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Pre-emptive correction for haemodialysis arteriovenous access stenosis (Review)

Ravani P, Quinn RR, Oliver MJ, Karsanji DJ, James MT, MacRae JM, Palmer SC, Strippoli GFM

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[Intervention Review]

Pre-emptive correction for haemodialysis arteriovenous access stenosis

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ABSTRACT

Background

Guidelines recommend routine arteriovenous (AV) graft and fistula surveillance (technology-based screening) in addition to clinical monitoring (physical examination) for early identification and pre-emptive correction of a stenosis before the access becomes dysfunctional. However, consequences on patient-relevant outcomes of pre-emptive correction of a stenosis in a functioning access as opposed to deferred correction, i.e. correction postponed to when the access becomes dysfunctional, are uncertain.

Objectives

We aimed to evaluate 1) whether pre-emptive correction of an AV access stenosis improves clinically relevant outcomes; 2) whether the effects of pre-emptive correction of an AV access stenosis differ by access type (fistula versus graft), aim (primary and secondary prophylaxis), and surveillance method for primary prophylaxis (Doppler ultrasound for the screening of functional and anatomical changes versus measurement of the flow in the access); and 3) whether other factors (dialysis duration, access location, configuration or materials, algorithm for referral for intervention, intervention strategies (surgical versus radiological or other), or study design) explain the heterogeneity that might exist in the effect estimates.

Search methods

We searched the Cochrane Kidney and Transplant Specialised Register to 30 November 2015 using search terms relevant to this review.

Selection criteria

We included all studies of any access surveillance method for early identification and pre-emptive treatment of an AV access stenosis.

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Data collection and analysis

We extracted data on potentially remediable and irremediable failure of the access (i.e. thrombosis and access loss respectively); infection and mortality; and resource use (hospitalisation, diagnostic and intervention procedures). Analysis was by a random effects model and results expressed as risk ratio (RR), hazard ratio (HR) or incidence rate ratio (IRR) with 95% confidence intervals (CI).

Main results

We identified 14 studies (1390 participants), nine enrolled adults without a known access stenosis (primary prophylaxis; three studies including people using fistulas) and five enrolled adults with a documented stenosis in a non-dysfunctional access (secondary prophylaxis; three studies in people using fistulas). Study follow-up ranged from 6 to 38 months, and study size ranged from 58 to 189 participants. In low- to moderate-quality evidence (based on GRADE criteria) in adults treated with haemodialysis, relative to no surveillance and deferred correction, surveillance with pre-emptive correction of an AV stenosis reduced the risk of thrombosis (RR 0.79, 95% CI 0.65 to 0.97; I^2 = 30%; 18 study comparisons, 1212 participants), and probably improves the longevity of AV access (RR 0.80, 95% CI 0.64 to 0.99; I^2 = 0%; 11 study comparisons, 972 participants). In analyses subgrouped by access type, pre-emptive stenosis correction did not reduce the risk of thrombosis (RR 0.95, 95% CI 0.8 to 1.12; I^2 = 0%; 11 study comparisons, 697 participants) or access loss in grafts (RR 0.87, 95% CI 0.69 to 1.11; I^2 = 0%; 7 study comparisons; 662 participants), but did reduce the risk of thrombosis (RR 0.5, 95% CI 0.35 to 0.71; I^2 = 0%; 7 study comparisons, 515 participants) and the risk of access loss in fistulas (RR 0.5, 95% CI 0.29 to 0.86; I^2 = 0%; 4 studies; 310 participants). Three of the four studies reporting access loss data in fistulas (199 participants) were conducted in the same centre. Insufficient data were available to assess whether benefits vary by prophylaxis aim in fistulas (i.e. primary and secondary prophylaxis). Although the magnitude of the effects of pre-emptive stenosis correction was considerable for patient-centred outcomes, results were either heterogeneous or imprecise. While pre-emptive stenosis correction may reduce the rates of hospitalisation (IRR 0.54, 95% CI 0.31 to 0.93; I^2 = 67%; 4 study comparisons, 219 participants) and use of catheters (IRR 0.58, 95% CI 0.35 to 0.98; I^2 = 53%; 6 study comparisons, 394 participants), it may also increase the rates of diagnostic procedures (IRR 1.78, 95% CI 1.18 to 2.67; I^2 = 62%; 7 study comparisons, 539 participants), infection (IRR 1.74, 95% CI 0.78 to 3.91; I^2 = 0%; 3 studies, 248 participants) and mortality (RR 1.38, 95% CI 0.91 to 2.11; I^2 = 0%; 5 studies, 386 participants).

In general, risk of bias was high or unclear in most studies for many domains we assessed. Four studies were published after 2005 and only one had evidence of registration within a trial registry. No study reported information on authorship and/or involvement of the study sponsor in data collection, analysis, and interpretation.

Authors' conclusions

Pre-emptive correction of a newly identified or known stenosis in a functional AV access does not improve access longevity. Although pre-emptive stenosis correction may be promising in fistulas existing evidence is insufficient to guide clinical practice and health policy. While pre-emptive stenosis correction may reduce the risk of hospitalisation, this benefit is uncertain whereas there may be a substantial increase (i.e. 80%) in the use of access-related procedures and procedure-related adverse events (e.g. infection, mortality). The net effects of pre-emptive correction on harms and resource use are thus unclear.

PLAIN LANGUAGE SUMMARY

Pre-emptive correction of stenosis of the arteriovenous access for haemodialysis

An arteriovenous access consists of a direct surgical connection between an artery and a vein in the arm (fistula) or a plastic conduit connecting an artery and a vein (graft). If these forms of access become dysfunctional the delivery of dialysis therapy becomes suboptimal. The most common cause of access dysfunction is the development of a restriction or conduit narrowing called 'stenosis'. Because early correction of stenosis is considered critical to maintain the patency (openness) of the access and prolong its use, guidelines recommend regular surveillance of the access (i.e. screening based on diagnostic tests) in addition to or instead of a physical exam (clinical monitoring) to identify and treat early lesions.

In this review we included 14 studies, randomising 1390 participants to either a pre-emptive correction of an access stenosis (i.e. before the access became dysfunctional) or a deferred correction of an access stenosis (i.e. if and when the access became dysfunctional). This review shows that pre-emptive correction of an arteriovenous access stenosis does not improve longevity of the access overall. In people using grafts pre-emptive correction does not reduce the risk of thrombosis or access loss. In people using fistulas pre-emptive stenosis correction reduces the risk of thrombosis and may prolong the longevity of the access. However, this surveillance and pre-emptive correction strategy may increase the number of access-related procedures and procedure-related adverse events.

This systematic review presents, to clinicians and patients, evidence-based data that do not support the use of access surveillance and pre-emptive correction of stenosis in grafts. Although surveillance and pre-emptive correction of stenosis reduce the risk of thrombosis and may reduce the risk of access loss in fistulas, they may also increase the risk of procedure-related adverse events and health-care cost. Large multicentre clinical trials are necessary in this patient population to better clarify potential harms and expected benefits of routine surveillance and pre-emptive correction of fistula stenosis.

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SUMMARY OF FINDINGS

Summary of findings for the main comparison. Scheduled surveillance versus clinical monitoring alone for preventing arteriovenous (AV) access failure

Scheduled surveillance versus clinical monitoring alone for the prevention of AV access failure (maintenance of suitability for haemodialysis in an established AV access)

Patient or population: people receiving haemodialysis to treat kidney failure and using a functioning AV access for haemodialysis.

Settings: inpatient, outpatient or home care setting

Intervention: Surveillance of the access with Doppler ultrasound or blood flow measurements with or without clinical monitoring of the access.

Comparison: clinical monitoring alone, i.e. physical examination with or without haemodynamic parameters measured during haemodialysis (e.g. pump blood flow, arterial and venous pressure)

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Monitoring alone	Surveillance in addition to monitoring				
Risk of access thrombosis Follow-up: 1 year	**Higher risk population (people using a graft for haemodialysis)**		**RR** 0.95 (0.8, 1.12)	697 (11 cohorts from 8 studies)	⊕⊕⊝⊝ **moderate**	Most studies are small with low-quality reporting
	500 per 1000	**475 per 1000** (400 to 560)				
	Lower risk population (people using a fistula for haemodialysis)		**RR** 0.5 (0.35, 0.71)	515 (7 cohorts from 6 studies)	⊕⊝⊝⊝ **low**	
	400 per 1000	**200 per 1000** (140 to 284)				
Rate of angiograms Follow-up: 1 year	**People using any AV access (fistula or graft)**		**RR** 1.78 (1.18, 2.67)	539 (7 cohorts from 5 studies)	⊕⊝⊝⊝ **low**	
	300 per 1000	**534 per 1000** (354 to 801)				

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **RR:** risk ratio.

GRADE Working Group grades of evidence

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High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

Baseline risks and rates (among controls - people receiving clinical monitoring without surveillance) were calculated from the survival plots or information the papers reported.

Summary of findings 2. Scheduled surveillance versus clinical monitoring alone for the prevention of arteriovenous (AV) access failure

Scheduled surveillance versus clinical monitoring alone for the prevention of AV access failure (maintenance of suitability for haemodialysis in an established AV access)

Patient or population: people receiving haemodialysis to treat kidney failure and using a functioning AV access for haemodialysis.

Settings: inpatient, outpatient or home care setting.

Intervention: Surveillance of the access with Doppler ultrasound or blood flow measurements with or without clinical monitoring of the access.

Comparison: clinical monitoring alone, i.e. physical examination with or without haemodynamic parameters measured during haemodialysis (e.g. pump blood flow, arterial and venous pressure)

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Monitoring alone	Surveillance in addition to monitoring				
Risk of access loss Follow-up: 1 year	**Higher risk population (people using a graft for haemodialysis)**		**RR** 0.90 (0.71, 1.15)	662 (7 cohorts from 6 studies)	⊕⊕⊝⊝ **moderate**	Most studies are small with low-quality reporting
	150 per 1000	**135 per 1000** (107 to 172)				
	Lower risk population (people using a fistula for haemodialysis)		**RR** 0.5 (0.29, 0.86)	310 (4 studies)	⊕⊝⊝⊝ **low**	
	100 per 1000	**50 per 1000** (29 to 86)				
Mortality Follow-up: 1 year	**People using any AV access (fistula or graft)**		**RR** 1.38 (0.90, 2.11)	586 (5 studies)	⊕⊝⊝⊝ **low**	
	150 per 1000	**207 per 1000** (135 to 317)				

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*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **RR:** risk ratio.

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

Baseline risks and rates (among controls - people receiving clinical monitoring without surveillance) were calculated from the survival plots or information the papers reported.

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BACKGROUND

Haemodialysis, the most common treatment for kidney failure globally, requires reliable access to the bloodstream by means of a vascular access. The native arteriovenous (AV) fistula and the AV graft are considered the best types of access (Allon 2008; Besarab 2008) because large observational studies have shown that their use is associated with better patient outcomes than central venous catheters (Dhingra 2001; Pastan 2002). This belief was reinforced by a recent meta-analysis that showed that people using catheters had the highest risk of death from all causes, infection and cardiovascular disease (Ravani 2013a).

Description of the condition

AV fistulas and grafts consist of a direct surgical connection between an artery and a vein (fistula), or a bridge conduit between an artery and a vein (graft), usually made of synthetic material. Remodelling of blood vessels after AV access creation results in access maturation (enlargement) and increased blood flow, which permits haemodialysis (Roy-Chaudhury 2006). However, scarring and abnormal remodelling may also contribute to access stenosis, dysfunction and thrombosis, a leading cause of hospitalisation in haemodialysis patients (Manns 2005). While early inflow complications within the first few months after access creation are more common in fistulas than in grafts (Dember 2008), late complications of an established and functioning access are more common in grafts, and include venous outflow, graft-vein, graft-artery and intra-graft lesions in grafts, and outflow and inflow lesions in fistulas (Roy-Chaudhury 2006). Additional procedures are performed in 80% of newly-created fistulas to salvage access function (1.45 to 3.3 procedures/access-year, three times higher than in grafts), with an overall cost to facilitate fistula maturation (CAD 7740 in the first year) similar to that of a successful graft creation (CAD 8130 in the first year) (Lok 2007). About half of the fistulas that mature without additional interventions (20% of all fistulas) require some revisions in the long-term (0.17 to 0.57 procedures/access-year) (Lok 2007). Since these rates are six times lower than in grafts in the long-term, fistulas are considered the most cost-effective haemodialysis access (USD 4862/year) (Besarab 2008).

Description of the intervention

In most haemodialysis programs, different screening methods are routinely used for early identification of a haemodynamically significant AV access stenosis (National Kidney Foundation 2006). These screening methods consist of physical examination (monitoring) and technology-based strategies (surveillance). Clinical monitoring includes examination of the access thrill and bruit, haemostasis time after needle removal and arm assessment. Haemodialysis parameters such as pump speed, and arterial and transmembrane pressure, and indices of dialysis adequacy (Kt/V or urea reduction ratio (URR)) are also part of clinical monitoring. Surveillance includes sequential measurements with trend analysis of intra-access flow, dynamic or static venous dialysis pressure (venous pressure to systolic blood pressure ratio), or duplex ultrasound.

How the intervention might work

In the presence of a trend toward critical values of these indices, guidelines recommend patient referral for an imaging study and, if a stenotic lesion is diagnosed, pre-emptive correction of stenoses greater than 50% is recommended to prevent further progression of vessel narrowing and thrombosis of the access (Jindal 2006; National Kidney Foundation 2006; Polkinghorne 2008; Tordoir 2007; Renal Association 2015). These pre-emptive radiological intervention procedures (angioplasty with or without stenting) or surgical corrections of a stenosis in a functioning access are expected to prevent thrombosis of the access, improve its suitability for dialysis, increase dialysis dose delivery and increase the longevity of the AV access with reduced long-term access-related procedures and cost, compared to deferred salvage interventions performed only if and when the access becomes dysfunctional. However, the evidence in support of such practice is controversial (Tonelli 2008). In addition, information regarding access loss, costs, and hospitalisation rates following implementation of these screening strategies (a measure of potential harm and use of health care resources) is scarce.

Why it is important to do this review

Current guidelines recommend routine surveillance of permanent AV accesses (National Kidney Foundation 2006; Renal Association 2015), but several studies and a systematic review (Tonelli 2008) have been published since these guidelines were last updated. Given the considerable morbidity associated with access dysfunction, but also the important resource implications and unclear benefits and harms of these screening strategies, knowledge synthesis about optimal ways to improve outcomes of a functioning access is a priority for patients, clinicians and health policy makers. In this systematic review we have summarised data from randomised controlled trials (RCTs) on the benefits and harms of pre-emptive correction of AV access stenosis on the risk of major vascular access and patient-centred endpoints. We conducted this systematic review and meta-analysis of RCTs according to a published peer-reviewed protocol (Ravani 2013b).

OBJECTIVES

1. To evaluate whether pre-emptive correction of an AV access stenosis improves clinically relevant outcomes
   a. Access outcomes: risk of thrombosis (potentially remediable unsuitability for haemodialysis) and access abandonment (irremediable access loss)
   b. Patient outcomes: infection rates and mortality; surrogate outcomes (measures of heart function and structure, of access flow, and of haemodialysis adequacy)
   c. Resource use: rates of diagnostic and intervention procedures to maintain access patency, and of hospitalisation.
2. To evaluate whether the effects of pre-emptive correction of an AV access stenosis differ by access type (fistula versus graft); aim (primary and secondary prophylaxis); and surveillance method for primary prophylaxis (Doppler ultrasound for the screening of functional and anatomical changes versus measurement of the flow in the access)
3. To evaluate whether other factors (dialysis duration, access location, configuration or materials, algorithm for referral for intervention, intervention strategies (surgical versus radiological or other), or study design) explain the heterogeneity that might exist in the effect estimates.

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METHODS

Criteria for considering studies for this review

Types of studies

We included RCTs and quasi-RCTs (RCTs in which allocation to treatment was obtained by predictable methods such as alternation, use of alternate medical records, or date of birth) evaluating the benefits and harms of a pre-emptive strategy to correct AV access stenosis in adults treated with haemodialysis or planned to start haemodialysis for end-stage kidney disease. We included studies of any follow-up duration without language restriction.

Types of participants

Inclusion criteria

We included RCTs that enrolled people who had an AV access (either a fistula or a graft) that was suitable for haemodialysis (or other extra-corporeal dialysis methods including haemofiltration and haemodiafiltration) regardless of the duration of their dialysis treatment. We included RCTs of pre-emptive stenosis correction in a mature AV access. These studies evaluated the effects of strategies planned to identify (through regular access surveillance) and correct pre-emptively a previously unknown/unidentified access stenosis (primary prophylaxis) or the effects of pre-emptive correction of a known stenosis in a non-dysfunctional access (secondary prophylaxis).

Exclusion criteria

We excluded studies in which participants received haemodialysis to treat acute kidney injury or used a central venous catheter for haemodialysis instead of an AV access. We also excluded studies comparing different approaches to salvage a dysfunctional, failing or clotted access (an access that was not suitable for haemodialysis).

Types of interventions

Active interventions

Interventions could be based on a surveillance method (alone or in addition to standard clinical monitoring) designed to identify early stenotic lesions in a functioning AV access that could be corrected pre-emptively, i.e. prior to access dysfunction (primary prophylaxis). Any screening strategy and diagnostic criteria defining the access eligibility for correction were allowed, including surveillance techniques and imaging tests, or a critical value for a documented stenosis or a lesion clinically suspected. Also, any pre-emptive correction procedure was allowed including surgical interventions (open or endovascular surgery) or imaging-assisted procedures (angioplasty), with or without stenting. In studies enrolling people with a documented stenotic lesion in an otherwise functioning AV fistula or graft the active intervention was any of these pre-emptive correction procedures (secondary prophylaxis).

Comparator

The comparator was either another surveillance method for pre-emptive correction of an access stenosis (active comparator) or a strategy based on deferred correction of a stenosis, i.e. a correction postponed to when the access became dysfunctional (inactive comparator). As for the intervention, for the comparator we considered any diagnostic criteria for eligibility for correction, including monitoring methods, surveillance techniques and imaging tests, or a critical value for a documented stenosis or a lesion clinically suspected.

Types of outcome measures

We considered access outcomes (primary outcomes) and outcomes related to the patient and the health care system (secondary outcomes).

Primary outcomes

The primary outcome was the achievement of long-term access suitability for cannulation and use for haemodialysis (longevity of the access or long-term patency). Two events could reduce access patency: a potentially remediable access failure (thrombosis or imminent thrombosis - an intermediate outcome) and an irremediable access failure (leading to access abandonment or loss - the most important outcome). Depending on whether the event affecting access survival was the initial problem of the access or the final access-terminating event we defined patency rates as follows.

- Primary (unassisted) patency: the event of interest was the first cause of dysfunction (i.e. thrombosis or imminent thrombosis), which could be remediable or irremediable, or the first intervention required to salvage the access (regardless of whether it was successful or unsuccessful).
- Secondary (assisted) patency: the event of interest is the final (irremediable) access failure, leading to abandonment of the access (i.e. access loss), regardless of previous procedures performed to prolong the life of the access up to that point.

We captured these events considering the information reported on access suitability, i.e. the ability to successfully use the AV access as defined in the included studies (Lok 2006).

Secondary outcomes

Secondary access-level outcomes

- Need for access evaluation defined as a formal clinical assessment or diagnostic imaging study, and intervention required to achieve maturation, maintain function, or correct dysfunction of an AV access, or as defined in the included studies
- Surgical interventions on the AV access defined as a vascular access procedure to maintain function, or correct dysfunction of an AV access, or as defined in the included studies
- Diagnostic or interventional radiological procedures on the access defined as a fistulogram or angioplasty of an AV access, or as defined in the included studies
- Any access complications (including infection, aneurysm, high flow and steal syndrome), as defined in the included studies.

Secondary patient-level and system-level outcomes

- All-cause mortality
- Cause-specific mortality (from infection or cardiovascular disease as evaluated in the included studies)

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- Non-fatal cardiovascular events
  - Myocardial infarction or acute coronary syndrome as defined in the included studies
  - Cerebrovascular accident of transient Ischaemic attack as defined in the included studies
  - Exacerbation of heart failure as defined in the included studies
  - Ventricular arrhythmia or sudden death or cardiac conduction disorder as defined in the included studies.
- All-cause hospitalisation and hospitalisation for any specific cause defined as admission to a hospital for any reason or as defined in the included studies
- Quality of life measured with the SF-36 scale or any kidney disease specific quality of life tool or any other measure provided in the included studies

We planned to capture the following surrogate outcomes

- Measurements of heart function and structure used to predict patient outcomes including left ventricular (LV) hypertrophy, LV mass index, LV systolic ejection fraction, and LV end diastolic dimension determined using any technique or threshold as defined in the included studies.
- Measurements of access function including access blood flow, dynamic or static venous pressure monitoring using the techniques and thresholds to determine dysfunction as defined in the included studies.
- Adequate dialysis dose delivery defined as a URR > 70%, single-pool Kt/V ≥ 1.2, or any other measure of dialysis adequacy as defined in the included studies.

Search methods for identification of studies

Electronic searches

We searched the Cochrane Kidney and Transplant Specialised Register (to 30 November 2015) using search terms relevant to this review. The Specialised Register contains studies identified from the following sources.

1. Monthly searches of the Cochrane Central Register of Controlled Trials (CENTRAL)
2. Weekly searches of MEDLINE OVID SP
3. Handsearching of renal-related journals and the proceedings of major nephrology conferences
4. Searching of the current year of EMBASE OVID SP
5. Weekly current awareness alerts for selected nephrology journals
6. Searches of the International Clinical Trials Register (ICTRP) Search Portal and ClinicalTrials.gov.

We identified studies contained in the Specialised Register through search strategies for CENTRAL, MEDLINE, and EMBASE based on the scope of the Cochrane Kidney and Transplant. Details of these strategies, as well as a list of handsearched journals, conference proceedings and current awareness alerts, are available in the Specialised Register section of information about the Cochrane Kidney and Transplant.

See Appendix 1 for search strategies.

Searching other resources

1. Reference lists of clinical practice guidelines, review articles and relevant studies.
2. Letters seeking information about unpublished or incomplete studies to investigators known to be involved in previous studies.
3. Information from the authors (see Acknowledgements).

Data collection and analysis

Selection of studies

Two authors independently screened the search results by title and abstract, then full text, to identify potentially eligible studies that fulfilled the inclusion criteria. Any study considered potentially eligible by at least one reviewer was retrieved for further review. We considered all RCTs of any AV access screening method or pre-emptive stenosis correction that reported data for adults receiving or planned to receive haemodialysis to treat kidney failure.

Data extraction and management

Two authors independently extracted data for population characteristics, interventions, non-randomised co-interventions, and risk of bias into a purpose-built database. Each author double-checked data extraction and data entry independently, and any discrepancies between authors were resolved by discussion. Where more than one publication of one study existed, we grouped the reports together.

Assessment of risk of bias in included studies

Two authors independently evaluated the following risk-of-bias items using the Cochrane risk of bias assessment tool (Higgins 2011) (see Appendix 2).

- Was there adequate sequence generation (selection bias)?
- Was allocation adequately concealed (selection bias)?
- Was the analysis done according to the intention-to-treat principle (selection bias)?
- Was knowledge of the allocated interventions adequately prevented during the study?
  - Participants and personnel (performance bias)
  - Outcome assessors (detection bias)
- Were incomplete outcome data adequately addressed (selection and attrition bias)?
- Are reports of the study free of suggestion of selective outcome reporting (reporting bias)?
- Was the study apparently free of other problems that could put it at a risk of bias?

For the latter item we considered failure to report a study hypothesis or assumptions of sample size estimation, unequal co-interventions, early termination of a study with failure to report pre-specified stopping rules, industry sponsor as author or involved in data handling and analysis, and flaws in data analysis. We also recorded whether studies reported information on registration in the primary study report.

Measures of treatment effect

We extracted data on all access-level, patient-level and system-level outcomes. To incorporate expected study-to-study variability

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beyond what would be expected by chance, analysis was by a random effects model. As all outcomes were dichotomous, results were expressed as risk ratio (RR), hazard ratio (HR) or incidence rate ratio (IRR) with 95% confidence intervals (CI).

Unit of analysis issues

In access-level outcome analyses the unit of analysis was the access. For patient- and system-level outcomes the unit of analysis was the patient.

Dealing with missing data

Where only proportions of participants experiencing an event were provided in the study report (rather than raw event data), we estimated the number of participants experiencing one or more events by multiplying the proportion affected by the sample size, and contacted the study authors for additional information. When not reported, we calculated rates of a binary event as the ratio of the event number and the reported average follow-up. For incomplete survival data reporting (i.e. available survival plots or life table data but lack of a HR estimate), we obtained the estimate of the HR using the method by Parmar 1998. We assumed a Poisson distribution for count data to calculate the variance of the log-IRR (when a measure of precision was not reported). We included all relevant studies in the systematic review and included in the meta-analysis the data that they reported (Higgins 2011).

Assessment of heterogeneity

We assessed for heterogeneity in summary effects using the Cochran Q and the I^2 test (with 95% CI), with P value of 0.1 used for statistical significance (Higgins 2003). We considered I^2 values of 0% to 25%, 26% to 50%, 51 to 75% and ≥ 76% indicating respectively low, moderate, considerable and substantial levels of heterogeneity.

Assessment of reporting biases

We used funnel plots of the log-RR in individual studies against their standard error to search for asymmetry but did not formally test for asymmetry or quantify the possible effect of any publication bias due to the low number of studies (Higgins 2011).

Data synthesis

We used the random-effects model for data synthesis, because of important differences between studies in terms of design, participants, interventions and co-interventions. For all analyses, a two-tailed P value < 0.05 indicated statistical significance. We conducted the analyses using R statistical software (R Foundation for Statistical Computing; www.R-project.org) and RevMan. Because three studies compared the effects of different interventions with the same comparator arm (Ram 2003; Sands 1999; Smits 2001) we split the comparator arm of these studies in meta-analyses.

Subgroup analysis and investigation of heterogeneity

We were aware that several factors were potentially responsible for heterogeneity including study population characteristics, publication year, gender, diabetes, presence of cardiovascular disease, age, time on dialysis, haemodialysis technique (including haemofiltration and haemodiafiltration) and anatomical location of the access, material, AV access configuration, or diagnostic criteria or type of intervention (angioplasty or surgery). However, due to the low number of studies, and to avoid inflation of the type I error rate (Higgins 2003), we conducted subgroup analyses according to the following pre-specified characteristics: type of access (fistula and graft); aim of the intervention (primary and secondary prophylaxis); and type of intervention (ultrasound-based surveillance, which provides both functional and anatomical information about the access, and access flow-measurement-based or access pressure-measurement-based surveillance, which provide only functional data). We did not study the impact of bias on heterogeneity. We considered moderate heterogeneity or higher (I^2 > 25%) as measure of support for separate data reporting by subgroup.

Sensitivity analysis

We performed sensitivity analyses by including and excluding studies according to the following criteria.

- Participants assigned to the comparator arm received an additional screening (i.e. measurement of dynamic or static pressure in addition to clinical monitoring)
- Participants assigned to the intervention arm received an additional screening (i.e. measurement of dynamic or static pressure in addition to Doppler ultrasound or flow measurement)
- Participants assigned to the comparator arm did not receive clinical monitoring
- Participants assigned to the intervention arm did not receive clinical monitoring
- HR calculated from the survival curves (as opposed to reported by authors).

We also compared meta-analyses of RR and HR for the same outcome.

Because the DerSimonian-Laird (DL) procedure is considered unstable with small numbers of studies, in sensitivity analyses we confirmed results using a restricted maximum likelihood (REML) method (equivalent to iterated Der-Simonian Laird) (Cornell 2014). We also used methods that incorporate in the variance estimation the uncertainty related to residual heterogeneity (Knapp-Hartung method). To account for potential correlation of effect estimates from the same study we used methods that account for potential correlation in the data (robust variance correction and mixed modelling). Finally we checked consistency of findings by summarizing binary events using a binomial approximation of the likelihood which may be preferred in relatively small studies.

Grading of Recommendations Assessment, Development and Evaluation (GRADE)

We summarised the quality of the evidence, together with absolute treatment effects based on estimated baseline risks, using GRADE guidelines (Guyatt 2008). According to this system the evidence from RCTs is initially graded as high, but is downgraded in the presence of bias in the studies, inconsistency in the direction or magnitude of study findings, indirectness related to differences in populations, interventions or outcomes between studies and the clinical context, imprecision of the estimated effects and publication bias. GRADE conceptualises the evidence quality as follows: high quality—further research is very unlikely to change our confidence in the estimate of effect; moderate quality—further

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research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; low quality—further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; very low quality—any estimate of effect is very uncertain. To estimate the absolute number of people using a fistula or a graft for haemodialysis who avoided a clotting event or incurred in an access procedure, the risk estimate and 95% CI were obtained from corresponding meta-analyses, together with the absolute population risk derived from data in the control groups of the included studies.

RESULTS

Description of studies

Results of the search

Our search of the Specialised Register identified 110 reports. After initial screening of the titles and abstracts 18 reports were excluded (not randomised, wrong population or intervention). The remaining 91 reports were assessed and we included 14 studies (30 reports) (Dember 2004; Lumsden 1997; Malik 2005; Mayer 1993; Moist 2003; Polkinghorne 2006; Ram 2003; Robbin 2006; Sands 1999; Scaffaro 2009; Smits 2001; Tessitore 2003; Tessitore 2004a; Tessitore 2014) and excluded 35 (50 reports) (Aftab 2014; Bacchini 2003; Beathard 1993; Beathard 1994; BRAVO II Study 2013; BRAVO I Study 2006; Brooks 1987; Cohen 2000; Dougherty 1999; Forauer 2008; HAPPI Study 2007; Haskal 2010; Haskal 2013; Hegab 2013; Hoffer 1997; Katsanos 2012; Khoo 2010; Kundu 2010; Marston 1997; Middlebrook 1995; Ono 2004; Quinn 1995; Roy-Chaudhury 2012; Saini 2008; Schuman 1994; Sheley 1996; Shemesh 2008; Teo 2013; Tessitore 2004b; Uflacker 1996; Veroux 2013; Vesely 1996; Vesely 1999; Vesely 2005; Whittier 2009. In addition there are three ongoing studies (NCT01200914; NCT01391975; NCT01538108) and two studies have recently been completed but as yet there are no published data (NCT01001676; NCT01544907) (see Figure 1). All 14 included studies contributed to qualitative and quantitative synthesis.

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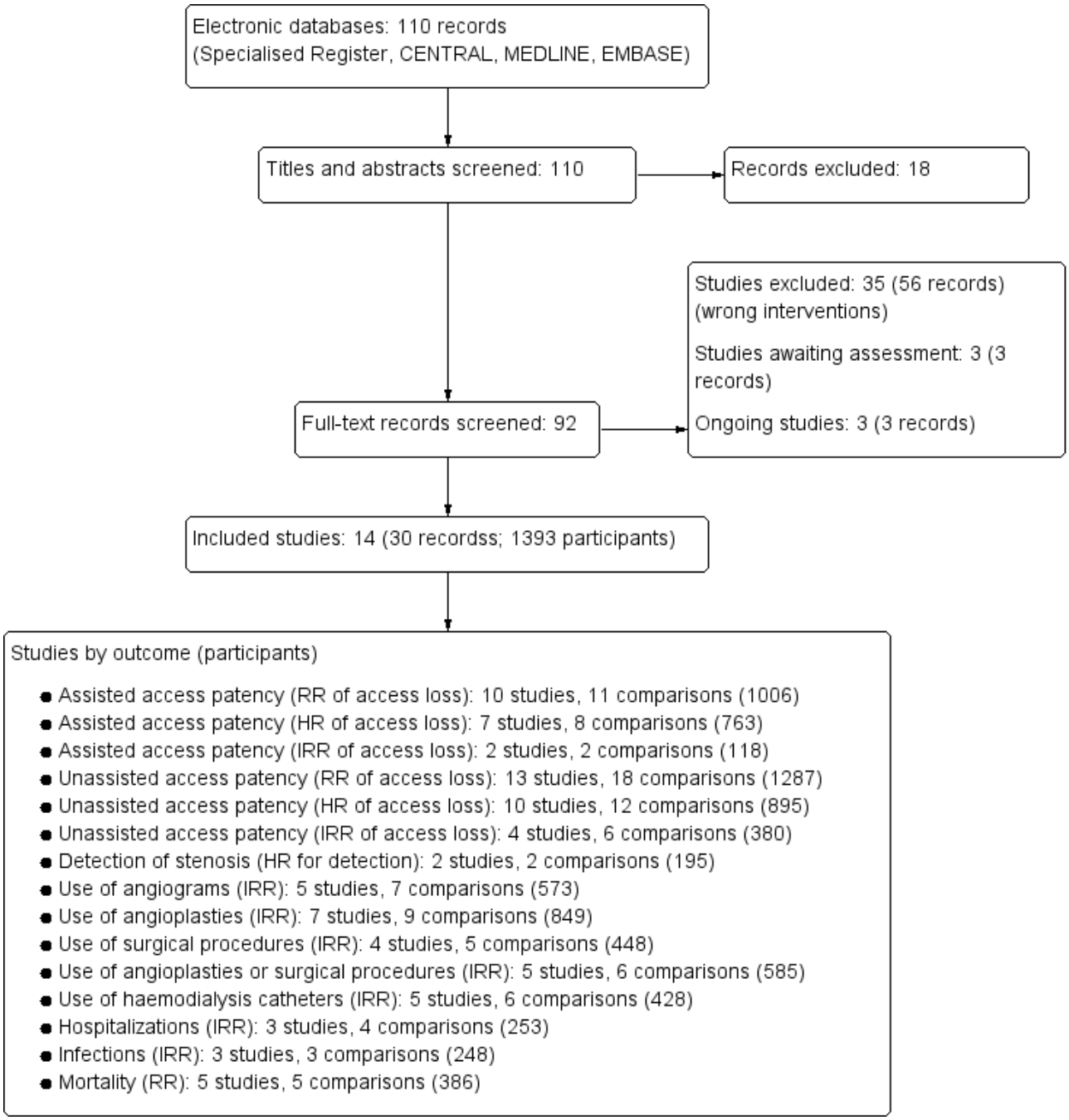
Figure 1. Study selection flow diagram-PRISMA



Prior to publication a final search of the Specialised Register identified one new report (Sands 1997). This will be assessed in a future update of this review.

Included studies

We included 14 studies comprising 1390 adult participants in this review, of which nine (1065 participants) enrolled adults without access stenosis (primary prophylaxis; three studies (313 participants) in people using fistulas) and five (325 participants) enrolled adults with a documented stenosis in a functioning access (secondary prophylaxis; three studies (197 participants) in people using fistulas).

Detailed information on the design, participants, intervention, comparator and outcomes of the included studies are summarised in Characteristics of included studies and Table 1. Nine studies (1065 participants) (Malik 2005; Mayer 1993; Moist 2003; Polkinghorne 2006; Ram 2003; Robbin 2006; Sands 1999; Scaffaro 2009; Smits 2001) enrolled people without a suspected or documented stenosis of the access (primary prophylaxis), and five (325 participants) enrolled people with either a documented (Lumsden 1997; Tessitore 2003; Tessitore 2004a; Tessitore 2014) or suspected (Dember 2004) stenosis of a functioning access (secondary prophylaxis).

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In studies of primary prophylaxis pre-emptive correction of a stenosis followed the identification of the stenosis by means of different surveillance strategies. These strategies involved Doppler ultrasound in at least one of the intervention arms (Malik 2005; Mayer 1993; Ram 2003; Robbin 2006; Scaffaro 2009), blood flow measurement in at least one of the intervention arms (Moist 2003; Polkinghorne 2006; Ram 2003; Sands 1999; Smits 2001) or measures of venous pressure in at least one intervention arm (Moist 2003; Sands 1999; Smits 2001). Three studies reported two comparisons each (Ram 2003; Sands 1999; Smits 2001). One study compared blood-flow measurement or static venous pressure and Doppler ultrasound every six months with Doppler ultrasound screening every six months (Sands 1999).

In 11 studies participants in both the intervention and control arms received clinical monitoring (Dember 2004; Malik 2005; Moist 2003; Polkinghorne 2006; Ram 2003; Robbin 2006; Scaffaro 2009; Smits 2001; Tessitore 2003; Tessitore 2004a; Tessitore 2014). In one study of secondary prophylaxis participants were randomised to undergo angiography confirmation and correction of a stenosis (suspected on the basis of an increase in the static venous pressure) or to continue venous pressure monitoring of the access until it became dysfunctional (Dember 2004). In the other four studies of secondary prophylaxis participants had an angiography documented stenosis and were randomised to undergo correction or continue clinical monitoring until the access became dysfunctional (Lumsden 1997; Tessitore 2003; Tessitore 2004a; Tessitore 2014).

Sample sizes ranged from 58 to 189 participants and the follow-up from 6 to 38 months. Participants' age in these studies ranged between 55.7 and 64.6 years; the proportion of males ranged between 41% and 68% and the proportion of diabetics ranged between 20% and 61%. Eight studies included only people using a graft (Dember 2004; Lumsden 1997; Malik 2005; Mayer 1993; Moist 2003; Ram 2003; Robbin 2006; Smits 2001), five only people using a fistula (Tessitore 2003; Tessitore 2004a; Scaffaro 2009; Polkinghorne 2006; Tessitore 2014), and one study included participants with a graft and participants with a fistula (Sands 1999).

Excluded studies

Reasons for exclusion of excluded studies are summarised in Characteristics of excluded studies. Most tested different interventions to correct a stenotic lesion in a dysfunctional access. Four of the five ongoing studies do not address the research question of this review. Information about the fifth study (NCT01391975) has not been updated since July 2011.

Risk of bias in included studies

Risk of bias is summarised in Figure 2 and Figure 3. In general, risk of bias was high or unclear in most studies for many domains we assessed. Four studies were published after 2005 (Robbin 2006; Polkinghorne 2006; Scaffaro 2009; Tessitore 2014) and only one had evidence of registration within a trial registry (Tessitore 2014). No study reported information on authorship and/or involvement of the study sponsor in data collection, analysis, and interpretation.

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

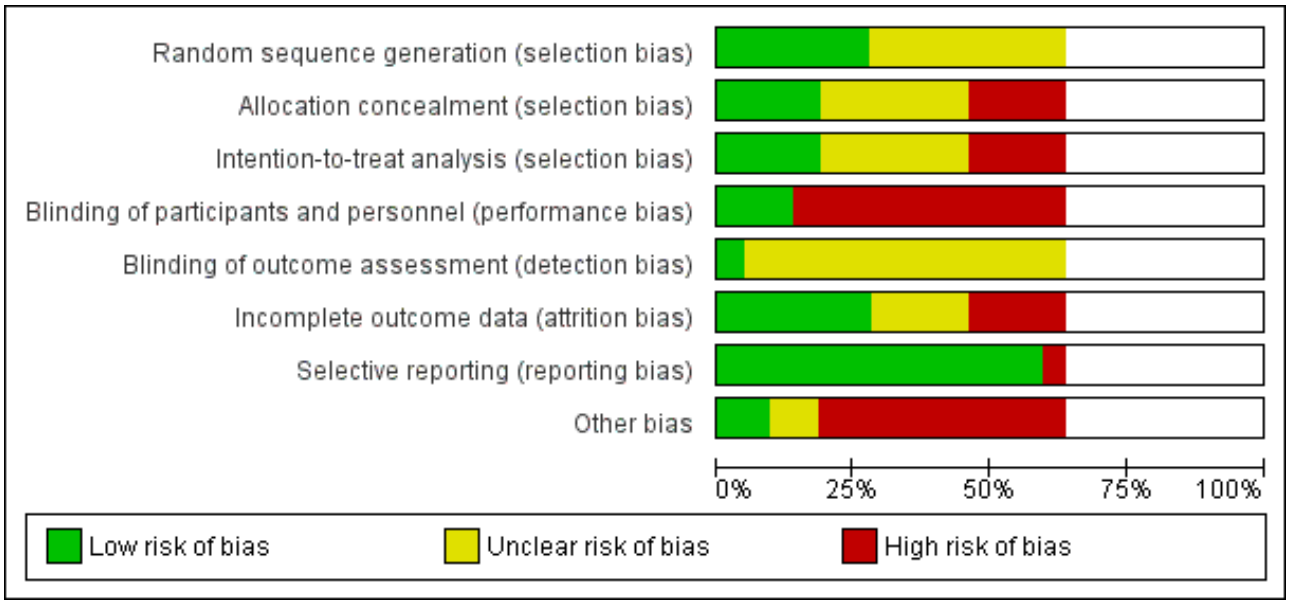

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Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

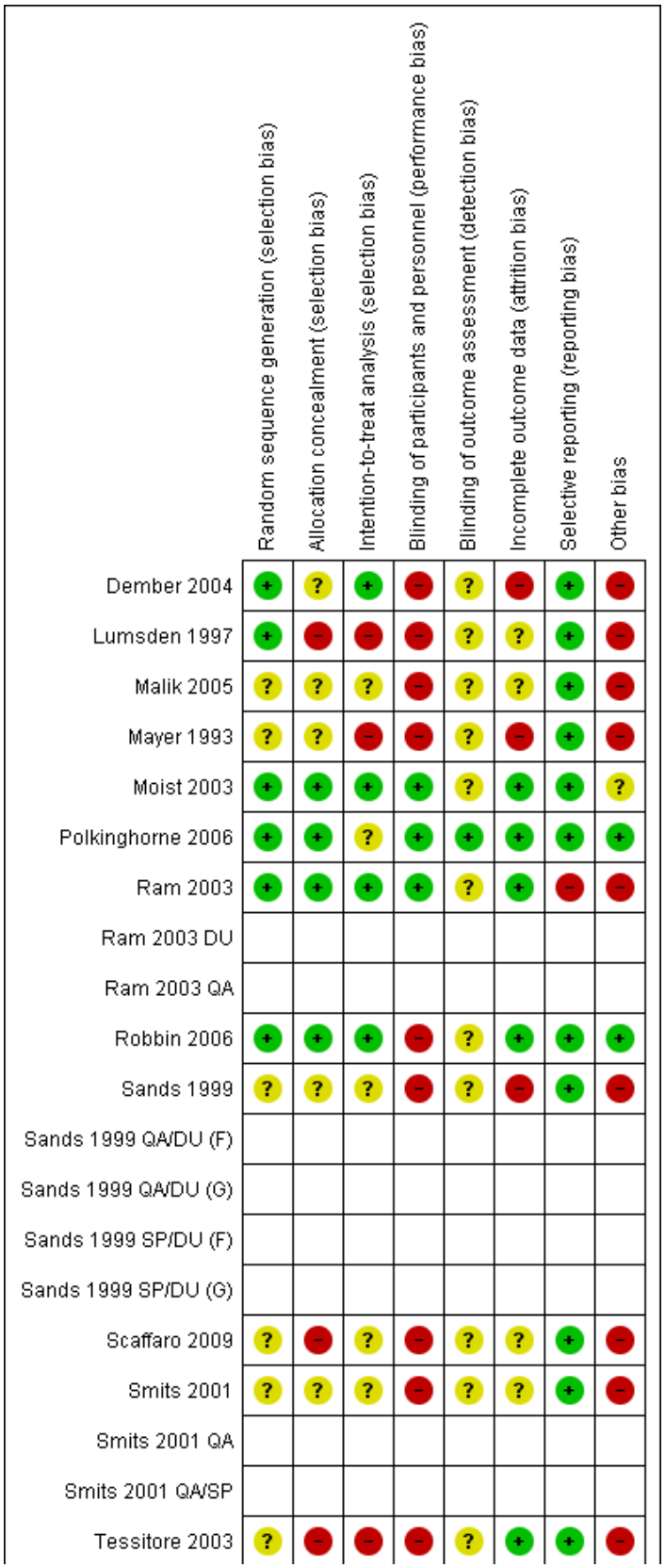

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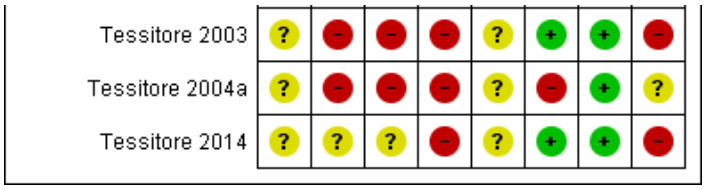
Figure 3. (Continued)



Allocation

Random sequence generation

Six studies were judged to be at low risk of bias (Dember 2004; Lumsden 1997; Moist 2003; Polkinghorne 2006; Ram 2003; Robbin 2006) and the remaining eight studies were judged unclear.

Allocation concealment

Four studies were judged to be at low risk of bias (Moist 2003; Polkinghorne 2006; Ram 2003; Robbin 2006), four studies were at high risk of bias (Lumsden 1997; Scaffaro 2009; Tessitore 2003; Tessitore 2004a), and the remaining six studies were judged unclear.

Intention-to-treat analysis

Four studies were judged to be at low risk of bias (Dember 2004; Moist 2003; Ram 2003; Robbin 2006), four studies were at high risk of bias (Lumsden 1997; Mayer 1993; Tessitore 2003; Tessitore 2004a), and the remaining six studies were unclear.

Blinding

Participants and personnel (performance bias)

Only two studies reported blinding of participants and personnel (Moist 2003; Polkinghorne 2006); one only blinded participants (Ram 2003). Eleven studies were judged to be at high risk of bias (Dember 2004; Lumsden 1997; Malik 2005; Mayer 1993; Robbin 2006; Sands 1999; Scaffaro 2009; Smits 2001; Tessitore 2003; Tessitore 2004a; Tessitore 2014).

Blinding of outcome assessment (detection bias)

Only one study reported on blinding of outcome assessors (Polkinghorne 2006). Although thrombosis and access loss are objective outcomes, reporting was unclear for the other 13 studies.

Incomplete outcome data

Five studies were at low risk of attrition bias (Moist 2003; Polkinghorne 2006; Ram 2003; Robbin 2006; Tessitore 2003), four studies were at high risk of bias (Dember 2004; Mayer 1993; Sands 1999; Tessitore 2004a) and the remaining studies were judged unclear.

Selective reporting

One study was at high risk of bias (Ram 2003) and the remaining 13 studies were judge to be at low risk of reporting bias.

Other potential sources of bias

Eight studies failed to report the study hypothesis or the sample size estimation (Lumsden 1997; Malik 2005; Mayer 1993; Ram 2003; Sands 1999; Scaffaro 2009; Smits 2001; Tessitore 2003). Two studies were stopped early but failed to report details on the stopping rule (Smits 2001; Tessitore 2014). In one study clinicians were notified about the results of the angiography only for participants of the intervention arm (Dember 2004). In three studies the unit of analysis was the access but the methods for handling correlated data were not reported (Scaffaro 2009; Smits 2001; Tessitore 2003). Only one study reported information on registration in a trial registry (Tessitore 2014).

Effects of interventions

See: **Summary of findings for the main comparison** Scheduled surveillance versus clinical monitoring alone for preventing arteriovenous (AV) access failure; **Summary of findings 2** Scheduled surveillance versus clinical monitoring alone for the prevention of arteriovenous (AV) access failure

Effects on access patency

Assisted patency (access loss)

In the meta-analysis of all studies (including people with a fistula or graft) we found that pre-emptive correction of an AV access stenosis probably improves the longevity of AV access (Analysis 1.1 (11 study comparisons, 972 participants): RR 0.80, 95% CI 0.63 to 0.99; I^2 = 0%). Subgroup analyses showed pre-emptive stenosis correction significantly reduced the risk of access loss in fistulas (Analysis 1.2.1 (4 studies, 310 participants): RR 0.50, 95% CI 0.29 to 0.86; I^2 = 0%) but not in grafts (Analysis 1.2.2 (7 study comparisons, 662 participants): RR 0.87, 95% CI 0.69 to 1.11; I^2 = 0%). Three of the four studies reporting access loss data in fistulas (199 participants) were conducted in the same centre and reported by the same authors (Tessitore 2003; Tessitore 2004a; Tessitore 2014). There were no significant subgroup differences by prevention aim (primary and secondary prophylaxis) and surveillance method in primary prophylaxis, and insufficient data for subgroup analysis by prevention aim in fistulas (Analysis 1.3; Analysis 1.4; Analysis 1.5). Meta-analyses of HR (with or without the inclusion of HR estimates we calculated from reported survival data) and IRR were essentially the same (Analysis 1.6; Analysis 1.7; Analysis 1.8; Analysis 1.9; Analysis 1.10).

Unassisted patency (access thrombosis)

In the meta-analysis of all studies (including people with a fistula or graft) we found that pre-emptive correction of an AV access stenosis had modest but precise effect on the risk of potentially remediable failure (thrombosis) (Analysis 1.11 (18 study comparisons, 1212 participants): RR 0.79, 95% CI 0.65 to 0.97; I^2 = 30%). There was moderate degree of heterogeneity in this meta-analysis, which was largely explained by the modifying effect of access type. We found that pre-emptive stenosis correction significantly reduced the risk of thrombosis in fistulas (Analysis 1.12.1 (7 study comparisons, 515 participants): RR 0.50, 95% CI 0.35 to 0.71; I^2 = 0%), but not in grafts (Analysis 1.12.2 (11 study comparisons, 697 participants): RR 0.95, 95% CI 0.80 to 1.12; I^2 = 0%). Subgroup analysis by

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prevention aim indicated that the effects of pre-emptive stenosis correction may differ in studies of primary (Analysis 1.13.1 (13 study comparisons, 885 participants): RR 0.94, 95% CI 0.78 to 1.12; I^2 = 0%) and secondary prophylaxis (Analysis 1.13.2 (5 study comparisons, 327 participants): RR 0.53, 95% CI 0.32 to 0.87; I^2 = 59%), but there remained moderate residual heterogeneity across studies in this analysis. In subgroup analysis by prevention aim limited to studies in fistulas we found that pre-emptive correction of stenosis had no effect on the risk of thrombosis in primary prophylaxis (Analysis 1.14.1 (4 study comparisons,316 participants): RR 0.75, 95% CI 0.42 to 1.36; I^2 = 0%) and significantly reduced the risk of thrombosis in studies of secondary prophylaxis (Analysis 1.14.2 (3 studies, 199 participants): RR 0.40, 95% CI 0.26 to 0.62; I^2 = 0%), with no residual heterogeneity across studies. However, the effect estimate in the secondary prophylaxis group was again derived from three studies (Tessitore 2003; Tessitore 2004a; Tessitore 2014). There were no significant subgroup differences in the risk of thrombosis by surveillance method in studies of primary prophylaxis (Analysis 1.15). Meta-analyses of HR (with or without the inclusion of HR estimates we calculated from reported survival data) and IRR were essentially the same (Analysis 1.16; Analysis 1.17; Analysis 1.18; Analysis 1.19; Analysis 1.20; Analysis 1.21; Analysis 1.22; Analysis 1.23).

Detection of stenosis and elective access repair

In Polkinghorne 2006, access surveillance increased the probability of identification of fistula stenosis (Analysis 1.24 (137 participants): RR 2.27, 95% CI 0.86 to 5.98). Tessitore 2014 reported elective fistula repair was over five times as likely in the treatment group (Analysis 1.25 (58 participants): RR 5.78, 95% CI 2.80 to 11.96).

Effects on health resource use and patient outcomes

Resource use

We found that pre-emptive correction of an AV access stenosis significantly increased the rates of diagnostic angiograms (Analysis 1.26 (7 study comparisons, 539 participants): IRR 1.78, 95% CI 1.18 to 2.67; I^2 = 62%); has uncertain or imprecise effects on the rates of angioplasties or surgical procedures (Analysis 1.27; Analysis 1.28; Analysis 1.29); and may reduce the rate of catheter use (Analysis 1.30 (6 study comparisons, 394 participants): IRR 0.58, 95% CI 0.35 to 0.98; I^2 = 53%) or hospitalisation (Analysis 1.31 (4 study comparisons, 219 participants): IRR 0.54, 95% CI 0.31 to 0.93; I^2 = 67%). Given the considerable heterogeneity in these analyses, effects on resource use are uncertain. We did not find data on resource and costs necessary to run a surveillance program. One study in secondary prophylaxis in people with fistulas did not find differences in costs between pre-emptive and deferred correction of stenosis (Tessitore 2014).

Patient outcomes

We found that pre-emptive correction of an AV access stenosis may increase the rates of infection (Analysis 1.32 (3 studies, 248 participants): IRR 1.74, 95% CI 0.78 to 3.91; I^2 = 0%) and mortality (Analysis 1.33 (5 studies, 386 participants): RR 1.38, 95% CI 0.91 to 2.11; I^2 = 0%). We did not find data on surrogate outcomes and quality of life.

Other comparisons

Insufficient data were available to assess the effects of two surveillance methods versus one or to compare two different surveillance methods head-to-head (Analysis 2.1; Analysis 2.2; Analysis 3.1; Analysis 3.2; Analysis 4.1; Analysis 4.2; Analysis 5.1; Analysis 5.2; Analysis 6.1; Analysis 6.2; Analysis 7.1; Analysis 7.2).

Sensitivity analyses

Results were the same in several sensitivity analyses we conducted by including and excluding studies of two surveillance methods, studies in which venous pressure was measured in the intervention and/or in the comparator arm and studies in which clinical monitoring was or was not a co-intervention. REML methods provided similar results as those based on the DL method, with the exception of the IRR diagnostic procedures, which was 1.64 (95% CI 1.24 to 2.18) (Figure 4) versus 1.78 (1.18 to 2.67) we found using the DL method (Analysis 1.26).

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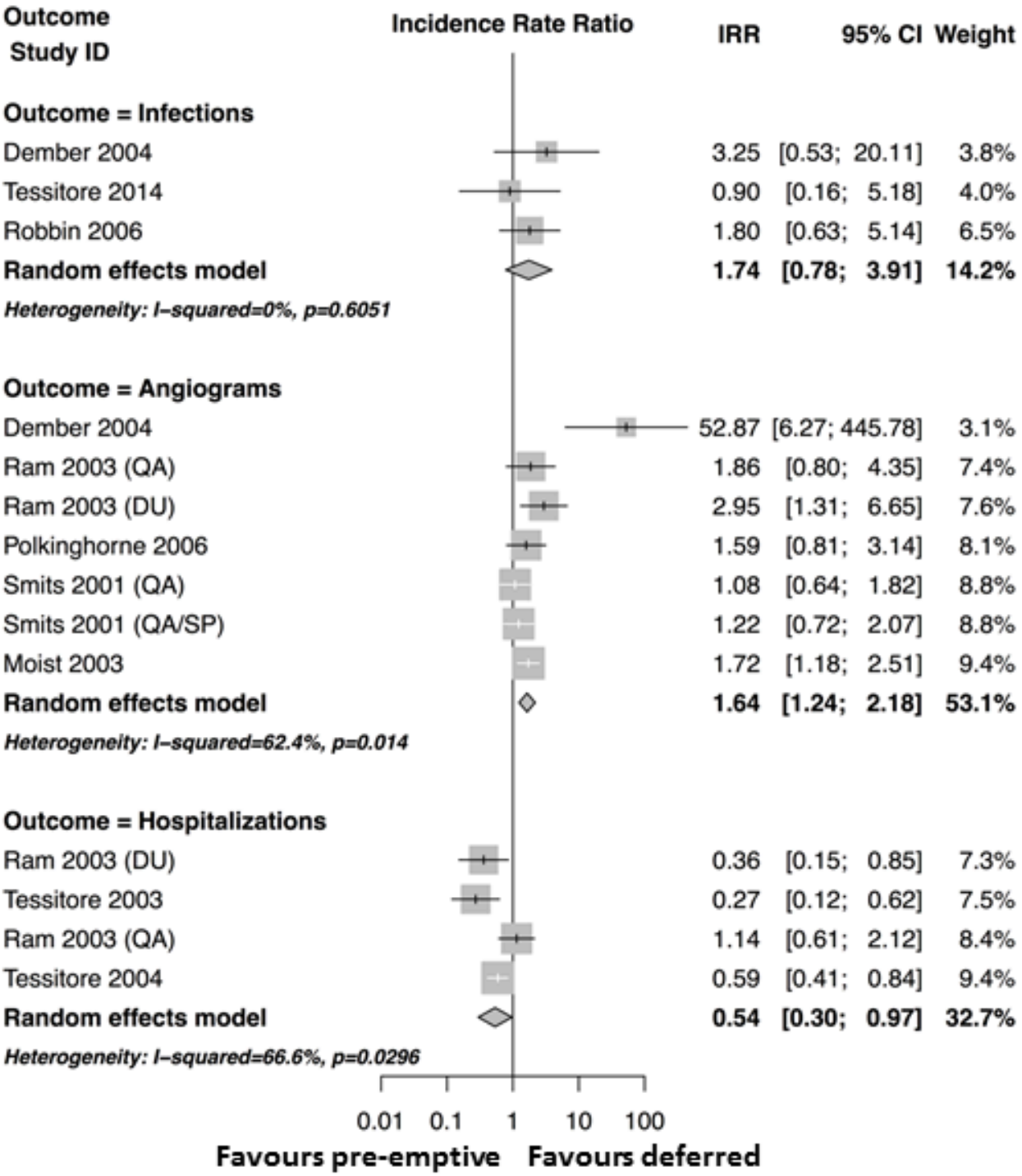
Figure 4. Sensitivity analyses using REML methods (Ravani 2016)



Small study effects

Funnel plots showed some evidence of asymmetry, suggesting the possible existence of small-study effects or publication bias (Figure 5; Figure 6). However, the low number of studies did not permit further analyses.

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Figure 5. Funnel plot of comparison: 1 Pre-emptive versus deferred correction, outcome: 1.2 Assisted patency: RR of access loss by access type.

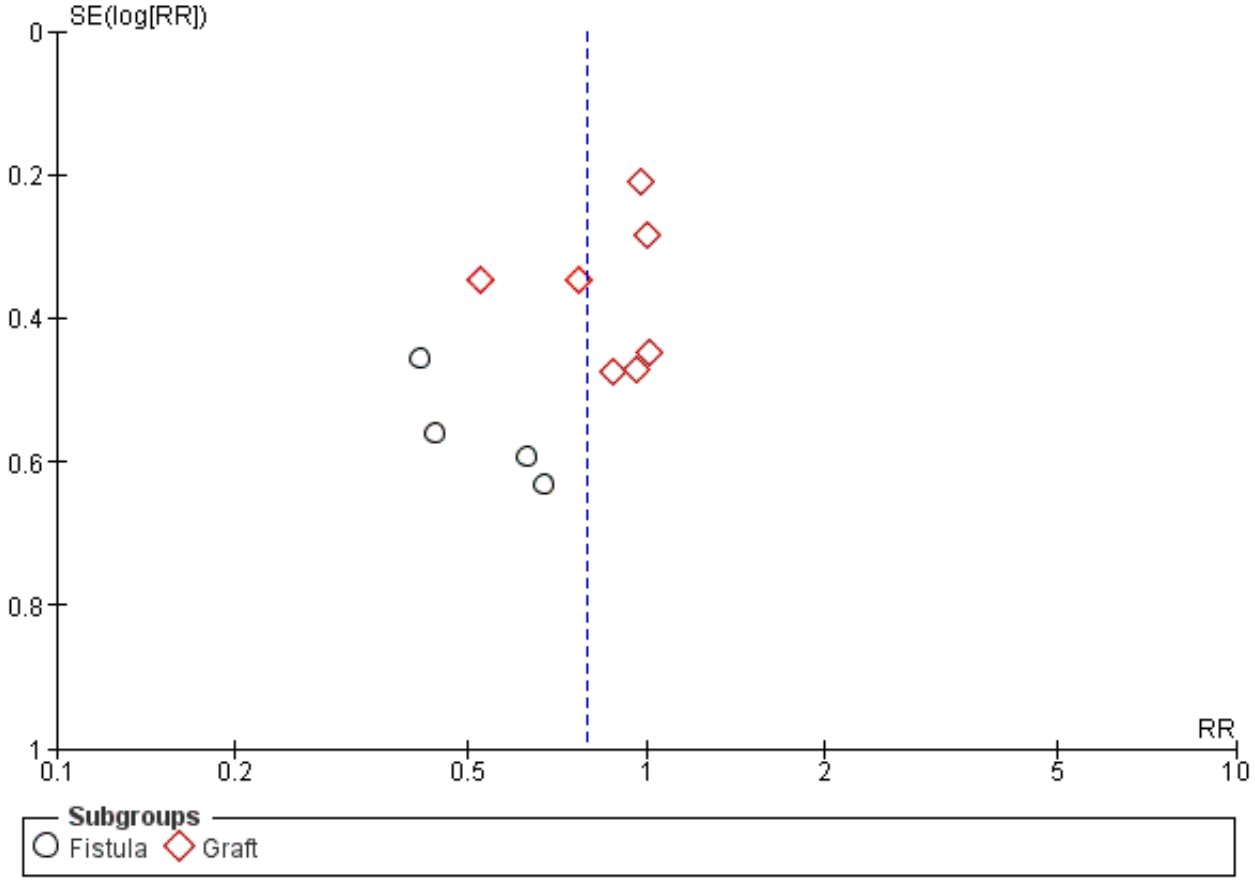

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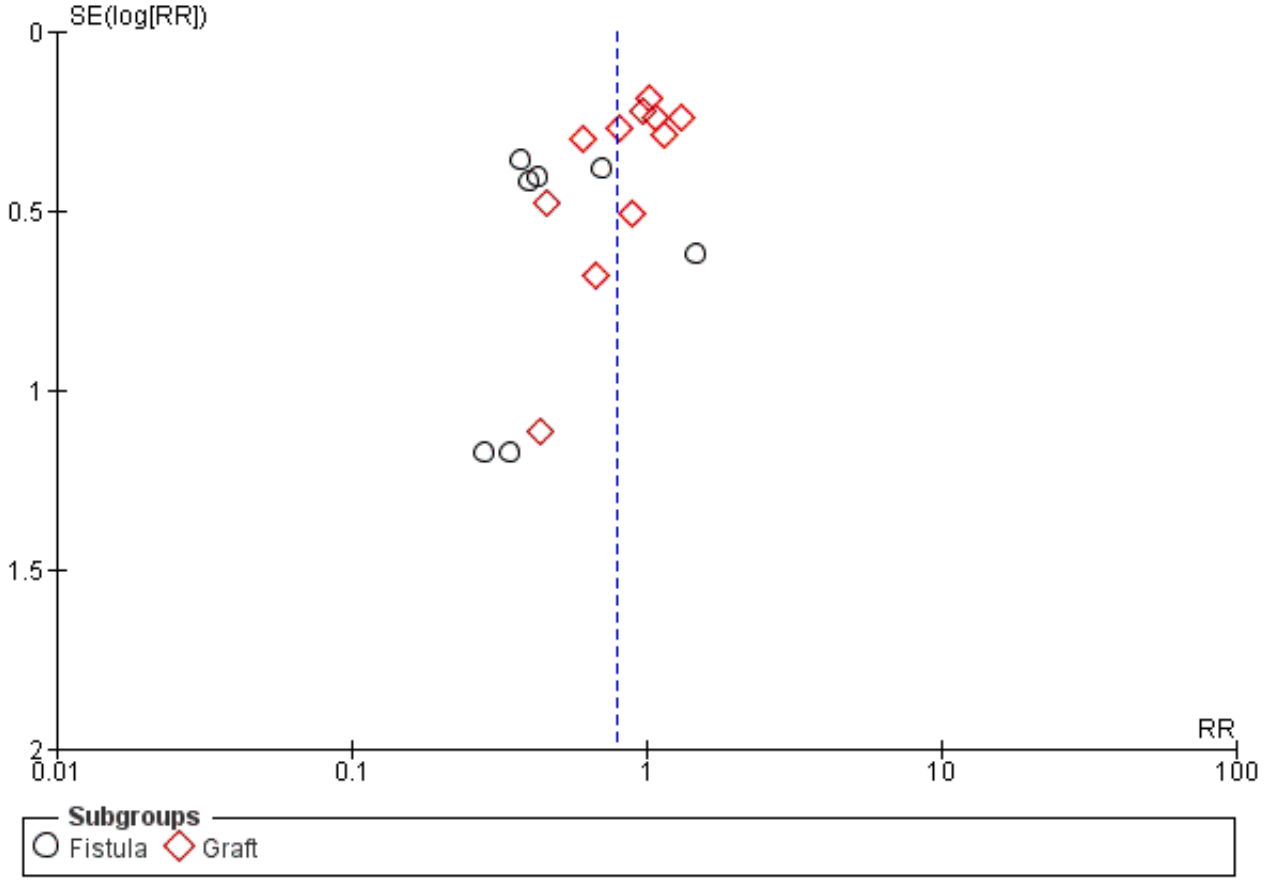
Figure 6. Funnel plot of comparison: 1 Pre-emptive versus deferred correction, outcome: 1.12 Unassisted patency: RR of access thrombosis by access type.



DISCUSSION

In our systematic review we identified 14 studies (1390 participants) that reported the effects of pre-emptive correction of AV access stenosis on access outcomes, health care resource use and patient outcomes. Nine studies assessed the effects of early identification of stenosis by means of access surveillance followed by its pre-emptive correction (primary prophylaxis) and five assessed the effects of pre-emptive correction of a known or suspected stenosis in an AV access (secondary prophylaxis).

Summary of main results

In low- to moderate-quality evidence from these studies, pre-emptive correction of AV access stenosis decreases the risk of thrombosis in fistulas and probably increases the longevity of fistulas, but has little or no effect on the risk of thrombosis and the risk of loss of grafts. Pre-emptive correction of access stenosis, however, may increase the rates of diagnostic procedures, has uncertain benefits in terms of avoidance of hospitalisation or catheters, and potential harms in terms of infection and mortality. On average, a strategy for pre-emptive correction of stenosis in 1000 people using a fistula can prevent thrombosis in 200 (baseline risk = 0.4) and access loss in 50 (baseline risk = 0.1), but may require additional invasive procedures in 234 (baseline risk = 0.3). While available evidence does not support surveillance and pre-emptive correction of graft stenosis, there is insufficient information about potential harms of access-related procedures to support pre-emptive correction of fistula stenosis.

Overall completeness and applicability of evidence

Considering that the effects of pre-emptive correction of a stenosis on primary and secondary patency rates of grafts are close to unity, we believe that further research is unlikely to change our confidence that this intervention is not beneficial in grafts. Consistency of findings in several sensitivity and subgroup analyses further support this statement.

Conversely, more data may be warranted for fistulas, considering that pre-emptive correction of a stenosis reduces the risk of thrombosis and that there are potential benefits on assisted patency, although they are heavily influenced by three small studies from a single centre. More data are also necessary on the health resource use, including resources necessary to run a surveillance program, and patient-centred outcomes, including quality of life, risk of infection and mortality.

Quality of the evidence

Overall the quality of available evidence is low to moderate. Most studies were at high risk of performance bias, although few showed that double blinding is possible in primary prophylaxis studies, and in most there was unclear risk of detection bias. Only one third

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of the studies were at low risk of selection bias. Because these forms of bias tend to inflate false positive results, we believe that additional RCTs of pre-emptive stenosis correction are very unlikely to change the confidence in the size and direction we observed in grafts. Conversely, further studies would be informative to test whether potential benefits may exist in fistulas.

Potential biases in the review process

Although based on a peer-reviewed protocol and conducted using methods developed by Cochrane, our review has limitations mostly related to the quality of the data on which the review is based. First, studies were few in number and small. Few were designed based on an explicit study question and none was powered to detect a meaningful effect. Second the overall quality of the studies was poor, as discussed above. Third most of the data were from grafts, a type of access used in < 10% of the haemodialysis population in most countries, and little information is available for fistula, the access believed to be the optimal form of access for haemodialysis. Fourth, insufficient information was available on important factors that may impact outcomes, including algorithms for referral for intervention or intervention strategies (surgical versus radiological or other). Finally, resource use and patient outcomes such as infections and mortality were under-reported and no information is available about cost of access surveillance programs and patient perspective or quality of life.

Agreements and disagreements with other studies or reviews

The findings of our systematic review are overall consistent with those by Tonelli 2008. Key differences include consideration of primary and secondary prophylaxis in our review; the addition of three studies (Dember 2004; Scaffaro 2009; Tessitore 2014); and analysis of patient outcomes. However, considering the high risk of access complications, and the morbidity burden and high cost associated with the effort to maintain a functioning AV access, the finding that only two studies were published since the publication of Tonelli 2008 raises several concerns about the reasons and consequences of the falling interest in this topic, which is relevant to patients and the healthcare system.

AUTHORS' CONCLUSIONS

Implications for practice

Our review does not support the use of pre-emptive correction of stenosis in grafts and casts doubts upon the use of pre-emptive correction of stenosis in fistulas. While available evidence shows that pre-emptive correction of a stenosis reduces the risk of thrombosis in fistulas, which in turn may result in prolonged fistula longevity, data on access loss (the most important outcome) are based on low- to moderate-quality evidence from only three small single-centre studies conducted in the same centre and reported by the same investigators. Although pre-emptive correction of fistula stenosis may be more effective in secondary prophylaxis, data supporting this practice come from these same studies. Until more research is available any prevention strategy should be weighed against potential harms of this practice (increased number of invasive procedures, procedure-related adverse events) and resource use. Considering the potential harms and inconvenience associated with these procedures, patients' involvement in decision-making is key to determine the management strategy that is more consistent with their preferences and values.

Implications for research

Considering the lack of benefits of pre-emptive correction of stenosis in graft, different questions need to be addressed in this area, including development of new vascular materials to reduce the risk of complications, interventions to prevent stenosis or reduce the risk of restenosis after a salvage procedure.

Conversely, considering the possible benefits of pre-emptive correction of an established stenosis in functioning fistulas, a large RCT with fistula loss as main outcome is warranted. Such secondary prophylaxis RCT must include also patient outcomes (QoL, infections and mortality) and data on resource use and cost as secondary outcomes (including staff time for access screening and data collection and interpretation). Based on the findings of our review we estimated (based on a log-rank test) that an RCT of 1020 participants per arm recruited over one year and followed for three years (480 total events) will have a power of 90% to detect as significant at the two-sided P value of 0.01 at least a 30% reduction in the HR for access loss, assuming a baseline risk of 10% per year and a withdrawal rate of 10%. Numbers are smaller (about 800/group) assuming an exponential model for time to event.

To better inform clinical practice in this area, and promote patient-centred care, data on patient preferences and views about expected benefits and potential harms of access surveillance and pre-emptive correction of access stenosis should be included in future research. These data will allow development of decision aids and incorporation of patient perspectives and informed decisions into a truly shared decision-making process at the bedside.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Dember 2004

Methods	• Study design: open-label. parallel, superiority RCT • Duration of study: not reported • Duration of follow-up: (months): 24 months
Participants	• Setting/data source: academic, multicentre (2) • Country: USA • Inclusion criteria: upper-extremity graft with SVP/systolic blood pressure ratio ≥ 0.4 • Stage of CKD; dialysis vintage: prevalent patients; not reported • Mean access age: 335 days • Access type: grafts, some with previous procedures • Access location; mean access age: treatment group (34% forearm; 321 days); control group (53% forearm; 350 days) • Mean QA; % of accesses with previous procedures: treatment group (not reported; 34%); control group (not reported; 28%) • Number: treatment group (32); control group (32) • Mean age ± SD (years): treatment group (58 ± 17); control group (60 ± 12) • Sex (men): treatment group (47%); control group (81%) • Diabetics: treatment group (63%); control group (47%) • Exclusion criteria: poor prognosis; anticipated change in RRT; allergy to contrast media
Interventions	Treatment group • Referred to angiography • Angioplasty if angiography confirmed > 50% stenosis Control group • Continued SVP monitoring • Stenosis repair if the graft became dysfunctional or clotted Other information • Stenosis criterion: > 50% • Radiologist involvement: not reported • Method of stenosis correction (%) (PTA/surgery): 88/12 • Prophylaxis: secondary suspected stenosis in non-dysfunctional access (increased SVP)
Outcomes	• Access abandonment (secondary survival - primary outcome) • Thrombotic events • Access-related diagnostic and intervention procedures • Access infections

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Dember 2004 *(Continued)*

	• CVC placements • Death
Notes	• Funding: "This study was funded by a Gambro Healthcare Research Program grant. We are grateful for the contributions of the nephrologists, interventional radiologists, and dialysis unit staff at Boston Medical centre, VA Boston Healthcare System, and Gambro Healthcare-Boston." • Contact with authors for additional data: no • Trial registration: no • Additional data on drug use (antiplatelet or anticoagulant): reported • The study was stopped early because of futility; however there was no pre-specified stopping rule

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random number generator and permuted block scheme; randomisation stratified by study site
Allocation concealment (selection bias)	Unclear risk	Not reported
Intention-to-treat analysis (selection bias)	Low risk	Pre-specified and done
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not reported; lack of blinding can influence access management
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Outcome assessors were not blinded, but outcomes are objective; radiologists and surgeons were blinded but they were not outcome assessors
Incomplete outcome data (attrition bias) All outcomes	High risk	Withdrawals only in the intervention arm
Selective reporting (reporting bias)	Low risk	Protocol not available but published report includes all pre-specified outcomes
Other bias	High risk	Physicians informed when patients referred to angioplasty (only intervention arm); among controls: more females and > body weight

Lumsden 1997

Methods	• Study design: open-label, parallel, superiority RCT • Duration of study: December 1993 to November 1996 • Duration of follow-up: 15 months
Participants	• Setting/data source: academic • Country: USA • Inclusion criteria: functional graft with > 50% stenosis (DUS screening + angiography confirmation) • Stage of CKD; dialysis vintage: prevalent patients; not reported • Mean access age: not reported

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Lumsden 1997 *(Continued)*

- Access type: graft, some with previous procedures
- Access location; mean access age: treatment group (25% forearm, 72% upper arm, 3% leg; not reported); control group (28% forearm, 72% upper arm; not reported)
- mean QA; % of accesses with previous procedures: treatment group (1716 mL/min; > 0); control group (1886 mL/min; > 0)
- Number of participants: treatment group (32); control group (32)
- Mean age ± SD (years): treatment group (56 ± 13); control group (58 ± 11)
- Sex(M/F): treatment group (17/15); control group (14/18)
- Diabetics: treatment group (41%); control group (38%)
- Exclusion criteria: allergy to contrast media; non-functioning PTFE graft

Interventions	Treatment group • Pre-emptive angioplasty • DUS repeated every 2 months Control group • Observation only • DUS repeated every 2 months; intervention if recirculation > 15% Other information • Stenosis criterion: > 50% • Radiologist involvement: not reported • Method of stenosis correction (PTA/surgery): not reported • Prophylaxis: secondary (documented stenosis in non-dysfunctional access)
Outcomes	• Functional failure: primary assisted patency (thrombosis, dysfunction, 6+ salvage procedures over 18 months) • Rates of procedures (only overall - not by group) • Death
Notes	• Funding: "Supported in part by NIH Grant # P50DK45215-03 and Clinical Research centre # 324" • Contact with authors for additional data: no • Trial registration: no • Additional data on drug use (antiplatelet or anticoagulant): not reported • Formal study hypothesis framed in the abstract; no sample size calculation reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Drawing cards
Allocation concealment (selection bias)	High risk	Strategy not reported; considering the method used to generate the random sequence, lack of reporting suggests high risk
Intention-to-treat analysis (selection bias)	High risk	Unclear reporting; number of participants at risk < number randomised
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not reported; lack of blinding can influence access management

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Lumsden 1997 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Strategy not reported, but outcomes are objective
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Total numbers included in outcome analyses not reported
Selective reporting (reporting bias)	Low risk	Outcomes reported as anticipated in the methods section
Other bias	High risk	Study hypothesis explicitly stated, but sample size not reported

Malik 2005

Methods	• Study design: open-label, parallel, superiority RCT • Duration of study: 1999 to 2004 • Duration of follow-up: 13 months
Participants	• Setting/data source: academic • Country: Czech Republic • Inclusion criteria: new graft • Stage of CKD; dialysis vintage: prevalent patients using a new graft; not reported • Mean access age: not reported • Access type: new graft • Access location; mean access age: treatment group (78% forearm, 20% upper arm, 2% subclavian; not reported); control group (78% forearm, 20% upper arm, 2% subclavian; not reported) • mean QA and % of accesses with previous procedures: treatment group (769; > 0); control group (not reported; > 0) • Number of participants: treatment group (97); control group (92) • Mean age ± SD (years): 58.7 ± 14.2); control group (58.3 ± 13.9) • Sex (men): treatment group (43%); control group (45%) • Diabetics: treatment group (53%); control group (51%) • Exclusion criteria: not reported
Interventions	Treatment group • DUS in addition to clinical monitoring and screening with DVP, recirculation and QA if available • DUS every 3 months; referral if peak systolic velocity ratio > 2 or > 25% decrease Control group • Clinical monitoring and screening with DVP, recirculation and QA if available • Clinical + DVP or recirculation or QA Other information • Stenosis criterion: not reported • Prophylaxis: primary (no stenosis at randomisation) • Radiologist involvement: not reported • Method of stenosis correction (%) (PTA/surgery): 94/6
Outcomes	• Secondary patency (graft loss) with thrombosis or infection requiring graft removal as terminating events

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Malik 2005 *(Continued)*

	• Intervention rates per access
Notes	• Funding: "This study was supported by the Research Project MSM-0021620807 of Ministry of Education, Czech Republic, and by the Grant Agency of Ministry of Health, Czech Republic No. NR 8334." • Contact with authors for additional data: no • Trial registration: no • Additional data on drug use (antiplatelet or anticoagulant): not reported • QA not available in all centres; eligibility criteria not reported; clinical criteria for angiogram referral are specified (abnormal physical findings, prolonged bleeding after needle removal, > VP, < QA < 600 or > 25%, abnormal recirculation, unexplained decreased in dialysis adequacy)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Intention-to-treat analysis (selection bias)	Unclear risk	Unclear reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not reported; lack of blinding can influence access management
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported, but outcome is objective
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Few missing data; unclear whether analyses followed the intention-to-treat principle
Selective reporting (reporting bias)	Low risk	Outcomes reported as anticipated in the methods section
Other bias	High risk	No explicit study hypothesis; no sample size estimation

Mayer 1993

Methods	• Study design: open-label, parallel, superiority RCT • Duration of study: not reported • Duration of follow-up: 21 months
Participants	• Setting/data source: academic • Country: USA • Inclusion criteria: not reported • Stage of CKD/dialysis vintage: prevalent patients using a new graft; not reported • Mean access age: not reported • Access type: new graft

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Mayer 1993 *(Continued)*

- Access location; mean access age: treatment group (57% forearm, 43% upper arm; not reported); control group (46% forearm, 54% upper arm; not reported)
- Mean QA and % of accesses with previous procedures: not reported
- Number of participants: treatment group (35); control group (35)
- Mean age ± SD (years): not reported
- Sex (M/F): not reported
- Diabetics: not reported
- Exclusion criteria: not reported

Interventions	Treatment group • DUS at 3, 6, 12 and yearly thereafter (looking at anatomical and haemodynamic changes) Control group • Clinical monitoring at 3, 6, 12 and yearly thereafter Other information • Stenosis criterion: > 50% • Prophylaxis: primary (no stenosis at randomisation) • Radiologist involvement: not reported • Method of stenosis correction (%) (PTA/surgery): 0/100
Outcomes	• Unassisted patency (thrombosis) • Intervention rate • Death
Notes	• Funding: not reported • Contact with authors for additional data: no • Trial registration: no • Additional data on drug use (antiplatelet or anticoagulant): not reported • Clinical monitoring components not described

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Intention-to-treat analysis (selection bias)	High risk	Unclear reporting; number of participants (accesses) at risk different from number randomised
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not reported; lack of blinding can influence access management
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported, but the outcome is objective
Incomplete outcome data (attrition bias)	High risk	Missing data are balanced; however, the percentage of loss to follow-up was > 10%

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Mayer 1993 *(Continued)*

All outcomes		
Selective reporting (reporting bias)	Low risk	Outcomes reported as anticipated in the methods section
Other bias	High risk	Lack of formal study hypothesis; no sample size estimation

Moist 2003

Methods	• Study design: double-blind, parallel, superiority RCT • Duration of study: January 2000 to December 2001 • Duration of follow-up: 12 months
Participants	• Setting/data source: academic, multicentre (2) • Country: Canada • Inclusion criteria: graft working; QA > 650 mL/min; no abnormality • Stage of CKD; dialysis vintage: prevalent patients; not reported • Mean access age: 734 days • Access type: grafts without previous procedure • Access location; mean access age: treatment group (68% forearm, 24% upper arm, 8% leg; 21 months); control group (76% forearm, 24% upper arm; 24 months) • Mean QA; % of accesses with previous procedures: treatment group (1116 mL/min; > 0); control group (1100 mL/min; > 0) • Number of participants: treatment group (59); control group (53) • Mean age ± SD (years): treatment group (62.9 ± 15.3); control group (66.5 ± 13.4) • Sex (men): treatment group (47.9%); control group (52.8%) • Diabetics: treatment group (26.2%); control group (28.3%) • Exclusion criteria: not reported
Interventions	Treatment group • Clinical monitoring + DVP + monthly QA measurement • DVP > 125 mm Hg (Baxter machines); DVP > 140 mm Hg (Gambro machines) or QA < 650 or > 20% decrease in QA Control group • Clinical monitoring + DVP • Referral for clinical signs Other information • Stenosis criterion: > 50% • Prophylaxis: primary (no stenosis at randomisation) • Radiologist involvement: reported • Method of stenosis correction (PTA/surgery): not reported
Outcomes	• Time to thrombosis • Rates of thrombosis episodes • Time to permanent graft loss • Rates of interventions/patient-years
Notes	• Funding: not reported • Contact with authors for additional data: no

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Moist 2003 *(Continued)*

- Trial registration: no
- Additional data on drug use (antiplatelet or anticoagulant): reported
- Study size < estimated sample size

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer randomised sequence in blocks of four.
Allocation concealment (selection bias)	Low risk	Done by an independent central coordinator
Intention-to-treat analysis (selection bias)	Low risk	Pre-specified and done
Blinding of participants and personnel (performance bias) All outcomes	Low risk	QA measurements encrypted (decoded only for participants of the intervention arm)
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported by outcomes were objective
Incomplete outcome data (attrition bias) All outcomes	Low risk	Missing data balanced; intention to treat analysis
Selective reporting (reporting bias)	Low risk	Similar baseline characteristics
Other bias	Unclear risk	Study size < estimated sample size

Polkinghorne 2006

Methods	• Study design: double-blind, parallel, superiority RCT • Duration of study: 2001 to 2003 • Duration of follow-up: 18 months
Participants	• Setting/data source: academic • Country: Australia • Inclusion criteria: age > 18 years; stable on HD for 3 + months; QA > 500 mL/min (flow in the access) • Stage of CKD; dialysis vintage: prevalent patients; 2.2 years • Mean access age: 2.17 years • Access type: prevalent fistulas (some with previous procedures) • Access location; median access age: treatment group (61% distal, 36% proximal, 3% others; 23 months); control group (62% forearm, 34% upper arm, 4% others; 29 months) • Mean access QA; % previous access procedures: treatment group (1243; not reported); control group (1145; not reported) • Number of participants: treatment group (69); control group (68) • Median age, range (years): treatment group (60.0, 23.8 to 82.8); control group (56.4, 21.4 to 79.7) • Sex (M/F): treatment group (45/24); control group (48/20)

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Polkinghorne 2006 *(Continued)*

	• Diabetics: treatment group (22%); control group (25%) • Exclusion criteria: home HD; waiting for living transplant
Interventions	Treatment group • Clinical monitoring (see control group) plus monthly QA • Monthly QA (US dilution); referred if QA < 500 or falls > 20% once < 1000 mL/min Control group • Clinical monitoring (referred if): DVP > 150 mm Hg, < arterial pressure requiring lowering QB, bleeding following needle removal, unexplained reduction in URR Other information • Stenosis criterion: > 50% • Prophylaxis: primary (no stenosis at randomisation) • Radiologist involvement: reported • Method of stenosis correction (%) (PTA/surgery): 33/66
Outcomes	• Fistula stenosis (> 50%) • Thrombosis • Diagnostic and intervention procedures
Notes	• Funding: "Dr K.R.P. is a recipient of the National Health and Medical Research Council (NH&MRC) Medical Postgraduate Scholarship" • Contact with authors for additional data: no • Trial registration: not reported • Additional data on drug use (antiplatelet or anticoagulant): reported • Follow-up was at least one year (1.5 years on average)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer generated sequence
Allocation concealment (selection bias)	Low risk	Done by one investigator not involved in patient enrolment
Intention-to-treat analysis (selection bias)	Unclear risk	Unclear reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Patients and clinicians were blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Missing data were balanced; intention-to-treat principle uncertain

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Polkinghorne 2006 *(Continued)*

Selective reporting (reporting bias)	Low risk	Outcomes reported as anticipated in the methods section
Other bias	Low risk	No other forms of bias were found

Ram 2003

Methods	• Study design: single-blind, three-arm parallel, superiority RCT • Duration of study: 1998 to 2001 • Duration of follow-up: 24 months
Participants	• Setting/data source: academic, multicentre (2) • Country: USA • Inclusion criteria: access flow measurement possible • Stage of CKD; dialysis vintage: prevalent patients; 276/502/414 days • Median access age: 170.8 days • Access type: prevalent grafts (some with previous procedures) • Access location; mean access age: treatment group 1 (not reported; 14 months) treatment group 2 (not reported; 16 months); control group (not reported; 9 months) • Mean QA; % of accesses with previous procedures: treatment group 1 (1253 mL/min; 26%); treatment group 2 (1243 mL/min; 41%); control group (1333 mL/min; 35%) • Number of participants: treatment group 1(32); treatment group 2 (35); control group (34) • Mean age ± SE (years): treatment group 1 (55 ± 3); treatment group 2 (59 ± 3); control group (53 ± 2) • Sex (men): treatment group 1 (44%); treatment group 2 (51%); control group (38%) • Diabetics: treatment group 1 (62%); treatment group 2 (51%); control group (44%) • Exclusion criteria: not reported
Interventions	All received clinical monitoring and screening (monthly QA and DUS every 3 months); then they were randomised to three possible criteria for angioplasty referral Treatment group 1 • Criterion based on QA (< 600 mL/min) Treatment group 2 • Criterion based on US > 50% stenosis Control group • Clinical criteria for angioplasty referral: unattained prescribed QB; > DVP; > bleeding following needle removal; swollen arm Other information • Stenosis criterion: > 50% • Prophylaxis: primary (no stenosis at randomisation) • Radiologist involvement: not reported • Method of stenosis correction (PTA/surgery): not reported
Outcomes	• Unassisted survival of the graft (thrombosis) • Assisted survival (graft loss)

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Ram 2003 *(Continued)*

Notes	• Funding: "The authors thank Dialysis Clinic, Inc., for a grant that funded part of this study, and Michael Perry (President) and Lori Ferrell (Operations Manager), U.S. Vascular Access Holdings, Fresenius Medical Care, Inc., for their assistance in providing duplex ultrasound procedures during this study." • Contact with authors for additional data: no • Trial registration: no • Additional data on drug use (antiplatelet or anticoagulant): not reported • Clinical criteria for angioplasty referral: unattained prescribed QB; > DVP; > bleeding following needle removal; swollen arm

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random number 'table' generated with a software (blocked randomisation)
Allocation concealment (selection bias)	Low risk	One single investigator not involved in patient management was responsible for allocation
Intention-to-treat analysis (selection bias)	Low risk	Pre-specified and done
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Single-blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported but outcome measures were objective
Incomplete outcome data (attrition bias) All outcomes	Low risk	Missing data were balanced
Selective reporting (reporting bias)	High risk	Outcomes not prespecified in the methods section
Other bias	High risk	Neither explicit hypothesis, nor sample size estimation

Ram 2003 DU

Methods	
Participants	
Interventions	
Outcomes	
Notes	This is the same study as Ram 2003; the reason for the different names is because we needed to separate data for the comparison of DU-based screening versus controls from QA-based screening versus controls

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Ram 2003 QA

Methods	
Participants	
Interventions	
Outcomes	
Notes	This is the same study as Ram 2003; the reason for the different names is because we needed to separate data for the comparison of DU-based screening versus controls from QA-based screening versus controls

Robbin 2006

Methods	• Study design: open-label, parallel, superiority RCT • Duration of study: not reported • Duration of follow-up: 38 months
Participants	• Setting/data source: academic • Country: USA • Inclusion criteria: stable on HD for 3+ months; outpatient; no previous procedures • Stage of CKD; dialysis vintage: prevalent patients; 0.75 months • Access type: an upper-extremity graft for 1 to 24 months • Access location; mean access age: treatment group (17% forearm, 83% upper arm; 9); control group (30% forearm, 70 upper arm; 9) • Mean QA; % of accesses with previous procedures: treatment group (not reported; 48); control group (not reported; 57) • Number of participants: treatment group (65); control group (61) • Mean age ± SD (years): treatment group (57 ± 12); control group (58 ± 13) • Sex (M/F): treatment group (31/34); control group (21/40) • Diabetics: treatment group (52%); control group (70%) • Exclusion criteria: poor prognosis; waiting for living transplant

Interventions	treatment group
	• Clinical monitoring plus DUS screening immediately after randomisation and then every four months
	• DUS every 4 months; referred if peak systolic velocity ratio = 2+
	Control group
	• Clinical monitoring
	  ○ Physical examination (inspection, palpation and auscultation)
	  ○ Indicators during dialysis (ease of cannulation, lack of clots, target QB, ease of haemostasis)
	  ○ Dialysis adequacy (Kt/V)
	Other information
	• Stenosis criterion: > 50%
	• Prophylaxis: primary (no stenosis at randomisation)
	• Radiologist involvement: reported
	• Method of stenosis correction (%) (PTA/surgery): 100/0

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Robbin 2006 *(Continued)*

Outcomes	• Secondary (assisted) graft patency (primary outcome) • Primary graft patency (thrombosis-free graft survival -- secondary outcome) • Rates of PTA procedures • Death
Notes	• Funding: "This study was funded by a grant from NIDDK (R01 DK54240-01A1) to Dr Robbin." • Contact with authors for additional data: no • Trial registration: no • Additional data on drug use (antiplatelet or anticoagulant): not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Not stated explicitly; however, stratification and blocking are reported -- implying a random number generator procedure
Allocation concealment (selection bias)	Low risk	Study coordinators opened 'sequentially numbered, opaque envelopes' to assign participants to either arm -- it is assumed that the envelopes were sealed, but it is not stated
Intention-to-treat analysis (selection bias)	Low risk	Pre-specified and done
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not reported; lack of blinding can influence access management
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported, but the outcome is an objective one
Incomplete outcome data (attrition bias) All outcomes	Low risk	Six participants assigned to the intervention arm withdrew their consent; however, all analyses followed the ITT principle
Selective reporting (reporting bias)	Low risk	Outcomes reported as anticipated in the methods section
Other bias	Low risk	None found

Sands 1999

Methods	• Study design: open-label, parallel three-arm, superiority RCT • Duration of study: not reported • Duration of follow-up: 6 months
Participants	• Setting/data source: non-academic • Country: USA • Inclusion criteria: not reported • Stage of CKD; dialysis vintage: prevalent patients; 542/542/851 days • Mean access age: 696 fistulas/609 grafts days • Access type: prevalent fistulas and grafts (some with previous procedures)

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Sands 1999 *(Continued)*

- Access location; mean access age: treatment groups (not reported; 18 months); control group (not reported; 28 months)
- Mean QA; % of accesses with previous procedures: not reported
- Number of participants: treatment group 1 (27); treatment group 2 (35); control group (41)
- Mean age (years): treatment groups (55.7); control group (59.7)
- Sex (M/F): not reported
- Diabetics: treatment groups (25.8%); control group (30%)
- Exclusion criteria: not reported

Interventions	Treatment group 1 • Monthly QA + DUS every 6 months • Referred if QA < 600 (fistula) or < 800 (graft) or DUS stenosis > 50% Treatment group 2 • Monthly SVP + DUS every 6 months • Referred if SVP = 0.5+ (both accesses) or DUS stenosis > 50% Control group • DUS every 6 months alone (no monitoring) • DUS stenosis > 50% Other information • Stenosis criterion: > 50% • Prophylaxis: primary (no stenosis at randomisation) • Radiologist involvement: not reported • Method of stenosis correction (PTA/surgery): not reported
Outcomes	• Thrombosis • Repeated thrombosis episodes • Number of procedures (angioplasties)
Notes	• Funding: "This work was supported in part by SBIR grant DK 50499-03" • Contact with authors for additional data: no • Trial registration: no • Additional data on drug use (antiplatelet or anticoagulant): not reported • No physical exam included in the protocol; two interventions vs one comparator (both comparisons by access type -- fistula or graft)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Intention-to-treat analysis (selection bias)	Unclear risk	Insufficient information reported
Blinding of participants and personnel (performance bias)	High risk	Not reported; lack of blinding can influence access management

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Sands 1999 *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported, but outcome is objective
Incomplete outcome data (attrition bias) All outcomes	High risk	Missing data not reported; intention-to-treat analysis uncertain
Selective reporting (reporting bias)	Low risk	Outcomes reported as anticipated in abstract and methods
Other bias	High risk	No sample size estimation; age of patients and accesses and diabetes vary substantially across groups; test used for outcome comparison not specified; rates of repeated events done using naive methods

Sands 1999 QA/DU (F)

Methods	
Participants	
Interventions	
Outcomes	
Notes	This is the same study as Sands 1999; the reason for the different names is because we needed to separate data for two comparisons in fistulas and two comparisons in grafts

Sands 1999 QA/DU (G)

Methods	
Participants	
Interventions	
Outcomes	
Notes	This is the same study as Sands 1999; the reason for the different names is because we needed to separate data for two comparisons in fistulas and two comparisons in grafts

Sands 1999 SP/DU (F)

Methods
Participants
Interventions

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Sands 1999 SP/DU (F) *(Continued)*

Outcomes	
Notes	This is the same study as Sands 1999; the reason for the different names is because we needed to separate data for two comparisons in fistulas and two comparisons in grafts

Sands 1999 SP/DU (G)

Methods	
Participants	
Interventions	
Outcomes	
Notes	This is the same study as Sands 1999; the reason for the different names is because we needed to separate data for two comparisons in fistulas and two comparisons in grafts

Scaffaro 2009

Methods	• Study design: open-label, parallel, superiority RCT • Duration of study: commenced 2005 • Duration of follow-up: 7.5 months
Participants	• Setting/data source: academic • Country: Brazil • Inclusion criteria: non-dysfunctional access • Stage of CKD; dialysis vintage: prevalent HD patients; not reported • Mean access age: 63% > 6 months • Access type: prevalent fistula • Access location; mean access age: treatment group (not reported; 64% > 6 months); control group (not reported; 62% > 6 months) • Mean QA; % of accesses with previous procedures: treatment group (not reported; 58%); control group (not reported; 57%) • Number of participants: treatment group (53); control group (58) • Mean age (years): treatment group (56.7); control group (54.9) • Sex (M/F): treatment group (32/21); control group (30/28) • Diabetics: treatment group (37.7%); control group (36.2%) • Exclusion criteria: not reported
Interventions	Treatment group • Clinical monitoring and haemodynamic assessment, plus DUS every 3 months • DUS detection of stenosis (> 50%) or QA < 500 mL/min, in addition to abnormalities at clinical monitoring Control group • Clinical monitoring including haemodynamic assessment • DVP > 150 mmHg or clinical indications Other information

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Scaffaro 2009 *(Continued)*

	• Stenosis criterion: > 50% • Prophylaxis: primary (no stenosis at randomisation) • Radiologist involvement: not reported • Method of stenosis correction (PTA/surgery): not reported
Outcomes	1. Need for a central venous catheter for vascular access 2. Thrombosis 3. Either 1 or 2
Notes	• Funding: not reported • Contact with authors for additional data: no • Trial registration: no • Additional data on drug use (antiplatelet or anticoagulant): not reported • Clinical examination described: weekly examination (inspection, palpation, auscultation) and assessment of QB and DVP

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	High risk	Sealed envelopes (whether envelopes were sequentially numbered, opened following the number order, and opaque is not reported) -- high risk considering the lack of reporting of the randomisation procedure
Intention-to-treat analysis (selection bias)	Unclear risk	Insufficient information reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not reported; lack of blinding can influence access management
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported but outcomes are objectives
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Some withdrawal; unclear whether the analyses followed to the intention-to-treat principle
Selective reporting (reporting bias)	Low risk	Outcomes reported as anticipated in the methods section
Other bias	High risk	No sample size estimation; differential treatment impacting one outcome (catheter): treatment for the control arm was surgery (more likely to require use of catheters), while it was angioplasty for the intervention arm; participants re-randomised after an event (111 fistulas in 108 participants) -- unclear whether methods for correlated date were used

Smits 2001

Methods	• Study design: open-label, parallel three-arm, superiority RCT

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Smits 2001 *(Continued)*

	• Duration of study: not reported • Duration of follow-up: 8 months

Participants	• Setting/data source: academic, multicentre (5)
	• Country: The Netherlands
	• Inclusion criteria: not reported
	• Stage of CKD dialysis vintage: prevalent patients; 2.5 years
	• Mean access age: 14.3 months
	• Access type: graft
	• Access location; mean access age
	  ○ study A: treatment group (93% forearm, 7% upper arm; 8 months); control group (92% forearm, 8% upper arm; 13 months)
	  ○ Study B: treatment group (90% forearm; 10% upper arm; 16 months); control group (100% forearm; 18 months)
	• Mean QA; % of accesses with previous procedures: not reported
	• Number of participants (treatment/control): study A (24/27); study B (31/37)
	• Number of grafts (treatment/control): study A (25/28); study B (31/41)
	• Mean age ± SD (years)
	  ○ Study A: treatment group (61 ± 17); control group (61 ± 18)
	  ○ Study B: treatment group (62 ± 14); control group (60 ± 17)
	• Sex (M/F)
	  ○ Study A: treatment group (9/15); control group (18/9)
	  ○ Study B: treatment group (15/16); control group (16/21)
	• Diabetics
	  ○ Study A: treatment group (16%); control group (26%)
	  ○ Study B: treatment group (26%); control group (11%)
	• Exclusion criteria: not reported

Interventions	Study A
	• Treatment group
	  ○ QA (screening) every 2 months
	  ○ QA (referral if < 600) + clinical monitoring
	• Control group
	  ○ Clinical (monitoring) + SVP and DVP
	  ○ referral if DVP > 150; SVP ratio > 0.5)
	Study B
	• Treatment group
	  ○ QA + SVP and DVP every 2 months
	  ○ QA (referral if < 600) + SVP and DVP + clinical monitoring
	• Control group
	  ○ Clinical (monitoring) + SVP and DVP
	  ○ Referral if DVP > 150; SVP ratio > 0.5
	Other information
	• Stenosis criterion: > 50%
	• Prophylaxis: primary (no stenosis at randomisation)
	• Radiologist involvement: not reported
	• Method of stenosis correction (%) (PTA/surgery): study A (87/13); study B (89/11)

Outcomes	• Thrombosis rate • Intervention rate

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Smits 2001 *(Continued)*

Notes	• Funding: "Dr. J.H.M. Smits is supported by a grant from the Dutch Kidney Foundation (C.97.1643)." • Contact with authors for additional data: no • Trial registration: no • Additional data on drug use (antiplatelet or anticoagulant): not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Intention-to-treat analysis (selection bias)	Unclear risk	Insufficient information reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not reported; lack of blinding can influence access management
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported; outcome are objective measures
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Missing data are balanced; whether the analyses followed the intention-to-treat principle is unclear
Selective reporting (reporting bias)	Low risk	Outcome reporting consistent with the methods section
Other bias	High risk	No consideration of multiple testing; unclear whether the access or the patient was randomised; sample size larger than the study size; the study was stopped early based on an unplanned interim analysis; age and gender varied across groups

Smits 2001 QA

Methods	
Participants	
Interventions	
Outcomes	
Notes	This is the same study as Smits 2001; the reason for the different names is because we needed to separate data for two comparisons from the same study

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Smits 2001 QA/SP

Methods	
Participants	
Interventions	
Outcomes	
Notes	This is the same study as Smits 2001; the reason for the different names is because we needed to separate data for two comparisons from the same study

Tessitore 2003

Methods	• Study design: open-label, parallel, superiority RCT • Duration of study: 1995 to 2001 • Duration of follow-up: 15 months
Participants	• Setting/data source: academic, single centre • Country: Italy • Inclusion criteria: functioning (Kt/V ≥ 1.2) virgin (never treated) fistula which had signs of stenosis at screening (dialysis QB > 30/mL/min, urea R > 5%, access R > 0% or QA < 850) and confirmed > 50% stenosis at angiography; no prior interventions • Stage of CKD; dialysis vintage: prevalent HD patients; 1 year • Mean access age: 12.6 months • Access type: prevalent fistulas • Access location; median access age: treatment group (forearm; 10 months); control group (forearm; 16 months) • Mean QA; % of accesses with previous procedures: treatment group (451; not reported); control group (473; not reported) • Number of participants: treatment group (30); control group (30) ○ number of accesses: treatment group (32); control group (30) • Mean age ± SD (years): treatment group (57.3 ± 16.7) control group (61.5 ± 13.4) • Sex (M/F): treatment group (18/12); control group (20/10) • Diabetics: treatment group (23.3%); control group (26.7%) • Exclusion criteria: already revised/salvaged fistula
Interventions	Treatment group • Pre-emptive angioplasty within 3 weeks of randomisation • Pre-emptive correction of stenosis if QA < 850 mL/min Control group • Deferred salvage procedures (angioplasty) • Correction if QB lowered by > 30 mL/min or recirculation > 5% Other information • Stenosis criterion: > 50% • Prophylaxis: secondary (documented stenosis in non-dysfunctional access) • Radiologist involvement: not reported • Method of stenosis correction (PTA/surgery): not reported
Outcomes	• Risk of thrombosis or surgery regardless of repeat angioplasties (assisted patency)

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Tessitore 2003 *(Continued)*

- Secondary (unassisted) patency
- Death
- Hospitalisation
- CVC placement
- Thrombectomy
- Elective surgery

Notes	• Funding: not reported • Contact with authors for additional data: yes • Trial registration: no • Additional data on drug use (antiplatelet or anticoagulant): not reported • Sample selected based on surveillance measurements

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Initial coin tossing subsequently replaced by a 'minimization' technique
Allocation concealment (selection bias)	High risk	Strategy not reported; considering the method used to generate the random sequence, lack of reporting suggests high risk
Intention-to-treat analysis (selection bias)	High risk	Not pre-specified; no sensitivity analyses assuming different scenarios for missing data
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not reported; lack of blinding can influence access management
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear, but outcomes are objective
Incomplete outcome data (attrition bias) All outcomes	Low risk	No losses to follow-up:
Selective reporting (reporting bias)	Low risk	Outcomes reported as anticipated in the methods section
Other bias	High risk	No sample size estimation; randomisation method changed during the study; baseline imbalances for participant and fistula age, diabetes, cardiovascular disease, severity of lesion (length of stenosis); clinical monitoring not described

Tessitore 2004a

Methods	• Study design: open-label, parallel, superiority RCT • Duration of study: commenced 1997 • Duration of follow-up: 30 months
Participants	• Setting/data source: academic, multicentre (2)

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Tessitore 2004a *(Continued)*

	• Country: Italy • Inclusion criteria: functioning (Kt/V ≥ 1.2) fistula which had signs of stenosis at screening (decreased QB > 40/mL/min, urea recirculation > 5% or QA < 750) and confirmed > 50% stenosis at angiography; no prior interventions • Stage of CKD; dialysis vintage: prevalent HD patients; 19.5 months • Mean access: 19.5 months • Access type: prevalent fistula • Access location; mean access age: treatment group (forearm; 17 months); control group (forearm; 22 months) • Mean QA; % of accesses with previous procedures: treatment group (450 mL/min; 0); control group (438 mL/min; 0) • Number of participants: treatment group (43); control group (36) • Mean age ± SD (years): treatment group (58.1 ± 14.9); control group (61.9 ± 13.0) • Sex (M/F): treatment group (23/20); control group (21/15) • Diabetics: treatment group (23.2%); control group (22.8%) • Exclusion criteria: other clinical trials
Interventions	Treatment group • Pre-emptive angioplasty within 3 weeks of randomisation (or surgery on the same conduit if lesion was not amenable to angioplasty) • Pre-emptive correction of stenosis if QA < 750 mL/min Control group • Deferred salvage procedures (angioplasty or surgery) • Correction if QB lowered by > 40 mL/min or recirculation > 5% Other information • Stenosis criterion: > 50% • Prophylaxis: secondary (documented stenosis in non-dysfunctional access) • Radiologist involvement: reported • Method of stenosis correction (%) (PTA/surgery): 79/21
Outcomes	• Secondary patency (primary outcome) • Primary survival (thrombosis)
Notes	• Funding: not reported • Contact with authors for additional data: yes • Trial registration: no • Additional data on drug use (antiplatelet or anticoagulant): not reported • Sample selected based on surveillance measurements

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Coin tossing
Allocation concealment (selection bias)	High risk	Not reported; considering the method used to generate the random sequence, lack of reporting indicates high risk
Intention-to-treat analysis (selection bias)	High risk	Not pre-specified; no sensitivity analyses assuming different scenarios for missing data

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Tessitore 2004a *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	Not reported; lack of blinding can influence access management
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear, but outcomes are objective
Incomplete outcome data (attrition bias) All outcomes	High risk	Four losses to follow-up excluded from final analysis
Selective reporting (reporting bias)	Low risk	Outcomes reported as anticipated in the methods section
Other bias	Unclear risk	Baseline imbalances for patient age and access age

Tessitore 2014

Methods	• Study design: open-label, parallel, superiority RCT • Duration of study: 2006 to 2013 • Duration of follow-up: 30 months
Participants	• Setting/data source: academic • Country: Italy • Inclusion criteria: functioning (Kt/V > 1.2) fistula with suspected stenosis at screening (QA < 900 and/or physical signs or static venous pressure ratio > 0.5) that was confirmed as > 50% stenosis at angiography • Stage of CKD; dialysis vintage: prevalent HD patients; not reported • Mean access age: 24 months • Access type: prevalent fistula • access location and mean access age: treatment group (17 forearm; 21 months); control group (22 forearm; 27 month) • Mean QA; % of accesses with previous procedures: treatment group (720 mL/min; 0 in the previous 3 months); control group (792 mL/min; 0) • Number of participants: treatment group (28); control group (30) • Mean age ± SD (years): treatment group (60 ± 17); control group (67 ± 14) • Sex (M/F): treatment group (18/10); control group (16/14) • Diabetics: treatment group (33%); control group (29%) • Exclusion criteria: access procedures in the previous three months
Interventions	Treatment group • Pre-emptive angioplasty or surgery within 3 weeks of randomisation • Pre-emptive correction of stenosis at baseline and repeated during follow-up if QA < 750 mL/min or QA dropped by > 25% Control group • Deferred salvage procedures (angioplasty or surgery) • Elective repair allowed if QA<400 (but 300 +) mL/min Other information

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Tessitore 2014 *(Continued)*

	• Stenosis criterion: > 50% • Prophylaxis: secondary (documented stenosis in non-dysfunctional access) • Radiologist involvement: reported • Method of stenosis correction (%) (PTA/surgery): 72/28
Outcomes	• Access failure (thrombosis or incipient thrombosis documented as QA < 300 mL/min) • Access loss (irremediable thrombosis or unsalvageable access) • Elective stenosis repair • Use of catheters • Catheter-related infections (bacteraemia and exit-site or tunnel infections) • Hospitalisations • Costs
Notes	• Funding: not reported • Contact with authors for additional data: no • Trial registration: yes • Additional data on drug use (antiplatelet or anticoagulant): not reported • Detailed description of cannulation method, US and angiography, manual or surgical thrombectomy, angioplasty and surgical repair of stenosis lesions

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Sealed envelopes (unclear whether they were opaque and numbered, and opened in order they were numbered)
Intention-to-treat analysis (selection bias)	Unclear risk	Not prespecified
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not reported; lack of blinding can influence access management
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear, but outcomes are objective
Incomplete outcome data (attrition bias) All outcomes	Low risk	All data included
Selective reporting (reporting bias)	Low risk	Outcomes reported as anticipated in the methods section
Other bias	High risk	Early termination without pre-specified stopping rules

CKD - chronic kidney disease; CVC - central venous catheters; DUS - duplex ultrasound; DVP - dynamic venous pressure; HD - haemodialysis; M/F - male/female; PTA - percutaneous transluminal angioplasty; PTFE -polytetrafluoroethylene; QA - access blood flow rate; QB - blood pump flow rate; RCT - randomised controlled trial; RRT - renal replacement therapy; SD - standard deviation; SVP - static venous pressure; URR - urea reduction ratio; US - ultrasound; VP - venous pressure

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Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Aftab 2014	Compared 2 interventions for established stenosis in a dysfunctional access (not pre-emptive intervention)
Bacchini 2003	Compared 2 interventions for established stenosis requiring an intervention
Beathard 1993	Compared 2 interventions for established stenosis requiring an intervention
Beathard 1994	Compared 2 interventions for established thrombosis
BRAVO I Study 2006	Compared 2 interventions for established stenosis requiring an intervention
BRAVO II Study 2013	Compared 2 interventions for established thrombosis
Brooks 1987	Compared 2 interventions for established stenosis requiring an intervention
Cohen 2000	Compared 2 interventions for established stenosis requiring an intervention
Dougherty 1999	Compared 2 interventions for established thrombosis
Forauer 2008	Compared 2 interventions for established stenosis requiring an intervention
HAPPI Study 2007	Compared 2 interventions for established stenosis requiring an intervention
Haskal 2010	Compared 2 interventions for established stenosis requiring an intervention
Haskal 2013	Compared 2 interventions for established thrombosis
Hegab 2013	Compared 2 interventions for established thrombosis
Hoffer 1997	Compared 2 interventions for established stenosis requiring an intervention
Katsanos 2012	Compared 2 interventions for established stenosis requiring an intervention
Khoo 2010	Compared 2 interventions for established stenosis requiring an intervention
Kundu 2010	Compared 2 interventions for established stenosis requiring an intervention
Marston 1997	Compared 2 interventions for established thrombosis
Middlebrook 1995	Compared 2 interventions for established stenosis requiring an intervention
Ono 2004	Compared 2 interventions for established stenosis requiring an intervention
Quinn 1995	Compared 2 interventions for established stenosis requiring an intervention
Roy-Chaudhury 2012	Compared 2 interventions for established stenosis requiring an intervention
Saini 2008	Compared 2 interventions for established stenosis requiring an intervention
Schuman 1994	Compared 2 interventions for established thrombosis
Sheley 1996	Compared 2 interventions for established stenosis requiring an intervention

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Study	Reason for exclusion
Shemesh 2008	Compared 2 interventions for established stenosis requiring an intervention
Teo 2013	Compared 2 interventions for established stenosis requiring an intervention
Tessitore 2004b	Compared 2 interventions for established stenosis requiring an intervention
Uflacker 1996	Compared 2 interventions for established stenosis requiring an intervention
Veroux 2013	Pre-operative interventions to promote maturation of an arteriovenous fistula
Vesely 1996	Compared 2 interventions for established thrombosis
Vesely 1999	Compared 2 interventions for established thrombosis
Vesely 2005	Compared 2 interventions for established stenosis/thrombosis requiring an intervention
Whittier 2009	Evaluated the correlation between two methods for blood flow measurement

Characteristics of studies awaiting assessment *[ordered by study ID]*

NCT01001676

Methods	RCT
Participants	People with access stenosis
Interventions	Paclitaxel Eluting Balloon Angioplasty versus standard angioplasty
Outcomes	Primary patency
Notes	

NCT01544907

Methods	RCT
Participants	People with stenosis of an arteriovenous graft or fistula
Interventions	Conventional angioplasty versus drug eluting balloon (DEB) - paclitaxel-eluting balloon
Outcomes	Patency rates
Notes	

Sands 1997

Methods	RCT
Participants	Patients with significant stenosis

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Sands 1997 *(Continued)*

Interventions	Ultrasound screening every 6 months versus no screening
Outcomes	Thrombosis rates, hospital admissions, hospital days, total charges and estimated payments
Notes	

Characteristics of ongoing studies *[ordered by study ID]*

NCT01200914

Trial name or title	Covered stents to treat haemodialysis access stenoses in the cephalic arch and central veins
Methods	RCT
Participants	People with upper-vein stenosis
Interventions	Angioplasty with GORE VIABAHN® endoprosthesis and heparin bioactive surface vs angioplasty without use of the GORE VIABAHN
Outcomes	Primary patency
Starting date	January 2011
Contact information	Dheeraj Rajan, University Health Network, Toronto
Notes	

NCT01391975

Trial name or title	Surveillance and proactive intervention for dialysis access (SPIDA)
Methods	RCT
Participants	People with fistulas (primary prophylaxis)
Interventions	Procedure: Active ultrasound surveillance of fistula and proactive treatment of stenosis Regular duplex ultrasound assessment of fistula from time of creation until 6 months post procedure with referral of all haemodynamically significant stenoses to further imaging and treatment
Outcomes	Secondary patency (access abandonment)
Starting date	Not reported
Contact information	Hull Royal Infirmary Not yet recruiting Hull, United Kingdom, HU3 2JZ Contact: Ian C Chetter, MBChB, MD, FRCS Contact: George E Smith, BSc, MBBS, MRCS Principal Investigator: Ian C Chetter, MBChB, MD, FRCS
Notes	

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NCT01538108	
Trial name or title	Study of NMB (Company's Name) drug ejecting balloon for arteriovenous fistulae
Methods	RCT
Participants	Obstructive lesions of arteriovenous dialysis fistulae
Interventions	Experimental: NMB's PTA balloon catheter with paclitaxel (device: PTA balloon catheter with paclitaxel patients treated by the NMB's PTA balloon catheter with paclitaxel) Active Comparator: standard angioplasty balloon (procedure: plain balloon angioplasty (PBA)
Outcomes	Restenosis rate
Starting date	Not yet recruiting
Contact information	The Chaim Sheba Medical centre Not yet recruiting Tel Hashomer, Israel Contact: Uri Rimon, MD
Notes	

DATA AND ANALYSES

Comparison 1. Pre-emptive versus deferred correction

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Assisted patency: RR of access loss overall	11	972	Risk Ratio (M-H, Random, 95% CI)	0.80 [0.64, 0.99]
2 Assisted patency: RR of access loss by access type	11	972	Risk Ratio (M-H, Random, 95% CI)	0.80 [0.64, 0.99]
2.1 Fistula	4	310	Risk Ratio (M-H, Random, 95% CI)	0.50 [0.29, 0.86]
2.2 Graft	7	662	Risk Ratio (M-H, Random, 95% CI)	0.87 [0.69, 1.11]
3 Assisted patency: RR of access loss by prevention aim	11	972	Risk Ratio (M-H, Random, 95% CI)	0.80 [0.64, 0.99]
3.1 Primary prophylaxis	7	709	Risk Ratio (M-H, Random, 95% CI)	0.82 [0.63, 1.06]
3.2 Secondary prophylaxis	4	263	Risk Ratio (M-H, Random, 95% CI)	0.75 [0.49, 1.13]

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Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4 Assisted patency: RR of fistula loss by prevention aim	4	310	Risk Ratio (M-H, Random, 95% CI)	0.50 [0.29, 0.86]
4.1 Primary prophylaxis	1	111	Risk Ratio (M-H, Random, 95% CI)	0.44 [0.15, 1.31]
4.2 Secondary prophylaxis	3	199	Risk Ratio (M-H, Random, 95% CI)	0.52 [0.28, 0.97]
5 Assisted patency: RR of access loss by surveillance method (primary prophylaxis)	7	709	Risk Ratio (M-H, Random, 95% CI)	0.82 [0.63, 1.06]
5.1 Doppler ultrasound (access flow and structure)	5	548	Risk Ratio (M-H, Random, 95% CI)	0.78 [0.59, 1.04]
5.2 Blood flow (access flow only)	2	161	Risk Ratio (M-H, Random, 95% CI)	0.98 [0.52, 1.86]
6 Assisted patency: HR of access loss overall	8	729	Risk Ratio (Random, 95% CI)	0.63 [0.39, 1.01]
7 Assisted patency: HR of access loss by access type	8	729	Risk Ratio (Random, 95% CI)	0.63 [0.39, 1.01]
7.1 Fistula	2	137	Risk Ratio (Random, 95% CI)	0.34 [0.16, 0.71]
7.2 Graft	6	592	Risk Ratio (Random, 95% CI)	0.75 [0.44, 1.28]
8 Assisted patency: HR of access loss by prevention aim	8	729	Risk Ratio (Random, 95% CI)	0.63 [0.39, 1.01]
8.1 Primary prophylaxis	5	528	Risk Ratio (Random, 95% CI)	0.63 [0.38, 1.03]
8.2 Secondary prophylaxis	3	201	Risk Ratio (Random, 95% CI)	0.60 [0.18, 1.97]
9 Assisted patency: HR of access loss by surveillance method (primary prophylaxis)	5	528	Risk Ratio (Random, 95% CI)	0.63 [0.38, 1.03]
9.1 Doppler ultrasound (access flow and structure)	3	367	Risk Ratio (Random, 95% CI)	0.54 [0.25, 1.19]
9.2 Blood flow (access flow only)	2	161	Risk Ratio (Random, 95% CI)	0.82 [0.39, 1.70]
10 Assisted patency: IRR of access loss overall	2	120	Risk Ratio (Random, 95% CI)	0.39 [0.22, 0.71]
11 Unassisted patency: RR of access thrombosis overall	18	1212	Risk Ratio (M-H, Random, 95% CI)	0.79 [0.65, 0.97]
12 Unassisted patency: RR of access thrombosis by access type	18	1212	Risk Ratio (M-H, Random, 95% CI)	0.79 [0.65, 0.97]

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Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
12.1 Fistula	7	515	Risk Ratio (M-H, Random, 95% CI)	0.50 [0.35, 0.71]
12.2 Graft	11	697	Risk Ratio (M-H, Random, 95% CI)	0.95 [0.80, 1.12]
13 Unassisted patency: RR of access thrombosis by prevention aim	18	1212	Risk Ratio (M-H, Random, 95% CI)	0.79 [0.65, 0.97]
13.1 Primary prophylaxis	13	885	Risk Ratio (M-H, Random, 95% CI)	0.94 [0.78, 1.12]
13.2 Secondary prophylaxis	5	327	Risk Ratio (M-H, Random, 95% CI)	0.53 [0.32, 0.87]
14 Unassisted patency: RR of fistula thrombosis by prevention aim	7	515	Risk Ratio (M-H, Random, 95% CI)	0.50 [0.35, 0.71]
14.1 Primary prophylaxis	4	316	Risk Ratio (M-H, Random, 95% CI)	0.75 [0.42, 1.36]
14.2 Secondary prophylaxis	3	199	Risk Ratio (M-H, Random, 95% CI)	0.40 [0.26, 0.62]
15 Unassisted patency: RR of access thrombosis by surveillance method (primary prophylaxis)	13	885	Risk Ratio (M-H, Random, 95% CI)	0.94 [0.78, 1.12]
15.1 Doppler ultrasound (access flow and structure)	4	359	Risk Ratio (M-H, Random, 95% CI)	0.84 [0.65, 1.08]
15.2 Blood flow (access flow only)	7	470	Risk Ratio (M-H, Random, 95% CI)	1.08 [0.83, 1.40]
15.3 Static venous pressure	2	56	Risk Ratio (M-H, Random, 95% CI)	0.54 [0.17, 1.70]
16 Unassisted patency: HR of access thrombosis overall	12	861	Risk Ratio (Random, 95% CI)	0.70 [0.51, 0.95]
17 Unassisted patency: HR of access thrombosis by access type	12	861	Risk Ratio (Random, 95% CI)	0.70 [0.51, 0.95]
17.1 Fistula	3	199	Risk Ratio (Random, 95% CI)	0.28 [0.16, 0.49]
17.2 Graft	9	662	Risk Ratio (Random, 95% CI)	0.91 [0.73, 1.15]
18 Unassisted patency: HR of access thrombosis by prevention aim	12	861	Risk Ratio (Random, 95% CI)	0.70 [0.51, 0.95]
18.1 Primary prophylaxis	7	534	Risk Ratio (Random, 95% CI)	0.97 [0.75, 1.25]
18.2 Secondary prophylaxis	5	327	Risk Ratio (Random, 95% CI)	0.42 [0.27, 0.67]

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Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
19 Unassisted patency: HR of access thrombosis by surveillance method (primary prophylaxis)	7	534	Risk Ratio (Random, 95% CI)	0.97 [0.75, 1.25]
19.1 Doppler ultrasound (access flow and structure)	3	248	Risk Ratio (Random, 95% CI)	0.97 [0.62, 1.52]
19.2 Blood flow (access flow only)	4	286	Risk Ratio (Random, 95% CI)	0.89 [0.58, 1.35]
20 Unassisted patency: IRR of access thrombosis overall	6	346	Risk Ratio (Random, 95% CI)	0.65 [0.39, 1.10]
21 Unassisted patency: IRR of access thrombosis by access type	6	346	Risk Ratio (Random, 95% CI)	0.65 [0.39, 1.10]
21.1 Fistula	2	120	Risk Ratio (Random, 95% CI)	0.29 [0.15, 0.57]
21.2 Graft	4	226	Risk Ratio (Random, 95% CI)	0.96 [0.66, 1.38]
22 Unassisted patency: IRR of access thrombosis by prevention aim	6	346	Risk Ratio (Random, 95% CI)	0.65 [0.39, 1.10]
22.1 Primary prophylaxis	4	226	Risk Ratio (Random, 95% CI)	0.96 [0.66, 1.38]
22.2 Secondary prophylaxis	2	120	Risk Ratio (Random, 95% CI)	0.29 [0.15, 0.57]
23 Unassisted patency: IRR of access thrombosis by surveillance method (primary prophylaxis)	4	226	Risk Ratio (Random, 95% CI)	0.96 [0.66, 1.38]
23.1 Doppler ultrasound (access flow and structure)	1	52	Risk Ratio (Random, 95% CI)	0.74 [0.40, 1.35]
23.2 Blood flow (access flow only)	3	174	Risk Ratio (Random, 95% CI)	1.06 [0.68, 1.66]
24 Detection of access stenosis (HR)	1		Risk Ratio (Random, 95% CI)	Totals not selected
25 Elective stenosis repair	1		Risk Ratio (Random, 95% CI)	Totals not selected
26 Health resource use: angiograms (IRR)	7	539	Risk Ratio (Random, 95% CI)	1.78 [1.18, 2.67]
27 Health resource use: angioplasties (IRR)	9	815	Risk Ratio (Random, 95% CI)	1.19 [0.87, 1.64]
28 Health resource use: surgical interventions (IRR)	5	448	Risk Ratio (Random, 95% CI)	0.95 [0.62, 1.47]
29 Health resource use: radiological or surgical interventions (IRR)	6	585	Risk Ratio (Random, 95% CI)	1.30 [0.80, 2.12]
30 Health resource use: use of catheters (IRR)	6	394	Risk Ratio (Random, 95% CI)	0.58 [0.35, 0.98]

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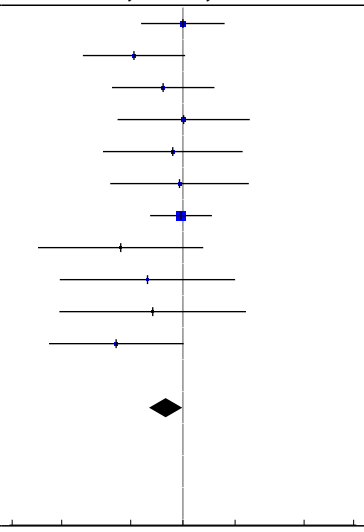
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
31 Health resource use: hospitalizations (IRR)	4	219	Risk Ratio (Random, 95% CI)	0.54 [0.31, 0.93]
32 Patient outcomes: infections (IRR)	3	248	Risk Ratio (Random, 95% CI)	1.74 [0.78, 3.91]
33 Patient outcomes: mortality (RR)	5	386	Risk Ratio (M-H, Random, 95% CI)	1.38 [0.91, 2.11]

Analysis 1.1. Comparison 1 Pre-emptive versus deferred correction, Outcome 1 Assisted patency: RR of access loss overall.

Study or subgroup	Pre-emptive correction n/N	Deferred correction n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Dember 2004	14/32	14/32		15.68%	1[0.57,1.74]
Malik 2005	11/97	20/92		10.53%	0.52[0.26,1.03]
Mayer 1993	10/35	13/35		10.52%	0.77[0.39,1.52]
Moist 2003	9/59	8/53		6.29%	1.01[0.42,2.43]
Ram 2003 DU	9/35	5/17		5.63%	0.87[0.35,2.21]
Ram 2003 QA	9/32	5/17		5.7%	0.96[0.38,2.4]
Robbin 2006	27/65	26/61		28.83%	0.97[0.65,1.47]
Scaffaro 2009	4/53	10/58		4.02%	0.44[0.15,1.31]
Tessitore 2003	4/32	6/30		3.58%	0.63[0.2,2]
Tessitore 2004a	4/43	5/36		3.16%	0.67[0.19,2.31]
Tessitore 2014	5/28	13/30		6.06%	0.41[0.17,1.01]
Total (95% CI)	**511**	**461**		**100%**	**0.8[0.64,0.99]**

Total events: 106 (Pre-emptive correction), 125 (Deferred correction)
Heterogeneity: Tau^2=0; Chi^2=7.21, df=10(P=0.71); I^2=0%
Test for overall effect: Z=2.04(P=0.04)

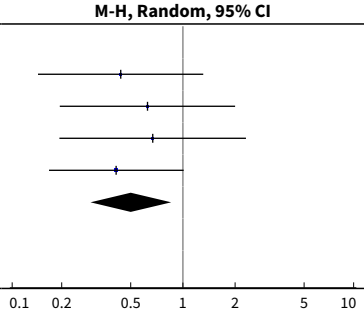


Favours pre-emptive — Favours deferred

Analysis 1.2. Comparison 1 Pre-emptive versus deferred correction, Outcome 2 Assisted patency: RR of access loss by access type.

Study or subgroup	Pre-emptive correction n/N	Deferred correction n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
1.2.1 Fistula					
Scaffaro 2009	4/53	10/58		4.02%	0.44[0.15,1.31]
Tessitore 2003	4/32	6/30		3.58%	0.63[0.2,2]
Tessitore 2004a	4/43	5/36		3.16%	0.67[0.19,2.31]
Tessitore 2014	5/28	13/30		6.06%	0.41[0.17,1.01]
Subtotal (95% CI)	**156**	**154**		**16.82%**	**0.5[0.29,0.86]**

Total events: 17 (Pre-emptive correction), 34 (Deferred correction)
Heterogeneity: Tau^2=0; Chi^2=0.59, df=3(P=0.9); I^2=0%



Favours pre-emptive — Favours deferred

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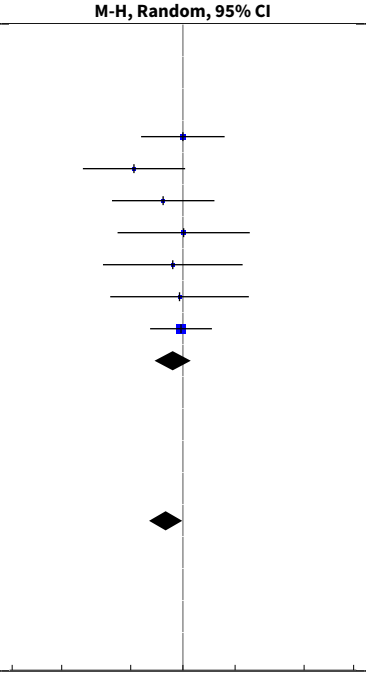
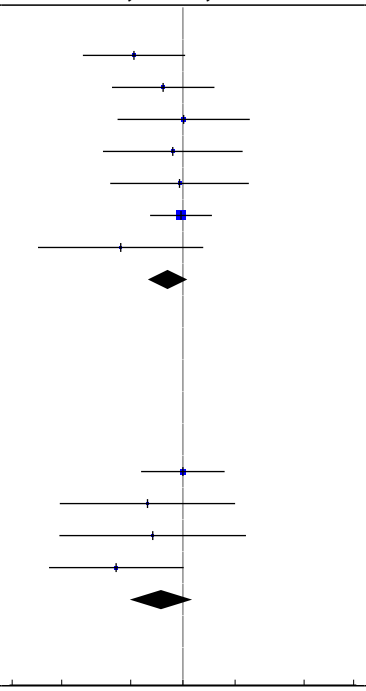
Study or subgroup	Pre-emptive correction n/N	Deferred correction n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Test for overall effect: Z=2.53(P=0.01)					
1.2.2 Graft					
Dember 2004	14/32	14/32		15.68%	1[0.57,1.74]
Malik 2005	11/97	20/92		10.53%	0.52[0.26,1.03]
Mayer 1993	10/35	13/35		10.52%	0.77[0.39,1.52]
Moist 2003	9/59	8/53		6.29%	1.01[0.42,2.43]
Ram 2003 DU	9/35	5/17		5.63%	0.87[0.35,2.21]
Ram 2003 QA	9/32	5/17		5.7%	0.96[0.38,2.4]
Robbin 2006	27/65	26/61		28.83%	0.97[0.65,1.47]
Subtotal (95% CI)	**355**	**307**		**83.18%**	**0.87[0.69,1.11]**
Total events: 89 (Pre-emptive correction), 91 (Deferred correction)					
Heterogeneity: Tau^2=0; Chi^2=3.05, df=6(P=0.8); I^2=0%					
Test for overall effect: Z=1.1(P=0.27)					
Total (95% CI)	**511**	**461**		**100%**	**0.8[0.64,0.99]**
Total events: 106 (Pre-emptive correction), 125 (Deferred correction)					
Heterogeneity: Tau^2=0; Chi^2=7.21, df=10(P=0.71); I^2=0%					
Test for overall effect: Z=2.04(P=0.04)					
Test for subgroup differences: Chi^2=3.44, df=1 (P=0.06), I^2=70.9%					



Analysis 1.3. Comparison 1 Pre-emptive versus deferred correction, Outcome 3 Assisted patency: RR of access loss by prevention aim.

Study or subgroup	Pre-emptive correction n/N	Deferred correction n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
1.3.1 Primary prophylaxis					
Malik 2005	11/97	20/92		10.53%	0.52[0.26,1.03]
Mayer 1993	10/35	13/35		10.52%	0.77[0.39,1.52]
Moist 2003	9/59	8/53		6.29%	1.01[0.42,2.43]
Ram 2003 DU	9/35	5/17		5.63%	0.87[0.35,2.21]
Ram 2003 QA	9/32	5/17		5.7%	0.96[0.38,2.4]
Robbin 2006	27/65	26/61		28.83%	0.97[0.65,1.47]
Scaffaro 2009	4/53	10/58		4.02%	0.44[0.15,1.31]
Subtotal (95% CI)	**376**	**333**		**71.52%**	**0.82[0.63,1.06]**
Total events: 79 (Pre-emptive correction), 87 (Deferred correction)					
Heterogeneity: Tau^2=0; Chi^2=4.12, df=6(P=0.66); I^2=0%					
Test for overall effect: Z=1.54(P=0.12)					
1.3.2 Secondary prophylaxis					
Dember 2004	14/32	14/32		15.68%	1[0.57,1.74]
Tessitore 2003	4/32	6/30		3.58%	0.63[0.2,2]
Tessitore 2004a	4/43	5/36		3.16%	0.67[0.19,2.31]
Tessitore 2014	5/28	13/30		6.06%	0.41[0.17,1.01]
Subtotal (95% CI)	**135**	**128**		**28.48%**	**0.75[0.49,1.13]**
Total events: 27 (Pre-emptive correction), 38 (Deferred correction)					
Heterogeneity: Tau^2=0; Chi^2=2.98, df=3(P=0.39); I^2=0%					



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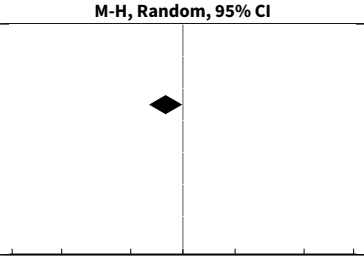
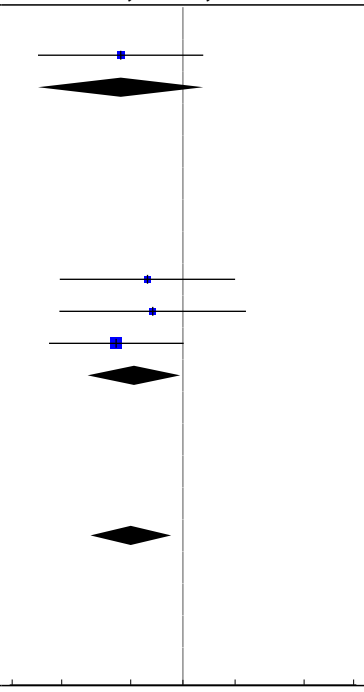
Study or subgroup	Pre-emptive correction n/N	Deferred correction n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Test for overall effect: Z=1.39(P=0.16)					
Total (95% CI)	**511**	**461**		**100%**	**0.8[0.64,0.99]**
Total events: 106 (Pre-emptive correction), 125 (Deferred correction)					
Heterogeneity: Tau²=0; Chi²=7.21, df=10(P=0.71); I²=0%					
Test for overall effect: Z=2.04(P=0.04)					
Test for subgroup differences: Chi²=0.12, df=1 (P=0.72), I²=0%					



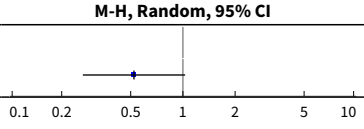
Analysis 1.4. Comparison 1 Pre-emptive versus deferred correction, Outcome 4 Assisted patency: RR of fistula loss by prevention aim.

Study or subgroup	Pre-emptive correction n/N	Deferred correction n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
1.4.1 Primary prophylaxis					
Scaffaro 2009	4/53	10/58		23.88%	0.44[0.15,1.31]
Subtotal (95% CI)	**53**	**58**		**23.88%**	**0.44[0.15,1.31]**
Total events: 4 (Pre-emptive correction), 10 (Deferred correction)					
Heterogeneity: Tau²=0; Chi²=0, df=0(P<0.0001); I²=100%					
Test for overall effect: Z=1.47(P=0.14)					
1.4.2 Secondary prophylaxis					
Tessitore 2003	4/32	6/30		21.29%	0.63[0.2,2]
Tessitore 2004a	4/43	5/36		18.78%	0.67[0.19,2.31]
Tessitore 2014	5/28	13/30		36.05%	0.41[0.17,1.01]
Subtotal (95% CI)	**103**	**96**		**76.12%**	**0.52[0.28,0.97]**
Total events: 13 (Pre-emptive correction), 24 (Deferred correction)					
Heterogeneity: Tau²=0; Chi²=0.52, df=2(P=0.77); I²=0%					
Test for overall effect: Z=2.07(P=0.04)					
Total (95% CI)	**156**	**154**		**100%**	**0.5[0.29,0.86]**
Total events: 17 (Pre-emptive correction), 34 (Deferred correction)					
Heterogeneity: Tau²=0; Chi²=0.59, df=3(P=0.9); I²=0%					
Test for overall effect: Z=2.53(P=0.01)					
Test for subgroup differences: Chi²=0.08, df=1 (P=0.78), I²=0%					



Analysis 1.5. Comparison 1 Pre-emptive versus deferred correction, Outcome 5 Assisted patency: RR of access loss by surveillance method (primary prophylaxis).

Study or subgroup	Pre-emptive correction n/N	Deferred correction n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
1.5.1 Doppler ultrasound (access flow and structure)					
Malik 2005	11/97	20/92		14.72%	0.52[0.26,1.03]



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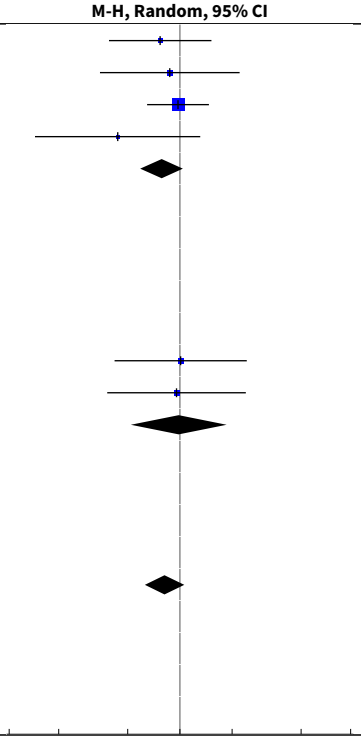
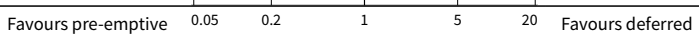
Study or subgroup	Pre-emptive correction n/N	Deferred correction n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Mayer 1993	10/35	13/35		14.71%	0.77[0.39,1.52]
Ram 2003 DU	9/35	5/17		7.88%	0.87[0.35,2.21]
Robbin 2006	27/65	26/61		40.31%	0.97[0.65,1.47]
Scaffaro 2009	4/53	10/58		5.61%	0.44[0.15,1.31]
Subtotal (95% CI)	**285**	**263**		**83.23%**	**0.78[0.59,1.04]**
Total events: 61 (Pre-emptive correction), 74 (Deferred correction)					
Heterogeneity: Tau^2=0; Chi^2=3.75, df=4(P=0.44); I^2=0%					
Test for overall effect: Z=1.67(P=0.1)					
1.5.2 Blood flow (access flow only)					
Moist 2003	9/59	8/53		8.8%	1.01[0.42,2.43]
Ram 2003 QA	9/32	5/17		7.97%	0.96[0.38,2.4]
Subtotal (95% CI)	**91**	**70**		**16.77%**	**0.98[0.52,1.86]**
Total events: 18 (Pre-emptive correction), 13 (Deferred correction)					
Heterogeneity: Tau^2=0; Chi^2=0.01, df=1(P=0.93); I^2=0%					
Test for overall effect: Z=0.05(P=0.96)					
Total (95% CI)	**376**	**333**		**100%**	**0.82[0.63,1.06]**
Total events: 79 (Pre-emptive correction), 87 (Deferred correction)					
Heterogeneity: Tau^2=0; Chi^2=4.12, df=6(P=0.66); I^2=0%					
Test for overall effect: Z=1.54(P=0.12)					
Test for subgroup differences: Chi^2=0.41, df=1 (P=0.52), I^2=0%					



Analysis 1.6. Comparison 1 Pre-emptive versus deferred correction, Outcome 6 Assisted patency: HR of access loss overall.

Study or subgroup	Pre-emptive correction N	Deferred correction N	log[Risk Ratio] (SE)	Risk Ratio IV, Random, 95% CI	Weight	Risk Ratio IV, Random, 95% CI
Dember 2004	32	32	0.6 (0.398)		14.09%	1.75[0.8,3.82]
Malik 2005	97	92	-1.3 (0.404)		13.95%	0.27[0.12,0.59]
Moist 2003	59	53	-0.1 (0.577)		9.92%	0.91[0.29,2.81]
Ram 2003 DU	35	17	-0.5 (0.495)		11.65%	0.58[0.22,1.54]
Ram 2003 QA	32	17	-0.3 (0.49)		11.77%	0.75[0.29,1.97]
Robbin 2006	65	61	-0.1 (0.287)		17.28%	0.93[0.53,1.63]
Tessitore 2004a	43	36	-1 (0.483)		11.95%	0.38[0.15,0.97]
Tessitore 2014	28	30	-1.3 (0.604)		9.41%	0.28[0.09,0.93]
Total (95% CI)					**100%**	**0.63[0.39,1.01]**
Heterogeneity: Tau^2=0.26; Chi^2=16.19, df=7(P=0.02); I^2=56.77%						
Test for overall effect: Z=1.9(P=0.06)						



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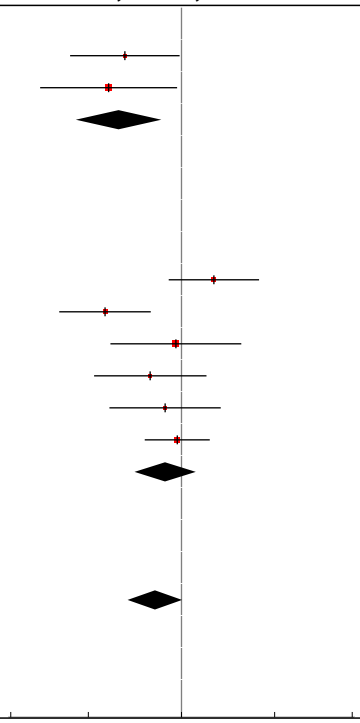
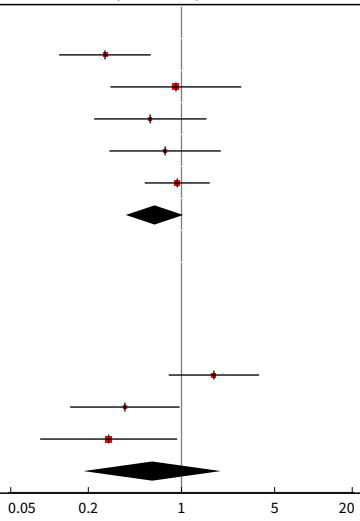
Analysis 1.7. Comparison 1 Pre-emptive versus deferred correction, Outcome 7 Assisted patency: HR of access loss by access type.

Study or subgroup	Pre-emptive correction N	Deferred correction N	log[Risk Ratio] (SE)	Risk Ratio IV, Random, 95% CI	Weight	Risk Ratio IV, Random, 95% CI
1.7.1 Fistula						
Tessitore 2004a	43	36	-1 (0.483)		11.95%	0.38[0.15,0.97]
Tessitore 2014	28	30	-1.3 (0.604)		9.41%	0.28[0.09,0.93]
Subtotal (95% CI)					**21.36%**	**0.34[0.16,0.71]**
Heterogeneity: Tau^2=0; Chi^2=0.13, df=1(P=0.72); I^2=0%						
Test for overall effect: Z=2.89(P=0)						
1.7.2 Graft						
Dember 2004	32	32	0.6 (0.398)		14.09%	1.75[0.8,3.82]
Malik 2005	97	92	-1.3 (0.404)		13.95%	0.27[0.12,0.59]
Moist 2003	59	53	-0.1 (0.577)		9.92%	0.91[0.29,2.81]
Ram 2003 DU	35	17	-0.5 (0.495)		11.65%	0.58[0.22,1.54]
Ram 2003 QA	32	17	-0.3 (0.49)		11.77%	0.75[0.29,1.97]
Robbin 2006	65	61	-0.1 (0.287)		17.28%	0.93[0.53,1.63]
Subtotal (95% CI)					**78.64%**	**0.75[0.44,1.28]**
Heterogeneity: Tau^2=0.25; Chi^2=11.99, df=5(P=0.03); I^2=58.28%						
Test for overall effect: Z=1.06(P=0.29)						
Total (95% CI)					**100%**	**0.63[0.39,1.01]**
Heterogeneity: Tau^2=0.26; Chi^2=16.19, df=7(P=0.02); I^2=56.77%						
Test for overall effect: Z=1.9(P=0.06)						
Test for subgroup differences: Chi^2=3, df=1 (P=0.08), I^2=66.71%						



Analysis 1.8. Comparison 1 Pre-emptive versus deferred correction, Outcome 8 Assisted patency: HR of access loss by prevention aim.

Study or subgroup	Pre-emptive correction N	Deferred correction N	log[Risk Ratio] (SE)	Risk Ratio IV, Random, 95% CI	Weight	Risk Ratio IV, Random, 95% CI
1.8.1 Primary prophylaxis						
Malik 2005	97	92	-1.3 (0.404)		13.95%	0.27[0.12,0.59]
Moist 2003	59	53	-0.1 (0.577)		9.92%	0.91[0.29,2.81]
Ram 2003 DU	35	17	-0.5 (0.495)		11.65%	0.58[0.22,1.54]
Ram 2003 QA	32	17	-0.3 (0.49)		11.77%	0.75[0.29,1.97]
Robbin 2006	65	61	-0.1 (0.287)		17.28%	0.93[0.53,1.63]
Subtotal (95% CI)					**64.55%**	**0.63[0.38,1.03]**
Heterogeneity: Tau^2=0.13; Chi^2=6.91, df=4(P=0.14); I^2=42.09%						
Test for overall effect: Z=1.83(P=0.07)						
1.8.2 Secondary prophylaxis						
Dember 2004	32	32	0.6 (0.398)		14.09%	1.75[0.8,3.82]
Tessitore 2004a	43	36	-1 (0.483)		11.95%	0.38[0.15,0.97]
Tessitore 2014	28	30	-1.3 (0.604)		9.41%	0.28[0.09,0.93]
Subtotal (95% CI)					**35.45%**	**0.6[0.18,1.97]**



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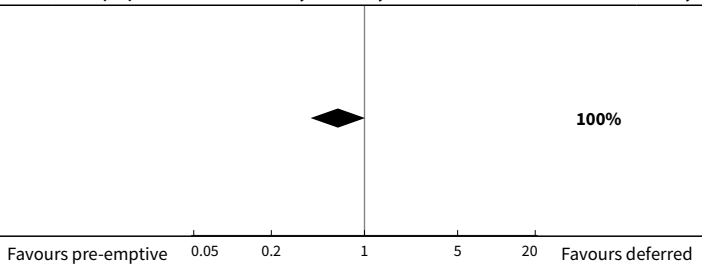
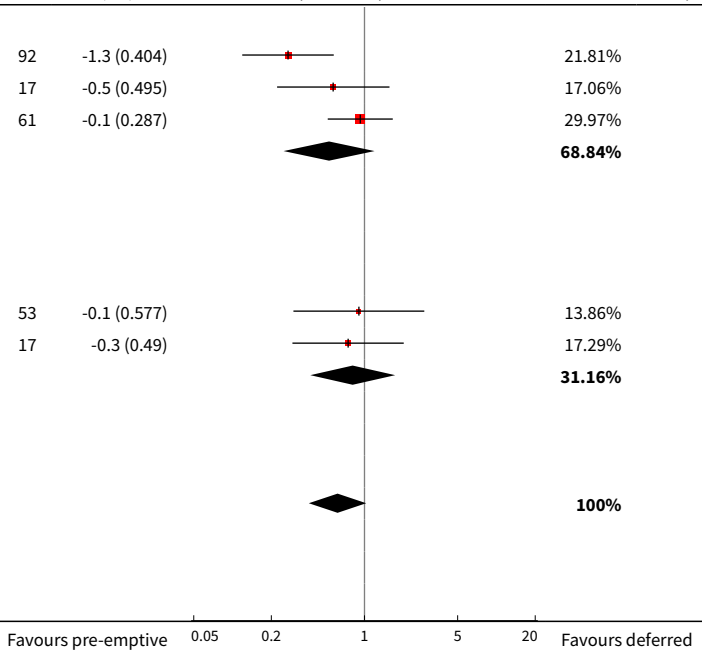
Study or subgroup	Pre-emptive correction N	Deferred correction N	log[Risk Ratio] (SE)	Risk Ratio IV, Random, 95% CI	Weight	Risk Ratio IV, Random, 95% CI
Heterogeneity: Tau²=0.85; Chi²=9.15, df=2(P=0.01); I²=78.15%						
Test for overall effect: Z=0.84(P=0.4)						
Total (95% CI)					**100%**	**0.63[0.39,1.01]**
Heterogeneity: Tau²=0.26; Chi²=16.19, df=7(P=0.02); I²=56.77%						
Test for overall effect: Z=1.9(P=0.06)						
Test for subgroup differences: Chi²=0, df=1 (P=0.95), I²=0%						



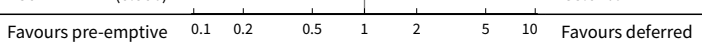
Analysis 1.9. Comparison 1 Pre-emptive versus deferred correction, Outcome 9 Assisted patency: HR of access loss by surveillance method (primary prophylaxis).

Study or subgroup	Pre-emptive correction N	Deferred correction N	log[Risk Ratio] (SE)	Risk Ratio IV, Random, 95% CI	Weight	Risk Ratio IV, Random, 95% CI
1.9.1 Doppler ultrasound (access flow and structure)						
Malik 2005	97	92	-1.3 (0.404)		21.81%	0.27[0.12,0.59]
Ram 2003 DU	35	17	-0.5 (0.495)		17.06%	0.58[0.22,1.54]
Robbin 2006	65	61	-0.1 (0.287)		29.97%	0.93[0.53,1.63]
Subtotal (95% CI)					**68.84%**	**0.54[0.25,1.19]**
Heterogeneity: Tau²=0.33; Chi²=6.37, df=2(P=0.04); I²=68.6%						
Test for overall effect: Z=1.53(P=0.13)						
1.9.2 Blood flow (access flow only)						
Moist 2003	59	53	-0.1 (0.577)		13.86%	0.91[0.29,2.81]
Ram 2003 QA	32	17	-0.3 (0.49)		17.29%	0.75[0.29,1.97]
Subtotal (95% CI)					**31.16%**	**0.82[0.39,1.7]**
Heterogeneity: Tau²=0; Chi²=0.06, df=1(P=0.81); I²=0%						
Test for overall effect: Z=0.55(P=0.58)						
Total (95% CI)					**100%**	**0.63[0.38,1.03]**
Heterogeneity: Tau²=0.13; Chi²=6.91, df=4(P=0.14); I²=42.09%						
Test for overall effect: Z=1.83(P=0.07)						
Test for subgroup differences: Chi²=0.56, df=1 (P=0.46), I²=0%						



Analysis 1.10. Comparison 1 Pre-emptive versus deferred correction, Outcome 10 Assisted patency: IRR of access loss overall.

Study or subgroup	Pre-emptive correction N	Deferred correction N	log[Risk Ratio] (SE)	Risk Ratio IV, Random, 95% CI	Weight	Risk Ratio IV, Random, 95% CI
Tessitore 2003	32	30	-0.9 (0.371)		64.98%	0.42[0.2,0.86]
Tessitore 2014	28	30	-1 (0.506)		35.02%	0.35[0.13,0.96]



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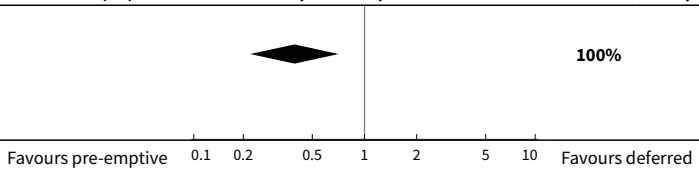
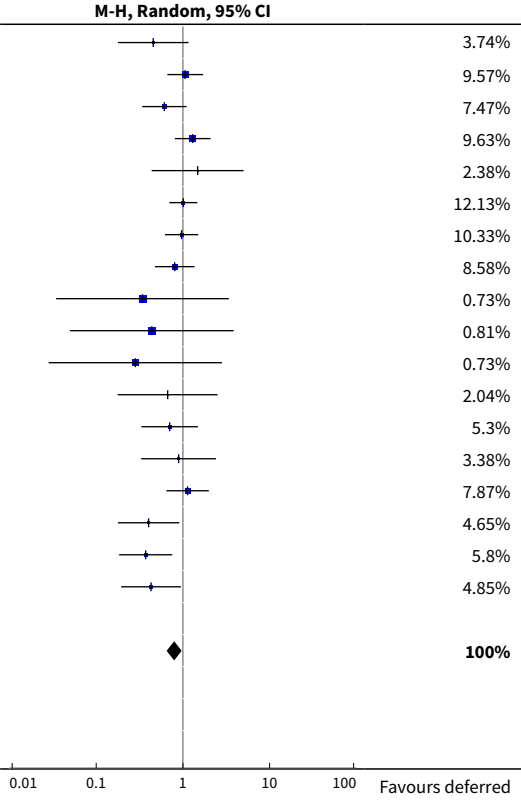
Study or subgroup	Pre-emptive correction N	Deferred correction N	log[Risk Ratio] (SE)	Risk Ratio IV, Random, 95% CI	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)					**100%**	**0.39[0.22,0.71]**
Heterogeneity: Tau²=0; Chi²=0.07, df=1(P=0.8); I²=0%						
Test for overall effect: Z=3.11(P=0)						



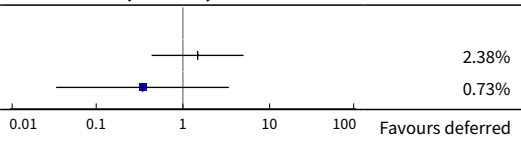
Analysis 1.11. Comparison 1 Pre-emptive versus deferred correction, Outcome 11 Unassisted patency: RR of access thrombosis overall.

Study or subgroup	Pre-emptive correction n/N	Deferred correction n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Dember 2004	5/32	11/32		3.74%	0.45[0.18,1.16]
Lumsden 1997	17/32	16/32		9.57%	1.06[0.66,1.71]
Mayer 1993	11/35	18/35		7.47%	0.61[0.34,1.1]
Moist 2003	26/59	18/53		9.63%	1.3[0.81,2.08]
Polkinghorne 2006	6/69	4/68		2.38%	1.48[0.44,5.01]
Ram 2003 DU	25/35	12/17		12.13%	1.01[0.7,1.47]
Ram 2003 QA	20/32	11/17		10.33%	0.97[0.62,1.5]
Robbin 2006	18/65	21/61		8.58%	0.8[0.48,1.36]
Sands 1999 QA/DU (F)	1/19	2/13		0.73%	0.34[0.03,3.39]
Sands 1999 QA/DU (G)	1/8	2/7		0.81%	0.44[0.05,3.85]
Sands 1999 SP/DU (F)	1/23	2/13		0.73%	0.28[0.03,2.82]
Sands 1999 SP/DU (G)	3/12	3/8		2.04%	0.67[0.18,2.51]
Scaffaro 2009	9/53	14/58		5.3%	0.7[0.33,1.49]
Smits 2001 QA	6/28	6/25		3.38%	0.89[0.33,2.41]
Smits 2001 QA/SP	18/41	12/31		7.87%	1.13[0.65,1.99]
Tessitore 2003	6/32	14/30		4.65%	0.4[0.18,0.91]
Tessitore 2004a	8/43	18/36		5.8%	0.37[0.18,0.75]
Tessitore 2014	6/28	15/30		4.85%	0.43[0.19,0.95]
Total (95% CI)	**646**	**566**		**100%**	**0.79[0.65,0.97]**
Total events: 187 (Pre-emptive correction), 199 (Deferred correction)					
Heterogeneity: Tau²=0.05; Chi²=24.23, df=17(P=0.11); I²=29.85%					
Test for overall effect: Z=2.28(P=0.02)					



Analysis 1.12. Comparison 1 Pre-emptive versus deferred correction, Outcome 12 Unassisted patency: RR of access thrombosis by access type.

Study or subgroup	Pre-emptive correction n/N	Deferred correction n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
1.12.1 Fistula					
Polkinghorne 2006	6/69	4/68		2.38%	1.48[0.44,5.01]
Sands 1999 QA/DU (F)	1/19	2/13		0.73%	0.34[0.03,3.39]



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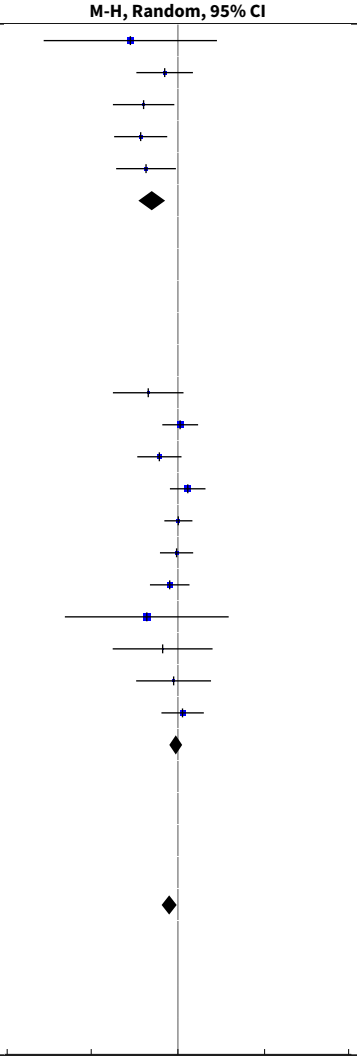
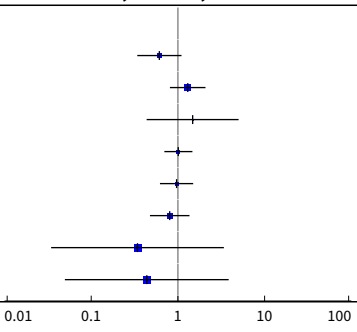
Study or subgroup	Pre-emptive correction n/N	Deferred correction n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Sands 1999 SP/DU (F)	1/23	2/13		0.73%	0.28[0.03,2.82]
Scaffaro 2009	9/53	14/58		5.3%	0.7[0.33,1.49]
Tessitore 2003	6/32	14/30		4.65%	0.4[0.18,0.91]
Tessitore 2004a	8/43	18/36		5.8%	0.37[0.18,0.75]
Tessitore 2014	6/28	15/30		4.85%	0.43[0.19,0.95]
Subtotal (95% CI)	**267**	**248**		**24.44%**	**0.5[0.35,0.71]**
Total events: 37 (Pre-emptive correction), 69 (Deferred correction)					
Heterogeneity: Tau^2=0; Chi^2=5.28, df=6(P=0.51); I^2=0%					
Test for overall effect: Z=3.83(P=0)					
1.12.2 Graft					
Dember 2004	5/32	11/32		3.74%	0.45[0.18,1.16]
Lumsden 1997	17/32	16/32		9.57%	1.06[0.66,1.71]
Mayer 1993	11/35	18/35		7.47%	0.61[0.34,1.1]
Moist 2003	26/59	18/53		9.63%	1.3[0.81,2.08]
Ram 2003 DU	25/35	12/17		12.13%	1.01[0.7,1.47]
Ram 2003 QA	20/32	11/17		10.33%	0.97[0.62,1.5]
Robbin 2006	18/65	21/61		8.58%	0.8[0.48,1.36]
Sands 1999 QA/DU (G)	1/8	2/7		0.81%	0.44[0.05,3.85]
Sands 1999 SP/DU (G)	3/12	3/8		2.04%	0.67[0.18,2.51]
Smits 2001 QA	6/28	6/25		3.38%	0.89[0.33,2.41]
Smits 2001 QA/SP	18/41	12/31		7.87%	1.13[0.65,1.99]
Subtotal (95% CI)	**379**	**318**		**75.56%**	**0.95[0.8,1.12]**
Total events: 150 (Pre-emptive correction), 130 (Deferred correction)					
Heterogeneity: Tau^2=0; Chi^2=8.24, df=10(P=0.61); I^2=0%					
Test for overall effect: Z=0.64(P=0.52)					
Total (95% CI)	**646**	**566**		**100%**	**0.79[0.65,0.97]**
Total events: 187 (Pre-emptive correction), 199 (Deferred correction)					
Heterogeneity: Tau^2=0.05; Chi^2=24.23, df=17(P=0.11); I^2=29.85%					
Test for overall effect: Z=2.28(P=0.02)					
Test for subgroup differences: Chi^2=10.05, df=1 (P=0), I^2=90.05%					



Analysis 1.13. Comparison 1 Pre-emptive versus deferred correction, Outcome 13 Unassisted patency: RR of access thrombosis by prevention aim.

Study or subgroup	Pre-emptive correction n/N	Deferred correction n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
1.13.1 Primary prophylaxis					
Mayer 1993	11/35	18/35		7.47%	0.61[0.34,1.1]
Moist 2003	26/59	18/53		9.63%	1.3[0.81,2.08]
Polkinghorne 2006	6/69	4/68		2.38%	1.48[0.44,5.01]
Ram 2003 DU	25/35	12/17		12.13%	1.01[0.7,1.47]
Ram 2003 QA	20/32	11/17		10.33%	0.97[0.62,1.5]
Robbin 2006	18/65	21/61		8.58%	0.8[0.48,1.36]
Sands 1999 QA/DU (F)	1/19	2/13		0.73%	0.34[0.03,3.39]
Sands 1999 QA/DU (G)	1/8	2/7		0.81%	0.44[0.05,3.85]



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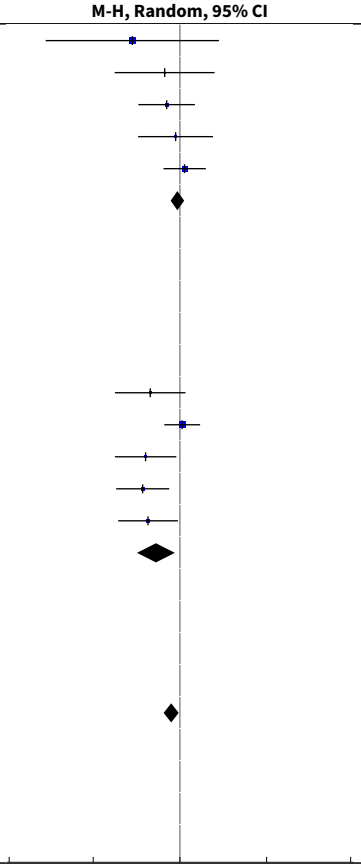
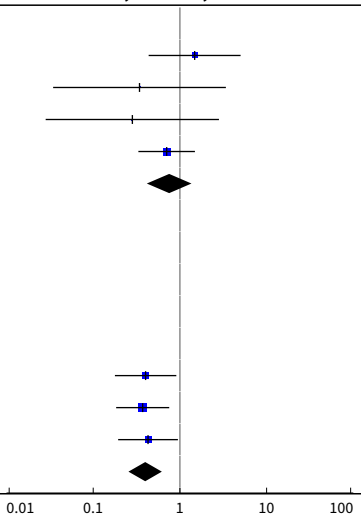
Study or subgroup	Pre-emptive correction n/N	Deferred correction n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Sands 1999 SP/DU (F)	1/23	2/13		0.73%	0.28[0.03,2.82]
Sands 1999 SP/DU (G)	3/12	3/8		2.04%	0.67[0.18,2.51]
Scaffaro 2009	9/53	14/58		5.3%	0.7[0.33,1.49]
Smits 2001 QA	6/28	6/25		3.38%	0.89[0.33,2.41]
Smits 2001 QA/SP	18/41	12/31		7.87%	1.13[0.65,1.99]
Subtotal (95% CI)	**479**	**406**		**71.39%**	**0.94[0.78,1.12]**
Total events: 145 (Pre-emptive correction), 125 (Deferred correction)					
Heterogeneity: Tau^2=0; Chi^2=8.53, df=12(P=0.74); I^2=0%					
Test for overall effect: Z=0.73(P=0.47)					
1.13.2 Secondary prophylaxis					
Dember 2004	5/32	11/32		3.74%	0.45[0.18,1.16]
Lumsden 1997	17/32	16/32		9.57%	1.06[0.66,1.71]
Tessitore 2003	6/32	14/30		4.65%	0.4[0.18,0.91]
Tessitore 2004a	8/43	18/36		5.8%	0.37[0.18,0.75]
Tessitore 2014	6/28	15/30		4.85%	0.43[0.19,0.95]
Subtotal (95% CI)	**167**	**160**		**28.61%**	**0.53[0.32,0.87]**
Total events: 42 (Pre-emptive correction), 74 (Deferred correction)					
Heterogeneity: Tau^2=0.19; Chi^2=9.7, df=4(P=0.05); I^2=58.78%					
Test for overall effect: Z=2.48(P=0.01)					
Total (95% CI)	**646**	**566**		**100%**	**0.79[0.65,0.97]**
Total events: 187 (Pre-emptive correction), 199 (Deferred correction)					
Heterogeneity: Tau^2=0.05; Chi^2=24.23, df=17(P=0.11); I^2=29.85%					
Test for overall effect: Z=2.28(P=0.02)					
Test for subgroup differences: Chi^2=4.39, df=1 (P=0.04), I^2=77.2%					



Analysis 1.14. Comparison 1 Pre-emptive versus deferred correction, Outcome 14 Unassisted patency: RR of fistula thrombosis by prevention aim.

Study or subgroup	Pre-emptive correction n/N	Deferred correction n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
1.14.1 Primary prophylaxis					
Polkinghorne 2006	6/69	4/68		8.48%	1.48[0.44,5.01]
Sands 1999 QA/DU (F)	1/19	2/13		2.4%	0.34[0.03,3.39]
Sands 1999 SP/DU (F)	1/23	2/13		2.38%	0.28[0.03,2.82]
Scaffaro 2009	9/53	14/58		22.44%	0.7[0.33,1.49]
Subtotal (95% CI)	**164**	**152**		**35.7%**	**0.75[0.42,1.36]**
Total events: 17 (Pre-emptive correction), 22 (Deferred correction)					
Heterogeneity: Tau^2=0; Chi^2=2.36, df=3(P=0.5); I^2=0%					
Test for overall effect: Z=0.94(P=0.35)					
1.14.2 Secondary prophylaxis					
Tessitore 2003	6/32	14/30		18.94%	0.4[0.18,0.91]
Tessitore 2004a	8/43	18/36		25.37%	0.37[0.18,0.75]
Tessitore 2014	6/28	15/30		20%	0.43[0.19,0.95]
Subtotal (95% CI)	**103**	**96**		**64.3%**	**0.4[0.26,0.62]**



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Study or subgroup	Pre-emptive correction n/N	Deferred correction n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Total events: 20 (Pre-emptive correction), 47 (Deferred correction)					
Heterogeneity: Tau²=0; Chi²=0.07, df=2(P=0.97); I²=0%					
Test for overall effect: Z=4.08(P<0.0001)					
Total (95% CI)	**267**	**248**		**100%**	**0.5[0.35,0.71]**
Total events: 37 (Pre-emptive correction), 69 (Deferred correction)					
Heterogeneity: Tau²=0; Chi²=5.28, df=6(P=0.51); I²=0%					
Test for overall effect: Z=3.83(P=0)					
Test for subgroup differences: Chi²=2.84, df=1 (P=0.09), I²=64.78%					

Analysis 1.15. Comparison 1 Pre-emptive versus deferred correction, Outcome 15 Unassisted patency: RR of access thrombosis by surveillance method (primary prophylaxis).

Study or subgroup	Pre-emptive correction n/N	Deferred correction n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
1.15.1 Doppler ultrasound (access flow and structure)					
Mayer 1993	11/35	18/35		9.35%	0.61[0.34,1.1]
Ram 2003 DU	25/35	12/17		23.23%	1.01[0.7,1.47]
Robbin 2006	18/65	21/61		11.69%	0.8[0.48,1.36]
Scaffaro 2009	9/53	14/58		5.7%	0.7[0.33,1.49]
Subtotal (95% CI)	**188**	**171**		**49.97%**	**0.84[0.65,1.08]**
Total events: 63 (Pre-emptive correction), 65 (Deferred correction)					
Heterogeneity: Tau²=0; Chi²=2.61, df=3(P=0.46); I²=0%					
Test for overall effect: Z=1.37(P=0.17)					
1.15.2 Blood flow (access flow only)					
Moist 2003	26/59	18/53		14.34%	1.3[0.81,2.08]
Polkinghorne 2006	6/69	4/68		2.15%	1.48[0.44,5.01]
Ram 2003 QA	20/32	11/17		16.42%	0.97[0.62,1.5]
Sands 1999 QA/DU (F)	1/19	2/13		0.61%	0.34[0.03,3.39]
Sands 1999 QA/DU (G)	1/8	2/7		0.68%	0.44[0.05,3.85]
Smits 2001 QA	6/28	6/25		3.24%	0.89[0.33,2.41]
Smits 2001 QA/SP	18/41	12/31		10.15%	1.13[0.65,1.99]
Subtotal (95% CI)	**256**	**214**		**47.6%**	**1.08[0.83,1.4]**
Total events: 78 (Pre-emptive correction), 55 (Deferred correction)					
Heterogeneity: Tau²=0; Chi²=2.88, df=6(P=0.82); I²=0%					
Test for overall effect: Z=0.59(P=0.56)					
1.15.3 Static venous pressure					
Sands 1999 SP/DU (F)	1/23	2/13		0.61%	0.28[0.03,2.82]
Sands 1999 SP/DU (G)	3/12	3/8		1.82%	0.67[0.18,2.51]
Subtotal (95% CI)	**35**	**21**		**2.43%**	**0.54[0.17,1.7]**
Total events: 4 (Pre-emptive correction), 5 (Deferred correction)					
Heterogeneity: Tau²=0; Chi²=0.41, df=1(P=0.52); I²=0%					
Test for overall effect: Z=1.06(P=0.29)					
Total (95% CI)	**479**	**406**		**100%**	**0.94[0.78,1.12]**

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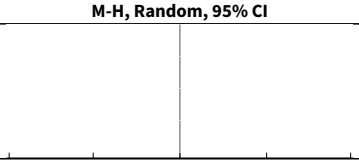
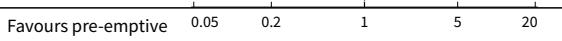
Study or subgroup	Pre-emptive correction n/N	Deferred correction n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Total events: 145 (Pre-emptive correction), 125 (Deferred correction)					
Heterogeneity: Tau²=0; Chi²=8.53, df=12(P=0.74); I²=0%					
Test for overall effect: Z=0.73(P=0.47)					
Test for subgroup differences: Chi²=2.82, df=1 (P=0.24), I²=29%					



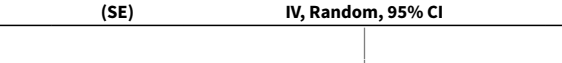
Analysis 1.16. Comparison 1 Pre-emptive versus deferred correction, Outcome 16 Unassisted patency: HR of access thrombosis overall.

Study or subgroup	Pre-emptive correction N	Deferred correction N	log[Risk Ratio] (SE)	Risk Ratio IV, Random, 95% CI	Weight	Risk Ratio IV, Random, 95% CI
Dember 2004	32	32	-0.4 (0.553)		5.74%	0.65[0.22,1.92]
Lumsden 1997	32	32	-0.4 (0.34)		10.26%	0.7[0.36,1.37]
Mayer 1993	35	35	-0.6 (0.373)		9.35%	0.53[0.26,1.11]
Moist 2003	59	53	-0 (0.418)		8.23%	0.96[0.42,2.19]
Ram 2003 DU	35	17	0.2 (0.269)		12.5%	1.24[0.73,2.1]
Ram 2003 QA	32	17	-0.2 (0.293)		11.7%	0.84[0.47,1.48]
Robbin 2006	65	61	0.1 (0.24)		13.48%	1.13[0.71,1.81]
Smits 2001 QA	28	25	0.2 (0.758)		3.54%	1.23[0.28,5.44]
Smits 2001 QA/SP	41	31	-0.2 (0.593)		5.19%	0.79[0.25,2.54]
Tessitore 2003	32	30	-1.2 (0.472)		7.11%	0.3[0.12,0.77]
Tessitore 2004a	43	36	-1.2 (0.43)		7.97%	0.3[0.13,0.69]
Tessitore 2014	28	30	-1.5 (0.614)		4.93%	0.22[0.07,0.74]
Total (95% CI)					**100%**	**0.7[0.51,0.95]**
Heterogeneity: Tau²=0.13; Chi²=20.41, df=11(P=0.04); I²=46.09%						
Test for overall effect: Z=2.28(P=0.02)						



Analysis 1.17. Comparison 1 Pre-emptive versus deferred correction, Outcome 17 Unassisted patency: HR of access thrombosis by access type.

Study or subgroup	Pre-emptive correction N	Deferred correction N	log[Risk Ratio] (SE)	Risk Ratio IV, Random, 95% CI	Weight	Risk Ratio IV, Random, 95% CI
1.17.1 Fistula						
Tessitore 2003	32	30	-1.2 (0.472)		7.11%	0.3[0.12,0.77]
Tessitore 2004a	43	36	-1.2 (0.43)		7.97%	0.3[0.13,0.69]
Tessitore 2014	28	30	-1.5 (0.614)		4.93%	0.22[0.07,0.74]
Subtotal (95% CI)					**20.01%**	**0.28[0.16,0.49]**
Heterogeneity: Tau²=0; Chi²=0.19, df=2(P=0.91); I²=0%						
Test for overall effect: Z=4.48(P<0.0001)						
1.17.2 Graft						



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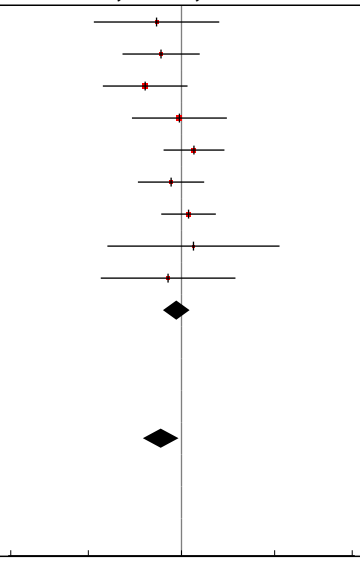
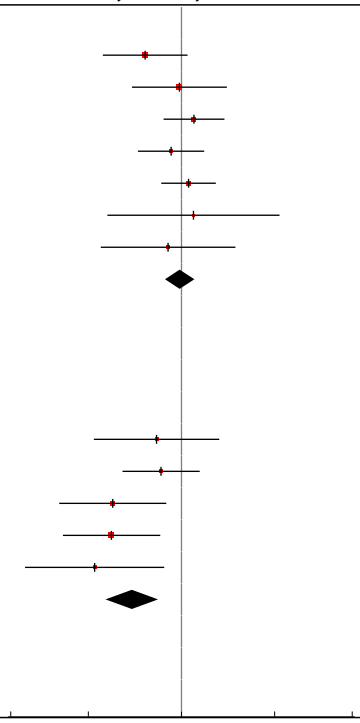
Study or subgroup	Pre-emptive correction N	Deferred correction N	log[Risk Ratio] (SE)	Risk Ratio IV, Random, 95% CI	Weight	Risk Ratio IV, Random, 95% CI
Dember 2004	32	32	-0.4 (0.553)		5.74%	0.65[0.22,1.92]
Lumsden 1997	32	32	-0.4 (0.34)		10.26%	0.7[0.36,1.37]
Mayer 1993	35	35	-0.6 (0.373)		9.35%	0.53[0.26,1.11]
Moist 2003	59	53	-0 (0.418)		8.23%	0.96[0.42,2.19]
Ram 2003 DU	35	17	0.2 (0.269)		12.5%	1.24[0.73,2.1]
Ram 2003 QA	32	17	-0.2 (0.293)		11.7%	0.84[0.47,1.48]
Robbin 2006	65	61	0.1 (0.24)		13.48%	1.13[0.71,1.81]
Smits 2001 QA	28	25	0.2 (0.758)		3.54%	1.23[0.28,5.44]
Smits 2001 QA/SP	41	31	-0.2 (0.593)		5.19%	0.79[0.25,2.54]
Subtotal (95% CI)					**79.99%**	**0.91[0.73,1.15]**
Heterogeneity: Tau^2=0; Chi^2=5.47, df=8(P=0.71); I^2=0%						
Test for overall effect: Z=0.76(P=0.45)						
Total (95% CI)					**100%**	**0.7[0.51,0.95]**
Heterogeneity: Tau^2=0.13; Chi^2=20.41, df=11(P=0.04); I^2=46.09%						
Test for overall effect: Z=2.28(P=0.02)						
Test for subgroup differences: Chi^2=14.74, df=1 (P=0), I^2=93.22%						



Analysis 1.18. Comparison 1 Pre-emptive versus deferred correction, Outcome 18 Unassisted patency: HR of access thrombosis by prevention aim.

Study or subgroup	Pre-emptive correction N	Deferred correction N	log[Risk Ratio] (SE)	Risk Ratio IV, Random, 95% CI	Weight	Risk Ratio IV, Random, 95% CI
1.18.1 Primary prophylaxis						
Mayer 1993	35	35	-0.6 (0.373)		9.35%	0.53[0.26,1.11]
Moist 2003	59	53	-0 (0.418)		8.23%	0.96[0.42,2.19]
Ram 2003 DU	35	17	0.2 (0.269)		12.5%	1.24[0.73,2.1]
Ram 2003 QA	32	17	-0.2 (0.293)		11.7%	0.84[0.47,1.48]
Robbin 2006	65	61	0.1 (0.24)		13.48%	1.13[0.71,1.81]
Smits 2001 QA	28	25	0.2 (0.758)		3.54%	1.23[0.28,5.44]
Smits 2001 QA/SP	41	31	-0.2 (0.593)		5.19%	0.79[0.25,2.54]
Subtotal (95% CI)					**63.98%**	**0.97[0.75,1.25]**
Heterogeneity: Tau^2=0; Chi^2=4.29, df=6(P=0.64); I^2=0%						
Test for overall effect: Z=0.26(P=0.8)						
1.18.2 Secondary prophylaxis						
Dember 2004	32	32	-0.4 (0.553)		5.74%	0.65[0.22,1.92]
Lumsden 1997	32	32	-0.4 (0.34)		10.26%	0.7[0.36,1.37]
Tessitore 2003	32	30	-1.2 (0.472)		7.11%	0.3[0.12,0.77]
Tessitore 2004a	43	36	-1.2 (0.43)		7.97%	0.3[0.13,0.69]
Tessitore 2014	28	30	-1.5 (0.614)		4.93%	0.22[0.07,0.74]
Subtotal (95% CI)					**36.02%**	**0.42[0.27,0.67]**
Heterogeneity: Tau^2=0.06; Chi^2=5.04, df=4(P=0.28); I^2=20.62%						
Test for overall effect: Z=3.71(P=0)						



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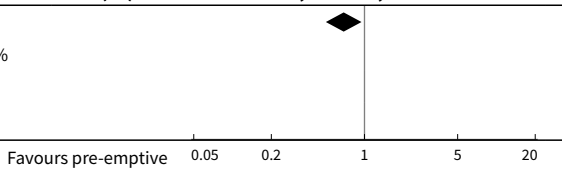
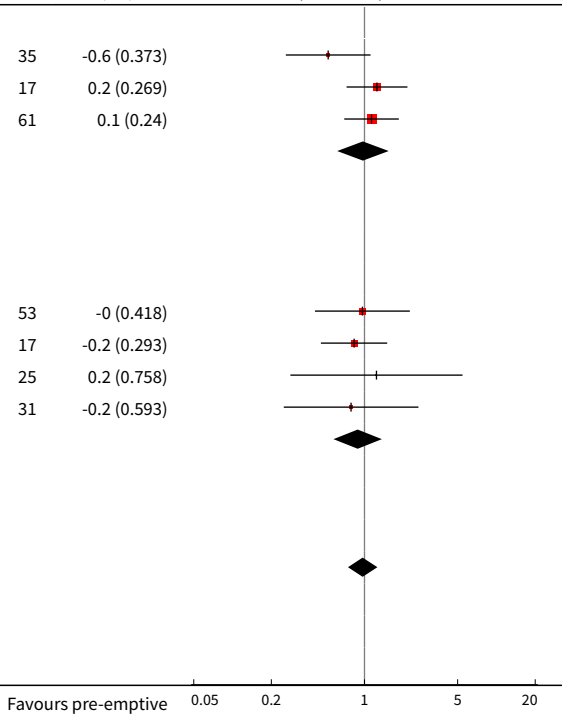
Study or subgroup	Pre-emptive correction N	Deferred correction N	log[Risk Ratio] (SE)	Risk Ratio IV, Random, 95% CI	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)					**100%**	**0.7[0.51,0.95]**
Heterogeneity: Tau²=0.13; Chi²=20.41, df=11(P=0.04); I²=46.09%						
Test for overall effect: Z=2.28(P=0.02)						
Test for subgroup differences: Chi²=9.71, df=1 (P=0), I²=89.7%						



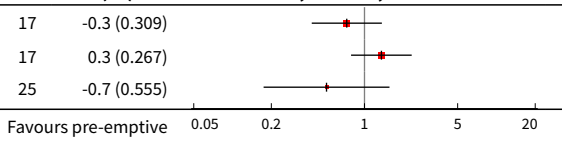
Analysis 1.19. Comparison 1 Pre-emptive versus deferred correction, Outcome 19 Unassisted patency: HR of access thrombosis by surveillance method (primary prophylaxis).

Study or subgroup	Pre-emptive correction N	Deferred correction N	log[Risk Ratio] (SE)	Risk Ratio IV, Random, 95% CI	Weight	Risk Ratio IV, Random, 95% CI
1.19.1 Doppler ultrasound (access flow and structure)						
Mayer 1993	35	35	-0.6 (0.373)		11.93%	0.53[0.26,1.11]
Ram 2003 DU	35	17	0.2 (0.269)		22.97%	1.24[0.73,2.1]
Robbin 2006	65	61	0.1 (0.24)		28.7%	1.13[0.71,1.81]
Subtotal (95% CI)					**63.6%**	**0.97[0.62,1.52]**
Heterogeneity: Tau²=0.07; Chi²=3.74, df=2(P=0.15); I²=46.52%						
Test for overall effect: Z=0.12(P=0.9)						
1.19.2 Blood flow (access flow only)						
Moist 2003	59	53	-0 (0.418)		9.48%	0.96[0.42,2.19]
Ram 2003 QA	32	17	-0.2 (0.293)		19.32%	0.84[0.47,1.48]
Smits 2001 QA	28	25	0.2 (0.758)		2.88%	1.23[0.28,5.44]
Smits 2001 QA/SP	41	31	-0.2 (0.593)		4.71%	0.79[0.25,2.54]
Subtotal (95% CI)					**36.4%**	**0.89[0.58,1.35]**
Heterogeneity: Tau²=0; Chi²=0.3, df=3(P=0.96); I²=0%						
Test for overall effect: Z=0.55(P=0.58)						
Total (95% CI)					**100%**	**0.97[0.75,1.25]**
Heterogeneity: Tau²=0; Chi²=4.29, df=6(P=0.64); I²=0%						
Test for overall effect: Z=0.26(P=0.8)						
Test for subgroup differences: Chi²=0.08, df=1 (P=0.77), I²=0%						



Analysis 1.20. Comparison 1 Pre-emptive versus deferred correction, Outcome 20 Unassisted patency: IRR of access thrombosis overall.

Study or subgroup	Pre-emptive correction N	Deferred correction N	log[Risk Ratio] (SE)	Risk Ratio IV, Random, 95% CI	Weight	Risk Ratio IV, Random, 95% CI
Ram 2003 DU	35	17	-0.3 (0.309)		19.65%	0.74[0.4,1.35]
Ram 2003 QA	32	17	0.3 (0.267)		21.05%	1.34[0.79,2.26]
Smits 2001 QA	28	25	-0.7 (0.555)		12.38%	0.52[0.18,1.54]



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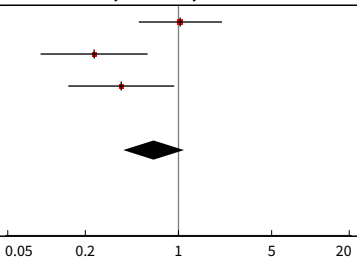
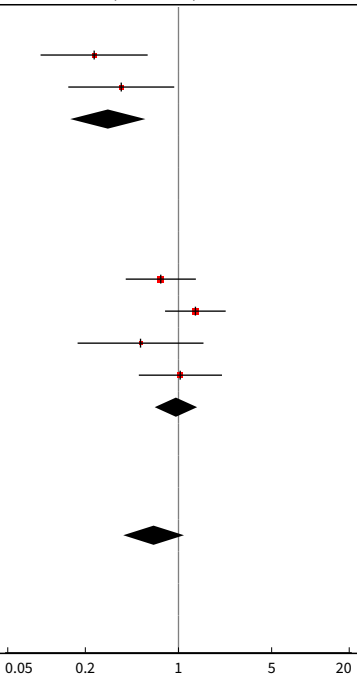
Study or subgroup	Pre-emptive correction N	Deferred correction N	log[Risk Ratio] (SE)	Risk Ratio IV, Random, 95% CI	Weight	Risk Ratio IV, Random, 95% CI
Smits 2001 QA/SP	41	31	0 (0.366)		17.74%	1.03[0.5,2.12]
Tessitore 2003	32	30	-1.5 (0.472)		14.52%	0.23[0.09,0.59]
Tessitore 2014	28	30	-1 (0.467)		14.66%	0.37[0.15,0.93]
Total (95% CI)					**100%**	**0.65[0.39,1.1]**
Heterogeneity: Tau²=0.27; Chi²=14.3, df=5(P=0.01); I²=65.04%						
Test for overall effect: Z=1.62(P=0.11)						



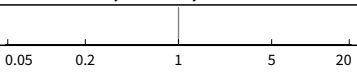
Analysis 1.21. Comparison 1 Pre-emptive versus deferred correction, Outcome 21 Unassisted patency: IRR of access thrombosis by access type.

Study or subgroup	Pre-emptive correction N	Deferred correction N	log[Risk Ratio] (SE)	Risk Ratio IV, Random, 95% CI	Weight	Risk Ratio IV, Random, 95% CI
1.21.1 Fistula						
Tessitore 2003	32	30	-1.5 (0.472)		14.52%	0.23[0.09,0.59]
Tessitore 2014	28	30	-1 (0.467)		14.66%	0.37[0.15,0.93]
Subtotal (95% CI)					**29.18%**	**0.29[0.15,0.57]**
Heterogeneity: Tau²=0; Chi²=0.5, df=1(P=0.48); I²=0%						
Test for overall effect: Z=3.68(P=0)						
1.21.2 Graft						
Ram 2003 DU	35	17	-0.3 (0.309)		19.65%	0.74[0.4,1.35]
Ram 2003 QA	32	17	0.3 (0.267)		21.05%	1.34[0.79,2.26]
Smits 2001 QA	28	25	-0.7 (0.555)		12.38%	0.52[0.18,1.54]
Smits 2001 QA/SP	41	31	0 (0.366)		17.74%	1.03[0.5,2.12]
Subtotal (95% CI)					**70.82%**	**0.96[0.66,1.38]**
Heterogeneity: Tau²=0.02; Chi²=3.55, df=3(P=0.31); I²=15.59%						
Test for overall effect: Z=0.24(P=0.81)						
Total (95% CI)					**100%**	**0.65[0.39,1.1]**
Heterogeneity: Tau²=0.27; Chi²=14.3, df=5(P=0.01); I²=65.04%						
Test for overall effect: Z=1.62(P=0.11)						
Test for subgroup differences: Chi²=9.53, df=1 (P=0), I²=89.5%						



Analysis 1.22. Comparison 1 Pre-emptive versus deferred correction, Outcome 22 Unassisted patency: IRR of access thrombosis by prevention aim.

Study or subgroup	Pre-emptive correction N	Deferred correction N	log[Risk Ratio] (SE)	Risk Ratio IV, Random, 95% CI	Weight	Risk Ratio IV, Random, 95% CI
1.22.1 Primary prophylaxis						



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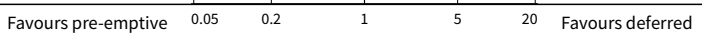
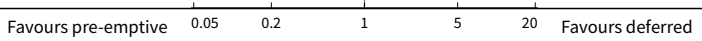
Study or subgroup	Pre-emptive correction N	Deferred correction N	log[Risk Ratio] (SE)	Risk Ratio IV, Random, 95% CI	Weight	Risk Ratio IV, Random, 95% CI
Ram 2003 DU	35	17	-0.3 (0.309)		19.65%	0.74[0.4,1.35]
Ram 2003 QA	32	17	0.3 (0.267)		21.05%	1.34[0.79,2.26]
Smits 2001 QA	28	25	-0.7 (0.555)		12.38%	0.52[0.18,1.54]
Smits 2001 QA/SP	41	31	0 (0.366)		17.74%	1.03[0.5,2.12]
Subtotal (95% CI)					**70.82%**	**0.96[0.66,1.38]**
Heterogeneity: Tau^2=0.02; Chi^2=3.55, df=3(P=0.31); I^2=15.59%						
Test for overall effect: Z=0.24(P=0.81)						
1.22.2 Secondary prophylaxis						
Tessitore 2003	32	30	-1.5 (0.472)		14.52%	0.23[0.09,0.59]
Tessitore 2014	28	30	-1 (0.467)		14.66%	0.37[0.15,0.93]
Subtotal (95% CI)					**29.18%**	**0.29[0.15,0.57]**
Heterogeneity: Tau^2=0; Chi^2=0.5, df=1(P=0.48); I^2=0%						
Test for overall effect: Z=3.68(P=0)						
Total (95% CI)					**100%**	**0.65[0.39,1.1]**
Heterogeneity: Tau^2=0.27; Chi^2=14.3, df=5(P=0.01); I^2=65.04%						
Test for overall effect: Z=1.62(P=0.11)						
Test for subgroup differences: Chi^2=9.53, df=1 (P=0), I^2=89.5%						



Analysis 1.23. Comparison 1 Pre-emptive versus deferred correction, Outcome 23 Unassisted patency: IRR of access thrombosis by surveillance method (primary prophylaxis).

Study or subgroup	Pre-emptive correction N	Deferred correction N	log[Risk Ratio] (SE)	Risk Ratio IV, Random, 95% CI	Weight	Risk Ratio IV, Random, 95% CI
1.23.1 Doppler ultrasound (access flow and structure)						
Ram 2003 DU	35	17	-0.3 (0.309)		29.71%	0.74[0.4,1.35]
Subtotal (95% CI)					**29.71%**	**0.74[0.4,1.35]**
Heterogeneity: Not applicable						
Test for overall effect: Z=0.99(P=0.32)						
1.23.2 Blood flow (access flow only)						
Ram 2003 QA	32	17	0.3 (0.267)		37.35%	1.34[0.79,2.26]
Smits 2001 QA	28	25	-0.7 (0.555)		10.6%	0.52[0.18,1.54]
Smits 2001 QA/SP	41	31	0 (0.366)		22.35%	1.03[0.5,2.12]
Subtotal (95% CI)					**70.29%**	**1.06[0.68,1.66]**
Heterogeneity: Tau^2=0.03; Chi^2=2.4, df=2(P=0.3); I^2=16.62%						
Test for overall effect: Z=0.27(P=0.79)						
Total (95% CI)					**100%**	**0.96[0.66,1.38]**
Heterogeneity: Tau^2=0.02; Chi^2=3.55, df=3(P=0.31); I^2=15.59%						
Test for overall effect: Z=0.24(P=0.81)						
Test for subgroup differences: Chi^2=0.92, df=1 (P=0.34), I^2=0%						



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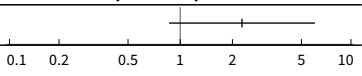
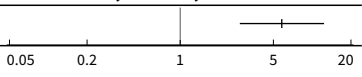
Analysis 1.24. Comparison 1 Pre-emptive versus deferred correction, Outcome 24 Detection of access stenosis (HR).

Study or subgroup	Pre-emptive correction N	Deferred correction N	log[Risk Ratio] (SE)	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Polkinghorne 2006	69	68	0.8 (0.494)		2.27[0.86,5.98]



Analysis 1.25. Comparison 1 Pre-emptive versus deferred correction, Outcome 25 Elective stenosis repair.

Study or subgroup	Pre-emptive correction N	Deferred correction N	log[Risk Ratio] (SE)	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Tessitore 2014	28	30	1.8 (0.371)		5.78[2.8,11.96]

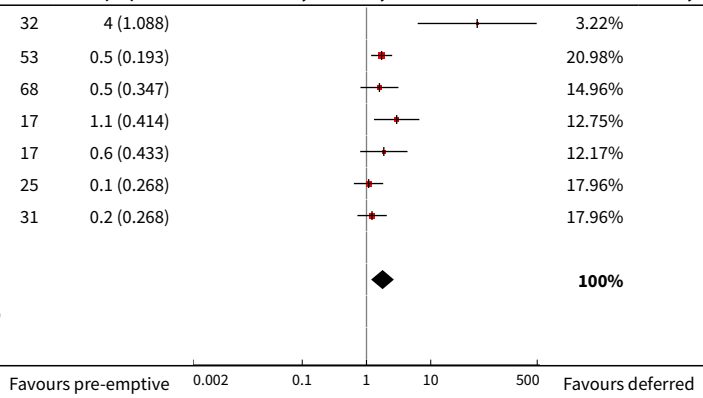


Analysis 1.26. Comparison 1 Pre-emptive versus deferred correction, Outcome 26 Health resource use: angiograms (IRR).

Study or subgroup	Pre-emptive correction N	Deferred correction N	log[Risk Ratio] (SE)	Risk Ratio IV, Random, 95% CI	Weight	Risk Ratio IV, Random, 95% CI
Dember 2004	32	32	4 (1.088)		3.22%	52.87[6.27,445.78]
Moist 2003	59	53	0.5 (0.193)		20.98%	1.72[1.18,2.51]
Polkinghorne 2006	69	68	0.5 (0.347)		14.96%	1.59[0.81,3.14]
Ram 2003 DU	35	17	1.1 (0.414)		12.75%	2.95[1.31,6.65]
Ram 2003 QA	32	17	0.6 (0.433)		12.17%	1.86[0.8,4.35]
Smits 2001 QA	28	25	0.1 (0.268)		17.96%	1.08[0.64,1.82]
Smits 2001 QA/SP	41	31	0.2 (0.268)		17.96%	1.22[0.72,2.07]
Total (95% CI)					**100%**	**1.78[1.18,2.67]**

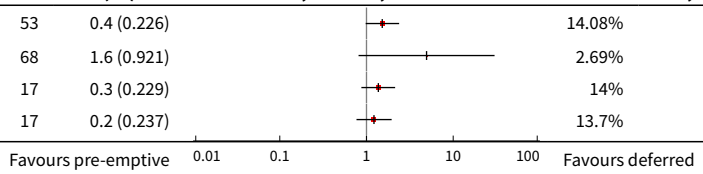
Heterogeneity: Tau^2=0.17; Chi^2=15.96, df=6(P=0.01); I^2=62.41%

Test for overall effect: Z=2.75(P=0.01)



Analysis 1.27. Comparison 1 Pre-emptive versus deferred correction, Outcome 27 Health resource use: angioplasties (IRR).

Study or subgroup	Pre-emptive correction N	Deferred correction N	log[Risk Ratio] (SE)	Risk Ratio IV, Random, 95% CI	Weight	Risk Ratio IV, Random, 95% CI
Moist 2003	59	53	0.4 (0.226)		14.08%	1.52[0.98,2.38]
Polkinghorne 2006	69	68	1.6 (0.921)		2.69%	4.93[0.81,29.98]
Ram 2003 DU	35	17	0.3 (0.229)		14%	1.37[0.87,2.14]
Ram 2003 QA	32	17	0.2 (0.237)		13.7%	1.22[0.77,1.95]



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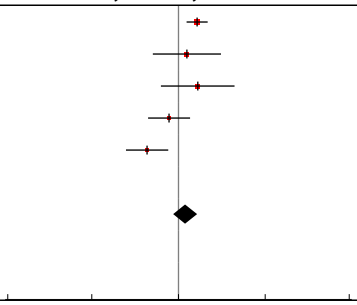
Study or subgroup	Pre-emptive correction N	Deferred correction N	log[Risk Ratio] (SE)	Risk Ratio IV, Random, 95% CI	Weight	Risk Ratio IV, Random, 95% CI
Robbin 2006	65	61	0.5 (0.143)		16.83%	1.64[1.24,2.17]
Sands 1999	62	41	0.2 (0.461)		7.57%	1.25[0.51,3.09]
Scaffaro 2009	53	58	0.5 (0.499)		6.86%	1.67[0.63,4.43]
Smits 2001 QA	28	25	-0.3 (0.283)		12.19%	0.78[0.45,1.36]
Smits 2001 QA/SP	41	31	-0.8 (0.287)		12.09%	0.43[0.25,0.76]
Total (95% CI)					**100%**	**1.19[0.87,1.64]**

Heterogeneity: Tau^2=0.14; Chi^2=23.45, df=8(P=0); I^2=65.88%

Test for overall effect: Z=1.09(P=0.28)

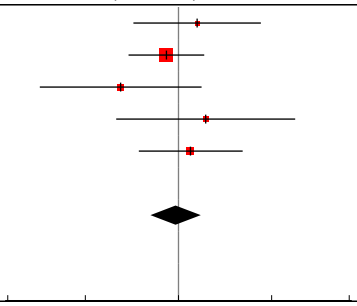


Analysis 1.28. Comparison 1 Pre-emptive versus deferred correction, Outcome 28 Health resource use: surgical interventions (IRR).

Study or subgroup	Pre-emptive correction N	Deferred correction N	log[Risk Ratio] (SE)	Risk Ratio IV, Random, 95% CI	Weight	Risk Ratio IV, Random, 95% CI
Polkinghorne 2006	69	68	0.3 (0.561)		15.5%	1.38[0.46,4.15]
Robbin 2006	65	61	-0.2 (0.334)		43.67%	0.81[0.42,1.56]
Smits 2001 QA	28	25	-1 (0.713)		9.62%	0.37[0.09,1.49]
Smits 2001 QA/SP	41	31	0.5 (0.789)		7.85%	1.6[0.34,7.51]
Tessitore 2003	30	30	0.2 (0.457)		23.36%	1.23[0.5,3.03]
Total (95% CI)					**100%**	**0.95[0.62,1.47]**

Heterogeneity: Tau^2=0; Chi^2=3.2, df=4(P=0.53); I^2=0%

Test for overall effect: Z=0.23(P=0.82)

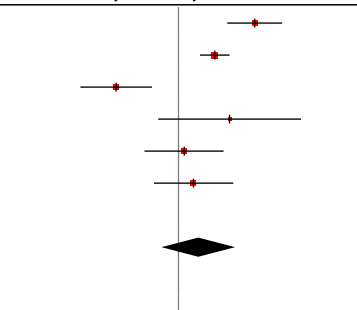


Analysis 1.29. Comparison 1 Pre-emptive versus deferred correction, Outcome 29 Health resource use: radiological or surgical interventions (IRR).

Study or subgroup	Pre-emptive correction N	Deferred correction N	log[Risk Ratio] (SE)	Risk Ratio IV, Random, 95% CI	Weight	Risk Ratio IV, Random, 95% CI
Dember 2004	32	32	1 (0.186)		18.37%	2.75[1.91,3.96]
Malik 2005	97	92	0.5 (0.1)		19.8%	1.62[1.33,1.97]
Mayer 1993	35	35	-0.8 (0.242)		17.16%	0.44[0.27,0.7]
Polkinghorne 2006	69	68	0.7 (0.484)		11.58%	1.97[0.76,5.09]
Smits 2001 QA	28	25	0.1 (0.268)		16.55%	1.08[0.64,1.82]
Smits 2001 QA/SP	41	31	0.2 (0.268)		16.55%	1.22[0.72,2.07]
Total (95% CI)					**100%**	**1.3[0.8,2.12]**

Heterogeneity: Tau^2=0.3; Chi^2=39.5, df=5(P<0.0001); I^2=87.34%

Test for overall effect: Z=1.05(P=0.29)



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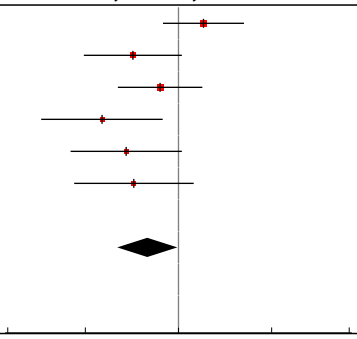
Analysis 1.30. Comparison 1 Pre-emptive versus deferred correction, Outcome 30 Health resource use: use of catheters (IRR).

Study or subgroup	Pre-emptive correction N	Deferred correction N	log[Risk Ratio] (SE)	Risk Ratio IV, Random, 95% CI	Weight	Risk Ratio IV, Random, 95% CI
Dember 2004	32	32	0.4 (0.357)		20.13%	1.54[0.77,3.1]
Ram 2003 DU	35	17	-0.8 (0.432)		17.21%	0.45[0.2,1.06]
Ram 2003 QA	32	17	-0.3 (0.371)		19.55%	0.73[0.35,1.51]
Scaffaro 2009	53	58	-1.3 (0.535)		13.82%	0.27[0.09,0.76]
Tessitore 2003	30	30	-0.9 (0.491)		15.19%	0.41[0.15,1.06]
Tessitore 2014	28	30	-0.8 (0.526)		14.09%	0.46[0.16,1.3]
Total (95% CI)					**100%**	**0.58[0.35,0.98]**

Heterogeneity: Tau^2=0.22; Chi^2=10.72, df=5(P=0.06); I^2=53.38%

Test for overall effect: Z=2.04(P=0.04)

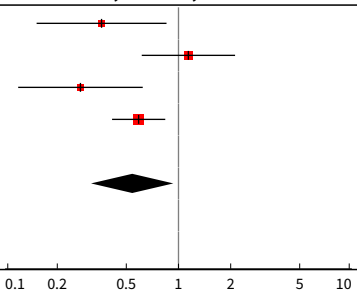


Analysis 1.31. Comparison 1 Pre-emptive versus deferred correction, Outcome 31 Health resource use: hospitalizations (IRR).

Study or subgroup	Pre-emptive correction N	Deferred correction N	log[Risk Ratio] (SE)	Risk Ratio IV, Random, 95% CI	Weight	Risk Ratio IV, Random, 95% CI
Ram 2003 DU	35	17	-1 (0.44)		19.78%	0.36[0.15,0.85]
Ram 2003 QA	32	17	0.1 (0.316)		26.02%	1.14[0.61,2.12]
Tessitore 2003	30	30	-1.3 (0.422)		20.6%	0.27[0.12,0.62]
Tessitore 2014	28	30	-0.5 (0.18)		33.6%	0.59[0.41,0.84]
Total (95% CI)					**100%**	**0.54[0.31,0.93]**

Heterogeneity: Tau^2=0.2; Chi^2=8.98, df=3(P=0.03); I^2=66.58%

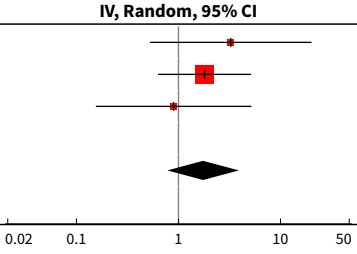
Test for overall effect: Z=2.2(P=0.03)



Analysis 1.32. Comparison 1 Pre-emptive versus deferred correction, Outcome 32 Patient outcomes: infections (IRR).

Study or subgroup	Pre-emptive correction N	Deferred correction N	log[Risk Ratio] (SE)	Risk Ratio IV, Random, 95% CI	Weight	Risk Ratio IV, Random, 95% CI
Dember 2004	32	32	1.2 (0.93)		19.64%	3.25[0.53,20.11]
Robbin 2006	65	61	0.6 (0.536)		59.14%	1.8[0.63,5.14]
Tessitore 2014	28	30	-0.1 (0.894)		21.22%	0.9[0.16,5.18]
Total (95% CI)					**100%**	**1.74[0.78,3.91]**

Heterogeneity: Tau^2=0; Chi^2=1, df=2(P=0.61); I^2=0%



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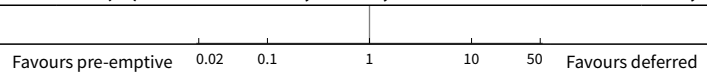
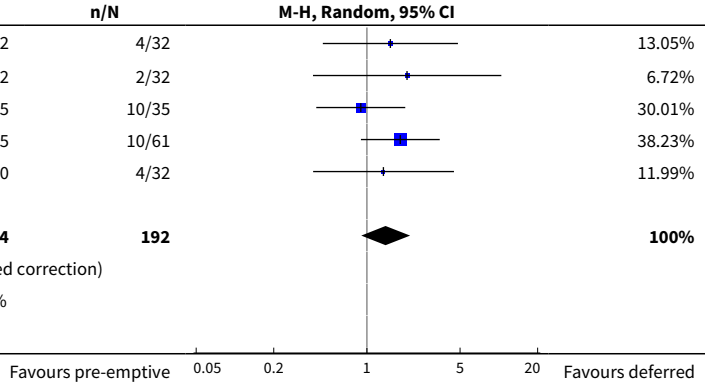
Study or subgroup	Pre-emptive correction N	Deferred correction N	log[Risk Ratio] (SE)	Risk Ratio IV, Random, 95% CI	Weight	Risk Ratio IV, Random, 95% CI
Test for overall effect: Z=1.35(P=0.18)						



Analysis 1.33. Comparison 1 Pre-emptive versus deferred correction, Outcome 33 Patient outcomes: mortality (RR).

Study or subgroup	Pre-emptive correction n/N	Deferred correction n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Dember 2004	6/32	4/32		13.05%	1.5[0.47,4.82]
Lumsden 1997	4/32	2/32		6.72%	2[0.39,10.16]
Mayer 1993	9/35	10/35		30.01%	0.9[0.42,1.94]
Robbin 2006	19/65	10/61		38.23%	1.78[0.9,3.52]
Tessitore 2003	5/30	4/32		11.99%	1.33[0.39,4.5]
Total (95% CI)	**194**	**192**		**100%**	**1.38[0.91,2.11]**
Total events: 43 (Pre-emptive correction), 30 (Deferred correction)					
Heterogeneity: Tau^2=0; Chi^2=1.96, df=4(P=0.74); I^2=0%					
Test for overall effect: Z=1.5(P=0.13)					



Comparison 2. Two surveillance methods versus one

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Access thrombosis (RR)	4	309	Risk Ratio (M-H, Random, 95% CI)	0.48 [0.28, 0.82]
1.1 All studies	4	103	Risk Ratio (M-H, Random, 95% CI)	0.48 [0.19, 1.22]
1.2 Ultrasound and static venous pressure	2	56	Risk Ratio (M-H, Random, 95% CI)	0.54 [0.17, 1.70]
1.3 Ultrasound and access flow	2	47	Risk Ratio (M-H, Random, 95% CI)	0.39 [0.08, 1.89]
1.4 Grafts	2	35	Risk Ratio (M-H, Random, 95% CI)	0.59 [0.19, 1.85]
1.5 Fistulas	2	68	Risk Ratio (M-H, Random, 95% CI)	0.31 [0.06, 1.58]
2 Health resource use: angioplasties (RR)	1	103	Risk Ratio (M-H, Random, 95% CI)	0.83 [0.36, 1.92]

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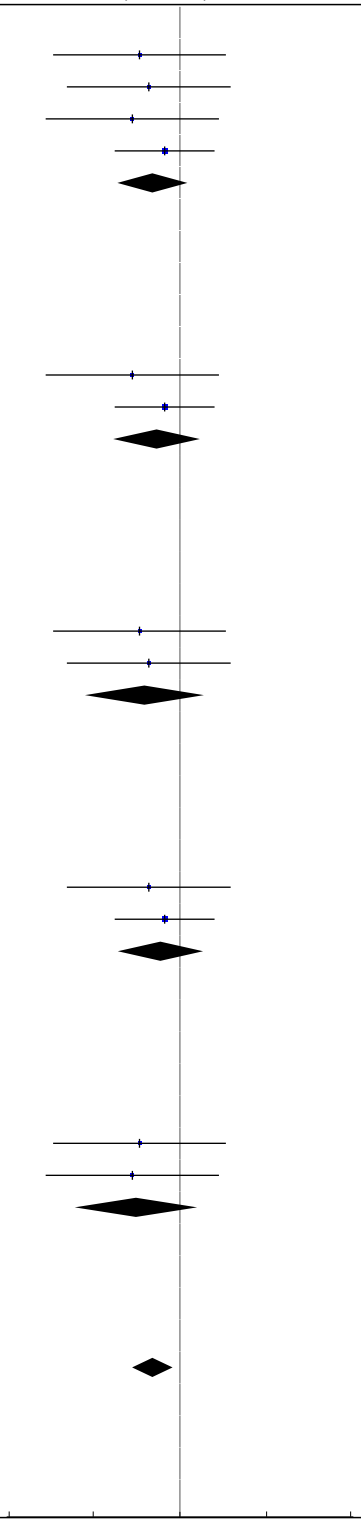
Analysis 2.1. Comparison 2 Two surveillance methods versus one, Outcome 1 Access thrombosis (RR).

Study or subgroup	Two methods n/N	One method n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
2.1.1 All studies					
Sands 1999 QA/DU (F)	1/19	2/13		5.47%	0.34[0.03,3.39]
Sands 1999 QA/DU (G)	1/8	2/7		6.08%	0.44[0.05,3.85]
Sands 1999 SP/DU (F)	1/23	2/13		5.43%	0.28[0.03,2.82]
Sands 1999 SP/DU (G)	3/12	3/8		16.35%	0.67[0.18,2.51]
Subtotal (95% CI)	**62**	**41**		**33.33%**	**0.48[0.19,1.22]**
Total events: 6 (Two methods), 9 (One method)					
Heterogeneity: Tau^2=0; Chi^2=0.54, df=3(P=0.91); I^2=0%					
Test for overall effect: Z=1.54(P=0.12)					
2.1.2 Ultrasound and static venous pressure					
Sands 1999 SP/DU (F)	1/23	2/13		5.43%	0.28[0.03,2.82]
Sands 1999 SP/DU (G)	3/12	3/8		16.35%	0.67[0.18,2.51]
Subtotal (95% CI)	**35**	**21**		**21.78%**	**0.54[0.17,1.7]**
Total events: 4 (Two methods), 5 (One method)					
Heterogeneity: Tau^2=0; Chi^2=0.41, df=1(P=0.52); I^2=0%					
Test for overall effect: Z=1.06(P=0.29)					
2.1.3 Ultrasound and access flow					
Sands 1999 QA/DU (F)	1/19	2/13		5.47%	0.34[0.03,3.39]
Sands 1999 QA/DU (G)	1/8	2/7		6.08%	0.44[0.05,3.85]
Subtotal (95% CI)	**27**	**20**		**11.55%**	**0.39[0.08,1.89]**
Total events: 2 (Two methods), 4 (One method)					
Heterogeneity: Tau^2=0; Chi^2=0.02, df=1(P=0.88); I^2=0%					
Test for overall effect: Z=1.17(P=0.24)					
2.1.4 Grafts					
Sands 1999 QA/DU (G)	1/8	2/7		6.08%	0.44[0.05,3.85]
Sands 1999 SP/DU (G)	3/12	3/8		16.35%	0.67[0.18,2.51]
Subtotal (95% CI)	**20**	**15**		**22.43%**	**0.59[0.19,1.85]**
Total events: 4 (Two methods), 5 (One method)					
Heterogeneity: Tau^2=0; Chi^2=0.11, df=1(P=0.74); I^2=0%					
Test for overall effect: Z=0.9(P=0.37)					
2.1.5 Fistulas					
Sands 1999 QA/DU (F)	1/19	2/13		5.47%	0.34[0.03,3.39]
Sands 1999 SP/DU (F)	1/23	2/13		5.43%	0.28[0.03,2.82]
Subtotal (95% CI)	**42**	**26**		**10.9%**	**0.31[0.06,1.58]**
Total events: 2 (Two methods), 4 (One method)					
Heterogeneity: Tau^2=0; Chi^2=0.01, df=1(P=0.91); I^2=0%					
Test for overall effect: Z=1.41(P=0.16)					
Total (95% CI)	**186**	**123**		**100%**	**0.48[0.28,0.82]**
Total events: 18 (Two methods), 27 (One method)					
Heterogeneity: Tau^2=0; Chi^2=1.63, df=11(P=1); I^2=0%					
Test for overall effect: Z=2.67(P=0.01)					
Test for subgroup differences: Chi^2=0.52, df=1 (P=0.97), I^2=0%					



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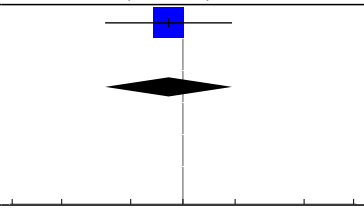
Analysis 2.2. Comparison 2 Two surveillance methods versus one, Outcome 2 Health resource use: angioplasties (RR).

Study or subgroup	Two methods n/N	One method n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Sands 1999	10/62	8/41		100%	0.83[0.36,1.92]
Total (95% CI)	**62**	**41**		**100%**	**0.83[0.36,1.92]**
Total events: 10 (Two methods), 8 (One method)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.44(P=0.66)					

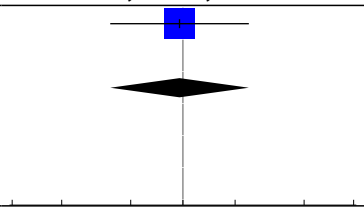


Comparison 3. Blood flow versus monitoring and venous pressure in grafts

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Assisted patency: RR of graft loss	1	49	Risk Ratio (M-H, Random, 95% CI)	0.96 [0.38, 2.40]
2 Unassisted patency: RR of graft thrombosis	2	102	Risk Ratio (M-H, Random, 95% CI)	0.95 [0.64, 1.43]

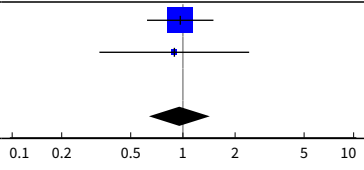
Analysis 3.1. Comparison 3 Blood flow versus monitoring and venous pressure in grafts, Outcome 1 Assisted patency: RR of graft loss.

Study or subgroup	Pre-emptive correction n/N	Deferred correction n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Ram 2003 QA	9/32	5/17		100%	0.96[0.38,2.4]
Total (95% CI)	**32**	**17**		**100%**	**0.96[0.38,2.4]**
Total events: 9 (Pre-emptive correction), 5 (Deferred correction)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.1(P=0.92)					



Analysis 3.2. Comparison 3 Blood flow versus monitoring and venous pressure in grafts, Outcome 2 Unassisted patency: RR of graft thrombosis.

Study or subgroup	Pre-emptive correction n/N	Deferred correction n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Ram 2003 QA	20/32	11/17		83.52%	0.97[0.62,1.5]
Smits 2001 QA	6/28	6/25		16.48%	0.89[0.33,2.41]
Total (95% CI)	**60**	**42**		**100%**	**0.95[0.64,1.43]**



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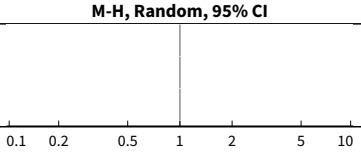
Study or subgroup	Pre-emptive correction n/N	Deferred correction n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Total events: 26 (Pre-emptive correction), 17 (Deferred correction)					
Heterogeneity: Tau²=0; Chi²=0.02, df=1(P=0.88); I²=0%					
Test for overall effect: Z=0.23(P=0.82)					

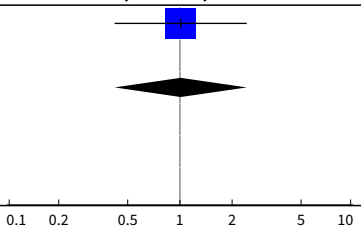


Comparison 4. Blood flow and venous pressure vs monitoring and venous pressure in grafts

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Assisted patency: RR of graft loss	1	112	Risk Ratio (M-H, Random, 95% CI)	1.01 [0.42, 2.43]
2 Unassisted patency: RR of graft thrombosis	2	184	Risk Ratio (M-H, Random, 95% CI)	1.23 [0.85, 1.76]

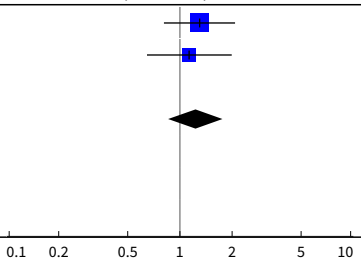
Analysis 4.1. Comparison 4 Blood flow and venous pressure vs monitoring and venous pressure in grafts, Outcome 1 Assisted patency: RR of graft loss.

Study or subgroup	Pre-emptive correction n/N	Deferred correction n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Moist 2003	9/59	8/53		100%	1.01[0.42,2.43]
Total (95% CI)	**59**	**53**		**100%**	**1.01[0.42,2.43]**
Total events: 9 (Pre-emptive correction), 8 (Deferred correction)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.02(P=0.98)					



Analysis 4.2. Comparison 4 Blood flow and venous pressure vs monitoring and venous pressure in grafts, Outcome 2 Unassisted patency: RR of graft thrombosis.

Study or subgroup	Pre-emptive correction n/N	Deferred correction n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Moist 2003	26/59	18/53		58.56%	1.3[0.81,2.08]
Smits 2001 QA/SP	18/41	12/31		41.44%	1.13[0.65,1.99]
Total (95% CI)	**100**	**84**		**100%**	**1.23[0.85,1.76]**
Total events: 44 (Pre-emptive correction), 30 (Deferred correction)					
Heterogeneity: Tau²=0; Chi²=0.13, df=1(P=0.72); I²=0%					
Test for overall effect: Z=1.11(P=0.27)					



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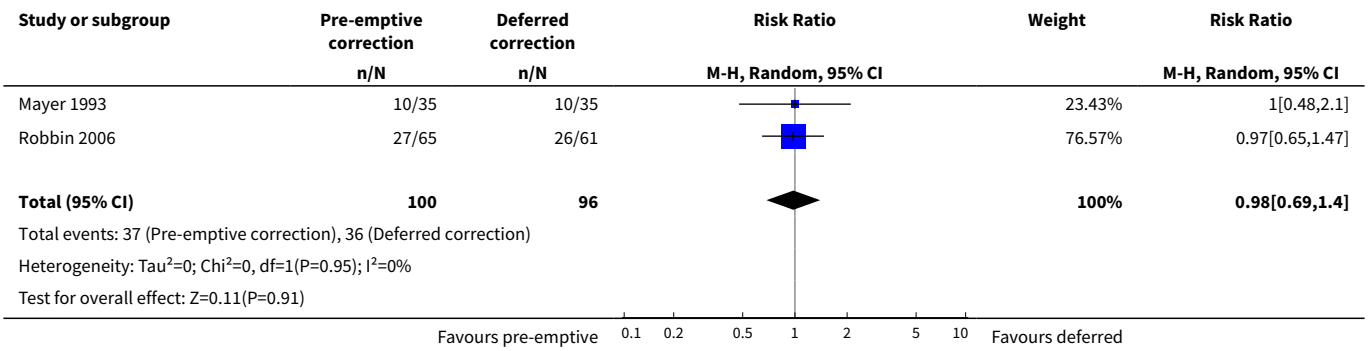
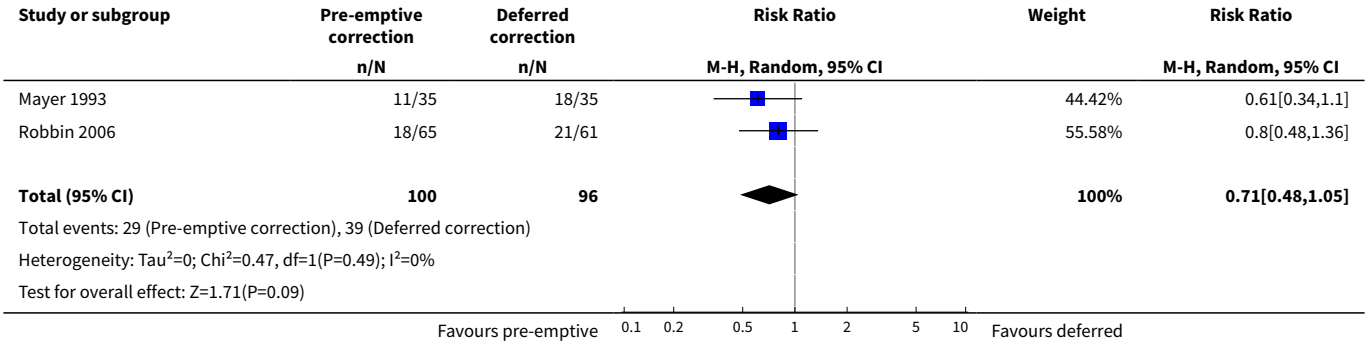
Comparison 5. Doppler versus monitoring alone in grafts

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Assisted patency: RR of graft loss	2	196	Risk Ratio (M-H, Random, 95% CI)	0.98 [0.69, 1.40]
2 Unassisted patency: RR of graft thrombosis	2	196	Risk Ratio (M-H, Random, 95% CI)	0.71 [0.48, 1.05]

Analysis 5.1. Comparison 5 Doppler versus monitoring alone in grafts, Outcome 1 Assisted patency: RR of graft loss.



Analysis 5.2. Comparison 5 Doppler versus monitoring alone in grafts, Outcome 2 Unassisted patency: RR of graft thrombosis.



Comparison 6. Doppler versus monitoring and venous pressure in grafts

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Assisted patency: RR of graft loss	2	241	Risk Ratio (M-H, Random, 95% CI)	0.62 [0.36, 1.08]

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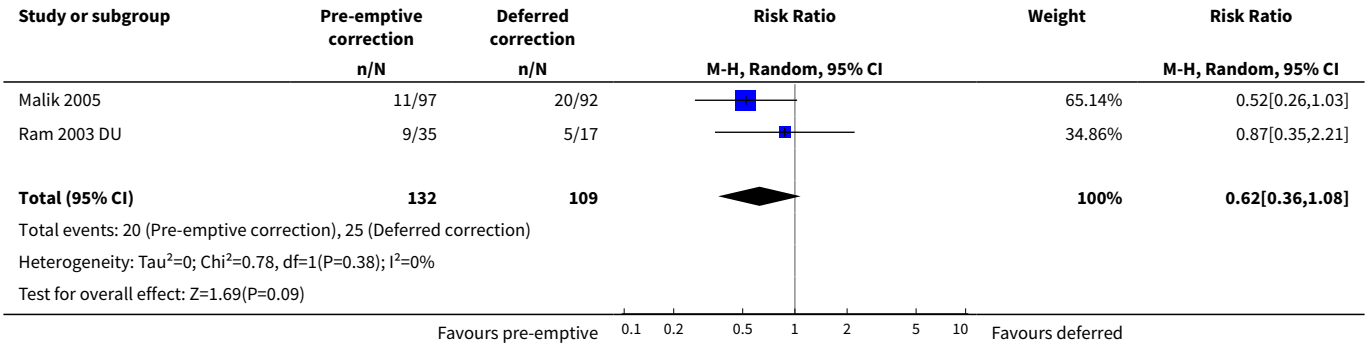
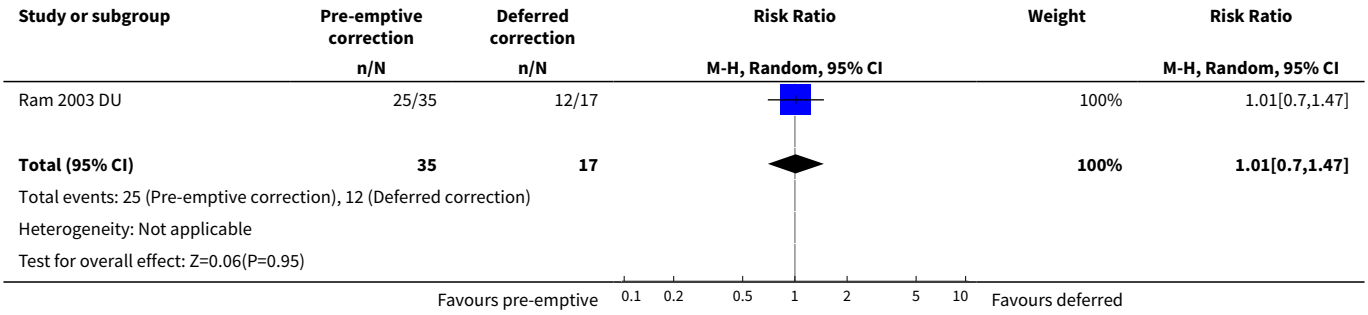
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2 Unassisted patency: RR of graft thrombosis	1	52	Risk Ratio (M-H, Random, 95% CI)	1.01 [0.70, 1.47]

Analysis 6.1. Comparison 6 Doppler versus monitoring and venous pressure in grafts, Outcome 1 Assisted patency: RR of graft loss.



Analysis 6.2. Comparison 6 Doppler versus monitoring and venous pressure in grafts, Outcome 2 Unassisted patency: RR of graft thrombosis.



Comparison 7. Unassisted patency: RR of access thrombosis by use of venous pressure

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Fistulas	4	209	Risk Ratio (M-H, Random, 95% CI)	0.38 [0.23, 0.63]
1.1 No VP measurement	3	173	Risk Ratio (M-H, Random, 95% CI)	0.38 [0.23, 0.64]
1.2 VP included	1	36	Risk Ratio (M-H, Random, 95% CI)	0.28 [0.03, 2.82]
2 Grafts	10	633	Risk Ratio (M-H, Random, 95% CI)	0.97 [0.81, 1.15]

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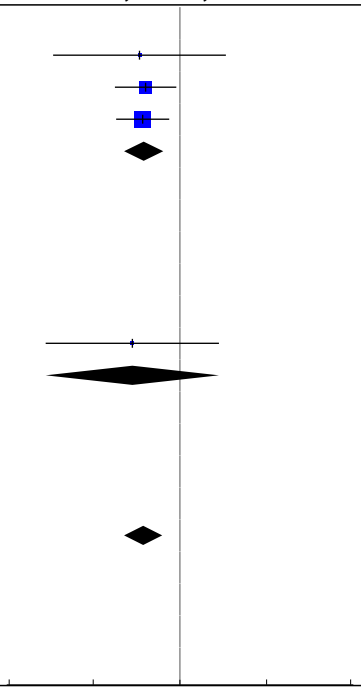
Outcome or sub-group title	No. of studies	No. of partici-pants	Statistical method	Effect size
2.1 No VP measure-ment	4	275	Risk Ratio (M-H, Random, 95% CI)	0.83 [0.61, 1.11]
2.2 VP included	6	358	Risk Ratio (M-H, Random, 95% CI)	1.05 [0.85, 1.31]

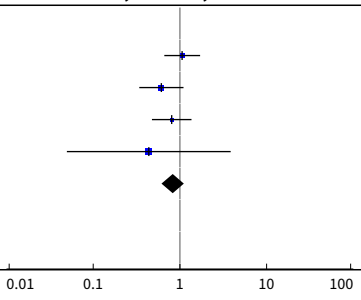
Analysis 7.1. Comparison 7 Unassisted patency: RR of access thrombosis by use of venous pressure, Outcome 1 Fistulas.

Study or subgroup	Two methods n/N	One method n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
7.1.1 No VP measurement					
Sands 1999 QA/DU (F)	1/19	2/13		4.88%	0.34[0.03,3.39]
Tessitore 2003	6/32	14/30		38.58%	0.4[0.18,0.91]
Tessitore 2004a	8/43	18/36		51.68%	0.37[0.18,0.75]
Subtotal (95% CI)	**94**	**79**		**95.15%**	**0.38[0.23,0.64]**
Total events: 15 (Two methods), 34 (One method)					
Heterogeneity: Tau^2=0; Chi^2=0.03, df=2(P=0.99); I^2=0%					
Test for overall effect: Z=3.63(P=0)					
7.1.2 VP included					
Sands 1999 SP/DU (F)	1/23	2/13		4.85%	0.28[0.03,2.82]
Subtotal (95% CI)	**23**	**13**		**4.85%**	**0.28[0.03,2.82]**
Total events: 1 (Two methods), 2 (One method)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.08(P=0.28)					
Total (95% CI)	**117**	**92**		**100%**	**0.38[0.23,0.63]**
Total events: 16 (Two methods), 36 (One method)					
Heterogeneity: Tau^2=0; Chi^2=0.09, df=3(P=0.99); I^2=0%					
Test for overall effect: Z=3.77(P=0)					
Test for subgroup differences: Chi^2=0.06, df=1 (P=0.8), I^2=0%					



Analysis 7.2. Comparison 7 Unassisted patency: RR of access thrombosis by use of venous pressure, Outcome 2 Grafts.

Study or subgroup	Two methods n/N	One method n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
7.2.1 No VP measurement					
Lumsden 1997	17/32	16/32		13.5%	1.06[0.66,1.71]
Mayer 1993	11/35	18/35		8.89%	0.61[0.34,1.1]
Robbin 2006	18/65	21/61		11.12%	0.8[0.48,1.36]
Sands 1999 QA/DU (G)	1/8	2/7		0.64%	0.44[0.05,3.85]
Subtotal (95% CI)	**140**	**135**		**34.16%**	**0.83[0.61,1.11]**
Total events: 47 (Two methods), 57 (One method)					
Heterogeneity: Tau^2=0; Chi^2=2.47, df=3(P=0.48); I^2=0%					



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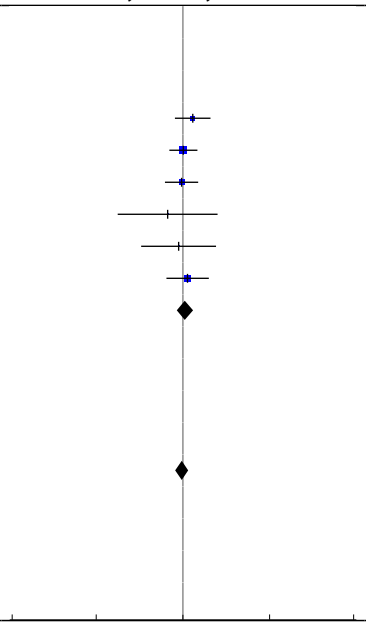
Study or subgroup	Two methods n/N	One method n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Test for overall effect: Z=1.25(P=0.21)					
7.2.2 VP included					
Moist 2003	26/59	18/53		13.65%	1.3[0.81,2.08]
Ram 2003 DU	25/35	12/17		22.1%	1.01[0.7,1.47]
Ram 2003 QA	20/32	11/17		15.62%	0.97[0.62,1.5]
Sands 1999 SP/DU (G)	3/12	3/8		1.73%	0.67[0.18,2.51]
Smits 2001 QA	6/28	6/25		3.08%	0.89[0.33,2.41]
Smits 2001 QA/SP	18/41	12/31		9.66%	1.13[0.65,1.99]
Subtotal (95% CI)	**207**	**151**		**65.84%**	**1.05[0.85,1.31]**
Total events: 98 (Two methods), 62 (One method)					
Heterogeneity: Tau^2=0; Chi^2=1.59, df=5(P=0.9); I^2=0%					
Test for overall effect: Z=0.48(P=0.63)					
Total (95% CI)	**347**	**286**		**100%**	**0.97[0.81,1.15]**
Total events: 145 (Two methods), 119 (One method)					
Heterogeneity: Tau^2=0; Chi^2=5.71, df=9(P=0.77); I^2=0%					
Test for overall effect: Z=0.35(P=0.73)					
Test for subgroup differences: Chi^2=1.67, df=1 (P=0.2), I^2=40.16%					



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ADDITIONAL TABLES

Table 1. Format of reported outcomes

Study ID	Loss	Thrombosis	Angiog-raphy	PTA	SX	PTA or SX	Need for CVC	Infec-tion	Hospital admis-sion	Stenosis detec-tion	Death
Dember 2004	RR; HR	RR; HR	RR; IRR	--	--	IRR	IRR	IRR; RR; HR	--	--	RR
Lumsden 1997	--	RR†; HR‡	--	--		--	--		--	--	RR
Malik 2005	HR; RR	--	--	--	--	IRR^	--	--	--	--	--
Mayer 1993	RR	RR; HR‡	--	--	--	RR; IRR	--	--	--	--	RR
Moist 2003	RR; HR‡	RR; HR‡	RR; IRR	RR; IRR		RR	--	--	--	--	--
Polkinghorne 2006	--	RR	RR	RR	RR	--	--	--	--	HR	--
Ram 2003	RR†;HR‡	IRR; RR; HR‡	RR; IRR	RR; IRR		--	RR; IRR	--	RR; IRR	--	--
Robbin 2006	HR; RR	HR; RR	--	RR; IRR	RR; IRR	--	--	RR	--	--	RR
Sands 1999	--	RR	--	RR	--	--	--	--	--	--	--
Scaffaro 2009	RR	RR	--	RR	--	--	RR; HR	--	--	--	--
Smits 2001	--	RR; IRR; HR‡	RR; IRR	RR; IRR	RR; IRR	IRR	--	--	--	--	--
Tessitore 2003	IRR; RR	IRR; RR; HR	--	--	RR; IRR	--	IRR; RR; HR	--	IRR; RR; HR	--	RR
Tessitore 2004a	RR; HR	RR; HR	--	--	--	--	--	--	--	--	--
Tessitore 2014	RR; HR; IRR	RR; HR; IRR	--	--	--	--	IRR	IRR	IRR	IRR	--

PTA indicates angioplasty; SX - surgical intervention; CVC - central venous catheter; RR - relative risk; HR - hazard ratio (time to event data); IRR - incidence rate ratio (from rate data).
^Rates and follow-up reported
†Events from survival plots
‡Log-HR (and their standard errors) were not reported by the authors but were estimated from survival plots (or tables) using the methods proposed by Parmar 1998.

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APPENDICES

Appendix 1. Electronic search strategies

Database	Search terms
CENTRAL	1. (fistula* or AVF* or graft or grafts or shunt or shunts):ti,ab,kw 2. "blood vessel prosthesis":kw 3. ("vascular access" or "venous access"):ti,ab,kw 4. ("dialysis access" or "hemodialysis access" or "haemodialysis access"):ti,ab,kw 5. (#1 OR #2 OR #3 OR #4) 6. "renal replacement therapy":ti,ab,kw 7. dialysis:ti,ab,kw 8. (haemodialysis or hemodialysis):ti,ab,kw 9. (hemofiltration or haemofiltration):ti,ab,kw 10.(hemodiafiltration or haemodiafiltration):ti,ab,kw 11.(predialysis or "pre-dialysis"):ti,ab,kw 12.("kidney failure" or "kidney disease" or "renal failure" or "renal disease"):ti,ab,kw 13.(CKD or CKF or CRD or CRF or ESKD or ESKF or ESRD or ESRF):ti,ab,kw 14.(#6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13) 15.constriction:kw 16.(stenosis or stenoses or stenosed or stenotic or restenos*):ti,ab,kw 17.(thrombosis or thrombosed or thrombotic):ti,ab,kw 18.(occlud* or occlusion or obstruct*):ti,ab,kw 19.(#15 OR #16 OR #17 OR #18) 20.angioplasty:ti,ab,kw 21."balloon dilation":ti,ab,kw 22.PTA:ti,ab,kw 23.((endovascular next treatment*) or (endovascular next procedure*) or (endoluminal next repair*) or (endovascular next surgery)):ti,ab,kw 24.(stent or stents or stenting):ti,ab,kw 25.((vein next patch*) or transposition* or interposition* or revision* or proximalization):ti,ab,kw 26.(("pre-emptive" or preemptive) next (strateg* or correction*)) 27.(#20 OR #21 OR #22 OR #23 OR #24 OR #25) 28.(#5 AND #14 AND #19 AND #26)
MEDLINE	1. Arteriovenous Shunt, Surgical/ 2. Arteriovenous Fistula/ 3. Blood Vessel Prosthesis/ 4. (fistula$ or AVF$ or graft or grafts or shunt or shunts).tw. 5. (vascular access or venous access).tw. 6. (dialysis access or hemodialysis access or haemodialysis access).tw. 7. or/1-6 8. Renal Dialysis/ 9. exp Hemofiltration/ 10.dialysis.tw. 11.(predialysis or pre-dialysis).tw. 12.(hemodialysis or haemodialysis).tw. 13.(hemofiltration or haemofiltration).tw. 14.(hemodiafiltration or haemodiafiltration).tw. 15.Renal Insufficiency/

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(Continued)

	16.exp Renal Insufficiency, Chronic/ 17.(kidney failure or kidney disease or renal failure or renal disease).tw. 18.(CKD or CKF or CRD or CRF or ESKD or ESKF or ESRD or ESRF).tw. 19.or/8-18 20.Constriction, Pathologic/ 21.Constriction/ 22.Graft Occlusion Vascular/ 23.Thrombosis/ 24.(stenosis or stenoses or stenosed or stenotic or restenos*).tw. 25.(thrombosis or thrombosed or thrombotic).tw. 26.(occlud* or occlusion or obstruct*).tw. 27.or/20-26 28.Angioplasty/ 29.Angioplasty, Balloon/ 30.exp Angioplasty, Laser/ 31.Balloon Dilation/ 32.angioplasty.tw. 33.balloon dilation.tw. 34.PTA.tw. 35.Endovascular Procedures/ 36.exp Stents/ 37.Implants, Artificial/ 38.(endovascular treatment* or endovascular procedure* or endoluminal repair or endovascular surgery*).tw. 39.(stent or stents or stenting).tw. 40.(vein patch* or transposition* or interposition* or revision* or proximalization).tw. 41.((pre-emptive or preemptive) adj (strateg* or correction*)).tw. 42.or/28-41 43.and/7,19,27,42
EMBASE	1. Arteriovenous Shunt/ 2. Arteriovenous Fistula/ 3. Kidney Arteriovenous Fistula/ 4. Blood Vessel Prosthesis/ 5. Blood Vessel Graft/ 6. Blood Vessel Shunt/ 7. (fistula* or AVF* or graft or grafts or shunt or shunts).tw. 8. (vascular access or venous access).tw. 9. (dialysis access or hemodialysis access or haemodialysis access).tw. 10.or/1-9 11.exp Renal Replacement Therapy/ 12.dialysis.tw. 13.(predialysis or pre-dialysis).tw. 14.(haemodialysis or hemodialysis).tw. 15.(hemofiltration or haemofiltration).tw. 16.(hemodiafiltration or haemodiafiltration).tw. 17.Kidney Failure/ 18.Chronic Kidney Disease/ 19.Chronic Kidney Failure/ 20.(kidney disease or kidney failure or renal disease or renal failure).tw. 21.(CRF or CRD or CKF or CKD or ESRF or ESRD or ESKF or ESKD).tw. 22.or/11-21

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(Continued)

23."Stenosis, Occlusion and Obstruction"/
24.Stenosis/
25.Occlusion/
26.Blood vessel Occlusion/
27.Artery Occlusion/
28.Vein Occlusion/
29.Graft Occlusion/
30.Thrombosis/
31.Artery Thrombosis/
32.Shunt Thrombosis/
33.Vein Thrombosis/
34.(stenosis or stenoses or stenosed or stenotic or restenos*).tw.
35.(thrombosis or thrombosed or thrombotic).tw.
36.(occlud* or occlusion or obstruct*).tw.
37.or/23-36
38.Angioplasty/
39.Percutaneous Transluminal Angioplasty/
40.Laser Angioplasty/
41.angioplasty.tw.
42.balloon dilation.tw.
43.PTA.tw.
44.Endovascular Surgery/
45.Stent/
46.Bare Metal Stent/
47.Drug Eluting Stent/
48.(endovascular treatment* or endovascular procedure* or endoluminal repair* or endovascular surgery).tw.
49.(stent or stents or stenting).tw.
50.(vein patch* or transposition* or interposition* or revision* or proximalization).tw.
51.((pre-emptive or preemptive) adj (strateg* or correction*)).tw.
52.or/38-51
53.and/10,22,37,52

Appendix 2. Risk of bias assessment tool

Potential source of bias	Assessment criteria
Random sequence generation Selection bias (biased allocation to interventions) due to inadequate generation of a randomised sequence	*Low risk of bias:* Random number table; computer random number generator; coin tossing; shuffling cards or envelopes; throwing dice; drawing of lots; minimization (minimization may be implemented without a random element, and this is considered to be equivalent to being random).
	High risk of bias: Sequence generated by odd or even date of birth; date (or day) of admission; sequence generated by hospital or clinic record number; allocation by judgement of the clinician; by preference of the participant; based on the results of a laboratory test or a series of tests; by availability of the intervention.
	Unclear: Insufficient information about the sequence generation process to permit judgement.
Allocation concealment	*Low risk of bias:* Randomisation method described that would not allow investigator/participant to know or influence intervention group before eligible participant entered in the study (e.g. central

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(Continued)

Selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment	allocation, including telephone, web-based, and pharmacy-controlled, randomisation; sequentially numbered drug containers of identical appearance; sequentially numbered, opaque, sealed envelopes).
	High risk of bias: Using an open random allocation schedule (e.g. a list of random numbers); assignment envelopes were used without appropriate safeguards (e.g. if envelopes were unsealed or non-opaque or not sequentially numbered); alternation or rotation; date of birth; case record number; any other explicitly unconcealed procedure.
	Unclear: Randomisation stated but no information on method used is available.
Blinding of participants and personnel Performance bias due to knowledge of the allocated interventions by participants and personnel during the study	*Low risk of bias*: No blinding or incomplete blinding, but the review authors judge that the outcome is not likely to be influenced by lack of blinding; blinding of participants and key study personnel ensured, and unlikely that the blinding could have been broken.
	High risk of bias: No blinding or incomplete blinding, and the outcome is likely to be influenced by lack of blinding; blinding of key study participants and personnel attempted, but likely that the blinding could have been broken, and the outcome is likely to be influenced by lack of blinding.
	Unclear: Insufficient information to permit judgement
Blinding of outcome assessment Detection bias due to knowledge of the allocated interventions by outcome assessors.	*Low risk of bias:* No blinding of outcome assessment, but the review authors judge that the outcome measurement is not likely to be influenced by lack of blinding; blinding of outcome assessment ensured, and unlikely that the blinding could have been broken.
	High risk of bias: No blinding of outcome assessment, and the outcome measurement is likely to be influenced by lack of blinding; blinding of outcome assessment, but likely that the blinding could have been broken, and the outcome measurement is likely to be influenced by lack of blinding.
	Unclear: Insufficient information to permit judgement
Incomplete outcome data Attrition bias due to amount, nature or handling of incomplete outcome data.	*Low risk of bias:* No missing outcome data; reasons for missing outcome data unlikely to be related to true outcome (for survival data, censoring unlikely to be introducing bias); missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups; for dichotomous outcome data, the proportion of missing outcomes compared with observed event risk not enough to have a clinically relevant impact on the intervention effect estimate; for continuous outcome data, plausible effect size (difference in means or standardized difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size; missing data have been imputed using appropriate methods.
	High risk of bias: Reason for missing outcome data likely to be related to true outcome, with either imbalance in numbers or reasons for missing data across intervention groups; for dichotomous outcome data, the proportion of missing outcomes compared with observed event risk enough to induce clinically relevant bias in intervention effect estimate; for continuous outcome data, plausible effect size (difference in means or standardized difference in means) among missing outcomes enough to induce clinically relevant bias in observed effect size; 'as-treated' analysis done with substantial departure of the intervention received from that assigned at randomisation; potentially inappropriate application of simple imputation.
	Unclear: Insufficient information to permit judgement
Selective reporting Reporting bias due to selective outcome reporting	*Low risk of bias:* The study protocol is available and all of the study's pre-specified (primary and secondary) outcomes that are of interest in the review have been reported in the pre-specified way; the study protocol is not available but it is clear that the published reports include all expected outcomes, including those that were pre-specified (convincing text of this nature may be uncommon).
	High risk of bias: Not all of the study's pre-specified primary outcomes have been reported; one or more primary outcomes is reported using measurements, analysis methods or subsets of the data (e.g. subscales) that were not pre-specified; one or more reported primary outcomes were not pre-

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(Continued)

	specified (unless clear justification for their reporting is provided, such as an unexpected adverse effect); one or more outcomes of interest in the review are reported incompletely so that they cannot be entered in a meta-analysis; the study report fails to include results for a key outcome that would be expected to have been reported for such a study.
	Unclear: Insufficient information to permit judgement
Other bias Bias due to problems not covered elsewhere in the table	*Low risk of bias:* The study appears to be free of other sources of bias.
	High risk of bias: Had a potential source of bias related to the specific study design used; stopped early due to some data-dependent process (including a formal-stopping rule); had extreme baseline imbalance; has been claimed to have been fraudulent; had some other problem.
	Unclear: Insufficient information to assess whether an important risk of bias exists; insufficient rationale or evidence that an identified problem will introduce bias.

WHAT'S NEW

Date	Event	Description
13 November 2017	Amended	Correction of control group number of events for Mayer 1993 from 10/35 to 13/35 for analyses 1.1, 1.2.2, 1.3.1 and 1.5

CONTRIBUTIONS OF AUTHORS

1. Draft the protocol: PR
2. Study selection: PR, MJ
3. Extract data from studies: PR, DK
4. Enter data into RevMan: PR
5. Carry out the analysis: PR
6. Interpret the analysis: PR, DK, MJ, SP, JM, MO, RQ, GS
7. Draft the final review: PR
8. Disagreement resolution: GS
9. Update the review: PR

DECLARATIONS OF INTEREST

- Pietro Ravani: none known
- Matthew T James: none known
- Jennifer M MacRae: none known
- Suetonia C Palmer: none known
- Robert R Quinn: is co-inventor of the Dialysis Measurement Analysis and Reporting (DMAR) System
- Matthew J Oliver: is co-inventor and co-owner of the Dialysis Measurement Analysis and Reporting (DMAR) which measures practice related to dialysis and vascular access.
- Giovanni FM Strippoli: none known.

This project received no specific funding. The authors had full responsibility for data collection, data interpretation, and writing of the report. The corresponding author had full access to all of the data and had the final responsibility to submit the manuscript for publication.

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Internal sources

- University of Calgary, Canada.

  Division of Nephrology

External sources

- No sources of support supplied

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We removed 'non-maturing access' from the inclusion criteria because this is unsuitable for haemodialysis. We found nine studies in which participants had a functioning access without known lesions and four studies that enrolled participants with a documented access stenosis. We conducted stratified analyses based on the study aim (primary and secondary prophylaxis).

Results for the sensitivity analyses were confirmed using the Restricted Maximum Likelihood (REML) method (Cornell 2014).

NOTES

This review has been co-published with the *American Journal of Kidney Diseases* (Ravani 2016).

INDEX TERMS

Medical Subject Headings (MeSH)

*Arteriovenous Shunt, Surgical [adverse effects]; *Renal Dialysis; Constriction, Pathologic [diagnosis] [prevention & control]; Kidney Failure, Chronic [*therapy]; Primary Prevention; Randomized Controlled Trials as Topic; Secondary Prevention; Thrombosis [diagnosis]

MeSH check words

Adult; Humans

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