservative therapy Total	Weight	Risk Ratio M-H, Fixed, 95% CI
REACT (1)	7	142	5	141	90.9%	1.39 [0.45, 4.28]
Sarullo 2000 (2)	1	45	0	45	9.1%	3.00 [0.13, 71.74]
Total (95% CI)		**187**		**186**	**100.0%**	**1.54 [0.54, 4.40]**
Total events	8		5			

Heterogeneity: $Chi^2 = 0.20$, df = 1 (P = 0.65); $I^2 = 0\%$
Test for overall effect: Z = 0.80 (P = 0.42)

(1) Inhospital
(2) Inhospital

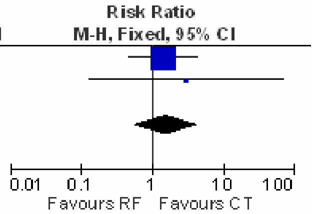
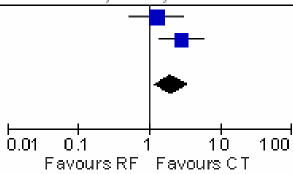


Figure 274: Minor bleeding (short-term)

Study or Subgroup	Repeated fibrinolysis Events	Total	Conservative therapy Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
REACT (1)	10	142	8	141	53.4%	1.24 [0.50, 3.05]
Sarullo 2000 (2)	20	45	7	45	46.6%	2.86 [1.34, 6.08]
Total (95% CI)		**187**		**186**	**100.0%**	**1.99 [1.13, 3.51]**
Total events	30		15			

Heterogeneity: Chi² = 1.94, df = 1 (P = 0.16); I² = 48%
Test for overall effect: Z = 2.39 (P = 0.02)



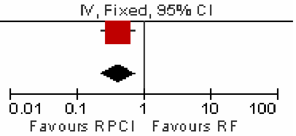
(1) Inhospital
(2) Inhospital

I.11.3 Rescue PCI versus repeated fibrinolysis

Figure 275: All-cause mortality – time to event

Study or Subgroup	log[Hazard Ratio]	SE	Rescue PCI Total	Repeated fibrinolysis Total	Weight	Hazard Ratio IV, Fixed, 95% CI
REACT (1)	-0.89	0.31	144	142	100.0%	0.41 [0.22, 0.75]
Total (95% CI)			144	142	100.0%	0.41 [0.22, 0.75]

Heterogeneity: Not applicable
Test for overall effect: Z = 2.87 (P = 0.004)

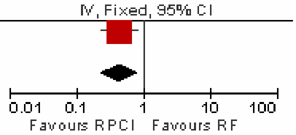


(1) At a median of 4.4 years

Figure 276: Cardiovascular mortality – time to event

Study or Subgroup	log[Hazard Ratio]	SE	Rescue PCI Total	Repeated fibrinolysis Total	Weight	Hazard Ratio IV, Fixed, 95% CI
REACT (1)	-0.84	0.34	144	142	100.0%	0.43 [0.22, 0.84]
Total (95% CI)			144	142	100.0%	0.43 [0.22, 0.84]

Heterogeneity: Not applicable
Test for overall effect: Z = 2.47 (P = 0.01)

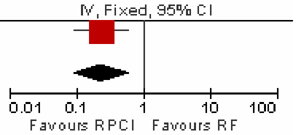


(1) At a median of 4.4 years

Figure 277: Reinfarction – time to event

Study or Subgroup	log[Hazard Ratio]	SE	Rescue PCI Total	Repeated fibrinolysis Total	Weight	Hazard Ratio IV, Fixed, 95% CI
REACT (1)	-1.47	0.49	144	142	100.0%	0.23 [0.09, 0.60]
Total (95% CI)			144	142	100.0%	0.23 [0.09, 0.60]

Heterogeneity: Not applicable
Test for overall effect: Z = 3.00 (P = 0.003)

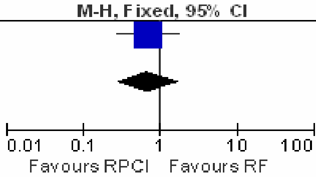


(1) At 6 months

Figure 278: Heart failure (longer-term)

Study or Subgroup	Rescue PCI Events	Total	Repeated fibrinolysis Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
REACT (1)	7	144	10	142	100.0%	0.69 [0.27, 1.76]
Total (95% CI)		**144**		**142**	**100.0%**	**0.69 [0.27, 1.76]**
Total events	7		10			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.77 (P = 0.44)

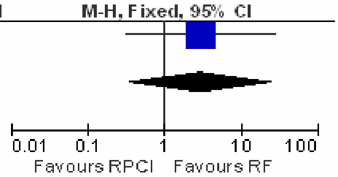


(1) At 6 months

Figure 279: Stroke (longer-term)

Study or Subgroup	Rescue PCI Events	Rescue PCI Total	Repeated fibrinolysis Events	Repeated fibrinolysis Total	Weight	Risk Ratio M-H, Fixed, 95% CI
REACT (1)	3	144	1	142	100.0%	2.96 [0.31, 28.10]
Total (95% CI)		**144**		**142**	**100.0%**	**2.96 [0.31, 28.10]**
Total events	3		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.94 (P = 0.35)

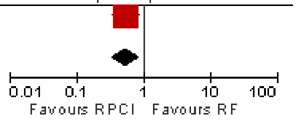


(1) At 6 months

Figure 280: Unplanned revascularisation – time to event

Study or Subgroup	log[Hazard Ratio]	SE	Rescue PCI Total	Repeated fibrinolysis Total	Weight	Hazard Ratio IV, Fixed, 95% CI
REACT (1)	-0.63	0.25	144	142	100.0%	0.53 [0.33, 0.87]
Total (95% CI)			144	142	100.0%	0.53 [0.33, 0.87]

Heterogeneity: Not applicable
Test for overall effect: Z = 2.52 (P = 0.01)

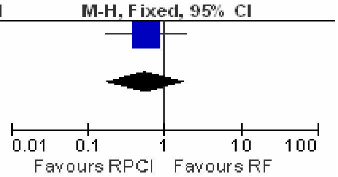


(1) At 12 months

Figure 281: Major bleeding (short-term)

Study or Subgroup	Rescue PCI Events	Rescue PCI Total	Repeated fibrinolysis Events	Repeated fibrinolysis Total	Weight	Risk Ratio M-H, Fixed, 95% CI
REACT (1)	4	144	7	142	100.0%	0.56 [0.17, 1.88]
Total (95% CI)		**144**		**142**	**100.0%**	**0.56 [0.17, 1.88]**
Total events	4		7			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.93 (P = 0.35)

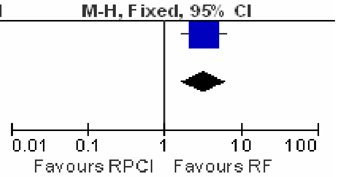


(1) Inhospital

Figure 282: Minor bleeding (short-term)

Study or Subgroup	Rescue PCI Events	Rescue PCI Total	Repeated fibrinolysis Events	Repeated fibrinolysis Total	Weight	Risk Ratio M-H, Fixed, 95% CI
REACT (1)	33	144	10	142	100.0%	3.25 [1.67, 6.35]
Total (95% CI)		**144**		**142**	**100.0%**	**3.25 [1.67, 6.35]**
Total events	33		10			

Heterogeneity: Not applicable
Test for overall effect: Z = 3.46 (P = 0.0005)



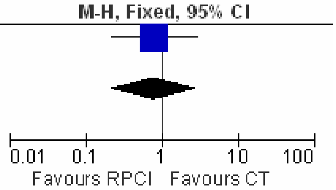
(1) Inhospital

I.11.4 Rescue PCI versus conservative therapy (sensitivity analysis – incidence of bleeding)

Figure 283: Major bleeding (short-term)

Study or Subgroup	Rescue PCI Events	Rescue PCI Total	Conservative therapy Events	Conservative therapy Total	Weight	Risk Ratio M-H, Fixed, 95% CI
REACT (1)	4	144	5	141	100.0%	0.78 [0.21, 2.86]
Total (95% CI)		**144**		**141**	**100.0%**	**0.78 [0.21, 2.86]**
Total events	4		5			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.37 (P = 0.71)

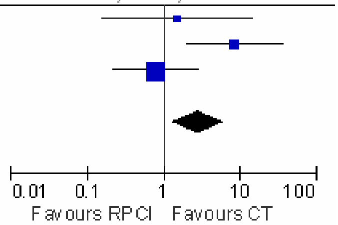


(1) Defined as major bleed in study

Figure 284: Major bleeding plus undefined bleeding (short-term)

Study or Subgroup	Rescue PCI Events	Rescue PCI Total	Conservative therapy Events	Conservative therapy Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Belenkie 1992 (1)	2	16	1	12	14.0%	1.50 [0.15, 14.68]
MERLIN (2)	17	153	2	154	24.3%	8.56 [2.01, 36.40]
REACT (3)	4	144	5	141	61.7%	0.78 [0.21, 2.86]
Total (95% CI)		**313**		**307**	**100.0%**	**2.78 [1.26, 6.09]**
Total events	23		8			

Heterogeneity: Chi² = 6.27, df = 2 (P = 0.04); I² = 68%
Test for overall effect: Z = 2.55 (P = 0.01)

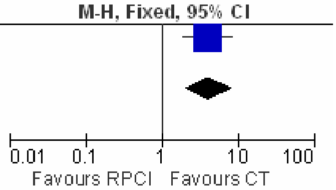


(1) No study definition. RPCI: 1 gastrointestinal bleeding,1 groin haematoma requiring transfusion. CT: 1 severe groin haematoma
(2) Transfusion required.Transfusion reserved for fall in haemoglobin of ≥2 g/dl, and only if this took total haemoglobin to <10 g/dl
(3) Defined as major bleed in study

Figure 285: Minor bleeding (short-term)

Study or Subgroup	Rescue PCI Events	Rescue PCI Total	Conservative therapy Events	Conservative therapy Total	Weight	Risk Ratio M-H, Fixed, 95% CI
REACT (1)	33	144	8	141	100.0%	4.04 [1.93, 8.44]
Total (95% CI)		**144**		**141**	**100.0%**	**4.04 [1.93, 8.44]**
Total events	33		8			

Heterogeneity: Not applicable
Test for overall effect: Z = 3.71 (P = 0.0002)

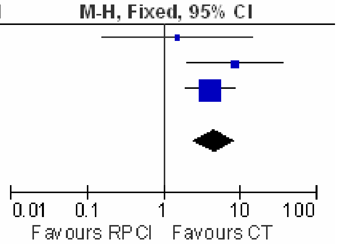


(1) Defined as minor bleed in study

Figure 286: Minor bleeding plus undefined bleeding (short-term)

Study or Subgroup	Rescue PCI Events	Rescue PCI Total	Conservative therapy Events	Conservative therapy Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Belenkie 1992 (1)	2	16	1	12	10.2%	1.50 [0.15, 14.68]
MERLIN (2)	17	153	2	154	17.8%	8.56 [2.01, 36.40]
REACT (3)	33	144	8	141	72.0%	4.04 [1.93, 8.44]
Total (95% CI)		**313**		**307**	**100.0%**	**4.58 [2.46, 8.55]**
Total events	52		11			

Heterogeneity: Chi² = 1.75, df = 2 (P = 0.42); I² = 0%
Test for overall effect: Z = 4.78 (P < 0.00001)

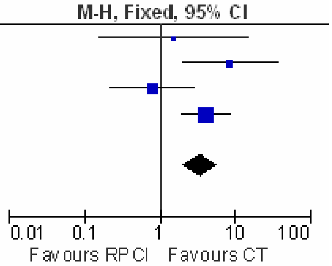


(1) No study definition. RPCI: 1 gastrointestinal bleeding,1 groin haematoma requiring transfusion. CT: 1 severe groin haematoma
(2) Transfusion required.Transfusion reserved for fall in haemoglobin of ≥2 g/dl, and only if this took total haemoglobin to <10 g/dl
(3) Defined as minor bleed in study

Figure 287: All bleeding (short-term)

Study or Subgroup	Rescue PCI Events	Rescue PCI Total	Conservative therapy Events	Conservative therapy Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Belenkie 1992 (1)	2	16	1	12	7.0%	1.50 [0.15, 14.68]
MERLIN (2)	17	153	2	154	12.3%	8.56 [2.01, 36.40]
REACT (3)	4	144	5	141	31.0%	0.78 [0.21, 2.86]
REACT. (4)	33	144	8	141	49.7%	4.04 [1.93, 8.44]
Total (95% CI)		**457**		**448**	**100.0%**	**3.40 [1.99, 5.81]**
Total events	56		16			

Heterogeneity: Chi² = 7.21, df = 3 (P = 0.07); I² = 58%
Test for overall effect: Z = 4.48 (P < 0.00001)



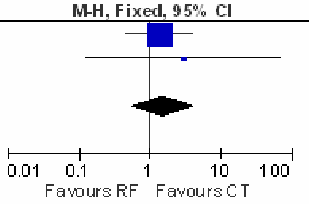
(1) No study definition. RPCI: 1 gastrointestinal bleeding,1 groin haematoma requiring transfusion. CT: 1 severe groin haematoma
(2) Transfusion required.Transfusion reserved for fall in haemoglobin of ≥2 g/dl, and only if this took total haemoglobin to <10 g/dl
(3) Defined as major bleed in study
(4) Defined as minor bleed in study

I.11.5 Repeated fibrinolysis versus conservative therapy (sensitivity analysis – incidence of bleeding)

Figure 288: Major bleeding (short-term)

Study or Subgroup	Repeated fibrinolysis Events	Repeated fibrinolysis Total	Conservative therapy Events	Conservative therapy Total	Weight	Risk Ratio M-H, Fixed, 95% CI
REACT (1)	7	142	5	141	90.9%	1.39 [0.45, 4.28]
Sarullo 2000 (2)	1	45	0	45	9.1%	3.00 [0.13, 71.74]
Total (95% CI)		**187**		**186**	**100.0%**	**1.54 [0.54, 4.40]**
Total events	8		5			

Heterogeneity: Chi² = 0.20, df = 1 (P = 0.65); I² = 0%
Test for overall effect: Z = 0.80 (P = 0.42)

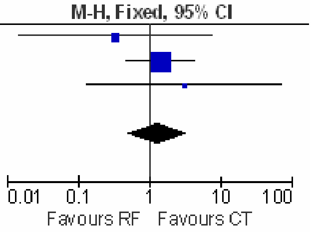


(1) Defined as major bleed in study
(2) Defined as major bleed in study

Figure 289: Major bleeding plus undefined bleeding (short-term)

Study or Subgroup	Repeated fibrinolysis Events	Repeated fibrinolysis Total	Conservative therapy Events	Conservative therapy Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Mounsey 1995 (1)	0	19	1	18	21.8%	0.32 [0.01, 7.30]
REACT (2)	7	142	5	141	71.1%	1.39 [0.45, 4.28]
Sarullo 2000 (3)	1	45	0	45	7.1%	3.00 [0.13, 71.74]
Total (95% CI)		**206**		**204**	**100.0%**	**1.27 [0.48, 3.34]**
Total events	8		6			

Heterogeneity: Chi² = 1.06, df = 2 (P = 0.59); I² = 0%
Test for overall effect: Z = 0.48 (P = 0.63)

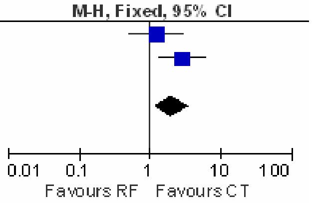


(1) No study definition. CT: 1 gastrointestinal haemorrhage requiring transfusion
(2) Defined as major bleed in study
(3) Defined as major bleed in study

Figure 290: Minor bleeding (short-term)

Study or Subgroup	Repeated fibrinolysis Events	Repeated fibrinolysis Total	Conservative therapy Events	Conservative therapy Total	Weight	Risk Ratio M-H, Fixed, 95% CI
REACT (1)	10	142	8	141	53.4%	1.24 [0.50, 3.05]
Sarullo 2000 (2)	20	45	7	45	46.6%	2.86 [1.34, 6.08]
Total (95% CI)		**187**		**186**	**100.0%**	**1.99 [1.13, 3.51]**
Total events	30		15			

Heterogeneity: Chi² = 1.94, df = 1 (P = 0.16); I² = 48%
Test for overall effect: Z = 2.39 (P = 0.02)

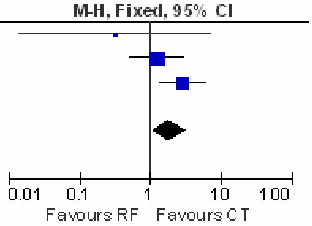


(1) Defined as minor bleed in study
(2) Defined as minor bleed in study

Figure 291: Minor bleeding plus undefined bleeding (short-term)

Study or Subgroup	Repeated fibrinolysis Events	Repeated fibrinolysis Total	Conservative therapy Events	Conservative therapy Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Mounsey 1995 (1)	0	19	1	18	9.3%	0.32 [0.01, 7.30]
REACT (2)	10	142	8	141	48.5%	1.24 [0.50, 3.05]
Sarullo 2000 (3)	20	45	7	45	42.3%	2.86 [1.34, 6.08]
Total (95% CI)		**206**		**204**	**100.0%**	**1.84 [1.06, 3.18]**
Total events	30		16			

Heterogeneity: Chi² = 3.25, df = 2 (P = 0.20); I² = 38%
Test for overall effect: Z = 2.17 (P = 0.03)

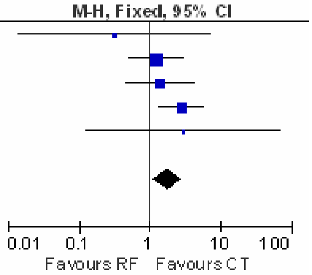


(1) No study definition. CT: 1 gastrointestinal haemorrhage requiring transfusion
(2) Defined as minor bleed in study
(3) Defined as minor bleed in study

Figure 292: All bleeding (short-term)

Study or Subgroup	Repeated fibrinolysis Events	Repeated fibrinolysis Total	Conservative therapy Events	Conservative therapy Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Mounsey 1995 (1)	0	19	1	18	7.0%	0.32 [0.01, 7.30]
REACT (2)	10	142	8	141	36.4%	1.24 [0.50, 3.05]
REACT. (3)	7	142	5	141	22.7%	1.39 [0.45, 4.28]
Sarullo 2000 (4)	20	45	7	45	31.7%	2.86 [1.34, 6.08]
Sarullo 2000. (5)	1	45	0	45	2.3%	3.00 [0.13, 71.74]
Total (95% CI)		**393**		**390**	**100.0%**	**1.76 [1.08, 2.87]**
Total events	38		21			

Heterogeneity: Chi² = 3.58, df = 4 (P = 0.47); I² = 0%
Test for overall effect: Z = 2.28 (P = 0.02)



(1) No study definition. CT: 1 gastrointestinal haemorrhage requiring transfusion
(2) Defined as minor bleed in study
(3) Defined as major bleed in study
(4) Defined as minor bleed in study
(5) Defined as major bleed in study

I.12 Routine early angiography following fibrinolysis

I.12.1 Routine early angiography versus selective or routine deferred angiography

Figure 293: All-cause mortality (short-term: 30 days unless specified)

Study or Subgroup	Early angiography Events	Early angiography Total	Comparator Events	Comparator Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.1.1 Selective approach						
CAPITAL-AMI	2	86	3	84	7.2%	0.65 [0.11, 3.80]
GRACIA-1	6	248	6	251	14.1%	1.01 [0.33, 3.10]
WEST	1	104	4	100	9.6%	0.24 [0.03, 2.11]
Subtotal (95% CI)		**438**		**435**	**30.9%**	**0.69 [0.30, 1.59]**
Total events	9		13			
Heterogeneity: Chi² = 1.36, df = 2 (P = 0.51); I² = 0%						
Test for overall effect: Z = 0.88 (P = 0.38)						
3.1.2 Routine deferred						
NORDISTEMI	3	134	3	132	7.1%	0.99 [0.20, 4.79]
SIAM III	4	82	8	81	19.0%	0.49 [0.15, 1.58]
TRANSFER-AMI	24	536	18	522	43.0%	1.30 [0.71, 2.36]
Subtotal (95% CI)		**752**		**735**	**69.1%**	**1.05 [0.64, 1.72]**
Total events	31		29			
Heterogeneity: Chi² = 2.11, df = 2 (P = 0.35); I² = 5%						
Test for overall effect: Z = 0.17 (P = 0.86)						
Total (95% CI)		**1190**		**1170**	**100.0%**	**0.93 [0.61, 1.43]**
Total events	40		42			

Heterogeneity: Chi² = 4.00, df = 5 (P = 0.55); I² = 0%
Test for overall effect: Z = 0.31 (P = 0.76)
Test for subgroup differences: Chi² = 0.71, df = 1 (P = 0.40), I² = 0%

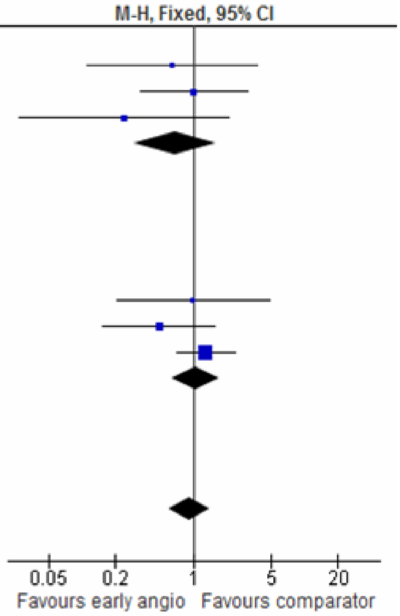
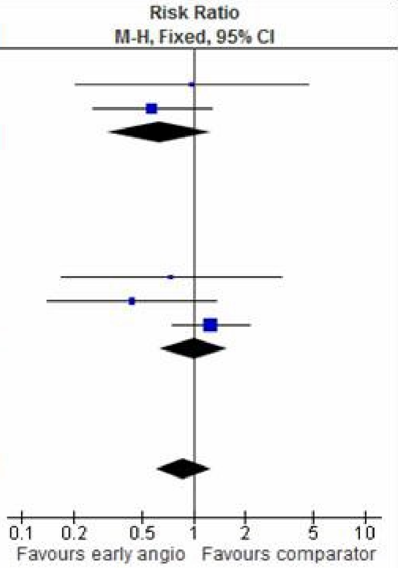


Figure 294: All-cause mortality (longer-term: 6 months unless specified)

Study or Subgroup	Early angiography Events	Early angiography Total	Comparator Events	Comparator Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.1.1 Selective approach						
CAPITAL-AMI	3	86	3	84	5.5%	0.98 [0.20, 4.70]
GRACIA-1 (1)	9	248	16	251	28.7%	0.57 [0.26, 1.26]
Subtotal (95% CI)		**334**		**335**	**34.2%**	**0.63 [0.31, 1.29]**
Total events	12		19			
Heterogeneity: Chi² = 0.36, df = 1 (P = 0.55); I² = 0%						
Test for overall effect: Z = 1.26 (P = 0.21)						
4.1.2 Routine deferred						
NORDISTEMI (2)	3	134	4	132	7.3%	0.74 [0.17, 3.24]
SIAM III	4	82	9	81	16.3%	0.44 [0.14, 1.37]
TRANSFER-AMI	30	528	23	511	42.2%	1.26 [0.74, 2.14]
Subtotal (95% CI)		**744**		**724**	**65.8%**	**1.00 [0.64, 1.56]**
Total events	37		36			
Heterogeneity: Chi² = 2.92, df = 2 (P = 0.23); I² = 31%						
Test for overall effect: Z = 0.00 (P = 1.00)						
Total (95% CI)		**1078**		**1059**	**100.0%**	**0.88 [0.60, 1.27]**
Total events	49		55			
Heterogeneity: Chi² = 4.44, df = 4 (P = 0.35); I² = 10%						
Test for overall effect: Z = 0.70 (P = 0.49)						
Test for subgroup differences: Chi² = 1.13, df = 1 (P = 0.29), I² = 11.9%						



(1) At 12 months
(2) At 12 months

Figure 295: Reinfarction (short-term: 30 days unless specified)

Study or Subgroup	Early angiography Events	Early angiography Total	Comparator Events	Comparator Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.3.1 Selective approach						
CAPITAL-AMI	4	86	11	84	17.5%	0.36 [0.12, 1.07]
GRACIA-1	3	248	4	251	6.2%	0.76 [0.17, 3.36]
WEST	6	104	9	100	14.4%	0.64 [0.24, 1.74]
Subtotal (95% CI)		**438**		**435**	**38.1%**	**0.53 [0.28, 1.02]**
Total events	13		24			
Heterogeneity: Chi² = 0.87, df = 2 (P = 0.65); I² = 0%						
Test for overall effect: Z = 1.90 (P = 0.06)						
3.3.2 Routine deferred						
NORDISTEMI	2	134	7	132	11.1%	0.28 [0.06, 1.33]
SIAM III	2	82	2	81	3.2%	0.99 [0.14, 6.84]
TRANSFER-AMI	18	536	30	522	47.7%	0.58 [0.33, 1.04]
Subtotal (95% CI)		**752**		**735**	**61.9%**	**0.55 [0.33, 0.92]**
Total events	22		39			
Heterogeneity: Chi² = 1.11, df = 2 (P = 0.57); I² = 0%						
Test for overall effect: Z = 2.28 (P = 0.02)						
Total (95% CI)		**1190**		**1170**	**100.0%**	**0.54 [0.36, 0.81]**
Total events	35		63			
Heterogeneity: Chi² = 1.99, df = 5 (P = 0.85); I² = 0%						
Test for overall effect: Z = 2.97 (P = 0.003)						
Test for subgroup differences: Chi² = 0.01, df = 1 (P = 0.93), I² = 0%						

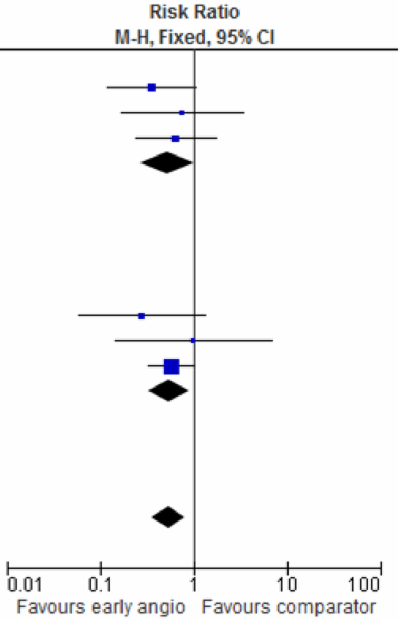
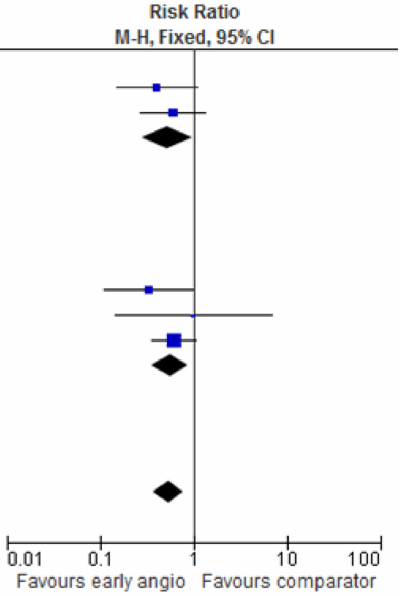


Figure 296: Reinfarction (longer-term: 6 months unless specified)

Study or Subgroup	Early angiography Events	Early angiography Total	Comparator Events	Comparator Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.3.1 Selective approach						
CAPITAL-AMI	5	86	12	84	16.3%	0.41 [0.15, 1.11]
GRACIA-1 (1)	9	248	15	251	20.0%	0.61 [0.27, 1.36]
Subtotal (95% CI)		**334**		**335**	**36.2%**	**0.52 [0.28, 0.97]**
Total events	14		27			
Heterogeneity: Chi² = 0.37, df = 1 (P = 0.54); I² = 0%						
Test for overall effect: Z = 2.07 (P = 0.04)						
4.3.2 Routine deferred						
NORDISTEMI (2)	4	134	12	132	16.2%	0.33 [0.11, 0.99]
SIAM III	2	82	2	81	2.7%	0.99 [0.14, 6.84]
TRANSFER-AMI	21	528	33	511	44.9%	0.62 [0.36, 1.05]
Subtotal (95% CI)		**744**		**724**	**63.8%**	**0.56 [0.35, 0.89]**
Total events	27		47			
Heterogeneity: Chi² = 1.35, df = 2 (P = 0.51); I² = 0%						
Test for overall effect: Z = 2.47 (P = 0.01)						
Total (95% CI)		**1078**		**1059**	**100.0%**	**0.54 [0.37, 0.79]**
Total events	41		74			
Heterogeneity: Chi² = 1.77, df = 4 (P = 0.78); I² = 0%						
Test for overall effect: Z = 3.21 (P = 0.001)						
Test for subgroup differences: Chi² = 0.04, df = 1 (P = 0.85), I² = 0%						



(1) At 12 months
(2) At 12 months

Figure 297: Heart failure (short-term: 30 days unless specified)

Study or Subgroup	Early angiography Events	Early angiography Total	Comparator Events	Comparator Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.4.1 Selective approach						
CAPITAL-AMI	11	86	10	84	18.5%	1.07 [0.48, 2.40]
WEST	15	104	15	100	27.9%	0.96 [0.50, 1.86]
Subtotal (95% CI)		**190**		**184**	**46.4%**	**1.01 [0.60, 1.68]**
Total events	26		25			
Heterogeneity: Chi² = 0.04, df = 1 (P = 0.83); I² = 0%						
Test for overall effect: Z = 0.02 (P = 0.98)						
3.4.2 Routine deferred						
TRANSFER-AMI	16	536	29	522	53.6%	0.54 [0.30, 0.98]
Subtotal (95% CI)		**536**		**522**	**53.6%**	**0.54 [0.30, 0.98]**
Total events	16		29			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.03 (P = 0.04)						
Total (95% CI)		**726**		**706**	**100.0%**	**0.75 [0.51, 1.11]**
Total events	42		54			
Heterogeneity: Chi² = 2.50, df = 2 (P = 0.29); I² = 20%						
Test for overall effect: Z = 1.43 (P = 0.15)						
Test for subgroup differences: Chi² = 2.45, df = 1 (P = 0.12), I² = 59.2%						

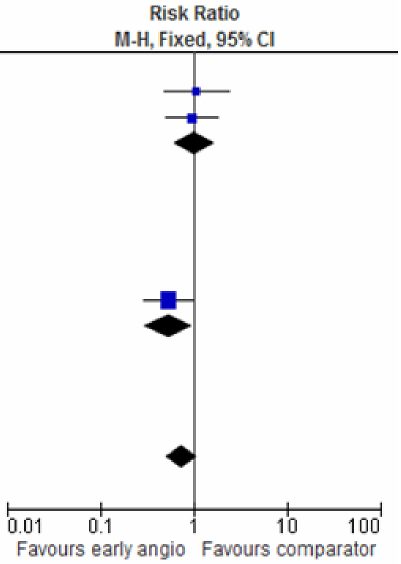


Figure 298: Heart failure (longer-term: 6 months unless specified)

Study or Subgroup	Early angiography Events	Early angiography Total	Comparator Events	Comparator Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.4.1 Selective approach						
CAPITAL-AMI	12	86	12	84	100.0%	0.98 [0.47, 2.05]
Subtotal (95% CI)		**86**		**84**	**100.0%**	**0.98 [0.47, 2.05]**
Total events	12		12			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.06 (P = 0.95)						
Total (95% CI)		**86**		**84**	**100.0%**	**0.98 [0.47, 2.05]**
Total events	12		12			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.06 (P = 0.95)						
Test for subgroup differences: Not applicable						

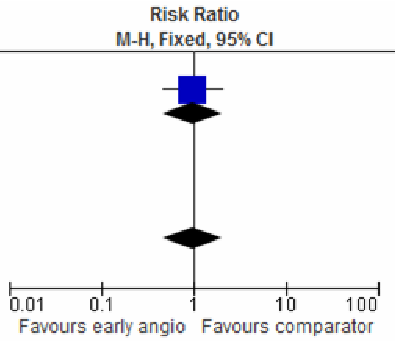


Figure 299: Stroke (short-term: 30 days unless specified)

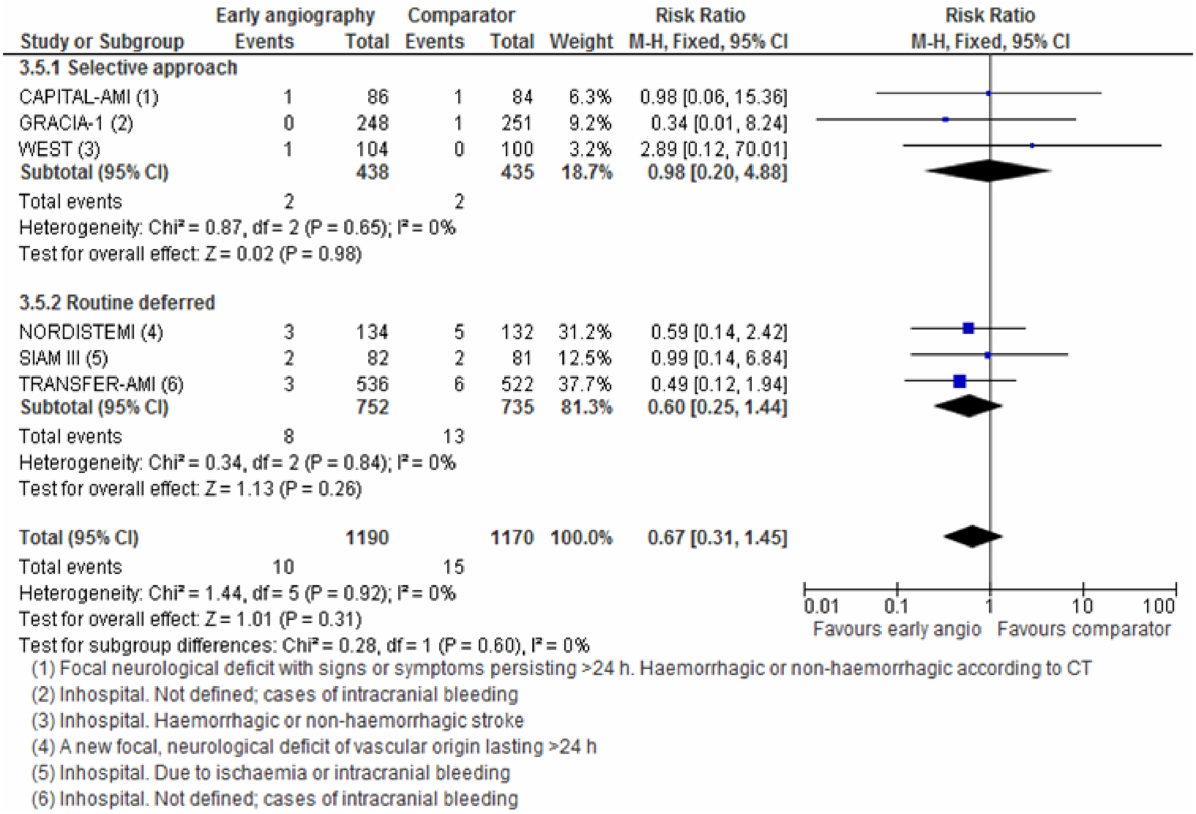


Figure 300: Stroke (longer-term: 6 months unless specified)

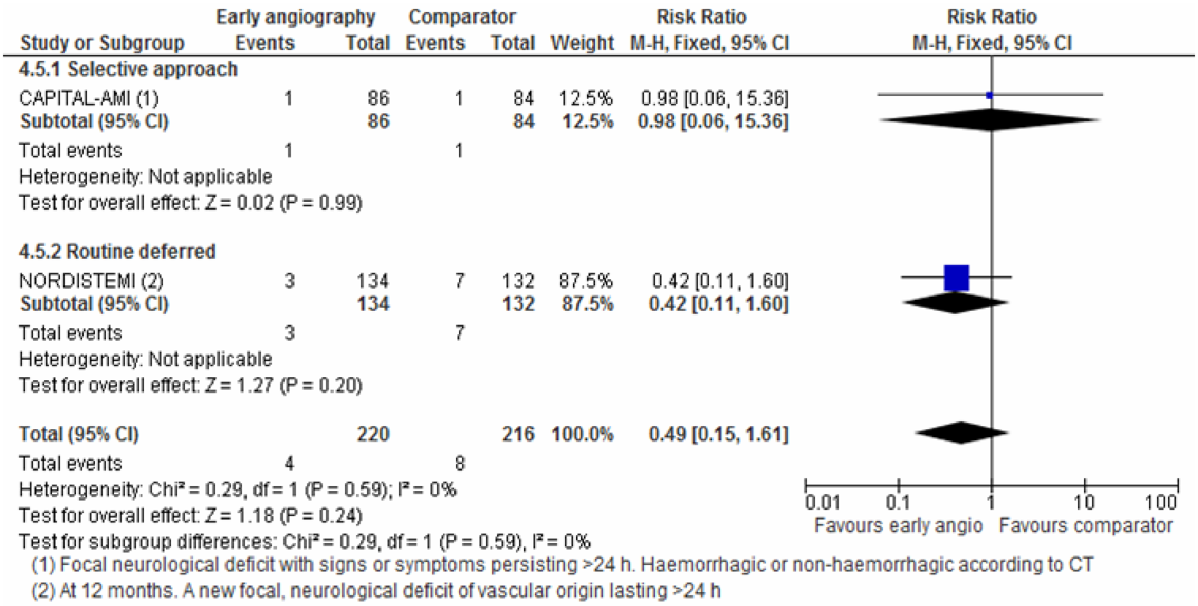
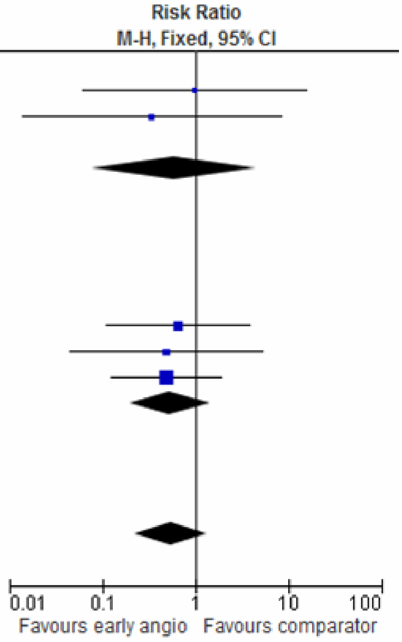


Figure 301: Intracranial bleeding (short-term: 30 days unless specified)

Study or Subgroup	Early angiography Events	Early angiography Total	Comparator Events	Comparator Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.10.1 Selective approach						
CAPITAL-AMI	1	86	1	84	7.4%	0.98 [0.06, 15.36]
GRACIA-1 (1)	0	248	1	251	10.9%	0.34 [0.01, 8.24]
WEST (2)	0	104	0	100		Not estimable
Subtotal (95% CI)		**438**		**435**	**18.4%**	**0.60 [0.08, 4.50]**
Total events	1		2			
Heterogeneity: Chi² = 0.25, df = 1 (P = 0.62); I² = 0%						
Test for overall effect: Z = 0.50 (P = 0.62)						
3.10.2 Routine deferred						
NORDISTEMI	2	134	3	132	22.2%	0.66 [0.11, 3.87]
SIAM III (3)	1	82	2	81	14.8%	0.49 [0.05, 5.34]
TRANSFER-AMI (4)	3	536	6	522	44.6%	0.49 [0.12, 1.94]
Subtotal (95% CI)		**752**		**735**	**81.6%**	**0.53 [0.20, 1.44]**
Total events	6		11			
Heterogeneity: Chi² = 0.07, df = 2 (P = 0.96); I² = 0%						
Test for overall effect: Z = 1.24 (P = 0.21)						
Total (95% CI)		**1190**		**1170**	**100.0%**	**0.55 [0.22, 1.33]**
Total events	7		13			
Heterogeneity: Chi² = 0.33, df = 4 (P = 0.99); I² = 0%						
Test for overall effect: Z = 1.34 (P = 0.18)						
Test for subgroup differences: Chi² = 0.01, df = 1 (P = 0.92), I² = 0%						



(1) Inhospital
(2) Inhospital
(3) Inhospital
(4) Inhospital

Figure 302: Intracranial bleeding (longer-term: 6 months unless specified)

Study or Subgroup	Early angiography Events	Early angiography Total	Comparator Events	Comparator Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.10.1 Selective approach						
CAPITAL-AMI	1	86	1	84	100.0%	0.98 [0.06, 15.36]
Subtotal (95% CI)		**86**		**84**	**100.0%**	**0.98 [0.06, 15.36]**
Total events	1		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.02 (P = 0.99)						
Total (95% CI)		**86**		**84**	**100.0%**	**0.98 [0.06, 15.36]**
Total events	1		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.02 (P = 0.99)						
Test for subgroup differences: Not applicable						

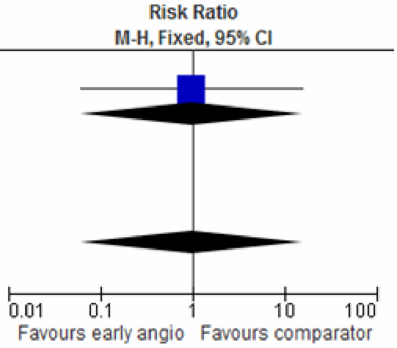
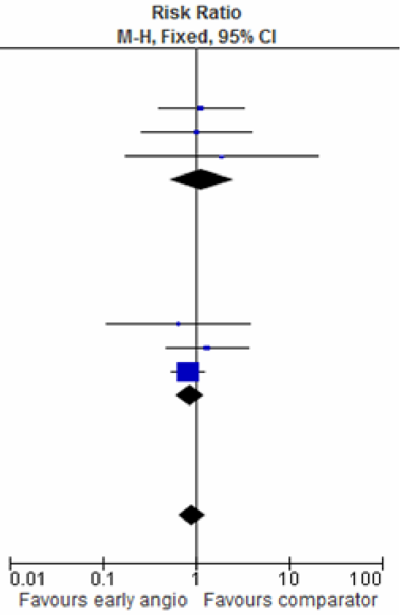


Figure 303: Major bleeding (short-term: 30 days unless specified)

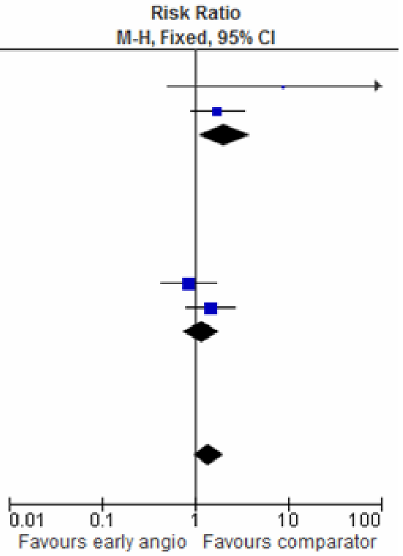
Study or Subgroup	Early angiography Events	Early angiography Total	Comparator Events	Comparator Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.8.1 Selective approach						
Agati et al. (1)	0	30	0	30		Not estimable
CAPITAL-AMI (2)	7	86	6	84	9.0%	1.14 [0.40, 3.25]
GRACIA-1 (3)	4	248	4	251	5.9%	1.01 [0.26, 4.00]
WEST (4)	2	104	1	100	1.5%	1.92 [0.18, 20.88]
Subtotal (95% CI)		**468**		**465**	**16.3%**	**1.17 [0.53, 2.55]**
Total events	13		11			
Heterogeneity: Chi² = 0.21, df = 2 (P = 0.90); I² = 0%						
Test for overall effect: Z = 0.38 (P = 0.70)						
3.8.2 Routine deferred						
NORDISTEMI (5)	2	134	3	132	4.5%	0.66 [0.11, 3.87]
SIAM III (6)	8	82	6	81	8.9%	1.32 [0.48, 3.63]
TRANSFER-AMI (7)	40	536	47	522	70.3%	0.83 [0.55, 1.24]
Subtotal (95% CI)		**752**		**735**	**83.7%**	**0.87 [0.60, 1.26]**
Total events	50		56			
Heterogeneity: Chi² = 0.80, df = 2 (P = 0.67); I² = 0%						
Test for overall effect: Z = 0.74 (P = 0.46)						
Total (95% CI)		**1220**		**1200**	**100.0%**	**0.92 [0.66, 1.28]**
Total events	63		67			
Heterogeneity: Chi² = 1.42, df = 5 (P = 0.92); I² = 0%						
Test for overall effect: Z = 0.50 (P = 0.62)						
Test for subgroup differences: Chi² = 0.43, df = 1 (P = 0.51), I² = 0%						



(1) Inhospital. Not defined
(2) Inhospital. TIMI criteria
(3) Inhospital. Any complication causing death, need for surgery or transfusion, or extended time in hospital
(4) Inhospital. Blood or fluid replacement, inotropic support, ventricular assist devices, surgery, or CPR required to maintain sufficient ca
(5) According to GUSTO scale (includes ICH)
(6) Inhospital. Need for transfusion, surgical intervention, documented by CT and/or u/s or >4g% decrease in haemoglobin within 72 h
(7) Inhospital; TIMI criteria (includes CABG related)

Figure 304: Minor bleeding (short-term: 30 days unless specified)

Study or Subgroup	Early angiography Events	Early angiography Total	Comparator Events	Comparator Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.9.1 Selective approach						
Agati et al. (1)	4	30	0	30	1.1%	9.00 [0.51, 160.17]
CAPITAL-AMI (2)	20	86	11	84	24.7%	1.78 [0.91, 3.48]
Subtotal (95% CI)		**116**		**114**	**25.9%**	**2.09 [1.09, 3.98]**
Total events	24		11			
Heterogeneity: Chi² = 1.21, df = 1 (P = 0.27); I² = 17%						
Test for overall effect: Z = 2.23 (P = 0.03)						
3.9.2 Routine deferred						
NORDISTEMI (3)	14	134	16	132	35.8%	0.86 [0.44, 1.69]
TRANSFER-AMI (4)	26	536	17	522	38.3%	1.49 [0.82, 2.71]
Subtotal (95% CI)		**670**		**654**	**74.1%**	**1.19 [0.76, 1.85]**
Total events	40		33			
Heterogeneity: Chi² = 1.41, df = 1 (P = 0.23); I² = 29%						
Test for overall effect: Z = 0.75 (P = 0.45)						
Total (95% CI)		**786**		**768**	**100.0%**	**1.42 [0.99, 2.04]**
Total events	64		44			
Heterogeneity: Chi² = 4.13, df = 3 (P = 0.25); I² = 27%						
Test for overall effect: Z = 1.89 (P = 0.06)						
Test for subgroup differences: Chi² = 1.99, df = 1 (P = 0.16), I² = 49.8%						



(1) Inhospital. Not defined
(2) Inhospital. TIMI criteria
(3) GUSTO scale (moderate plus minor)
(4) Inhospital. TIMI criteria

Figure 305: Recurrent ischaemia (short-term: 30 days unless specified)

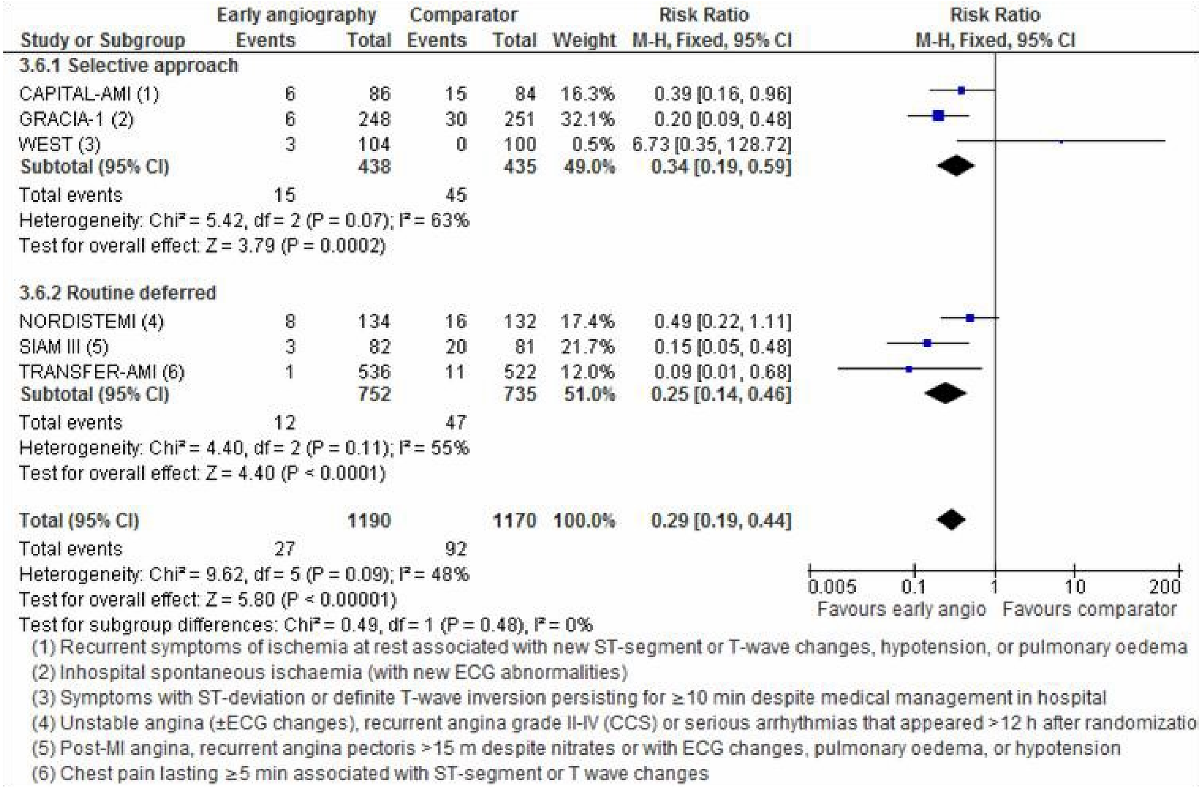


Figure 306: Recurrent ischaemia (longer-term: 6 months unless specified)

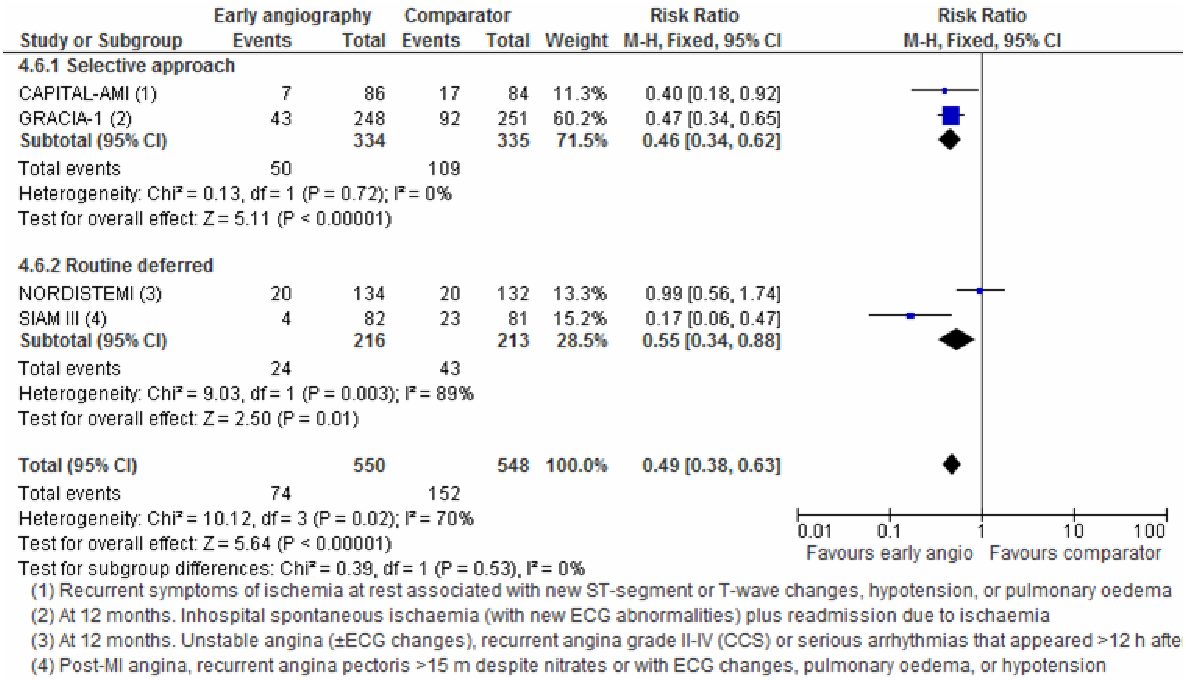
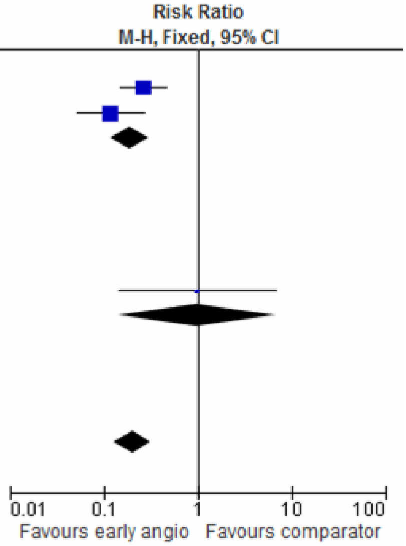


Figure 307: Unplanned revascularisation (short-term: 30 days unless specified)

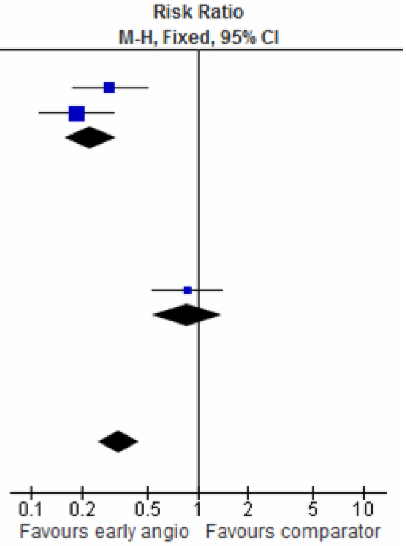
Study or Subgroup	Early angiography Events	Early angiography Total	Comparator Events	Comparator Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.7.1 Selective approach						
CAPITAL-AMI (1)	12	86	44	84	45.8%	0.27 [0.15, 0.47]
GRACIA-1 (2)	6	248	51	251	52.1%	0.12 [0.05, 0.27]
Subtotal (95% CI)		**334**		**335**	**97.9%**	**0.19 [0.12, 0.30]**
Total events	18		95			
Heterogeneity: Chi² = 2.64, df = 1 (P = 0.10); I² = 62%						
Test for overall effect: Z = 6.97 (P < 0.00001)						
3.7.2 Routine deferred						
SIAM III (3)	2	82	2	81	2.1%	0.99 [0.14, 6.84]
Subtotal (95% CI)		**82**		**81**	**2.1%**	**0.99 [0.14, 6.84]**
Total events	2		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.01 (P = 0.99)						
Total (95% CI)		**416**		**416**	**100.0%**	**0.20 [0.13, 0.32]**
Total events	20		97			
Heterogeneity: Chi² = 5.03, df = 2 (P = 0.08); I² = 60%						
Test for overall effect: Z = 6.91 (P < 0.00001)						
Test for subgroup differences: Chi² = 2.67, df = 1 (P = 0.10), I² = 62.5%						



(1) Non-protocol PCI or CABG
(2) Inhospital. Induced by spontaneous ischaemia or non-invasive stress tests (PCI or CABG)
(3) Any reintervention or CABG involving the IRA

Figure 308: Unplanned revascularisation (longer-term: 6 months unless specified)

Study or Subgroup	Early angiography Events	Early angiography Total	Comparator Events	Comparator Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.7.1 Selective approach						
CAPITAL-AMI (1)	14	86	46	84	30.6%	0.30 [0.18, 0.50]
GRACIA-1 (2)	15	248	81	251	52.9%	0.19 [0.11, 0.32]
Subtotal (95% CI)		**334**		**335**	**83.5%**	**0.23 [0.16, 0.33]**
Total events	29		127			
Heterogeneity: Chi² = 1.55, df = 1 (P = 0.21); I² = 36%						
Test for overall effect: Z = 7.84 (P < 0.00001)						
4.7.2 Routine deferred						
SIAM III (3)	22	82	25	81	16.5%	0.87 [0.54, 1.41]
Subtotal (95% CI)		**82**		**81**	**16.5%**	**0.87 [0.54, 1.41]**
Total events	22		25			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.57 (P = 0.57)						
Total (95% CI)		**416**		**416**	**100.0%**	**0.33 [0.25, 0.44]**
Total events	51		152			
Heterogeneity: Chi² = 19.93, df = 2 (P < 0.0001); I² = 90%						
Test for overall effect: Z = 7.52 (P < 0.00001)						
Test for subgroup differences: Chi² = 18.58, df = 1 (P < 0.0001), I² = 94.6%						



(1) Non-protocol PCI or CABG
(2) At 12 months. Induced by spontaneous ischaemia or noninvasive stress tests (PCI or CABG)
(3) Any reintervention or CABG involving the IRA

Figure 309: Quality of life (short-term: 30 days unless specified)

Study or Subgroup	Early angiography Mean	Early angiography SD	Early angiography Total	Comparator Mean	Comparator SD	Comparator Total	Weight	Mean Difference IV, Fixed, 95% CI
NORDISTEMI	0.873	0.156	130	0.856	0.167	129	100.0%	0.02 [-0.02, 0.06]
Total (95% CI)			**130**			**129**	**100.0%**	**0.02 [-0.02, 0.06]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.85 (P = 0.40)								

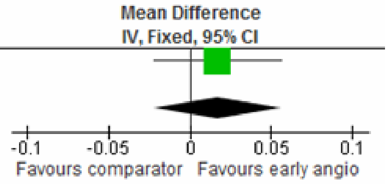


Figure 310: Quality of life (longer-term: 6 months unless specified)

	Early angiography			Comparator				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
NORDISTEMI (1)	0.889	0.16	130	0.872	0.182	129	100.0%	0.02 [-0.02, 0.06]
Total (95% CI)			**130**			**129**	**100.0%**	**0.02 [-0.02, 0.06]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.80 (P = 0.42)

(1) At 7 months

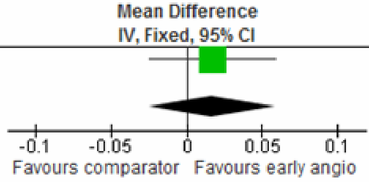
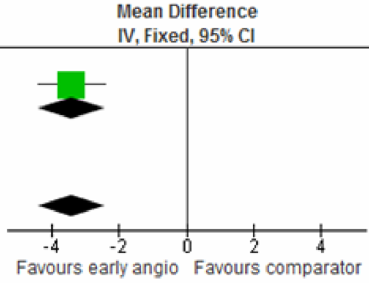


Figure 311: Length of hospital stay – index admission

	Early angiography			Comparator				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
3.11.1 Selective approach								
GRACIA-1	7.1	5.6	248	10.5	5.7	251	100.0%	-3.40 [-4.39, -2.41]
Subtotal (95% CI)			**248**			**251**	**100.0%**	**-3.40 [-4.39, -2.41]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 6.72 (P < 0.00001)								
Total (95% CI)			**248**			**251**	**100.0%**	**-3.40 [-4.39, -2.41]**

Heterogeneity: Not applicable
Test for overall effect: Z = 6.72 (P < 0.00001)
Test for subgroup differences: Not applicable



Appendix J: Excluded clinical studies

J.1 Time to reperfusion

Exclusion List	Reason for exclusion
Aasa M, Dellborg M, Herlitz J, Svensson L, Grip L. Risk reduction for cardiac events after primary coronary intervention compared with thrombolysis for acute ST-elevation myocardial infarction (five-year results of the Swedish early decision reperfusion strategy [SWEDES] trial). American Journal of Cardiology. 2010; 106(12):1685-1691.	Follow-up of RCT that does not stratify study participants according to time to intervention
Aasa M, Dellborg M, Herlitz J, Svensson L, Grip L. Superior long-term outcome after primary PCI compared to early thrombolysis in acute ST-segment elevation myocardial infarction. European Heart Journal. 2009; 30:474.	Follow-up of RCT that does not stratify study participants according to time to intervention
Agati L, Voci P, Hickle P, et al. Tissue-type plasminogen activator therapy versus primary coronary angioplasty: impact on myocardial tissue perfusion and regional function 1 month after uncomplicated myocardial infarction. J Am Coll Cardiol 1998; 31:338-43.	No outcomes of interest
Agati L, Voci P, Hickle P, Vizza DC, Autore C, Fedele F et al. Tissue-type plasminogen activator therapy versus primary coronary angioplasty: impact on myocardial tissue perfusion and regional function 1 month after uncomplicated myocardial infarction. Journal of the American College of Cardiology. 1998; 31(2):338-343.	No outcomes of interest, RCT does not stratify study participants according to time to intervention
Akdemir R, Karakurt O, Kilic H, Yesilay AB, Dogan M, Cagirci G et al. Effect of reperfusion therapy on index of myocardial performance in acute myocardial infarction: thrombolytics versus primary angioplasty. Heart and Vessels. 2010; 25(2):87-91.	RCT does not stratify study participants according to time to intervention
Akhras F, Abu Ousa A, Swann.G., Duncan H, Chamsi-Pasha H, Jabbad H. Primary coronary angioplasty or intraveneous thrombolysis for pateines with acute myocardial infarction? Acute and late follow up results in a new cardiac unit. Journal of the American College of Cardiology. 2011; 29(Suppl 1):A235.	RCT does not stratify study participants according to time to intervention
Andersen,Henning R.; Nielsen,Torsten T.; Rasmussen,Klaus; Thuesen,Leif; Kelbaek,Henning; Thayssen,Per; Abildgaard,Ulrik; Pedersen,Flemming; Madsen,Jan K.; Grande,Peer; Villadsen,Anton B.; Krusell,Lars R.; Haghfelt,Torben; Lomholt,Preben; Husted,Steen E. Vigholt,Else; Kjaergard,Henrik K.; Mortensen,Leif Spange; DANAMI-2 Investigators. A comparison of coronary angioplasty with fibrinolytic therapy in acute myocardial infarction. New England Journal of Medicine.2003; 349(8)733-742.	RCT does not stratify study participants according to time to intervention
Andersen,Henning R.; Nielsen,Torsten T.; Rasmussen,Klaus; Thuesen,Leif; Kelbaek,Henning; Thayssen,Per; Abildgaard,Ulrik; Pedersen,Flemming; Madsen,Jan K.; Grande,Peer; Villadsen,Anton B.; Krusell,Lars R.; Haghfelt,Torben; Lomholt,Preben; Husted,Steen E. Vigholt,Else; Kjaergard,Henrik K.; Mortensen,Leif Spange; DANAMI-2 Investigators. A comparison of coronary angioplasty with fibrinolytic therapy in acute myocardial infarction. New England Journal of Medicine.2003; 349(8)733-742.	RCT does not stratify study participants according to time to intervention
Angeja BG, Gibson CM, Chin R, Frederick PD, Every NR, Ross AM et al. Predictors of door-to-balloon delay in primary angioplasty. American Journal of Cardiology. 2002; 89(10):1156-1161.	Not RCT, cohort (n = 40,077)
Antoniucci D, Valenti R, Migliorini A, Moschi G, Trapani M, Buonamici P et al. Relation of time to treatment and mortality in patients with acute myocardial infarction undergoing primary coronary angioplasty. American Journal of Cardiology. 2002; 89(11):1248-1252.	Not question of interest
Aoki H, Suzuki T, Shibata M, Takino T, Sato N, Mukaida H et al. A prospective	RCT does not stratify study

Exclusion List	Reason for exclusion
randomized trial of intracoronary t-PA vs. coronary angioplasty in acute myocardial infarction: Japanese Intervention trial in Myocardial Infarction (JIMI). Circulation. 1997; 96(Suppl.):3003.	participants according to time to intervention
Armstrong PW, WEST Steering Committee. A comparison of pharmacologic therapy with/without timely coronary intervention vs. primary percutaneous intervention early after ST-elevation myocardial infarction: the WEST (Which Early ST-elevation myocardial infarction Therapy) study. European Heart Journal. 2006; 27(13):1530-1538.	RCT does not stratify study participants according to time to intervention
Aversano T, Aversano LT, Passamani E, Knatterud GL, Terrin ML, Williams DO et al. Thrombolytic therapy vs primary percutaneous coronary intervention for myocardial infarction in patients presenting to hospitals without on-site cardiac surgery: a randomized controlled trial. JAMA. 2002; 287(15):1943-1951.	Not RCT, narrative review
Aversano T, Aversano LT, Passamani E, Knatterud GL, Terrin ML, Williams DO et al. Thrombolytic therapy vs primary percutaneous coronary intervention for myocardial infarction in patients presenting to hospitals without on-site cardiac surgery: a randomized controlled trial. JAMA.2002; 287(15):1943-1951.	RCT does not stratify study participants according to time to intervention
Barbagelata A, Perna ER, Clemmensen P, Uretsky BF, Canella JPC, Califf RM et al. Time to reperfusion in acute myocardial infarction. It is time to reduce it! Journal of Electrocardiology. 2007; 40(3):257-264.	Not question of interest, meta-analysis does not examine timing
Bates DW, Miller E, Bernstein SJ, Hauptman PJ, Leape LL. Coronary angiography and angioplasty after acute myocardial infarction. Annals of Internal Medicine. 1997; 126(7):539-550.	Not RCT, narrative review
Bauer T, Hoffmann R, Junger C, Koeth O, Zahn R, Gitt A et al. Efficacy of a 24-h primary percutaneous coronary intervention service on outcome in patients with ST elevation myocardial infarction in clinical practice. Clinical Research in Cardiology. 2009; 98(3):171-178.	Not RCT, cohort study < 100,000 (n = 6350)
Beck CA, Eisenberg MJ, Pilote L. Invasive versus noninvasive management of ST-elevation acute myocardial infarction: a review of clinical trials and observational studies. American Heart Journal. 2005; 149(2):194-199.	Not RCT, narrative review
Bednar F, Widimsky P, Krupicka J, Groch L, Aschermann M, Zelizko M et l. Interhospital transport for primary angioplasty improves the long-term outcome of acute myocardial infarction compared with immediate thrombolysis in the nearest hospital (one-year follow-up of the PRAGUE-1 study). Canadian Journal of Cardiology. 2003; 19(10):1133-1137.	RCT does not stratify study participants according to time to intervention
Berger AK, Radford MJ, Krumholz HM. Factors associated with delay in reperfusion therapy in elderly patients with acute myocardial infarction: Analysis of the cooperative cardiovascular project. American Heart Journal. 2000; 139(6):985-992.	Not RCT, cohort (n = 17,379)
Berger PB, Ellis SG, Holmes J, Granger CB, Criger DA, Betriu A et al. Relationship between delay in performing direct coronary angioplasty and early clinical outcome in patients with acute myocardial infarction: Results from the global use of strategies to open occluded arteries in acute coronary syndromes (GUSTO-IIb) trial. Circulation. 1999; 100(1):14-20.	Not question of interest, substudy examined outcome according to timing of PCI from onset of symptoms without comparison of data from fibrinolysis arm
Berger PB, Bell MR, Holmes J, Gersh BJ, Hopfenspirger M, Gibbons R. Time to reperfusion with direct coronary angioplasty and thrombolytic therapy in acute myocardial infarction. American Journal of Cardiology. 1994; 73(4):231-236.	No outcome of interest
Beri A, Printz M, Hassan A, Babb JD. Fibrinolysis versus primary percutaneous intervention in ST-elevation myocardial infarction with long interhospital transfer distances. Clin Cardiol. 2010 Mar; 33(3):162-7	Not RCT, cohort study
Berrocal DH, Cohen MG, Spinetta AD, Ben MG, Rojas Matas CA, Gabay JM et al.	Not outcome of interest

Exclusion List	Reason for exclusion
Early reperfusion and late clinical outcomes in patients presenting with acute myocardial infarction randomly assigned to primary percutaneous coronary intervention or streptokinase. American Heart Journal. 2003; 146(6):E22.	
Betriu A, Masotti M. Comparison of mortality rates in acute myocardial infarction treated by percutaneous coronary intervention versus fibrinolysis. Am J Cardiol. 2005; 95(1):100-1.	Post hoc meta-regression that only reported absolute risk reductions
Birnbaum Y, Goodman S, Barr A, Gates KB, Barbash GI, Battler A et al. Comparison of primary coronary angioplasty versus thrombolysis in patients with ST-segment elevation acute myocardial infarction and grade II and grade III myocardial ischemia on the enrollment electrocardiogram. American Journal of Cardiology. 2001; 88(8):842-847.	RCT does not stratify study participants according to time to intervention
Boersma E, Steyerberg EW, Van der Vlugt MJ, Simoons ML. Reperfusion therapy for acute myocardial infarction. Which strategy for which patient? Drugs. 1998; 56(1):31-48.	Not RCT, not question of interest
Boersma H, Califf R, Collins R, Deckers JW, Simoons ML. Selection of reperfusion therapy for individual patients with evolving myocardial infarction. European Heart Journal. 1997; 18(9):1371-1381.	Not RCT, not question of interest
Boersma H, Van der Vlugt MJ, Arnold AER, Deckers JW, Simoons ML. Estimated gain in life expectancy. A simple tool to select optimal reperfusion treatment in individual patients with evolving myocardial infarction. European Heart Journal. 1996; 17(1):64-75.	Not RCT, not question of interest
Bonnefoy E, Steg PG, Boutitie F, Dubien PY, Lapostolle F, Roncalli J et al. Comparison of primary angioplasty and pre-hospital fibrinolysis in acute myocardial infarction (CAPTIM) trial: a 5-year follow-up. European Heart Journal. 2009; 30(13):1598-1606.	Follow-up of RCT that does not stratify study participants according to time to intervention
Bonnefoy E, Steg PG, Chabaud S, Dubien PY, Lapostolle F, Boudet F et al. Is primary angioplasty more effective than prehospital fibrinolysis in diabetics with acute myocardial infarction? Data from the CAPTIM randomized clinical trial. European Heart Journal. 2005; 26(17):1712-1718.	RCT does not stratify study participants according to time to intervention
Bonnefoy E, Lapostolle F, Leizorovicz A, Steg G, McFadden EP, Dubien PY et al. Primary angioplasty versus prehospital fibrinolysis in acute myocardial infarction: a randomised study. Lancet. 2002; 360(9336):825-829.	Not question of interest RCT does not stratify study participants according to time to intervention
Bradley EH, Herrin J, Wang Y, McNamara RL, Radford MJ, Magid DJ et al. Door-to-drug and door-to-balloon times: where can we improve? Time to reperfusion therapy in patients with ST-segment elevation myocardial infarction (STEMI). American Heart Journal. 2006; 151(6):1281-1287.	Not RCT, cohort study National Registry of Myocardial Infarction (NRMI-4), population < 100,000 (n = 33,822)
Bradley EH, Herrin J, Wang Y, McNamara RL, Webster TR, Magid DJ et al. Racial and ethnic differences in time to acute reperfusion therapy for patients hospitalized with myocardial infarction. JAMA. 2004; 292(13):1563-1572.	Not RCT, cohort study Second National Registry of Myocardial Infarction (NRMI-3 or NRMI-4), population < 100,000 (n = 73,032), not question of interest
Bravo Vergel Y, Palmer S, Asseburg C, Fenwick E, de Belder M, Abrams K et al. Is primary angioplasty cost effective in the UK? Results of a comprehensive decision analysis. Heart. 2007; 93(10):1238-1243.	Cost-effectiveness analysis
Brieger DB, Mak K-H, White HD, Kleiman NS, Miller DP, Vahanian A et al. Benefit of early sustained reperfusion in patients with prior myocardial infarction (The GUSTO-I Trial). American Journal of Cardiology. 1998; 81(3):282-287.	Not question of interest
Brodie BR, Stuckey TD, Muncy DB, Hansen CJ, Wall TC, Pulsipher M et al.	Not RCT, cohort study (n =

Exclusion List	Reason for exclusion
Importance of time-to-reperfusion in patients with acute myocardial infarction with and without cardiogenic shock treated with primary percutaneous coronary intervention. American Heart Journal. 2003; 145(4):708-715.	1843)
Brodie BR, Stone GW, Morice MC, Cox DA, Garcia E, Mattos LA et al. Importance of time to reperfusion on outcomes with primary coronary angioplasty for acute myocardial infarction (results from the Stent Primary Angioplasty in Myocardial Infarction Trial). American Journal of Cardiology. 2001; 88(10):1085-1090.	Not question of interest
Brodie BR, Stuckey TD, Wall TC, Kissling G, Hansen CJ, Muncy DB et al. Importance of time to reperfusion for 30-day and late survival and recovery of left ventricular function after primary angioplasty for acute myocardial infarction. Journal of the American College of Cardiology. 1998; 32(5):1312-1319.	Not RCT (cohort; n = 1352) no comparator for PCI, not question of interest, study examined outcomes for differential timing of PCI from onset of symptoms
Brooks SC, Allan KS, Welsford M, Verbeek PR, Arntz HR, Morrison LJ. Prehospital triage and direct transport of patients with ST-elevation myocardial infarction to primary percutaneous coronary intervention centres: a systematic review and meta-analysis. Canadian Journal of Emergency Medicine. 2009; 11(5):481-492.	Not question of interest, meta-analysis of RCTs with varying comparators to PCI
Brophy JM, Bogaty P. Primary angioplasty and thrombolysis are both reasonable options in acute myocardial infarction. Annals of Internal Medicine. 2004; 141(4):292-297.	Not RCT, narrative review
Bueno H, Betriu A, Heras M, Alonso JJ, Cequier A, Garcia EJ et al. Primary angioplasty vs. fibrinolysis in very old patients with acute myocardial infarction: TRIANA (TRatamiento del Infarto Agudo de miocardio eN Ancianos) randomized trial and pooled analysis with previous studies. European Heart Journal. 2011; 32(1):51-60.	RCT does not stratify study participants according to time to intervention
Busk M, Maeng M, Rasmussen K, Kelbaek H, Thayssen P, Abildgaard U et al. The Danish multicentre randomized study of fibrinolytic therapy vs. primary angioplasty in acute myocardial infarction (the DANAMI-2 trial): outcome after 3 years follow-up. European Heart Journal. 2008; 29(10):1259-1266.	Follow-up of RCT that does not stratify study participants according to time to intervention
Cannon CP, Gibson CM, Lambrew CT, Shoultz DA, Levy D, French WJ et al. Relationship of symptom-onset-to-balloon time and door-to-balloon time with mortality in patients undergoing angioplasty for acute myocardial infarction. JAMA. 2000; 283(22):2941-2947.	Not RCT, cohort studyNational Registry of Myocardial Infarction (NRMI-2), population < 100,000 (n = 27,080) study examined outcomes for differential timing of PCI from onset of symptoms, no data on fibrinolysis
Cannon CP, Sayah AJ, Walls RM. Prehospital thrombolysis: an idea whose time has come. Clinical Cardiology. 1999; 22(Suppl 4):IV10-IV19.	Not RCT, not question of interest
Cannon CP. Time to treatment: A crucial factor in thrombolysis and primary angioplasty. Journal of Thrombosis and Thrombolysis. 1996; 3(3):249-255.	Not RCT, narrative review
Cannon CP. Time to treatment of acute myocardial infarction revisited. Current Opinion in Cardiology. 1998; 13(4):254-266.	Not RCT, narrative review
Canto JG, Every NR, Magid DJ, Rogers WJ, Malmgren JA, Frederick PD et al. The volume of primary angioplasty procedures and survival after acute myocardial infarction. National Registry of Myocardial Infarction 2 Investigators. New England Journal of Medicine. 2000; 342(21):1573-1580.	Not RCT, cohort study National Registry of Myocardial Infarction (NRMI), not question of interest, examined volume of PCI procedures
Caspi A, Gottlieb S, Behar S. Delayed percutaneous transluminal coronary	Not RCT, cohort (n = 1940)

Exclusion List	Reason for exclusion
angioplasty after acute myocardial infarction. International Journal of Cardiology. 1998; 63(3):199-204.	
Chen K-Y, Rha SW, Li Y-J, Choi B-G, Choi C-U, Park C-G et al. Impact of presentation time on the management and clinical outcomes of acute myocardial infarction in Korea. European Heart Journal. 2011; 32(Suppl 1):726.	Not RCT, cohort study population < 100,000 (n = 7883)
Chen B, Wang W, Zhao H, Hu D, Xu C, Zhao M et al. Efficacy of recombinant tissue-type plasminogen activator thrombolysis and primary coronary stenting after acute myocardial infarction. Chinese Medical Journal. 2003; 116(1):142-144.	Not question of interest
Chong JJH, Ganesan AN, Eipper V, Kovoor P. Comparison of left ventricular ejection fraction and inducible ventricular tachycardia in ST-elevation myocardial infarction treated by primary angioplasty versus thrombolysis. American Journal of Cardiology. 2008; 101(2):153-157.	Not RCT, cohort (n = 420)
Cox JL, Lee E, Langer A, Armstrong PW, Naylor CD. Time to treatment with thrombolytic therapy: determinants and effect on short-term nonfatal outcomes of acute myocardial infarction. Canadian GUSTO Investigators. Global Utilization of Streptokinase and + PA for Occluded Coronary Arteries. CMAJ : Canadian Medical Association Journal = Journal De L'Association Medicale Canadienne. 1997; 156(4):497-505.	RCT does not stratify study participants according to time to intervention
Dalby M, Bouzamondo A, Lechat P, Montalescot G. Transfer for primary angioplasty versus immediate thrombolysis in acute myocardial infarction: a meta-analysis. Circulation. 2003; 108(15):1809-1814.	Meta-analysis PCI versus fibrinolysis, not question of interest, no analysis on time to intervention
De Boer SPM, Barnes EH, Westerhout CM, Simes RJ, Granger CB, Kastrati A et al. High-risk patients with ST-elevation myocardial infarction derive greatest absolute benefit from primary percutaneous coronary intervention: results from the Primary Coronary Angioplasty Trialist versus thrombolysis (PCAT)-2 collaboration. American Heart Journal. 2011; 161(3):500.	No data on timing
de Boer SPM, Westerhout CM, Simes RJ, Granger CB, Zijlstra F, Boersma E et al. Mortality and morbidity reduction by primary percutaneous coronary intervention is independent of the patient's age. JACC Cardiovascular Interventions. 2010; 3(3):324-331.	Not question of interest
De Boer MJ, Ottervanger JP, van 't Hof AW, Hoorntje JC, Suryapranata H, Zijlstra F. Reperfusion therapy in elderly patients with acute myocardial infarction: a randomized comparison of primary angioplasty and thrombolytic therapy. Journal of the American College of Cardiology. 2002; 39(11):1723-1728.	RCT does not stratify study participants according to time to intervention
De Boer MJ, Hoorntje JC, Ottervanger JP, Reiffers S, Suryapranata H, Zijlstra F. Immediate coronary angioplasty versus intravenous streptokinase in acute myocardial infarction: left ventricular ejection fraction, hospital mortality and reinfarction. Journal of the American College of Cardiology. 1994; 23(5):1004-1008.	RCT does not stratify study participants according to time to time
Dhingra R, Conley S, Niles NW. Time delay to percutaneous coronary intervention and 30-day mortality in patients with ST-elevation myocardial infarction: Single center registry. Journal of the American College of Cardiology. 2012; 59(13 SUPPL. 1):E467.	Not study type of interest; cohort analysis
De Jaegere PP, Serruys PW, Simoons ML. Should all patients with an acute myocardial infarction be referred for direct PTCA? Heart. 2004; 90(11):1352-1357.	Not RCT, narrative review
de Labriolle A, Pacouret G, Giraudeau B, Fremont B, Desveaux B, Quilliet L et al. Effect of time to treatment and age on one year mortality in acute STEMI: difference between thrombolysis and primary percutaneous coronary intervention. Archives of Cardiovascular Diseases. 2008; 101(1):48-54.	Not RCT, cohort (n = 794)

Exclusion List	Reason for exclusion
DeLuca G, et al. Percutaneous coronary intervention-related time delay, patient's risk profile, and survival benefits of primary angioplasty vs lytic therapy in ST-segment elevation myocardial infarction. Am J Emerg Med. 2009; 27(6):712-9.	Post hoc meta-regression included 2 RCTs not matching our inclusion criteria (fPPCI versus fibrinolysis)
De Luca G, Biondi-Zoccai G, Marino P. Transferring patients with ST-segment elevation myocardial infarction for mechanical reperfusion: a meta-regression analysis of randomized trials. Annals of Emergency Medicine. 2008; 52(6):665-676.	Not question of interest
De Luca L, Bolognese L, Casella G, Savonitto S, Gonzini L, Di Chiara A et al. Modalities of treatment and 30-day outcomes of unselected patients older than 75 years with acute ST-elevation myocardial infarction: data from the BLITZ study. Journal of Cardiovascular Medicine. 2008; 9(10):1045-1051.	Not RCT, cohort (n = 1959)
De Luca G, Suryapranata H, Marino P. Reperfusion strategies in acute ST-elevation myocardial infarction: an overview of current status. Progress in Cardiovascular Diseases. 2008; 50(5):352-382.	Not RCT, narrative review
De Luca G, Suryapranata H, Marino P. Primary angioplasty vs. thrombolysis. Indian Heart Journal. 2007; 59(4):302-310.	Not RCT, narrative review
De Luca G. Overview of contemporary reperfusion strategies in acute ST-elevation myocardial infarction. Cardiology International. 2007; 8(3):92-98.	Not RCT, narrative review
De Luca G, Suryapranata H, Ottervanger JP, Antman EM. Time delay to treatment and mortality in primary angioplasty for acute myocardial infarction: every minute of delay counts. Circulation. 2004; 109(10):1223-1225.	Not question of interest, no comparator for PCI
De Luca G, Suryapranata H, Zijlstra F, van 't Hof AWJ, Hoorntje JCA, Gosselink ATM et al. Symptom-onset-to-balloon time and mortality in patients with acute myocardial infarction treated by primary angioplasty. Journal of the American College of Cardiology. 2003; 42(6):991-997.	Not question of interest, no comparator for PCI, data from 4 RCTs
DeWood MA. Surgical reperfusion vs. rt-PA vs. PTCA as therapy for single vessel LAD anterior myocardial infarction. Circulation 1992; 86:772.	RCT does not stratify study participants according to time to intervention
DeWood MA, Fisher MJ. Direct PTCA versus intravenous r-tPA in acute myocardial infarction: preliminary results from a prospective randomized trial. Circulation. 1989; 80(2):418.	RCT does not stratify study participants according to time to intervention
Deng HQ, Zhou XS, Dong XF, Hu GY, Liao YQ, Liu GD et al. Comparisons of immediate and delayed PTCA/stenting with intravenous thrombolytic therapy for patients with acute myocardial infarction. Chinese Journal of Coal Industry Medine. 2002; 5(7):647-649.	Not RCT, narrative review
Dudek D, Rakowski T, Dziewierz A, Mielecki W. Time delay in primary angioplasty: How relevant is it? Heart. 2007; 93(10):1164-1166.	Not RCT, narrative review
Dussoix P, Reuille O, Verin V, Gaspoz JM, Unger PF. Time savings with prehospital thrombolysis in an urban area. European Journal of Emergency Medicine. 2003; 10(1):2-5.	Not question of interest, RCT did not examine PCI versus fibrinolysis
Eisenhauer AC. Prolonged door-to-balloon time: is treatment delayed always treatment denied? Progress in Cardiovascular Diseases. 2010; 53(3):195-201.	Retrospective cohort study
Every NR, Parsons LS, Fihn SD, Larson EB, Maynard C, Hallstrom AP et al. Long-term outcome in acute myocardial infarction patients admitted to hospitals with and without on-site cardiac catheterization facilities. Circulation. 1997; 96(6):1770-1775.	Not question of interest
Fernandez-Aviles F. Primary versus facilitated percutaneous coronary intervention (tenecteplase plus stenting) in patients with ST-elevated myocardial infarction: the final results of the GRACIA-2 randomized trial. European Heart Journal. 2004; 25(Suppl):33.	RCT does not stratify study participants according to time to intervention

Exclusion List	Reason for exclusion
Fernandez-Aviles F, Alonso JJ, Castro-Beiras A, Vazquez N, Blanco J, Alonso-Briales J et al. Routine invasive strategy within 24 hours of thrombolysis versus ischaemia-guided conservative approach for acute myocardial infarction with ST-segment elevation (GRACIA-1): a randomised controlled trial. Lancet. 2004; 364(9439):1045-1053.	Not question of interest
Fernandez-Aviles F, Alonso JJ, Pena G, Blanco J, Alonso-Briales J, Lopez-Mesa J et al. Primary angioplasty vs. early routine post-fibrinolysis angioplasty for acute myocardial infarction with ST-segment elevation: the GRACIA-2 non-inferiority, randomized, controlled trial. European Heart Journal. 2007; 28(8):949-960.	RCT does not stratify study participants according to time to intervention
Fosbol EL, Thune JJ, Kelbaek H, Andersen HR, Saunamaki K, Nielsen TT et al. Long-term outcome of primary angioplasty compared with fibrinolysis across age groups: a Danish Multicenter Randomized Study on Fibrinolytic Therapy Versus Acute Coronary Angioplasty in Acute Myocardial Infarction (DANAMI-2) substudy. American Heart Journal. 2008; 156(2):391-396.	Follow-up of RCT that does not stratify study participants according to time to intervention
Fu Y, Goodman S, Chang W-C, De Werf FV, Granger CB, Armstrong PW. Time to treatment influences the impact of ST-segment resolution on one-year prognosis: Insights from the Assessment of the Safety and Efficacy of a New Thrombolytic (ASSENT-2) Trial. Circulation. 2001; 104(22):2653-2659.	Not question of interest, original RCT examined alteplase versus tenecteplase
Gao Rl, Han Yl, Yang Xc, Mao Jm, Fang Wy, Wang L et al. Thrombolytic therapy with rescue percutaneous coronary intervention versus primary percutaneous coronary intervention in patients with acute myocardial infarction: a multicenter randomized clinical trial. Chinese Medical Journal. 2010; 123(11):1365-1372.	RCT does not stratify study participants according to time to intervention
Gao R, Han Y, Yang X, Mao J, Fang W, Wang L et al. Thrombolytic therapy with rescue percutaneous coronary intervention versus primary percutaneous coronary intervention in patients with acute myocardial infarction: A multicenter randomized clinical trial. Circulation. 2010; 122(2):e249.	RCT does not stratify study participants according to time to intervention
Garcia E, Elizaga J, Soriano J, Abeytua M, Botas J, Fernandez A et al. Primary angioplasty versus thrombolysis with t-PA in the anterior myocardial infarction: results from a single center trial. Journal of the American College of Cardiology. 1997; 29(Suppl):389A.	RCT does not stratify study participants according to time to intervention
Garcia E, Elizaga J, Perez-Castellano N, Serrano JA, Soriano J, Abeytua M et al. Primary angioplasty versus systemic thrombolysis in anterior myocardial infarction. Journal of the American College of Cardiology. 1999; 33(3):605-611.	RCT does not stratify study participants according to time to intervention
Gibbons RJ, Holmes DR, Reeder GS, Bailey KR, Hopfenspirger MR, Gersh BJ. Immediate angioplasty compared with the administration of a thrombolytic agent followed by conservative treatment for myocardial infarction. The Mayo Coronary Care Unit and Catheterization Laboratory Groups. N Engl J Med. 1993 Mar 11; 328(10):685-91.	No outcomes of interest
Gibson CM, Pride YB, Frederick PD, Pollack CVJ, Canto JG, Tiefenbrunn AJ et al. Trends in reperfusion strategies, door-to-needle and door-to-balloon times, and in-hospital mortality among patients with ST-segment elevation myocardial infarction enrolled in the National Registry of Myocardial Infarction from 1990 to 2006. American Heart Journal. 2008; 156(6):1035-1044.	Not question of interest
Gibson CM, Murphy SA, Kirtane AJ, Giugliano RP, Cannon CP, Antman EM et al. Association of duration of symptoms at presentation with angiographic and clinical outcomes after fibrinolytic therapy in patients with ST-segment elevation myocardial infarction. Journal of the American College of Cardiology. 2004; 44(5):980-987.	Not RCT, not question of interest, no comparator for fibrinolysis
Giugliano RP, Sabatine MS, Gibson CM, Roe MT, Harrington RA, Murphy SA et al. Combined assessment of thrombolysis in myocardial infarction flow grade, myocardial perfusion grade, and ST-segment resolution to evaluate epicardial	Not question of interest

Exclusion List	Reason for exclusion
and myocardial reperfusion. American Journal of Cardiology. 2004; 93(11):1362-1366.	
Giugliano RP, Braunwald E. Selecting the Best Reperfusion Strategy in ST-Elevation Myocardial Infarction: It's All a Matter of Time. Circulation. 2003; 108(23):2828-2830.	Not RCT, not question of interest
Goldberg RJ, Mooradd M, Gurwitz JH, Rogers WJ, French WJ, Barron HV et al. Impact of time to treatment with tissue plasminogen activator on morbidity and mortality following acute myocardial infarction (The second National Registry of Myocardial Infarction). American Journal of Cardiology. 1998; 82(3):259-264.	Not question of interest
Goldenberg I, Matetzky S, Halkin A, Roth A, Di SE, Freimark D et al. Primary angioplasty with routine stenting compared with thrombolytic therapy in elderly patients with acute myocardial infarction. American Heart Journal. 2003; 145(5):862-867.	Not RCT, cohort (n = 160)
Grines CL, Block PC. Senior PAMI - Final results. ACC Cardiosource Review Journal. 2007; 16(3):35-38.	RCT does not stratify study participants according to time to intervention
Grines C, Patel A, Zijlstra F, Weaver WD, Granger C, Simes RJ et al. Primary coronary angioplasty compared with intravenous thrombolytic therapy for acute myocardial infarction: six-month follow up and analysis of individual patient data from randomized trials. American Heart Journal. 2003; 145(1):47-57.	Meta-analysis PCI versus fibrinolysis, not question of interest, no analysis on time to intervention
Grines CL, Westerhausen DRJ, Grines LL, Hanlon JT, Logemann TL, Niemela M et al. A randomized trial of transfer for primary angioplasty versus on-site thrombolysis in patients with high-risk myocardial infarction: the Air Primary Angioplasty in Myocardial Infarction study. Journal of the American College of Cardiology. 2002; 39(11):1713-1719.	RCT does not stratify study participants according to time to interventions, thrombolytic arm either streptokinase or rt-PA
Grines CL, Browne KF, Marco J, Rothbaum D, Stone GW, O'Keefe J et al. A comparison of immediate angioplasty with thrombolytic therapy for acute myocardial infarction. The Primary Angioplasty in Myocardial Infarction Study Group. New England Journal of Medicine. 1993; 328(10):673-679.	RCT does not stratify study participants according to time to intervention
Guerra DR, Gibson CM. Door-to-balloon delays with PCI in acute myocardial infarction. Current Treatment Options in Cardiovascular Medicine. 2004; 6(1):69-77.	Not RCT, narrative review
Guo L, Mai X, Deng J, Liu A, Bu L, Wang H. Early percutaneous intervention improves survival in elderly patients with acute myocardial infarction complicated by cardiogenic shock. Kardiologia Polska. 2008; 66(7):722-728.	Not RCT, cohort study (n = 94)
Syndromes (GUSTO IIb) Angioplasty Substudy Investigators. A clinical trial comparing primary coronary angioplasty with tissue plasminogen activator for acute myocardial infarction. New England Journal of Medicine. 1997; 336(23):1621-1628.	RCT does not stratify study participants according to time to intervention
Hartwell D, Colquitt J, Loveman E, Clegg AJ, Brodin H, Waugh N et al. Clinical effectiveness and cost-effectiveness of immediate angioplasty for acute myocardial infarction: systematic review and economic evaluation. Health Technology Assessment. 2005; 9(17):1-114.	Not question of interest, meta-analysis does not examine timing
Herlitz J, Dellborg M, Hartford M, Karlsson T, Risenfors M, Karlson BW et al. Mortality and morbidity 1 year after early thrombolysis in suspected AMI: results from the TEAHAT Study. Journal of Internal Medicine Supplement. 1991; 734:43-51.	Not question of interest
Hochman JS, Sleeper LA, Webb JG, Sanborn TA, White HD, Talley JD et al. Early revascularization in acute myocardial infarction complicated by cardiogenic shock. New England Journal of Medicine. 1999; 341(9):625-634.	Not question of interest

Exclusion List	Reason for exclusion
Hudson MP, Armstrong PW, O'Neil WW, Stebbins AL, Weaver WD, Widimsky P et al. Mortality implications of primary percutaneous coronary intervention treatment delays: insights from the Assessment of Pexelizumab in Acute Myocardial Infarction trial. Circulation Cardiovascular Quality and Outcomes. 2011; 4(2):183-192.	Not question of interest, study on PPCI only
Hugenholtz PG. Expanding indications for thrombolytic therapy in acute myocardial infarction. How late is too late, and how early is early: the clinician's view of the first 100 minutes. American Journal of Cardiology. 1993; 72(19):22G-29G.	Not RCT, narrative review
Huynh T, Perron S, O'Loughlin J, Joseph L, Labrecque M, Tu JV et al. Comparison of primary percutaneous coronary intervention and fibrinolytic therapy in ST-segment-elevation myocardial infarction: bayesian hierarchical meta-analyses of randomized controlled trials and observational studies. Circulation. 2009; 119(24):3101-3109.	Not question of interest, meta-analysis of RCTs that did not stratify study participants according to time to intervention
Jezewski T, Konopa B, Tarchalski J, Kasprzak JD. Comparison of clinical results and life quality after myocardial infarction therapy with primary percutaneous coronary intervention and fibrinolytic angents. Polskie Achiwum Medycyny Wewnetrznej. 2009; 119(1-2):26-31.	Not RCT, cohort study (n = 200)
Karha J, Topol EJ. Primary percutaneous coronary intervention vs. fibrinolytic therapy for acute ST-elevation myocardial infarction in the elderly. American Journal of Geriatric Cardiology. 2006; 15(1):19-21.	Not RCT, narrative review
Kastrati A, Mehilli J, Dirschinger J, Schricke U, Neverve J, Pache J et al. Myocardial salvage after coronary stenting plus abciximab vs. FL plus abciximab in patients with acute myocardial infarction: a randomised trial. Lancet. 2002; 359(9310):920-925.	RCT does not stratify study participants according to time to intervention
Kedev S, Petrovksi B, Kotevski V, Antov S, Sokolov I, Jovanova S. Primary coronary angioplasty vs. intravenous streptokinase in acute myocardial infarction. Journal of the American College of Cardiology. 1997; 29(Suppl):91A.	RCT does not stratify study participants according to time to intervention
Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. Lancet. 2003; 361(9351):13-20.	Not question of interest, meta-analysis of RCTs that did not stratify study participants according to time to intervention
Kent DM, Lau J, Selker HP. Balancing the benefits of primary angioplasty against the benefits of thrombolytic therapy for acute myocardial infarction: the importance of timing. Effective Clinical Practice. 2001; 4(5):214-220.	Not RCT, narrative review
Kent DM, Ruthazer R, Griffith JL, Beshansky JR, Concannon TW, Aversano T et al. A percutaneous coronary intervention-thrombolytic predictive instrument to assist choosing between immediate thrombolytic therapy versus delayed primary percutaneous coronary intervention for acute myocardial infarction. American Journal of Cardiology. 2008; 101(6):790-795.	Not question of interest
Kent DM, Ruthazer R, Griffith JL, Beshansky JR, Grines CL, Aversano T et al. Comparison of mortality benefit of immediate thrombolytic therapy versus delayed primary angioplasty for acute myocardial infarction. American Journal of Cardiology. 2007; 99(10):1384-1388.	Not question of interest
Kent DM, Schmid CH, Lau J, Selker HP. Is primary angioplasty for some as good as primary angioplasty for all? Journal of General Internal Medicine. 2002; 17(12):887-894.	Not question of interest, meta-analysis of RCTs that did not stratify study participants according to time to intervention
Lamas GA, Escolar E, Faxon DP. Review article: Examining treatment of st-elevation myocardial infarction: The importance of early intervention. Journal of Cardiovascular Pharmacology and Therapeutics. 2010; 15(1):6-16.	Not RCT, narrative review

Exclusion List	Reason for exclusion
Leizorovicz A, Boissel JP, Robert F. Coronary reperfusion rates in acute myocardial infarction patients after thrombolytic treatment with anistreplase: correlation with the delay from onset of symptoms to treatment: a review of 424 case records of patients admitted to coronary reperfusion studies with anistreplase. Journal of Cardiovascular Pharmacology. 1992; 19(1):34-39.	Not question of interest
Le May MR, Labinaz M, Davies RF, Marquis JF, Laramee LA, O'Brien ER et al. Stenting versus thrombolysis in acute myocardial infarction trial (STAT). Journal of the American College of Cardiology. 2001; 37(4):985-991.	RCT does not stratify study participants according to time to intervention
Leonard S. Reperfusion therapy for acute st-elevation myocardial infarction (STEMI). Cardiovascular Journal of Africa. 2011; 22(3 SUPPL. 1):S26.	Not RCT, narrative review
Lundergan CF, Reiner JS, Ross AM. How long is too long? Association of time delay to successful reperfusion and ventricular function outcome in acute myocardial infarction: The case for thrombolytic therapy before planned angioplasty for acute myocardial infarction. American Heart Journal. 2002; 144(3):456-462.	Not outcome of interest
Madan M, Tan M, Halvorsen S, Westernout CM, Cantor W, Le May MR et al. Timing of angiography and clinical outcomes after fibrinolysis: A patient-level analysis of randomized early invasive clinical trials. Journal of the American College of Cardiology. 2012; 59(13 SUPPL. 1):E353.	Not question of interest
Madsen MM, Busk M, Sondergaard HM, Bottcher M, Mortensen LS, Andersen HR et al. Does diabetes mellitus abolish the beneficial effect of primary coronary angioplasty on long-term risk of reinfarction after acute ST-segment elevation myocardial infarction compared with fibrinolysis? (A DANAMI-2 substudy). American Journal of Cardiology. 2005; 96(11):1469-1475.	Not question of interest
Maeng M, Nielsen PH, Busk M, Mortensen LS, Kristensen SD, Nielsen TT et al. Time to treatment and three-year mortality after primary percutaneous coronary intervention for ST-segment elevation myocardial infarction-a DANish Trial in Acute Myocardial Infarction-2 (DANAMI-2) substudy. American Journal of Cardiology. 2010; 105(11):1528-1534.	Subgroup analysis of RCT that does not stratify study participants according to time to intervention
Magid DJ, Wang Y, Herrin J, McNamara RL, Bradley EH, Curtis JP et al. Relationship between time of day, day of week, timeliness of reperfusion, and in-hospital mortality for patients with acute ST-segment elevation myocardial infarction. JAMA. 2005; 294(7):803-812.	Not RCT, cohort study National Registry of Myocardial Infarction (NRMI-3 or NRMI-4), population < 100,000 (n = 68,439)
Martinez-Rios MA, Rosas M, Gonzalez H, Pena-Duque MA, Martinez-Sanchez C, Gaspar J et al. Comparison of reperfusion regimens with or without tirofiban in ST-elevation acute myocardial infarction. American Journal of Cardiology. 2004; 93(3):280-287.	Not question of interest
Morais J, Faria H, Goncalves F, Brandao V, Calisto J, Goncalves L et al. Primary angioplasty in better than front loaded t-PA to preserve left ventricular function after acute anterior myocardial infarction. European Heart Journal. 1997; 18(Suppl):59.	RCT does not stratify study participants according to time to intervention
Moreno R, Lopez-Sendon J, Garcia E, Perez de Isla L, Lopez de Sa E, Ortega A et al. Primary angioplasty reduces the risk of left ventricular free wall rupture compared with thrombolysis in patients with acute myocardial infarction. Journal of the American College of Cardiology. 2002; 39(4):598-603.	No outcome of interest
Nallamothu BK, Bradley EH, Krumholz HM. Time to treatment in primary percutaneous coronary intervention. New England Journal of Medicine. 2007; 357(16):1631-1638.	Not RCT, narrative review
Nallamothu BK, Wang Y, Magid DJ, McNamara RL, Herrin J, Bradley EH et al. Relation between hospital specialization with primary percutaneous coronary intervention and clinical outcomes in ST-segment elevation myocardial	Not RCT, cohort study National Registry of Myocardial Infarction

Exclusion List	Reason for exclusion
infarction: National Registry of Myocardial Infarction-4 analysis. Circulation. 2006; 113(2):222-229.	(NRMI-4), population < 100,000 (n = 37,233), not question of interest
Nallamothu BK, et al. Primary percutaneous coronary intervention versus fibrinolytic therapy in acute myocardial infarction: does the choice of fibrinolytic agent impact on the importance of time-to-treatment? Am J Cardiol. 2004; 94(6):772-4.	Post hoc meta-regression that only reported absolute risk reductions
Nallamothu BK, Bates ER. Percutaneous coronary intervention versus fibrinolytic therapy in acute myocardial infarction: is timing (almost) everything?Am J Cardiol. 2003; 92(7):824-6.	Post hoc meta-regression that only reported absolute risk reductions
Nielsen PH, Terkelsen CJ, Nielsen TT, Thuesen L, Krusell LR, Thayssen P et al. System delay and timing of intervention in acute myocardial infarction (from the Danish Acute Myocardial Infarction-2 [DANAMI-2] Trial). American Journal of Cardiology. 2011; 108(6):776-781.	Subgroup analysis of RCT that does not stratify study participants according to time to intervention
Nielsen PH, Maeng M, Busk M, Mortensen LS, Kristensen SD, Nielsen TT et al. Primary angioplasty versus fibrinolysis in acute myocardial infarction: long-term follow-up in the Danish acute myocardial infarction 2 trial. Circulation. 2010; 121(13):1484-1491.	RCT does not stratify study participants according to time to intervention
Nielsen PH, Maeng M, Busk M, Mortensen LS, Nielsen TT, Andersen HR. Primary angioplasty versus fibrinolysis in acute myocardial infarction: Long-term follow-up in the DANAMI-2 trial. Journal of the American College of Cardiology. 2009; 53(10):A459-A460.	RCT does not stratify study participants according to time to intervention
Noguchi Y, Yamaguchi I, Sugishita Y. [Comparison of thrombolytic therapy and direct percutaneous transluminal coronary angioplasty for acute myocardial infarction: prospective multicenter trial at 16 clinical centers in Ibaraki prefecture TUGMI. Tsukuba University Group for Myocardial Infarction]. Journal of Cardiology. 1996; 27(3):111-120.	RCT does not stratify study participants according to time to time
Nunn CM, O'Neill WW, Rothbaum D, Stone GW, O'Keefe J, Overlie P et al. Long-term outcome after primary angioplasty: report from the primary angioplasty in myocardial infarction (PAMI-I) trial. Journal of the American College of Cardiology. 1999; 33(3):640-646.	RCT does not stratify study participants according to time to intervention
O'Keefe JHJ, Bailey WL, Rutherford BD, Hartzler GO. Primary angioplasty for acute myocardial infarction in 1,000 consecutive patients. Results in an unselected population and high-risk subgroups. American Journal of Cardiology. 1993; 72(19):107G-115G.	Not RCT, cohort
Ornato JP. Timely lessons in heart attack management. Heart attack patients may benefit more from angioplasty than clot-busting drugs, even if it means waiting two hours. Health News. 2003; 9(10):8-9.	Not RCT, narrative review
Pinto DS, Frederick PD, Chakrabarti AK, Kirtane AJ, Ullman E, Dejam A et al. Benefit of Transferring ST-Segment-Elevation Myocardial Infarction Patients for Percutaneous Coronary Intervention Compared With Administration of Onsite Fibrinolytic Declines as Delays Increase. Circulation. 2011; 124(23):2512-2521.	Not RCT, cohort study population < 100,000 (n = 19,012)
Pinto DS, Southard M, Ciaglo L, Gibson CM. Door-to-balloon delays with percutaneous coronary intervention in ST-elevation myocardial infarction. American Heart Journal. 2006; 151(6 Suppl):S24-S29.	Not RCT, narrative review
Shiraishi J, Kohno Y, Sawada T, Arihara M, Hyogo M, Yagi T et al. Effects of hospital volume of primary percutaneous coronary interventions on angiographic results and in-hospital outcomes for acute myocardial infarction. Circulation Journal. 2008; 72(7):1041-1046.	Not RCT, cohort (n = 1785)
Rihal CS, Jaffe AS, Holmes J, Ting HH, Gersh BJ, Bell MR. Percutaneous coronary intervention vs thrombolysis for ST-elevation myocardial infarction. Journal of the American Medical Association. 2007; 297(12):1313.	Not RCT, narrative review

Exclusion List	Reason for exclusion
Rollins G. Time delays negate advantage of primary balloon angioplasty over fibrinolytic therapy in heart attack treatment. Report on Medical Guidelines and Outcomes Research. 2003; 14(21):1-6.	Not RCT, narrative review
Ribeiro EE, Silva LA, Carneiro R, D'Oliveira LG, Gasquez A, Amino JG et al. Randomized trial of direct coronary angioplasty versus intravenous streptokinase in acute myocardial infarction. Journal of the American College of Cardiology. 1993; 22(2):376-380.	RCT does not stratify study participants according to time to intervention
Ribichini F, Steffenino G, Dellavalle A, Ferrero V, Vado A, Feola M et al. Comparison of thrombolytic therapy and primary coronary angioplasty with liberal stenting for inferior myocardial infarction with precordial ST-segment depression: immediate and long-term results of a randomized study. Journal of the American College of Cardiology. 1998; 32(6):1687-1694.	RCT does not stratify study participants according to time to intervention
Ripa R, Sejersten M, Grande P, Wagner GS, Clemmensen P. Time to treatment has little influence on myocardial salvage after AMI: A DANAMI-2 substudy. Journal of Electrocardiology. 2004; 37(SUPPL.):173.	No outcome of interest
Ross AM, Huber K, Zeymer U, Armstrong PW, Granger CB, Goldstein P et al. The impact of place of enrollment and delay to reperfusion on 90-day post-infarction mortality in the ASSENT-4 PCI trial: assessment of the safety and efficacy of a new treatment strategy with percutaneous coronary intervention. JACC Cardiovascular Interventions. 2009; 2(10):925-930.	Not question of interest, RCT of fPPCI versus PCI
Ross AM, Coyne KS, Reiner JS, et al. A randomized trial comparing primary angioplasty with a strategy of short-acting thrombolysis and immediate planned rescue angioplasty in acute myocardial infarction: the PACT trial. PACT investigators. Plasminogen-activator Angioplasty Compatibility Trial. J Am Coll Cardiol 1999 Dec; 34:1954-62.	Not question of interest
Sadeghi HM, Grines CL, Chandra HR, Mehran R, Fahy M, Cox DA et al. Magnitude and impact of treatment delays on weeknights and weekends in patients undergoing primary angioplasty for acute myocardial infarction (the cadillac trial). American Journal of Cardiology. 2004; 94(5):637-640.	Not question of interest
Schömig A, Kastrati A, Dirschinger J, Mehilli J, Schricke U, Pache J, Martinoff S, Neumann FJ, Schwaiger M. Coronary stenting plus platelet glycoprotein IIb/IIIa blockade compared with tissue plasminogen activator in acute myocardial infarction. Stent versus Thrombolysis for Occluded Coronary Arteries in Patients with Acute Myocardial Infarction Study Investigators. N Engl J Med. 2000 Aug 10; 343(6):385-91.	Not question of interest
Schomig A, Ndrepepa G, Mehilli J, Schwaiger M, Schuhlen H, Nekolla S et al. Therapy-dependent influence of time-to-treatment interval on myocardial salvage in patients with acute myocardial infarction treated with coronary artery stenting or thrombolysis. Circulation. 2003; 108(9):1084-1088.	Not question of interest, 2 RCTs examined PCI with stent and abciximab versus fibrinolysis
Sejersten M, Ripa RS, Maynard C, et al. Timing of ischemic onset estimated from the electrocardiogram is better than historical timing for predicting outcome after reperfusion therapy for acute anterior myocardial infarction: a DANish trial in Acute Myocardial Infarction 2 (DANAMI-2) substudy. Am Heart J 2007; 154:61-8.	No outcome of interest
Sejersten M, Birnbaum Y, Ripa RS, Maynard C, Wagner GS, Clemmensen P et al. Influences of electrocardiographic ischaemia grades and symptom duration on outcomes in patients with acute myocardial infarction treated with thrombolysis versus primary percutaneous coronary intervention: results from the DANAMI-2 trial. Heart. 2006; 92(11):1577-1582.	RCT does not stratify study participants according to time to intervention
Sejersten M, Ripa RS, Maynard C, Grande P, Andersen HR, Wagner GS et al. Timing of ischemic onset estimated from the electrocardiogram is better than historical timing for predicting outcome after reperfusion therapy for acute anterior myocardial infarction: a DANish trial in Acute Myocardial Infarction 2	No outcomes of interest

Exclusion List	Reason for exclusion
(DANAMI-2) substudy. American Heart Journal. 2007; 154(1):61-68.	
Simek S, Lubanda JC, Aschermann M, Humhal J, Hork J, Kovarnik T et al. How does delaying treatment affect the long-term prognosis for patients with acute myocardial infarction treated with primary coronary angioplasty? Kardiologia Polska. 2004; 61(8):91-100.	Not RCT, narrative review
Smalling RW, Giesler GM, Julapalli VR, Denktas AE, Sdringola SM, Vooletich MT et al. Pre-hospital reduced-dose fibrinolysis coupled with urgent percutaneous coronary intervention reduces time to reperfusion and improves angiographic perfusion score compared with prehospital fibrinolysis alone or primary percutaneous coronary intervention: results of the PATCAR Pilot Trial. Journal of the American College of Cardiology. 2007; 50(16):1612-1614.	Not question of interest, RCT of fibrinolysis plus PCI versus stenting plus abciximab
Soon CY, Chan WX, Tan HC. The impact of time-to-balloon on outcomes in patients undergoing modern primary angioplasty for acute myocardial infarction. Singapore Medical Journal. 2007; 48(2):131-136.	Not RCT, cohort study (n = 2008
Stanislaw S, Lubanda JC, Aschermann M, et al. How does thetime to treatment affects the long term prognosis with patients with acute myocardial infarction treated with PPCI. 2004, 61, 91.	Not RCT, cohort (n = 339)
Steffenino G, Santoro GM, Maras P, Mauri F, Ardissino D, Violini R et al. In-hospital and one-year outcomes of patients with high-risk acute myocardial infarction treated with thrombolysis or primary coronary angioplasty. Italian Heart Journal. 2004; 5(2):136-145.	Not RCT, cohort (n = 2227)
Steg PG, Bonnefoy E, Chabaud S, Lapostolle F, Dubien PY, Cristofini P et al. Impact of time to treatment on mortality after prehospital fibrinolysis or primary angioplasty: data from the CAPTIM randomized clinical trial. Circulation. 2003; 108(23):2851-2856.	Not question of interest, substudy of RCT that did not stratify study participants according to time to intervention
Stenestrand U, Lindback J, Wallentin L, RIKS-HIA R. Long-term outcome of primary percutaneous coronary intervention vs prehospital and in-hospital thrombolysis for patients with ST-elevation myocardial infarction. JAMA. 2006; 296(14):1749-1756.	Not RCT, cohort study, Register of Information and Knowledge about Swedish Heart Intensive Care Admissions (RIKS-HIA), population < 100,000 (n = 26,205)
Swanson N, Nunn C, Holmes S, Devlin G. Door to balloon times: streamlining admission for primary percutaneous coronary intervention. New Zealand Medical Journal. 2010; 123(1309):18-25.	Not question of interest, RCT on PPCI
Tarantini G, Van de Werf F, Bilato C, Gersh B. Primary percutaneous coronary intervention for acute myocardial infarction: Is it worth the wait? The risk-time relationship and the need to quantify the impact of delay. American Heart Journal. 2011; 161(2):247-253.	Not RCT, narrative review
Tarantini G, Ramondo A, Napodano M, Bilato C, Buja P, Isabella G et al. Time delay-adjusted survival benefit of angioplasty over thrombolysis in acute myocardial infarction: influence of time from symptom onset. Italian Heart Journal. 2004; 5(11):844-850.	Post hoc meta-regression that only reported absolute risk reductions
Terkelsen CJ, Sorensen JT, Nielsen TT. Is there any time left for primary percutaneous coronary intervention according to the 2007 updated American College of Cardiology/American Heart Association ST-segment elevation myocardial infarction guidelines and the D2B alliance? Journal of the American College of Cardiology. 2008; 52(15):1211-1215.	Not RCT, narrative review
Thomas K, Ottervanger JP, De Boer MJ, Suryapranata H, Hoorntje JC, Zijlstra F. Primary angioplasty compared with thrombolysis in acute myocardial infarction in diabetic patients. Diabetes Care. 1999; 22(4):647-649.	Subgroup analysis of RCT that does not stratify study participants according to time to

Exclusion List	Reason for exclusion
	intervention
Valente S, Lazzeri C, Saletti E, Chiostri M, Gensini GF. Primary percutaneous coronary intervention in comatose survivors of cardiac arrest with ST-elevation acute myocardial infarction: a single-center experience in Florence. Journal of Cardiovascular Medicine. 2008; 9(11):1083-1087.	Not RCT, cohort (n = 31)
Vermeer F, Oude Ophuis AJ, vd Berg EJ, Brunninkhuis LG, Werter CJ, Boehmer AG et al. Prospective randomised comparison between thrombolysis, rescue PTCA, and primary PTCA in patients with extensive myocardial infarction admitted to a hospital without PTCA facilities: a safety and feasibility study. Heart. 1999; 82(4):426-431.	No outcomes of interest, RCT does not stratify study participants according to time to intervention
Vrachatis AD, Alpert MA, Georgulas VP, Nikas DJ, Petropoulou EN, Lazaros GI et al. Comparative efficacy of primary angioplasty with stent implantation and thrombolysis in restoring basal coronary artery flow in acute ST segment elevation myocardial infarction: quantitative assessment using the corrected TIMI frame count. Angiology. 2001; 52(3):161-166.	No outcomes of interest
Wang TY, Nallamothu BK, Krumholz HM, Li S, Roe MT, Jollis JG et al. Association of door-in to door-out time with reperfusion delays and outcomes among patients transferred for primary percutaneous coronary intervention. JAMA. 2011; 305(24):2540-2547.	Not RCT, cohort study, National Cardiovascular Data Registry (NCDR) Acute Coronary Treatment and Intervention Outcomes Network Registry-Get with the Guidelines (ATCION Registry-GWTG), population < 100,000 (n = 14,821) study examined outcomes for differential timing of PCI from onset of symptoms, no data on fibrinolysis
Weaver WD, Simes RJ, Betriu A, Grines CL, Zijlstra F, Garcia E, Grinfeld L, Gibbons RJ, Ribeiro EE, DeWood MA, Ribichini F. Comparison of primary coronary angioplasty and intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review. JAMA. 1997 Dec 17; 278(23):2093-8. Erratum in: JAMA 1998 Jun 17; 279(23):1876.	Not question of interest, meta-analysis of RCTs that did not stratify study participants according to time to intervention
Widimsky P, Bilkova D, Penicka M, et al. Long-term outcomes of patients with acute myocardial infarction presenting to hospitals without catheterization laboratory and randomized to immediate thrombolysis or interhospital transport for primary percutaneous coronary intervention. Five years' follow-up of the PRAGUE-2 Trial. Eur Heart J 2007; 28:679-84.	RCT does not stratify study participants according to time to intervention
Widimsky P, Budesinsky T, Vorac D, Groch L, Zelizko M, Aschermann M et al. Long distance transport for primary angioplasty vs immediate thrombolysis in acute myocardial infarction. Final results of the randomized national multicentre trial--PRAGUE-2. European Heart Journal. 2003; 24(1):94-104.	RCT does not stratify study participants according to time to intervention
Widimsky P, Groch L, Zelizko M, Aschermann M, Bednar F, Suryapranata H. Multicentre randomized trial comparing transport to primary angioplasty vs immediate thrombolysis vs combined strategy for patients with acute myocardial infarction presenting to a community hospital without a catheterization laboratory. The PRAGUE study. European Heart Journal. 2000; 21(10):823-831.	RCT does not stratify study participants according to time to intervention
Wong A, Koh T-H, Mak K-H, Sim K-H, Ahmad TRL, Tan KH et al. A randomized multicenter trial comparing primary angioplasty and combined fibrinolytic therapy with or without rescue angioplasty-apamit extended pilot study. American Journal of Cardiology. 2009; 103(9):3B.	RCT does not stratify study participants according to time to intervention

Exclusion List	Reason for exclusion
Woollard M. Early thrombolysis: Time to change? A discussion paper. Journal of Emergency Primary Health Care. 2005; 3(4).	Not RCT, narrative review
Zeymer U, Schroder R, Machnig T, Neuhaus KL. Primary percutaneous transluminal coronary angioplasty accelerates early myocardial reperfusion compared to thrombolytic therapy in patients with acute myocardial infarction. American Heart Journal. 2003; 146(4):686-691.	Not question of interest
Zeymer U, Neuhaus K-L. Thrombolysis and percutaneous transluminal coronary angioplasty in patients with acute myocardial. Zeitschrift Fur Kardiologie. 2000; 89(SUPPL. 4):IV30-IV40.	Not RCT, narrative review
Zijlstra F, Patel A, Jones M, Grines CL, Ellis S, Garcia E et al. Clinical characteristics and outcome of patients with early (<2 h), intermediate (2-4 h) and late (>4 h) presentation treated by primary coronary angioplasty or thrombolytic therapy for acute myocardial infarction. European Heart Journal. 2002; 23(7):550-557.	Superseded by newer regression analyses (found 10 RCTs that are identified in newer studies)
Zijlstra F, Hoorntje JC, de BM, Reiffers S, Medema K, Ottervanger JP et al. Long-term benefit of primary angioplasty as compared with thrombolytic therapy for acute myocardial infarction. New England Journal of Medicine. 1999; 341(19):1413-1419.	Not RCT, narrative review
Zijlstra F, Beukema WP, van't Hof AW, Liem A, Reiffers S, Hoorntje JC et al. Randomized comparison of primary coronary angioplasty with thrombolytic therapy in low risk patients with acute myocardial infarction. Journal of the American College of Cardiology. 1997; 29(5):908-912.	RCT does not stratify study participants according to time to intervention
Zijlstra F, de Boer MJ, Hoorntje JC, Reiffers S, Reiber JH, Suryapranata H. A comparison of immediate coronary angioplasty with intravenous streptokinase in acute myocardial infarction. N Engl J Med. 1993 Mar 11; 328(10):680-4.	RCT does not stratify study participants according to time to intervention
Zijlstra F, De Boer MJ, Ottervanger JP, Liem AL, Hoorntje JC, Suryapranata H. Primary coronary angioplasty versus intravenous streptokinase in acute myocardial infarction: differences in outcome during a mean follow-up of 18 months. Coronary Artery Disease. 1994; 5(8):707-712.	RCT does not stratify study participants according to time to time

J.2 Facilitated PPCI

Reference	Reason for exclusion
Anonymous. Platelet glycoprotein IIb/IIIa receptor blockade and low-dose heparin during percutaneous coronary revascularization. The EPILOG Investigators. N.Engl.J.Med. 336 (24):1689-1696, 1997.	Wrong population: not STEMI (STEMI excluded)
Anonymous. Promising results with argatroban as an adjunctive thrombolytic therapy. Br.J.Cardiol. 4 (5):180, 1997.	Wrong treatment: thrombolysis not fPPCI; trial overview not full study publication
J. Afilalo, A. Michael Roy, and M. J. Eisenberg. Systematic review of fibrinolytic-facilitated percutaneous coronary intervention: potential benefits and future challenges. Can.J.Cardiol. 25 (3):141-148, 2009.	Systematic review with no meta-analysis
L. Agati, S. Funaro, M. Madonna, G. Sardella, B. Garramone, and L. Galiuto. Does coronary angioplasty after timely thrombolysis improve microvascular perfusion and left ventricular function after acute myocardial infarction? Am.Heart J. 154 (1):151-157, 2007.	Not true fPPCI as PCI performed anytime within 24hrs
F. V. Aguirre, R. P. McMahon, H. Mueller, N. S. Kleiman, M. J. Kern, P. Desvigne-Nickens, W. P. Hamilton, and B. R. Chaitman. Impact of age on clinical outcome and postlytic management strategies in patients treated with intravenous thrombolytic therapy: Results from the TIMI II study. Circulation 90 (1):78-86, 1994.	TIMI-II subanalysis – wrong treatment: patients received fibrinolysis and not additional PCI (thus not fPPCI versus PPCI)

Reference	Reason for exclusion
H.-R. Amtz, J. F. Schroeder, K. Pels, P. Schwimmbeck, B. Witzenbichler, and H. P. Schultheiss. Prehospital versus periprocedural administration of abciximab in STEMI: early and late results from the randomised REOMOBILE-study. Eur.Heart J. 24 (Suppl 1):268, 2003.	REOMOBILE study - abstract. This has not been published into a full article yet.
H Andersen, T Nielsen, T Vesterlund, P Grande, U Abildgaard, P Thayssen, F Pedersen, L Mortensen, and DANAMI-2 Investigators. Danish multicenter randomized study on fibrinolytic therapy versus acute coronary angioplasty in acute myocardial infarction: rationale and design of the DANish trial in Acute Myocardial Infarction-2 (DANAMI-2). Am.Heart J. 146 (2):234-241, 2003.	DANAMI-2 trial – wrong intervention: thrombolysis not fPPCI
F. Andreotti, S. B. Ujang, P. Sritara, C. Kluft, G. J. Davies, and A. Maseri. Can we reduce thrombin generation during coronary thrombolysis or coronary angioplasty? Fibrinolysis 9 (SUPPL. 1):74-77, 1995.	Wrong comparison: different doses of t-PA
E. M. Antman, H. W. Louwerenburg, H. F. Baars, J. C. Wesdorp, B. Hamer, J. P. Bassand, F. Bigonzi, G. Pisapia, C. M. Gibson, H. Heidbuchel, E. Braunwald, and F. Van de Werf. Enoxaparin as adjunctive antithrombin therapy for ST-elevation myocardial infarction: results of the ENTIRE-Thrombolysis in Myocardial Infarction (TIMI) 23 Trial. Circulation 105 (14):1642-1649, 2002.	TIMI 23 trial – wrong treatment: PCI was given at physician's discretion thus not true PCI versus fPPCI (only 47% of patients had PCI)
E. M. Antman, C. M. Gibson, J. A. de Lemos, R. P. Giugliano, C. H. McCabe, P. Coussement, I. Menown, C. A. Nienaber, et al. Combination reperfusion therapy with abciximab and reduced dose reteplase: Results from TIMI 14. Eur.Heart J. 21 (23):1944-1953, 2000.	TIMI 14 trial – wrong intervention: groups just fibrinolysis with out PCI
D. Antoniucci, R. Valenti, A. Migliorini, G. Moschi, M. Trapani, P. Buonamici, G. Cerisano, L. Bolognese, and G. M. Santoro. Abciximab therapy improves 1-month survival rate in unselected patients with acute myocardial infarction undergoing routine infarct artery stent implantation. Am.Heart J. 144 (2):315-322, 2002.	Not RCT
D. Antoniucci, R. Valenti, A. Migliorini, G. Moschi, M. Trapani, E. V. Dovellini, L. Bolognese, and G. M. Santoro. Abciximab therapy improves survival in patients with acute myocardial infarction complicated by early cardiogenic shock undergoing coronary artery stent implantation. Am.J.Cardiol. 90 (4):353-357, 2002.	Not RCT
R. J. Applegate, M. A. Grabarczyk, D. C. Sane, M. T. Sacrinty, J. E. Goodin, G. S. Statonk, T. T. Baki, S. K. Gandhi, M. A. Kutcher, and W. C. Little. PCI with and without abciximab after upstream eptifibatide use: outcomes in high-risk patients. J.Invasive Cardiol. 18 (12):604-613, 2006.	Not RCT
P W. Armstrong, A Gershlick, P Goldstein, R Wilcox, T Danays, E Bluhmki, F Van de Werf, and STREAM Steering Committee. The Strategic Reperfusion Early After Myocardial Infarction (STREAM) study. Am.Heart J. 160 (1):30, 2010.	STREAM study: study protocol.
P. W. Armstrong and WEST Steering Committee. A comparison of pharmacologic therapy with/without timely coronary intervention vs. primary percutaneous intervention early after ST-elevation myocardial infarction: the WEST (Which Early ST-elevation myocardial infarction Therapy) study. Eur.Heart J. 27 (13):1530-1538, 2006.	WEST study - wrong percentage had PCI in the fPPCI arm: <85% (78%) and 50% of this was rescue PCI. More pts in the PPCI arm had PCI (91%).
P. W. Armstrong, N. Bett, D. Brieger, D. Chew, R. Dick, A. Farshid, P. Garrahy, B. Gunalingham, R. Hendriks, J. Horowitz, N. Jepson, J. Lefkovits, S. Lo, et al. PexeLizumab for Acute ST-elevation myocardial infarction in patients undergoing primary percutaneous coronary intervention: A randomized controlled trial. JAMA 297 (1):43-51, 2007.	Wrong drug: pexelizumab not licensed in UK
A. E. Arnold, M. L. Simoons, F. Van de Werf, D. P. de Bono, J. Lubsen, J. G. Tijssen, P. W. Serruys, and M. Verstraete. Recombinant tissue-type	Wrong population: suspected MI

Reference	Reason for exclusion
plasminogen activator and immediate angioplasty in acute myocardial infarction. One-year follow-up. The European Cooperative Study Group. Circulation 86 (1):111-120, 1992.	
A. T. Askari and A. M. Lincoff. GUSTO V: Combination drug treatment of acute myocardial infarction. Cleve.Clin.J.Med. 69 (7):554-560, 2002.	GUSTO V trial overview - wrong comparison: abciximab versus reteplase (both fPPCI) using different drugs given at the same time rather than early versus later thus not fPPCI versus PPCI.
R Bagur, OF. Bertrand, J Rodes-Cabau, E Larose, S Rinfret, CM. Nguyen, B Noel et al. Long term efficacy of abciximab bolus-only compared to abciximab bolus and infusion after transradial coronary stenting. Catheter.Cardiovasc.Interv. 74 (7):1010-1016, 2009.	EASY trial: wrong comparisons: All patients received abciximab + stenting, then randomised to same day discharge + no abciximab infusion versus overnight hospital stay + abciximab infusion.
F. W. Bar, J. Meyer, F. Vermeer, R. Michels, B. Charbonnier, K. Haerten, M. Spiecker, C. Macaya, et al. Comparison of saruplase and alteplase in acute myocardial infarction. SESAM Study Group. The Study in Europe with Saruplase and Alteplase in Myocardial Infarction. Am.J.Cardiol. 79 (6):727-732, 1997.	SESAM trial - wrong comparison: fPPCI versus fPPCI using different drugs (patients randomised to saruplase versus alteplase), and drugs given at the same time rather than early versus later (thus not fPPCI versus PPCI). Additionally 0% stents used (not mentioned their use in the protocol or results)
G. I. Barbash, A. Roth, H. Hod, M. Modan, H. I. Miller, S. Rath, Y. H. Zahav, G. Keren, M. Motro, and A. Shachar. Randomized controlled trial of late in-hospital angiography and angioplasty versus conservative management after treatment with recombinant tissue-type plasminogen activator in acute myocardial infarction. Am.J.Cardiol. 66 (5):538-545, 1990.	Wrong comparison: fPPCI vs thrombolysis; not true fPPCI as PCI performed 5 days after giving the thrombolytics
F. Bellandi, M. Maioli, M. Gallopin, A. Toso, and R. P. Dabizzi. Increase of myocardial salvage and left ventricular function recovery with intracoronary abciximab downstream of the coronary occlusion in patients with acute myocardial infarction treated with primary coronary intervention. Catheter.Cardiovasc.Interv. 62 (2):186-192, 2004.	Wrong comparisons: abciximab + PCI by different routes of administration
J. Bengtson, M. Adolphson, D. L. Brewer, D. Jacobs, J. L. Gard, L. Cahoon, M. Bloom, B. Kennelly, K. Porter, J. Kmonicek, F. M. Krainin, J. Shane, J. F. Marquis, et al. Multicenter, dose-ranging study of efegatran sulfate versus heparin with thrombolysis for acute myocardial infarction: The Promotion of Reperfusion in Myocardial Infarction Evolution (PRIME) trial. Am.Heart J. 143 (1):95-105, 2002.	PRIME trial - wrong intervention and comparison: thrombolysis at different doses
P. B. Berger, M. R. Bell, Jr Holmes, B. J. Gersh, M. Hopfenspirger, and R. Gibbons. Time to reperfusion with direct coronary angioplasty and thrombolytic therapy in acute myocardial infarction. Am.J.Cardiol. 73 (4):231-236, 1994.	Wrong outcomes: reperfusion directly after procedure (no clinical outcomes)

Reference	Reason for exclusion
J. S. Berger, M. T. Roe, C. M. Gibson, R. Kilaru, C. L. Green, L. Melton, J. D. Blankenship et al. Safety and feasibility of adjunctive antiplatelet therapy with intravenous elinogrel, a direct-acting and reversible P2Y12 ADP-receptor antagonist, before primary percutaneous intervention in patients with ST-elevation myocardial infarction: The Early Rapid ReversAl of Platelet ThromboSis with Intravenous Elinogrel before PCI to Optimize REperfusion in Acute Myocardial Infarction (ERASE MI). Am.Heart J. 158 (6):998, 2009.	Wrong study drugs: patients randomised to elinogrel versus placebo
J. S. Berger, M. T. Roe, C. M. Gibson, R. Kilaru, C. L. Green, L. Melton, J. D. Blankenship, D. C. Metzger, C. B. Granger, D. D. Gretler, C. L. Grines, K. Huber, U. Zeymer, P. Buszman, R. A. Harrington, and P. W. Armstrong. Safety and feasibility of adjunctive antiplatelet therapy with intravenous elinogrel, a direct-acting and reversible P2Y12 ADP-receptor antagonist, before primary percutaneous intervention in patients with ST-elevation myocardial infarction: The Early Rapid ReversAl of Platelet ThromboSis with Intravenous Elinogrel before PCI to Optimize REperfusion in Acute Myocardial Infarction (ERASE MI). Am.Heart J. 158 (6):998, 2009.	Not RCT – comparison of data from several trials
N. Bhala. Enoxaparin in elective percutaneous coronary intervention [6]. N.Engl.J.Med. 355 (26):2788, 2006.	Letter
D L. Bhatt, B I. Lee, P J. Casterella, M Pulsipher, M Rogers, M Cohen, V E. Corrigan, T J. J. Ryan, J A. Breall, et al., and Coronary Revascularization Using Integrilin and Single bolus Enoxaparin Study. Safety of concomitant therapy with eptifibatide and enoxaparin in patients undergoing percutaneous coronary intervention: results of the Coronary Revascularization Using Integrilin and Single bolus Enoxaparin Study. J.Am.Coll.Cardiol. 41 (1):20-25, 2003.	CRUISE trial - wrong comparison: both groups randomised to fPPCI (fPPCI using eptifibatide + enoxaparin versus fPPCI using eptifibatide + UFH); drugs given in both groups at the same time (at time of PCI) rather than early versus later thus would have been fPPCI versus PPCI. Additionally 0% stents used (not mentioned their use in the protocol or results)
D. L. Bhatt and E. J. Topol. Long-term protection from myocardial ischemic events after coronary angioplasty. Cardiol.Rev. 15 (7):18-22, 1998.	Wrong population: not STEMI but mixed
L Bolognese, G Falsini, F Liistro, P Angioli, K Ducci, T Taddei, R Tarducci, F Cosmi et al. Randomized comparison of upstream tirofiban versus downstream high bolus dose tirofiban or abciximab on tissue-level perfusion and troponin release in high-risk acute coronary syndromes treated with percutaneous coronary interventions: the EVEREST trial. J.Am.Coll.Cardiol. 47 (3):522-528, 2006.	EVEREST trial - wrong population: high risk ACS.
E Bonnefoy, P G Steg, F Boutitie, P Y Dubien, F L, J Roncalli, F Dissait, G Vanzetto, A Leizorowicz, G Kirkorian, Investigators CAPTIM, C. Mercier, E. P. McFadden, and P. Touboul. Comparison of primary angioplasty and pre-hospital fibrinolysis in acute myocardial infarction (CAPTIM) trial: a 5-year follow-up. Eur.Heart J. 30 (13):1598-1606, 2009.	CAPTIM trial - wrong comparison: PPCI vs thrombolysis
E Bonnefoy, F Lapostolle, A Leizorovicz, G Steg, E P. McFadden, P Y Dubien, S Cattan, E Boullenger, J Machecourt, et al, and Comparison of Angioplasty and Prehospital Thromboysis in Acute Myocardial Infarction study group. Primary angioplasty versus prehospital fibrinolysis in acute myocardial infarction: a randomised study. Lancet 360 (9336):825-829, 2002.	Wrong comparison: PPCI vs thrombolysis

Reference	Reason for exclusion
D. P. de Bono. What is the role of invasive intervention after coronary thrombolysis? Eur.Heart J. 12 Suppl G:43-46, 1991.	Review
W. B. Borden and D. P. Faxon. Facilitated Percutaneous Coronary Intervention. J.Am.Coll.Cardiol. 48 (6):1120-1128, 2006.	Literature review
J. C. Braga, F. P. Esteves, J. P. Esteves, A. L. Latado, A. G. Godinho, A. Azevedo Junior, J. C. Brito, P. R. Silva, M. S. Teixeira, V. P. Souza, A. Rabelo Junior, and M. S. Rocha. Confirmation that heparin is an alternative means of promoting early reperfusion. Coron.Artery Dis. 9 (6):335-338, 1998.	Wrong % stents used: <85% stents used (66%)
C. E. Buller, G. E. Pate, P. W. Armstrong, B. J. O'Neill, J. G. Webb, R. Gallo, and R. C. Welsh. Catheter thrombosis during primary percutaneous coronary intervention for acute ST elevation myocardial infarction despite subcutaneous low-molecular-weight heparin, acetylsalicylic acid, clopidogrel and abciximab pretreatment. Can.J.Cardiol. 22 (6):511-515, 2006.	Not RCT (case report of 3 patients in an RCT – WEST study)
C. P. Cannon. Bridging the gap with new strategies in acute ST elevation myocardial infarction: bolus thrombolysis, glycoprotein IIb/IIIa inhibitors, combination therapy, percutaneous coronary intervention, and facilitated PCI. Journal of Thrombosis and Thrombolysis 9 (3):235-241, 2000.	Literature review
S. M Chen, Y. K. Hsieh, G. B. Guo, C. Y. Fang, H. K. Yip, C.J. Wu, and M. Fu. Angiographic and clinical outcome in ST-segment elevation myocardial infarction patients receiving an adjunctive double bolus regimen of tirofiban for primary percutaneous coronary intervention. Circulation Journal 70 (5):536-541, 2006.	Not RCT (patients not randomised)
D. P. Chew, P. Aylward, and H. D. White. Facilitated percutaneous coronary intervention: is this strategy ready for implementation? Curr.Cardiol.Rep. 7 (4):235-241, 2005.	Review / overview
J. S. Cho, S.-H. Her, J. Y. Baek, M.-W. Park, H. D. Kim, M. H. Jeong, Y. K. Ahn, S. C. Chae, S. H. Hur, et al. Clinical benefit of low molecular weight heparin for ST-segment elevation myocardial infarction patients undergoing primary percutaneous coronary intervention with glycoprotein IIb/IIIa inhibitor. J.Korean Med.Sci. 25 (11):1601-1608, 2010.	KAMIR study – not RCT: patients divided into 2 groups rather than randomised. Additionally wrong comparison: both groups fPPCI using different drugs GPI versus no GPI then subdivided into use of LMWH versus UFH. Also drugs given at the same time not early versus later, thus is not fPPCI versus PPCI.
W.-Y. Chung, M.-J. Han, Y.-S. Cho, K.-I. Kim, H.-J. Chang, T.-J. Youn, I.-H. Chae, D.-J. Choi, C.-H. Kim, B.-H. Oh, Y.-B. Park, and Y.-S. Choi. Effects of the early administration of heparin in patients with ST-elevation myocardial infarction treated by primary angioplasty. Circulation Journal 71 (6):862-867, 2007.	Not Randomised
B. E. P. M. Claessen, G. D. Dangas, R. Mehran, B. Witzenbichler, G. Gaugliumi, J. Peruga, K. Xu, and G. W. Stone. Clinical outcomes following stent thrombosis occurring in-hospital versus out-of-hospital; Results of the HORIZONS-AMI trial. Eur.Heart J. 32:655, 2011.	Abstract
N. Curzen. Viewpoint: thrombolysis or angioplasty in the real world: a UK perspective. Circulation 113 (23):f89-f91, 2006.	Viewpoint
M. J. De Boer, J. P. Ottervanger, A. W. van 't Hof, J. C. Hoorntje, H. Suryapranata, and F. Zijlstra. Reperfusion therapy in elderly patients with acute myocardial infarction: a randomized comparison of primary angioplasty and	Wrong comparison: thrombolysis not fPPCI

Reference	Reason for exclusion
thrombolytic therapy. J.Am.Coll.Cardiol. 39 (11):1723-1728, 2002.	
Luca G. De, N. Ernst, H. Suryapranata, J. P. Ottervanger, J. C. Hoorntje, A. T. Gosselink, J. H. Dambrink, M. J. De Boer, and A. W. van 't Hof. Relation of interhospital delay and mortality in patients with ST-segment elevation myocardial infarction transferred for primary coronary angioplasty. Am J Cardiol 95 (11):1361-1363, 2005.	Wrong population: all patients undergoing angioplasty (not just STEMI).
G De Luca, H Suryapranata, G W. Stone, D Antoniucci, J E. Tcheng, F J Neumann, F Van de Werf, E M. Antman, and E J. Topol. Abciximab as adjunctive therapy to reperfusion in acute ST-segment elevation myocardial infarction: a meta-analysis of randomized trials. JAMA 293 (14):1759-1765, 2005.	Old meta-analysis in STEMI patients (published 2005 and included trials only up to 2004)
G. De Luca, C. M. Gibson, F. Bellandi, S. Murphy, M. Maioli, M. Noc, U. Zeymer, D. Dudek, H. R. Arntz, S. Zorman, H. M. Gabriel, A. Emre, et al. Early glycoprotein IIb-IIIa inhibitors in primary angioplasty (EGYPT) cooperation: an individual patient data meta-analysis. Heart 94 (12):1548-1558, 2008.	Newer IPD meta-analysis in STEMI patients (published 2008) but included trials only up to 2007)
G. De Luca and P. Marino. Facilitated angioplasty with combo therapy among patients with ST-segment elevation myocardial infarction: a meta-analysis of randomized trials. Am.J.Emerg.Med. 27 (6):683-690, 2009.	Newer meta-analysis in STEMI patients (published 2009) but included trials only up to 2007)
G De Luca, C. M Gibson, F Bellandi, S Murphy, M Maioli, M Noc, U Zeymer, D Dudek, H R Arntz et al. Benefits of pharmacological facilitation with glycoprotein IIb-IIIa inhibitors in diabetic patients undergoing primary angioplasty for STEMI. A subanalysis of the EGYPT cooperation. Journal of Thrombosis and Thrombolysis 28 (3):288-298, 2009.	Newer meta-analysis in STEMI patients (published 2009) but included trials only up to 2007). Also only gives results for diabetic patients with STEMI.
G De Luca, E P Navarese, E Cassetti, M Verdoia, and H Suryapranata. Meta-analysis of randomized trials of glycoprotein IIb/IIIa inhibitors in high-risk acute coronary syndromes patients undergoing invasive strategy. Am.J.Cardiol. 107 (2):198-203, 2011.	Newer meta-analysis (published 2011 and included trials up to 2010) – but wrong population: ACS patients
A. E. Denktas, H. Athar, T. D. Henry, D. M. Larson, M. Simons, R. S. Chan, N. W. Niles, H. Thiele, et al. Reduced-Dose Fibrinolytic Acceleration of ST-Segment Elevation Myocardial Infarction Treatment Coupled With Urgent Percutaneous Coronary Intervention Compared to Primary Percutaneous Coronary Intervention Alone. Results of the AMICO (Alliance for Myocardial Infarction Care Optimization) Registry. JACC: Cardiovascular Interventions 1 (5):504-510, 2008.	AMICO trial: not RCT (registry data)
P Di Pasquale, S Cannizzaro, F Giambanco, S Scalzo, G Tricoli, S Fasullo, and S Paterna. Immediate versus delayed facilitated percutaneous coronary intervention: a pilot study. J.Cardiovasc.Pharmacol. 46 (1):83-88, 2005.	Low % stents used: 38 and 40% in each group.
Hendrik Jan Dieker, Elvira V. van Horssen, Ferry M. R. J. Hersbach, Marc A. Brouwer, Ad J. van Boven, Arnoud W. J. van 't Hof, Wim R. M. Aengevaeren, Freek W. A. Verheugt, and Frits W. H. M. Bar. Transport for abciximab facilitated primary angioplasty versus on-site thrombolysis with a liberal rescue policy: the randomised Holland Infarction Study (HIS). Journal of Thrombosis and Thrombolysis 22 (1):39-45, 2006.	HIS study - wrong fPPCI intervention: fibrinolysis + rescue PCI. Also PCI performed in <85% patients (26% and 98% in each arm; mean 75%).
P DiPasquale, S Cannizzaro, G Parrinello, F Giambanco, G Vitale, S Fasullo, S Scalzo, F Ganci et al. Is delayed facilitated percutaneous coronary intervention better than immediate in reperfused myocardial infarction? Six months follow up findings. Journal of Thrombosis and Thrombolysis 21 (2):147-157, 2006.	Wrong comparison: although this is immediate PCI versus delayed PCI (correct comparison), however different drugs may have been used as before randomisation

Reference	Reason for exclusion
	patients had combination treatment either tirofiban + rtPA or abciximab + rtPA
S Doggrell. Can bivalirudin and provisional GP IIb/IIIa blockade REPLACE heparin and planned glycoprotein IIb/IIIa blockade during percutaneous coronary intervention? Expert Opin Pharmacother 4 (8):1431-1433, 2003.	REPLACE trial - wrong population: not STEMI but mixed all pts undergoing PCI
L. Dong-Bao, H. Qi, L. Hong-Wei, C. Hui, and Z. Shu-Mei. Effects of early angioplasty after fibrinolysis on prognosis of patients with ST-segment elevation acute myocardial infarction. Afr.J.Biotechnol. 10 (70):15801-15804, 2011.	Wrong comparison: fPPCI versus standard treatment (fibrinolytics with PCI only in some patients 7 days later)
C L. Dubois, A Belmans, C B. Granger, P W. Armstrong, L Wallentin, P M. Fioretti, J L. Lopez-Sendon, F W. Verheugt, J Meyer, F Van de Werf, and ASSENT-3 Investigators. Outcome of urgent and elective percutaneous coronary interventions after pharmacologic reperfusion with tenecteplase combined with unfractionated heparin, enoxaparin, or abciximab. J.Am.Coll.Cardiol. 42 (7):1178-1185, 2003.	ASSENT-3 substudy – loss of randomisation: subgroups of urgent versus elective PCI patients
S. G. Ellis, P. Armstrong, A. Betriu, B. Brodie, H. Herrmann, G. Montalescot, F. J. Neumann, J. J. Smith, E. Topol, and Facilitated INtervention with Enhanced Reperfusion Speed to Stop Events Investigators. Facilitated percutaneous coronary intervention versus primary percutaneous coronary intervention: design and rationale of the Facilitated Intervention with Enhanced Reperfusion Speed to Stop Events (FINESSE) trial. Am.Heart J. 147 (4):E16, 2004.	No results: methods and design of FINESSE trial
S. G. Ellis. A clinical trial comparing primary coronary angioplasty with tissue plasminogen activator for acute myocardial infarction. N.Engl.J.Med. 336 (23):1621-1628, 1997.	GUSTO IIb trial – loss of randomisation / indirect comparison: 2 sets of patients randomised. 1 set to PCI versus fibrinolysis (wrong comparison); 2nd set to PCI + hirudin versus PCI + heparin (wrong comparison). To be included in our review we would need to compare 1 arm from each of the randomised sets: PCI versus PCI + heparin, and this is an indirect comparison (as loss of randomisation).
Nicolette M. S. K. Ernst, Harry Suryapranata, Kor Miedema, Robbert J. Slingerland, Jan Paul Ottervanger, Jan C. A. Hoorntje, A. T. M. Gosselink, Jan Henk Dambrink, Menko Jan de Boer, Felix Zijlstra, and Arnoud W. J. van 't Hof. Achieved platelet aggregation inhibition after different antiplatelet regimens during percutaneous coronary intervention for ST-segment elevation myocardial infarction. J.Am.Coll.Cardiol. 44 (6):1187-1193, 2004.	Randomised patients with STEMI to abciximab, tirofiban or no GPI in the cath lab after angiography and just before the PPCI procedure (not a facilitated PPCI strategy – using GPI conventionally in the cath lab). Also the main outcome was platelet aggregation and relevant clinical outcomes beyond hospital admission are not reported.

Reference	Reason for exclusion
J. Exaire, S Butman, R Ebrahimi, N. Kleiman, R. Harrington, M. Schweiger, J. Bittl, K Wolski, E. Topol, A Lincoff, and REPLACE-2 Investigators. Provisional glycoprotein IIb/IIIa blockade in a randomized investigation of bivalirudin versus heparin plus planned glycoprotein IIb/IIIa inhibition during percutaneous coronary intervention: predictors and outcome in the Randomized Evaluation in Percutaneous coronary intervention Linking Angiomax to Reduced Clinical Events (REPLACE)-2 trial. Am.Heart J. 152 (1):157-163, 2006.	Subgroup analysis of REPLACE-2 trial – wrong population: not STEMI but mixed elective and urgent PCI
F. Fernandez-Aviles, J. J. Alonso, G. Pena, J. Blanco, J. Alonso-Briales, J. Lopez-Mesa, F. Fernandez-Vazquez, et al. Primary angioplasty vs. early routine post-fibrinolysis angioplasty for acute myocardial infarction with ST-segment elevation: the GRACIA-2 non-inferiority, randomized, controlled trial. Eur.Heart J. 28 (8):949-960, 2007.	GRACIA-2 trial - wrong comparison: both groups randomised to PCI at different times (early versus later) however the drugs used in each arm were different (abciximab versus tenecteplase).
F. Fernandez-Aviles. Primary versus facilitated percutaneous coronary intervention (tenecteplase plus stenting) in patients with ST-elevated myocardial infarction: the final results of the GRACIA-2 randomized trial. Eur.Heart J. 25 (Suppl):33, 2004.	Abstract. GRACIA-2 trial - wrong comparison: both groups randomised to PCI at different times (early versus later) however the drugs used in each arm were different (abciximab versus tenecteplase).
I. Ferreira-Gonzalez, G. Permanyer-Miralda, J. Marrugat, M. Heras, J. Cunat, E. Civeira, F. Aros, J. J. Rodriguez, P. L. Sanchez, et al. MASCARA (Manejo del Sindrome Coronario Agudo. Registro Actualizado) study. General findings. Rev.Esp.Cardiol. 61 (8):803-816, 2008.	MASCARA trial: not an RCT.
J. Franke. HORIZONS AMI. Harmonizing outcomes with revascularization and stents in AMI: A prospective, randomized comparison of bivalirudin vs. heparin plus glycoprotein IIb/IIIa inhibitors during primary angioplasty in acute myocardial infarction - 30-Day results. Herz 32 (8):671, 2007.	In German; abstract
X.-H. Fu, Q.-Q. Hao, X.-W. Jia, W.-Z. Fan, X.-S. Gu, W.-L. Wu, G.-Z. Hao, S.-Q. Li, Y.-F. Jiang, and W. Geng. Effect of tirofiban plus clopidogrel and aspirin on primary percutaneous coronary intervention via transradial approach in patients with acute myocardial infarction. Chin.Med.J.(Engl). 121 (6):522-527, 2008.	Wrong intervention: not true fPPCI as thrombolysis given 24h before PCI
R l Gao, Y Han, X Yang, J Mao, W Fang, L Wang, W Shen, Z Li, G Jia, S Lu, M Wei, D Zeng, J Chen, X Qin, B Xu, C DU, and Collaborative Research Group of Reperfusion Therapy in Acute Myocardial Infarction (RESTART). Thorombolytic therapy with rescue percutaneous coronary intervention versus primary percutaneous coronary intervention in patients with acute myocardial infarction: a multicenter randomized clinical trial. Chin.Med.J.(Engl). 123 (11):1365-1372, 2010.	RESTART study - wrong comparison: thrombolysis with rescue PCI not fPPCI (55% had rescue PCI)
B. J. Gersh, G. W. Stone, H. D. White, and D. R. J. Holmes. Pharmacological facilitation of primary percutaneous coronary intervention for acute myocardial infarction: is the slope of the curve the shape of the future? JAMA 293 (8):979-986, 2005.	Literature review
C. Michael Gibson, Yuli Ten, Sabina A. Murphy, Lauren N. Ciaglo, Matthew C. Southard, A. Michael Lincoff, and Ron Waksman. Association of	Sunanalysis of REPLACE-2 trial – wrong subgroups:

Reference	Reason for exclusion
prerandomization anticoagulant switching with bleeding in the setting of percutaneous coronary intervention (A REPLACE-2 analysis). Am.J.Cardiol. 99 (12):1687-1690, 2007.	stratified by anti-coagulant use
R R. Giraldez, S D. Wiviott, J C. Nicolau, S Mohanavelu, D A. Morrow, E M. Antman, and R P. Giugliano. Streptokinase and enoxaparin as an alternative to fibrin-specific lytic-based regimens: an ExTRACT-TIMI 25 analysis. Drugs 69 (11):1433-1443, 2009.	EXTRACT-TIMI 25 substudy post-hoc analysis – wrong treatment: patients received streptokinase or alteplase, reteplase or tenecteplase at physician's discretion and were randomised to enoxaparin or UFH. Results have been stratified here by type of fibrinolytic.
R P. Giugliano, L. K Newby, R A. Harrington, C. M Gibson, F Van de Werf, P Armstrong, G Montalescot, J Gilbert, J T. Strony, R M. Califf, E Braunwald, and EARLY ACS Steering Committee. The early glycoprotein IIb/IIIa inhibition in non-ST-segment elevation acute coronary syndrome (EARLY ACS) trial: a randomized placebo-controlled trial evaluating the clinical benefits of early front-loaded eptifibatide in the treatment of patients with non-ST-segment elevation acute coronary syndrome--study design and rationale. Am.Heart J. 149 (6):994-1002, 2005.	Wrong population: NSTEMI-ACS
R P. Giugliano, J A. White, C Bode, P W. Armstrong, G Montalescot, B S. Lewis, A van 't Hof, et al., and A. C. S. EARLY, I. Early versus delayed, provisional eptifibatide in acute coronary syndromes. N.Engl.J.Med. 360 (21):2176-2190, 2009.	Wrong population: NSTEMI
C. L. Grines, D. A. Cox, G. W. Stone, E. Garcia, L. A. Mattos, A. Giambartolomei, B. R. Brodie, O. Madonna, M. Eijgelshoven, A. J. Lansky, W. W. O'Neill, and M. C. Morice. Coronary angioplasty with or without stent implantation for acute myocardial infarction. Stent Primary Angioplasty in Myocardial Infarction Study Group. N Engl J Med 341 (26):1949-1956, 1999.	PAMI trial – wrong comparison: PCI with stenting versus PCI without stenting
M. Gyongyosi, H. Domanovits, W. Benzer, M. Haugk, B. Heinisch, G. Sodeck, R. Hodl, G. Gaul, G. Bonner, et al. Use of abciximab prior to primary angioplasty in STEMI results in early recanalization of the infarct-related artery and improved myocardial tissue reperfusion - results of the Austrian multi-centre randomized ReoPro-BRIDGING Study. Eur.Heart J. 25 (23):2125-2133, 2004.	ReoPRO-BRIDGING study – wrong timing of outcomes: outcome results are only for pre-PCI not post PCI (thus shows effect of fibrinolysis NOT fPPCI)
D. Hartwell, J. Colquitt, E. Loveman, A. J. Clegg, H. Brodin, N. Waugh, P. Royle, P. Davidson, L. Vale, and L. MacKenzie. Clinical effectiveness and cost-effectiveness of immediate angioplasty for acute myocardial infarction: systematic review and economic evaluation. Health.Technol.Assess. 9 (17):1-114, 2005.	Wrong comparison: thrombolysis not fPPCI
T Heestermans, H Suryapranata, J M. ten Berg, A Mosterd, A. T. M. Gosselink, W Kochman, T Dill et al. Facilitated reperfusion with prehospital glycoprotein IIb/IIIa inhibition: predictors of complete ST-segment resolution before primary percutaneous coronary intervention in the On-TIME 2 trial: correlates of reperfusion before primary PCI. J.Electrocardiol. 44 (1):42-48, 2011.	On-TIME 2 SUBSTUDY – wrong outcomes: outcomes during transport and predictors
A. A. C. M. Heestermans, J. W. Van Werkum, C. Hamm, T. Dill, A. T. M. Gosselink, M. J. De Boer, G. Van Houwelingen, J. C. A. Hoorntje, P. C. Koopmans, J. M. Ten Berg, and A. W. J. Van 't Hof. Marked reduction of early stent thrombosis with pre-hospital initiation of high-dose Tirofiban in ST-segment elevation myocardial infarction. J Thromb Haemost 7 (10):1612-1618,	On-TIME 2 SUBSTUDY – wrong outcomes: occurrence of early stent thrombosis

Reference	Reason for exclusion
2009.	
T Heestermans, A W. J. van 't Hof, J M. ten Berg, J W. van Werkum, E Boersma, A Mosterd, P R. Stella et al. The golden hour of prehospital reperfusion with triple antiplatelet therapy: a sub-analysis from the Ongoing Tirofiban in Myocardial Evaluation 2 (On-TIME 2) trial early initiation of triple antiplatelet therapy. Am.Heart J. 160 (6):1079-1084, 2010.	On-TIME 2 SUBSTUDY – wrong outcomes: patency according to time
R. S. Hermanides, Houwelingen G. Van, J. P. Ottervanger, Boer M. J. De, T. Dill, C. Hamm, P. R. Stella, E. Boersma, J. M. Ten Berg, and A. W. J. van't Hof. The impact of age on effects of pre-hospital initiation of high bolus dose of tirofiban before primary angioplasty for st-elevation myocardial infarction. Cardiovasc.Drugs Ther. 25 (4):323-330, 2011.	ONTIME-2 substudy – results stratified by age.
H. C. Herrmann, D. J. Moliterno, E. M. Ohman, A. L. Stebbins, C. Bode, A. Betriu, F. Forycki, et al. Facilitation of early percutaneous coronary intervention after reteplase with or without abciximab in acute myocardial infarction: results from the SPEED (GUSTO-4 Pilot) Trial. J.Am.Coll.Cardiol. 36 (5):1489-1496, 2000.	Substudy of the SPEED (GUSTO-4 pilot) trial - wrong comparison / loss of randomisation: patients originally randomised to abciximab + reteplase (different doses) + PCI versus abciximab + PCI (correct comparison). However this substudy assessed all patients who underwent PCI and divided them into 2 groups and compared – those who had early PCI versus not early PCI.
H. C. Herrmann, J. Lu, B. R. Brodie, P. W. Armstrong, G. Montalescot, A. Betriu, F. J. Neuman, M. B. Effron, E. S. Barnathan, E. J. Topol, S. G. Ellis, and Investigators FINESSE. Benefit of facilitated percutaneous coronary intervention in high-risk ST-segment elevation myocardial infarction patients presenting to nonpercutaneous coronary intervention hospitals. JACC Cardiovasc Interv 2 (10):917-924, 2009.	Retrospective analysis of FINESSE trial – stratification by TIMI risk score
T. Itoh, K. Fukami, T. Suzuki, T. Kimura, Y. Kanaya, M. Orii, I. Goto, H. Matsui, S. Sugawara, S. Nakajima, T. Fusazaki, and M. Nakamura. Comparison of long-term prognostic evaluation between pre-intervention thrombolysis and primary coronary intervention: A prospective randomized trial - Five-year results of the IMPORTANT study. Circulation Journal 74 (8):1625-1634, 2010.	Not true randomisation. The 2 groups of interest were a subgroup of 1 of the original 2 randomised groups. Patients randomised to prior t-PA (n = 50) versus PPCI (n = 51) but the t-PA group was then subdivided into fPPCI (n = 19) and t-PA alone (n = 27). The t-PA alone half of the arm we are not interested in so it would be loss of randomisation to compare the originally randomised PPCI arm (n = 51) to just the fPPCI subgroup (n = 19) of the originally randomised prior t-PA arm (n = 50).
S Khoobiar, N Mejevoi, K Kaid, C Boiangiu, S Setty, A Tanwir, K Khalid, and M Cohen. Primary percutaneous coronary intervention for ST-elevation	Not RCT

Reference	Reason for exclusion
myocardial infarction using an intravenous and subcutaneous enoxaparin low molecular weight heparin regimen. Journal of Thrombosis and Thrombolysis 26 (2):85-90, 2008.	
A. Kastrati, J. Mehilli, K. Schlotterbeck, F. Dotzer, J. Dirschinger, C. Schmitt, S. G. Nekolla, M. Seyfarth, S. Martinoff et al. Early administration of reteplase plus abciximab vs abciximab alone in patients with acute myocardial infarction referred for percutaneous coronary intervention: a randomized controlled trial. JAMA 291 (8):947-954, 2004.	Wrong timing for PPCI arm: adjunctive therapy given in the emergency department or ICU rather than cath lab (as specified in our protocol) thus is a type of fPPCI (patients randomsied to reteplse + abciximab versus abciximab) and drugs in both arms given at the same time in either the ER or ICU.
E. C. Keeley, J. A. Boura, and C. L. Grines. Comparison of primary and facilitated percutaneous coronary interventions for ST-elevation myocardial infarction: quantitative review of randomised trials. Lancet 367 (9510):579-588, 2006.	Old meta-analysis in STEMI patients (published 2006 and included trials only up to 2005)
R. V. Kelly, M. G. Cohen, and E. M. Ohman. Facilitated percutaneous coronary w intervention in acute myocardial infarction: attractive concept but difficult to	Revie
D. J. Kereiakes, N. S. Kleiman, J. Ambrose, M. Cohen, S. Rodriguez, T. Palabrica, H. C. Herrmann, J. M. Sutton, W. D. Weaver, D. B. McKee, V. Fitzpatrick, and F. L. Sax. Randomized, double-blind, placebo-controlled dose-ranging study of tirofiban (MK-383) platelet IIb/IIIa blockade in high risk patients undergoing coronary angioplasty. J.Am.Coll.Cardiol. 27 (3):536-542, 1996.	Wrong population: Angina
T. J. Kiernan, H. H. Ting, and B. J. Gersh. Facilitated percutaneous coronary intervention: current concepts, promises, and pitfalls. Eur.Heart J. 28 (13):1545-1553, 2007.	Literature review
W. Kochman, S. Dobrzycki, K.S. Nowak, S. Chlopicki, P. Kralisz, P. Prokopczuk, H. Bachorzewska-Gajewska, K. Gugala, M. Niewada, G. Mezynski, B. Poniatowski, J. Korecki, and W.J. Musial. Safety and feasibility of a novel dosing regimen of tirofiban administered in patients with acute myocardial infarction with ST elevation before primary coronary angioplasty: a pilot study. Journal of Thrombosis and Thrombolysis 17 (2):127-131, 2004.	Not RCT
V Kodumuri, S Adigopula, P Singh, P Swaminathan, R Arora, and S Khosla. Comparison of low molecular weight heparin with unfractionated heparin during percutaneous coronary interventions: a meta-analysis. Am.J.Ther. 18 (3):180-189, 2011.	Wrong population: not STEMI but mixed
D. D. Kontogianni, N. T. Kouris, and D. D. Babalis. The use of low molecular weight heparins and platelet GP IIb/IIIa inhibitors as adjuncts to thrombolysis: Are there any perspectives? Hell.J.Cardiol. 45 (5):312-323, 2004.	Literature review
J. M. Lablanche, E. P. McFadden, N. Meneveau, J. R. Lusson, B. Bertrand, J. P. Metzger, V. Legrand, et al. Effect of nadroparin, a low-molecular-weight heparin, on clinical and angiographic restenosis after coronary balloon angioplasty: the FACT study. Fraxiparine Angioplastie Coronaire Transluminale. Circulation 96 (10):3396-3402, 1997.	Wrong population: angina
M. Lablanche, E. P. McFadden, N. Meneveau, J. R. Lusson, B. Bertrand, J. P. Metzger, V. Legrand, G. Grollier, C. Macaya,et al. Effect of nadroparin, a low-molecular-weight heparin, on clinical and angiographic restenosis after coronary balloon angioplasty: the FACT study. Fraxiparine Angioplastie	FACT study – wrong population: not STEMI but elective PCI after arterial injury

Reference	Reason for exclusion
Coronaire Transluminale. Circulation 96 (10):3396-3402, 1997.	
A. J. Lansky, Y. Tsuchiya, M. Brener, R. Mehran, E. Cristea, C. Pietras, C. L. Grines, D. A. Cox, E. Garcia, J. E. Tcheng, G. Guagliumi, T. Stuckey, M. Turco, J. D. Carroll, B. D. Rutherford, M. B. Leon, J. Moses, and G. W. Stone. Comparison between ticlopidine and clopidogrel in patients undergoing primary stenting in acute myocardial infarction: Results from the CADILLAC trial. Catheter.Cardiovasc.Interv. 72 (7):917-924, 2008.	Subgroup analysis of CADILLAC trial – wrong subgroups: results stratified by pts who received clopidogrel vs ticlopidine after PCI with stenting
M. Lee, H Liao, T Yang, J Dhoot, J Tobis, G Fonarow, and E Mahmud. Comparison of bivalirudin versus heparin plus glycoprotein IIb/IIIa inhibitors in patients undergoing an invasive strategy: a meta-analysis of randomized clinical trials. Int.J.Cardiol. 152 (3):369-374, 2011.	Meta-analysis – wrong population: not STEMI but mixed
C. W. Lee, D.-H. Moon, M.-K. Hong, J.-H. Lee, S. I. W. Choi, H. S. Yang, J.-J. Kim, S.-W. Park, and S.-J. Park. Effect of Abciximab on myocardial salvage in patients with acute myocardial infarction undergoing primary angioplasty. Am.J.Cardiol. 90 (11):1243-1246, 2002.	Wrong outcomes: pre-PCI results (angiographic only) thus not show effects of fPPCI
Y J Li, S W Rha, K Y Chen, K L. Poddar, Z Jin, Y Minami, L Wang, Q Dang, G P Li, S Ramasamy, J Y Park, C U Choi, et al, and other Korea Acute Myocardial infarction Registry Investigators. Low-molecular-weight heparin versus unfractionated heparin in acute ST-segment elevation myocardial infarction patients undergoing primary percutaneous coronary intervention with drug-eluting stents. Am.Heart J. 159 (4):684, 2010.	KAMIR study – not RCT: patients divided into 2 groups rather than randomised. Additionally wrong comparison: both groups fPPCI using different drugs GPI versus no GPI then subdivided into use of LMWH versus UFH. Also drugs given at the same time not early versus later, thus is not fPPCI versus PPCI.
F. Liang, D. Hu, X. Shi, M. Gao, J. Wei, H. Zhao, L. Wang, S. Jia, H. Wang, R. Liu, Y. Chen, and Y. Lu. Efficacy and safety of single-bolus tenecteplase compared with front-loaded alteplase in Chinese patients with acute myocardial infarction. J.Geriatr.Cardiol. 4 (3):137-141, 2007.	Wrong comparison: both groups randomised to fPPCI (fPPCI using tenecteplase versus fPPCI using alteplase); drugs given in both groups in either the ER or ICU. Additionally <85% had PCI: Only 60-70% had PCI in the end (PCI or CABG was given at the discretion of the physician depending on the angiogram results, angiography was done 90 minutes after the study drugs were administered)
J. P. Leitner and J. D. Abbott. Drug-eluting stents and glycoprotein IIbIIIa inhibitors in the pharmacoinvasive management of ST elevation MI. Intervent.Cardiol. 3 (1):17-21, 2011. Original trial GRACIA-3 = SANCHEZ 2010	GRACIA-3 substudy – results stratified by type of stent rather than GPI versus placebo.
W M Li, X Yang, L F Wang, Y G Ge, H S Wang, L Xu, Z H Ni, and D P Zhang.	Wrong comparison: both

Reference	Reason for exclusion
Comparison of tirofiban combined with dalteparin or unfractionated heparin in primary percutaneous coronary intervention of acute ST-segment elevation myocardial infarction patients. Chin.Med.J.(Engl). 124 (20):3275-3280, 2011.	groups had fPPCI but randomsied to different drugs tirofiban + UFH vs tirofiban + dalteparin. Also drugs given at the same time not early vs. later, thus is not fPPCI vs PPCI.
G.-M. Lin and C.-L. Han. Risk profile and benefits from Gp IIb-IIIa inhibitors among patients with ST-segment elevation myocardial infarction treated with primary angioplasty: A meta-regression analysis of randomized trials. Eur.Heart J. 31 (6):753-754, 2010.	Letter
A. M. Lincoff, R. M. Califf, D. J. Moliterno, S. G. Ellis, J. Ducas, J. H. Kramer, N. S. Kleiman, E. A. Cohen, J. E. Booth, S. K. Sapp, C. F. Cabot, E. J. Topol, J. E. Tcheng, J. D. Talley, P. O. Caramori, J. R. Burton, T. A. Kelly, and T. B. Ivanc. Complementary clinical benefits of coronary-artery stenting and blockade of platelet glycoprotein IIb/IIIa receptors. N.Engl.J.Med. 341 (5):319-327, 1999.	Wrong population: not STEMI (AMI excluded)
T Liu, Ying Xie, Yu jie Zhou, Yue ping Li, Han ying Ma, Yong he Guo, Yu yang Liu, Ying xin Zhao, and Dong mei Shi. Effects of upstream tirofiban versus downstream tirofiban on myocardial damage and 180-day clinical outcomes in high-risk acute coronary syndromes patients undergoing percutaneous coronary interventions. Chin.Med.J.(Engl). 122 (15):1732-1737, 2009.	Wrong population: NSTEMI
M. A. McDonald, Y. Fu, U. Zeymer, G. Wagner, S. G. Goodman, A. Ross, C. B. Granger, F. Van de Werf, P. W. Armstrong, and P. C. I. investigators. Adverse outcomes in fibrinolytic-based facilitated percutaneous coronary intervention: insights from the ASSENT-4 PCI electrocardiographic substudy. Eur.Heart J. 29 (7):871-879, 2008.	ASSENT-4 substudy: wrong outcomes – ECG outcomes
M A. McDonald, Y Fu, U Zeymer, G Wagner, S G. Goodman, A Ross, C B. Granger, F Van de Werf, P W. Armstrong, and P. C. I. investigators. Adverse outcomes in fibrinolytic-based facilitated percutaneous coronary intervention: insights from the ASSENT-4 PCI electrocardiographic substudy. Eur.Heart J. 29 (7):871-879, 2008.	ASSENT-4 SUBSTUDY-wrong outcomes: outcomes stratified by extent of ST resolution
T. Mann, G. Cubeddu, J. Bowen, J. E. Schneider, M. Arrowood, W. N. Newman, M. J. Zellinger, and G. C. Rose. Stenting in acute coronary syndromes: a comparison of radial versus femoral access sites. J.Am.Coll.Cardiol. 32 (3):572-576, 1998.	Not RCT – randomisation not mentioned. Patients in each group were matched by specific characteristics.
L. Marcoff, Z. Zhang, W. Zhang, E. Ewen, C. Jurkovitz, P. Leguet, P. Kolm, and W. S. Weintraub. Cost effectiveness of enoxaparin in acute ST-segment elevation myocardial infarction: the ExTRACT-TIMI 25 (Enoxaparin and Thrombolysis Reperfusion for Acute Myocardial Infarction Treatment-Thrombolysis In Myocardial Infarction 25) study. J.Am.Coll.Cardiol. 54 (14):1271-1279, 2009.	EXTRACT-TIMI 25 study - wrong comparison: thrombolysis with 2 different drugs rather than fPPCI
J. D. Marmur, C. A. Mitre, E. Barnathan, and E. Cavusoglu. Benefit of bolus-only platelet glycoprotein IIb/IIIa inhibition during percutaneous coronary intervention: Insights from the very early outcomes in the Evaluation of 7E3 for the Prevention of Ischemic Complications (EPIC) trial. Am.Heart J. 152 (5):876-881, 2006.	EPIC trial – wrong population: not STEMI but mixed
Marco A. Martinez-Rios, Martin Rosas, Hector Gonzalez, Marco A. Pena-Duque, Carlos Martinez-Sanchez, Jorge Gaspar, Hector Garcia, Efrain Gaxiola, Luis Delgado, Jorge Carrillo, Jose Luis Leyva, Eulo Lupi, and Investigators SASTRE. Comparison of reperfusion regimens with or without tirofiban in ST-elevation acute myocardial infarction. Am.J.Cardiol. 93 (3):280-287, 2004.	Randomised patients with STEMI to 'usual reperfusion' (group A) or to 'combined reperfusion with tirofiban' (group B). They then randomised patients again to either fibrinolysis or PPCI, creating 4 groups (A1, A2,

Reference	Reason for exclusion
	B1,B2). It is unclear whether the PPCI procedures were carried out as quickly as possible and whether the tirofiban was administered as part of a facilitation strategy and the authors refer to 'standard primary stenting PCI'.
A Marzocchi, A Manari, G Piovaccari, C Marrozzini, S Marra, P Magnavacchi, P Sangiorgio et al. and F. A. T. A. Investigators. Randomized comparison between tirofiban and abciximab to promote complete ST-resolution in primary angioplasty: results of the facilitated angioplasty with tirofiban or abciximab (FATA) in ST-elevation myocardial infarction trial. Eur.Heart J. 29 (24):2972-2980, 2008.	FATA trial – wrong comparison: both groups randomised to fPPCI with different drugs (fPPCI using abciximab versus fPPCI using tirofiban); drugs could be administered in ER, ambulance or cath lab in either group (it was not given at a prespecified different time in each group).
G. Medic, M. Schwenkglenks, I. Eijgelshoven, A. Smith, J. Day, S. Plent, G. Bergman, and T. Toward. Relative efficacy of bivalirudin vs. heparin alone in stemi patients treated with primary PCI - An indirect treatment comparison. Value in Health 14 (7):A367, 2011.	Abstract
R Mehran, A J. Lansky, B Weitzenbichler, G Guagliumi, J Z. Peruga, B R. Brodie, et al, and Trial HORIZONS-AMI, I. Bivalirudin in patients undergoing primary angioplasty for acute myocardial infarction (HORIZONS-AMI): 1-year results of a randomised controlled trial. Lancet 374 (9696):1149-1159, 2009.	HORIZONS-AMI trial - wrong comparison: both arms fPPCI using different drugs (Bivalirudin versus Heparin + GPI) then PCI in both.
S. R. Mehta, W. E. Boden, J. W. Eikelboom, M. Flather, P. G. Steg, A. Avezum, R. Afzal, L. S. Piegas, et al, and OASIS 5 and 6 Investigators. Antithrombotic therapy with fondaparinux in relation to interventional management strategy in patients with ST- and non-ST-segment elevation acute coronary syndromes: an individual patient-level combined analysis of the Fifth and Sixth Organization to Assess Strategies in Ischemic Syndromes (OASIS 5 and 6) randomized trials. Circulation 118 (20):2038-2046, 2008.	OASIS 5 and 6 trials – wrong population: NSTEMI/STEMI mixed (not separated into each group)
M. G. Midei, V. J. Coombs, D. R. Lowry, M. N. Drossner, K. C. Prewitt, J. C. Wang, M. B. Loughrey, and S. O. Gottlieb. Clinical outcomes comparing eptifibatide and abciximab in ST elevation acute myocardial infarction patients undergoing percutaneous coronary interventions. Cardiology 107 (3):172-177, 2007.	Not RCT
G. J. Mishkel, A. L. Moore, S. J. Markwell, and R. W. Ligon. Bivalirudin versus heparin plus glycoprotein IIb/IIIa inhibitors in drug-eluting stent implantations in the absence of acute myocardial infarction: clinical and economic results (Provisional abstract). J.Invasive Cardiol. 19 (2):63-68, 2007.	Not RCT
G Montalescot, U Zeymer, J Silvain, B Boulanger, M Cohen, P Goldstein, P Ecollan, X Combes, K Huber et al, and Investigators ATOLL. Intravenous enoxaparin or unfractionated heparin in primary percutaneous coronary intervention for ST-elevation myocardial infarction: the international randomised open-label ATOLL trial. Lancet 378 (9792):693-703, 2011.	ATOLL trial - wrong comparison: both arms fPPCI using different drugs (enoxaparin versus heparin) then PCI in both.

Reference	Reason for exclusion
D. J. Moliterno and E. J. Topol. Conjunctive use of platelet glycoprotein IIb/IIIa antagonists and thrombolytic therapy for acute myocardial infarction. Thromb.Haemost. 78 (1):214-219, 1997.	Literature review
G Montalescot, SG. Ellis, MA. de Belder, L Janssens, O Katz, W Pluta, P Ecollan, M Tendera, Ad J. van Boven, P Widimsky, HR. Andersen et al, and Facilitated INtervention with Enhanced Reperfusion Speed to Stop Events Investigators. Enoxaparin in primary and facilitated percutaneous coronary intervention A formal prospective nonrandomized substudy of the FINESSE trial (Facilitated INtervention with Enhanced Reperfusion Speed to Stop Events). JACC Cardiovasc Interv 3 (2):203-212, 2010.	FINESSE substudy: non-randomised data and wrong comparison. Analysed results by dividing the fPPCI arm into people who had enoxaparin or unfractionated heparin, depending which was given (so both these groups are fPPCI – the wrong comparison).
G Montalescot, M Borentain, L Payot, J P Collet, and D Thomas. Early vs late administration of glycoprotein IIb/IIIa inhibitors in primary percutaneous coronary intervention of acute ST-segment elevation myocardial infarction: a meta-analysis. JAMA 292 (3):362-366, 2004.	Old meta-analysis in STEMI patients (published 2004 and included trials only up to 2004)
G. Montalescot, D. Antoniucci, A. Kastrati, F. J. Neumann, M. Borentain, A. Migliorini, C. Boutron, J.-P. Collet, and E. Vicaut. Abciximab in primary coronary stenting of ST-elevation myocardial infarction: A European meta-analysis on individual patients' data with long-term follow-up. Eur.Heart J. 28 (4):443-449, 2007.	IPD meta-analysis of just 3 trials (all pre-2008) and not a systematic search.
M K. Natarajan, J L. Velianou, A G. G. Turpie, S R. Mehta, D Raco, D M. Goodhart, R Afzal, and J S. Ginsberg. A randomized pilot study of dalteparin versus unfractionated heparin during percutaneous coronary interventions. Am.Heart J. 151 (1):175, 2006.	Wrong population: not STEMI (mixed)
F. J. Neumann, R. Blasini, C. Schmitt, E. Alt, J. Dirschinger, M. Gawaz, A. Kastrati, and A. Schomig. Effect of glycoprotein IIb/IIIa receptor blockade on recovery of coronary flow and left ventricular function after the placement of coronary-artery stents in acute myocardial infarction. Circulation 98 (24):2695-2701, 1998.	Not true fPPCI: had intervention within 48h of symptoms
F. J. Neumann, A. Kastrati, C. Schmitt, R. Blasini, M. Hadamitzky, J. Mehilli, M. Gawaz, M. Schleef, M. Seyfarth, J. Dirschinger, and A. Schomig. Effect of glycoprotein IIb/IIIa receptor blockade with abciximab on clinical and angiographic restenosis rate after the placement of coronary stents following acute myocardial infarction. J.Am.Coll.Cardiol. 35 (4):915-921, 2000.	Not true fPPCI: had intervention within 48h of symptoms
C. M. O'Connor, R. B. Meese, S. McNulty, K. D. Lucas, R. J. Carney, R. M. LeBoeuf, W. Maddox, C. F. Bethea, N. Shadoff, T. F. Trahey, J. A. Heinsimer, J. M. Burks, G. O'Donnell, M. W. Krucoff, and R. M. Califf. A randomized factorial trial of reperfusion strategies and aspirin dosing in acute myocardial infarction. Am.J.Cardiol. 77 (10):791-797, 1996.	Wrong drug: anisteprase (not used in UK)
W. W. O'Neill, R. Weintraub, C. L. Grines, T. B. Meany, B. R. Brodie, H. Z. Friedman, R. G. Ramos, V. Gangadharan, R. N. Levin, N. Choksi, and . A prospective, placebo-controlled, randomized trial of intravenous streptokinase and angioplasty versus lone angioplasty therapy of acute myocardial infarction. Circulation 86 (6):1710-1717, 1992.	PRAGUE study – wrong intevention: streptokinase (not used in UK)
G. Parodi, R. Sciagra, A. Migliorini, G. Memisha, G. Moschi, R. Valenti, A. Pupi, and D. Antoniucci. A randomized trial comparing clopidogrel versus ticlopidine therapy in patients undergoing infarct artery stenting for acute myocardial infarction with abciximab as adjunctive therapy. *Am.Heart J.* 150 (2):220, 2005.	Wrong comparison: both arms fPPCI using different drugs (clopidogrel versus ticlopidine).
K. Pels, J. Schroder, B. Witzenbichler, D. Muller, A. Morguet, M. Pauschinger, H.	0% stents used (not

Reference	Reason for exclusion
P. Schultheiss, and H. R. Arntz. Prehospital versus periprocedural abciximab in ST-elevation myocardial infarction treated by percutaneous coronary intervention. European journal of emergency medicine : official journal of the European Society for Emergency Medicine 15 (6):324-329, 2008.	mentioned their use in the protocol or results). Comparison fPPCI versus PPCI (early abciximab versus later abciximab).
S Peters, M Truemmel, and B Koehler. Facilitated PCI by combination fibrinolysis or upstream tirofiban in acute ST-segment elevation myocardial infarction: results of the Alteplase and Tirofiban in Acute Myocardial Infarction (ATAMI) trial. Int.J.Cardiol. 130 (2):235-240, 2008.	ATAMI trial – wrong timing (not true fPPCI): PCI given only 43 and 112 hours later
A. S. Petronio, D. Rovai, G. Musumeci, R. Baglini, C. Nardi, U. Limbruno, C. Palagi, D. Volterrani, and M. Mariani. Effects of abciximab on microvascular integrity and left ventricular functional recovery in patients with acute infarction treated by primary coronary angioplasty. Eur.Heart J. 24 (1):67-76, 2003.	Wrong sample size: n<60 (n = 31) already have larger studies or abciximab.
M. Piorkowski, J. Priess, U. Weikert, M. Jaster, P.-L. Schwimmbeck, H.-P. Schultheiss, and U. Rauch. Abciximab therapy is associated with increased platelet activation and decreased heparin dosage in patients with acute myocardial infarction. Thromb.Haemost. 94 (2):422-426, 2005.	Wrong sample size (N<60, 30) for abciximab studies as got larger studies; wrong outcomes: not clinical just platelet activation markers
F Prati, S Petronio, Ad J. van Boven, M Tendera, L De Luca, M A. de Belder, A R. Galassi, F Imola, et al, and substudy investigators FINESSE-ANGIO. Evaluation of infarct-related coronary artery patency and microcirculatory function after facilitated percutaneous primary coronary angioplasty: the FINESSE-ANGIO (Facilitated Intervention With Enhanced Reperfusion Speed to Stop Events-Angiographic) study. JACC Cardiovasc Interv 3 (12):1284-1291, 2010.	FINESSE trial substudy – wrong patients and wrong outcomes: ony looked at a subset of patients and outcomes of TIMI score change.
M. Rabah, D. Mason, D. W. Muller, R. Hundley, A. D. Kugelmass, B. Weiner, L. Cannon, W. W. O'Neill, and R. D. Safian. Heparin after percutaneous intervention (HAPI): a prospective multicenter randomized trial of three heparin regimens after successful coronary intervention. J.Am.Coll.Cardiol. 34 (2):461-467, 1999.	HAPI trial - wrong treatment: treatment post-PCI (not initiated before PCI thus not true fPPCI).
LE. Rabbani, S Iyengar, GD. Dangas, CL. Grines, DA. Cox, E Garcia, JE. Tcheng, JJ. Griffin, G Guagliumi et al. Impact of thienopyridine administration prior to primary stenting in acute myocardial infarction. J.Intervent.Cardiol. 22 (4):378-384, 2009. Original CADILLAC trial = STONE 2006 and STONE 2002	CADILLAC trial substudy - (loss of randomisation) and wrong comparison: looked at effect of patients who received thienopyradine versus no thienopyradine prior to stenting. The original trial randomsied groups were stent + abciximab versus stent.
T. Rakowski, J. Zalewski, J. Legutko, S. Bartus, L. Rzeszutko, A. Dziewierz, D. Sorysz, L. Bryniarski, K. Zmudka, G. L. Kaluza, J. S. Dubiel, and D. Dudek. Early abciximab administration before primary percutaneous coronary intervention improves infarct-related artery patency and left ventricular function in high-risk patients with anterior wall myocardial infarction: A randomized study. Am.Heart J. 153 (3):360-365, 2007.	Early vs later abciximab trial but wrong sample size: N<60 (N=59) already got much larger abciximab studies.
T. Rakowski, Z. Siudak, A. Dziewierz, R. Birkemeyer, J. Legutko, W. Mielecki, R. Depukat, M. Janzon, J. Stefaniak, K. Zmudka, J. S. Dubiel, L. Partyka, and D. Dudek. Early abciximab administration before transfer for primary percutaneous coronary interventions for ST-elevation myocardial infarction reduces 1-year mortality in patients with high-risk profile. Results from EUROTRANSFER Registry. Am.Heart J. 158 (4):569-575, 2009.	EUROTRANSFER study – not an RCT.

Reference	Reason for exclusion
M. T. Roe. Facilitated percutaneous coronary intervention for acute ST-segment elevation myocardial infarction: Results from the prematurely terminated ADdressing the Value of facilitated ANgioplasty after Combination therapy or Eptifibatide monotherapy in acute Myocardial Infarction (ADVANCE MI) trial. Am.Heart J. 150 (1):116-122, 2005.	ADVANCE-MI trial – wrong comparison: although this is fPPCI versus PPCI (tenecteplase + eptifibatide versus placebo + eptifibatide), half the patients in each group were given UFH and the other half no UFH. Additionally 0% stents used (not mentioned their use in the protocol or results).
A. M. Ross, K. S. Coyne, J. S. Reiner, S. W. Greenhouse, C. Fink, A. Frey, E. Moreyra, M. Traboulsi, et al. A randomized trial comparing primary angioplasty with a strategy of short-acting thrombolysis and immediate planned rescue angioplasty in acute myocardial infarction: the PACT trial. PACT investigators. Plasminogen-activator Angioplasty Compatibility Trial. J.Am.Coll.Cardiol. 34 (7):1954-1962, 1999.	Wrong percentage stents: <50% - only 26% received stents
M. S. Sabatine, C. P. Cannon, C. M. Gibson, J. L. Lopez-Sendon, G. Montalescot, P. Theroux, B. S. Lewis, S. A. Murphy, C. H. McCabe, and E. Braunwald. Effect of clopidogrel pretreatment before percutaneous coronary intervention in patients with ST-elevation myocardial infarction treated with fibrinolytics: The PCI-CLARITY study. JAMA 294 (10):1224-1232, 2005.	PCI-CLARITY study – loss of randomisation: subanalysis of the CLARITY study. Only looking at the results of the subgroup of people who had PCI in each of the original randomsied groups (clopidogrel versus placebo).
P. L. Sanchez, F. Gimeno, P. Ancillo, J. J. Sanz, J. H. Alonso-Briales, F. Bosa, I. Santos, J. Sanchis, A. Bethencourt, J. Lopez-Messa et al. Role of the paclitaxel-eluting stent and tirofiban in patients with ST-elevation myocardial infarction undergoing postfibrinolysis angioplasty: the GRACIA-3 randomized clinical trial. Circ Cardiovasc.Interv 3 (4):297-307, 2010.	GRACIA-3 trial: percentage of patients who had PCI <85% (83% overall, range was 77%-90% in each of the 4 arms).
J Saw, A. M Lincoff, W Desmet, A Betriu, W Rutsch, R G. Wilcox, N S. Kleiman, K Wolski, E J. Topol, and REPLACE-2 Investigators. Lack of clopidogrel pretreatment effect on the relative efficacy of bivalirudin with provisional glycoprotein IIb/IIIa blockade compared to heparin with routine glycoprotein IIb/IIIa blockade: a REPLACE-2 substudy. J.Am.Coll.Cardiol. 44 (6):1194-1199, 2004.	REPLACE-2 substudy – wrong population: not STEMI
U. Schaefer, T. Kurz, H. Bonnemeier, A. Dendorfer, F. Hartmann, H. Schunkert, and G. Richardt. Intracoronary enalaprilat during angioplasty for acute myocardial infarction: Alleviation of postischaemic neurohumoral and inflammatory stress? J.Intern.Med. 261 (2):188-200, 2007.	Wrong treatment: treatment DURING angioplasty (not initiated before PCI thus not true fPPCI).
A. Sethi, A. Bahekar, H. Doshi, R. Bhuriya, U. Bedi, S. Singh, and S. Khosla. Tirofiban Use With Clopidogrel and Aspirin Decreases Adverse Cardiovascular Events After Percutaneous Coronary Intervention for ST-Elevation Myocardial Infarction: A Meta-analysis of Randomized Trials. Can.J.Cardiol. 27 (5):548-554, 2011.	New 2011 SR/MA (serch until 2010 so some missing studies) – used for references /conclusions
Rahul A. Shimpi. Low-molecular-weight heparins and glycoprotein IIb/IIIa inhibitors with percutaneous coronary intervention in acute coronary syndromes. J.Invasive Cardiol. 15 (8):460-465, 2003.	Literature review

Reference	Reason for exclusion
J. M. Siller-Matula, K. Huber, G. Christ, K. Schror, J. Kubica, H. Herkner, and B. Jilma. Impact of clopidogrel loading dose on clinical outcome in patients undergoing percutaneous coronary intervention: A systematic review and meta-analysis. Heart 97 (2):98-105, 2011.	Wrong population: not just STEMI
J. Silvain, O. Barthelemy, F. Beygui, J.-P. Collet, and G. Montalescot. Enoxaparin versus unfractionated heparin in percutaneous coronary intervention: A meta-analysis. Circulation 124 (21 SUPPL. 1), 2011.	Abstract
R. W. Smalling, G. M. Giesler, V. R. Julapalli, A. E. Denktas, S. M. Sdringola, M. T. Vooletich, J. J. McCarthy, R. N. Bradley, D. E. Persse, B. K. Richter, M. Yagi, K. Fujise, and H. V. Anderson. Pre-hospital reduced-dose fibrinolysis coupled with urgent percutaneous coronary intervention reduces time to reperfusion and improves angiographic perfusion score compared with prehospital fibrinolysis alone or primary percutaneous coronary intervention: results of the PATCAR Pilot Trial. J.Am.Coll.Cardiol. 50 (16):1612-1614, 2007.	PACTAR pilot trial - short report (not enough detail); feasibility study not powered; results pooled for the two PPCI arms.
J. J. J. Smit, J. W. Van Werkum, Berg J. Ten, R. Slingerland, J. P. Ottervanger, T. Heestermans, T. Dill, C. Hamm, and A. W. J. Van 't Hof. Prehospital triple antiplatelet therapy in patients with acute ST elevation myocardial infarction leads to better platelet aggregation inhibition and clinical outcome than dual antiplatelet therapy. Heart 96 (22):1815-1820, 2010.	ON-TIME 2 substudy – wrong outcomes: effect on platelet aggregation.
J. J. J. Smit, N. M. S. K. Ernst, R. J. Slingerland, J. J. E. Kolkman, H. Suryapranata, J. C. A. Hoorntje, J. H. Dambrink, J. P. Ottervanger, A. T. M. Gosselink, M. J. De Boer, and A. W. J. van't Hof. Platelet microaggregation inhibition in patients with acute myocardial infarction pretreated with tirofiban and relationship with angiographic and clinical outcome. Am.Heart J. 151 (5):1109-1114, 2006.	Wrong outcomes: platelet aggregation
D. Y. So, A. C. Ha, R. F. Davies, M. Froeschl, G. A. Wells, and M. R. Le May. ST segment resolution in patients with tenecteplase-facilitated percutaneous coronary intervention versus tenecteplase alone: Insights from the Combined Angioplasty and Pharmacological Intervention versus Thrombolysis ALone in Acute Myocardial Infarction (CAPITAL AMI) trial. Can.J.Cardiol. 26 (1):e7-12, 2010.	CAPITAL-AMI substudy: wrong outcomes – ST segment resolution in each of the randomised groups
S. R. Steinhubl, S. G. Ellis, K. Wolski, A. M. Lincoff, and E. J. Topol. Ticlopidine pretreatment before coronary stenting is associated with sustained decrease in adverse cardiac events: Data from the evaluation of platelet IIb/IIIa inhibitor for stenting (EPISTENT) trial. Circulation 103 (10):1403-1409, 2001.	EPISTENT trial – wrong population: not STEMI (STEMI excluded)
G. W. Stone, C. L. Grimes, K. F. Browne, J. Marco, D. Rothbaum, J. O'Keefe, G. O. Hartzler, P. Overlie, B. et al. Predictors of in-hospital and 6-month outcome after acute myocardial infarction in the reperfusion era: The primary angioplasty in myocardial infarction (PAMI) trial. J.Am.Coll.Cardiol. 25 (2):370-377, 1995.	PAMI trial subanalysis – wrong outcomes: predictors of outcomes (not RCT results)
G. W. Stone. Impact of new pharmacologic agents in the treatment of acute thrombotic syndromes. Am.J.Cardiol. 83 (9 A):16E-20E, 1999.	Literature review
G. W. Stone, C. L. Grines, D. A. Cox, E. Garcia, J. E. Tcheng, J. J. Griffin, G. Guagliumi, T. Stuckey, M. Turco, J. D. Carroll, B. D. Rutherford, and A. J. Lansky. Comparison of angioplasty with stenting, with or without abciximab, in acute myocardial infarction. N Engl J Med 346 (13):957-966, 2002.	CADILLAC trial - wrong comparison - not representative of current clinical practice / not fPPCI: PPCI with stenting vs. PPCI with no stenting vs. thrombolysis with no stenting
L Svensson, M Aasa, M Dellborg, C. M Gibson, A Kirtane, J Herlitz, A Ohlsson, T Karlsson, and L Grip. Comparison of very early treatment with either fibrinolysis or percutaneous coronary intervention facilitated with abciximab with respect to ST recovery and infarct-related artery epicardial flow in	SWEDES trial – wrong comparison: no PCI in 1 arm (fPPCI versus fibrinolysis)

Reference	Reason for exclusion
patients with acute ST-segment elevation myocardial infarction: the Swedish Early Decision (SWEDES) reperfusion trial. Am.Heart J. 151 (4):798-7, 2006.	
H. Thiele, M. Scholz, L. Engelmann, W. H. Storch, A. Hartmann, G. Dimmel, D. Pfeiffer, G. Schuler, and Leipzig Prehospital Fibrinolysis Group. ST-segment recovery and prognosis in patients with ST-elevation myocardial infarction reperfused by prehospital combination fibrinolysis, prehospital initiated facilitated percutaneous coronary intervention, or primary percutaneous coronary intervention. Am.J.Cardiol. 98 (9):1132-1139, 2006.	PPCI group not randomised
H. Thiele, L. Engelmann, K. Elsner, M. J. Kappl, W. H. Storch, K. Rahimi, A. Hartmann, D. Pfeiffer, G. D. Kneissl, D. Schneider, T. Moller, H. J. Heberling, I. Weise, G. Schuler, and Leipzig Prehospital Fibrinolysis Group. Comparison of pre-hospital combination-fibrinolysis plus conventional care with pre-hospital combination-fibrinolysis plus facilitated percutaneous coronary intervention in acute myocardial infarction. Eur.Heart J. 26 (19):1956-1963, 2005.	Wrong comparison: fPPCI vs thrombolysis
Tilsted-Hansen, L. Thuesen, K. Rasmussen, H. R. Andersen, T. Vesterlund, A. B. Villadsen, A. P. Schroeder, S. E. Husted, and T. T. Nielsen. Percutaneous transluminal coronary angioplasty versus thrombolysis in acute myocardial infarction. Scand.Cardiovasc.J. 34 (4):365-370, 2000.	Wrong intervention: thrombolysis not fPPCI
E. J. Topol, R. M. Califf, M. Vandormael, C. L. Grines, B. S. George, M. L. Sanz, T. Wall, M. O'Brien, M. Schwaiger, et al. A randomized trial of late reperfusion therapy for acute myocardial infarction. Circulation 85 (6):2090-2099, 1992.	Patients randomised twice: second randomisation meant that 50% of patients did not receive angioplasty (angioplasty versus no angioplasty).
M. Valgimigli, G. Percoco, P. Malagutti, G. Campo, F. Ferrari, D. Barbieri, G. Cicchitelli, E. P. McFadden, F. Merlini, et al. Tirofiban and sirolimus-eluting stent vs abciximab and bare-metal stent for acute myocardial infarction: A randomized trial. JAMA 293 (17):2109-2117, 2005.	STRATEGY trial - wrong comparison: both arms fPPCI using different drugs and different stents (abciximab + BMS versus tirofiban + DES).
M. Valgimigli, G. Campo, G. Percoco, L. Bolognese, C. Vassanelli, S. Colangelo, Cesare N. De, A. E. Rodriguez, M. Ferrario, et al. Comparison of angioplasty with infusion of tirofiban or abciximab and with implantation of sirolimus-eluting or uncoated stents for acute myocardial infarction: The Multistrategy randomized trial. JAMA 299 (15):1788-1799, 2008.	MULTISTRATEGY trial - wrong comparison: both arms fPPCI using different drugs and different stents (abciximab versus tirofiban) then PCI with different stents (DES or BMS).
M. Valgimigli, L. Bolognese, M. Anselmi, G. Campo, A. E. Rodriguez, Cesare N. De, D. J. Cohen, I. Sheiban, S. Colangelo, et al. Two-by-two factorial comparison of high-bolus-dose tirofiban followed by standard infusion versus abciximab and sirolimus-eluting versus bare-metal stent implantation in patients with acute myocardial infarction. Design and rationale for the MULTI-STRATEGY trial. Am.Heart J. 154 (1):39-45, 2007.	MULTISTRATEGY trial – wrong comparison: tirofiban + PCI vs abciximab + PCI (both fPPCI arms with different drugs not PPCI)
F. Vermeer, A. J. Oude Ophuis, E. J. vd Berg, L. G. Brunninkhuis, C. J. Werter, A. G. Boehmer, A. H. Lousberg, W. R. Dassen, and F. W. Bar. Prospective randomised comparison between thrombolysis, rescue PTCA, and primary PTCA in patients with extensive myocardial infarction admitted to a hospital without PTCA facilities: a safety and feasibility study. Heart 82 (4):426-431, 1999.	Wrong fPPCI intervention: fibrinolysis + rescue PCI. Also PCI performed in <85% patients (53% and 85% in each arm; mean 74%). Percentage stents <50% (4% and 17% in each arm
C. M. Westerhout, E. Bonnefoy, R. C. Welsh, P. G. Steg, F. Boutitie, and P. W.	IPD analysis of WEST and

Reference	Reason for exclusion
Armstrong. The influence of time from symptom onset and reperfusion strategy on 1-year survival in ST-elevation myocardial infarction: A pooled analysis of an early fibrinolytic strategy versus primary percutaneous coronary intervention from CAPTIM and WEST. Am.Heart J. 161 (2):283-290, 2011.	CAPTIM trials – wrong intervention: thrombolysis not fPPCI
P. Widimsky, L. Groch, M. Zelizko, M. Aschermann, F. Bednar, and H. Suryapranata. Multicentre randomized trial comparing transport to primary angioplasty vs immediate thrombolysis vs combined strategy for patients with acute myocardial infarction presenting to a community hospital without a catheterization laboratory. The PRAGUE study. Eur.Heart J. 21 (10):823-831, 2000.	PRAGUE study – wrong intevention: streptokinase (not used in UK)
P. Widimsky, T. Budesinsky, D. Vorac, L. Groch, M. Zelizko, M. Aschermann, M. Branny, J. St'asek, P. Formanek, and 'PRAGUE' Study Group. Long distance transport for primary angioplasty vs immediate thrombolysis in acute myocardial infarction. Final results of the randomized national multicentre trial--PRAGUE-2. Eur.Heart J. 24 (1):94-104, 2003.	Wrong comparison: thrombolysis not fPPCI
A. Wong, K.-H. Mak, C. Chan, T.-H. Koh, K.-W. Lau, T.-T. Lim, S.-T. Lim, P. Wong, L.-L. Sim, Y.-T. Lim, H.-C. Tan, and Y.-L. Lim. Combined fibrinolysis using reduced-dose alteplase plus abciximab with immediate rescue angioplasty versus primary angioplasty with adjunct use of abciximab for the treatment of acute myocardial infarction: Asia-Pacific Acute Myocardial Infarction Trial (APAMIT) pilot study. Catheter.Cardiovasc.Interv. 62 (4):445-452, 2004.	APAMIT pilot study - wrong intervention: thrombolysis + rescue PCI (not true fPPCI)
B. S. Young, J.-Y. Hahn, H.-C. Gwon, H. K. Jun, Y. L. Sang, H. C. Yeon, S.-H. Choi, J.-H. Choi, and H. L. Sang. Upstream high-dose tirofiban does not reduce myocardial infarct size in patients undergoing primary percutaneous coronary intervention: A magnetic resonance imaging pilot study. Clinical Cardiology 32 (6):321-326, 2009.	Wrong outcomes (MI infarct size and LVEF)
J Zalewski, K Bogaerts, W Desmet, P Sinnaeve, P Berger, C Grines, T Danays, P Armstrong, and F Van de Werf. Intraluminal thrombus in facilitated versus primary percutaneous coronary intervention: an angiographic substudy of the ASSENT-4 PCI (Assessment of the Safety and Efficacy of a New Treatment Strategy with Percutaneous Coronary Intervention) trial. J.Am.Coll.Cardiol. 57 (19):1867-1873, 2011.	ASSENT-4 SUBSTUDY- wrong outcomes: occurrence of intraluminal thrombus
U. Zeymer. The role of eptifibatide in patients undergoing percutaneous coronary intervention. Expert Opin Pharmacother 8 (8):1147-1154, 2007.	Literature review

J.3 Radial versus femoral arterial access for PPCI

Reference	Reason for exclusion
Agostoni P, Biondi-Zoccai GG, de Benedictis ML, Rigattieri S, Turri M, Anselmi M, Vassanelli C, Zardini P, Louvard Y, Hamon M. Radial versus femoral approach for percutaneous coronary diagnostic and interventional procedures; Systematic overview and meta-analysis of randomized trials. J Am Coll Cardiol. 2004; 44(2):349-56.	Not RCT; meta-analysis (used for cross checking)
Bagur R, Bertrand OF, Rodés-Cabau J, Rinfret S, Larose E, Tizón-Marcos H, Gleeton O, Nguyen CM, Roy L, Costerousse O, De Larochellière R. Comparison of outcomes in patients ≥70 years versus <70 years after transradial coronary stenting with maximal antiplatelet therapy for acute coronary syndrome. Am J Cardiol. 2009; 104(5):624-9.	All patients treated using radial access approach; patients presenting with STEMI within 72 hrs were excluded
Bell BP, Pyne CT, and Rao SV. Transradial percutaneous coronary intervention in patients with acute coronary syndromes. Acute Coronary Syndromes.2011; 10: 64-72.	Not RCT; narrative review
Bertrand OF, Belisle P, Joyal D, Costerousse O, Rao S, Jolly S et al. Comparison of transradial and femoral approaches for percutaneous coronary	Not RCT; meta-analysis (used for cross checking)

Reference	Reason for exclusion
interventions: A hierarchical bayesian meta-analysis. Canadian Journal of Cardiology. 2011; 27(5 SUPPL. 1):S114.	
Brueck M, Bandorski D, Kramer W, Wieczorek M, Höltgen R, Tillmanns H. A randomized comparison of transradial versus transfemoral approach for coronary angiography and angioplasty. JACC Cardiovasc Interv. 2009; 2(11):1047-54.	Only 8% of the study population had acute STEMI, remaining recent MI and previous PCI
Cantor WJ, Puley G, Natarajan MK, Dzavik V, Madan M, Fry A et al. Radial versus femoral access for emergent percutaneous coronary intervention with adjunct glycoprotein IIb/IIIa inhibition in acute myocardial infarction--the RADIAL-AMI pilot randomized trial. American Heart Journal. 2005; 150(3):543-549.	RCT intervention not restricted to PPCI
Cantor WJ, Mahaffey KW, Huang Z, Das P, Gulba DC, Glezer S, Gallo R, Ducas J, Cohen M, Antman EM, Langer A, Kleiman NS, White HD, Chisholm RJ, Harrington RA, Ferguson JJ, Califf RM, Goodman SG. Bleeding complications in patients with acute coronary syndrome undergoing early invasive management can be reduced with radial access, smaller sheath sizes, and timely sheath removal. Catheter Cardiovasc Interv. 2007; 69(1):73-83.	Patients not randomised according to femoral versus radial access Wrong population (NSTEMI)
Chung WJ, Fang HY, Tsai TH, Yang CH, Chen CJ, Chen SM, Cheng CI, Fang CY, Hsieh YK, Hang CL, Yip HK, Wu CJ. Transradial approach percutaneous coronary interventions in an out-patient clinic. Int Heart J. 2010; 51(6):371-6.	Not RCT; all patients managed using radial approach
Cohen A, Bertrand OF, Meerkin D. Transradial angioplasty for ST-elevation myocardial infarction. Interventional Cardiology 2011; 3(3): 337-46.	Not RCT, narrative review
Dahm JB, Wolpers HG, Becker J, Hansen C, Felix SB. Transradial access in percutaneous coronary interventions: technique and procedure. Herz. 2010; 35(7):482-487.	Not RCT; narrative review
Dahm JB, van Buuren F. Transradial percutaneous coronary interventions: indications, success rates & clinical outcome. Indian Heart J. 2010; 62(3):218-20.	Not RCT; narrative review
Eichhöfer J, Horlick E, Ivanov J, Seidelin PH, Ross JR, Ing D, Daly P, Mackie K, Ridley B, Schwartz L, Barolet A, Dzavík V. Decreased complication rates using the transradial compared to the transfemoral approach in percutaneous coronary intervention in the era of routine stenting and glycoprotein platelet IIb/IIIa inhibitor use: a large single-center experience. Am Heart J. 2008; 156(5):864-70.	Not RCT; registry
Franchi E, Marino P, Biondi-Zoccai GG, Luca G, Vassanelli C, and Agostoni P. Transradial versus transfemoral approach for percutaneous coronary procedures. Current Cardiology Reports. 2009; 11:391-7.	Not RCT; narrative review
George BS, Candela RJ, Topol EJ, Stack RS, Kereiakes DJ, Abbottsmith CW, Masek R, Pickel A, Dillon J, Harrelson L, et al. Brachial approach to emergency cardiac catheterization during thrombolytic therapy for acute myocardial infarction. TAMI Study Group. Cathet Cardiovasc Diagn. 1990; 20(4):221-6.	Patients randomised to brachial versus femoral approach
Hamon M, Rasmussen LH, Manoukian SV, Cequier A, Lincoff MA, Rupprecht HJ, Gersh BJ, Mann T, Bertrand ME, Mehran R, Stone GW. Choice of arterial access site and outcomes in patients with acute coronary syndromes managed with an early invasive strategy: the ACUITY trial. EuroIntervention. 2009; 5(1):115-20.	Patients not randomised to radial versus femoral radial
Jang J-S, Chung S-R, Jin H-Y, Seo J-S, Yang T-H, Kim D-K et al. Radial versus femoral approach for primary percutaneous coronary intervention in patients with acute myocardial infarction: An update meta-analysis. Journal of the American College of Cardiology. 2011; 58(20 SUPPL. 1):B143.	Not RCT; meta-analysis (used for cross checking)
Jimenez Diaz VA, Colin E, Ortiz A, De MA, Bastos G, Gomez IT et al. Transradial versus transfemoral approach in elderly patients with ST-segment elevation	Not RCT; cohort study

Reference	Reason for exclusion
acute myocardial infarction treated with primary angioplasty: Feasibility, predictors of success and outcome. Journal of the American College of Cardiology. 2011; 58(20 SUPPL. 1):B142.	
Jolly SS, Amlani S, Hamon M, Yusuf S, Mehta SR. Radial versus femoral access for coronary angiography or intervention and the impact on major bleeding and ischemic events: a systematic review and meta-analysis of randomized trials. Am Heart J. 2009; 157(1):132-40.	Not RCT; meta-analysis (used for cross checking)
Joyal D, Bertrand OF, Rinfret S, Shimony A, Eisenberg MJ. Meta-analysis of ten trials on the effectiveness of the radial versus the femoral approach in primary percutaneous coronary intervention. American Journal of Cardiology. 2012; 109(6):813-818.	Not RCT; meta-analysis (used for cross checking)
Kar S, Drury JK, Hajduczki I, Eigler N, Wakida Y, Litvack F, Buchbinder N, Marcus H, Nordlander R, Corday E. Synchronized coronary venous retroperfusion for support and salvage of ischemic myocardium during elective and failed angioplasty. J Am Coll Cardiol. 1991; 18(1):271-82.	Not RCT; cohort study on wrong population
Kassam S, Cantor WJ, Patel D, Gilchrist IC, Winegard LD, Rea ME, Bowman KA, Chisholm RJ, Strauss BH. Radial versus femoral access for rescue percutaneous coronary intervention with adjuvant glycoprotein IIb/IIIa inhibitor use. Can J Cardiol. 2004; 20(14):1439-42.	Not RCT; retrospective analysis
Kim JY, Yoon J, Jung HS, Ko JY, Yoo BS, Hwang SO, Lee SH, Choe KH. Feasibility of the radial artery as a vascular access route in performing primary percutaneous coronary intervention. Yonsei Med J. 2005; 46(4):503-10.	Not RCT; retrospective analysis
Kowalczuk AM, Chodór P, Streb W, Kurek T, Kalarus Z, Zembala M. The utility of duplex ultrasound scanning in reporting the vascular complications after heart catheterization performed from new arterial approaches - Radial or femoral artery access with StarClose usage - A substudy of the RADIAMI II trial. Postepy w kardiologii interwencyjnej. 2010; 6(3):112-6.	Substudy of RADIAMI II (which was included); no additional outcomes of interest reported
Li X-S, Chen Q-W, Wang Z-G, Ke D-Z, Wu Q. Comparison on transradial versus transfemoral approach for coronary angiography and angioplasty in the elderlys with coronary heart disease. Chinese Journal of Interventional Imaging and Therapy. 2011; 8(4):259-262.	Publication not in English
Louvard Y, Lefèvre T, Allain A, Morice M. Coronary angiography through the radial or the femoral approach: The CARAFE study. Catheter Cardiovasc Interv. 2001; 52(2):181-7.	Excluded patients with acute myocardial infarction
Louvard Y, Krol M, Pezzano M, Sheers L, Piechaud JF, Marien C, Benaim R, Lardoux H, Morice MC. Feasibility of routine transradial coronary angiography: a single operator's experience. J Invasive Cardiol. 1999; 11(9):543-8.	Not RCT
Mamas MA, Ratib K, Routledge H, Fath-Ordoubadi F, Neyses L, Louvard Y et al. Influence of access site selection on PCI-related adverse events in patients with STEMI: meta-analysis of randomised controlled trials. Heart. 2012; 98(4):303-311.	Not RCT; meta-analysis (used for cross checking)
Mann T, Cubeddu G, Bowen J, Schneider JE, Arrowood M, Newman WN, Zellinger MJ, Rose GC. Stenting in acute coronary syndromes: a comparison of radial versus femoral access sites. J Am Coll Cardiol. 1998; 32(3):572-6.	Only 14% of patients had Q wave myocardial infarction (29% non-Q-wave MI; 57% unstable angina); no patient underwent direct angioplasty for myocardial infarction
Pristipino C, Trani C, Nazzaro MS, Berni A, Patti G, Patrizi R, Pironi B, Mazzarotto P, Gioffrè G, Biondi-Zoccai GG, Richichi G; Prospective REgistry of Vascular Access in Interventions in Lazio Region Study Group. Major improvement of percutaneous cardiovascular procedure outcomes with radial	Not RCT; cohort study

Reference	Reason for exclusion
artery catheterisation: results from the PREVAIL study. Heart. 2009; 95(6):476-82.	
Ruzsa Z, Ungi I, Horváth T, Sepp R, Zimmermann Z, Thury A, Jambrik Z, Sasi V, Tóth G, Forster T, Nemes A. Five-year experience with transradial coronary angioplasty in ST-segment-elevation myocardial infarction. Cardiovasc Revasc Med. 2009; 10(2):73-9.	Not RCT; cohort study
Schaufele TG et al. Radial access versus conventional femoral puncture: outcome and resource effectiveness in a daily routine: the raptor trial. Circulation 2009; 120:2152-61. Abstract 41	Insufficient information on population (does not appear to be STEMI or to be managed by PPCI);
Siudak Z, Zawislak B, Dziewierz A, Rakowski T, Jakala J, Bartus S, Noworolnik B, Zasada W, Dubiel JS, Dudek D. Transradial approach in patients with ST-elevation myocardial infarction treated with abciximab results in fewer bleeding complications: data from EUROTRANSFER registry. Coron Artery Dis. 2010; 21(5):292-7.	Not RCT; registry analysis
Slagboom T, Kiemeneij F, Laarman GJ, van der Wieken R. Outpatient coronary angioplasty: feasible and safe. Catheter Cardiovasc Interv. 2005; 64(4):421-7.	Excluded patients with acute myocardial infarction
Tizón-Marcos H, Bertrand OF, Rodés-Cabau J, Larose E, Gaudreault V, Bagur R, Gleeton O, Courtis J, Roy L, Poirier P, Costerousse O, De Larochellière R. Impact of female gender and transradial coronary stenting with maximal antiplatelet therapy on bleeding and ischemic outcomes. Am Heart J. 2009; 157(4):740-5.	All patients treated using transradial approach; patients presenting with STEMI within 72 hrs were excluded
Valsecchi O, Musumeci G, Vassileva A, Tespili M, Guagliumi G, Gavazzi A, Ferrazzi P. Safety, feasibility and efficacy of transradial primary angioplasty in patients with acute myocardial infarction. Ital Heart J. 2003; 4(5):329-34.	Not RCT; cohort study
Vazquez-Rodriguez JM et al. Radial vs femoral arterial access in emergent coronary interventions for acute myocardial infarction with ST segment elevation. J Am Coll Cardiol 2007; 49(Suppl 2):12B	Sufficient information detailed in included studies
Vorobcsuk A, Kónyi A, Aradi D, Horváth IG, Ungi I, Louvard Y, Komócsi A. Transradial versus transfemoral percutaneous coronary intervention in acute myocardial infarction Systematic overview and meta-analysis. Am Heart J. 2009; 158(5):814-21.	Not RCT; meta-analysis (used for cross checking)
Wang YB, Fu XH, Wang XC, Gu XS, Zhao YJ, Hao GZ et al. Randomized comparison of radial versus femoral approach for patients with STEMI undergoing early PCI following intravenous thrombolysis. Journal of Invasive Cardiology. 2012; 24(8):412-416.	Indirect intervention, rescue PPCI
Yan ZX, Zhou YJ, Zhao YX, Liu YY, Shi DM, Guo YH, Cheng WJ. Safety and feasibility of transradial approach for primary percutaneous coronary intervention in elderly patients with acute myocardial infarction. Chin Med J (Engl). 2008; 121(9):782-6.	Not RCT; cohort study
Ziakas A, Klinke P, Mildenberger R, Fretz E, Williams M, Della Siega A, Kinloch D, Hilton D. Comparison of the radial and the femoral approaches in percutaneous coronary intervention for acute myocardial infarction. Am J Cardiol. 2003; 91(5):598-600.	Not RCT; retospective study
Ziakas AG, Koskinas KC, Gavrilidis S, Giannoglou GD, Hadjimiltiades S, Gourassas I, Theofilogiannakos E, Economou F, Styliadis I. Radial versus femoral access for orally anticoagulated patients. Catheter Cardiovasc Interv. 2010; 76(4):493-9.	Only 29% of patients underwent PPCI after angiography; ACS (46%, but not stated if NSTEMI or STEMI), stable angina (23%), congestive heart failure (21%) and other (8%) were indications for

Reference	Reason for exclusion
	angiography

J.4 Thrombus extraction during PPCI

Reference	Reason for exclusion
Abdelhamid MA, Tamara AF, Khalil MA, Farag NM. Presenting thrombus aspiration versus standard percutaneous coronary intervention in patients with acute coronary syndrome having large thrombus burden. American Journal of Cardiology. 2011; 107(8 SUPPL. 1):44A.	Wrong population
Amin AP, Mamtani MR, Kulkarni H. Factors influencing the benefit of adjunctive devices during percutaneous coronary intervention in ST-segment elevation myocardial infarction: meta-analysis and meta-regression. Journal of Interventional Cardiology. 2009; 22(1):49-60.	Not RCT; systematic review
Andersen NH, Karlsen FM, Gerdes JC, Kaltoft A, Sloth E, Thuesen L et al. No beneficial effects of coronary thrombectomy on left ventricular systolic and diastolic function in patients with acute S-T elevation myocardial infarction: a randomized clinical trial. Journal of the American Society of Echocardiography: Official Publication of the American Society of Echocardiography. 2007; 20(6):724-730.	No outcomes of interest
Antoniucci D. JETSTENT trial results: impact on ST-segment elevation myocardial infarction interventions. Journal of Invasive Cardiology. 2010; 22(10 Suppl B):23B-25B.	Abstract
Antoniucci D, Migliorini A, Valenti R, Colombo A, Stabile A, Afredo R et al. Randomised comparison of angiojet rheolytic thrombectomy before direct infarct artery stenting to direct stenting alone in patients with acute myocardial infarction: The Jetstent trial. EuroIntervention. 2010; 6.	Abstract
Antoniucci D, Migliorini A, Valenti R, Colombo A, Stabile A, Afredo R et al. Randomised comparison of angiojet rheolytic thrombectomy before direct infarct artery stenting to direct stenting alone in patients with acute myocardial infarction: The Jetstent trial. EuroIntervention Conference: EuroPCR. 2010; 20100525(20100528).	Abstract
Antoniucci D. Rheolytic thrombectomy in acute myocardial infarction: the Florence experience and objectives of the multicenter randomized JETSTENT trial. Journal of Invasive Cardiology. 2006; 18 Suppl C:32C-34C.	Abstract
Ashraf T, Rasool SI, Saghir T, Rizvi SN, Qamar N, Zaman KS et al. Aspiration of thrombus in st segment elevation myocardial infarction. Journal of the Pakistan Medical Association. Pakistan: Pakistan Medical Association. 2007; 57(7):359-362.	Not RCT
Baim DS, Wahr D, George B, Leon MB, Greenberg J, Cutlip DE et al. Randomized trial of a distal embolic protection device during percutaneous intervention of saphenous vein aorto-coronary bypass grafts. Circulation. 2002; 105(11):1285-1290.	Not question of interest
Bar FW, Tzivoni D, Dirksen MT, Fernandez-Ortiz A, Heyndrickx GR, Brachmann J et al. Results of the first clinical study of adjunctive CAldaret (MCC-135) in patients undergoing primary percutaneous coronary intervention for ST-Elevation Myocardial Infarction: the randomized multicentre CASTEMI study. European Heart Journal. 2006; 27(21):2516-2523.	Wrong comparison
Bavry AA, Kumbhani DJ, Bhatt DL. Role of adjunctive thrombectomy and embolic protection devices in acute myocardial infarction: a comprehensive meta-analysis of randomized trials (Structured abstract). European Heart Journal. 2008; 29(24):2989-3001.	Not RCT; systematic review
Bejarano J. Mechanical protection of cardiac microcirculation during percutaneous coronary intervention of saphenous vein grafts. International	Not question of interest

Reference	Reason for exclusion
Journal of Cardiology. 2005; 99(3):365-372.	
Bertrand OF, Larose E, Costerousse O, Mongrain R, Rodés-Cabau J, DéRy JP et al. Effects of aspiration thrombectomy on necrosis size and ejection fraction after transradial percutaneous coronary intervention in acute ST-elevation myocardial infarction. Catheterization and Cardiovascular Interventions: Official Journal of the Society for Cardiac Angiography and Interventions. 2011; 77(4):475-482.	Not RCT; cohort study
Brodie BR. Adjunctive thrombectomy with primary percutaneous coronary intervention for ST-elevation myocardial infarction: summary of randomized trials. Journal of Invasive Cardiology. 2006; 18 Suppl C:C24-C27.	Not RCT; narrative review
Brodie BR. Aspiration thrombectomy with primary PCI for STEMI: review of the data and current guidelines. Journal of Invasive Cardiology. 2010; 22(10 Suppl B):2B-5B.	Not RCT; narrative review
Burzotta F, Testa L, Giannico F, Biondi-Zoccai GGL, Trani C, Romagnoli E et al. Adjunctive devices in primary or rescue PCI: a meta-analysis of randomized trials. International Journal of Cardiology. 2008; 123(3):313-321.	Not RCT
Burzotta F, De Vita M, Gu YL, Isshiki T, Lefevre T, Kaltoft A et al. Clinical impact of thrombectomy in acute ST-elevation myocardial infarction: an individual patient-data pooled analysis of 11 trials. European Heart Journal. 2009; 30(18):2193-2203.	Not RCT; systematic review
Cassese S, Esposito G, Mauro C, Varbella F, Carraturo A, Montinaro A et al. MGUard versus bAre-metal stents plus manual thRombectomy in ST-elevation myocarDial infarction pAtieNts-(GUARDIAN) trial: study design and rationale. Catheterization and Cardiovascular Interventions. 2012; 79(7):1118-1126.	Not question of interest
Chinnaiyan KM, Grines CL, O'Neill WW, Shah D, Raju A, Decker J et al. Safety of AngioJet thrombectomy in acute ST-segment elevation myocardial infarction: a large, single-center experience. Journal of Invasive Cardiology. 2006; 18 Suppl C:17C-21C.	Participants not randomised to intervention
Ciszewski M, Pregowski J, Teresinska A, Karcz M, Kalinczuk L, Pracon R et al. Aspiration coronary thrombectomy for acute myocardial infarction increases myocardial salvage: single center randomized study. Catheterization & Cardiovascular Interventions. 2011; 78(4):523-531.	No outcomes of interest
Cohen R, Domniez T, Foucher R, Sfaxi A, Elhadad S. Intracoronary thrombectomy with the export aspiration catheter before angioplasty in patients with ST-segment elevation myocardial infarction. Journal of Interventional Cardiology. 2007; 20(2):136-142.	Not RCT, cohort
Cutlip DE, Ricciardi MJ, Ling FS, Carrozza JPJ, Dua V, Garringer J et al. Effect of tirofiban before primary angioplasty on initial coronary flow and early ST-segment resolution in patients with acute myocardial infarction. American Journal of Cardiology. 2003; 92(8):977-980.	Wrong comparison
De Luca G, Verdoia M, Cassetti E. Thrombectomy during primary angioplasty: methods, devices, and clinical trial data. Current Cardiology Reports. 2010; 12(5):422-428.	Not RCT; review
De Luca G, Dudek D, Sardella G, Marino P, Chevalier B, Zijlstra F. Adjunctive manual thrombectomy improves myocardial perfusion and mortality in patients undergoing primary percutaneous coronary intervention for ST-elevation myocardial infarction: a meta-analysis of randomized trials (Structured abstract). European Heart Journal. 2008; 29(24):3002-3010.	Not RCT; systematic review
De Luca G, Suryapranata H, Stone GW, Antoniucci D, Neumann FJ, Chiariello M. Adjunctive mechanical devices to prevent distal embolization in patients undergoing mechanical revascularization for acute myocardial infarction: a meta-analysis of randomized trials (Structured abstract). American Heart Journal. 2007; 153(3):343-353.	Not RCT; systematic review

Reference	Reason for exclusion
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Guetta V, Mosseri M, Shechter M, Matetzky S, Assali A, Almagor Y et al. Safety and efficacy of the FilterWire EZ in acute ST-segment elevation myocardial infarction. American Journal of Cardiology. 2007; 99(7):911-915.	Not question of interest
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Henriques JPS, Zijlstra F, Van 't Hof AWJ, De Boer MJ, Dambrink J-HE, Gosselink ATM et al. Primary percutaneous coronary intervention versus thrombolytic treatment: long term follow up according to infarct location. Heart. 2006; 92(1):75-79.	Wrong comparison
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Kampinga MA, Vlaar PJ, Fokkema ML, Gu YL, Zijlstra F. Thrombus aspiration during percutaneous coronary intervention in acute non-ST-elevation myocardial infarction study (TAPAS II) - study design. Netherlands Heart Journal. 2009; 17(11):409-413.	Wrong comparison
Kelbaek H, Terkelsen CJ, Helqvist S, Lassen JF, Clemmensen P, Kløvgaard L et al. Randomized comparison of distal protection versus conventional treatment in primary percutaneous coronary intervention: the drug elution and distal protection in ST-elevation myocardial infarction (DEDICATION) trial. Journal of the American College of Cardiology. 2008; 51(9):899-905.	Not question of interest
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Ko B, Malaiapan Y, Hutchison A, Lehman S, Potvin J, Meredith I. Novel thrombus burden guided thrombus aspiration catheter use during primary percutaneous coronary intervention in the management of ST elevation myocardial infarction. Heart Lung and Circulation. 2010; 19:S32.	Abstract
Krstic N, Perisic Z, Pavlovic M, Koracevic G, Salinger-Martinovic S, Apostolovic S et al. Thrombus aspiration during primary percutaneous coronary intervention. Circulation. 2010; 122 (2):e250.	Abstract
Kukreja N, Costopoulos C, Gorog D, Di Mario C. Use of thrombectomy devices in primary percutaneous coronary intervention. Journal of the American College of Cardiology. 2011; 1):B98.	Abstract
Lanjewar C, Jolly S, Mehta SR. Effects of aspiration thrombectomy on mortality in patients with acute myocardial infarction undergoing primary percutaneous coronary intervention: a meta-analysis of the randomized trials (Structured abstract). Indian Heart Journal. 2009; 61(4):335-340.	Not RCT; systematic rveiew
Laarman GJ, Suttorp MJ, Dirksen MT, van Heerebeek L, Kiemeneij F, Slagboom	Wrong comparison

Reference	Reason for exclusion
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Lee MS, Singh V, Wilentz JR, Makkar RR. AngioJet thrombectomy. Journal of Invasive Cardiology. 2004; 16(10):587-591.	Not RCT; narrative review
Li N, Yan HB, Zhu XL, Gao H, Ai H, Wang J et al. [Diver CE versus Guardwire Plus for thrombectomy during primary angioplasty for inferior myocardial infarction]. Zhonghua Xin Xue Guan Bing Za Zhi [Chinese Journal of Cardiovascular Diseases]. 2007; 35(5):461-465.	Study not in English
Liem A, Zijlstra F, Ottervanger JP, Hoorntje JC, Suryapranata H, De Boer MJ et al. High dose heparin as pretreatment for primary angioplasty in acute myocardial infarction: the Heparin in Early Patency (HEAP) randomized trial. Journal of the American College of Cardiology. 2000; 35(3):600-604.	Wrong comparison
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Lipiecki J, Monzy S, Durel N, Cachin F, Chabrot P, Muliez A et al. Effect of thrombus aspiration on infarct size and left ventricular function in high-risk patients with acute myocardial infarction treated by percutaneous coronary intervention. Results of a prospective controlled pilot study. American Heart Journal. 2009; 157(3):583.	No outcomes of interest
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Margheri M, Vittori G, Chechi T, Falchetti E, Cosgrave J, Spaziani G et al. Thrombus aspiration with export catheter in ST elevation myocardial infarction. Journal of Interventional Cardiology. 2007; 20(1):38-43.	Not RCT; cohort study
McCormick LM, Brown AJ, Gajendragadkar PR, Basavarajaiah S, West NE. Routine thrombus aspiration and glycoprotein inhibitor use during primary percutaneous coronary intervention for ST elevation myocardial infarction: Do all patients benefit? Journal of the American College of Cardiology. 2011; 1):B103.	Not RCT; cohort study
Mongeon FP, Belisle P, Joseph L, Eisenberg MJ, Rinfret S. Adjunctive thrombectomy for acute myocardial infarction: A bayesian meta-analysis. Circulation: Cardiovascular Interventions. 2010; 3(1):6-16.	Not RCT; systematic review
Naidu SS, Turco MA, Mauri L, Coolong A, Popma JJ, Kereiakes DJ. Contemporary incidence and predictors of major adverse cardiac events after saphenous vein graft intervention with embolic protection (an AMEthyst trial substudy). American Journal of Cardiology. 2010; 105(8):1060-1064.	Not question of interest
Nakagawa Y, Matsuo S, Kimura T, Yokoi H, Tamura T, Hamasaki N et al. Thrombectomy with AngioJet catheter in native coronary arteries for patients with acute or recent myocardial infarction. American Journal of Cardiology. 1999; 83(7):994-999.	Not RCT
Ochala A, Smolka G, Wojakowski W, Gabrylewicz B, Garbocz P, Tendera M. Prospective randomised study to evaluate effectiveness of distal embolic protection compared to abciximab administration in reduction of microembolic complications of primary coronary angioplasty. Kardiologia Polska. 2007; 65(6):672-680.	Not question of interest

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Petronio AS, Musumeci G, Limbruno U, De Carlo M, Baglini R, Paterni G et al. Abciximab improves 6-month clinical outcome after rescue coronary angioplasty. American Heart Journal. 2002; 143(2):334-341.	Wrong comparison
Rajagopal R, Musto C, La Manna A, Tanigawa J, Goktekin O, Di Mario C. Thrombectomy and distal protection devices. Minerva Cardioangiologica. 2005; 53(5):415-430.	Not RCT
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Segev A, Elian D, Marai I, Matetzky S, Agranat O, Har-Zahav Y et al. Thrombus aspiration during primary percutaneous coronary intervention in acute ST-elevation myocardial infarction. Cardiovascular Revascularization Medicine. 2008; 9(3):140-143.	Not RCT; cohort study
Sharma SK, Tamburrino F, Mares AM, Kini AS. Improved outcome with AngioJet thrombectomy during primary stenting in acute myocardial infarction patients with high-grade thrombus. Journal of Invasive Cardiology. 2006; 18 Suppl C:C8-11.	Abstract
Sherev DA, Shavelle DM, Abdelkarim M, Shook T, Mayeda GS, Burstein S et al. AngioJet Rheolytic thrombectomy during rescue PCI for failed thrombolysis: a single-center experience. Journal of Invasive Cardiology. 2006; 18 Suppl C:12C-16C.	Wrong population
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Spaulding C, Henry P, Teiger E, Beatt K, Bramucci E, Carrie D et al. Sirolimus-eluting versus uncoated stents in acute myocardial infarction. New England Journal of Medicine. 2006; 355(11):1093-1104.	Wrong comparison
Stone GW, Rogers C, Ramee S, White C, Kuntz RE, Popma JJ et al. Distal filter protection during saphenous vein graft stenting: technical and clinical correlates of efficacy. Journal of the American College of Cardiology. 2002; 40(10):1882-1888.	Wrong intervention
Stone GW, Webb J, Cox DA, Brodie BR, Qureshi M, Kalynych A et al. Distal microcirculatory protection during percutaneous coronary intervention in acute ST-segment elevation myocardial infarction: a randomized controlled trial. JAMA : the Journal of the American Medical Association. 2005; 293(9):1063-1072.	Wrong intervention
Stone GW, Cox DA, Babb J, Nukta D, Bilodeau L, Cannon L et al. Prospective, randomized evaluation of thrombectomy prior to percutaneous intervention in diseased saphenous vein grafts and thrombus-containing coronary arteries. Journal of the American College of Cardiology. 2003; 42(11):2007-2013.	Wrong intervention
Stone GW, Rogers C, Hermiller J, Feldman R, Hall P, Haber R et al. Randomized comparison of distal protection with a filter-based catheter and a balloon occlusion and aspiration system during percutaneous intervention of diseased saphenous vein aorto-coronary bypass grafts. Circulation. 2003; 108(5):548-553.	Not question of interest
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Suryapranata H, De Luca G, Van 't Hof AWJ, Ottervanger JP, Hoorntje JCA, Dambrink J-HE et al. Is routine stenting for acute myocardial infarction superior to balloon angioplasty? A randomised comparison in a large cohort of unselected patients. Heart. 2005; 91(5):641-645.	Wrong comparison
Tamhane UU, Chetcuti S, Hameed I, Grossman PM, Moscucci M, Gurm HS. Safety and efficacy of thrombectomy in patients undergoing primary percutaneous coronary intervention for acute ST elevation MI: a meta-analysis of randomized controlled trials (Structured abstract). BMC Cardiovascular Disorders. 2010; 10:10.	Not RCT; systematic review
Tanabe K, Kozuma K, Ikari Y, Fujii K, Sakurada M, Hashimoto H et al. Five-year clinical follow-up of the vampire study in ST elevation acute myocardial infarction (STEMI) patients with thrombus aspiration prior to coronary intervention. Circulation Conference: American Heart Association's Scientific Sessions. 2011; 124(21 SUPPL. 1).	Abstract
Tarsia G, De Michele M, Polosa D, Biondi-Zoccai G, Costantino F, Del Prete G et al. Manual versus nonmanual thrombectomy in primary and rescue percutaneous coronary angioplasty (Provisional abstract). Heart and Vessels. 2010; 25(4):275-281.	Not applicable to question
Uribe J, Ici DO, Hovasse T, Unterseeh T, Benamer H, Chevalier B et al. A randomized comparison of systematic vs angiographic-guided thrombus aspiration (Export catheter) prior to coronary stenting in patients with < 12 h ST-elevation MI. European Heart Journal. 2010; 31:877.	Abstract
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Vink MA, Dirksen MT, Tijssen JGP, Suttorp MJ, Patterson MS, van Geloven N et al. Lack of long-term clinical benefit of thrombus aspiration during primary percutaneous coronary intervention with paclitaxel-eluting stents or bare-metal stents: post-hoc analysis of the PASSION-trial. Catheterization and Cardiovascular Interventions. 2012; 79(6):870-877.	Post-hoc analysis
Wei L, Li-Rong W, Ming-Yu L, Wei-Min W, Jian L, Yu-Liang M. Clinical study of utilisation of thrombus aspiration catheters in patients with recovering from acute myocardial infarction underwent elective percutaneous. Heart. 2011; 97:A157-A158.	Abstract
Whisenant BK, Baim DS, Kuntz RE, Garcia LA, Ramee SR, Carrozza JP. Rheolytic thrombectomy with the Possis AngioJet: technical considerations and initial clinical experience. Journal of Invasive Cardiology. 1999; 11(7):421-426.	Not RCT; narrative review
Yan HB, Wang J, Li N, Zhu XL, Gao H, Ai H et al. Diver CE versus Guardwire Plus for thrombectomy in patients with inferior myocardial infarction: a trial of aspiration of thrombus during primary angioplasty for inferior myocardial infarction. Chinese Medical Journal. 2007; 120(7):557-561.	Wrong comparison
Zhang J, Zhong M-H, Zhang Y-Q, Mi J, Qi X-Q. [Thrombus aspiration during percutaneous coronary intervention in patients with acute myocardial infarction]. Chinese Journal of Interventional Imaging and Therapy. 2006; 3(6):406-409.	Study not in English
Zorman S, Zorman D, Noc M. Effects of abciximab pretreatment in patients with acute myocardial infarction undergoing primary angioplasty. American Journal of Cardiology. 2002; 90(5):533-536.	Not question of interest

J.5 Culprit versus complete revascularisation **Updated, see 2020 evidence review**

Reference	Reason for exclusion
Alhulaimi N, Midodzi W, Welsh RC. Culprit and non-culprit PCI compared to culprit only PCI in multi-vessel coronary artery disease patients with acute ST elevation myocardial infarction treated by primary percutaneous coronary intervention: A systematic review. Journal of the American College of Cardiology. 2010; 55 (10 SUPPL 1):A97.	Systematic review ordered for cross-checking purposes
Aggarwal V, Rajpathak S, Singh M, Romick B, Srinivas VS. Clinical outcomes based on completeness of revascularisation in patients undergoing percutaneous coronary intervention: a meta-analysis of multivessel coronary artery disease studies. EuroIntervention. 2012; 7(9):1095-1102.	Systematic review ordered for cross-checking purposes
Akhtar MM, Graham A, Jones D, Rathod K, Gallagher S, Jain A et al. Treatment of multi-vessel coronary artery disease (CAD) in primary percutaneous coronary intervention (PPCI) for ST segment elevation myocardial infarction (STEMI): Culprit only revascularization is associated with higher major adverse cardiovascular event (MACE) rates. Circulation. 2011; 124(21 SUPPL. 1).	Insufficient details for inclusion in review
Arampatzis CA, Hoye A, Lemos PA, Saia F, Tanabe K, Degertekin M et al. Elective sirolimus-eluting stent implantation for multivessel disease involving significant LAD stenosis: one-year clinical outcomes of 99 consecutive patients-	Not question of interest

Reference	Reason for exclusion
-the Rotterdam experience. Catheterization and Cardiovascular Interventions. 2004; 63(1):57-60.	
Aronow WS, Sukhija R, Palaniswamy C, Singh T, Ahn C, Kalapatapu K et al. Major adverse cardiac events at long-term follow-up in patients treated with single versus multiple stents during single-vessel percutaneous coronary intervention. Journal of Interventional Cardiology. 2009; 22(5):427-430.	Not question of interest
Bagai A, Thavendiranathan P, Sharieff W, Cheema A. Multivessel stenting during primary percutaneous coronary intervention for acute myocardial infarction: A quantitative review. Journal of the American College of Cardiology. 2010; 1):B13.	Systematic review ordered for cross-checking purposes
Bagai A, Thavendiranathan P, Waseem S, Cheema AN. Multivessel stenting during primary percutaneous coronary intervention for acute myocardial infarction: A quantitative review. Canadian Journal of Cardiology. 2010; 26:127D.	Insufficient details for inclusion in review
Bangalore S, Kumar S, Poddar KL, Ramasamy S, Rha SW, Faxon DP. Meta-analysis of multivessel coronary artery revascularization versus culprit-only revascularization in patients with ST-segment elevation myocardial infarction and multivessel disease. American Journal of Cardiology. 2011; 107(9):1300-1310.	Systematic review ordered for cross-checking purposes
Bauer T, Zeymer U, Hochadel M, Mollmann H, Weidinger F, Zahn R et al. Use and outcomes of multivessel percutaneous coronary intervention in patients with acute myocardial infarction complicated by cardiogenic shock (from the EHS-PCI Registry). American Journal of Cardiology. 2012; 109(7):941-946.	Not question of interest
Bedossa M, Guillaume L, Coudert I, Pennec P, Moquet B, Hacot JP et al. Acute myocardial infarction and multi vessel disease: Results of PCI on non culprit lesion in a prospective french brittany registry about 2700 patients (ORBI). Catheterization and Cardiovascular Interventions. 2011; 77:S3.	Not question of interest
Bedotto JB, Rutherford BD, McConahay DR, Johnson WL, Giorgi LV, Shimshak TM et al. Results of multivessel percutaneous transluminal coronary angioplasty in persons aged 65 years and older. American Journal of Cardiology. 1991; 67(13):1051-1055.	Not question of interest
Bell MR, Bailey KR, Reeder GS, Lapeyre AC, Holmes DRJ. Percutaneous transluminal angioplasty in patients with multivessel coronary disease: how important is complete revascularization for cardiac event-free survival? Journal of the American College of Cardiology. 1990; 16(3):553-562.	Wrong population
Berger A, Botman KJ, MacCarthy PA, Wijns W, Bartunek J, Heyndrickx GR et al. Long-term clinical outcome after fractional flow reserve-guided percutaneous coronary intervention in patients with multivessel disease. Journal of the American College of Cardiology. 2005; 46(3):438-442.	Wrong population
Biondi-Zoccai G, Lotrionte M, Moretti C, Sciuto F, Omede P, Agostoni A et al. Culprit-only stenting should be sought instead of multivessel stenting in patients with ST-elevation myocardial infarction and multivessel disease: Evidence from a 30,886-patient meta-analysis. European Heart Journal. 2010; 31:456.	Systematic review ordered for cross-checking purposes
Brener SJ, Murphy SA, Gibson CM, DiBattiste PM, Demopoulos LA, Cannon CP et al. Efficacy and safety of multivessel percutaneous revascularization and tirofiban therapy in patients with acute coronary syndromes. American Journal of Cardiology. 2002; 90(6):631-633.	Wrong population
Brener SJ, Milford-Beland S, Roe MT, Bhatt DL, Weintraub WS, Brindis RG et al. Culprit-only or multivessel revascularization in patients with acute coronary syndromes: an American College of Cardiology National Cardiovascular Database Registry report. American Heart Journal. 2008; 155(1):140-146.	Wrong population
Cavallini C, Risica G, Olivari Z, Marton F, Franceschini E, Giommi L. Clinical and	Wrong population

Reference	Reason for exclusion
angiographic follow-up after coronary angioplasty in patients with two-vessel disease: influence of completeness and adequacy of revascularization on long-term outcome. American Heart Journal. 1994; 127(6):1504-1509.	
Celik T, Iyisoy A, Jata B, Kardesoglu E, Isik E. Culprit only versus multivessel coronary revascularization in patients presenting with acute ST elevation myocardial infarction: unending debate. International Journal of Cardiology. 2009; 137(1):65-66.	Narrative review
Chen LY, Lennon RJ, Grantham JA, Berger PB, Mathew V, Singh M et al. In-hospital and long-term outcomes of multivessel percutaneous coronary revascularization after acute myocardial infarction. American Journal of Cardiology. 2005; 95(3):349-354.	Wrong population
Dib C, Hanna EB, Chaudhry MA, Hennebry TA, Stavrakis S, Abu-Fadel MS. Culprit-Vessel Percutaneous Coronary Intervention Followed by Contralateral Angiography versus Complete Angiography in Patients with ST-Elevation Myocardial Infarction. Texas Heart Institute Journal / From the Texas Heart Institute of St Luke's Episcopal Hospital, Texas Children's Hospital. 2012; 39(3):359-364.	Not question of interest
Faxon DP, Ghalilli K, Jacobs AK, Ruocco NA, Christellis EM, Kellett MAJ et al. The degree of revascularization and outcome after multivessel coronary angioplasty. American Heart Journal. 1992; 123(4 Pt 1):854-859.	Cohort study < 500 patients
Fei G, Yu JZ, Zhi JW, Wei YS, De AJ, Hua S. Three years clinical outcomes in patients with acute myocardial infarction undergoing single versus multiple vessel percutaneous coronary intervention. Heart. 2011; 97:A150.	Insufficient details for inclusion in review
Gaglia J, Torguson R, Xue Z, Gonzalez MA, Ben-Dor I, Suddath WO et al. Outcomes of patients with acute myocardial infarction rom a saphenous vein graft culprit undergoing percutaneous coronary intervention. Catheterization and Cardiovascular Interventions. 2011; 78(1):23-29.	Not question of interest
Gambhir DS, Singh S, Sinha SC, Jain R, Trehan V, Arora R. Immediate and follow-up clinical outcome after multivessel coronary stenting. Indian Heart Journal. 1997; 49(4):391-396.	Not question of interest
Gierlotka M, Gasior M, Tajstra M, Lekston A, Buszman P, Opolski G et al. 12-months mortality of STEMI patients treated by primary PCI with multivessel disease and chronic total occlusions: Analysis from PL-ACS registry. European Heart Journal. 2010; 31:195-196.	Not question of interest
Glaser R, Selzer F, Faxon DP, Laskey WK, Cohen HA, Slater J et al. Clinical progression of incidental, asymptomatic lesions discovered during culprit vessel coronary intervention. Circulation. 2005; 111(2):143-149.	Not question of interest
Grantham J, Culprit vs. complete revascularisation in acute myocardial infarction with multivessel coronary artery disease. Circulation 2008; 114(suppl);P98.	STEMI cohort study < 500 patients
Guttmann O, Jones DA, Rathod K, Weerackody R, Akthar M, Wicks E et al. Treatment of multivessel coronary artery disease in primary PCI for STEMI: Culprit only revascularisation is associated with higher MACE rates. Journal of the American College of Cardiology. 2011; 58(20 SUPPL. 1):B19.	Insufficient details for inclusion in review
Han B, Liu L, Aboud M, Nahir M, Hasin Y. Provisional stenting for multivessel PCI. International Journal of Cardiovascular Interventions. 2005; 7(1):46-51.	Not question of interest
Han Yl, Wang B, Wang Xz, Li Y, Wang Sl, Jing Qm et al. Comparative effects of percutaneous coronary intervention for infarct-related artery only or for both infarct- and non-infarct-related arteries in patients with ST-elevation myocardial infarction and multi-vessel disease. Chinese Medical Journal. 2008; 121(23):2384-2387.	STEMI cohort study < 500 patients
Ho PC, Nguyen ME. Multivessel coronary drug-eluting stenting alone in	Not question of interest

Reference	Reason for exclusion
patients with significant ischemic mitral regurgitation: a 4-year follow up. Journal of Invasive Cardiology. 2008; 20(1):41-43.	
Hollman J, Simpfendorfer C, Franco I, Whitlow P, Goormastic M. Multivessel and single-vessel coronary angioplasty: a comparative study. American Heart Journal. 1992; 124(1):9-12.	Not intervention of interest
Hudzik B, Lekston A, Gasior M, et al. Prognostic impact of complete revascularization and diabetes mellitus in patients with acute myocardial infarction and multivessel coronary artery disease. Eur Heart J 2009; 925.	Insufficient details for inclusion in review
Ijsselmuiden AJJ, Ezechiels J, Westendorp ICD, Tijssen JGP, Kiemeneij F, Slagboom T et al. Complete versus culprit vessel percutaneous coronary intervention in multivessel disease: a randomized comparison. American Heart Journal. 2004; 148(3):467-474.	Wrong population
Jaski BE, Cohen JD, Trausch J, Marsh DG, Bail GR, Overlie PA et al. Outcome of urgent percutaneous transluminal coronary angioplasty in acute myocardial infarction: comparison of single-vessel versus multivessel coronary artery disease. American Heart Journal. 1992; 124(6):1427-1433.	Not question of interest
Jeger RV, Pfisterer ME. Primary PCI in STEMI--dilemmas and controversies: multivessel disease in STEMI patients. Complete versus Culprit Vessel revascularization in acute ST--elevation myocardial infarction. Minerva Cardioangiologica. 2011; 59(3):225-233.	Narrative review
Jensen LO, Thayssen P, Horvath-Puho E, Terkelsen CJ, Tilsted HH, Maeng M et al. Influence of single-vessel disease or multivessel disease with or without further revascularisation on mortality in patients with STEMI. EuroIntervention. 2012; 8:N122.	Insufficient details for inclusion in review
Jo HS, Park JS, Sohn JW, Yoon JC, Sohn CW, Lee SH et al. Culprit-Lesion-Only Versus Multivessel Revascularization Using Drug-Eluting Stents in Patients With ST-Segment Elevation Myocardial Infarction: A Korean Acute Myocardial Infarction Registry-Based Analysis. Korean Circ J. 2011; 41(12):718-725.	More recent publication included in review
Kalarus Z, Lenarczyk R, Kowalczyk J, Kowalski O, Gasior M, Was T et al. Importance of complete revascularization in patients with acute myocardial infarction treated with percutaneous coronary intervention. American Heart Journal. 2007; 153(2):304-312.	Wrong population
Kaul U, Singh B, Sudan D, Sapra R, Kachru R, Ghose T et al. Multi-vessel coronary stenting--procedural results and late clinical outcomes: a comparison with single-vessel stenting. Journal of Invasive Cardiology . 2000; 12(8):410-415.	Wrong population
Khattab AA, Abdel-Wahab M, Rother C, Liska B, Toelg R, Kassner G et al. Multi-vessel stenting during primary percutaneous coronary intervention for acute myocardial infarction: A single-center experience. Clinical Research in Cardiology. 2008; 97(1):32-38.	STEMI cohort study < 500 patients
Kornowski R, Mehran R, Dangas G, Nikolsky E, Assali A, Claessen BE et al. Prognostic impact of staged versus 'one-time' multivessel percutaneous intervention in acute myocardial infarction: analysis from the HORIZONS-AMI (harmonizing outcomes with revascularization and stents in acute myocardial infarction) trial. Journal of the American College of Cardiology. 2011; 58(7):704-711.	Wrong comparison, not staged PCI
Kugelmass AD, Brown PP, Reynolds MR, Culler SD, Simon AW, Cohen DJ. Is multi-vessel primary pci advisable? differences in clinical outcomes among medicare beneficiaries undergoing single versus multi-vessel PCI during a primary ST-segment elevated myocardial infarction hospitalization in fiscal year 2007. Journal of the American College of Cardiology. 2010; 55(10 SUPPL 1):A97.	Insufficient details for inclusion in review
Laham RJ, Ho KK, Baim DS, Kuntz RE, Cohen DJ, Carrozza JPJ. Multivessel	Not question of interest

Reference	Reason for exclusion
Palmaz-Schatz stenting: early results and one-year outcome. Journal of the American College of Cardiology. 1997; 30(1):180-185.	
Lawand S. One year clinical outcomes of patients undergoing multi-vessel PCI who are considered poor candidates for CABG: A single tertiary care center experience. EuroIntervention. 2010; 6.	Wrong population
Le Feuvre C, Bonan R, Cote G, Crepeau J, De Guise P, Lesperance J et al. Five- to ten-year outcome after multivessel percutaneous transluminal coronary angioplasty. American Journal of Cardiology. 1993; 71(13):1153-1158.	Not question of interest
Lee HW, Hong TJ, Ahn SK, Yang MJ, Choi JH, Kim BW et al. Long-term clinical outcomes of infarct-related artery versus multivessel revascularization in acute ST-segment elevation myocardial infarction with multivessel disease: An analysis from KAMIR. European Heart Journal. 2011; 32:869-870.	Duplicate of included study
Lee JM, Wong SC, Minutello RM, Bergman G, Moussa I, Feldman DN. Long-term survival following multivessel versus single-vessel percutaneous coronary interventions in the contemporary drug-eluting stent era. Journal of the American College of Cardiology. 2010; 55(10 SUPPL 1):A191.	Duplicate of included study
Lehmann R, Fichtlscherer S, Schachinger V, Held L, Hobler C, Baier G et al. Complete revascularization in patients undergoing multivessel PCI is an independent predictor of improved long-term survival. Journal of Interventional Cardiology. 2010; 23(3):256-263.	Wrong population
Lo HS, Chen ML, Ong ET, Chiou HC. Double-Vessel Primary Angioplasty in Acute Inferior Myocardial Infarction - Is It a Feasible Therapeutic Modality? Acta Cardiologica Sinica. 2003; 19(4):243-250.	Not question of interest
Lelek M, Wita K, Drzewiecki J, Trusz-Gluza M. Impact of thrombus aspiration on myocardial perfusion and left ventricle function in patients with anterior STEMI treated with primary angioplasty. EuroIntervention. 2011; 7:M176.	Insufficient details for inclusion in review
Maamoun W, Elkhaeat N, Elarasy R. Safety and feasibility of complete simultaneous revascularization during primary PCI in patients with STEMI and multi-vessel disease. Egyptian Heart Journal. 2011; 63(1):39-43.	Not question of interest
Mathew V, Garratt KN, Holmes DRJ. Clinical outcome after multivessel coronary stent implantation. American Heart Journal. 1999; 138(6 Pt 1):1105-1110.	Not question of interest
Mohamad T, Bernal JM, Kondur A, Hari P, Nelson K, Niraj A et al. Coronary revascularization strategy for ST elevation myocardial infarction with multivessel disease: Experience and results at 1-year follow-up. American Journal of Therapeutics. 2011; 18(2):92-100.	Cohort study < 500 patients
Mylotte D, Lefevre T, Eltchaninoff H, Briole N, Tazarourte K, Margenet A et al. Complete revascularization improves survival in patients with STEMI complicated by cardiac arrest and cardiogenic shock. Journal of the American College of Cardiology. 2011; 58(20 SUPPL. 1):B133.	Wrong population
Mylotte D, Lefevre T, Eltchaninoff H, Briole N, Tazarourte K, Margenet A et al. Multivessel versus target lesion percutaneous coronary intervention in resuscitated cardiac arrest patients with STEMI. Circulation. 2011; 124(21 SUPPL. 1).	Wrong population
Navarese E, Buffon A, De Luca G, Napodano M, De Servi S. Clinical impact of complete revascularisation vs. culprit only primary angioplasty in patients with ST-segment elevation myocardial infarction and multivessel disease: A meta-analysis. EuroIntervention. 2010; 20100525(20100528).	Systematic review ordered for cross-checking purposes
Navarese EP, De SS, Buffon A, Suryapranata H, De LG. Clinical impact of simultaneous complete revascularization vs. culprit only primary angioplasty in patients with ST-elevation myocardial infarction and multivessel disease: a meta-analysis (Structured abstract). Journal of Thrombosis and Thrombolysis.	Systematic review ordered for cross-checking purposes

Reference	Reason for exclusion
2011; 31(2):217-225.	
Nikolsky E, Halabi M, Roguin A, Zdorovyak A, Gruberg L, Hir J et al. Staged versus one-step approach for multivessel percutaneous coronary interventions. American Heart Journal. 2002; 143(6):1017-1026.	Wrong population
Norwa-Otto B, Kadziela J, Malek LA, Debski A, Witkowski A, Demkow M et al. Functionally driven complete vs incomplete revascularisation in multivessel coronary artery disease - Long-term results from a large cohort. Kardiologia Polska. 2010; 68(12):1344-1350.	Not question of interest
Novack V, Tsyvine D, Cohen DJ, Pencina M, Dubin J, Dehghani H et al. Multivessel drug-eluting stenting and impact of diabetes mellitus--a report from the EVENT registry. Catheterization and Cardiovascular Interventions. 2009; 73(7):874-880.	Not question of interest
Oemrawsingh P, Imami S, Bax M, Schotborgh C, Savalle L, Bech JW et al. Long term follow up of 4 treatment strategies in multivessel disease following primary percutaneous intervention for acute myocardial infarction. Journal of the American College of Cardiology. 2011; 58(20 SUPPL. 1):B18.	Not question of interest
Pain TE, Jones DA, Rathod K, Weerackody R, Gallagher S, Jain A et al. Treatment of multivessel coronary artery disease in primary PCI for ST elevation myocardial infarction: Culprit only revascularisation is associated with higher MACE rates. European Heart Journal. 2011; 32:867.	Insufficient details for inclusion in review
Palmer ND, Causer JP, Ramsdale DR, Perry RA. Effect of completeness of revascularization on clinical outcome in patients with multivessel disease presenting with unstable angina who undergo percutaneous coronary intervention. Journal of Invasive Cardiology. 2004; 16(4):185-188.	Wrong population
Piraino RA, Calenta CH, Luchessi E, Kirschmann DF. The oculo-stenotic reflex improves survival in patients with acute myocardial infarction and multivessels disease treated with primary angioplasty. European Heart Journal. 2009; 30:791.	STEMI cohort study < 500 patients
Qarawani D, Nahir M, Abboud M, Hazanov Y, Hasin Y. Culprit only versus complete coronary revascularization during primary PCI. International Journal of Cardiology. 2008; 123(3):288-292.	STEMI cohort study < 500 patients
Rha S-W, Choi BG, Choi SY, Im SI, Kim SW, Na JO et al. Chronic total occlusion lesion revascularization alone versus complete revascularization in chronic total occlusion patients with multivessel disease. Journal of the American College of Cardiology. 2012; 60:B128.	Insufficient details for inclusion in review
Rahman M, Nfor T, Allaqaband S, et al. Clinical and angiographic outcomes in patients with ST-segment elevation myocardial infarction undergoing single versus multiple vessel percutaneous coronary intervention. J Am Coll Cardiol 2010; 55:A98.	Insufficient details for inclusion in review
Rathod KS, McGill LA, Sammut E, Rathod VS, Jones DA, Weerackody R et al. Treatment of multivessel coronary artery disease in primary PCI for ST elevation myocardial infarction: Culprit only revascularisation is associated with higher mace rates. Heart. 2011; 97:A15-A16.	No outcome of interest
Rigattieri S, Biondi-Zoccai G, Silvestri P, Russo CD, Musto C, Ferraiuolo G et al. Management of multivessel coronary disease after ST elevation myocardial infarction treated by primary angioplasty. Journal of Interventional Cardiology. 2008; 21(1):1-7.	STEMI cohort study < 500 patients
Roe MT, Cura FA, Joski PS, Garcia E, Guetta V, Kereiakes DJ, Zijlstra F, Brodie BR, Grines CL, Ellis SG. Initial experience with multivessel percutaneous coronary intervention during mechanical reperfusion for acute myocardial infarction. Am J Cardiol. 2001 Jul 15; 88(2):170-3, A6.	STEMI cohort study < 500 patients
Samson M, Meester HJ, De Feyter PJ, Strauss B, Serruys PW. Successful	Not question of interest

Reference	Reason for exclusion
multiple segment coronary angioplasty: Effect of completeness of revascularization in single-vessel multilesions and multivessels. American Heart Journal. 1990; 120(1):1-12.	
Sarno G, Garg S, Onuma Y, Gutierrez-Chico JL, van den Brand MJBM, Rensing BJWM et al. Impact of completeness of revascularization on the five-year outcome in percutaneous coronary intervention and coronary artery bypass graft patients (from the ARTS-II study). American Journal of Cardiology . 2010; 106(10):1369-1375.	Not question of interest
Sen S, Francis D, Petraco R, Broyd C, Nijjer S, Foin N et al. Should we discourage the use of multi-vessel angioplasty during stemi or the use of registry data in comparative efficacy research? An analysis of 35,008 patients. Journal of the American College of Cardiology. 2012; 59(13 SUPPL. 1):E515.	Not question of interest
Seo J-S, Park D-W, Kim SS, et al. Long-term outcomes of culprit only versus complete coronary revascularization during primary percutaneous coronary intervention. J Am Coll Cardiol 2009; 53:A58.	STEMI cohort study < 500 patients
Sheiban I, Sillano D, Biondi-Zoccai G, Moretti C, Garrone P, Lombardi P et al. Impact of multivessel stenting on top of percutaneous revascularization for unprotected left main disease in the drug-eluting stent era: insights from the Turin registry. Journal of Cardiovascular Medicine. 2009; 10(6):461-468.	Not question of interest
Shishehbor MH, Topol EJ, Mukherjee D, Hu T, Cohen DJ, Stone GW et al. Outcome of multivessel coronary intervention in the contemporary percutaneous revascularization era. American Journal of Cardiology. 2006; 97(11):1585-1590.	Not population of interest
Shishehbor MH, Lauer MS, Singh IM, Chew DP, Karha J, Brener SJ et al. In unstable angina or non-ST-segment acute coronary syndrome, should patients with multivessel coronary artery disease undergo multivessel or culprit-only stenting? Journal of the American College of Cardiology. 2007; 49(8):849-854.	Not population of interest
Srinivas VS, Brooks MM, Detre KM, King SB, III, Jacobs AK, Johnston J et al. Contemporary percutaneous coronary intervention versus balloon angioplasty for multivessel coronary artery disease: a comparison of the National Heart, Lung and Blood Institute Dynamic Registry and the Bypass Angioplasty Revascularization Investigation (BARI) study. Circulation. 2002; 106(13):1627-1633.	Not question of interest
Tamburino C, Angiolillo DJ, Capranzano P, Dimopoulos K, La Manna A, Barbagallo R et al. Complete versus incomplete revascularization in patients with multivessel disease undergoing percutaneous coronary intervention with drug-eluting stents. Catheterization and Cardiovascular Interventions. 2008; 72(4):448-456.	Not population of interest
Telayna J. Percutaneous interventional approach in acute myocardial infarction: treatment of culprit lesion versus complete revascularization. Am J Cardiol 2002; 90 (suppl):47H-8H.	STEMI cohort study < 500 patients
Varani E, Balducelli M, Aquilina M, Vecchi G, Hussien MN, Frassineti V et al. Single or multivessel percutaneous coronary intervention in ST-elevation myocardial infarction patients. Catheterization and Cardiovascular Interventions. 2008; 72(7):927-933.	STEMI cohort study < 500 patients
Vlaar PJ, Mahmoud KD, Holmes DR, Jr., van VG, Hillege HL, van der Horst IC et al. Culprit vessel only versus multivessel and staged percutaneous coronary intervention for multivessel disease in patients presenting with ST-segment elevation myocardial infarction: a pairwise and network meta-analysis. Journal of the American College of Cardiology. 2011; 58(7):692-703.	Systematic review ordered for cross-checking purposes
Yang HH, Chen Y, Gao CY. The influence of complete coronary revascularization on long-term outcomes in patients with multivessel coronary heart disease undergoing successful percutaneous coronary intervention. Journal of	Wrong population

Reference	Reason for exclusion
International Medical Research. 2010; 38(3):1106-1112.	
Zapata GO, Lasave LI, Kozak F, Damonte A, Meirino A, Rossi M et al. Culprit-only or multivessel percutaneous coronary stenting in patients with non-ST-segment elevation acute coronary syndromes: one-year follow-up. Journal of Interventional Cardiology. 2009; 22(4):329-335.	Wrong population

J.6 Cardiogenic shock

Reference	Reason for exclusion
Bauer T, Zeymer U, Hochadel M, Mollmann H, Weidinger F, Zahn R et al. Use and outcomes of multivessel percutaneous coronary intervention in patients with acute myocardial infarction complicated by cardiogenic shock (from the EHS-PCI Registry). American Journal of Cardiology. 2012; 109(7):941-946.	Not question of interest
Buerke M, et al. Pathophysiology, diagnosis, and treatment of infarction-related cardiogenic shock. Herz. 2011 Mar; 36(2):73-83. Review.	Review
Hochman, JS et al. One-year survival following: early revascularization for cardiogenic shock. Commentary; JAMA2001:240	Commentary
Jeger RV et al. Interhospital transfer for early revascularization in patients with ST-elevation myocardial infarction complicated by cardiogenic shock--a report from the SHould we revascularize Occluded Coronaries for cardiogenic shocK? (SHOCK) trial and registry. Am Heart J. 2006 Oct; 152(4):686-92.	Subgroup analysis of transfer patients
Lee MS, et al. Outcome after surgery and percutaneous intervention for cardiogenic shock and left main disease. Ann Thorac Surg. 2008 Jul; 86(1):29-34.	Wrong comparison: PCI versus CABG
MarKusohn E et al. Primary percutaneous coronary intervention after out-of-hospital cardiac arrest: patients and outcomes. Isr Med Assoc J. 2007 Apr; 9(4):257-9.	No control group
Prasad A et al. Outcomes of elderly patients with cardiogenic shock treated with early percutaneous revascularization. Am Heart J. 2004 Jun; 147(6):1066-70.	Analysis of early revascularisation patients
Ramanathan K et al. Rapid complete reversal of systemic hypoperfusion after intra-aortic balloon pump counterpulsation and survival in cardiogenic shock complicating an acute myocardial infarction. Am Heart J. 2011 Aug; 162(2):268-75.	Subgroup of IABP patients
Rogers PA, Huang H, Alam M, Paniagua D, Kar B, Jneid H. Early revascularization improves mortality in elderly patients with acute myocardial infarction complicated by cardiogenic shock. Circulation. 2011; 124(21 SUPPL. 1).	Abstract
Webb JG et al. SHOCK Investigators. Percutaneous coronary intervention for cardiogenic shock in the SHOCK Trial Registry. Am Heart J. 2001 Jun; 141(6):964-70.	Analysis of PCI patients only
Webb JG et al SHOCK Investigators. Percutaneous coronary intervention for cardiogenic shock in the SHOCK trial. J Am Coll Cardiol. 2003 Oct 15; 42(8):1380-6.	Investigates only patients who had PCI
White HD et al. Comparison of percutaneous coronary intervention and coronary artery bypass grafting after acute myocardial infarction complicated by cardiogenic shock: results from the Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock (SHOCK) trial. Circulation. 2005 Sep 27; 112(13):1992-2001.	PCI versus CABG
Wong SC et al. SHOCK Investigators. Absence of gender differences in clinical outcomes in patients with cardiogenic shock complicating acute myocardial infarction. A report from the SHOCK Trial Registry. J Am Coll Cardiol. 2001 Nov	Did not compare early revascularisation versus initial medical stabilisation

Reference	Reason for exclusion
1; 38(5):1395-401.	

J.7 People who remain unconscious after a cardiac arrest

Reference	Reason for exclusion
Aguila A, Aktas MK, Funderburk M, McNitt S, Delehanty J, Traub D et al. Outcomes following therapeutic hypothermia for patients presenting with cardiac arrest. Heart Rhythm. 2009 (1):S429-S430.	Not study type of interest; abstract
Al-Senani FM, Graffagnino C, Grotta JC, Saiki R, Wood D, Chung W et al. A prospective, multicenter pilot study to evaluate the feasibility and safety of using the CoolGard System and Icy catheter following cardiac arrest. Resuscitation. 2004; 62(2):143-150.	Not question of interest
Aldhoon B, Kettner J, Cihlova M, Kohoutek J, Wiendl M, Al-Hiti H et al. Short-term outcomes of out-of-hospital cardiac arrest after successful resuscitation. Heart Rhythm. 2009; 1):S182.	Not study type of interest; abstract
Alla V, Mathias S, Hunter C, Holmberg M. Aortic and coronary thrombosis following methamphetamine use and resuscitated SCD: Coincidence or shared pathogenesis? Journal of General Internal Medicine. 2010; 25:S493.	Wrong study type; case control
Andrade Ferreira I, Schutte M, Oosterloo E, Dekker W, Mooi BW, Dambrink JHE et al. Therapeutic mild hypothermia improves outcome after out-of-hospital cardiac arrest. Netherlands Heart Journal. 2009; 17(10):378-384.	Not question of interest
Anyfantakis ZA, Baron G, Aubry P, Himbert D, Feldman LJ, Juliard JM et al. Acute coronary angiographic findings in survivors of out-of-hospital cardiac arrest. American Heart Journal. 2009; 157(2):312-318.	Wrong population
Athanasuleas CL, Buckberg GD, Allen BS, Beyersdorf F, Kirsh MM. Sudden cardiac death: Directing the scope of resuscitation towards the heart and brain. Resuscitation. 2006; 70(1):44-51.	Not question of interest
Aurore A, Jabre P, Liot P, Margenet A, Lecarpentier E, Combes X. Predictive factors for positive coronary angiography in out-of-hospital cardiac arrest patients. European Journal of Emergency Medicine. 2011; 18(2):73-76.	Wrong population (mixed STEMI, NSTEMI, Q wave)
Batista LM, Lima FO, Januzzi JL, Donahue V, Snydeman C, Greer DM. Combined cardiac catheterization and therapeutic hypothermia following cardiac arrest is feasible and safe. Stroke. 2010; 41 (4):e260.	Not study type of interest; abstract
Bendz B, Eritsland J, Nakstad AR, Brekke M, Klow NE, Steen PA et al. Long-term prognosis after out-of-hospital cardiac arrest and primary percutaneous coronary intervention. Resuscitation. 2004; 63(1):49-53.	Not study type of interest; case series
Borger Van Der Burg AE, Bax JJ, Boersma E, Bootsma M, Van Erven L, Van Der Wall EE et al. Impact of percutaneous coronary intervention or coronary artery bypass grafting on outcome after nonfatal cardiac arrest outside the hospital. American Journal of Cardiology. 2003; 91(7):785-789.	Wrong population
Borger Van Der Burg AE, Bax JJ, Boersma E, Van Erven L, Bootsma M, Van Der Wall EE et al. Standardized screening and treatment of patients with life-threatening arrhythmias: The leiden out-of-hospital cardiac arrest evaluation study. Heart Rhythm. 2004; 1(1):51-57.	Wrong population
Bray J, Stub D, Bernard S, Smith K. Exploring gender differences and the 'estrogen effect' in an Australian out-of-hospital cardiac arrest (OHCA) population. Academic Emergency Medicine. 2012; 19(6):739.	Not question of interest
Bro-Jeppesen J, Kjaergaard J, Pedersen F, Wanscher M, Nielsen S, Moller J et al. Does the combination of therapeutic hypothermia and acute coronary angiography improve outcome. European Heart Journal. 2011; 32:930.	Not study type of interest; abstract
Busch M, Sooreide E. Have the 2005 european resuscitation council guidelines and the use of percutaneous coronary intervention improved outcome in	Not study type of interest; abstract

Reference	Reason for exclusion
unconscious out-of-hospital cardiac arrest survivors? Intensive Care Medicine. 2010; 36:S297.	
Chakravarthy M, Mitra S, Nonis L. Outcomes of in-hospital, out of intensive care and operation theatre cardiac arrests in a tertiary referral hospital. Indian Heart Journal. 2012; 64(1):7-11.	Not study type of interest; audit
Choudry FA, Weerackody RP, Mills PG, Kjain A. Survival following acute ST elevation myocardial infarction complicated by out of hospital cardiopulmonary arrest. Journal of the American College of Cardiology. 2010; 1):B106.	Not study type of interest; abstract
Chow-In Ko P, Xiong GH, Chiang WC, Wang HC, Yang CW, Huei-Ming Ma M. Hospital characteristics associated with survival after out-of-hospital cardiac arrest: Resuscitation center designation. Circulation Conference: American Heart Association's Scientific Sessions. 2011; 124(21 SUPPL. 1).	Not study type of interest; abstract
Cokkinos P. Post-resuscitation care: current therapeutic concepts. Acute Cardiac Care. 2009; 11(3):131-137.	Not study type of interest; narrative review used for crosschecking purposes
Derksen R, Van Hemel NM. Coronary revascularisation or ICD implantation in selected survivors of an out-of-hospital cardiac arrest after myocardial infarction? European Journal of Cardiac Pacing and Electrophysiology. 1996; 6(3):171-172.	Not study type of interest; narrative review
Dooris M. Emergency cardiac catheterisation for resuscitated out of hospital cardiac arrest: An ongoing challenge but not futile. Heart Lung and Circulation. 2010; 19:S129-S130.	Not study type of interest; abstract
Dumas F, White L, Stubbs BA, Cariou A, Rea TD. Long-term prognosis following resuscitation from out of hospital cardiac arrest: Role of percutaneous coronary intervention and therapeutic hypothermia. Journal of the American College of Cardiology. 2012; 60(1):21-27.	Not question of interest
Dumas F, Cariou A, Manzo-Silberman S, Grimaldi D, Vivien B, Rosencher J et al. Immediate percutaneous coronary intervention is associated with better survival after out-of-hospital cardiac arrest: Insights from the PROCAT (Parisian Region Out of Hospital Cardiac Arrest) registry. Circulation: Cardiovascular Interventions. 2010; 3(3):200-207.	Not study type of interest; case series
Dumas F, Silberman SM, Giovanetti O, Lemiale V, Vivien B, Carli P et al. Outcome after immediate invasive strategy in out-of-hospital cardiac arrest. Archives of Cardiovascular Diseases Supplements. 2010; 2 (1):111.	Not study type of interest; abstract
Farhat A, Godin M, Abriou C, Borz B, Tron C, Baala B et al. Does primary coronary angioplasty improve outcome in patients who are victims of out-of-hospital cardiac arrest? Circulation Conference: American Heart Association's Scientific Sessions. 2011; 124(21 SUPPL. 1).	Not study type of interest; abstract
Garot P, Lefevre T, Eltchaninoff H, Morice MC, Tamion F, Abry B et al. Six-month outcome of emergency percutaneous coronary intervention in resuscitated patients after cardiac arrest complicating ST-elevation myocardial infarction. Circulation. 2007; 115(11):1354-1362.	Not study type of interest; case series
Golia E, Piro M, Tubaro M. Out-of-hospital CPR: Better outcome for our patients. Critical Care. 2011; 15(2).	Narrative review
Gorjup V, Radsel P, Kocjancic ST, Erzen D, Noc M. Acute ST-elevation myocardial infarction after successful cardiopulmonary resuscitation. Resuscitation. 2007; 72(3):379-385.	Not study type of interest; case series
Grasner JT, Meybohm P, Caliebe A, Bottiger BW, Wnent J, Messelken M et al. Postresuscitation care with mild therapeutic hypothermia and coronary intervention after out-of-hospital cardiopulmonary resuscitation: A prospective registry analysis. Critical Care. 2011; 15(1).	Not study type of interest; case series

Reference	Reason for exclusion
Gupta N, Kontos MC, Gupta A, Vetrovec GW, Messenger J. Clinical and angiographic characteristics of patients undergoing percutaneous coronary intervention following sudden cardiac arrest: Insights from the ncdr. Circulation Conference: American Heart Association's Scientific Sessions. 2011; 124(21 SUPPL. 1).	Not study type of interest; abstract
Hosmane VR, Mustafa NG, Reddy VK, Reese ICL, DiSabatino A, Kolm P et al. Survival and Neurologic Recovery in Patients With ST-Segment Elevation Myocardial Infarction Resuscitated From Cardiac Arrest. Journal of the American College of Cardiology. 2009; 53(5):409-415.	Not question of interest
Hovdenes J, Laake JH, Aaberge L, Haugaa H, Bugge JF. Therapeutic hypothermia after out-of-hospital cardiac arrest: Experiences with patients treated with percutaneous coronary intervention and cardiogenic shock. Acta Anaesthesiologica Scandinavica. 2007; 51(2):137-142.	Wrong population
Hreybe H, Singla I, Razak E, Saba S. Predictors of cardiac arrest occurring in the context of acute myocardial infarction. PACE - Pacing and Clinical Electrophysiology. 2007; 30(10):1262-1266.	No outcome of interest
Johnson NJ, Salhi RA, Abella BS, Neumar RW, Carr BG. Emergency department factors associated with survival after out-of-hospital cardiac arrest. Academic Emergency Medicine. 2012; 19:S272-S273.	Narrative review
Kahn JK, Glazier S, Swor R, Savas V, O'Neill WW. Primary coronary angioplasty for acute myocardial infarction complicated by out-of-hospital cardiac arrest. American Journal of Cardiology. 1995; 75(15):1069-1070.	Not study type of interest; case series
Kamal Z, Andersen GO, Eritsland J, Draegni T, Sunde K, Mangschau A. Coronary angiographic findings in patients with or without st-segment elevation resuscitated after out-of-hospital cardiac arrest. Circulation Conference: American Heart Association's Scientific Sessions. 2011; 124(21 SUPPL. 1).	Not study type of interest; abstract
Kebed KY, Schwartz RS, Newell MC, Browning JA, Sharkey SW, Hauser RG et al. Cardiac arrest: Who goes to the catheterization lab? Circulation Conference: American Heart Association's Scientific Sessions. 2011; 124(21 SUPPL. 1).	Not study type of interest; abstract
Keelan PC, Bunch TJ, White RD, Packer DL, Holmes Jr DR. Early direct coronary angioplasty in survivors of out-of-hospital cardiac arrest. American Journal of Cardiology. 2003; 91(12):1461-1463.	Not study type of interest; case series
Kelley M, Huang R, Wells Q, Scott C, Fredi J, McPherson J. Outcomes in comatose cardiac arrest patients with st elevation myocardial infarction treated with therapeutic hypothermia and percutaneous coronary intervention. Critical Care Medicine. 2010; 38:A127.	Not study type of interest; abstract
Kelly P, Ruskin JN, Vlahakes GJ, Buckley Jr MJ, Freeman CS, Garan H. Surgical coronary revascularization in survivors of prehospital cardiac arrest: Its effect on inducible ventricular arrhythmias and long-term survival. Journal of the American College of Cardiology. 1990; 15(2):267-273.	Wrong intervention
Kern KB. Importance of invasive interventional strategies in resuscitated patients following sudden cardiac arrest. Interventional Cardiology. 2011; 3(6):649-661.	Narrative review
Keuper W, Dieker HJ, Brouwer MA, Verheugt FWA. Reperfusion therapy in out-of-hospital cardiac arrest: current insights. Resuscitation. 2007; 73(2):189-201.	Narrative review
Kirkland L, Parham W, Edelstein K, Unger B, Mooney M. Simultaneous percutaneous coronary intervention and mild therapeutic hypothermia in comatose survivors of cardiac arrest with st-segment elevation acute myocardial infarction. Critical Care Medicine. 2009; 37 (12 SUPPL.):A32.	Not study type of interest; abstract
Knafelj R, Radsel P, Ploj T, Noc M. Primary percutaneous coronary intervention and mild induced hypothermia in comatose survivors of ventricular fibrillation with ST-elevation acute myocardial infarction. Resuscitation. 2007; 74(2):227-	Not study type of interest; case series

Reference	Reason for exclusion
234.	
Koester R, Kaehler J, Barmeyer A, Mullerleile K, Priefler M, Soeffker G et al. Coronary angiography and intervention during hypothermia can be performed safely without cardiac arrhythmia or vasospasm. Clinical Research in Cardiology. 2011; 100(11):1013-1019.	Not study type of interest; case series (information not included in case series table as no mortality or neurological status outcomes reported)
Kokubu N, Hase M, Nishida J, Funayama N, Mochizuki A, Muranaka A et al. Impacts of gensini score for coronary angiographic severity on outcomes of out-of-hospital cardiac arrest due to acute myocardial infarction patients. American Journal of Cardiology. 2011; 1):5A.	Not study type of interest; abstract
Lee CH, Lemos PA, Degertekin M, Saia F, Tanabe K, Serruys PW In-hospital versus out-of-hospital cardiac arrest complicating myocardial infarction: survival after percutaneous coronary revascularization. Int J Cardiol. 2005 Feb 15; 98(2):359-60.	Not study type of interest; case series
Lettieri C, Savonitto S, De Servi S, Guagliumi G, Belli G, Repetto A et al. Emergency percutaneous coronary intervention in patients with ST-elevation myocardial infarction complicated by out-of-hospital cardiac arrest: Early and medium-term outcome. American Heart Journal. 2009; 157(3):569-575.	Not study type of interest; case series
Lyon RM, Shepherd J, Clegg GR. Early in-hospital management of out-of-hospital cardiac arrest in Scotland: A national survey. European Journal of Emergency Medicine. 2011; 18(2):102-104.	Not study type of interest (survey)
Mager A, Kornowski R, Murninkas D, Vaknin-Assa H, Ukabi S, Brosh D et al. Outcome of emergency percutaneous coronary intervention for acute ST-elevation myocardial infarction complicated bv cardiac arrest. Coronary Artery Disease. 2008; 19(8):615-618.	Not study type of interest (compared cardiac arrest versus non-cardiac arrest patients)
Markusohn E, Roguin A, Sebbag A, Aronson D, Dragu R, Amikam S et al. Primary percutaneous coronary intervention after out-of-hospital cardiac arrest: Patients and outcomes. Israel Medical Association Journal. 2007; 9(4):257-259.	Not study type of interest; case series
Maze R, Le May M, Glover C, So D, Froeschl M, Marquis J et al. Therapeutic hypothermia in patients with ST-segment elevation myocardial infarction surviving out of hospital cardiac arrest in the context of a regional primary PCI program. Canadian Journal of Cardiology. 2010; 26:127D.	Not study type of interest; abstract
Molnar L, Zima E, Geller L, Szabo G, Merkely B. Primary percutaneous coronary intervention during resuscitation with the AutoPulse is feasible. Resuscitation. 2011; 82:S10.	Not study type of interest; abstract
Mylotte D, Lefevre T, Eltchaninoff H, Briole N, Tazarourte K, Margenet A et al. Multivessel versus target lesion percutaneous coronary intervention in resuscitated cardiac arrest patients with STEMI. Circulation Conference: American Heart Association's Scientific Sessions. 2011; 124(21 SUPPL. 1).	Not study type of interest; abstract
Nanjayya V, Nayyar V, Kim C. Does immediate coronary intervention for patients with out-of-hospital VT/VF arrest improve outcome. Anaesthesia and Intensive Care. 2009; 37 (6):1033.	Insufficient information for inclusion in review
Nanjayya VB, Nayyar V. Immediate coronary angiogram in comatose survivors of out-of-hospital cardiac arrest-An Australian study. Resuscitation. 2012; 83(6):699-704.	Study reported population of acute MI, unclear number of STEMI patients
Nielsen N, Hovdenes J, Nilsson F, Rubertsson S, Stammet P, Sunde K et al. Outcome, timing and adverse events in therapeutic hypothermia after out-of-hospital cardiac arrest. Acta Anaesthesiologica Scandinavica. 2009; 53(7):926-934.	Not study type of interest; case series
Noc M. Mild induced hypothermia and an urgent invasive coronary strategy - a	Narrative review ordered

Reference	Reason for exclusion
Promising protocol for comatose survivors of sudden cardiac arrest. Serbian Journal of Experimental and Clinical Research. 2011; 12(2):53-55.	for cross checking
Noc M. Patients with resuscitated sudden cardiac arrest: Forgotten 'orphans of interventional cardiology? Interventional Cardiology. 2011; 3(6):623-625.	Narrative review ordered for cross checking
Noc M. Urgent coronary angiography and percutaneous coronary intervention as a part of postresuscitation management. Critical Care Medicine. 2008; 36(11 Suppl):S454-S457.	Narrative review ordered for cross checking
Noc M, Radsel P. Urgent invasive coronary strategy in patients with sudden cardiac arrest. Current Opinion in Critical Care. 2008; 14(3):287-291.	Narrative review ordered for cross checking
Panchal AR, Vadeboncoeur TF, Stolz U, Roosa JR, Berg RA, Ewy GA et al. Impact of an aha guideline-based, statewide postarrest system of care on survival from out-of-hospital cardiac arrest. Circulation Conference: American Heart Association's Scientific Sessions. 2011; 124(21 SUPPL. 1).	Not study type of interest; abstract
Quintero-Moran B, Moreno R, Villarreal S, Perez-Vizcayno MJ, Hernandez R, Conde C et al. Percutaneous coronary intervention for cardiac arrest secondary to ST-elevation acute myocardial infarction. Influence of immediate paramedical/medical assistance on clinical outcome. Journal of Invasive Cardiology. 2006; 18(6):269-272.	Not study type of interest; case series
Reddy VK, Hosmane VR, Doorey A, Weintraub WS, Rahman E. Is it appropriate to take all post-resuscitation patients suspected of having an acute MI for urgent angiography? Journal of the American College of Cardiology. 2011; 1):B131.	Not study type of interest; abstract
Reynolds JC, Callaway CW, El Khoudary SR, et al. Coronary angiography predicts improved outcome following cardiac arrest: Propensity-adjusted analysis. J Intensive Care Med 2009; 24:179-86.R	Not study type of interest; case series
Schefold JC, Storm C, Joerres A, Hasper D. Mild therapeutic hypothermia after cardiac arrest and the risk of bleeding in patients with acute myocardial infarction. International Journal of Cardiology. 2009; 132(3):387-391.	Not question of interest
Siudak Z, Birkemeyer R, Dziewierz A, Rakowski T, Zmudka K, Dubiel JS et al. Out-of-hospital cardiac arrest in patients treated with primary PCI for STEMI. Long-term follow up data from EUROTRANSFER registry. Resuscitation. 2012; 83(3):303-306.	Not question of interest
Spaulding CM, Joly LM, Rosenberg A, Monchi M, Weber SN, Dhainaut JFA et al. Immediate coronary angiography in survivors of out-of-hospital cardiac arrest. New England Journal of Medicine. 1997; 336(23):1629-1633.	Wrong population (mixed STEMI, NSTEMI, Q wave)
Stub D, Hengel C, Chan W, Jackson D, Sanders K, Dart A et al. Cooling and coronary catheterisation is associated with improved survival in out of hospital cardiac arrest. Heart Lung and Circulation. 2010; 19:S127.	Not study type of interest; abstract
Stub D, Hengel C, Chan W, Jackson D, Sanders K, Dart AM et al. Usefulness of cooling and coronary catheterization to improve survival in out-of-hospital cardiac arrest. American Journal of Cardiology. 2011; 107(4):522-527.	Not question of interest
Swanson LA, Edelstein KM, Parham WM, Kapsner CE, Unger BT, Kalb ME et al. Cool it: Therapeutic hypothermia for cardiac arrest in patients with ST-elevation myocardial infarction and unique benefits with combined treatment. Journal of the American College of Cardiology. 2009; 53 (10):A347.	Not study type of interest; abstract
Tachibana E, Nagao K, Kikushima K, Takayama T, Satoh N, Yamada A et al. The effect of emergency percutaneous coronary intervention for patients with post cardiac arrest syndrome in tokyo CCU network. Circulation Conference: American Heart Association's Scientific Sessions. 2011; 124(21 SUPPL. 1).	Not study type of interest; abstract
Tadel-Kocjancic S, Radsel P, Knafelj R, Gorjup V, Noc M. Improved hospital outcome of comatose survivors of cardiac arrest of presumed cardiac origin. European Heart Journal, Supplement. 2010; 12:F123.	Not study type of interest; abstract

Reference	Reason for exclusion
Valente S, Lazzeri C, Saletti E, Chiostri M, Gensini GF. Primary percutaneous coronary intervention in comatose survivors of cardiac arrest with ST-elevation acute myocardial infarction: a single-center experience in Florence. Journal of Cardiovascular Medicine (Hagerstown, Md). 2008; 9(11):1083-1087.	Not study type of interest; case series
Werling M, Thoren AB, Axelsson C, Herlitz J. Treatment and outcome in post-resuscitation care after out-of-hospital cardiac arrest when a modern therapeutic approach was introduced. Resuscitation. 2007; 73(1):40-45.	Data on population of interest not analysed separately from other populations
Wijesekera V, Mullany D, Savage M, Walters D. Survivors of out of hospital cardiac arrests proceeding to coronary angiogram: Clinical, angiographic features and in-hospital outcomes-a single centre experience. Heart Lung and Circulation. 2010; 19:S35-S36.	Wrong population
Wolfrum S, Pierau C, Radke PW, Schunkert H, Kurowski V. Mild therapeutic hypothermia in patients after out-of-hospital cardiac arrest due to acute ST-segment elevation myocardial infarction undergoing immediate percutaneous coronary intervention. Critical Care Medicine. 2008; 36(6):1780-1786.	Not study type of interest; case series
Zanuttini D, Armellini I, Nucifora G, Carchietti E, Trillo G, Spedicato L et al. Impact of Emergency Coronary Angiography on In-Hospital Outcome of Unconscious Survivors After Out-of-Hospital Cardiac Arrest. American Journal of Cardiology. 2012.	Mixed population; only 34% STEMI
Zoffoli G, Nicolini F, Beghi C, Budillon AM, Agostinelli A, Borrello B et al. Acute coronary syndromes without persistent st-segment elevation: Advances in surgical revascularization. Acta Biomedica De L'Ateneo Parmense. 2005; 76(2):99-106+127.	Wrong population

J.8 Hospital volumes of PPCI

Reference	Reason for exclusion
Adogwa, Owoicho, Costich, Julia F., Hill, Raymond, and Slavova, Svetla. Does higher surgical volume predict better patient outcomes? Journal of the Kentucky Medical Association 107(1), 10-16. 2009.	Wrong intervention - all PCIs
Birkmeyer, J. D., Finlayson, E. V., and Birkmeyer, C. M. Volume standards for high-risk surgical procedures: potential benefits of the Leapfrog initiative. Surgery 130(3), 415-422. 2001.	Wrong intervention - all PCIs
Birkmeyer, John D. and Dimick, Justin B. Potential benefits of the new Leapfrog standards: effect of process and outcomes measures. Surgery 135(6), 569-575. 2004.	Wrong intervention - all PCIs
Brown, David L. Analysis of the institutional volume-outcome relations for balloon angioplasty and stenting in the stent era in California. American Heart Journal 146(6), 1071-1076. 2003.	Wrong intervention - all PCIs
Burton, K. R., Slack, R., Oldroyd, K. G., Pell, A. C. H., Flapan, A. D., Starkey, I. R., Eteiba, H., Jennings, K. P., Northcote, R. J., Hillis, W. Stewart, and Pell, J. P. Hospital volume of throughput and periprocedural and medium-term adverse events after percutaneous coronary intervention: retrospective cohort study of all 17,417 procedures undertaken in Scotland, 1997-2003. Heart 92(11), 1667-1672. 2006.	Wrong intervention - all PCIs
Carey, Joseph S., Danielsen, Beate, Junod, Forrest L., Rossiter, Stephen J., and Stabile, Bruce E. The California Cardiac Surgery and Intervention Project: evolution of a public reporting program. American Surgeon 72(10), 978-983. 2006	Wrong intervention - all PCIs
Epstein, Andrew J., Rathore, Saif S., Volpp, Kevin G. M., and Krumholz, Harlan M. Hospital percutaneous coronary intervention volume and patient mortality, 1998 to 2000: does the evidence support current procedure volume	Wrong intervention - all PCIs

Reference	Reason for exclusion
minimums? Journal of the American College of Cardiology 43(10), 1755-1762. 2004.	
Hannan, E. L., Racz, M., Ryan, T. J., McCallister, B. D., Johnson, L. W., Arani, D. T., Guerci, A. D., Sosa, J., and Topol, E. J. Coronary angioplasty volume-outcome relationships for hospitals and cardiologists. JAMA 277(11), 892-898. 1997.	Wrong intervention - all PCIs
Hannan, Edward L., Wu, Chuntao, Walford, Gary, King, Spencer B., Holmes, David R. J., Ambrose, John A., Sharma, Samin, Katz, Stanley, Clark, Luther T., and Jones, Robert H. Volume-outcome relationships for percutaneous coronary interventions in the stent era. Circulation 112(8), 1171-1179. 2005.	Narative review
Ho, V. Evolution of the volume-outcome relation for hospitals performing coronary angioplasty. Circulation 101(15), 1806-1811. 2000.	Data collected before cut-off and wrong intervention (all PCIs)
Ho, Vivian. Certificate of need, volume, and percutaneous transluminal coronary angioplasty outcomes. American Heart Journal 147(3), 442-448. 2004.	Wrong intervention - all PCIs
Jollis, J. G., Peterson, E. D., DeLong, E. R., Mark, D. B., Collins, S. R., Muhlbaier, L. H., and Pryor, D. B. The relation between the volume of coronary angioplasty procedures at hospitals treating Medicare beneficiaries and short-term mortality. New England Journal of Medicine 331(24), 1625-1629. 1994.	Data collected before cut-off and wrong intervention (all PCIs)
Jollis, J. G., Peterson, E. D., Nelson, C. L., Stafford, J. A., DeLong, E. R., Muhlbaier, L. H., and Mark, D. B. Relationship between physician and hospital coronary angioplasty volume and outcome in elderly patients. Circulation 95(11), 2485-2491. 1997.	Data collected before cut-off and wrong intervention (all PCIs)
Kenney, Kimberly M., Marzo, Mitchell C., Ondrasik, Nicholas R., and Wisenbaugh, Thomas. Percutaneous coronary intervention outcomes in a low-volume center: survival, stent thrombosis, and repeat revascularization. Circulation.Cardiovascular quality and outcomes 2(6), 671-677. 2009.	Population not specified. Wrong intervention - all PCIs
Kimmel, Stephen E., Sauer, William H., Brensinger, Colleen, Hirshfeld, John, Haber, Howard L., and Localio, A. Russell. Relationship between coronary angioplasty laboratory volume and outcomes after hospital discharge. American Heart Journal 143(5), 833-840. 2002.	Data collected before cut-off and wrong intervention (all PCIs)
Kuwabara, Hiroyo, Fushimi, Kiyohide, and Matsuda, Shinya. Relationship between hospital volume and outcomes following primary percutaneous coronary intervention in patients with acute myocardial infarction. Circulation Journal 75(5), 1107-1112. 2011.	Wrong population. Codes for inclusion relate to both STEMI and NSTEMI.
Lin, Herng Ching, Lee, Hsin Chien, and Chu, Chien Heng. The volume-outcome relationship of percutaneous coronary intervention: can current procedure volume minimums be applied to a developing country? American Heart Journal 155(3), 547-552. 2008.	Wrong intervention - all PCIs
Machino, T. O., Toyama, M., Obara, K., Takeyasu, N., Watanabe, S., and Aonuma, K. Effect of hospital case volume on treatment and in-hospital outcomes in patients undergoing percutaneous coronary intervention for acute myocardial infarction: Results from the Ibaraki Coronary Artery Disease Study (ICAS) registry. International heart journal 49(3), 249-260. 2008.	Wrong population – STEMI and NSTEMI
Maynard, C., Every, N. R., Chapko, M. K., and Ritchie, J. L. Institutional volumes and coronary angioplasty outcomes before and after the introduction of stenting. Effective Clinical Practice 2(3), 108-113. 1999.	Wrong intervention - all PCIs
Maynard, C., Every, N. R., Chapko, M. K., and Ritchie, J. L. Outcomes of coronary angioplasty procedures performed in rural hospitals. American Journal of Medicine 108(9), 710-713. 2000.	Wrong intervention - all PCIs
McGrath, P. D., Wennberg, D. E., Malenka, D. J., Kellett, M. A. J., Ryan, T. J. J., O'Meara, J. R., Bradley, W. A., Hearne, M. J., Hettleman, B., Robb, J. F.,	Wrong intervention - all PCIs

Reference	Reason for exclusion
Shubrooks, S., VerLee, P., Watkins, M. W., Lucas, F. L., and O'Connor, G. T. Operator volume and outcomes in 12,998 percutaneous coronary interventions. Northern New England Cardiovascular Disease Study Group. Journal of the American College of Cardiology 31(3), 570-576. 1998	
McGrath, P. D., Wennberg, D. E., Dickens, J. D. J., Siewers, A. E., Lucas, F. L., Malenka, D. J., Kellett, M. A. J., and Ryan, T. J. J. Relation between operator and hospital volume and outcomes following percutaneous coronary interventions in the era of the coronary stent. JAMA 284(24), 3139-3144. 2000.	Wrong intervention - all PCIs
Mukherjee, Debabrata, Wainess, Reid M., Dimick, Justin B., Cowan, John A., Rajagopalan, Sanjay, Chetcuti, Stanley, Grossman, Paul M., and Upchurch, Gilbert R. Variation in outcomes after percutaneous coronary intervention in the United States and predictors of periprocedural mortality. Cardiology 103(3), 143-147. 2005.	Wrong intervention - all PCIs
Ohtsuka Machino, Tomoko, Toyama, Masahiro, Obara, Kenichi, Takeyasu, Noriyuki, Watanabe, Shigeyuki, Aonuma, Kazutaka, and Ibaraki Coronary Artery Disease Study (ICAS) Registry. Effect of hospital case volume on treatment and in-hospital outcomes in patients undergoing percutaneous coronary intervention for acute myocardial infarction. Results from the Ibaraki Coronary Artery Disease Study (ICAS) Registry. International heart journal 49(3), 249-260. 2008.	Wrong population – STEMI and NSTEMI reported together
Spaulding, C. M., Joly, L. M., Rosenberg, A., Monchi, M., Weber, S. N., Dhainaut, J. F. A., and Carli, P. Immediate coronary angiography in survivors of out-of-hospital cardiac arrest. New England Journal of Medicine 336(23), 1629-1633. 1997.	Not relevant to question
Spaulding, Christian, Morice, Marie Claude, Lancelin, Bernard, El Haddad, Simon, Lepage, Eric, Bataille, Sophie, Tresca, Jean Pierre, Mouranche, Xavier, Fosse, Sandrine, Monchi, Mehran, de Vernejoul, Nikita, and CARDIO-ARIF, registry, I. Is the volume-outcome relation still an issue in the era of PCI with systematic stenting? Results of the greater Paris area PCI registry. European Heart Journal 27(9), 1054-1060. 2006.	Unclear population – contained 'emergency' PCI for AMI of more than 12 hours but less than 24 hours of duration if the operator considered emergency PCI necessary because of continuous ischaemia.
Tsuchihashi, Miyuki, Tsutsui, Hiroyuki, Tada, Hideo, Shihara, Miwako, Takeshita, Akira, Kono, Suminori, and Japanese Coronary Intervention Study (JCIS) Group. Volume-outcome relation for hospitals performing angioplasty for acute myocardial infarction: results from the Nationwide Japanese Registry. Circulation Journal 68(10), 887-891. 2004.	Wrong intervention - all PCIs
Vakili, Babak A., Brown, David L., and Coronary Angioplasty Reporting System of the New York State Department of Health. Relation of total annual coronary angioplasty volume of physicians and hospitals on outcomes of primary angioplasty for acute myocardial infarction (data from the 1995 Coronary Angioplasty Reporting System of the New York State Department of Health). American Journal of Cardiology 91(6), 726-728. 2003.	Mixed population – elective and emergent PCI
Vakili, B. A., Kaplan, R., and Brown, D. L. Volume-outcome relation for physicians and hospitals performing angioplasty for acute myocardial infarction in New York state. Circulation 104(18), 2171-2176. 2001.	Mixed population – elective and emergent PCI
Vakili, B. A., Kaplan, R., and Brown, D. L. Volume-outcome relation for physicians and hospitals performing angioplasty for acute myocardial infarction in New York state. Circulation 104(18), 2171-2176. 2001.	Unclear population and intervention
West, Robert M., Cattle, Brian A., Bouyssie, Marianne, Squire, Iain, de Belder, Mark, Fox, Keith A. A., Boyle, Roger, McLenachan, Jim M., Batin, Philip D., Greenwood, Darren C., and Gale, Chris P. Impact of hospital proportion and volume on primary percutaneous coronary intervention performance in	No outcomes of interest reported

Reference	Reason for exclusion
England and Wales. European Heart Journal 32(6), 706-711. 2011.	
Zahn, R., Vogt, A., Zeymer, U., Gitt, A. K., Seidl, K., Gottwik, M., Weber, M. A., Niederer, W., Modl, B., Engel, H. J., Tebbe, U., Senges, J., and Arbeitsgemeinschaft Leitender, Kardiologischer Krankenhausarzte. In-hospital time to treatment of patients with acute ST elevation myocardial infarction treated with primary angioplasty: determinants and outcome. Results from the registry of percutaneous coronary interventions in acute myocardial infarction of the Arbeitsgemeinschaft Leitender Kardiologischer Krankenhausarzte. Heart 91(8), 1041-1046. 2005.	Not relevant to question
Zahn, R., Gottwik, M., Hochadel, M., Senges, J., Zeymer, U., Vogt, A., Meinertz, T., Dietz, R., Hauptmann, K. E., Grube, E., Kerber, S., Sechtem, U., and Registry of Percutaneous Coronary Interventions of the Arbeitsgemeinschaft Leitende Kardiologische Krankenhausarzte (ALKK). Volume-outcome relation for contemporary percutaneous coronary interventions (PCI) in daily clinical practice: is it limited to high-risk patients? Results from the Registry of Percutaneous Coronary Interventions of the Arbeitsgemeinschaft Leitende Kardiologische Krankenhausarzte (ALKK). Heart 94(3), 329-335. 2008.	Wrong intervention - all PCIs

J.9 Pre-hospital versus in-hospital fibrinolysis

Reference	Reason for exclusion
P. W. Armstrong and WEST Steering Committee. A comparison of pharmacologic therapy with/without timely coronary intervention vs. primary percutaneous intervention early after ST-elevation myocardial infarction: the WEST (Which Early ST-elevation myocardial infarction Therapy) study. Eur.Heart J. 27 (13):1530-1538, 2006.	Wrong comparison – pooled in-hospital and pre-hospital data
H. R. Arntz. Prehospital thrombolysis in acute myocardial infarction. Thromb Res 103 Suppl 1:S91-S96, 2001.	Review
I. Bata, P. W. Armstrong, C. M. Westerhout, A. Travers, S. Sookram, E. Caine, J. Christenson, and R. C. Welsh. Time from first medical contact to reperfusion in ST elevation myocardial infarction: A Which Early ST Elevation Myocardial Infarction Therapy (WEST) substudy. Can.J.Cardiol. 25 (8):463-468, 2009.	Considers time to reperfusion, not pre-hospital versus in-hospital fribrinolysis
L. Belle, D. Savary, N. Dumonteil, M. Villaceque, S. Charpentier, L. Soulat, C. Loubeyre, P.-G. Steg, Y. Cottin, D. Miljkovic, and J. Puel. Are there good and bad responders to prehospital thrombolysis in the acute phase of myocardial infarction? OPTIMAL study rationale. Arch.Mal.Coeur Vaiss. 99 (9):823-827, 2006.	Not English language
BEPS Collaborative Group. Prehospital thrombolysis in acute myocardial infarction: the Belgian eminase prehospital study (BEPS). Eur.Heart J. 12 (9):965-967, 1991.	Not RCT
A. Boland, Y. Dundar, A. Bagust, A. Haycox, R. Hill, R. M. Mota, T. Walley, and R. Dickson. Early thrombolysis for the treatment of acute myocardial infarction: a systematic review and economic evaluation (Provisional abstract). Health.Technol.Assess. 7 (15):1-136, 2003.	Wrong comparison – considers drugs used in pre-hospital fibrinolysis
M. J. M. Bouten and M. L. Simoons. Strategies for pre-hospital thrombolysis: An overview. Eur.Heart J. 12 (SUPPL. G):39-42, 1991.	Review
D. B. Brieger, K.-H. Mak, H. D. White, N. S. Kleiman, D. P. Miller, A. Vahanian, A. M. Ross, R. M. Califf, and E. J. Topol. Benefit of early sustained reperfusion in patients with prior myocardial infarction (The GUSTO-I Trial). Am.J.Cardiol. 81 (3):282-287, 1998.	Wrong comparison
J. Brugemann, J. van der Meer, P. A. de Graeff, L. H. Takens, and K. I. Lie. Logistical problems in prehospital thrombolysis. Eur.Heart J. 13 (6):787-788, 1992.	None of the specified outcomes were reported in trial

Reference	Reason for exclusion
C. P. Cannon, A. J. Sayah, and R. M. Walls. ER TIMI-19: testing the reality of prehospital thrombolysis. J.Emerg.Med. 19 (3 Suppl):21S-25S, 2000.	Not RCT
C. P. Cannon and M. Smith. Advances in alliteration in acute myocardial infarction: From 'Time to treatment' to 'Onset to opening'. Journal of Thrombosis and Thrombolysis 6 (1):5-7, 1998.	Review
A. D. Castaigne, C. Hervé, A. M. Duval-Moulin, M. Gaillard, J. L. Dubois-Randé, and D. Lellouche. Pre-hospital thrombolysis, is it useful? Eur.Heart J. 11 Suppl F:43-47, 1990.	Review article
P. A. Castillo, C. S. Palmer, M. T. Halpern, E. J. Hatziandreu, and B. J. Gersh. Cost-effectiveness of thrombolytic therapy for acute myocardial infarction. Ann.Pharmacother. 31 (5):596-603, 1997.	Cost-effectiveness analysis with incorrect comparison
P. Chareonthaitawee, R. J. Gibbons, R. S. Roberts, T. F. Christian, R. Burns, and S. Yusuf. The impact of time to thrombolytic treatment on outcome in patients with acute myocardial infarction. Heart 84 (2):142-148, 2000.	Considered time to reperfusion, not relevant comparison
S. Coccolini, G. Berti, S. Bosi, M. Pretolani, and G. Tumiotto. Prehospital thrombolysis in rural emergency room and subsequent transport to a coronary care unit: Ravenna Myocardial Infarction (RaMI) trial. Int.J.Cardiol. 49 Suppl:S47-S58, 1995.	Wrong comparison - emergency room versus coronary care unit
J. L. Cox, E. Lee, A. Langer, P. W. Armstrong, and C. D. Naylor. Time to treatment with thrombolytic therapy: determinants and effect on short-term nonfatal outcomes of acute myocardial infarction. Canadian GUSTO Investigators. Global Utilization of Streptokinase and + PA for Occluded Coronary Arteries. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne 156 (4):497-505, 1997.	Secondary cohort analysis
Joseph S. Crowder, Michael W. Hubble, Sanjay Gandhi, Henderson McGinnis, Stacie Zelman, William Bozeman, and James Winslow. Prehospital Administration of Tenecteplase for ST-segment Elevation Myocardial Infarction in a Rural EMS System. Prehosp.Emerg.Care 15 (4):499-505, 2011.	Retrospective case series
J. E. Dalen, J. M. Gore, E. Braunwald, J. Borer, R. J. Goldberg, E. R. Passamani, S. Forman, and G. Knatterud. Six- and twelve-month follow-up of the phase I Thrombolysis in Myocardial Infarction (TIMI) trial. Am.J.Cardiol. 62 (4):179-185, 1988.	Wrong comparison (recombinant tissue plasminogen activator (rt-PA) versus streptokinase)
P. Dussoix, O. Reuille, V. Verin, J. M. Gaspoz, and P. F. Unger. Time savings with prehospital thrombolysis in an urban area. Eur.J.Emerg.Med. 10 (1):2-5, 2003.	Reported on time saving in pre-hospital fibrinolysis – no relevant outcomes reported
R. Gatenby, K. Lyons, T. Stewart, J. Taylor, J. Scott, G. Payne, J. Reid, D. Glass, D. Carroll, A. McLean, G. Mennie, F. Mair, D. Barclay, M. McCrone, K. Morton, N. Kennedy, J. Anderson, D. Innes, and D. Scott. Feasibility, safety, and efficacy of domiciliary thrombolysis by general practitioners: Grampian region early anistreplase trial. Br.Med.J. 305 (6853):548-553, 1992.	Not STEMI population
R. J. Goldberg, M. Mooradd, J. H. Gurwitz, W. J. Rogers, W. J. French, H. V. Barron, and J. M. Gore. Impact of time to treatment with tissue plasminogen activator on morbidity and mortality following acute myocardial infarction (The second National Registry of Myocardial Infarction). Am.J.Cardiol. 82 (3):259-264, 1998.	Retrospective registry data
V. Gomes, J. Trigo, P. Gago, J. Mimoso, R. Faria, N. Marques, W. Santos, and V. Brandao. Emergency department bypass reduces the time to reperfusion therapy. Eur.Heart J. 30:337, 2009.	Abstract
E. W. M. Grijseels, M. J. M. Bouten, T. Lenderink, J. W. Deckers, A. W. Hoes, J. A. M. Hartman, Dde Van, and M. L. Simoons. Pre-hospital thrombolytic therapy with either alteplase or streptokinase. Practical applications, complications and	Wrong comparison – pre-hospital alteplase versus pre-hospital streptokinase

Reference	Reason for exclusion
long-term results in 529 patients. Eur.Heart J. 16 (12):1833-1838, 1995.	
D. G. Julian. Time as a factor in thrombolytic therapy. Eur.Heart J. 11 Suppl F:53-55, 1990.	Review article
J. W. Kennedy and W. D. Weaver. Potential use of thrombolytic therapy before hospitalization. Am.J.Cardiol. 64 (2):8A-26A, 1989.	Phase 1 results of MITI trial
N. S. Kleiman, H. D. White, E. M. Ohman, A. M. Ross, L. H. Woodlief, R. M. Califf, D. R. Holmes, E. Bates, M. Pfisterer, and A. Vahanian. Mortality within 24 hours of thrombolysis for myocardial infarction. The importance of early reperfusion. The GUSTO Investigators, Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries. Circulation 90 (6):2658-2665, 1994.	Considered mortality within 24 hours of fibrinolysis; not relevant comparison
J. Koefoed-Nielsen, E. F. Christensen, H. Melchiorsen, and A. Foldspang. Acute myocardial infarction: does pre-hospital treatment increase survival? Eur.J.Emerg.Med. 9 (3):210-216, 2002.	Not RCT
C. T. Lambrew, L. J. Bowlby, W. J. Rogers, N. C. Chandra, and Weaver W. Douglas. Factors influencing the time to thrombolysis in acute myocardial infarction. Arch.Intern.Med. 157 (22):2577-2582, 1997.	Identifies factors that delay fibrinolytic treatment
A. Leizorovicz, M. C. Haugh, C. Mercier, and J.-P. Boissel. Pre-hospital and hospital time delays in thrombolytic treatment in patients with suspected acute myocardial infarction. Analysis of data from the EMIP study. Eur.Heart J. 18 (2):248-253, 1997.	Considers time delay information only. No relevant outcomes reported
J. A. de Lemos, E. M. Antman, R. P. Giugliano, D. A. Morrow, C. H. McCabe, S. S. Cutler, A. Charlesworth, R. Schröder, and E. Braunwald. Comparison of a 60- versus 90-minute determination of ST-segment resolution after thrombolytic therapy for acute myocardial infarction. In TIME-II Investigators. Intravenous nPA for Treatment of Infarcting Myocardium Early-II. Am.J.Cardiol. 86 (11):1235-7, A5, 2000..	Wrong comparison
B. McAleer, B. Ruane, E. Burke, M. Cathcart, A. Costello, G. Dalton, J. R. Williams, and M. P. Varma. Prehospital thrombolysis in a rural community: short- and long-term survival. Cardiovasc Drugs Ther 6 (4):369-372, 1992.	Open allocation; participants not randomly allocated
C. Maynard, R. Althouse, M. Olsufka, J. L. Ritchie, K. B. Davis, and J. W. Kennedy. Early versus late hospital arrival for acute myocardial infarction in the western Washington thrombolytic therapy trials. Am.J.Cardiol. 63 (18):1296-1300, 1989.	Wrong comparison
Laurie J. Morrison, Valeria E. Rac, James M. Bowen, Brian Schwartz, Tyrone Perreira, Welson Ryan, Cathy Zahn, Rishab Chadha, Alan Craig, Daria O'Reilly, and Ron Goeree. Prehospital evaluation and economic analysis of different coronary syndrome treatment strategies--PREDICT--rationale, development and implementation. BMC Emergency Medicine 11:4, 2011.	Systematic review that didn't meet protocol requirements
David A. Morrow, Elliott M. Antman, Assaad Sayah, Kristin C. Schuhwerk, Robert P. Giugliano, James A. deLemos, Michael Waller, Sidney A. Cohen, Donald G. Rosenberg, Sally S. Cutler, Carolyn H. McCabe, Ron M. Walls, and Eugene Braunwald. Evaluation of the time saved by prehospital initiation of reteplase for ST-elevation myocardial infarction: results of The Early Retavase-Thrombolysis in Myocardial Infarction (ER-TIMI) 19 trial. J.Am.Coll.Cardiol. 40 (1):71-77, 2002.	Feasibility study – retavase given at different time points
L. K. Newby, W. R. Rutsch, R. M. Califf, M. L. Simoons, P. E. Aylward, P. W. Armstrong, L. H. Woodlief, K. L. Lee, E. J. Topol, and F. Van de Werf. Time from symptom onset to treatment and outcomes after thrombolytic therapy. GUSTO-1 Investigators. J.Am.Coll.Cardiol. 27 (7):1646-1655, 1996.	Secondary cohort analysis from GUSTO on time to fibrinolytic treatment
P. Ohlmann, P. Reydel, L. Jacquemin, F. Adnet, O. Wolf, J.-C. Bartier, A. Weiss, F. Lapostolle, C. Gaultier, E. Salengro, H. Benamer, P. Guyon, B. Chevalier, S. Catan, P. Ecollan, T. Chouihed, M. Angioi, M. Zupan, F. Bronner, P. Bareiss, G.	Wrong intervention

Reference	Reason for exclusion
Steg, G. Montalescot, J.-P. Monassier, and O. Morel. Prehospital abciximab in st-segment elevation myocardial infarction results of the randomized, double-blind MISTRAL study. Circ.Cardiovasc.Interventions 5 (1):69-76, 2012.	
E. Rapaport. Early versus late opening of coronary arteries: the effect of timing. Clinical Cardiology 13 (8 Suppl 8):VIII18-VIII22, 1990.	Review article
J. Rawles. Halving of mortality at 1 year by domiciliary thrombolysis in the Grampian Region Early Anistreplase Trial (GREAT). J.Am.Coll.Cardiol. 23 (1):1-5, 1994.	Inclusion criteria did not include ECG diagnosis – mixed population
Alyson M. Smith, Pamela J. Hardy, David A. Sandler, and Justin Cooke. Paramedic decision making: prehospital thrombolysis and beyond. Emergency Medicine Journal 28 (8):700-702, 2011.	Observational data
S. A. Spinler and P. A. Mikhail. Prehospital-initiated thrombolysis. Ann.Pharmacother. 31 (11):1339-1346, 1997.	Review

J.10 Use of antithrombin as an adjunct to fibrinolysis

Exclusion List	Reason for exclusion
Armstrong PW, et al. Efficacy and safety of unfractionated heparin versus enoxaparin: a pooled analysis of ASSENT-3 and -3 PLUS data CMAJ. 2006; 174(10):1421-6.	Not RCT
Bates ER. Anticoagulant therapy in acute coronary syndromes. Future Cardiol. 2007; 3(3):301-8.	Not RCT
Bogaty P, et al. Routine invasive management after fibrinolysis in patients with ST-elevation myocardial infarction: A systematic review of randomized clinical trials. BMC Cardiovasc Disord. 2011; 11:34	Not question of interest
Bøhmer E, et al. Health and cost consequences of early versus late invasive strategy after thrombolysis for acute myocardial infarction. Eur J Cardiovasc Prev Rehabil. 2011; 18(5):717-23	Not question of interest
Brouwer MA, et al. Influence of early prehospital thrombolysis on mortality and event-free survival (the Myocardial Infarction Triage and Intervention [MITI] Randomized Trial). MITI Project Investigators. Am J Cardiol. 1996; 78(5):497-502.	Patients randomised to pre-hospital versus in-hospital fibrinolysis
Cannon CP, et al. ER TIMI-19: testing the reality of prehospital thrombolysis. J Emerg Med. 2000; 19(3 Suppl):21S-25S.	Not question of interest
Clever YP et al. Long-term follow-up of early versus delayed invasive approach after fibrinolysis in acute myocardial infarction. Circ Cardiovasc Interv. 2011; 4(4):342-8.	Not question of interest
Crowder JS et al. Prehospital Administration of Tenecteplase for ST-segment Elevation Myocardial Infarction in a Rural EMS System. Prehosp Emerg Care. 2011; 15(4):499-505	Not RCT
Danchin N et al. Pre-hospital thrombolysis in perspective. Eur Heart J. 2008; 29(23):2835-42.	Not RCT
Dawson S et al. Guidelines for pre-hospital administration of fibrinolytic therapy by New Zealand general practitioners. N Z Med J. 2004; 117(1197):U958.	Not RCT
Dussoix P et al. Time savings with prehospital thrombolysis in an urban area. Eur J Emerg Med. 2003; 10(1):2-5.	Patients randomised to pre-hospital versus in-hospital fibrinolysis or PPCI
Eikelboom JW, et al. Unfractionated and low-molecular-weight heparin as adjuncts to thrombolysis in aspirin-treated patients with ST-elevation acute	Not RCT

Exclusion List	Reason for exclusion
myocardial infarction: A meta-analysis of the randomized trials. Circulation. 2005; 112(25):3855-67.	
Ferreira-Gonzalez I, et al. Composite endpoints in clinical trials. Rev Esp Cardiol. 2008; 61(3):283-90.	Not question of interest
Gatenby R, et al. Feasibility, safety, and efficacy of domiciliary thrombolysis by general practitioners: Grampian region early anistreplase trial. BMJ. 1992; 305(6853):548-53.	Not question of interest; anistreplase was used
Hermanides RS, et al. Net clinical benefit of prehospital glycoprotein IIb/IIIa inhibitors in patients with ST-elevation myocardial infarction and high risk of bleeding: effect of tirofiban in patients at high risk of bleeding using CRUSADE bleeding score. Journal of invasive cardiology: 2012; 24: 84-89.	Not RCT
Herve C, Castaigne A, Jan F. Pre-hospital thrombolysis in myocardial infarction. Therapie 1988; 80	Non-English language
Horne S, et al. The impact of pre-hospital thrombolytic treatment on varction rates: analysis of the Myocardial Infarction National Audit Project (MINAP). Heart 2009; 95(7):559-63.	Not RCT
Huber K et al. Pre-hospital reperfusion therapy: A strategy to improve therapeutic outcome in patients with ST-elevation myocardial infarction. Eur Heart J. 2005; 26(19):2063-74.	Not RCT
Kennedy JW, Weaver WD. Potential use of thrombolytic therapy before hospitalization. Am J Cardiol. 1989; 64(2):8A-11A; discussion 24A-26A.	Not question of interest
Koefoed-Nielsen J, et al. Acute myocardial infarction: does pre-hospital treatment increase survival? Eur J Emerg Med. 2002; 9(3):210-6.	Not RCT
Koeth O, et al. Primary PCI and thromboysis in survivors of prehospital resuscitation. Eur Heart J. 2009; 30:693	Not question of interest
Morrison LJ, et al. Mortality and prehospital thrombolysis for acute myocardial infarction: A meta-analysis. JAMA. 2000; 283(20):2686-92.	Not RCT
Morrow DA, et al. One-year outcomes after a strategy using enoxaparin vs. unfractionated heparin in patients undergoing fibrinolysis for ST-segment elevation myocardial infarction: 1-year results of the ExTRACT-TIMI 25 Trial. Eur Heart J. 2010; 31(17):2097-102.	Not question of interest
Rubboli A. Efficacy and safety of low-molecular-weight heparins as an adjunct to thrombolysis in acute ST-elevation myocardial infarction. Curr Cardiol Rev. 2008; 4(1):63-71.	Not RCT
Rubboli A, et al. Low-molecular-weight heparins in conjunction with thrombolysis for ST-elevation acute myocardial infarction: A critical review of the literature. Cardiology. 2007; 107(2):132-9.	Not RCT
Smith AM, et al. Paramedic decision making: prehospital thrombolysis and beyond. Emerg Med J. 2011; 28(8):700-2.	Not RCT
Svensson L et al. Safety and delay time in prehospital thrombolysis of acute myocardial infarction in urban and rural areas in Sweden. Am J Emerg Med. 2003; 21(4):263-70.	All patients received pre-hospital heparin immediately before pre-hospital fibrinolysis
The Task Force on the Management of Acute Myocardial Infarction of the European Society of Cardiology. Acute myocardial infarction: pre-hospital and in-hospital management. Eur Heart J. 1996; 17(1):43-63.	Not RCT
Woollard M. Early thrombolysis: Time to change? A discussion paper. Journal of Emergency Primary Health Care: 2005; 3.	Not RCT

J.11 Rescue PCI

Exclusion List	Reason for exclusion
After thrombolysis for myocardial infarction, early routine angiography reduces cardiac events and death compared with conservative treatment. Evidence-Based Healthcare and Public Health.2005; 9:127-8	Not question of interest
Outcome of attempted rescue coronary angioplasty after failed thrombolysis for acute myocardial infarction. The CORAMI Study Group. Cohort of Rescue Angioplasty in Myocardial Infarction. Am J Cardiol. 1994; 74(2):172-4.	Not RCT
SWIFT trial of delayed elective intervention v conservative treatment after thrombolysis with anistreplase in acute myocardial infarction. SWIFT (Should We Intervene Following Thrombolysis?) Trial Study Group. BMJ. 1991; 302(6776):555-60.	Not question of interest
Barbash GI, Birnbaum Y, Bogaerts K, Hudson M, Lesaffre E, Fu Y, Goodman S, Houbracken K, Munsters K, Granger CB, Pieper K, Califf RM, Topol EJ, Van De Werf F. Treatment of reinfarction after thrombolytic therapy for acute myocardial infarction: an analysis of outcome and treatment choices in the global utilization of streptokinase and tissue plasminogen activator for occluded coronary arteries (gusto I) and assessment of the safety of a new thrombolytic (assent 2) studies. Circulation. 2001; 103(7):954-60.	Not RCT
Barbash GI, Roth A, Hod H, Modan M, Miller HI, Rath S, Zahav YH, Keren G, Motro M, Shachar A, et al. Randomized controlled trial of late in-hospital angiography and angioplasty versus conservative management after treatment with recombinant tissue-type plasminogen activator in acute myocardial infarction. Am J Cardiol. 1990; 66(5):538-45.	Not question of interest
Baron SJ, Giugliano RP. Effectiveness and safety of percutaneous coronary intervention after fibrinolytic therapy for ST-segment elevation acute myocardial infarction. Am J Cardiol. 2011; 107(7):1001-9.	Not RCT
Bonnet JL, Bory M, Jau P, Joly P, D'Houdain F, Habib G. Immediate or delayed coronary angioplasty after intravenous thrombolytic therapy for acute myocardial infarction. A prospective study. Original: ANGIOPLASTIE CORONAIRE PRECOCE OU DIFFEREE APRES THROMBOLYSE INTRAVEINEUSE POUR INFARCTUS DU MYOCARDE. ETUDE PROSPECTIVE. Archives Des Maladies Du Coeur Et Des Vaisseaux. 1990; 83(9):1375-1379.	Non-English language
Borgia F, Goodman SG, Halvorsen S, Cantor WJ, Piscione F, Le May MR, Fernández-Avilés F, Sánchez PL, Dimopoulos K, Scheller B, Armstrong PW, Di Mario C. Early routine percutaneous coronary intervention after fibrinolysis vs. standard therapy in ST-segment elevation myocardial infarction: a meta-analysis. Eur Heart J. 2010; 31(17):2156-69.	Not RCT
Buller CE, Welsh RC, Westerhout CM, Webb JG, O'Neill B, Gallo R, Armstrong PW. Guideline adjudicated fibrinolytic failure: incidence, findings, and management in a contemporary clinical trial. Am Heart J. 2008; 155(1):121-7	Not question of interest; No comparator
Cantor WJ, Brunet F, Ziegler CP, Kiss A, Morrison LJ. Immediate angioplasty after thrombolysis: a systematic review. CMAJ. 2005; 173(12):1473-81.	Not RCT
Cantor WJ, Burnstein J, Choi R, Heffernan M, Dzavik V, Lazzam C, Duic M, Fitchett D, Tan M, Wawrzyniak J, Kassam S, Dhingra S, Morrison LJ, Langer A, Goodman SG. Transfer for urgent percutaneous coronary intervention early after thrombolysis for ST-elevation myocardial infarction: the TRANSFER-AMI pilot feasibility study. Can J Cardiol. 2006; 22(13):1121-6.	Not question of interest
Cantor WJ, Fitchett D, Borgundvaag B, Ducas J, Heffernan M, Cohen EA, Morrison LJ, Langer A, Dzavik V, Mehta SR, Lazzam C, Schwartz B, Casanova A, Goodman SG; TRANSFER-AMI Trial Investigators. Routine early angioplasty after fibrinolysis for acute myocardial infarction. N Engl J Med. 2009; 360(26):2705-18.	Not question of interest

Exclusion List	Reason for exclusion
Cantor WJ, Kaplan AL, Velianou JL, Sketch MH Jr, Barsness GW, Berger PB, Ohman EM. Effectiveness and safety of abciximab after failed thrombolytic therapy. Am J Cardiol. 2001; 87(4):439-42, A4.	Not RCT
Collet JP, Montalescot G, Le May M, Borentain M, Gershlick A. Percutaneous coronary intervention after fibrinolysis: a multiple meta-analyses approach according to the type of strategy. J Am Coll Cardiol. 2006; 48(7):1326-35	Not RCT
Czarnecki A, Welsh RC, Yan RT, DeYoung JP, Gallo R, Rose B et al. Reperfusion strategies and outcomes of ST-segment elevation myocardial infarction patients in Canada: observations from the Global Registry of Acute Coronary Events (GRACE) and the Canadian Registry of Acute Coronary Events (CANRACE). Canadian Journal of Cardiology. 2012; 28(1):40-47.	Observational data
Dakik HA, Kleiman NS, Farmer JA, He ZX, Wendt JA, Pratt CM, Verani MS, Mahmarian JJ. Intensive medical therapy versus coronary angioplasty for suppression of myocardial ischemia in survivors of acute myocardial infarction: a prospective, randomized pilot study. Circulation. 1998; 98(19):2017-23.	Not question of interest
Desch S, Eitel I, Rahimi K, de Waha S, Schuler G, Thiele H. Timing of invasive treatment after fibrinolysis in ST elevation myocardial infarction--a meta-analysis of immediate or early routine versus deferred or ischemia-guided randomised controlled trials. Heart. 2010; 96(21):1695-702	Not RCT
Di Mario C, Dudek D, Piscione F, Mielecki W, Savonitto S, Murena E, Dimopoulos K, Manari A, Gaspardone A, Ochala A, Zmudka K, Bolognese L, Steg PG, Flather M; CARESS-in-AMI (Combined Abciximab RE-teplase Stent Study in Acute Myocardial Infarction) Investigators. Immediate angioplasty versus standard therapy with rescue angioplasty after thrombolysis in the Combined Abciximab REteplase Stent Study in Acute Myocardial Infarction (CARESS-in-AMI): an open, prospective, randomised, multicentre trial. Lancet. 2008; 371(9612):559-68.	Not question of interest
Di Pasquale P, Cannizzaro S, Scalzo S, Maringhini G, Vitrano GM, Giubilato A, Giambanco F, Sarullo FM, Paterna S. Safety and tolerability of abciximab in patients with acute myocardial infarction and failed thrombolysis. Int J Cardiol. 2003; 92(2-3):265-70	Abciximab versus placebo
Di Pasquale P, Sarullo FM, Cannizzaro S, Vitrano MG, Giubilato A, Scalzo S, Giambanco F, Paterna S. Increased reperfusion by glycoprotein IIb/IIIa receptor antagonist administration in case of unsuccessful and failed thrombolysis in patients with acute myocardial infarction: a pilot study. Ital Heart J. 2001; 2(10):751-6.	Not question of interest
Di Pasquale P, Sarullo FM, Cannizzaro S, Vitrano MG, Vincenzo B, Giambanco F, Scandurra A, Calcaterra G, and Paterna S. Effects of administration of glycoprotein IIb/IIIa receptor antagonists in patients with failed thrombolysis: A pilot study. Clinical Drug Investigation.2001; 21:545-3	Not question of interest
D'Souza SP, Mamas MA, Fraser DG, Fath-Ordoubadi F. Routine early coronary angioplasty versus ischaemia-guided angioplasty after thrombolysis in acute ST-elevation myocardial infarction: a meta-analysis. Eur Heart J. 2011; 32(8):972-82.	Not RCT
Edmond JJ, French JK, Aylward PE, Wong CK, Stewart RA, Williams BF, De Pasquale CG, O'connell RL, Van den Berg K, Van de Werf FJ, Simes RJ, White HD; for the HERO-2 Investigators. Variations in the use of emergency PCI for the treatment of re-infarction following intravenous fibrinolytic therapy: impact on outcomes in HERO-2. Eur Heart J. 2007; 28(12):1418-24	Not question of interest
Ellis SG, Lincoff AM, George BS, Kereiakes DJ, Ohman EM, Krucoff MW, Califf RM, Topol EJ. Randomized evaluation of coronary angioplasty for early TIMI 2 flow after thrombolytic therapy for the treatment of acute myocardial infarction: a new look at an old study. The Thrombolysis and Angioplasty in	Post-hoc subgroup analysis of a study published < 1990 (Enrolment ended October

Exclusion List	Reason for exclusion
Myocardial Infarction (TAMI) Study Group. Coron Artery Dis. 1994; 5(7):611-5.	1986)
Ellis SG, Van de Werf F, Ribeiro-daSilva E, Topol EJ. Present status of rescue coronary angioplasty: current polarization of opinion and randomized trials. J Am Coll Cardiol. 1992; 19(3):681-6.	Not RCT
Feit F, Mueller HS, Braunwald E, Ross R, Hodges M, Herman MV, Knatterud GL. Thrombolysis in Myocardial Infarction (TIMI) phase II trial: outcome comparison of a 'conservative strategy' in community versus tertiary hospitals. The TIMI Research Group. J Am Coll Cardiol. 1990; 16(7):1529-34.	Wrong comparators
Geltman EM. Conservative management after thrombolysis: the strategy of choice. J Am Coll Cardiol. 1990; 16(7):1535-7.	Not RCT
Gibson CM, Cannon CP, Greene RM, Sequeira RF, Margorien RD, Leya F, Diver DJ, Baim DS, Braunwald E. Rescue angioplasty in the thrombolysis in myocardial infarction (TIMI) 4 trial. Am J Cardiol. 1997; 80(1):21-6.	Not RCT
Gibson CM, Murphy SA, Montalescot G, Morrow DA, Ardissino D, Cohen M, Gulba DC, Kracoff OH, Lewis BS, Roguin N, Antman EM, Braunwald E; ExTRACT-TIMI 25 Investigators. Percutaneous coronary intervention in patients receiving enoxaparin or unfractionated heparin after fibrinolytic therapy for ST-segment elevation myocardial infarction in the ExTRACT-TIMI 25 trial. J Am Coll Cardiol. 200; 49(23):2238-46.	Not question of interest
Gill S, Haastrup B, Haghfelt T, Dellborg M, Clemmensen PM. Early reperfusion assessment and repeated thrombolysis in acute myocardial infarction estimated by repeated standard electrocardiography. A randomised, double-blind, placebo-controlled pilot study. Cardiology. 2000; 94(1):58-65.	No outcomes of interest
Granger CB, Califf RM, Young S, Candela R, Samaha J, Worley S, Kereiakes DJ, Topol EJ. Outcome of patients with diabetes mellitus and acute myocardial infarction treated with thrombolytic agents. The Thrombolysis and Angioplasty in Myocardial Infarction (TAMI) Study Group. J Am Coll Cardiol. 1993; 21(4):920-5.	Not RCT
Gulba DC, Merx, W., Kochs, M., Altstidel, H., Sabin, G., and R, A.M. The 'planned rescue PTCA' after thrombolytic therapy of acute heart attack shortens the duration of reperfusion, but is not connected with an extra PTCA risk. Zeitschrift Fur Kardiologie. 1998; 87(Suppl. 1):208.	Non-English language
Harrington RA, Califf RM. The role of angioplasty after failed thrombolysis for acute myocardial infarction. Coron Artery Dis. 1994; 5(5):392-8.	Not RCT
Jariwala P, Chandra S. Diagnosis and management of failed thrombolytic therapy for acute myocardial infarction. Indian Heart J. 2010; 62(1):21-8.	Not RCT
Jovell AJ, Lau J, Berkey C, Kupelnick B, and Chalmers TC. Early angiography and angioplasty following thrombolytic therapy of acute myocardial infarction. Metaanalysis of the randomized control trials. Online Journal of Current Clinical Trials. 1993;Doc No 67: 3714	Not RCT
Kunadian B, Vijayalakshmi K, Dunning J, Sutton A, de Belder MA. Towards an understanding of the role of rescue angioplasty for failed fibrinolysis: comparison of the MERLIN, RESCUE and REACT trials. J Invasive Cardiol. 2007; 19(9):359-68	Not RCT
La Vecchia L, Favero L, Martini M, Vincenzi P, Rubboli A, Ottani F, Bottero M, Fontanelli A. Systematic coronary stenting after failed thrombolysis in high-risk patients with acute myocardial infarction: procedural results and long-term follow-up. Coron Artery Dis. 2003; 14(5):395-400.	No comparator
Madsen JK, Grande P, Saunamäki K, Thayssen P, Kassis E, Eriksen U, Rasmussen K, Haunsø S, Nielsen TT, Haghfelt T, Fritz-Hansen P, Hjelms E, Paulsen PK, Alstrup P, Arendrup H, Niebuhr-Jørgensen U, Andersen LI. Danish multicenter randomized study of invasive versus conservative treatment in patients with	Not question of interest

Exclusion List	Reason for exclusion
inducible ischemia after thrombolysis in acute myocardial infarction (DANAMI). DANish trial in Acute Myocardial Infarction. Circulation. 1997; 96(3):748-55.	
Madsen JK, Nielsen TT, Grande P, Eriksen UH, Saunamäki K, Thayssen P, Kassis E, Rasmussen K, Haunsø S, Haghfelt T, Fritz-Hansen P, Hjelms E, Paulsen PK, Alstrup P, Arendrup H, Niebuhr-Jørgensen U, Andersen LI; DANAMI study group. Revascularization compared to medical treatment in patients with silent vs. symptomatic residual ischemia after thrombolyzed myocardial infarction--the DANAMI study. Cardiology. 2007; 108(4):243-51.	Not question of interest
Mendoza CE, Bhatt MR, Virani S, Schob AH, Levine S, Ferreira AC, de Marchena E. Management of failed thrombolysis after acute myocardial infarction: an overview of current treatment options. Int J Cardiol. 2007; 114(3):291-9	Not RCT
Miller JM, Smalling R, Ohman EM, Bode C, Betriu A, Kleiman NS, Schildcrout JS, Bastos E, Topol EJ, Califf RM. Effectiveness of early coronary angioplasty and abciximab for failed thrombolysis (reteplase or alteplase) during acute myocardial infarction (results from the GUSTO-III trial). Global Use of Strategies To Open occluded coronary arteries. Am J Cardiol. 1999; 84(7):779-84.	Abciximab versus placebo
Ozbek C, Dyckmans J, Sen S, Rettig G, Isringhaus H, Hammer B, and SH. Invasive vs conservative procedures after streptokinase therapy (SK) of acute myocardial infarction (AMI); Results of a randomised study (SIAM). Zeitschrift Fur Kardiologie. 1990; 79 Suppl 1:53.	Non-English language
Patel TN, Bavry AA, Kumbhani DJ, Ellis SG. A meta-analysis of randomized trials of rescue percutaneous coronary intervention after failed fibrinolysis. Am J Cardiol. 2006; 97(12):1685-90	Not RCT (used for quality assessment)
Rebuzzi AG, Niccoli G, Ferrante G. Acute myocardial infarction interventional procedures: primary percutaneous coronary intervention versus facilitated percutaneous coronary intervention, rescue angioplasty, rescue excimer laser. Minerva Cardioangiol. 2007; 55(1):73-82.	Not RCT
Rekik S, Mnif S, Sahnoun M, Krichen S, Charfeddine H, Trabelsi I, Triki F, Hentati M, Kammoun S. Total absence of ST-segment resolution after failed thrombolysis is correlated with unfavorable short- and long-term outcomes despite successful rescue angioplasty. J Electrocardiol. 2009; 42(1):73-8	No comparator
Rogers WJ, Baim DS, Gore JM, Brown BG, Roberts R, Williams DO, Chesebro JH, Babb JD, Sheehan FH, Wackers FJ, et al. Comparison of immediate invasive, delayed invasive, and conservative strategies after tissue-type plasminogen activator. Results of the Thrombolysis in Myocardial Infarction (TIMI) Phase II-A trial. Circulation. 1990; 81(5):1457-76.	Not question of interest
Ross AM, Lundergan CF, Rohrbeck SC, Boyle DH, van den Brand M, Buller CH, Holmes DR Jr, Reiner JS. Rescue angioplasty after failed thrombolysis: technical and clinical outcomes in a large thrombolysis trial. GUSTO-1 Angiographic Investigators. Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries. J Am Coll Cardiol. 1998; 31(7):1511-7.	Patients not randomised to rescue PCI versus conservative therapy
Ruocco NA Jr, Bergelson BA, Jacobs AK, Frederick MM, Faxon DP, Ryan TJ. Invasive versus conservative strategy after thrombolytic therapy for acute myocardial infarction in patients with antecedent angina. A report from Thrombolysis in Myocardial Infarction Phase II (TIMI II). J Am Coll Cardiol. 1992; 20(7):1445-51	Not question of interest
Sarullo FM, Schicchi R, Schiro M, Americo L, Bonni G, Faraone N, Di PP, Castello A, Mauri F. Safety and efficacy of rescue thrombolysis in acute myocardial infarction. Italian Heart Journal Supplement. 2000; 1(1):81-87.	Non-English language
Scheller B, Hennen B, Hammer B, Walle J, Hofer C, Hilpert V, Winter H, Nickenig G, Böhm M; SIAM III Study Group. Beneficial effects of immediate	Not question of interest

Exclusion List	Reason for exclusion
stenting after thrombolysis in acute myocardial infarction. J Am Coll Cardiol. 2003; 42(4):634-41.	
Shavelle DM, Salami A, Abdelkarim M, French WJ, Shook TL, Mayeda GS, Burstein S, Matthews RV. Rescue percutaneous coronary intervention for failed thrombolysis. Catheter Cardiovasc Interv. 2006; 67(2):214-20.	Not RCT
Sohal M, Foo F, Sirker A, Rajani R, Khawaja MZ, Pegge N, Hatrick R, Kneale B, Signy M, Holmberg S, de Belder A, Hildick-Smith D. Rescue angioplasty for failed fibrinolysis--long-term follow-up of a large cohort. Catheter Cardiovasc Interv. 2011; 77(5):599-604.	Not RCT
Steg PG, Francois L, Iung B, Himbert D, Aubry P, Charlier P, Benamer H, Feldman LJ, Juliard JM. Long-term clinical outcomes after rescue angioplasty are not different from those of successful thrombolysis for acute myocardial infarction. Eur Heart J. 2005; 26(18):1831-7	Not RCT
Taglieri N, Di Mario C. Percutaneous coronary intervention following thrombolysis: for whom and when? Acute Card Care. 2009; 11(4):195-203.	Not RCT
Testa L, van Gaal WJ, Biondi-Zoccai GG, Abbate A, Agostoni P, Bhindi R, Banning AP. Repeat thrombolysis or conservative therapy vs. rescue percutaneous coronary intervention for failed thrombolysis: systematic review and meta-analysis. QJM. 2008; 101(5):387-95	Not RCT (used for quality assessment)
Verheugt FW. Timing of angiography after fibrinolysis for ST-elevation acute myocardial infarction. Curr Opin Cardiol. 2010; 25(4):302-4	Not RCT
Vetrano A, Carotenuto R, Corsini F, Schioppa M, Martone A, Melorio S, Sideri F, Romano S, Chieffo C, Corsini G. Effectiveness of tirofiban for failed thrombolysis during acute myocardial infarction. Am J Cardiol. 2004; 93(7):914-6.	Not RCT
Wijeysundera HC, Vijayaraghavan R, Nallamothu BK, Foody JM, Krumholz HM, Phillips CO, Kashani A, You JJ, Tu JV, Ko DT. Rescue angioplasty or repeat fibrinolysis after failed fibrinolytic therapy for ST-segment myocardial infarction: a meta-analysis of randomized trials. J Am Coll Cardiol. 2007; 49(4):422-30.	Not RCT (used for quality assessment)
Yan AT, Yan RT, Cantor WJ, Borgundvaag B, Cohen EA, Fitchett DH et al. Relationship between risk stratification at admission and treatment effects of early invasive management following fibrinolysis: insights from the Trial of Routine ANgioplasty and Stenting After Fibrinolysis to Enhance Reperfusion in Acute Myocardial Infarction (TRANSFER-AMI). European Heart Journal . 2011; 32(16):1994-2002.	Post-hoc analysis
Yan AT, Yan RT, Mehta SR, Morrison LJ, Cantor WJ, Heffernan M et al. Efficacy of early invasive management postfibrinolysis in men versus women with ST-elevation myocardial infarction: A subgroup analysis from transfer-AMI. Canadian Journal of Cardiology. 2011; 27(5 SUPPL. 1):S152-S153.	Abstract

J.12 Routine early angiography following fibrinolysis

Study	Reason for exclusion
Abdul-Rahman S, Nammas W, Gamal A, Adel A, Zaki T. Routine invasive versus ischemia-guided strategy in patients with acute inferior ST-elevation myocardial infarction who received fibrinolytic therapy: a prospective randomized controlled pilot trial. J Invasive Cardiol. 2011; 23(8):316-21.	Protocol specified that angiography in the 'early routine group' was performed within 48 hours (actual time to angiography was not recorded)
Arnold AE, Simoons ML, Detry JM, von Essen R, Van de Werf F, Deckers JW, Lubsen J, Verstraete M. Prediction of mortality following hospital discharge	Not RCT

Study	Reason for exclusion
after thrombolysis for acute myocardial infarction: is there a need for coronary angiography? European Cooperative Study Group. Eur Heart J. 1993; 14(3):306-15.	
Barbash GI, Roth A, Hod H, Modan M, Miller HI, Rath S, Zahav YH, Keren G, Motro M, Shachar A, et al. Randomized controlled trial of late in-hospital angiography and angioplasty versus conservative management after treatment with recombinant tissue-type plasminogen activator in acute myocardial infarction. Am J Cardiol. 1990; 66(5):538-45.	Early routine angio was performed 3–7 days after fibrinolysis; quasi randomisation (alternating 2 month periods); enrolment started before 1996
Baron SJ, Giugliano RP. Effectiveness and safety of percutaneous coronary intervention after fibrinolytic therapy for ST-segment elevation acute myocardial infarction. Am J Cardiol. 2011; 107(7):1001-9.	Not RCT
Bednár F, et al. Interhospital transport for primary angioplasty improves the long-term outcome of acute myocardial infarction compared with immediate thrombolysis in the nearest hospital (one-year follow-up of the PRAGUE-1 study). Can J Cardiol. 2003; 19(10):1133-7.)	PCI rather than fibrinolysis was the primary reperfusion strategy in the routine early arm; randomised patients in the early routine arm to pre-hospital streptokinase
Bøhmer E, Arnesen H, Abdelnoor M, Mangschau A, Hoffmann P, Halvorsen S. The NORwegian study on DIstrict treatment of ST-elevation myocardial infarction (NORDISTEMI). Scand Cardiovasc J. 2007; 41(1):32-8.	Preliminary results – final results reported in another article that was included
SWIFT trial of delayed elective intervention v conservative treatment after thrombolysis with anistreplase in acute myocardial infarction. SWIFT (Should We Intervene Following Thrombolysis?) Trial Study Group.	Enrolment finished November 1988 and <50% stenting
Borgia F, Goodman SG, Halvorsen S, Cantor WJ, Piscione F, Le May MR, Fernández-Avilés F, Sánchez PL, Dimopoulos K, Scheller B, Armstrong PW, Di Mario C. Early routine percutaneous coronary intervention after fibrinolysis vs. standard therapy in ST-segment elevation myocardial infarction: a meta-analysis. Eur Heart J. 2010; 31(17):2156-69.	Not RCT (used for quality assessment)
Califf RM, Topol EJ, Stack RS, Ellis SG, George BS, Kereiakes DJ, Samaha JK, Worley SJ, Anderson JL, Harrelson-Woodlief L, et al. Evaluation of combination thrombolytic therapy and timing of cardiac catheterization in acute myocardial infarction. Results of thrombolysis and angioplasty in myocardial infarction--phase 5 randomized trial. TAMI Study Group. Circulation. 1991; 83(5):1543-56.	Factorial design that does not directly compare routine early angiography with deferred or selective approach; enrolment ended May 1989 and <50% stenting
Cantor WJ, Brunet F, Ziegler CP, Kiss A, Morrison LJ. Immediate angioplasty after thrombolysis: a systematic review. CMAJ. 2005; 173(12):1473-81.	Not RCT
Cantor WJ, Burnstein J, Choi R, Heffernan M, Dzavik V, Lazzam C, Duic M, Fitchett D, Tan M, Wawrzyniak J, Kassam S, Dhingra S, Morrison LJ, Langer A, Goodman SG. Transfer for urgent percutaneous coronary intervention early after thrombolysis for ST-elevation myocardial infarction: the TRANSFER-AMI pilot feasibility study. Can J Cardiol. 2006; 22(13):1121-6.	Not RCT
Cantor WJ, Fitchett D, Borgundvaag B, Heffernan M, Cohen EA, Morrison LJ, Ducas J, Langer A, Mehta S, Lazzam C, Schwartz B, Dzavik V, Goodman SG. Rationale and design of the Trial of Routine ANgioplasty and Stenting After Fibrinolysis to Enhance Reperfusion in Acute Myocardial Infarction (TRANSFER-AMI). Am Heart J. 2008; 155(1):19-25.	Trial design – no results
Chaitman BR, Thompson BW, Kern MJ, Vandormael MG, Cohen MB, Ruocco NA, Solomon RE, Braunwald E. Tissue plasminogen activator followed by	Original article published before 1990 cut-off and

Study	Reason for exclusion
percutaneous transluminal coronary angioplasty: one-year TIMI phase II pilot results. TIMI Investigators. Am Heart J. 1990; 119(2 Pt 1):213-23.	<50% stenting
Desch S, Eitel I, Rahimi K, de Waha S, Schuler G, Thiele H. Timing of invasive treatment after fibrinolysis in ST elevation myocardial infarction--a meta-analysis of immediate or early routine versus deferred or ischemia-guided randomised controlled trials. Heart. 2010; 96(21):1695-702	Not RCT (used for quality assessment)
Dieker H-J, Aengevaeren WR, French J, Huber K, Brouwer M, Verheugt F. Early stenting versus conservative treatment after successful fibrinolysis for stemi: Results of the randomized angiographic APRICOT-3 trial. Journal of the American College of Cardiology. 2012; 59(13 SUPPL. 1):E373.	Abstract
Di Mario C, Bolognese L, Maillard L, Dudek D, Gambarati G, Manari A, Guiducci V, Patrizi G, Rusconi LC, Piovaccari G, Hibon AR, Belpomme V, Indolfi C, Olivari Z, Steffenino G, Zmudka K, Airoldi F, Panzarasa R, Flather M, Steg PG. Combined Abciximab REteplase Stent Study in acute myocardial infarction (CARESS in AMI). Am Heart J. 2004; 148(3):378-85.	Trial design – no results
Di Mario C, et al. Immediate angioplasty versus standard therapy with rescue angioplasty after thrombolysis in the Combined Abciximab REteplase Stent Study in Acute Myocardial Infarction (CARESS-in-AMI): an open, prospective, randomised, multicentre trial. Lancet. 2008; 371(9612):559-68.	Randomised both treatment arms to unconventional fibrinolysis strategies not used in the UK (that is, half-dose reteplase plus abciximab, rather than a full-dose fibrinolytic agent)
Dong-Bao L, Qi H, Hong-Wei L, Hui C, Shu-Mei Z. Effects of early angioplasty after fibrinolysis on prognosis of patients with ST-segment elevation acute myocardial infarction. African Journal of Biotechnology. 2011; 10(70):15801-15804.	Not randomised data
D'Souza SP, Mamas MA, Fraser DG, Fath-Ordoubadi F. Routine early coronary angioplasty versus ischaemia-guided angioplasty after thrombolysis in acute ST-elevation myocardial infarction: a meta-analysis. Eur Heart J. 2011; 32(8):972-82.	Not RCT (used for quality assessment)
Dudek D, Dziewierz A, Rakowski T, Siudak Z, Wizimirski M, Legutko J, Batruś S, Mielecki W, Rzeszutko L, Zmudka K, Dubiel JS. Angiographic and clinical outcome after percutaneous coronary interventions following combined fibrinolytic therapy in acute myocardial infarction. Kardiol Pol. 2006; 64(3):239-47	Not RCT
Hochman, JS et al. One-year survival following: early revascularization for cardiogenic shock. Commentary; JAMA2001:240	Commentary
Krupicka J, Widimský P, Nechvatál L, Bednár F, Línková H, Gregor P, Groch L, Zelízko M, Aschermann M. Inter-hospital transport for primary angioplasty does not compromise left ventricular function: six-month echocardiographic follow-up of the PRAGUE 1 Study. Jpn Heart J. 2003; 44(3):313-22.	No outcomes of interest
Lee MS, Tseng CH, Barker CM, Menon V, Steckman D, Shemin R, Hochman JS. Outcome after surgery and percutaneous intervention for cardiogenic shock and left main disease. Ann Thorac Surg. 2008 Jul; 86(1):29-34.	PCI versus CABG
McCullough PA, Gibson CM, Dibattiste PM, Demopoulos LA, Murphy SA, Weintraub WS, Neumann FJ, Khanal S, Cannon CP; TACTICS-TIMI-18 Investigators. Timing of angiography and revascularization in acute coronary syndromes: an analysis of the TACTICS-TIMI-18 trial. J Interv Cardiol. 2004; 17(2):81-6.	Not RCT (analysis of single arm)
Marcusohn E, Roguin A, Sebbag A, Aronson D, Dragu R, Amikam S, Boulus M, Grenadier E, Kerner A, Nikolsky E, Markiewicz W, Hammerman H, Kapeliovich M. Primary percutaneous coronary intervention after out-of-hospital cardiac	No control group

Study	Reason for exclusion
arrest: patients and outcomes. Isr Med Assoc J. 2007 Apr; 9(4):257-9.	
Muller DW, Topol EJ, Ellis SG, Woodlief LH, Sigmon KN, Kereiakes DJ, George BS, Worley SJ, Samaha JK, Phillips H 3rd, et al. Determinants of the need for early acute intervention in patients treated conservatively after thrombolytic therapy for acute myocardial infarction. TAMI-5 Study Group. J Am Coll Cardiol. 1991; 18(7):1594-601.	Factorial design that does not directly compare routine early angiography with deferred or selective approach; enrolment ended May 1989 and <50% stenting
Pilote L, Miller DP, Califf RM, Rao JS, Weaver WD, Topol EJ. Determinants of the use of coronary angiography and revascularization after thrombolysis for acute myocardial infarction. N Engl J Med. 1996; 335(16):1198-205.	Not question of interest
Reiner JS, Lundergan CF, van den Brand M, Boland J, Thompson MA, Machecourt J, Py A, Pilcher GS, Fink CA, Burton JR, et al. Early angiography cannot predict postthrombolytic coronary reocclusion: observations from the GUSTO angiographic study. Global Utilization of Streptokinase and t-PA for Occluded Coronary Arteries. J Am Coll Cardiol. 1994; 24(6):1439-44.	Study design does not directly compare routine early angiography with deferred or selective approach; enrolment ended February 1993 and <50% stenting
Rogers WJ, Babb JD, Baim DS, Chesebro JH, Gore JM, Roberts R, Williams DO, Frederick M, Passamani ER, Braunwald E. Selective versus routine predischarge coronary arteriography after therapy with recombinant tissue-type plasminogen activator, heparin and aspirin for acute myocardial infarction. TIMI II Investigators. J Am Coll Cardiol. 1991; 17(5):1007-16.	Not RCT (comparison of arms from 2 different trials)
Rogers WJ, Baim DS, Gore JM, Brown BG, Roberts R, Williams DO, Chesebro JH, Babb JD, Sheehan FH, Wackers FJ, et al. Comparison of immediate invasive, delayed invasive, and conservative strategies after tissue-type plasminogen activator. Results of the Thrombolysis in Myocardial Infarction (TIMI) Phase II-A trial. Circulation. 1990; 81(5):1457-76.	Enrolment finished June 1988 and <50% stenting
Ross AM, Lundergan CF, Rohrbeck SC, Boyle DH, van den Brand M, Buller CH, Holmes DR Jr, Reiner JS. Rescue angioplasty after failed thrombolysis: technical and clinical outcomes in a large thrombolysis trial. GUSTO-1 Angiographic Investigators. Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries. J Am Coll Cardiol. 1998; 31(7):1511-7.	Not question of interest
Ruocco NA Jr, Bergelson BA, Jacobs AK, Frederick MM, Faxon DP, Ryan TJ. Invasive versus conservative strategy after thrombolytic therapy for acute myocardial infarction in patients with antecedent angina. A report from Thrombolysis in Myocardial Infarction Phase II (TIMI II). J Am Coll Cardiol. 1992; 20(7):1445-51.	Enrolment finished June 1988; wrong population
Simes RJ, Topol EJ, Holmes DR Jr, White HD, Rutsch WR, Vahanian A, Simoons ML, Morris D, Betriu A, Califf RM, et al. Link between the angiographic substudy and mortality outcomes in a large randomized trial of myocardial reperfusion. Importance of early and complete infarct artery reperfusion. GUSTO-I Investigators. Circulation. 1995; 91(7):1923-8.	Not question of interest
Smalling RW, Giesler GM, Julapalli VR, Denktas AE, Sdringola SM, Vooletich MT, McCarthy JJ, Bradley RN, Persse DE, Richter BK, Yagi M, Fujise K, Anderson HV. Pre-hospital reduced-dose fibrinolysis coupled with urgent percutaneous coronary intervention reduces time to reperfusion and improves angiographic perfusion score compared with prehospital fibrinolysis alone or primary percutaneous coronary intervention: results of the PATCAR Pilot Trial. J Am Coll Cardiol. 2007; 50(16):1612-4	Not question of interest
So DY, Ha AC, Davies RF, Froeschl M, Wells GA, Le May MR. ST segment resolution in patients with tenecteplase-facilitated percutaneous coronary intervention versus tenecteplase alone: Insights from the Combined	No outcomes of interest

Study	Reason for exclusion
Angioplasty and Pharmacological Intervention versus Thrombolysis ALone in Acute Myocardial Infarction (CAPITAL AMI) trial. Can J Cardiol. 2010; 26(1):e7-12	
Terrin ML, Williams DO, Kleiman NS, Willerson J, Mueller HS, Desvigne-Nickens P, Forman SA, Knatterud GL, Braunwald E. Two- and three-year results of the Thrombolysis in Myocardial Infarction (TIMI) Phase II clinical trial. J Am Coll Cardiol. 1993; 22(7):1763-72.	Original article published before 1990 cut-off; enrolment finished June 1988 and <50% stenting
Thiele H, et al. Comparison of pre-hospital combination-fibrinolysis plus conventional care with pre-hospital combination-fibrinolysis plus facilitated percutaneous coronary intervention in acute myocardial infarction. Eur Heart J. 2005; 26(19):1956-63.	Randomised both treatment arms to unconventional fibrinolysis strategies not used in the UK (that is, half-dose reteplase plus abciximab, rather than a full-dose fibrinolytic agent)
Thiele H, Scholz M, Engelmann L, Storch WH, Hartmann A, Dimmel G, Pfeiffer D, Schuler G; Leipzig Prehospital Fibrinolysis Group. ST-segment recovery and prognosis in patients with ST-elevation myocardial infarction reperfused by prehospital combination fibrinolysis, prehospital initiated facilitated percutaneous coronary intervention, or primary percutaneous coronary intervention. Am J Cardiol. 2006; 98(9):1132-9.	Original study excluded, no additional outcomes of interest, or further follow-up data of outcomes of interest
Topol EJ, Califf RM, George BS, Kereiakes DJ, Abbottsmith CW, Candela RJ, Lee KL, Pitt B, Stack RS, O'Neill WW. A randomized trial of immediate versus delayed elective angioplasty after intravenous tissue plasminogen activator in acute myocardial infarction. N Engl J Med. 1987; 317(10):581-8.	Article published before 1990 cut-off; enrolment finished October 1986 and <50% stenting
Tsukahara K, Kimura K, Usui T, Okuda J, Kitamura Y, Kosuge M, Sano T, Tohyama S, Nemoto T, Yamanaka O, Yoshii Y, Tochikubo O, Umemura S. Efficacy of low-dose mutant tissue-type plasminogen activator followed by planned rescue percutaneous transluminal coronary angioplasty as reperfusion therapy for acute myocardial infarction. J Cardiol. 2001; 37(3):143-50.	Non-English language
Widimský P, et al. Multicentre randomized trial comparing transport to primary angioplasty vs immediate thrombolysis vs combined strategy for patients with acute myocardial infarction presenting to a community hospital without a catheterization laboratory. The PRAGUE study. Eur Heart J. 2000; 21(10):823-31.	PCI rather than fibrinolysis was the primary reperfusion strategy in the routine early arm; randomised patients in the early routine arm to pre-hospital streptokinase
Wijeysundera HC, You JJ, Nallamothu BK, Krumholz HM, Cantor WJ, Ko DT An early invasive strategy versus ischemia-guided management after fibrinolytic therapy for ST-segment elevation myocardial infarction: a meta-analysis of contemporary randomized controlled trials. Am Heart J. 2008; 156(3):564-572, 572.e1-2.	Not RCT (used for quality assessment)
Williams DO, Braunwald E, Knatterud G, Babb J, Bresnahan J, Greenberg MA, Raizner A, Wasserman A, Robertson T, Ross R. One-year results of the Thrombolysis in Myocardial Infarction investigation (TIMI) Phase II Trial. Circulation. 1992; 85(2):533-42.	Original article published before 1990 cut-off; enrolment finished 1988; <50% stenting
van Den Brand MJ, Betriu A, Bescos LL, Nijssen K, Pfisterer ME, Renkin J, Cusi LS, Zijlstra F, Simoons ML. Randomized trial of deferred angioplasty after thrombolysis for acute myocardial infarction. Coronary Artery Disease 1993; 3:393-401.	Patients not initially randomised to early versus deferred angiography; angiography was undertaken 48–120 hours after fibrinolysis; performed balloon angioplasty

Study	Reason for exclusion
Verheugt FW. Timing of angiography after fibrinolysis for ST-elevation acute myocardial infarction. Curr Opin Cardiol. 2010; 25(4):302-4.	Not RCT
Vermeer F, Oude Ophuis AJ, vd Berg EJ, Brunninkhuis LG, Werter CJ, Boehmer AG, Lousberg AH, Dassen WR, Bär FW. Prospective randomised comparison between thrombolysis, rescue PTCA, and primary PTCA in patients with extensive myocardial infarction admitted to a hospital without PTCA facilities: a safety and feasibility study. Heart. 1999; 82(4):426-31.	Enrolment: Sep 1995 – August 1997 and <50% stenting
Webb JG, Lowe AM, Sanborn TA, White HD, Sleeper LA, Carere RG, Buller CE, Wong SC, Boland J, Dzavik V, Porway M, Pate G, Bergman G, Hochman JS; SHOCK Investigators. Percutaneous coronary intervention for cardiogenic shock in the SHOCK trial. J Am Coll Cardiol. 2003 Oct 15; 42(8):1380-6.	Investigates only patients who had PCI
Buerke M, Lemm H, Dietz S, Werdan K. Pathophysiology, diagnosis, and treatment of infarction-related cardiogenic shock. Herz. 2011 Mar; 36(2):73-83. Review.	Review
Wong SC, Sleeper LA, Monrad ES, Menegus MA, Palazzo A, Dzavik V, Jacobs A, Jiang X, Hochman JS; SHOCK Investigators. Absence of gender differences in clinical outcomes in patients with cardiogenic shock complicating acute myocardial infarction. A report from the SHOCK Trial Registry. J Am Coll Cardiol. 2001 Nov 1; 38(5):1395-401.	Wrong comparison
White HD, Assmann SF, Sanborn TA, Jacobs AK, Webb JG, Sleeper LA, Wong CK, Stewart JT, Aylward PE, Wong SC, Hochman JS. Comparison of percutaneous coronary intervention and coronary artery bypass grafting after acute myocardial infarction complicated by cardiogenic shock: results from the Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock (SHOCK) trial. Circulation. 2005 Sep 27; 112(13):1992-2001.	PCI versus CABG
Ramanathan K, Farkouh ME, Cosmi JE, French JK, Harkness SM, Džavík V, Sleeper LA, Hochman JS. Rapid complete reversal of systemic hypoperfusion after intra-aortic balloon pump counterpulsation and survival in cardiogenic shock complicating an acute myocardial infarction. Am Heart J. 2011 Aug; 162(2):268-75.	Registry data. Subgroup analysis of patients who underwent IABP
Webb JG, Sanborn TA, Sleeper LA, Carere RG, Buller CE, Slater JN, Baran KW, Koller PT, Talley JD, Porway M, Hochman JS; SHOCK Investigators. Percutaneous coronary intervention for cardiogenic shock in the SHOCK Trial Registry. Am Heart J. 2001 Jun; 141(6):964-70.	Analysis of PCI patients only
Jeger RV, Tseng CH, Hochman JS, Bates ER. Interhospital transfer for early revascularization in patients with ST-elevation myocardial infarction complicated by cardiogenic shock--a report from the SHould we revascularize Occluded Coronaries for cardiogenic shocK? (SHOCK) trial and registry. Am Heart J. 2006 Oct; 152(4):686-92.	Subgroup analysis of transfer patients
Prasad A, Lennon RJ, Rihal CS, Berger PB, Holmes DR Jr. Outcomes of elderly patients with cardiogenic shock treated with early percutaneous revascularization. Am Heart J. 2004 Jun; 147(6):1066-70.	Analysis of only early revascularisation patients
Madan M, Tan M, Halvorsen S, Westernout CM, Cantor W, Le May MR et al. Timing of angiography and clinical outcomes after fibrinolysis: A patient-level analysis of randomized early invasive clinical trials. Journal of the American College of Cardiology. 2012; 59(13 SUPPL. 1):E353.	Abstract
Magno JDA, Alcover JD, Javier ADC, Punzalan FER. Routine angioplasty after fibrinolytic therapy for ST-segment elevation myocardial infarction: An updated meta-analysis (RAFT-STEMI). Journal of the American College of Cardiology. 2011; 58(20 SUPPL. 1):B94.	Abstract
Rodriguez De Leiras OS, Prado GB, Sayago S, I, Vizcaino AM, Marcos SF,	Abstract

Study	Reason for exclusion
Carrascosa RC et al. Primary percutaneous coronary intervention and culprit vessel revascularisation versus thrombolysis and early complete revascularisation: Comparison of two strategies. EuroIntervention. 2010; 6.	
van Loon RB, Veen G, Baur LHB, Kamp O, Bronzwaer JGF, Twisk JWR et al. Improved clinical outcome after invasive management of patients with recent myocardial infarction and proven myocardial viability: primary results of a randomized controlled trial (VIAMI-trial). Trials. 2012; 13:1.	Not all patients received fibrinolysis
Yan AT, Cantor WJ, Yan RT, Borgundvaag B, Cohen EA, Dzavik V et al. Risk stratification at admission to identify ST-segment elevation myocardial infarction patients receiving fibrinolysis who may benefit from early angioplasty: Insights from the trial of routine angioplasty and stenting after fibrinolysis to enhance reperfusion in acute myocardial infarction (transfer-AMI). Circulation. 2010; 122:A15640.	Post-hoc subgroup analysis and abstract
Yan AT, Yan RT, Mehta SR, Morrison LJ, Cantor WJ, Heffernan M et al. Efficacy of early invasive management postfibrinolysis in men versus women with ST-elevation myocardial infarction: A subgroup analysis from transfer-AMI. Canadian Journal of Cardiology. 2011; 27(5 SUPPL. 1):S152-S153.	Abstract
Yan AT, Yan RT, Cantor WJ, Borgundvaag B, Cohen EA, Fitchett DH et al. Relationship between risk stratification at admission and treatment effects of early invasive management following fibrinolysis: insights from the Trial of Routine ANgioplasty and Stenting After Fibrinolysis to Enhance Reperfusion in Acute Myocardial Infarction (TRANSFER-AMI). European Heart Journal. 2011; 32(16):1994-2002.	Post-hoc analysis
Zhang B-C. A meta-analysis of early percutaneous coronary intervention within 24 hours of thrombolysis in acute st-elevation myocardial infarction. American Journal of Cardiology. 2012; 109(7 SUPPL. 1):6S-7S.	Abstract

Appendix K: Excluded economic studies

K.1 Time to reperfusion

Reference	Reason for exclusion
Concannon TWK. Comparative effectiveness of ST-segment-elevation myocardial infarction regionalization strategies. Circulation: Cardiovascular Quality and Outcomes 3(5): 506-513, 2010.	Excluded due to availability of more applicable evidence. US perspective used and effectiveness data based on PCI-TPI (Percutaneous Coronary Intervention-Thrombolytic Predictive Instrument) which was not included in the clinical review. The 2 included studies both used a UK perspective.

K.2 Facilitated PPCI

Reference	Reason for exclusion
Coleman CI, McKay RG, Boden WE, Mather JF, and White CM. Effectiveness and cost-effectiveness of facilitated percutaneous coronary intervention compared with primary percutaneous coronary intervention in patients with ST-segment elevation myocardial infarction transferred from community hospitals. Clinical Therapeutics. 28(7): 1054-1062, 2006.	Excluded due to a combination of lack of applicability and very serious methodological limitations. The clinical review was based on RCTs only, and so within-trial economic analyses were included only if based on RCTs. This was an observational study and so was not randomised. Health outcomes were based on this study only and not on the full effectiveness evidence included in the clinical review. In addition fPPCI with fibrinolytics and/or GPIs was compared with PPCI without any fibrinolytics or GPIs, which has limited applicability to the current context where periprocedural GPI use is common.

K.3 Radial versus femoral arterial access for PPCI

Reference	Reason for exclusion
Saito S, Tanaka S, Hiroe Y, Miyashita Y, Takahashi S, Tanaka K, et al. Comparative study on transradial approach vs. transfemoral approach in primary stent implantation for patients with acute myocardial infarction: results of the test for myocardial infarction by prospective unicenter randomization for access sites (TEMPURA) trial. Cathetarization and cardiovascular intervention. 59(1): 26-33, 2003.	Excluded due to a combination of partial lack of applicability and very serious methodological limitations. Based on a trial carried out in Japan more than 10 years ago. No explanation of which costs are included in the total costs or of the sources of resource and cost data used. The length of stay for patients is unrepresentative of current UK practice, which would alter the costs by a substantial but incalculable amount.

K.4 Thrombus extraction during PPCI

Reference	Reason for exclusion
Anzai H, Yoneyama S, Tsukagoshi M, Miyake T, Kikuchi T, and Sakurada M. Rescue percutaneous thrombectomy system provides better angiographic coronary flow and does not increase the in-hospital cost in patients with acute myocardial infarction. Circulation Journal 67(9): 768-774, 2003.	Excluded due to a combination of partial lack of applicability and very serious methodological limitations. The clinical review was based on RCTs only, and so within-trial economic analyses were included only if based on RCTs. This was based on a before-after observational study without randomisation or blinding. Some patients were non-randomly excluded from the intervention arm but not from the control arm due to doctor decision about their suitability for the procedure. Health outcomes were based on this study only and not on the full effectiveness evidence included in the clinical review. The resource use and unit costs are Japanese and more than 10 years old.
Tarsia G, De MM, Polosa D, Biondi ZG, Costantino F, Del PG, et al. Manual versus nonmanual thrombectomy in primary and rescue percutaneous coronary angioplasty. Heart and Vessels 25(4): 275-281, 2010.	Excluded due to a combination of lack of applicability and very serious methodological limitations. The clinical review was based on RCTs only, and so within-trial economic analyses were included only if based on RCTs. This was based on a before-after observational study without randomisation or blinding and with a substantial time difference between arms (2000–2005 versus 2005–2007). Exclusion criteria are not clear. Health outcomes were based on this study only and not on the full effectiveness evidence included in the clinical review. No information was given on the source of resource use and unit cost data.

K.5 Culprit versus complete revascularisation **Updated, see 2020 evidence review**

None.

K.6 Cardiogenic shock

None.

K.7 People who remain unconscious after a cardiac arrest

None.

K.8 Hospital volumes of PPCI

None.

K.9 Pre-hospital versus in-hospital fiobrinolysis

Reference	Reason for exclusion
Vale L, Silcock J, and Rawles J. An economic evaluation of thrombolysis in a remote rural community. BMJ. 314(7080): 570-572, 1997.	Excluded due to a combination of lack of applicability and very serious methodological limitations. Analysis based on GREAT study, the inclusion criteria of which did not include a definitive diagnosis of STEMI by electrocardiogram and hence the population included people without STEMI. It also used only a simple outcome measure and so is less relevant than Vale 2004.
Vale L, Steffens H, and Donaldson C. The costs and benefits of community thrombolysis for acute myocardial infarction: a decision-analytic model. PharmacoEconomics 22(14): 943-954, 2004.	Excluded due to a combination of lack of applicability and potentially serious methodological limitations. Analysis based on GREAT study, the inclusion criteria of which did not include a definitive diagnosis of STEMI by electrocardiogram and hence the population included people without STEMI. It also does not reflect the whole effectiveness evidence identified in the clinical review or include long-term healthcare costs.

K.10 Use of antithrombin as an adjunct to fibrinolysis

None.

K.11 Rescue PCI

None.

K.12 Routine early angiography following fibrinolysis

None.

Appendix L: Comparative cost analysis: Radial versus femoral arterial access for PPCI

L.1 Introduction

No relevant economic evaluations were identified that compared radial access with femoral access for PPCI. Given that both approaches are in common usage in England and Wales, and that it is not clear which approach is most cost effective, the GDG decided to conduct a comparative cost analysis for an NHS context.

L.2 Methods

L.2.1 Approach to analysis

The analysis was undertaken in line with the NICE reference case.[86] The population and interventions considered were the same as in the clinical evidence review for this question (see review protocol, Appendix C). The costs considered were the direct cost of all healthcare received by individuals from an NHS and personal social services perspective. As this is a cost analysis, health outcomes, including health-related quality of life, were not considered. Only costs incurred during the initial hospital stay were included. The time horizon was less than 1 year, and hence discounting was not required. In line with the NICE Guide to the methods of technology appraisal,[86] VAT was excluded from the analysis, and hence the costs quoted below do not include VAT.

Five factors were considered, each of which the GDG believed may give rise to a difference in costs between procedures carried out by radial access and those carried out by femoral access.

- Equipment used in standard PPCI procedures.
- Equipment used in crossover PPCI procedures.
- Treatment of complications.
- Length of PPCI procedures.
- Length of hospital stay.

The GDG did not believe that there were any other factors likely to give rise to differences in procedural or in-hospital costs. Differences in healthcare usage after the initial hospital stay were not considered due to a lack of biological plausibility that the arterial access route used could affect the need for healthcare beyond the initial hospital stay, and because the clinical evidence review for this question found no evidence of difference in long-term outcomes.

L.2.2 Resource use

L.2.2.1 Equipment used in standard PPCI procedures

The opinion of the GDG was that the equipment used during uncomplicated PPCI procedures is largely equivalent regardless of which arterial approach is used. The only difference identified was in the equipment needed to close the artery at the end of the procedure.

In femoral procedures this may be carried out in one of three ways:

- pressing manually on the entry site
- using an external compression device
- using an vascular closure device.

The relative use of each of these 3 methods in the UK is unknown as practice varies between PPCI centres.

In radial procedures closure may be carried out either by manual pressure or by using a vascular closure device. In practice manual pressure is rarely used as the vascular closure devices are relatively inexpensive. It was assumed that closure devices are used in 100% of radial PPCI procedures.

L.2.2.2 Equipment used in crossover PPCI procedures

A 'crossover' occurs when access to the coronary arteries is found not to be possible through the intended access route, in which case the operator will withdraw any equipment already inserted from that artery and instead attempt to access the coronary arteries through the alternative approach. For example a crossover occurs in a radial procedure when the operator intends to carry out the procedure through the radial artery and initially attempts this, but is not able to complete the procedure using the radial artery and so instead restarts the process using a femoral artery and continues as for a standard femoral procedure.

The repetition involved in this process means that some addition equipment is required in crossover procedures.

Crossovers are also likely to increase the total length of a PPCI procedure. However this effect will be captured in the mean lengths of procedures reported in studies and analysed below, which average the lengths of all procedures carried out in the included trials, whether or not a crossover was involved.

Crossovers are more common in radial procedures than in femoral procedures. The weighted frequency of crossovers observed in the clinical evidence review is shown in Table 111 and in Figure 157, Appendix I.

Table 111: Crossover rates

	Radial access	Femoral access	Increase in rate with radial access	Studies reporting crossover
Crossover rate	6.8%	2.0%	4.8%	TEMPURA 2003,[95] Brasselet 2007,[14] Li 2007,[73] Gan 2009,[48] RADIAMI 2009,[26] Hou 2010,[56] RIVAL 2011,[60] RADIAMI II 2011,[27] RIFLE-STEACS 2012[93]

The opinion of the GDG was that the additional equipment needed when a crossover occurs (either from radial to femoral access or from femoral to radial access) is as follows:

- In approximately 70% of cases the decision to crossover is taken early due to difficulties in initially accessing the artery. In these cases a replacement sheath only is required.
- In approximately 30% of cases the decision to crossover is taken later due to a failure to successfully negotiate the artery. In these cases a replacement sheath is still needed but a new introducing wire is also likely to be required. In around half of these cases (approximately 15% of all cases) a new guide catheter is also likely to be necessary.
- It was noted that small quantities of additional supplies would also be needed, such as an additional introducing needle, one or two syringes, some local anaesthetic and cleaning swabs. However, the low cost of these items compared with the overall extra costs calculated in this section meant that adding the cost of these items into this calculation explicitly would be unnecessary as the extra cost involved would be insignificant.

L.2.2.3 Treatment of complications

The clinical trials reported a variety of complications, with differing definitions (see Chapter 7). Some of these complications would not need any treatment (for example, some minor bleeding). The GDG judged that the complications which were likely to need treatment and so were most relevant for costing were cases with bleeding requiring blood transfusion, and haematomas (which were assumed to include all cases of pseudoaneurysm). Weighted means of the complication rates observed in the clinical evidence review are shown in Table 112.

Table 112: Frequencies of complications requiring treatment

Complication rate	Radial acces	Femoral access	Increase in rate with femoral access	Studies reporting complication
Bleeding requiring blood transfusion (Figure 164)	0.8%	2.7%	1.9%	TEMPURA 2003,[95] Brasselet 2007,[14] RADIAMI 2009,[26] Hou 2010,[56] RIVAL 2011,[60] RIFLE-STEACS 2012,[93] RADIAMI II 2011[27]
Haematoma (Figure 165)	7.3%	14.4%	7.1%	Brasselet 2007,[14] Li 2007,[73] Gan 2009,[48] RADIAMI 2009,[26] Hou 2010,[56] RADIAMI II 2011[27]

Small haematomas require no additional treatment. Larger haematomas will be investigated by ultrasound to check for the presence of a pseudoaneursym. Pseudoaneursym may be treated by compression, by thrombin injection or, in rare cases, by surgery. The relative frequencies of these interventions are not known, and so the GDG estimated these values based on their clinical experience.

The opinion of the GDG was that the additional resources needed to treat complications would be as follows:

- Every patient requiring blood transfusion is assumed to receive on average a transfusion of two units of blood.
- It is assumed that 50% of patients with a haematoma will receive an ultrasound to check for pesudoaneursym (false aneurysm).
- It is assumed that 50% of those given an ultrasound will be diagnosed with pesudoaneursym.
- It is assumed that 50% of those diagnosed with pesudoaneursym will be treated with compression, requiring an external compression device; that 45% will be treated by injection with thrombin; and that 5% would require surgery.
    - o It is noted that, depending on which means of closing femoral arteries is routinely adopted (as discussed in L.2.2.1 above) the use of an external compression device may not be an additional cost.

L.2.2.4 Length of PPCI procedures

If PPCI procedures using one arterial approach take longer than those using the other approach, then that will involve additional staff time and additional time using the cardiac catheter laboratory with the overheads that that involves. If the difference in length of time is sufficient that the staff and laboratory time could have alternatively been used in treating another patient then that will mean that this approach has additional costs.

The mean procedure length in each of the clinical studies is recorded and meta-analysed in Figure 163, Appendix I. As already noted, the mean length will take into account any additional time spent in crossover procedures and in treating complications which arise during the procedure, as well as any difference in the length of uncomplicated procedures.

The results, shown in Figure 163, are that radial procedures are 1.66 minutes (95% CI 0.73, 2.59) longer than femoral procedures. This is an increase of only 100 seconds in a procedure which usually takes between 30 and 60 minutes, and was considered by the GDG not to be clinically significant, as it is implausible that a difference of that magnitude would in practice lead to staff and facility resources being available to treat another patient instead.

It was therefore concluded that there was no evidence that there would be a significant difference in costs between the two approaches on the basis of procedure length. It was therefore not found to be necessary to establish the exact resources used in a PPCI procedure for each additional minute, or the cost of these resources, and hence these are not reported here or in the cost section below.

L.2.2.5 Length of hospital stay

The weighted means of the studies included in the clinical evidence review (Figure 162, Appendix I and Table 113 below) gave the length of stay as 7.3 days for radial access, and 8.0 days for femoral access (evidence quality: Very Low). The reduction in length of stay varied between 0.3 days[14] and 4.1 days.[56] These data were from studies undertaken in France, China, Japan and Poland and published between 2003 and 2010. The GDG agreed that these were not applicable to the current UK context since current UK length of stay for both radial and femoral access is typically very much shorter.

The British Cardiovascular Intervention Society (BCIS) carries out an annual audit of all PPCI procedures carried out in the UK.[77] This includes the arterial access route used in each procedure. BCIS does not routinely publish length of stay data by access route, but have made that available for this guideline (Ludman PF: unpublished evidence 2012). It shows 3.28 days for radial access and 4.58 days for femoral access (Table 113). This is the only UK hospital data routinely collected which is separated by access route, as other sources such as NHS episode statistics and NHS reference costs do not disaggregate their data. No UK clinical trial has been identified which published disaggregated data.

Table 113: Length of stay in hospital during and following a PPCI procedure

Data source	Population	LOS (days), radial access	LOS (days), femoral access	Reduction in LOS with radial (days)
Clinical trial data				
TEMPURA 2003,[95] Brasselet 2007,[14] Gan 2009,[48] RADIAMI 2009,[26] Hou 2010[56] (Figure 162)	n = 758	7.9 (mean) 7.3 (weighted mean)	10.5 (mean) 8.0 (weighted mean)	2.5 (24%) 0.6 (8%)
UK data				
BCIS audit 2011[77] (a)	n = 19,787	3.28	4.58	1.30 (28%)

LOS = Length of hospital stay, mean
(a) Non-randomised cohort. Does not account for patients treated then transferred to a different hospital. Does not include crossovers (mean LOS: 5.19 days).

The BCIS audit data are therefore likely to be the most applicable data for the context of England and Wales. However, they have a number of significant limitations. They are non-randomised and as such are likely to be heavily confounded. In the opinion of the GDG, patients with some of the most complicated cases, such as those patients with cardiogenic shock, are very much more likely to be treated using a femoral procedure than a radial procedure. These patients have poorer outcomes than patients without complications (see Chapter 10), and are more likely to require intensive care following the PPCI procedure. As a result, the population receiving femoral access PPCI may be expected to have worse outcomes and a longer length of stay than the population receiving radial access on this account.

Procedures including crossovers are associated with a longer length of stay (5.19 days), but are omitted from the mean lengths of stay by approach. Assuming that the rate of excess crossovers in radial access in the UK is 4.8%, as in the clinical review, adding in this effect would be likely to increase the mean length of stay for patient receiving radial access, but only by around 0.07 days.

The BCIS data is also complicated by the fact that it only records the length of stay in the hospital carrying out the procedure. There is at least one high volume PPCI centre in England and Wales, which carries out a majority of radial procedures, whose patients routinely transfer to other hospitals for their recovery, staying at the first centre for less than one day. This would be expected to make the data favour radial access. It is possible that there are other centres following a similar practice of transferring patients, and they may predominantly have patients with radial access or femoral access.

As a result of these limitations, it is the opinion of the GDG that the difference in mean length of stay seen in the BCIS data (1.3 days) is likely to be the upper bound of the possible difference in length of stay between radial and femoral access. It is therefore judged that the true difference in length of stay is likely to lie between 0 days and 1.3 days. The GDG does not believe there is sufficient evidence to judge the likely true difference within this range. No evidence has been identified suggesting a shorter length of stay for femoral access compared to radial access.

L.2.3 Costs

L.2.3.1 Equipment used in standard PPCI procedures

The prices of the items of equipment needed were agreed by the GDG by consensus, based on their experience of purchasing these items in clinical practice in the previous year. It was agreed that the range of prices shown in Table 114 represents the costs at which NHS providers were able to purchase these items in 2012 across England and Wales. These items are not reusable.

The staff time involved in applying manual pressure has not been costed, as the length of time for which manual pressure needs to be maintained has not been measured, and it is not clear whether the staff member responsible might have spent his or her time otherwise observing, talking to or attending to the patient during this time if they had not been applying pressure, so it is unclear whether this is additional staff time which could otherwise have been used in dealing with a different patient, or not. If it was to be costed it would be expected to be less than £10.

Table 114: Cost of equipment used in standard PPCI procedures

Item	Price (range)
Femoral closure	
Manual pressure	Staff time only
External compression device	£50–£60
Vascular closure device (femoral)	£90–£130
Radial closure	
Vascular closure device (radial)	£10–£14

L.2.3.2 Equipment used in crossover PPCI procedures

The prices of the items of equipment needed were agreed by the GDG by consensus, based on their experience of purchasing these items in clinical practice in the previous year. It was agreed that the range of prices shown in Table 115 represents the costs at which NHS providers were able to purchase these items in 2012 across England and Wales. These items are not reusable.

Table 115: Cost of equipment used in crossover PPCI procedures

Item	Price (range)
Sheath	£10–£20
Introducing wire	£17–£21
Guide catheter	£20–£30

L.2.3.3 Treatment of complications

The costs of the procedures needed to treat the complications referred to above were found or estimated from the most appropriate sources (Table 116). Standard NHS Reference Costs were used where available.[31,32] There are no NHS costs specifically for a minor vascular operation to repair a pseudoaneursym. It was therefore assumed that the cost of this would be similar to a simple hernia operation.

Table 116: Cost of procedures used in treating complications

Item	Price	Source
Blood transfusion	£58	NHS Reference Costs (2010-11)[31]: transfusion for outpatient, mean. Number of units not stated; equivalent cost not available for inpatients or for 2011-12[32]
Blood transfusion of 2 units	£58–£116	Based on the assumption that this will cost between the price of 1 and 2 average blood transfusions
Ultrasound	£50 (£33–£59)	NHS Reference Costs[32]: ultrasound < 20 minutes, direct access patients, mean (interquartile range)
Compression device	£50–£60	GDG opinion (where not already used and paid for as standard)
Thrombin injection	£200–£300	GDG opinion
Vascular surgery	£1100–£1500	GDG opinion, assumed to be similar to hernia surgery (NHS Reference Costs[32]: adult day-case hernia surgery)

L.2.3.4 Length of hospital stay

The national average unit cost for one excess bed day for PCI in non-elective patients is £326 (NHS Reference Costs, 2011-12).[32]

L.3 Results

L.3.1 Equipment used in standard PPCI procedures

The equipment needed to close a radial artery costs £10–£14 per procedure.

No data come be found regarding the relative usage of different strategies of femoral closure in the UK, and so it can only be stated with certainty that the cost of the equipment needed to close a femoral artery lies between £0 and £130 per procedure. It is most likely to lie around the middle of that range, and is very likely to be greater than the £10–£14 cost in radial procedures. It is therefore very likely that the equipment used for femoral procedures is more expensive than that used in radial procedures by around £0–£120 per procedure.

L.3.2 Equipment used in crossover PPCI procedures

Based on the costs and resource use assumptions stated above:

- The average additional cost per crossover (radial to femoral or femoral to radial) is between £18.10 and £30.80 (midpoint £24.45).

- Therefore, the average excess cost per radial PPCI procedure, given an excess rate of crossover in radial cases of 4.8%, is between £0.88 and £1.49 (midpoint £1.18).
- It is noted that if the additional low cost items referred to in Section L.2.2.2 were added in, this average cost would increase slightly, but not by more than a few pence.

L.3.3 Treatment of complications

Based on the costs and resource use assumptions stated above:

- The additional cost for patients requiring a blood transfusion is £58–£116.
- The average excess cost of blood transfusions per femoral PPCI patient is hence £1.08–£2.17.
- The additional cost of treating a patient with haematoma is £51.50–£82 if external compression devices are already being used as standard, and £57.75–£89.50 if manual pressure would otherwise have been used and so additional external compression devices are needed.
- The average excess cost of treating haematomas per femoral PPCI patient is hence £3.65–£5.82 without compression devices or £4.10–£6.35 including compression devices.
- Therefore, the average excess cost due to complications for each femoral PPCI procedure is £4.74–£7.99 without compression devices or £5.18–£8.52 including compression devices.

There are further comments on these figures in Section L.4.2 below.

L.3.4 Length of PPCI procedures

There was found to be no evidence of a clinically significant difference in procedure times between the two approaches, and it was hence concluded that there was likely to be no difference in costs on the basis of procedure length.

L.3.5 Length of hospital stay

Based on an additional length of stay for procedures using femoral access of between 0 and 1.3 days, there could be an excess cost of between £0 and £425 for femoral procedures, but the GDG is unable to judge with any confidence where in that range the cost difference is most likely to lie.

L.4 Discussion

L.4.1 Summary of results

The analysis presented here suggests:

- Equipment used in standard PPCI procedures costs £0–£120 more in femoral procedures.
- Equipment used in crossover PPCI procedures costs around £1 more in radial procedures.
- Treating complications costs around £5–£8 more in femoral procedures.
- The length of PPCI procedures does not give rise to any difference in costs.
- The length of hospital stay could cost £0–£425 more in femoral procedures.

No difference is seen in procedure length, and the excess costs incurred by crossovers and complications are negligible in the context of an intervention which cost around £2900 per procedure (NHS Reference Costs, 2010-11).[32,32] The remaining two factors both favour radial over femoral access, but with a very high degree of uncertainty.

L.4.2 Limitations and interpretation

All the data presented and analysed above are subject to substantial limitations, with the exception of the procedure length, which was found to be differ between approaches by a very small amount with a high degree of confidence (95% CI 0.73 minutes, 2.59 minutes).

It is not clear whether the excess rate of crossovers in radial access procedures in England and Wales is in line with the 4.8% difference found in the clinical evidence review. However the very small absolute value of the excess cost (88p–£1.49) means that if this rate was somewhat higher or lower this would have minimal impact for NHS resources.

The assumptions regarding complications are subject to substantial uncertainty as to which complications should be considered, the proportion of patients with a complication needing treatment, the methods of treatment used, and the proportion of patients receiving each treatment method. The costs of each treatment method were presented as a range of prices available in the NHS and not as exact values, and the cost of vascular surgery was estimated based on hernia surgery. The costs of these 2 procedures are unlikely to be the same, and using the hernia surgery cost as an estimate may be an overestimate as it will include double-counting of hospital bed stay costs. However, the small absolute value of the excess cost (£5.18–£8.52) means that these findings would be robust to very different assumptions. Even if the proportion of patients treated for complications was to double, the average net cost per femoral patient would not be greater than £17, still a very small difference.

It is clear that the cost of arterial closure in femoral procedures is highly likely to be higher than in radial procedures, but without data on the relative use and effectiveness of the 3 alternative closure methods outlined it is not possible to calculate how much higher. The experience of the GDG members suggests that each method is currently used in England and Wales to at least a moderate extent, and so the difference in cost is perhaps more likely to be towards the centre than at the extremes of the £0–£120 range suggested.

The cost difference resulting from potential differences in length of stay is even more uncertain. As previously stated, there is no data on length of stay from randomised controlled trials of femoral access versus radial access in a UK or directly equivalent context. The BCIS data which is available must be highly qualified by the fact that it is non-randomised, and the case mix of those patients selected for femoral and radial access are not equivalent. Due to this, and the additional effects of not including crossovers or inter-hospital transfers, the difference in length of stay in a typical PPCI patient is very unlikely to be as high as 1.3 days. The cost difference due to this factor is therefore very likely to be lower than £425. However, it is not possible to be more precise in this result. This is particularly regrettable since this factor has the potential to give rise to the largest cost difference in this analysis if length of stay with radial access is indeed substantially reduced from length of stay with femoral access. It would however be inappropriate to attempt greater certainty than the evidence permits.

L.4.3 Conclusion

Taking together the costs of the equipment used in standard PPCI procedures, in crossover procedures and to treat complications, the length of the PPCI procedure and the length of hospital stay, the evidence suggests that PPCI carried out in the NHS in England and Wales by femoral access is very likely to be more expensive than PPCI carried out by radial access. There is insufficient evidence to reliably predict the size of the cost difference which might be expected.

L.4.4 Implications for future research

Research into the frequency, cost and effectiveness of arterial closure methods used in femoral access PPCI procedures in the UK would be beneficial.

Research into the length of stay of comparable patients following PPCI by radial access versus femoral access in the UK would be highly beneficial.

Appendix M: Comparative cost analysis: The use of thrombus extraction devices during PPCI

M.1 Introduction

No relevant economic evaluations were identified that compared PPCI with and without the use of thrombus extraction devices. Given that both approaches are in common usage in England and Wales, and that it is not clear which approach is most cost effective, the GDG decided to conduct a comparative cost analysis for an NHS context.

M.2 Methods

M.2.1 Approach to analysis

The analysis was undertaken in line with the NICE reference case.[86] The population and interventions considered were the same as in the clinical evidence review for this question (see review protocol, Appendix C). The costs considered were the direct cost of all healthcare received by individuals from an NHS and personal social services perspective. As this is a cost analysis, health outcomes, including health-related quality of life, were not considered. Only costs incurred during the PPCI procedure were included. The time horizon was less than 1 year, and hence discounting was not relevant. In line with the NICE Guide to the methods of technology appraisal,[86] VAT was excluded from the analysis, and hence the costs quoted below do not include VAT.

This analysis examines the usage and costs of three items of equipment used in PPCI procedures:

- thrombus extraction devices
  - thrombus aspiration devices (these are also referred to as manual devices, suction devices or aspiration catheters)
  - mechanical thrombus extraction devices (these are also referred to as non-manual or fragmenting devices)
- stents
- balloon catheters.

The use of thrombus extraction devices results in an additional cost for the procedure as these are single-use items which must be purchased for each procedure. However, the use of such devices may also be associated with differential usage of stents or balloon catheters. The GDG therefore believed it was important to investigate the usage of these items of equipment with and without thrombus extraction to see if this use differed, and if so what effect that would have on the cost of each approach.

The duration of PPCI procedures with and without thrombus extraction was also investigated as a difference in procedure length could give rise to differential costs between the two approaches.

The GDG did not believe that the usage of any other items of equipment (including guide catheters and guidewires) were likely to vary between PPCI procedures with or without thrombus extraction. The costs of healthcare beyond the initial procedure were not included. It was considered that the evidence that future healthcare usage could differ according to whether or not thrombus extraction was carried out was not sufficiently certain or accurate to allow useful costing to be undertaken, and so it was assumed that there would not be any difference in longer-term costs.

M.2.2 Resource use

M.2.2.1 Thrombus extraction devices

By definition there is clearly additional resource use in PPCI procedures adopting a thrombus-extraction approach compared to procedures not carrying out thrombus extraction. These procedures will use either one thrombus aspiration device or one mechanical thrombus extraction device. There is no other resource use directly connected with the use of a thrombus extraction device. Mechanical thrombus extraction devices require the PPCI centre to have use of a machine which allows the delivery of the device. However these machines are typically loaned to hospitals by the device manufacturers in return for commitments to purchase individual devices from the company and so are not an additional cost on the NHS provider.

Unpublished data from the BCIS 2011 audit shows that 0.2% of devices used in PPCI procedures were mechanical thrombus extraction devices, 84.5% were thrombus aspiration devices, with the remaining 15.3% of devices not stated (Ludman PF: unpublished evidence 2012). The GDG agreed that in their clinical experience mechanical thrombus extraction devices are used only rarely.

M.2.2.2 Stents

The proportion of procedures in which at least one stent was used with and without thrombus extraction devices in shown in Table 117 and in the forest plot in Figure 177, Appendix I. The number of stents used per procedure with and without thrombus extraction devices in shown in Table 118.

Table 117: Proportion of procedures in which ≥1 stent was used during PPCI when thrombus extraction device used versus when no thrombus extraction device used

Study	Stent use: thrombus device used	Stent use: no thrombus device used	Difference in usage rate
Thrombus aspiration devices			
Bulum 2012[17]	100%	100%	0
DEAR-MI 2006[102]	99%	97%	+1.4%
De Luca 2006[30]	100%	100%	0
EXPIRA 2010[96]	100%	100%	0
INFUSE-AMI 2012[106] (a)	74%	71%	+3.4%
Kaltoft 2006[61]	95%	97%	−1.8%
Liistro 2009[74]	100%	100%	0
PIHRATE 2010[34]	99%	96.9%	+2.1%
TAPAS 2008[118]	100%	100%	0
VAMPIRE 2008[57]	94%	93%	+0.7%
Mechanical thrombus extraction devices			
AIMI 2006[2]	93%	95%	−1.3%
Antoniucci 2004[3]	98%	98%	0
Napodano 2003[85]	93%	91%	+2.2%
X AMINE ST[72]	100%	98%	+2.0%

Beran 2002,[9] JETSTENT 2010,[83] EXPORT 2008,[25] ITTI 2012[75] and REMEDIA 2005[19] did not report stent usage.
(a) Use of drug-eluting stents. It was not reported whether or not bare metal stents were used in additional cases

Table 118: Number of stents used per procedure in patients when thrombus extraction device used versus when no thrombus extraction device used

Study	Number of stents: thrombus device used	Number of stents: no thrombus device used	Difference in means
Thrombus aspiration devices			
Bulum 2012[17]	1.50	1.47	+0.03
ITTI 2012[75] (a)	1.4 ± 0.7 (a)	1.1 ± 0.3 (a)	+0.3
REMEDIA 2005[19] (a)	1.3 ± 0.6 (a)	1.3 ± 0.6 (a)	0
Mechanical thrombus extraction devices			
AIMI 2006[2] (b)	1.28 (b)	1.21 (b)	+0.07
Beran 2002[9]	1.26 ± 0.54	1.03 ± 0.48	+0.23
JETSTENT 2010[83]	1.26 ± 0.54	1.40 ± 0.73	−0.14
Napodano 2003[85]	1.20 ± 0.65	1.13 ± 0.50	+0.07
X AMINE ST 2005[72]	1.32 ± 0.61	1.37 ± 0.65	−0.05

Antoniucci 2004,[3] DEAR-MI 2006,[102] De Luca 2006,[30] EXPORT 2008,[25] EXPIRA 2010,[96] INFUSE-AMI 2012,[106] Kaltoft 2006,[61] LIISTRO 2009,[74] PIHRATE 2010,[34] TAPAS 2008,[118] and VAMPIRE 2008[57] did not report number of stents used.

(a) Number of stents used per lesion not per procedure

(b) Calculated from number of procedures using 0,1,2,≥3 stents, assuming 3 for ≥3

Figure 177 shows a risk ratio of 1.01 (95% CI 0.99, 1.02): that is that there is no difference in the number of procedures using at least one stent. Those studies which reported the actual numbers of stents used do not give evidence for concluding that the numbers of stents used would differ either.

The GDG has hence concluded that there is no evidence that the usage of stents will differ dependent on the usage of thrombus extraction devices, and therefore there would be no difference in costs due to stent usage.

M.2.2.3 Balloon catheters

Balloon catheter usage is reported in Table 119 and Figure 178, Appendix I. Most studies did not report balloon catheter usage directly, but reported direct stenting (that is, inserting a stent without first using a balloon) and so it is only possible to state the relative usage of balloons in patients who also received a stent. Since stents were used in a large majority of procedures in all of these studies (see Section M.2.2.2), this is unlikely to affect the results.

Table 119: Proportion of patients who received a stent during PPCI procedure who also received ≥ 1 balloon catheter when thrombus extraction device used versus when no thrombus extraction device used

Study	Balloon use: device	Balloon use: no device	Difference
Thrombus aspiration devices			
DEAR-MI 2006[102] (a)	28%	73%	−45%
De Luca 2006A[30] (b)	8%	95%	−87%
EXPIRA 2010[96] (b)	24%	98%	−74%
Liistro 2009[74] (b)	78%	91%	−13%
PIHRATE 2010[34] (c)(d)	24%	92%	−68%
TAPAS 2008[118] (b)(e)	34%	100%	−66%
Mechanical thrombus extraction devices			
Antoniucci 2004[3] (f)	4%	16%	−12%
JETSTENT 2010[83] (b)(g)	10%	14%	−4%

Study	Balloon use: device	Balloon use: no device	Difference
Napodano 2003[85] (h)	33%	63%	−30%
X AMINE ST 2005[72] (i)	40%	64%	−24%

AIMI 2006,[2] Bulum 2012,[17] EXPORT 2008,[25] INFUSE-AMI 2012,[106] ITTI 2012,[75] Kaltoft 2006,[61] REMEDIA 2005[19] and VAMPIRE 2008[57] did not report balloon catheter usage. Beran 2002[9] reported the mean number of balloons used (0.60 ± 0.62 with device; 1.45 ± 0.72 with no device)

(a) 1 patient (1%) in device arm and 2 patients (3%) in no device arm did not receive a stent; balloon use in these patients not reported

(b) 0 patients in each arm did not receive a stent; results therefore reflect all patients

(c) 1 patient (1%) in device arm and 3 patients (3%) in no device arm did not receive a stent; balloon use in these patients not reported

(d) Protocol directed that direct stenting be attempted in procedures using a thrombus extraction device and that balloons be used in procedures not using a thrombus extraction device

(e) Protocol directed that balloons be used in procedures not using a thrombus extraction device

(f) 1 patient (2%) in each arm did not receive a stent; balloon use in these patients not reported

(g) Protocol directed that direct stenting be attempted in all cases

(h) 3 patients (7%) in device arm and 4 patients (9%) in no device arm did not receive a stent; balloon use in these patients not reported

(i) 0 patients in device arm and 2 patients (2%) in no device arm did not receive a stent; balloon use in these patients not reported

Figure 178 shows a risk ratio of 0.35 (95% CI 0.31, 0.38) for thrombus aspiration devices: that is a relative reduction of 65% in the proportion of procedures using at least one balloon catheter when aspiration devices are used. This relates to a reduction from a mean of 95.6% of procedures without aspiration receiving at least one balloon to 33.0% of procedures with aspiration receiving a balloon, an absolute reduction of 62.6% of procedures.

Figure 178 shows a risk ratio of 0.60 (95% CI 0.48, 0.75) for mechanical thrombus extraction devices: that is a relative reduction of 40% in the proportion of procedures using at least one balloon catheter when mechanical devices are used, and an absolute reduction of 12.6% from 30.8% to 18.1%. The usage of balloon catheters in the control groups in these two comparisons are very different (95.6% versus 30.8%) which makes it hard to compare the two groups directly. This is partially explained by the protocol for JETSTENT[83] which directed that direct stenting be attempted in all patients in both arms of the trial wherever possible.

With the exception of Beran 2002,[9] the studies did not report the number of balloons used in each patient. It is assumed that either one or no balloons will normally be used in the initial phase of the procedure (before stent implantation). Additional balloons may also be used at later points in the procedure, but this usage will be unaffected by the use of thrombus extraction devices.

M.2.2.4 Length of PPCI procedures

If PPCI procedures using thrombus extraction take longer than without thrombus extraction this will involve additional time spent by staff and additional time using the cardiac catheter laboratory with the overheads that that involves. If the difference in length of time is sufficient that the staff and laboratory time could have alternatively been used in treating another patient then that will mean that this approach has additional costs.

The mean procedure length in each of the clinical studies is shown in Table 120 and Figure 179, Appendix I.

Table 120: Procedure time for PPCI when thrombus extraction device used versus when no thrombus extraction device used

Study	Procedure time (minutes): thrombus device used (mean ± SD)	Procedure time (minutes): no thrombus device used (mean ± SD)
Thrombus aspiration devices		
DEAR-MI 2006[102]	57 ± 19	54 ± 21
EXPORT 2008[25]	36.7 ± 18.0	34.5 ± 21.5
ITTI 2012[75]	53 ± 32	41 ± 16
REMEDIA 2005[19]	81 ± 43	72 ± 34
VAMPIRE 2008[57]	87.0 ± 32.4	93.6 ± 78.6
Mechanical thrombus extraction devices		
AIMI 2006[2]	75.4 ± 30.9	59.2 ± 26.8
JETSTENT 2010[83]	59.5 (44.7–70) (a)	46 (35–50) (a)
X AMINE ST 2005[72]	54 ± 28	45 ± 25

Antoniucci 2004,[3] Beran 2002,[9] Bulum 2012,[17] Napodano 2003,[85] De Luca 2006,[30] EXPIRA 2010,[96] INFUSE-AMI 2012,[106] Kaltoft 2006,[61] Liistro 2009,[74] PIHRATE 2010,[34] and TAPAS 2008[118] did not report procedure length.

(a) *Median (interquartile range)*

Figure 179 shows that the use of thrombus aspiration devices was associated with an increase in procedure length of 2.94 minutes (95% CI −1.29, 7.17) compared to procedures not involving thrombus extraction. This increase is not statistically significant, but it is also considered by the GDG not to be a clinically significant increase, as it is implausible that a difference of that magnitude would in practice lead to staff and facility resources actually being available to treat another patient instead.

Figure 179 further shows that the use of mechanical thrombus extraction devices was associated with an increase of 13.81 minutes (CI 9.58, 18.04) compared to procedures not involving thrombus extraction. This result is based on only two studies,[2,72] but is also consistent with the median procedure length reported for JETSTENT [83] (see Table 120 above). This provides relatively good evidence that there is a real increase in procedure length when mechanical thrombus extraction devices are used.

Whether a difference of 14 minutes is clinically significant depends to a great extent on the organisation of coronary services in a particular PCI centre. Saving time – meaning that the staff and the cardiac catheter laboratory are free to treat other patients – is only an advantage if there are other patients needing treatment at that particular time. This is a particularly significant consideration for an emergency procedure such as PPCI, but is complicated by the overlap of staff and facilities between PPCI and non-emergency procedures such as elective PCI. For further discussion on this point see Chapter 12. In the opinion of the GDG, an increase in procedure length of 14 minutes is unlikely to be clinically significant in any but very high volume centres. Any possible cost implications would also be small in comparison to the effect of the cost of the mechanical thrombus extraction devices themselves. It was therefore concluded that it would be both very difficult to attempt to reliably cost the effect of differing procedure length, and it was unnecessary. No costs were therefore calculated.

M.2.3 Costs

M.2.3.1 Thrombus extraction devices

Thrombus extraction devices are not procured by the NHS centrally, and there are no published national list prices. Prices are set by manufacturers in negotiation with NHS buyers.

We contacted the manufacturers of all thrombus extraction devices currently used in the UK and they provided us with the price or range of prices at which they sell their products. The prices given were the nationally available prices at which these items could be purchased by an NHS buyer in 2012. The prices for individual devices were provided on a confidential basis, but summary measures for each class of device are presented below, with the consent of the manufacturers. The products for which prices were received were: AngioJet, ThrombCat, Diver CE, Export, Eliminate, QuickCat and Pronto. The distributer of Hunter aspiration catheters agreed to provide cost data but did not do so in time for the publication of this guideline, so Hunter has been excluded from these calculations.

Thrombus aspiration devices

Thrombus aspiration devices cost between £140 and £180, with a mean of £153.

Mechanical thrombus extraction devices

Mechanical thrombus extraction devices have a mean cost of £1244 with a small range.

M.2.3.2 Balloon catheters

The price of balloon catheters was agreed by the GDG by consensus, based on their experience of purchasing these items in clinical practice in the previous year. It was agreed that the range of prices shown in Table 121 represent the costs at which NHS providers were able to purchase these items in 2012 across England and Wales.

Table 121: Cost of balloon catheters

Item	Price (range)
Balloon catheter	£45–£65

M.3 Results

M.3.1 Thrombus extraction devices

Thrombus aspiration devices

Procedures involving the use of a thrombus aspiration device will cost an average of £153 more than procedures involving no thrombus extraction device.

Mechanical thrombus extraction devices

Procedures involving the use of a mechanical thrombus extraction device will cost an average of £1244 more than procedures involving no thrombus extraction device.

M.3.2 Stents

There was found to be no evidence of a difference in usage of stents between the two approaches, and it was hence concluded that there was not likely to be any difference in costs between the approaches on the basis of stent usage.

M.3.3 Balloon catheters

Given the frequency of balloon catheter use shown in the studies included in the clinical evidence review, and a cost of £45–£65 per balloon catheter:

- For thrombus aspiration devices: an absolute reduction of 62.6% will lead to a cost saving of £28–£41 per procedure when a thrombus aspiration device is used compared to no thrombus extraction.
- For mechanical thrombus extraction devices: an absolute reduction of 12.6% will lead to a cost saving of £5.70–£8.20 per procedure when a mechanical thrombus extraction device is used compared to no thrombus extraction.

The results for mechanical thrombus extraction devices are based on a baseline rate of balloon catheter usage in the control group much lower than in the aspiration group, and lower than seems likely in clinical practice. If the baseline rate was higher then greater savings would be expected, though the savings would remain lower than the savings shown above for the use of aspiration devices, due to the lesser relative reduction in use of balloon catheters seen with mechanical devices.

M.3.4 Length of PPCI procedures

There was found to be no evidence of a clinically significant difference in procedure times between thrombus aspiration and no thrombus extraction, and it is hence concluded that there was likely to be no difference in costs on the basis of procedure length for thrombus extraction.

There was found to be an increase of procedure length by 14 minutes with mechanical thrombus extraction compared to no thrombus extraction. In some settings this will not give rise to any difference in costs; in other settings this may cause mechanical thrombus extraction to be more expensive than no thrombus extraction.

M.4 Discussion

M.4.1 Summary of results

The analysis presented here suggests that there will not be any cost difference on account of the usage of stents or, for thrombus aspiration devices, procedure length.

The greatest impact on costs is the price of the thrombus extraction devices themselves: around £150 per PPCI procedure for thrombus aspiration devices and over £1200 per PPCI procedure for mechanical thrombus extraction devices.

The use of balloon catheters partly counteracts this for thrombus aspiration devices, with a reduction in costs of £28–41 when a thrombus aspiration device is used. The result is that procedures using thrombus aspiration devices are likely to cost around £110–£125 more than procedures not using any thrombus extraction device.

The cost saving in the use of balloon catheters for mechanical thrombus extraction procedures is smaller but less certain, due to less reliable clinical evidence. However, any possible cost saving will be minimal compared to the cost of the mechanical thrombus extraction device itself. There is also a possibility of increased cost due to longer procedure times with mechanical thrombus extraction devices, however that will be dependent on the setting: it is unlikely to make any difference in most centres, and even in the busier centres the additional effect is unlikely to be large. Hence the overall additional cost of using a mechanical thrombus extraction device is likely to be around £1200 compared to procedures not using any thrombus extraction device.

M.4.2 Limitations and interpretation

This analysis was informed wherever possible with data from the clinical evidence review for this question. It is not clear whether current UK practice is the same. Stent use in the UK is widespread

(92.3% of all PPCI procedures in the UK, 2011[77]) and there is no evidence to suggest that it differs between procedures using or not using a thrombus extraction device. The usage of balloon catheters is much less certain however.

The clinical data for balloon catheter usage were limited in two ways. Firstly, figures were not available for the absolute number of balloon catheters used or saved, only the cases receiving at least one balloon catheter. Secondly, the control groups for the two classes of devices were not comparable, which suggests that one or both of the reductions in usage shown may have been substantially inaccurate. No UK data were identified for balloon usage. However, the relatively small saving (up to £41) shown with a large (63%) reduction in balloon usage for thrombus aspiration devices indicates that it is unlikely the maximum saving could be much larger than this.

Thus the finding that both classes of thrombus extraction devices incur increased costs seems robust, but the exact magnitude of the increased cost is not certain for aspiration devices.

M.4.3 Conclusion

The evidence considered here suggests that a PPCI procedure carried out in the NHS in England and Wales using a thrombus aspiration device will cost more than PPCI carried out with no thrombus extraction device, the cost difference is most likely to be around £110–£125.

The evidence considered here suggests that a PPCI procedure carried out in the NHS in England and Wales using a thrombus aspiration device will cost around £1200 more than PPCI carried out with no thrombus extraction device.

M.4.4 Implications for future research

Research into the usage of balloon catheters in comparable patients undergoing PPCI in the UK with and without the use of thrombus aspiration devices would be beneficial.

Appendix N: Additional review data

N.1 Time to reperfusion (chapter 5)

Table 122: Search strategies of the pooled RCT analysis studies of PPCI versus fibrinolysis

Study	RCTs identified	RCTs analysed	Search strategy
Kent 2001	10	10	• Based on earlier meta-analysis (Weaver 1997) RCTs identified through MEDLINE (January 1985–March 1996) and by queries of principal investigators for exact data and additional studies. Also searched the scientific session abstracts in Circulation, The Journal of the American College of Cardiology and the European Heart Journal over the same period. • One study was excluded because individual patient data were unavailable (DeWood 1992) • One additional study identified (Akhras 1997); published after Weaver 1997 meta-analysis
Zijlstra 2002	11	10	• Based on earlier meta-analysis (Weaver 1997) RCTs identified through MEDLINE (January 1985–March 1996) and by queries of principal investigators for exact data and additional studies. Also searched the scientific session abstracts in Circulation, The Journal of the American College of Cardiology and the European Heart Journal over the same period. • One study was excluded because individual patient data were unavailable (DeWood 1992) • One additional study identified (Akhras 1997); published after Weaver 1997 meta-analysis
Boersma 2006	25	22	• All RCTs (n > 50) published between January 1990 and December 2002 were considered (non-English articles were not excluded). They were identified by OVID MEDLINE and ISI Web of Science® using a broad range of key words; References of identified papers and abstract listings of annual meetings of the American Heart Association, American College of Cardiology and European Society of Cardiology were also examined during the same period. • Two studies were excluded because individual patient data were unavailable (DeWood 1992; Morais 1997) • One study was excluded because CAPTIM investigators judged that their protocol (which included pre-hospital fibrinolysis) was incompatible with the other trials included in the pooled analysis (Steg 2003); included in sensitivity analysis
Asseburg 2007	24	22	• Updated earlier meta-analysis http://www.ncbi.nlm.nih.gov/pubmed/12517460 (Keeley 2003) by searching: Cochrane Controlled Trials Register, UK National Research Register, Medline, Embase, Database of Abstracts of Reviews of Effects, UK National Health Service Economic Evaluation Databases, and the Health Technology Assessment Database for English language studies published between 2002 and 2004. Inclusion criteria were consistent with Keeley 2003 and Cochrane review (Cucherat 2003) • One additional trial was identified (de Boer 1994) • One study was excluded because emergency revascularisation arm did not differentiate results by type of intervention

Study	RCTs identified	RCTs analysed	Search strategy
			(angioplasty 64%, surgery 36%) (Hochman 1999) • An additional study was excluded because it did not report data on the delay to primary angioplasty (Akhras 1997) • Preliminary data from 3 conference abstracts was updated with final trial reports (Berrocal 2003; Widimsky 2003; Andersen 2003) • Other inaccuracies were corrected
Tarantini 2010	19	16	• All RCTs (n > 50), published and unpublished (non-English articles were not excluded) comparing fibrin-specific fibrinolysis to PPCI. MEDLINE, CENTRAL, EMBASE, and the Cochrane Central Register of Controlled Trials were searched from January 1990 to December 2008 using a broad range of keywords. Also searched for abstracts reported in the New England Journal of Medicine, Circulation, European Heart Journal, Journal of the American College of Cardiology, and Heart. References of identified papers, relevant studies, and meta-analyses were additionally scanned. Furthermore, oral presentations and expert slide presentations identified from www.theheart.org, www.tctmd.com, www.crtonline.com, www.clinicaltrialresults.org, www.esccardio.org, www.europcr.com, and www.acc.org were also examined. • Two studies were excluded due to missing data (Aoki 1997; Morais 1997) • One study was excluded because it did not directly compare PPCI to fibrinolysis (Hochman 1999)

Table 123: RCTs published subsequent to the pooled RCT analysis studies of PPCI versus fibrinolysis

		Fibrinolysis				PPCI				
Study	Age (years)	n	Agent	TN (min)	1-month all-cause mortality n (%)	n	Stent used	TB (min)	1-month all-cause mortality n (%)	OR (95%CI) PPCI versus fibrinolysis
Armstrong PW, WEST Steering Committee. A comparison of pharmacologic therapy with/without timely coronary intervention vs. primary percutaneous intervention early after ST-elevation myocardial infarction: the WEST (Which Early ST-elevation myocardial infarction Therapy) study. European Heart Journal. 2006; 27(13):1530-1538.	≥18	100	TNK	113*	4(4.0)	100	Yes (97%)	176*	1(1.0)	0.24 (0.027 to 2.21)
Bueno H, Betriu A, Heras M, Alonso JJ, Cequier A, Garcia EJ et al. Primary angioplasty vs. fibrinolysis in very old patients with acute myocardial infarction: TRIANA (TRatamiento del Infarto Agudo de miocardio eN Ancianos) randomized trial and pooled analysis with previous studies. European Heart Journal. 2011;	≥ 75	134	TNK	195*	23(17.2)	132	Yes (93%)	245*	18(13.6)	0.76(0.39 to 1.49)

Study	Age	Fibrinolysis	PPCI	OR (95%CI)
32(1):51-60.				

** from symptom onset, **from randomisation; ¥59% of patients in fibrinolysis armunderwent PPCI*
TNK = Telecteplase, rt-PA = XX = recombinant tissue-type plasminogen activator, r-Sak = staphylokinase

N.2 Facilitated primary percutaneous coronary intervention (fPPCI) (chapter 6)

N.2.1 GPIs: fPPCI versus PPCI – all GPIs subgroup analysis

Table 124: Clinical evidence profile: fPPCI with GPIs – fPPCI versus PPCI – all GPIs, subgroup analysis of trials using background of clopidogrel + aspirin or aspirin alone

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	GPIs (all): fPPCI	PPCI (clopidogrel subgroup)	Relative (95% CI)	Absolute	Quality	Importance
Mortality - all-cause (In-hospital) - Clopidogrel + aspirin (background treatment) (assessed with: No studies)												
0	No studies											CRITICAL
Mortality - all-cause (In-hospital) - Aspirin (background treatment) (assessed with: Zorman)												
1	Randomised trials	Very serious (a)	No serious inconsistency	No serious indirectness	Very serious (b)	None	0/56 (0%)	5/51 (9.8%)	RR 0.08 (0 to 1.46)	90 fewer per 1000 (from 98 fewer to 45 more)	VERY LOW	CRITICAL
Mortality - all-cause (short-term) - Clopidogrel + aspirin (background treatment) (assessed with: ASSIST; BRAVE-3; ON-TIME2)												
3	Randomised trials	Very serious (c)	No serious inconsistency	No serious indirectness	Very serious (b)	None	31/1075 (2.9%)	33/1075 (3.1%)	RR 0.94 (0.58 to 1.52)	2 fewer per 1000 (from 13 fewer to 16 more)	VERY LOW	CRITICAL
Mortality - all-cause (short-term) - Aspirin (background treatment) (assessed with: No studies)												
0	No studies											CRITICAL
Mortality - all-cause (longer-term) - Clopidogrel + aspirin (background treatment) (assessed with: ASSIST; BRAVE-3; ON-TIME 2)												
3	Randomised	Very serious	Serious (d)	No serious	Serious (e)	None	52/1069	47/1068	RR 1.11 (0.75 to	5 more per 1000 (from	VERY	CRITICAL

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**GPIs (all): fPPCI**	**PPCI (clopidogrel subgroup)**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
	trials	(c)		indirectness			(4.9%)	(4.4%)	1.63)	11 fewer to 28 more)	LOW	
Mortality - all-cause (longer-term) - Aspirin (background treatment) (assessed with: Zorman)												
1	Randomised trials	Very serious (a)	No serious inconsistency	No serious indirectness	Serious (f)	None	0/56 (0%)	7/51 (13.7%)	RR 0.06 (0 to 1.04)	129 fewer per 1000 (from 137 fewer to 5 more)	VERY LOW	CRITICAL
Stroke - all-cause (short-term) - Clopidogrel + aspirin (background treatment) (assessed with: ASSIST; BRAVE-3; ON-TIME 2)												
3	Randomised trials	Very serious (c)	No serious inconsistency	No serious indirectness	Serious (f)	None	2/1075 (0.19%)	9/1075 (0.84%)	RR 0.26 (0.07 to 1.06)	6 fewer per 1000 (from 8 fewer to 1 more)	VERY LOW	CRITICAL
Stroke - all-cause (short-term) - Aspirin (background treatment) (assessed with: FINESSE)												
1	Randomised trials	Serious (g)	No serious inconsistency	No serious indirectness	Very serious (b)	None	9/814 (1.1%)	8/715 (1.1%)	RR 1.10 (0.43 to 2.83)	1 more per 1000 (from 6 fewer to 20 more)	VERY LOW	CRITICAL
Stroke - all-cause (longer-term) - Clopidogrel + aspirin (background treatment) (assessed with: ASSIST; BRAVE-3)												
2	Randomised trials	Very serious (h)	Serious (d)	No serious indirectness	Very serious (b)	None	3/602 (0.5%)	5/598 (0.84%)	RR 0.63 (0.17 to 2.4)	3 fewer per 1000 (from 7 fewer to 12 more)	VERY LOW	CRITICAL
Stroke - all-cause (longer-term) - Aspirin (background treatment) (assessed with: No Studies)												
0	No studies											CRITICAL
Reinfarction / non-fatal reinfarction / recurrent myocardial infarction (short-term) - Clopidogrel + aspirin (background treatment) (assessed with: ASSIST; BRAVE-3; ON-TIME 2)												
3	Randomised trials	Very serious (c)	No serious inconsistency	No serious indirectness	Very serious (b)	None	19/1075 (1.8%)	19/1075 (1.8%)	RR 1 (0.54 to 1.88)	0 fewer per 1000 (from 8 fewer to 16 more)	VERY LOW	IMPORTANT
Reinfarction / non-fatal reinfarction / recurrent myocardial infarction (short-term) - Aspirin (background treatment) (assessed with: FINESSE)												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	GPIs (all): fPPCI	PPCI (clopidogrel subgroup)	Relative (95% CI)	Absolute	Quality	Importance
1	Randomised trials	Serious (g)	No serious inconsistency	No serious indirectness	Very serious (b)	None	16/602 (2.7%)	13/598 (2.2%)	RR 1.05 (0.52 to 2.11)	1 more per 1000 (from 10 fewer to 24 more)	VERY LOW	IMPORTANT
Reinfarction / non-fatal reinfarction / recurrent myocardial infarction (longer-term) - Clopidogrel + aspirin (background treatment) (assessed with: ASSIST; BRAVE-3)												
2	Randomised trials	Very serious (h)	No serious inconsistency	No serious indirectness	Very serious (b)	None	16/602 (2.7%)	13/598 (2.2%)	RR 1.22 (0.59 to 2.52)	5 more per 1000 (from 9 fewer to 33 more)	VERY LOW	IMPORTANT
Major bleeding (In-hospital) - Aspirin (background treatment) (assessed with: Zorman)												
1	Randomised trials	Very serious (a)	No serious inconsistency	No serious indirectness	Serious (i)	None	16/56 (28.6%)	6/51 (11.8%)	RR 2.43 (1.03 to 5.73)	168 more per 1000 (from 4 more to 556 more)	VERY LOW	IMPORTANT
Major bleeding (short-term) - Clopidogrel + aspirin (background treatment) (assessed with: BRAVE-3; ON-TIME 2)												
2	Randomised trials	Serious (j)	No serious inconsistency	No serious indirectness	Very serious (b)	None	26/874 (3%)	21/876 (2.4%)	RR 1.24 (0.71 to 2.19)	6 more per 1000 (from 7 fewer to 29 more)	VERY LOW	IMPORTANT
Major bleeding (short-term) - Aspirin (background treatment) (assessed with: FINESSE)												
1	Randomised trials	Serious (g)	No serious inconsistency	No serious indirectness	Serious (i)	None	39/814 (4.8%)	21/795 (2.6%)	RR 1.81 (1.08 to 3.06)	21 more per 1000 (from 2 more to 54 more)	LOW	IMPORTANT
Heart failure (In-hospital) - Aspirin (background treatment) (assessed with: Zornam)												
1	Randomised trials	Very serious (a)	No serious inconsistency	No serious indirectness	No serious imprecision	None	4/56 (7.1%)	15/51 (29.4%)	RR 0.24 (0.09 to 0.68)	224 fewer per 1000 (from 94 fewer to 268 fewer)	LOW	IMPORTANT

(a)1/1 study poor/unclear randomisation, allocation concealment and blinding.

(b) Confidence interval crosses both default MIDs (0.75 and 1.25) and line of no effect
(c) 3/3 studies poor/unclear allocation concealment; 1/3 studies poor/unclear blinding
(d) Heterogeneity: I^2 > 50% and < 75%
(e) Confidence interval crosses 1 default MID (1.25) and line of no effect
(f) Confidence interval crosses 1 default MID (0.75) and line of no effect
(g) 1/1 study poor/unclear allocation concealment
(h) 2/2 studies poor/unclear allocation concealment; 1/2 studies poor/open blinded
(i) onfidence interval crosses 1 default MID (1.25)
(j) 2/2 studies poor/unclear allocation concealment

N.2.2 GPIs: fPPCI versus PPCI – individual GPIs

Table 125: Clinical evidence profile: fPPCI with GPIs – fPPCI versus PPCI: abciximab

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	GPIs: Abciximab fPPCI	PPCI (placebo / no drug)	Relative (95% CI)	Absolute	Quality	Importance
Mortality - all-cause (In-hospital) (assessed with: Zorman)												
1	Randomised trials	Very serious (a)	No serious inconsistency	No serious indirectness	Very serious (b)	None	0/56 (0%)	5/51 (9.8%)	RR 0.08 (0 to 1.46)	90 fewer per 1000 (from 98 fewer to 45 more)	VERY LOW	CRITICAL
Mortality - all-cause (short-term) (assessed with: BRAVE-3)												
1	Randomised trials	Serious (c)	No serious inconsistency	No serious indirectness	Very serious (b)	None	13/401 (3.2%)	10/399 (2.5%)	RR 1.29 (0.57 to 2.92)	7 fewer per 1000 (from 11 fewer to 48 more)	VERY LOW	CRITICAL
Mortality - all-cause (longer-term) (assessed with: BRAVE-3; Zorman)												
2	Randomised trials	Very serious (d)	Very serious (e)	No serious indirectness	Very serious (b)	None	27/457 (5.9%)	23/450 (5.1%)	RR 1.15 (0.67 to 1.96)	8 more per 1000 (from 17 fewer to 49 more)	VERY LOW	CRITICAL
Stroke - all-cause (short-term) (assessed with: BRAVE-3; FINESSE)												
2	Randomised	Serious	No serious	No serious	Very serious	None	10/1215	9/1194	RR 1.09	1 more per	VERY LOW	CRITICAL

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	GPIs: Abciximab fPPCI	PPCI (placebo / no drug)	Relative (95% CI)	Absolute	Quality	Importance
	trials	(f)	inconsistency	indirectness	(b)		(0.82%)	(0.75%)	(0.44 to 2.66)	1000 (from 4 fewer to 13 more)		
Stroke - all-cause (longer-term) (assessed with: BRAVE-3)												
1	Randomised trials	Serious (c)	No serious inconsistency	No serious indirectness	Very serious (b)	None	3/401 (0.75%)	1/399 (0.25%)	RR 2.99 (0.31 to 28.58)	5 more per 1000 (from 2 fewer to 69 more)	VERY LOW	CRITICAL
Stroke - fatal (short-term) (assessed with: FINESSE)												
1	Randomised trials	Serious (c)	No serious inconsistency	No serious indirectness	Very serious (b)	None	3/814 (0.37%)	0/795 (0%)	RR 6.84 (0.35 to 132.14)	Not estimable as 0 events in 1 arm	VERY LOW	CRITICAL
Reinfarction / non-fatal reinfarction / recurrent myocardial infarction (short-term) (assessed with: BRAVE-3; FINESSE)												
2	Randomised trials	Serious (f)	No serious inconsistency	No serious indirectness	Serious (h)	None	19/1219 (1.6%)	19/1205 (1.6%)	RR 0.99 (0.53 to 1.85)	0 fewer per 1000 (from 7 fewer to 13 more)	LOW	IMPORTANT
Reinfarction / non-fatal reinfarction / recurrent myocardial infarction (longer-term) (assessed with: BRAVE-3)												
1	Randomised trials	Serious (c)	No serious inconsistency	No serious indirectness	Serious (b)	None	12/401 (3%)	11/309 (3.6%)	RR 1.09 (0.48 to 2.43)	3 more per 1000 (from 19 fewer to 51 more)	LOW	IMPORTANT
Intracranial bleeding / intracranial haemorrhage (short-term) (assessed with: FINESSE)												
1	Randomised trials	Serious (c)	No serious inconsistency	No serious indirectness	Very serious (b)	None	5/814 (0.61%)	1/795 (0.13%)	RR 4.88 (0.57 to 41.71)	5 more per 1000 (from 1 fewer to 51 more)	VERY LOW	CRITICAL
Major bleeding (In-hospital) (assessed with: Zorman)												
1	Randomised trials	Very serious	No serious inconsistency	No serious indirectness	Serious (j)	None	16/56 (28.6%)	6/51 (11.8%)	RR 2.43 (1.03 to	168 more per 1000	VERY LOW	IMPORTANT

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	GPIs: Abciximab fPPCI	PPCI (placebo / no drug)	Relative (95% CI)	Absolute		
				(i)					5.73)	(from 4 more to 556 more)		
Major bleeding (short-term) (assessed with: BRAVE-3; FINESSE)												
2	Randomised trials	Serious (f)	No serious inconsistency	No serious indirectness	Serious (j)	None	46/1215 (3.8%)	28/1194 (2.3%)	RR 1.61 (1.01 to 2.56)	14 more per 1000 (from 0 more to 37 more)	LOW	IMPORTANT
Minor bleeding (short-term) (assessed with: BRAVE-3; FINESSE)												
2	Randomised trials	Serious (f)	No serious inconsistency	No serious indirectness	No serious imprecision	None	94/1215 (7.7%)	41/1194 (3.4%)	RR 1.61 (1.01 to 2.56)	21 more per 1000 (from 0 more to 51 more)	MODERATE	IMPORTANT
Repeat revascularisation (revascularisation or reintervention); (short-term) (assessed with: FINESSE)												
1	Randomised trials	Serious (c)	No serious inconsistency	No serious indirectness	No serious imprecision	None	111/818 (13.6%)	111/806 (13.8%)	RR 0.99 (0.77 to 1.26)	1 fewer per 1000 (from 32 fewer to 36 more)	MODERATE	IMPORTANT
Repeat revascularisation (revascularisation or reintervention); (longer-term) (assessed with: BRAVE-3)												
1	Randomised trials	Serious (k)	No serious inconsistency	No serious indirectness	Serious (l)	None	53/401 (13.2%)	76/399 (19%)	RR 0.69 (0.5 to 0.96)	59 fewer per 1000 (from 8 fewer to 95 fewer)	LOW	IMPORTANT
Heart failure / fatal heart failure (In-hospital) (assessed with: Zorman)												
1	Randomised trials	Very serious (a)	No serious inconsistency	No serious indirectness	No serious imprecision	None	4/56 (7.1%)	15/51 (29.4%)	RR 0.24 (0.09 to 0.68)	224 fewer per 1000 (from 94 fewer to 268 fewer)	LOW	IMPORTANT

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	GPIs: Abciximab fPPCI	PPCI (placebo / no drug)	Relative (95% CI)	Absolute	Quality	Importance
Heart failure / fatal heart failure (short-term) (assessed with: FINESSE)												
1	Randomised trials	Serious (c)	No serious inconsistency	No serious indirectness	Very serious (b)	None	45/818 (5.5%)	52/806 (6.5%)	RR 0.85 (0.58 to 1.26)	10 fewer per 1000 (from 27 fewer to 17 more)	VERY LOW	IMPORTANT

(a) 1/1 study unclear randomisation and allocation concealment, 1/1 study unblinded.
(b) Confidence interval crosses both default MIDs (0.75 and 1.25) and line of no effect
(c) 1/1 study poor/unclear allocation concealment
(d) 1/2 studies poor randomisation, 2/2 studies unclear allocation concealment, 1/2 studies poor blinding
(e) Unexplained heterogeneity I^2 >75%
(f) 2/2 studies poor/unclear allocation concealment
(g) 1/1 study poor/open blinded
(h) Confidence interval crosses 1 default MID (0.75) and line of no effect
(i) 1/1 study poor/unclear randomisation; 1/1 study poor/unclear allocation concealment; 1/1 study poor/open blinded
(j) 95% CI crosses 1 default MID (1.25)
(k) 1/1 studies poor/unclear allocation concealment
(l) 96% CI crosses 1 MID (0.75)

Table 126: Clinical evidence profile: fPPCI with GPIs – fPPCI versus PPCI: tirofiban

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	GPIs: Tirofiban fPPCI	PPCI (placebo)	Relative (95% CI)	Absolute		
Mortality - all-cause (short-term) (assessed with: ON-TIME 2)												
1	Randomised trials	Serious (a)	No serious inconsistency	No serious indirectness	Serious (b)	None	11/473 (2.3%)	19/477 (4%)	RR 0.58 (0.28 to 1.21)	17 fewer per 1000 (from 29 fewer to 8 more)	LOW	CRITICAL
Mortality - all-cause (longer-term) (assessed with: ON-TIME 2)												
1	Randomised trials	Serious (a)	No serious inconsistency	No serious indirectness	Serious (b)	None	16/467 (3.4%)	25/470 (5.3%)	RR 0.64 (0.35 to 1.19)	19 fewer per 1000 (from 35 fewer to 10 more)	LOW	CRITICAL
Stroke - all-cause (short-term) (assessed with: ON-TIME 2)												
1	Randomised trials	Serious (a)	No serious inconsistency	No serious indirectness	Serious (b)	None	1/473 (0.2%)	7/477 (1.5%)	RR 0.14 (0.02 to 1.17)	13 fewer per 1000 (from 14 fewer to 2 more)	LOW	CRITICAL
Reinfarction /non-fatal reinfarction/recurrent myocardian infarction (short-term) (assessed with: ON-TIME 2)												
1	Randomised trials	Serious (a)	No serious inconsistency	No serious indirectness	Very serious (c)	None	13/473 (2.7%)	14/477 (2.9%)	RR 0.94 (0.44 to 1.97)	2 fewer per 1000 (from 16 fewer to 28 more)	VERY LOW	IMPORTANT
Major bleeding (short-term) (assessed with: ON-TIME 2)												
1	Randomised trials	Serious (a)	No serious inconsistency	No serious indirectness	Very serious (c)	None	19/473 (4%)	14/477 (2.9%)	RR 1.37 (0.69 to 2.7)	11 more per 1000 (from 9 fewer to 50 more)	VERY LOW	IMPORTANT
Minor bleeding (short-term) (assessed with: ON-TIME 2)												
1	Randomised trials	Serious (a)	No serious inconsistency	No serious indirectness	Serious (d)	None	29/473 (6.1%)	21/477 (4.4%)	RR 1.39 (0.81 to 2.41)	17 more per 1000 (from 8 fewer to 62 more)	LOW	LESS IMPORTANT

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	GPIs: Tirofiban fPPCI	PPCI (placebo)	Relative (95% CI)	Absolute	Quality	Importance
Repeat revascularisation (repeat or urgent revascularisation); (short-term) (assessed with: ON-TIME 2)												
1	Randomised trials	Serious (a)	No serious inconsistency	No serious indirectness	Very serious (c)	None	18/473 (3.8%)	20/477 (4.2%)	RR 0.91 (0.49 to 1.69)	4 fewer per 1000 (from 21 fewer to 29 more)	VERY LOW	IMPORTANT

(a) 1/1 study poor/unclear allocation concealment
(b) Confidence interval crosses 1 default MIDs (0.75) and line of no effect
(c) Confidence interval crosses both default MIDs (0.75 and 1.25) and line of no effect
(d) Confidence interval crosses 1 default MID (1.25) and line of no effect

Table 127: Clinical evidence profile: fPPCI with GPIs – fPPCI versus PPCI: eptifibatide

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	GPIs: Eptifibatide fPPCI	PPCI	Relative (95% CI)	Absolute	Quality	Importance
Mortality - all-cause (short-term) (assessed with: ASSIST)												
1	Randomised trials	Serious (a)	No serious inconsistency	No serious indirectness	Very serious (b)	None	7/201 (3.5%)	4/199 (2%)	RR 1.73 (0.52 to 5.83)	15 more per 1000 (from 10 fewer to 97 more)	VERY LOW	CRITICAL
Mortality - all-cause (longer-term) (assessed with: ASSIST)												
1	Randomised trials	Serious (a)	No serious inconsistency	No serious indirectness	Very serious (b)	None	9/201 (4.5%)	6/199 (3%)	RR 1.49 (0.54 to 4.09)	15 more per 1000 (from 14 fewer to 93 more)	VERY LOW	CRITICAL
Stroke - all-cause (short-term) (assessed with: ASSIST)												
1	Randomised	Serious	No serious	No serious	Very serious	None	0/201	1/199	RR 0.33	3 fewer	VERY LOW	CRITICAL

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	GPIs: Eptifibatide fPPCI	PPCI	Relative (95% CI)	Absolute	Quality	Importance
	trials	(a)	inconsistency	indirectness	(b)		(0%)	(0.5%)	(0.01 to 8.05)	per 1000 (from 5 fewer to 35 more)		
Stroke - all-cause (longer-term) (assessed with: ASSIST)												
1	Randomised trials	Serious (a)	No serious inconsistency	No serious indirectness	Very serious (b)	None	0/201 (0%)	4/199 (2%)	RR 0.11 (0.01 to 2.03)	18 fewer per 1000 (from 20 fewer to 21 more)	VERY LOW	CRITICAL
Reinfarction / non-fatal reinfarction / recurrent myocardial infarction (short-term) (assessed with: ASSIST)												
1	Randomised trials	Serious (a)	No serious inconsistency	No serious indirectness	Very serious (b)	None	3/201 (1.5%)	1/199 (0.5%)	RR 2.97 (0.31 to 28.31)	10 more per 1000 (from 3 fewer to 137 more)	VERY LOW	IMPORTANT
Reinfarction / non-fatal reinfarction / recurrent myocardial infarction (longer-term) (assessed with: ASSIST)												
1	Randomised trials	Serious (a)	No serious inconsistency	No serious indirectness	Very serious (b)	None	4/201 (2%)	2/199 (1%)	RR 1.98 (0.37 to 10.69)	10 more per 1000 (from 6 fewer to 97 more)	VERY LOW	IMPORTANT
Heart failure / fatal heart failure (short-term) (assessed with: ASSIST)												
1	Randomised trials	Serious (a)	No serious inconsistency	No serious indirectness	Very serious (b)	None	15/201 (7.5%)	22/199 (11.1%)	RR 0.68 (0.36 to 1.26)	35 fewer per 1000 (from 71 fewer to 29 more)	VERY LOW	IMPORTANT
Heart failure / fatal heart failure (longer-term) (assessed with: ASSIST)												
1	Randomised trials	Serious (a)	No serious inconsistency	No serious indirectness	Serious imprecision	None	15/201 (7.5%)	24/199 (12.1%)	RR 0.62 (0.33 to	46 fewer per 1000	LOW	IMPORTANT

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	GPIs: Eptifibatide fPPCI	PPCI	Relative (95% CI)	Absolute	Quality	Importance
					(c)				1.14)	(from 81 fewer to 17 more)		
Repeat revascularisation (repeat or urgent revascularisation); (short-term) (assessed with: ASSIST)												
1	Randomised trials	Serious (a)	No serious inconsistency	No serious indirectness	Very serious (b)	None	8/201 (4%)	4/199 (2%)	RR 1.98 (0.61 to 6.47)	20 more per 1000 (from 8 fewer to 110 more)	VERY LOW	IMPORTANT
Repeat revascularisation (repeat or urgent revascularisation); (longer-term) (assessed with: ASSIST)												
1	Randomised trials	Serious (a)	No serious inconsistency	No serious indirectness	Very serious (b)	None	8/201 (4%)	6/199 (3%)	RR 1.32 (0.47 to 3.74)	10 more per 1000 (from 16 fewer to 83 more)	VERY LOW	IMPORTANT

(a) 1/1 study unclear allocation concealment and poor blinding
(b) Confidence interval crosses both default MIDs (0.75 and 1.25) and line of no effect
(c) Confidence interval crosses one default MID (0.75) and line of no effect

N.2.3 GPIs: pre-catheter laboratory versus in-catheter laboratory administration – individual GPIs

Table 128: Clinical evidence profile: fPPCI with GPIs – pre-catheter laboratory versus in-catheter laboratory administration: abciximab

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	FPPCI - Early	Later - ABCIXIMAB	Relative (95% CI)	Absolute	Quality	Importance
Mortality - all-cause (In-hospital) (assessed with: MISTRAL; Zorman)												
2	Randomised trials	Very serious	Serious (b)	No serious indirectness	Very serious (c)	None	2/183 (1.1%)	5/185 (2.7%)	RR 0.46 (0.10 to	15 fewer per 1000	VERY LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	FPPCI - Early	Later - ABCIXIMAB	Relative (95% CI)	Absolute		
		(a)							2.01)	(from 24 fewer to 27 more)		
Mortality - all-cause (short-term) (assessed with: Bellandi; Dudek; MISTRAL; ERAMI)												
4	Randomised trials	Very serious (d)	No serious inconsistency	No serious indirectness	Very serious (c)	None	8/214 (3.7%)	7/222 (3.2%)	RR 1.19 (0.47 to 3.06)	6 more per 1000 (from 17 fewer to 65 more)	VERY LOW	CRITICAL
Mortality - all-cause (longer-term) (assessed with: MISTRAL; Zorman)												
2	Randomised trials	Very serious (a)	Serious (e)	No serious indirectness	Very serious (c)	None	2/183 (1.1%)	6/185 (3.2%)	RR 0.39 (0.09 to 1.64)	20 fewer per 1000 (from 30 fewer to 21 more)	VERY LOW	CRITICAL
Intracranial bleeding / intracranial haemorrhage (In-hospital) (assessed with: Bellandi)												
1	Randomised trials	Serious (f)	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/27 (0%)	0/28 (0%)	Not pooled	Not pooled	MODERATE	CRITICAL
Intracranial bleeding / intracranial haemorrhage (short-term) (assessed with: Dudek; RELAX-AMI)												
2	Randomised trials	Very serious (g)	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/129 (0%)	0/132 (0%)	Not pooled	Not pooled	LOW	CRITICAL
Reinfarction / non-fatal reinfarction / recurrent myocardial infarction (In-hospital) (assessed with: MISTRAL)												
1	Randomised trials	Serious (h)	No serious inconsistency	No serious indirectness	Very serious (c)	None	2/127 (1.6%)	2/129 (1.6%)	RR 1.02 (0.15 to 7.1)	0 more per 1000 (from 13 fewer to 95 more)	VERY LOW	IMPORTANT
Reinfarction / non-fatal reinfarction / recurrent myocardial infarction (short-term) (assessed with: Bellandi, Dudek, MISTRAL, ERAMI, RELAX-AMI)												
5	Randomised trials	Very serious (i)	No serious inconsistency	No serious indirectness	Very serious (c)	None	5/319 (1.6%)	7/327 (2.1%)	RR 0.74 (0.25 to 2.21)	6 fewer per 1000 (from 16 fewer to 26 more)	VERY LOW	IMPORTANT
Reinfarction / non-fatal reinfarction / recurrent myocardial infarction (longer-term) (assessed with: MISTRAL)												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	FPPCI - Early	Later - ABCIXIMAB	Relative (95% CI)	Absolute	Quality	Importance
1	Randomised trials	Serious (h)	No serious inconsistency	No serious indirectness	Very serious (c)	None	3/127 (2.4%)	2/129 (1.6%)	RR 1.52 (0.26 to 8.97)	8 more per 1000 (from 11 fewer to 124 more)	VERY LOW	IMPORTANT
Bleeding (In-hospital) (assessed with: Zorman)												
1	Randomised trials	Very serious (j)	No serious inconsistency	No serious indirectness	Serious (k)	None	16/56 (28.6%)	11/56 (19.6%)	RR 1.45 (0.74 to 2.85)	88 more per 1000 (from 51 fewer to 363 more)	VERY LOW	CRITICAL
Major bleeding (short-term) (assessed with: Bellandi, Dudek, ERAMI, RELAX-AMI)												
4	Randomised trials	Very serious (l)	No serious inconsistency	No serious indirectness	Very serious (c)	None	4/192 (2.1%)	4/198 (2%)	RR 1.05 (0.29 to 3.8)	1 more per 1000 (from 14 fewer to 57 more)	VERY LOW	IMPORTANT
Minor bleeding (short-term) (assessed with: Dudek; ERAMI; RELAX-AMI)												
3	Randomised trials	Very serious (m)	No serious inconsistency	No serious indirectness	Very serious (c)	None	12/165 (7.3%)	8/170 (4.7%)	RR 1.54 (0.65 to 3.67)	25 more per 1000 (from 16 fewer to 126 more)	VERY LOW	IMPORTANT
Repeat revascularisation (repeat or urgent revascularisation); (short-term) (assessed with: Bellandi; Dudek; ERAMI; RELAX-AMI)												
4	Randomised trials	Very serious (l)	No serious inconsistency	No serious indirectness	Very serious (c)	None	3/192 (1.6%)	1/198 (0.51%)	RR 2.38 (0.36 to 15.84)	7 more per 1000 (from 3 fewer to 75 more)	VERY LOW	IMPORTANT
Heart failure (In-hospital) (assessed with: Zorman)												
1	Randomised trials	Very serious (j)	No serious inconsistency	No serious indirectness	Serious (n)	None	4/56 (7.1%)	10/56 (17.9%)	RR 0.40 (0.13 to 1.20)	107 fewer per 1000 (from 155 fewer to 36 more)	VERY LOW	CRITICAL

(a) 2/2 studies poor/unclear randomisation and allocation concealment; 1/2 studies poor/unclear blinding
(b) Significant heterogeneity: I^2 = 59%
(c) Confidence interval crosses both default MIDs (0.75 and 1.25) and line of no effect

(d) 4/4 studies poor/unclear randomisation; 3/4 studies poor/unclear allocation concealment; 2/4 studies poor/open blinded; 1/4 studies no/unclear ITT analysis
(e) Significant heterogeneity: I^2 = 65%
(f) 1/1 studies poor/unclear randomisation; 1/1 studies poor/open blinded
(g) 2/2 studies poor/unclear randomisation; 2/2 studies poor/unclear allocation concealment; 2/2 studies poor/open blinded; 2/2 studies no/unclear ITT analysis
(h) 1/1 study poor/unclear randomisation; 1/1 study poor/unclear allocation concealment
(i) 5/5 studies poor/unclear randomisation; 4/5 studies poor/unclear allocation concealment; 3/5 studies poor/open blinded; 2/5 studies no/unclear ITT analysis
(j) 1/1 study poor/unclear randomisation, allocation concealment and blinding
(k) Confidence interval crosses 1 default MID (1.25) and line of no effect
(l) 4/4 studies poor/unclear randomisation; 3/4 studies poor/unclear allocation concealment; 3/4 studies poor/open blinded; 2/4 studies no/unclear ITT analysis
(m) 3/3 studies poor/unclear randomisation; 3/3 studies poor/unclear allocation concealment; 2/3 studies poor/open blinded; 2/3 studies no/unclear ITT analysis
(n) Confidence Interval crosses 1 default MID (0.75) and line of no effect

Table 129: Clinical evidence profile: fPPCI with GPIs – pre-catheter laboratory versus in-catheter laboratory administration: tirofiban

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Early	Later TIROFIBAN	Relative (95% CI)	Absolute	Quality	Importance
Mortality- all-cause (in-hospital) (assessed with: AGIR)												
1	Randomised trials	Serious (a)	No serious inconsistency	No serious indirectness	Very serious (b)	None	5/156 (3.2%)	9/164 (5.5%)	RR 0.58 (0.2 to 1.7)	23 fewer per 1000 (from 44 fewer to 38 more)	VERY LOW	CRITICAL
Mortality - all-cause (short-term) (assessed with: Emre; ON-TIME)												
2	Randomised trials	Very serious (c)	No serious inconsistency	No serious indirectness	Serious (d)	None	9/277 (3.2%)	2/281 (0.7%)	RR 4.54 (0.99 to 20.78)	25 more per 1000 (from 0 fewer to 141 more)	VERY LOW	CRITICAL
Mortality - all-cause (longer-term) (assessed with: ON-TIME)												
1	Randomised trials	Very serious (e)	No serious inconsistency	No serious indirectness	Very serious (b)	None	11/245 (4.5%)	9/244 (3.7%)	RR 1.22 (0.51 to 2.88)	8 more per 1000 (from 18 fewer to 69 more)	VERY LOW	CRITICAL
Stroke - all-cause (in-hospital) (assessed with: AGIR)												
1	Randomised trials	Serious (a)	No serious inconsistency	No serious indirectness	Very serious (b)	None	1/156 (0.6%)	2/164 (1.2%)	RR 0.53 (0.05 to 5.74)	6 fewer per 1000 (from 12 fewer to 58 more)	VERY LOW	CRITICAL

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Early	Later TIROFIBAN	Relative (95% CI)	Absolute	Quality	Importance
Stroke - all-cause (short-term) (assessed with: ON-TIME)												
1	Randomised trials	Very serious (e)	No serious inconsistency	No serious indirectness	Very serious (b)	None	0/245 (0%)	1/256 (0.4%)	RR 0.35 (0.01 to 8.51)	3 fewer per 1000 (from 4 fewer to 29 more)	VERY LOW	CRITICAL
Reinfarction or non-fatal reinfarction or recurrent myocardial infarction (short-term) (assessed with: Emre; ON-TIME)												
2	Randomised trials	Very serious (c)	No serious inconsistency	No serious indirectness	Very serious (b)	None	3/277 (1.1%)	3/281 (1.1%)	RR 1.02 (0.23 to 4.48)	0 more per 1000 (from 8 fewer to 37 more)	VERY LOW	IMPORTANT
Reinfarction / non-fatal reinfarction / recurrent myocardial infarction (longer-term) (assessed with: ON-TIME)												
1	Randomised trials	Very serious (e)	No serious inconsistency	No serious indirectness	Very serious (b)	None	6/245 (2.4%)	9/244 (3.7%)	RR 0.66 (0.24 to 1.84)	13 fewer per 1000 (from 28 fewer to 31 more)	VERY LOW	IMPORTANT
Intracranial bleeding or intracranial haemorrhage (short-term) (assessed with: ON-TIME)												
1	Randomised trials	Very serious (e)	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/245 (0%)	0/256 (0%)	Not estimable as zero events in each arm		LOW	CRITICAL
Major bleeding (In hospital) (assessed with: AGIR)												
1	Randomised trials	Serious (a)	No serious inconsistency	No serious indirectness	Very serious (b)	None	2/156 (1.3%)	6/164 (3.7%)	RR 0.35 (0.07 to 1.71)	24 fewer per 1000 (from 34 fewer to 26 more)	VERY LOW	IMPORTANT
Major bleeding (short-term) (assessed with: Emre; ON-TIME)												
2	Randomised trials	Very serious (c)	No serious inconsistency	No serious indirectness	Very serious (b)	None	11/277 (4%)	8/290 (2.8%)	RR 1.44 (0.59 to 3.51)	12 more per 1000 (from 11 fewer to 69 more)	VERY LOW	IMPORTANT
Minor bleeding (short-term) (assessed with: Emre)												
1	Randomised	Very serious	No serious	No serious	Very serious	None	3/32	2/34	RR 1.59 (0.28 to	35 more per 1000 (from 42	VERY	IMPORTANT

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Early	Later TIROFIBAN	Relative (95% CI)	Absolute	Quality	Importance
	trials	(f)	inconsistency	indirectness	(b)		(9.4%)	(5.9%)	8.93)	fewer to 466 more)	LOW	

(a) 1/1 study poor/unclear bliding; 1/1 study no/unclear ITT analysis
(b) Confidence interval crosses both default MIDs (0.75 and 1.25) and line of no effect
(c) 2/2 studies poor/unclear randomisation; 2/2 studies poor/unclear allocation concealment; 1/2 studies poor/open blinded; 1/2 studies no/unclear ITT analysis
(d) Confidence interval crosses 1 default MID (1.25) and line of no effect
(e) 1/1 study poor/unclear randomisation; 1/1 study poor/unclear allocation concealment
(f) 1/1 study poor/unclear randomisation; 1/1 study poor/unclear allocation concealment; 1/1 study poor/open blinded; 1/1 study no/unclear ITT analysis

Table 130: Clinical evidence profile: fPPCI with GPIs – pre-catheter laboratory versus in-catheter laboratory administration: eptifibatide

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Early	Later EPTIFIBATIDE	Relative (95% CI)	Absolute	Quality	Importance
Mortality - all-cause (short-term) (assessed with: INTAMI-pilot)												
1	Randomised trials	Very serious	No serious inconsistency	No serious indirectness (a)	Very serious (b)	None	2/53 (3.8%)	2/49 (4.1%)	RR 0.92 (0.14 to 6.31)	3 fewer per 1000 (from 35 fewer to 217 more)	VERY LOW	CRITICAL
Stroke - all-cause (short-term) (assessed with: INTAMI-pilot)												
1	Randomised trials	Very serious (a)	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/53 (0%)	0/49 (0%)	Not estimable as zero events in each arm		LOW	CRITICAL
Reinfarction / non-fatal reinfarction /recurrent myocardial infarction (short-term) (assessed with: INTAMI-pilot)												
1	Randomised trials	Very serious (a)	No serious inconsistency	No serious indirectness	Very serious (b)	None	3/53 (5.7%)	0/49 (0%)	RR 6.48 (0.34 to 122.37)	Not estimable as 0 events in 1 arm	VERY LOW	IMPORTANT
Major bleeding (short-term) (assessed with: INTAMI-pilot)												
1	Randomised trials	Very serious	No serious inconsistency	No serious indirectness	Very serious (b)	None	2/53 (3.8%)	2/49 (4.1%)	RR 0.92 (0.14 to	3 fewer per 1000 (from	VERY LOW	IMPORTANT

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Early	Later EPTIFIBATIDE	Relative (95% CI)	Absolute	Quality	Importance
		(a)							6.31)	35 fewer to 217 more)		
Repeat revascularisation (repeat TVR); (short-term) (assessed with: INTAMI-pilot)												
1	Randomised trials	Very serious (a)	No serious inconsistency	No serious indirectness	Very serious (b)	None	2/53 (3.8%)	1/49 (2%)	RR 1.85 (0.17 to 19.76)	17 more per 1000 (from 17 fewer to 383 more)	VERY LOW	IMPORTANT

(a) 1/1 study poor/unclear randomisation; 1/1 study poor/open blinded; 1/1 study no/unclear ITT analysis
(b) Confidence interval crosses both default MIDs (0.75 and 1.25) and line of no effect

N.2.4 Fibrinolytics: fPPCI versus PPCI – individual fibrinolytics

Table 131: Clinical evidence profile: fPPCI with fibrinolytics – fPPCI versus PPCI: tenecteplase

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	FIBRINOLYTICS : Tenecteplase fPPCI	PPCI	Relative (95% CI)	Absolute	Quality	Importance
Mortality- all-cause (In hospital) (assessed with: ASSENT; ATHENS)												
2	Randomised trials	Very serious (a)	Very serious (b)	No serious indirectness	No serious imprecision	None	23/862 (2.7%)	5/904 (0.6%)	RR 4.33 (1.74 to 10.75)	18 more per 1000 (from 4 more to 54 more)	VERY LOW	CRITICAL
Mortality - all-cause(short-term) (assessed with: ASSENT; LIPSIA-STEMI)												
2	Randomised trials	Very serious (c)	No serious inconsistency	No serious indirectness	Serious (d)	None	60/903 (6.6%)	45/909 (5%)	RR 1.34 (0.92 to 1.95)	17 more per 1000 (from 4 fewer to 47 more)	VERY LOW	CRITICAL
Stroke - all-cause (In hospital) (assessed with: ATHENS; ASSENT-4)												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	FIBRINOLYTICS : Tenecteplase fPPCI	PPCI	Relative (95% CI)	Absolute	Quality	Importance
2	Randomised trials	Very serious (e)	No serious inconsistency	No serious indirectness	No serious imprecision	None	16/972 (1.6%)	0/979 (0%)	RR 17.06 (2.29 to 127.32)	Not estimable as 0 events in 1 arm	LOW	CRITICAL
Stroke - all-cause (short-term) (assessed with: LIPSIA-STEMI; ASSENT-4)												
2	Randomised trials	Very serious (f)	No serious inconsistency	No serious indirectness	Serious (d)	None	8/909 (0.88%)	2/916 (0.22%)	RR 4.00 (0.86 to 18.67)	7 more per 1000 (from 0 fewer to 39 more)	VERY LOW	CRITICAL
Stroke - non-fatal (In hospital) (assessed with: ATHENS)												
1	Randomised trials	Very serious (e)	No serious inconsistency	No serious indirectness	Very serious (g)	None	1/143 (0.7%)	0/141 (0%)	RR 2.96 (0.12 to 72.01)	Not estimable as 0 events in 1 arm	VERY LOW	CRITICAL
Reinfarction /non-fatal reinfarction/recurrent MI (short-term) (assessed with: ASSENT; LIPSIA-STEMI)												
2	Randomised trials	Very serious (c)	No serious inconsistency	No serious indirectness	No serious imprecision	None	54/885 (6.1%)	34/898 (3.8%)	RR 1.61 (1.06 to 2.45)	23 more per 1000 (from 2 more to 55 more)	LOW	IMPORTANT
Intracranial bleeding / intracranial haemorrhage (In hospital) (assessed with: ASSENT; ATHENS)												
2	Randomised trials	Very serious (a)	No serious inconsistency	No serious indirectness	No serious imprecision	None	8/862 (0.9%)	0/904 (0%)	RR 18.04 (1.04 to 311.96)	Not estimable as 0 events in 1 arm	LOW	CRITICAL
Intracranial bleeding / intracranial haemorrhage (short-term) (assessed with: ASSENT)												
1	Randomised trials	Very serious	No serious inconsistency	No serious indirectness	Very serious (g)	None	1/829 (0.1%)	1/838 (0.1%)	RR 1.01 (0.06 to	0 more per 1000	VERY LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	FIBRINOLYTICS: Tenecteplase fPPCI	PPCI	Relative (95% CI)	Absolute		
		(h)							16.13)	(from 1 fewer to 18 more)		
Major bleeding (In hospital) (assessed with: ASSENT; ATHENS)												
2	Randomised trials	Very serious (a)	No serious inconsistency	No serious indirectness	Serious (d)	None	54/862 (6.3%)	42/904 (4.6%)	RR 1.35 (0.91 to 2)	16 more per 1000 (from 4 fewer to 46 more)	VERY LOW	IMPORTANT
Minor bleeding (In hospital) (assessed with: ASSENT)												
1	Randomised trials	Very serious (h)	No serious inconsistency	No serious indirectness	No serious imprecision	None	210/719 (29.2%)	159/763 (20.8%)	RR 1.4 (1.17 to 1.68)	83 more per 1000 (from 35 more to 142 more)	LOW	IMPORTANT
Heart failure (In hospital) (assessed with: ATHENS)												
1	Randomised trials	Very serious (e)	No serious inconsistency	No serious indirectness	No serious imprecision	None	24/143 (16.8%)	5/141 (3.5%)	RR 4.73 (1.86 to 12.06)	132 more per 1000 (from 30 more to 392 more)	LOW	IMPORTANT
Heart failure (short-term) (assessed with: ASSENT; LIPSIA-STEMI)												
2	Randomised trials	Very serious (c)	No serious inconsistency	No serious indirectness	No serious imprecision	None	103/887 (11.6%)	78/896 (8.7%)	RR 1.34 (1.01 to 1.77)	30 more per 1000 (from 1 more to 67 more)	LOW	IMPORTANT
Repeat revascularisation (repeat or urgent revascularisation); (short-term) (assessed with: ASSENT)												
1	Randomised trials	Very serious (h)	No serious inconsistency	No serious indirectness	No serious imprecision	None	53/805 (6.6%)	28/818 (3.4%)	RR 1.92 (1.23 to 3.01)	31 more per 1000 (from 8 more to	LOW	IMPORTANT

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	FIBRINOLYTICS : Tenecteplase fPPCI	PPCI	Relative (95% CI)	Absolute	Quality	Importance
										69 more)		

(a) 1/2 studies poor/unclear randomisation; 1/2 studies poor/unclear allocation concealment; 2/2 studies poor/open blinded; 2/2 studies no/unclear ITT analysis
(b) Unexplained heterogeneity I^2 >75%
(c) 1/2 studies poor/unclear randomisation; 1/2 studies poor/unclear allocation concealment; 2/2 studies poor/open blinded; 1/2 studies no/unclear ITT analysis
(d) Confidence interval crosses 1 default MID (1.25) and line of no effect
(e) 1/1 studies poor/unclear randomisation; 1/1 studies poor/unclear allocation concealment; 1/1 studies poor/open blinded; 1/1 studies no/unclear ITT analysis
(f) 1/2 studies poor/unclear randomisation; 1/2 studies poor/unclear allocation concealment; 2/2 studies poor/open blinded; 1/2 studies no / unclear ITT analysis
(g) Confidence interval crosses both default MIDs (0.75 and 1.25) and line of no effect
(h) 1/1 study poor/unclear allocation concealment; 1/1 study poor/open blinded; 1/1 study no/unclear ITT analysis

Table 132: Clinical evidence profile: fPPCI with fibrinolytics - fPPCI versus PPCI: reteplase

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	FIBRINOLYTICS: Reteplase fPPCI	PPCI	Relative (95% CI)	Absolute	Quality	Importance
Mortality - all-cause (longer-term) (assessed with: Liu)												
1	Randomised trials	Very serious (a)	No serious inconsistency	No serious indirectness	Very serious (b)	None	1/72 (1.4%)	6/71 (8.5%)	RR 0.16 (0.02 to 1.33)	71 fewer per 1000 (from 83 fewer to 28 more)	VERY LOW	CRITICAL
Reinfarction /Non-fatal reinfarction/recurrent MI (short-term) (assessed with: Liu)												
1	Randomised trials	Very serious (a)	No serious inconsistency	No serious indirectness	Very serious (b)	None	1/72 (1.4%)	3/71 (4.2%)	RR 0.33 (0.04 to 3.09)	28 fewer per 1000 (from 41 fewer to 88 more)	VERY LOW	IMPORTANT
Intracranial bleeding / intracranial haemorrhage (longer-term) (assessed with: Liu)												
1	Randomised trials	Very serious (a)	No serious inconsistency	No serious indirectness	No serious imprecision (c)	None	0/72 (0%)	0/71 (0%)	Not estimable as zero events in both arms		LOW	CRITICAL

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	FIBRINOLYTICS: Reteplase fPPCI	PPCI	Relative (95% CI)	Absolute	Quality	Importance
Major bleeding (long term) (assessed with: Liu)												
1	Randomised trials	Very serious (a)	No serious inconsistency	No serious indirectness	No serious imprecision (c)	None	0/72 (0%)	0/71 (0%)	Not estimable as zero events in both arms		LOW	IMPORTANT
Minor bleeding (longer-term) (assessed with: Liu)												
1	Randomised trials	Very serious (a)	No serious inconsistency	No serious indirectness	Very serious (b)	None	8/72 (11.1%)	7/71 (9.9%)	RR 1.13 (0.43 to 2.94)	13 more per 1000 (from 56 fewer to 191 more)	VERY LOW	IMPORTANT
Heart failure (longer-term) (assessed with: Liu)												
1	Randomised trials	Very serious (a)	No serious inconsistency	No serious indirectness	Serious (d)	None	2/72 (2.8%)	9/71 (12.7%)	RR 0.22 (0.05 to 0.98)	99 fewer per 1000 (from 3 fewer to 120 fewer)	VERY LOW	IMPORTANT

(a) Randomisation and allocation concealment not reported. Unblinded.
(b) Confidence interval crosses both default MIDs (0.75 and 1.25) and line of no effect
(c) Zero events in both arms
(d) Confidence interval crosses 1 default MID (0.75)

Appendix O: Research recommendations

O.1 PPCI and fibrinolyis in people with acute STEMI who present very early

****This research question has been removed from the 2020 update****

Research question:

If a person with acute STEMI presents within 1 hour of the onset of symptoms, is it better for that person to be given fibrinolysis with a short call to needle time rather than to be transferred to a centre that carries out primary PCI for primary PCI with a delay of up to 120 minutes?

Why this is important:

Fibrinolytic drugs are administered intravenously and can be given out of hospital by an ambulance crew or in the emergency department of a hospital. Benefit from fibrinolysis declines significantly with time from onset of symptoms. Primary PCI, on the other hand, requires transfer to an interventional cardiology service, which inevitably delays the start of reperfusion treatment. Regardless of the reperfusion method used, delays to treatment are associated with an increased risk of impaired left ventricular systolic function and death.

It is unclear whether people with acute STEMI with a very short presentation delay would benefit more from immediate fibrinolysis (usually pre-hospital for people who do not self-present to hospital emergency departments) compared with transfer to a centre that carries out primary PCI.

To answer this question, a randomised controlled trial of pre-hospital fibrinolysis versus primary PCI in people with acute STEMI who have a short presentation delay of 1 hour or less is needed. Primary end points would include cardiovascular and all-cause mortality and other major adverse cardiovascular events. The STREAM study has recruited people who present early (less than 3 hours from onset of symptoms), and those presenting very early (less than 1 hour) could be analysed as a subgroup. However, it is not known whether this cohort will be big enough to allow a statistically significant conclusion to be drawn.

Criteria for selecting high-priority research recommendations:

PICO question	If a person with acute STEMI presents within 1 hour of the onset of symptoms, is it better for that person to be given fibrinolysis with a short call to needle time rather than to be transferred to a centre that carries out primary PCI for primary PCI with a delay of up to 120 minutes?
Importance to patients or the population	Delays to reperfusion treatment in STEMI are associated with an increased risk of death or heart failure. Up to 60 deaths per thousand treated are prevented if fibrinolysis is delivered within one hour of onset of symptoms. For people with acute STEMI who have a very short presentation delay but an anticipated long PPCI-delay this scenario potentially maximises the benefit of fibrinolysis when compared to a strategy of PPCI.
Relevance to NICE guidance	Results would inform a recommendation for, or against, fibrinolysis for people with acute STEMI who present within 1 hour after the onset of chest pain.
Relevance to the NHS	If results show benefit for fibrinolysis versus PPCI, a recommendation could state that for people with STEMI and short presentation delay, paramedics should make a judgement on acute management. This would require a more bespoke service than currently delivered and would have implications for ambulance services delivering fibrinolysis as soon as possible, which include training in pre-hospital fibrinolysis, potential for transmitting ECGs to hospitals for diagnosis

	and ambulance coverage if people are to be taken to a PPCI centre for rescue PCI.
National priorities	No
Current evidence base	Limited. The CAPTIM study[105] found a trend to mortality benefit in STEMI patients with presentation delay less than 2 hours who received pre-hospital fibrinolysis compared to PPCI.
Equality	The research question has no particular equality issues.
Study design	Randomised controlled trial of early fibrinolysis (usually pre-hospital since only a minority of people [around 15%] self-present to hospital emergency departments) versus PPCI in people with STEMI who have a very short presentation delay of 1 hour or less and an anticipated PPCI-related delay of up to 120 minutes. Primary end points would include cardiovascular and all-cause mortality and other major adverse cardiovascular events.
Feasibility	This research would require close collaboration between ambulance services and PPCI capable hospitals.
Other comments	None
Importance	Medium: the research is relevant to the recommendations in the guideline, but the research recommendations are not key to future updates

O.2 Primary PCI and fibrinolysis in people with acute STEMI who have a long anticipated transfer time for primary PCI

Research question:

In people with acute STEMI who present more than 1 hour after the onset of symptoms, is a primary PCI-related delay of 120-180 minutes associated with outcomes similar to, better or worse than pre-hospital administered fibrinolysis?

Why this is important:

Primary PCI is the preferred coronary reperfusion therapy provided it can be delivered ‘in a timely fashion’. It is suggested that primary PCI is the preferred reperfusion strategy for primary PCI-related delays of at least up to 2 hours. However, there is inadequate evidence to conclude whether primary PCI is still preferable at primary PCI-related time delays of more than 2 hours.

No specifically designed randomised controlled trial or observational study has addressed the issue of the extent to which primary PCI-related time delay (and other factors such as presentation delay and a person’s risk profile) diminishes the advantages of primary PCI over fibrinolysis. For example, in more geographically remote areas, a short presentation delay together with an anticipated long primary PCI-related delay could favour a strategy of pre-hospital fibrinolysis.

To answer this question, a randomised controlled trial of pre-hospital fibrinolysis versus primary PCI in people with acute STEMI who have a primary PCI-related time delay of 2 hours or more is needed. Primary end points would include cardiovascular and all-cause mortality and other major adverse cardiovascular events.

Criteria for selecting high-priority research recommendations:

PICO question	In people with acute STEMI who present more than 1 hour after the onset of symptoms, is a primary PCI-related delay of 120–180 minutes associated with outcomes similar to, better or worse than pre-hospital administered fibrinolysis?
Importance to patients or the population	Time to reperfusion is crucial in STEMI and for those people with acute STEMI who have long PPCI-related delays, it is important to ascertain whether PPCI is still preferable to fibrinolysis.

Relevance to NICE guidance	If results show a benefit for fibrinolysis versus PPCI then this would inform a recommendation of a bespoke revascularisation service in geographically remote areas. A negative result would inform a recommendation of PPCI for all people with STEMI, irrespective of PPCI-related time delay.
Relevance to the NHS	If results show a benefit for fibrinolysis versus PPCI, a recommendation could state that for people with long travel times to a PPCI centre the paramedics should make a judgement on acute STEMI management. This would require a more bespoke service than currently delivered and would have implications for ambulance services delivering fibrinolysis as soon as possible, which include training in pre-hospital fibrinolysis, potential for transmitting ECGs to hospitals for diagnosis and ambulance coverage if people are to be taken to a PPCI centre for rescue PCI.
National priorities	No
Current evidence base	There are no studies addressing this issue.
Equality	The research focuses on those people who live in geographically more remote areas of the UK.
Study design	Randomised controlled trial of pre-hospital fibrinolysis versus PPCI, in people with STEMI who present within 12 hours of chest pain and who have a PPCI-related delay of 2 hours or more. Primary end points should include all-cause and cardiovascular mortality.
Feasibility	This would require recruitment of patients in geographically remote areas and there are few areas in England and Wales where patients could not be transferred to a PPCI service within a PPCI related delay of 2 hours.
Other comments	None
Importance	Medium: the research is relevant to the recommendations in the guideline, but the research recommendations are not key to future updates.

O.3 Radial arterial access primary PCI versus femoral arterial access primary PCI

****This research recommendation has been removed from the 2020 update****

Research question:

What is the clinical and cost effectiveness of radial arterial access compared with femoral arterial access for coronary angiography or primary PCI in people with acute STEMI managed by primary PCI?

Why this is important:

There is no current evidence that demonstrates if there is a mortality difference between radial arterial access primary PCI compared with femoral arterial access primary PCI. It is unclear if operator experience has influenced current evidence. Operators may need additional training if 1 approach was shown to be superior. A randomised controlled trial comparing the 2 interventions for longer- term outcomes of all-cause mortality and major adverse cardiovascular events would answer the question. The trial would need to address the impact of operator expertise on the clinical outcomes. In addition, the need for operator training could be informed by an observational study that looked at the effectiveness and impact on clinical outcomes of experienced radial operators primarily using the radial approach versus experienced femoral operators primarily using the femoral approach including closure devices. The study would need a sufficient number of participants to enable differences in outcomes to be detected

Criteria for selecting high-priority research recommendations:

PICO question	What is the clinical and cost effectiveness of radial arterial access compared with femoral arterial access for coronary angiography or primary PCI in people with acute STEMI managed by primary PCI?
Importance to patients or the population	Demonstration of superiority of one intervention over another would provide the appropriate intervention for patients presenting with STEMI.
Relevance to NICE guidance	Results would inform a recommendation for either radial arterial access PPCI or femoral access PPCI.
Relevance to the NHS	Additional training of operators may be required, dependent upon the results.
National priorities	No.
Current evidence base	Published randomised controlled trials do not reflect current UK practice, furthermore, the femoral arms of the trials do not have a consistent approach with respect to haemostasis, and the femoral arms have low closure device utilisation.
Equality	No equality issues.
Study design	Randomised controlled trial comparing radial access PPCI versus femoral access PPCI with adjustment for operator expertise, non-randomised comparison of experienced radial operators primarily using the radial approach versus experienced femoral operators primarily using the femoral approach with closure device. A non-randomised study would require very large patient numbers. Outcomes should include: All-cause mortality, major adverse cardiovascular events, vascular complications, requirement for transfusion, length of hospital stay, cost of procedure, door to balloon times.
Feasibility	A randomised controlled trial and a non-randomised study would require sufficient patient numbers for adequate power to detect differences in clinical end points.
Other comments	None
Importance	Medium: the research is relevant to the recommendations in the guideline, but the research recommendations are not key to future updates.

O.4 Culprit vessel primary PCI versus multivessel PCI

****This research recommendation has been removed by the 2020 update****

Research question:

Does multivessel PCI, at the time of presentation of people with acute STEMI, confer an advantage over a strategy of 'culprit vessel only' primary PCI, followed by further elective revascularisation driven by symptoms and evidence of ischaemia?

Why this is important:

One-third of people presenting with STEMI have multivessel coronary artery disease at the time of presentation. Currently, there is uncertainty about whether to initially treat only the vessel likely to have caused the presentation or whether to treat all significant lesions. Most of the current evidence that examines 'culprit vessel only' primary PCI versus multivessel PCI in these people comes from studies that are underpowered or non-randomised. Answering this question would clarify the appropriate revascularisation strategy for this patient group. A randomised controlled trial powered to examine all-cause mortality and major adverse cardiovascular events with a 5-year follow-up would be the optimum design.

Criteria for selecting high-priority research recommendations:

PICO question	Does multivessel PCI, at the time of presentation of people with acute STEMI, confer an advantage over a strategy of 'culprit vessel only' primary PCI, followed by further elective revascularisation driven by symptoms and evidence of ischaemia?
Importance to patients or the population	Approximately 20,000 people per annum are treated in England with PPCI for STEMI. Of these, around one-third will have multivessel disease at the time of presentation. Answering this question would clarify the appropriate initial treatment for this population.
Relevance to NICE guidance	Results would inform a recommendation for an appropriate revascularisation strategy in people with STEMI and multivessel disease.
Relevance to the NHS	If research demonstrated that multivessel PCI at the time of initial presentation of STEMI was superior to culprit vessel only PCI, this would have limited consequences for the setting up of PPCI services and would have downstream effects on the subsequent investigation and management of people presenting with STEMI.
National priorities	No
Current evidence base	Most of the current evidence base comes from studies that are under-powered or non-randomised. One current ongoing study is randomised but the randomisation occurs only after the angiogram has been performed. This introduces a bias and will reduce the applicability of the results.
Equality	The research recommendation would be relevant to all people presenting with STEMI although the population with multivessel disease will include a higher proportion of elderly people and people with diabetes.
Study design	A randomised controlled trial powered to examine major adverse cardiovascular events over a 5-year follow-up would be the optimum design. One of the key issues is whether it is possible to assess the severity of non-culprit lesions in the setting of acute myocardial infarction. To address this, people presenting with STEMI and multivessel disease could have the culprit vessel treated in the usual way and the remaining lesions assessed visually by the operator and classed as significant or non-significant. People could then be assessed electively with functional imaging or with pressure wire assessment to determine the reliability of the operator's initial assessment of the significance of non-culprit coronary lesion(s). Outcomes should include: all-cause mortality, myocardial infarction, stroke and the need for unplanned revascularisation at 5 years.
Feasibility	A study examining clinically relevant end points including all-cause mortality, recurrent myocardial infarction, stroke and the need for further unplanned revascularisation would probably require 5-year follow-up and several thousand patients. This may present considerable organisational difficulties.
Other comments	It is quite likely that the differences between the two strategies will be relatively small. In the absence of data favouring multivessel PCI at the time of STEMI presentation, most operators favour the more conservative treatment of culprit vessel only PCI at the time of initial presentation followed by outpatient assessment of residual ischaemia 4–8 weeks after the acute event. This may involve stress perfusion scanning, stress echo, stress MRI or pressure wire assessment.
Importance	Medium: the research is relevant to the recommendations in the guideline, but the research recommendations are not key to future updates

O.5 Relationship between volume of procedures and clinical outcomes

Research question:

What is the relationship between hospital volume of primary PCI procedures and optimal outcomes in people with acute STEMI?

Why this is important:

There is a suggestion that outcomes may be better in larger-volume primary PCI units, and some retrospective registries have reported data to support this. However, the quality of the data is poor and still leaves the question open. In the UK, primary PCI is provided by units that vary greatly in the number of cases per year. The development of services has been ad hoc and not designed specifically around the provision of primary PCI. If it was possible to conclusively show that people were or were not better off being treated in larger volume units, then it would have important implications for the national provision of primary PCI.

Criteria for selecting high-priority research recommendations:

PICO question	What is the relationship between hospital volume of primary PCI procedures and optimal outcomes in people with acute STEMI?
Importance to patients or the population	The results would have important implications for service provision. If no significant difference was noted then PPCI service could be devolved to smaller local centres thus providing shorter call to balloon times and better outcomes. If there were a significant difference then provision would need to be concentrated in larger but more distant centres and transport and delivery of patients would become a focus.
Relevance to NICE guidance	Findings would inform a recommendation for optimal centre volumes of PPCI procedures, most likely aimed at commissioners.
Relevance to the NHS	Results could inform the strategy for delivery of PPCI across the country.
National priorities	No
Current evidence base	The current evidence base is not applicable to modern UK practice. It is in the form of retrospective registry analysis in the 1990s in the US, at a time when the majority of hospitals involved were using both fibrinolysis and PPCI and most of the 'low volume' centres were providing very low levels of PPCI (< 5 patients).
Equality	No equality issues.
Study design	It would be very difficult to conduct an RCT to answer this question. Retrospective registry data or cohorts of small patient number would not necessarily answer the question, because many other confounders may influence the outcomes. A prospective comparison of low volume centres versus high volume centres ensuring that total number patients were included in each group (for example, 2 units at 600 (high volume) versus 6 units at 100 (low volume) for 3 years may be the best way of providing a comparison. Outcomes should include: risk-adjusted in-hospital and 30-day all-cause mortality.
Feasibility	The variation in the presentation of STEMI is great so the trial would have to go on for a sufficient length of time to gather enough patient numbers to make robust statistical analysis possible. There are no technical or ethical issues.
Other comments	None
Importance	Low: the research is of interest and will fill existing evidence gaps.

O.6 People who remain unconscious after a cardiac arrest

****This research recommendation has been removed from the 2020 update****

Research question:

In people with return of spontaneous circulation following out-of-hospital cardiac arrest, does acute coronary angiography with coronary intervention compared to conventional treatment improve survival?

Why this is important:

The majority of people resuscitated from out-of-hospital cardiac arrest due to acute STEMI remain unconscious. Although early revascularisation is a treatment priority for all patients with ST-elevation myocardial infarction, people who remain unconscious following resuscitation from cardiac arrest may require immediate medical stabilisation. This competes with, and may take priority over, early revascularisation, delaying intervention in these people. With the knowledge that the benefits of early revascularisation are time-critical, it is not known whether the delays that inevitably occur in order to stabilise these people may contribute further to their mortality and morbidity.

A prospective randomised study of people resuscitated from cardiac arrest who remain unconscious (requiring intubation) following return of spontaneous circulation, comparing concurrent PPCI (while medical stabilisation is carried out), with delayed PCI in people admitted to intensive care for a period of stabilisation is needed to assess the clinical and cost effectiveness of these two strategies in this population. Outcomes should include survival to neurologically intact hospital discharge, myocardial function at 30 days and length of hospital stay. Although patient numbers are relatively small, with minimal cost implications for the NHS, the individual benefits to patients may be significant.

Criteria for selecting high-priority research recommendations:

PICO question	In people with return of spontaneous circulation following out-of-hospital cardiac arrest, does acute coronary angiography with coronary intervention compared to conventional treatment improve survival?
Importance to patients or the population	The majority of people resuscitated from out-of-hospital cardiac arrest are unconscious on arrival in the Emergency Department. Understanding the optimal management strategies could potentially benefit a large proportion of people admitted with return of spontaneous circulation from out-of-hospital cardiac arrest.
Relevance to NICE guidance	The answer to this question would directly influence the recommendations in NICE guidelines for people who remain unconscious following out-of-hospital cardiac arrest, where evidence is currently limited.
Relevance to the NHS	People with STEMI are likely to require PPCI shortly after admission to hospital. Prioritising or delaying this intervention is unlikely to have significant financial impact, effect on staff, impact on strategic planning or service delivery.
National priorities	Although clinically important, this question is not considered a national priority area.
Current evidence base	No randomised studies exist on acute coronary angiography following out-of-hospital cardiac arrest. An increasing number of observational studies support feasibility and a possible survival benefit of an early invasive approach, but a randomised controlled trial is required to address this question adequately.
Equality	There are no equality issues with regards to this research recommendation.
Study design	Prospective randomised studies would be required to address this question definitively.

Feasibility	A randomised study would present significant ethical challenges. Outcomes should include survival to neurologically intact hospital discharge, myocardial

	function at 30 days and length of hospital stay.
Other comments	Outcome from cardiac arrest varies significantly between hospitals and relatively large numbers of patients would therefore be required to control for cofounding variables.
Importance	Low: the research is of interest and will fill existing evidence gaps.

Appendix P: References

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