SUPPLEMENTAL MATERIAL

Global burden of atherosclerotic cardiovascular disease in people living with the human immunodeficiency virus: a systematic review and meta-analysis

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Supplement text

Supplement text 1: Search criteria

Medline – Ovid MEDLINE 1946 to August week 4 2016 - 1164 hits
Embase – OVID EMBASE 1974 to 30TH August 2016; 4572 hits
Global health - OVID GLOBAL HEALTH 1910 TO WEEK 35 2016; 1352 hits
WoS (exc medline) – 1946 to Week 21 2015 – 30TH August 2016; 622 hits

Medline

1. human immunodeficiency virus infection.mp. or exp Human immunodeficiency virus infection/
2. hiv.ab. or hiv-1.ti. or hiv-1.ab. or hiv-2.ti. or hiv-2.ab. or human immunodeficiency virus.ti. or human immunodeficiency virus.ab. or human immuno-deficiency virus.ti. or human immuno-deficiency virus.ab. or human immunedeficiency virus.ti. or human immunedeficiency virus.ab. or human immune-deficiency virus.ti. or human immune-deficiency virus.ab. or acquired immune-deficiency syndrome.ti. or acquired immune-deficiency syndrome.ab. or acquired immunedeficiency syndrome.ti. or acquired immunedeficiency syndrome.ab. or acquired immunodeficiency syndrome.ti. or acquired immunodeficiency syndrome.ab. or acquired immuno-deficiency syndrome.ti. or acquired immuno-deficiency syndrome.ab.
3. hiv.ti.
4. 1 or 2 or 3
5. exp Myocardial Infarction/ or Cardiovascular Disease/
6. exp Coronary Thrombosis/
7. acute coronary.mp.
8. exp Angina, Unstable/
9. Myocardial infarct$.mp.
10. heart infarct:.mp.
11. acs.mp.
12. ami.mp.
13. (coronary adj3 syndrome$).mp.
14. acute angina.mp.
15. (unstable adj3 angina).mp.
16. unstable coronary.mp.
17. 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16
18. cerebrovascular disorders/ or basal ganglia cerebrovascular disease/ or brain ischemia/ or exp brain infarction/ or hypoxia-ischemia, brain/ or carotid artery diseases/ or carotid artery thrombosis/ or carotid artery, internal, dissection/ or intracranial arterial diseases/ or cerebral arterial diseases/ or infarction, anterior cerebral artery/ or infarction, middle cerebral artery/ or infarction, posterior cerebral artery/ or exp "intracranial embolism and thrombosis"/ or exp stroke/ or vertebral artery dissection/
19. (isch?emi$ adj5 (stroke$ or apoplex$ or cerebral vasc$ or cerebrovasc$ or cva)).tw.
20. ((brain or cerebr$ or cerebell$ or vertebrobasil$ or hemispher$ or intracran$ or intracerebral or infratentorial or supratentorial or middle cerebr$ or mca$ or anterior circulation or basilar artery or vertebral artery) adj5 (isch?emi$ or infarct$ or thrombo$ or emboli$ or occlus$ or hypoxi$)).tw.

21. 18 or 19 or 20
22. 17 or 21
23. 4 and 22
24. exp Antiretroviral Therapy, Highly Active/ or antiretroviral therapy.mp. or exp Anti-Retroviral Agents/
25. zidovudine.mp. or exp Zidovudine/
26. lamivudine.mp. or exp Lamivudine/
27. indinavir.mp. or exp Indinavir/
28. stavudine.mp. or exp Stavudine/
29. saquinivir.mp. or exp Saquinivir/
30. nelfinavir.mp. or exp Nelfinavir/
31. didanosine.mp. or exp Didanosine/
32. zalcitabine.mp. or exp Zalcitabine/
33. ritonavir.mp. or exp Ritonavir/
34. anti-HIV agents.mp. or exp Anti-HIV Agents/
35. 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34
36. 4 or 35
37. 22 and 36
38. limit 37 to humans

Embase

1. human immunodeficiency virus infection.mp. or exp Human immunodeficiency virus infection/
2. hiv.ab. or hiv-1.ti. or hiv-1.ab. or hiv-2.ti. or hiv-2.ab. or human immunodeficiency virus.ti. or human immunodeficiency virus.ab. or human immuno-deficiency virus.ti. or human immuno-deficiency virus.ab. or human immunedeficiency virus.ti. or human immunedeficiency virus.ab. or human immune-deficiency virus.ti. or human immune-deficiency virus.ab. or acquired immune-deficiency syndrome.ti. or acquired immune-deficiency syndrome.ab. or acquired immunedeficiency syndrome.ti. or acquired immunedeficiency syndrome.ab. or acquired immunodeficiency syndrome.ti. or acquired immunodeficiency syndrome.ab. or acquired immuno-deficiency syndrome.ti. or acquired immuno-deficiency syndrome.ab.
3. hiv.ti.
4. exp zalcitabine/ or exp didanosine/ or exp nevirapine/ or exp highly active antiretroviral therapy/ or exp antiretrovirus agent/ or exp efavirenz/ or exp stavudine/ or exp zidovudine/ or antiretroviral therapy.mp. or exp lamivudine/
5. exp indinavir plus ritonavir/ or exp indinavir/
6. exp acquired immune deficiency syndrome/
7. exp ritonavir/ or exp nelfinavir/ or exp amprenavir/ or exp saquinavir/
8. exp zalcitabine derivative/ or exp zalcitabine/
9. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8
10. exp Heart Infarction/ or Cardiovascular Disease/
11. coronary thrombosis.mp. or exp Coronary Artery Thrombosis/
12. acute coronary.mp.
13. exp Unstable Angina Pectoris/
14. Myocardial infarct$.mp.
15. heart infarct:.mp.
16. acs.mp.
17. ami.mp.
18. (coronary adj3 syndrome$).mp.
19. acute angina.mp.
20. (unstable adj3 angina).mp.
21. brain infarction/ or brain stem infarction/ or cerebellum infarction/ or exp brain ischemia/ or carotid artery disease/ or exp carotid artery obstruction/ or cerebral artery disease/ or exp cerebrovascular accident/ or exp occlusive cerebrovascular disease/ or stroke patient/
22. (isch?emi$ adj5 (stroke$ or apoplex$ or cerebral vasc$ or cerebrovasc$ or cva)).tw.
23. ((brain or cerebr$ or cerebell$ or vertebrobasil$ or hemispher$ or intracran$ or intracerebral or infratentorial or supratentorial or middle cerebr$ or mca$ or anterior circulation or basilar artery or vertebral artery) adj5 (isch?emi$ or infarct$ or thrombo$ or emboli$ or occlus$ or hypoxi$)).tw.
24. 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23
25. 9 and 24
26. limit 25 to human

Global health

1. brain infarction.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]
2. brain stem infarction.mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]
3. stroke.mp. or exp stroke/
4. exp infarction/
5. carotid artery disease.mp.
6. carotid artery obstruction.mp.
7. cerebrovascular accident.mp. or cerebrovascular disorders.sh.
8. exp Myocardial Infarction/
9. acute coronary syndrome.mp. or cardiovascular diseases.sh. or myocardial ischaemia.sh.
10. acs.mp.
11. ami.mp.
12. (unstable adj3 angina).mp.
13. acute angina.mp.
14. unstable angina.mp.
15. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14
16. hiv.mp. or exp human immunodeficiency viruses/
17. hiv.ab. or hiv-1.ti. or hiv-1.ab. or hiv-2.ti. or hiv-2.ab. or human immunodeficiency virus.ti. or human immunodeficiency virus.ab. or human immuno-deficiency virus.ti. or human immuno-deficiency virus.ab. or human immunedeficiency virus.ti. or human immunedeficiency virus.ab. or human immune-deficiency virus.ti. or human immune-deficiency virus.ab. or acquired immune-deficiency syndrome.ti. or acquired immune-deficiency syndrome.ab. or acquired immunedeficiency syndrome.ti. or acquired immunedeficiency syndrome.ab. or acquired immunodeficiency syndrome.ti. or acquired immunodeficiency syndrome.ab. or acquired immuno-deficiency syndrome.ti. or acquired immuno-deficiency syndrome.ab.
18. aids.mp. or exp acquired immune deficiency syndrome/
19. (proteinase inhibitors or antiretroviral agents or highly active antiretroviral therapy).sh.
20. zidovudine.mp. or exp Zidovudine/
21. lamivudine.mp. or exp Lamivudine/
22. indinavir.mp. or exp Indinavir/
23. stavudine.mp. or exp Stavudine/
24. saquinivir.mp. or exp Saquinivir/
25. nelfinavir.mp. or exp Nelfinavir/
26. didanosine.mp. or exp Didanosine/
27. zalcitabine.mp. or exp Zalcitabine/
28. ritonavir.mp. or exp Ritonavir/
29. anti-HIV agents.mp.
30. 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29
31. 15 and 30

Web of science

1. TS=(Myocardial Infarction OR Coronary Thrombosis OR acute coronary syndrome OR ACS OR unstable angina OR cerebrovascular disease OR stroke OR brain infarction OR brain ischaemia OR brain ischemia)

2. TS = (human immunodeficiency virus OR acquired immune deficiency syndrome OR zidovudine OR lamivudine OR indinavir OR stavudine OR saquinivir OR nelfinavir OR didanosine OR zalcitabine OR ritonavir OR anti-HIV agents OR antiretroviral agents OR highly active antiretroviral therapy)

3. 1 and 2

Supplementary text 2: Method for calculating country specific estimates for cardiovascular mortality and morbidity attributable to HIV

Step 1

We anticipated heterogeneity between studies when estimating both the crude incidence rates and the risk ratio. We therefore used a random-effects model to account for both within and between study heterogeneity. For estimating the pooled crude rate of cardiovascular disease in HIV populations we extracted the number of events and the person-follow up time from the relevant studies. The count data was then used to calculate the pooled crude rate using a random effects generalised linear mixed model with the rma.glmm function in the metafor package in R. The pooled rates were standardised per 10,000 persons.

Step 2

We obtained estimates, with uncertainty intervals, on the prevalence of HIV at global and regional levels (age group 15 to 49 years) by year from 1990 to 2015. We further obtained previously unpublished national-level estimates of prevalence (age group >15 years) for 2016 from the United Nations programme on HIV/AIDS (UNAIDS). Similarly, we obtained global and national level data for cardiovascular disability adjusted life years from the most recent global burden of series estimates.

Step 3

Assumptions

- We assume that the pooled risk ratios obtained from a range of case-control/cohort studies were applicable across both developed and developing country.
- The prevalence data from UNAIDS at a global and regional level was available for the 15 to 49-year-old age group. At the national level, prevalence data for people living with HIV were available for the entire population (15+ year old age group). At the global and regional level, we applied the prevalence estimates of the 15 to 49-year-

old age group estimates to calculate the population attributable fraction which was applied to the entire adult population.

- We were limited to adjustment of confounders available in the primary studies, and while most studies adjusted for patient demographics and some risk factors there remains the potential for residual confounding.

Step 4

We estimated the population attributable fraction and DALY as follows:-

Population attributable fraction

$$Population\ Attributable\ Fraction = \frac{Prevalence * \ (RR - 1)}{1 + Prevalence * (RR - 1)}$$

DALY due to HIV

$$DALY\ due\ to\ HIV\ = Cardiovascular\ DALYs\ \times\ PAF$$

We obtained uncertainty intervals for the DALY-due to HIV and PAF via simulation. Briefly, we sampled from probability distributions which captured the uncertainty around the estimate for each component (specifically, log normal for the rate ratios, normal for the cardiovascular disability adjusted life years and beta for the prevalence) calculating the PAF and DALY for each of 10,000 samples for each global, regional and national estimate. We report these uncertainty estimates as the 95% confidence interval. The uncertainty ranges can be viewed as approximate Bayesian posterior probability limits with very diffuse priors for the estimates and risk factor rate ratios.

For calculating the HIV attributable cardiovascular DALYs at the regional and global level, the cardiovascular DALY data were available at 5-year intervals, from 1990 to 2015, with intervening years being obtained via linear interpolation. The HIV prevalence data were available annually between 1990 and 2015 to calculate the annual trends in the population

attributable fraction. As such whilst the cardiovascular DALYs are changing in linear fashion between each 5-year bracket the actual annual HIV prevalence rates contribute to the smoothing noticed in Figure 2A.

The schematic in ***Supplementary Figure 1A and 1B*** illustrates the steps involved to derive the cardiovascular DALYs due to HIV for Kenya.

Supplement tables

Supplementary table 1: PRISMA checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	2,4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	2,4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	1
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supplement
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5,6

Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5, table 1
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	6,7,8
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	6
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	7,8
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	7,8
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	6,7,8
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	9, supplement
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Table 1 and 2
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Supplement
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Figure 1 and 2; supplement
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Figure 1 and 2; supplement
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Supplement
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	9, 10, Supplement
DISCUSSION			

Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	12
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	14,15
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	13
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	1

Supplementary table 2: Risk of bias in studies providing relative risk estimates.
Risk of bias assessed by level of adjustment. Low risk – adjustment of age, sex and at least one other covariate; moderate risk – adjustment of at least age or sex; high risk – no adjustment

		Adjusted confounders			
Author	**Year**	**Age**	**Sex**	**Other confounders**	**Risk of bias**
Qureshi et al	1997	Yes	Yes	Hypertension, smoking, diabetes mellitus, cardiac disease, alcohol, and cocaine use	Low
Gardner et al	2003	No	No	None	High
Cole et al	2004	Yes	Yes	Race	Low
Triant et al	2009	Yes	Yes	Race, hypertension, diabetes, dyslipidemia and CRP	Low
Aldaz et al	2011	Yes	Yes	None	Moderate
Durand et al	2011	Yes	Yes	Prior use of antihypertensive drugs, antidiabetic drugs, lipid-lowering drugs, and antiplatelets, or anticoagulation drugs	Low
Chow et al	2012	Yes	Yes	Race, hypertension, diabetes, dyslipidemia, smoking (ever vs. never), structural heart disease (at least one diagnosis of cardiomyopathy, left-sided valvular heart disease, or heart failure), atrial fibrillation/flutter, aspirin use, warfarin use	Low
Helleberg et al	2012	Yes	Yes	None	Moderate
Walker et al	2013	Yes	Yes	Hypertension, smoking status, alcohol consumption, presence of diabetes mellitus, having had a	Low

				previous stroke or transient ischaemic attack, and a high ratio of total cholesterol to HDL cholesterol	
Mateen et al	2013	Yes	Yes	Systolic blood pressure, diabetes, smoking	Low
Tripathi et al	2014	Yes	Yes	Race/ethnicity, year of enrollment in Medicaid, tobacco use variables, preexisting conditions (ie, essential hypertension, diabetes, dyslipidemia, and obesity that developed prior to a CVD event), hepatitis B coinfection, and hepatitis C coinfection	Low
Womack et al	2014	Yes	Yes	Ethnicity, lipids, smoking, blood pressure, diabetes, renal disease, obesity, HCV infection, substance use and abuse (cocaine and alcohol)	Low
Sico et al	2015	Yes	Yes	Race/ethnicity, hypertension (controlled or uncontrolled), diabetes, smoking status, dyslipidemia, atrial fibrillation, body mass index, hepatitis C infection, history of cocaine and alcohol abuse or dependence, HMG-CoA reductase inhibitor use, estimated glomerular filtration rate, and hemoglobin.	Low
Rasmussen et al	2015	Yes	Yes	None	Moderate

Althoff et al	2015	Yes	Yes	Race, hepatitis C infection, body mass index (BMI), alcohol use, smoking, anemia, diabetes, hyperlipidemia, hypertension, antihypertensive medications, and statin use	Low
Klein et al	2015	Yes	Yes	Year, census-based socioeconomic status, race/ethnicity, hypertension, smoking, diabetes, alcohol/drug abuse, overweight/obesity, and lipid-lowering therapy	Low

Supplementary table 3: Countries by UNAIDS region

UNAIDS Region - Western & Central Europe and North America

Country	ISO Code	Country	ISO Code
Andorra	AND	**Italy**	ITA
Austria	AUT	**Latvia**	LVA
Belgium	BEL	**Lithuania**	LTU
Bulgaria	BGR	**Luxembourg**	LUX
Canada	CAN	**Netherlands**	NLD
Croatia	HRV	**Norway**	NOR
Cyprus	CYP	**Poland**	POL
Czech Republic	CZE	**Portugal**	PRT
Denmark	DNK	**Romania**	ROU
Estonia	EST	**Serbia**	SRB
Finland	FIN	**Slovakia**	SVK
France	FRA	**Slovenia**	SVN
Germany	DEU	**Spain**	ESP
Greece	GRC	**Sweden**	SWE
Hungary	HUN	**Switzerland**	CHE
Iceland	ISL	**Turkey**	TUR
Ireland	IRL	**United Kingdom**	GBR
Israel	ISR	**United States**	USA

UNAIDS Region - West and Central Africa

Country	ISO Code	Country	ISO Code
Benin	BEN	**Guinea**	GIN
Burkina Faso	BFA	**Guinea-Bissau**	GNB
Burundi	BDI	**Liberia**	LBR
Cameroon	CMR	**Mali**	MLI
Cape Verde	CPV	**Mauritania**	MRT
Central African Republic	CAF	**Niger**	NER
Chad	TCD	**Nigeria**	NGA
Congo	COG	**Sao Tome and Principe**	STP
Cote d'Ivoire	CIV	**Senegal**	SEN
Democratic Republic of the Congo	COD	**Sierra Leone**	SLE
Equatorial Guinea	GNQ	**The Gambia**	GMB
Gabon	GAB	**Togo**	TGO
Ghana	GHA		

UNAIDS Region - Middle East and North Africa

Country	ISO Code
Algeria	DZA
Bahrain	BHR
Djibouti	DJI
Egypt	EGY
Iran	IRN
Iraq	IRQ
Jordan	JOR
Kuwait	KWT
Lebanon	LBN
Libya	LBY
Morocco	MAR
Oman	OMN
Qatar	QAT
Saudi Arabia	SAU

UNAIDS Region - Latin America and the Caribbean

Country	ISO code	Country	ISO code
Antigua and Barbuda	ATG	**Haiti**	HTI
Argentina	ARG	**Honduras**	HND
Barbados	BRB	**Jamaica**	JAM
Belize	BLZ	**Mexico**	MEX
Bolivia	BOL	**Nicaragua**	NIC
Brazil	BRA	**Panama**	PAN
Chile	CHL	**Paraguay**	PRY
Colombia	COL	**Peru**	PER
Costa Rica	CRI	**Saint Kitts and Nevis**	KNA
Cuba	CUB	**Saint Lucia**	LCA
Dominica	DMA	**Saint Vincent and the Grenadines**	VCT
Dominican Republic	DOM	**Suriname**	SUR
Ecuador	ECU	**The Bahamas**	BMH
El Salvador	SLV	**Trinidad and Tobago**	TTO
Grenada	GRD	**Uruguay**	URY
Guatemala	GTM	**Venezuela**	VEN
Guyana	GUY		

UNAIDS Region - Eastern Europe and Central Asia

Country	ISO code	Country	ISO code
Albania	ALB	Macedonia	MKD
Armenia	ARM	Moldova	MDA
Azerbaijan	AZE	Montenegro	MNE
Belarus	BLR	Russia	RUS
Bosnia and Herzegovina	BIH	Tajikistan	TJK
Georgia	GEO	Turkmenistan	TKM
Kazakhstan	KAZ	Ukraine	UKR
Kyrgyzstan	KGZ	Uzbekistan	UZB

UNAIDS Region - East and Southern Africa

Country	ISO code	Country	ISO code	Country	ISO code
Angola	AGO	**Seychelles**	SYC	**Georgia**	GEO
Botswana	BWA	**South Africa**	ZAF	**Kazakhstan**	KAZ
Comoros	COM	**South Sudan**	SSD	**Kyrgyzstan**	KGZ
Eritrea	ERI	**Swaziland**	SWZ	**Macedonia**	MKD
Ethiopia	ETH	**Tanzania**	TZA	**Moldova**	MDA
Kenya	KEN	**Uganda**	UGA	**Montenegro**	MNE
Lesotho	LSO	**Zambia**	ZMB	**Russia**	RUS
Madagascar	MDG	**Zimbabwe**	ZWE	**Tajikistan**	TJK
Malawi	MWI	**Albania**	ALB	**Turkmenistan**	TKM
Mauritius	MUS	**Armenia**	ARM	**Ukraine**	UKR
Mozambique	MOZ	**Azerbaijan**	AZE	**Uzbekistan**	UZB
Namibia	NAM	**Belarus**	BLR		
Rwanda	RWA	**Bosnia and Herzegovina**	BIH		

UNAIDS Region - Asia and the Pacific

Country	ISO code	Country	ISO code	Country	ISO code
Afghanistan	AFG	**Laos**	LAO	**Philippines**	PHL
Australia	AUS	**Malaysia**	MYS	**Singapore**	SGP
Bangladesh	BGD	**Maldives**	MDV	**Solomon Islands**	SLB
Bhutan	BTN	**Marshall Islands**	MHL	**South Korea**	KOR
Brunei	BRN	**Mongolia**	MNG	**Sri Lanka**	LKA
Cambodia	KHM	**Myanmar**	MMR	**Thailand**	THA
China	CHN	**Nauru**	NRU	**Timor-Leste**	TLS
Federated States of Micronesia	FSM	**Nepal**	NPL	**Tonga**	TON
Fiji	FJI	**New Zealand**	NZL	**Tuvalu**	TUV
India	IND	**North Korea**	PRK	**Vanuatu**	VUT
Indonesia	IDN	**Pakistan**	PAK	**Vietnam**	VNM
Japan	JPN	**Palau**	PLW		
Kiribati	KIR	**Papua New Guinea**	PNG		

UNAIDS Global plan priority countries

Country	ISO code
Angola	AGO
Botswana	BWA
Burundi	BDI
Cameroon	CMR
Chad	TCD
Cote dvoire	CIV
Democratic Republic of the Congo	COD
Ethiopia*	ETH
Ghana	GHA
Kenya	KEN
Lesotho	LSO
Malawi	MWI
Mozambique	MOZ
Namibia	NAM
Nigeria	NGA
South Africa	ZAF
Swaziland	SWZ
Tanzania	TZA
Uganda	UGA
Zambia	ZMB
Zimbabwe	ZWE

*** Prevalence and DALY estimates available for 20 of the 21 Global Plan Priority countries with data missing for Ethiopia**

Supplementary Table 4: Baseline characteristics of studies providing estimates of crude rate

Author and year	Country	LMIC	Study type	Source of data	From	To	Outcome classification	Outcome type	Outcome sub-type	% Males	Mean (or median) Age at baseline	Cohort size	Patient years
Rickerts et al, 2000[1]	Germany	No	Cohort study	Clinical database	1983	1998	Physician diagnosis	Incidence	MI	82	32	4993	16478
Coplan et al, 2001[2]	USA	No	RCT	Trial register	multiple cohorts	multiple cohorts	Investigator report	Incidence	CVD, stroke and MI	NA	NA	2680	2597
Holmberg et al, 2002[3]	USA	No	Cohort study	Clinical database	1993	2002	Physician diagnosis	Incidence	MI	82	43	5672	17712
Escaut et al, 2003[4]	France	No	Cohort study	Clinical data	NA	NA	Physician diagnosis	Incidence	MI	NA	43	840	2520
Evers et al, 2003[5]	Germany	No	Cohort study	Clinical data	1993	2001	Physician diagnosis	Incidence	Stroke	81	36	772	6944
Mary-Krause et al, 2003[6]	France	No	Cohort study	Clinical database	1996	1999	ICD coding	Incidence	MI	100	38	34976	88029
Barbaro et al, 2003[7]	Italy	No	Cohort study	Clinical database	1999	2002	NA	Incidence	MI	64	35	1551	4653
Bozette et al, 2003[8]	USA	No	Cohort study	National Clinical database	1993	2001	ICD coding	Incidence and mortality	CVD	98	NA	36766	121936
Currier et al, 2003[9]	USA	No	Cohort study	MediCal database	1994	2000	ICD coding	Incidence	MI	73	39	28513	71286
Gardner et al, 2003[10]	USA	No	Cohort study	Clinical database	1993	2000	Physician diagnosis	Incidence	CVD and MI	0	38	885	3803
Coplan et al, 2003[11]	Multicentre	No	RCT	Clinical Trial database	NA	1999	Investigator report	Incidence	MI	92	38	10986	2150
Reisler et al, 2003[12]	USA	No	Cohort study	Clinical Trial database	1996	2001	ICD coding	Incidence	CVD	83	39	2947	5940
Cole et al, 2004[13]	USA	No	Cohort study	Hospital database	1988	1991	ICD coding	Incidence	Stroke	83	35	557	2826
Jerico et al, 2004[14]	Spain	No	Cohort study	Clinical database	1999	2003	Physician diagnosis	Incidence	CVD, stroke and MI	NA	NA	1459	5836

Author and year	Country	LMIC	Study type	Source of data	From	To	Outcome classification	Outcome type	Outcome sub-type	% Males	Mean (or median) Age at baseline	Cohort size	Patient years
Iloeje et al, 2005[15]	USA	No	Cohort study	Cohort database and hospital discharge reports	1996	2003	Physician diagnosis	Incidence	CVD, stroke and MI	86	39	7542	23765
Krentz et al, 2005[16]	Canada	No	Cohort study	Clinical database	1984	2003	ICD coding	Mortality	CVD	NA	NA	1987	6955
INITIO cohort, 2006[17]	Multicentre	No	RCT	Clinical data	1999	2004	US Center for Disease Control and Prevention criteria	Incidence	CVD and MI	79	39	911	2733
Sackoff et al, 2006[18]	USA	No	Cohort study	DOHMH	1999	2004	ICD coding	Mortality	CVD, stroke and MI	70	46	68669	313331
ATCC cohort, 2006[19]	Europe, North America	No	Cohort study	Cohort database	1996	2006	ICD coding	Mortality	CVD, stroke and MI	73	37	1876	154667
DAD cohort, 2006[20]	Multicentre	No	Cohort study	Clinical database	1999	2008	CoDe system	Mortality	CVD, stroke and MI	74	39	33308	180176
Kwong et al, 2006[21]	USA	No	Cohort study	Hospital discharge letters	1983	2004	WHO Monica criteria	Incidence	CVD, stroke and MI	83	36	18603	77480
Triant et al, 2007[22]	USA	No	Cohort study	Clinical database	1996	2004	ICD coding	Incidence	MI	70	38	3851	16983
Bonnet et al, 2007[23]	France	No	Cohort study	Hospital database	2000	2004	ICD coding	Incidence	CVD, stroke and MI	74	40	3650	11357
Vaughn et al, 2007[24]	USA	No	Cohort study	Clinical database	1990	2000	ICD coding	Incidence	CVD and stroke	79	35	5667	15550
Martinez et al, 2007[25]	Spain	No	Cohort study	Clinical database and national registry	1997	2003	Physician diagnosis and patient's friends or relatives	Mortality	CVD	NA	NA	4471	34400
Bozzette et al, 2008[26]	USA	No	Cohort study	National Clinical database	1993	2003	ICD coding	Incidence	MI	98	NA	41213	168213
Tedaldi et al, 2008[27]	USA	No	RCT	Trial register	1999	2005	Division of AIDS at the National Institutes of	Incidence	CVD	80	38	1397	5929

Author and year	Country	LMIC	Study type	Source of data	From	To	Outcome classification	Outcome type	Outcome sub-type	% Males	Mean (or median) Age at baseline	Cohort size	Patient years
							Health, adverse-event grading scale						
Brothers et al, 2009[28]	UK	No	RCT	Clinical trials database	1997	2004	MedDRA coding	Incidence	MI	82	37	14174	11932
Corral et al, 2009[29]	Spain	No	Cohort study	clinic data	1996	2008	TOAST Criteria	Incidence	Stroke	72	NA	2012	13228
Falster et al, 2009[30]	Australia	Yes	Cohort study	Asia Pacific HIV Observational Database	1999	2007	CoDe system	Mortality	CVD and MI	80	41	3151	7630
Bedimo et al, 2010[31]	USA	No	Cohort study	National Clinical database	1996	2004	ICD coding	Incidence	Stroke	98	46	19424	75000
Lang et al, 2010[32]	France	No	Cohort study	National Hospital Database	2000	2006	ICD coding	Incidence	MI	89	47	74958	298156
Belloso et al, 2010[33]	Latin America	Yes	Cohort study	Clinical data	1997	2007	Physician diagnosis	Incidence	CVD, stroke and MI	70	NA	6007	15018
Serraino et al, 2010[34]	Italy	No	Cohort study	Death Certificates	1999	2005	ICD coding	Mortality	MI	78	NA	9662	34814
Triant et al, 2010[35]	USA	No	Cohort study	Clinical database	1998	2008	ICD coding	Incidence	MI	69	46	6517	33237
Durand et al, 2011[36]	Canada	No	Cohort study	Quebec public health insurance database	1985	2007	ICD coding	Incidence	MI	78	40	7053	35787
Pinzon et al, 2011[37]	USA	No	Cohort study	Hospital medical record and death certificate review	NA	NA	Physician diagnosis	Incidence and mortality	MI	74	52	311	902
Ribaudo et al, 2011[38]	USA	No	RCT	ACTG database	1998	2007	Division of AIDS at the National Institutes of Health, adverse-event grading scale	Incidence	MI	82	37	5056	17404
Aldaz et al, 2011[39]	Spain	No	Cohort study	AIDS case register	1999	2006	ICD coding	Mortality	CVD	68	NA	1145	7113
Palella et al, 2011[40]	USA	No	Cohort study	Social Security Death Index	1996	2007	Physician diagnosis	Mortality	CVD	84	39	3569	19543

Author and year	Country	LMIC	Study type	Source of data	From	To	Outcome classification	Outcome type	Outcome sub-type	% Males	Mean (or median) Age at baseline	Cohort size	Patient years
Bedimo et al, 2011[41]	USA	No	Cohort study	Clinical database	1996	2004	ICD coding	Mortality	Stroke and MI	98	46	19424	76376
Hasse et al, 2011[42]	Switzerland	No	Cohort study	Clinical database	2008	2010	WHO Monica criteria	Incidence	Stroke and MI	71	36	8444	22591
Reekie et al, 2011[43]	Europe, Argentina and Israel	No	Cohort study	EuroSIDA study	1994	2001	CoDe system	Incidence	CVD	76	NA	10869	43784
Bhowmik et al, 2012[44]	India	Yes	Cohort study	ART patient register	2009	2010	Inpatient records, telephone contact and home visits	Mortality	CVD, stroke and MI	66	35	759	731
Mateen et al, 2012[45]	USA	No	Cohort study	MACS database	1996	2011	ICD coding	Incidence	Stroke	100	41	1776	17159
Tseng et al, 2012[46]	USA	No	Cohort study	National Death Index/ Clinic records	2000	2009	ICD coding	Mortality	MI	87	39	2860	10582
Berry et al, 2012[47]	USA	No	Cohort study	Clinical database	2001	2008	ICD coding	Incidence	MI	72	40	11645	40499
Chow et al, 2012[48]	USA	No	Cohort study	Research Patient Data Registry	1996	2009	ICD coding	Incidence	Stroke	69	42	4308	25100
Marin et al, 2012[49]	Multicentre	No	Cohort study	CASACADE database	1996	2006	ICD coding and CoDe system	Mortality	CVD	77	30	9858	71230
Monforte et al, 2013[50]	Multicentre	No	Cohort study	Clinical database	1999	2011	WHO Monica criteria	Incidence	Stroke and MI	74	43	49734	301907
Ruppik et al, 2013[51]	Switzerland	No	Cohort study	Clinical database	2005	2009	ICD coding	Mortality	CVD, stroke and MI	74	47	9053	36720
Sabin et al, 2013[52]	Multicentre	No	Cohort study	Clinical database	1999	2011	WHO Monica criteria	Incidence	CVD	74	38	33301	221505
Flexor et al, 2013[53]	France	No	Cohort study	Cohort database	2000	2004	NA	Mortality	CVD	77	65	132	500
Rodger et al, 2013[54]	Multicentre	No	RCT	Trial register; human mortality database	2000	2008	CoDe system	Mortality	CVD and MI	80	43	3280	12357

Author and year	Country	LMIC	Study type	Source of data	From	To	Outcome classification	Outcome type	Outcome sub-type	% Males	Mean (or median) Age at baseline	Cohort size	Patient years
Vinikoor et al, 2013[55]	USA	No	Cohort study	electronic institutional records;	1999	2010	WHO Monica criteria; AHA criteria	Incidence	Stroke	70	39	2574	13708
Overton et al, 2013[56]	USA	No	Cohort study	Cohort database	2000	2009	MedDRA coding	Incidence	CVD, stroke and MI	83	39	3601	15135
Masia et al, 2013[57]	Spain	No	Cohort study	Clinical database	2004	2010	CoDe system	Incidence	CVD, stroke and MI	79	36	5185	12669
Brouwer et al, 2014[58]	USA	No	Cohort study	Medicaid database	2002	2008	ICD coding	Incidence	MI	52	41	3500	6399
Cooper et al, 2014[59]	Multicentre	No	RCT	Trial register	2004	2010	Sponsor defined	Incidence	MI	71	37	721	2447
Gillis et al, 2014[60]	Canada	No	Cohort study	HIV Ontario Observational Database; medical charts	1995	2011	ICD coding	Incidence	CVD, stroke and MI	85	36	4501	19914
Gulick et al, 2014[61]	USA, Europe and Australia	No	RCT	Trial register	2004	2006	Division of AIDS at the National Institutes of Health, adverse-event grading scale	Incidence and mortality	CVD (mortality) and MI (incident)	85	46	938	2639
Marcus et al, 2014[62]	USA	No	Cohort study	HIV registry and electronic medical record	1996	2011	ICD coding	Incidence	Stroke	91	41	24768	120588
Sarfo et al, 2014[63]	Ghana	Yes	Cohort study	Clinical database	2004	2011	Division of AIDS at the National Institutes of Health, adverse-event grading scale	Incidence	Stroke	32	38	10400	11237
Womack et al, 2014[64]	USA	No	Cohort study	MediCare/ IHD Quality Enhancement Initiative	2003	2009	ICD coding	Incidence	CVD	0	44	710	4260
Zoufaly et al, 2014[65]	Europe, Argentina and Israel	No	Cohort study	EuroSIDA study	2001	2011	CoDe system	Incidence	Stroke	72	42	2913	11491

Author and year	Country	LMIC	Study type	Source of data	From	To	Outcome classification	Outcome type	Outcome sub-type	% Males	Mean (or median) Age at baseline	Cohort size	Patient years
Berry et al, 2014[66]	USA	No	Cohort study	Clinical database	2003	2010	ICD coding	Incidence	CVD	46	10	579	3516
Ehren et al, 2014[67]	Germany	No	Cohort study	Clinical database	2004	2010	CoDe system	Mortality	CVD	80	47	3165	22155
Miller et al, 2014[68]	Multicentre	No	RCT	Trial register; medical records	2000	2008	NA	Incidence and mortality	CVD (incident and mortality), MI (incident) and stroke (incident)	77	42	3570	15351
Klein et al, 2015[69]	USA	No	Cohort study	HIV registry and electronic medical record	1996	2011	ICD coding	Incidence	MI	91	41	24768	119587
Althoff et al, 2015[70]	USA	No	Cohort study	MediCare/ IHD Quality Enhancement Initiative	2003	2010	ICD coding	Incidence	MI	97	48	27253	144346
Rasmussen et al, 2015[71]	Denmark	No	CCS	Danish Civil Registration System, national registry	1995	2014	ICD coding	Incidence	Stroke and MI	76	36	5897	56953
Sico et al, 2015[72]	USA	No	Cohort study	MediCare Quality Enhancement Initiative	2003	2009	ICD coding	Incidence	Stroke	100	48	25355	149595
Marcus et al, 2016[73]	USA	No	Cohort study	HIV registry; electronic medical record	1998	2011	ICD coding	Incidence	CVD	89	42	8154	34472

Abbreviations: RCT – Randomised control trials; CCS – Case control studies; NA – Not available

Supplementary table 5: Crude rates for cardiovascular events in studies that provided data for both HIV and non-HIV populations

			HIV population			Non-HIV population		
Author	**Year**	**Outcome**	**Patient years**	**Events**	**Rate per 10,000**	**Patient years**	**Events**	**Rate per 10,000**
Womack et al	2014	Incidence - CVD	4260	46	108.0	8862	40	45.1
Durand et al	2011	Incidence - MI	35787	137	38.3	101782	226	22.2
Klein et al	2015	Incidence - MI	119587	320	26.8	1506676	2483	16.5
Triant et al	2007	Incidence - MI	16983	189	111.3	3747329	26142	69.8
Althoff et al	2015	Incidence - MI	144346	291	20.2	309507	398	12.9
Currier et al	2003	Incidence - MI	71286	294	41.2	8052939	26777	33.3
Rasmussen et al	2015	Incidence - MI	56953	170	29.8	648720	1068	16.5
Cole et al	2004	Incidence - Stroke	2826	6	21.2	4104734	545	1.3
Sico et al	2015	Incidence - Stroke	149595	910	60.8	303266	570	18.8
Marcus et al	2014	Incidence - Stroke	120588	151	12.5	1516250	1128	7.4
Chow et al	2012	Incidence - Stroke	25100	132	52.6	208600	782	37.5
Rasmussen et al	2015	Incidence - Stroke	56777	222	39.1	648720	1563	24.1

Supplementary table 6: Ethnicity mix in studies providing relative risk estimates

Author	Year	Ethnicity
Qureshi et al	1997	Black: 85%
Gardner et al	2003	Black: 60.8%; Caucasian: 20.7%; Hispanic: 17.2%
Cole et al	2004	Black: 100%
Triant et al	2009	Caucasian: 49.6%
Aldaz et al	2011	Not specified
Durand et al	2011	Not specified
Chow et al	2012	Black: 21%; Caucasian: 53%; Hispanic: 17%
Helleberg et al	2012	Black: 13%; Caucasian: 73%; Asian: 5%
Walker et al	2013	Zamaro: 28%; Ndengereko: 14%
Mateen et al	2013	Black: 29%; Caucasian: 65%; Hispanic: 7%
Tripathi et al	2014	Black: 35.6%; Caucasian: 10.3%
Womack et al	2014	Black: 61.6%; Caucasian: 28.7%
Sico et al	2015	Black: 47%; Caucasian: 39%; Hispanic: 7%
Rasmussen et al	2015	Not specified
Althoff et al	2015	Black: 48%; Caucasian: 38%;
Klein et al	2015	Black: 18%; Caucasian: 56%; Hispanic: 21%

Supplementary table 7: Sensitivity and subgroup analysis for the risk ratio

	Number of estimates	Risk ratio	Lower limit	Upper limit
Overall	17	2.16	1.68	2.77
Outcome				
Cardiovascular disease	5	2.36	1.50	3.70
Stroke	7	2.56	1.43	4.61
Myocardial infarction	5	1.79	1.54	2.08
Risk of bias*				
Low	12	2.09	1.49	2.92
Moderate / High	5	2.12	1.84	2.45
Publication year**				
Pre 2013	8	2.86	1.79	4.58
Post 2013	9	1.73	1.41	2.14
Publication bias***				
Imputed risk ratio	22	1.73	1.25	2.40
Follow-up				
Long (≥6 years [median])	6	2.01	1.43	2.82
Short (<6 years[median])	4	1.73	1.28	2.33

*Risk of bias assessed by level of adjustment. Low risk – adjustment of age, sex and at least one other covariate

** Median publication year was 2013. Using the publication year as continuous variable, we noticed some attenuation of risk by year from 1997 to 2015 (HR 0.91, 95%CI [0.87 to 0.96]

***Publication bias assessed by using the regression test for funnel plot asymmetry: p=0.002: five additional estimates imputed using the trim and fill method to provide the imputed risk ratio

Supplementary table 8: Population attributable fraction (95% CI) and cardiovascular DALY's attributable to HIV in all patients and stratified by sex and year (using prevalence data for HIV for the 15-49 year age group)

			Population attributable fraction, %			HIV attributable CVD Burden in DALYs ('000's)		
Sex	**Area**	**Year**	**CE**	**LL**	**UL**	**CE**	**LL**	**UL**
All	Global	1990	0.36%	0.21%	0.56%	744	437	1156
	Global	1995	0.70%	0.41%	1.07%	1595	950	2455
	Global	2000	0.93%	0.55%	1.42%	2281	1346	3481
	Global	2005	0.93%	0.55%	1.41%	2416	1440	3675
	Global	2010	0.89%	0.53%	1.35%	2368	1408	3596
	Global	2015	0.92%	0.55%	1.41%	2571	1533	3916
Female	Global	1990	0.33%	0.20%	0.52%	305	178	478
	Global	1995	0.69%	0.41%	1.06%	691	406	1060
	Global	2000	0.95%	0.57%	1.45%	1005	597	1535
	Global	2005	0.96%	0.57%	1.45%	1054	621	1599
	Global	2010	0.93%	0.55%	1.42%	1001	596	1530
	Global	2015	0.98%	0.58%	1.49%	1085	642	1653
Male	Global	1990	0.39%	0.23%	0.60%	444	260	693
	Global	1995	0.70%	0.42%	1.08%	911	540	1399
	Global	2000	0.91%	0.54%	1.38%	1265	750	1928
	Global	2005	0.90%	0.53%	1.37%	1353	801	2063
	Global	2010	0.86%	0.51%	1.31%	1348	794	2060
	Global	2015	0.87%	0.51%	1.32%	1461	865	2232

Supplementary table 9: Population attributable fraction (95% CI) and cardiovascular DALY's attributable to HIV in stratified by region and year (using prevalence data for HIV for the 15-49-year age group)

		Population attributable fraction, %			HIV attributable CVD Burden in DALYs ('000's)			Rate of change of DALYs per year ('000)		
Area	**Year**	**CE**	**LL**	**UL**	**CE**	**LL**	**UL**	**CE**	**LL**	**UL**
Asia and the Pacific	1990	0.03%	0.02%	0.05%	32	17	55	13.93	8.09	21.75
	1995	0.15%	0.08%	0.25%	173	95	293			
	2000	0.23%	0.13%	0.36%	299	174	472			
	2005	0.25%	0.14%	0.38%	360	209	563			
	2010	0.24%	0.14%	0.37%	374	218	586			
	2015	0.24%	0.14%	0.37%	394	227	620			
East and Southern Africa	1990	4.61%	2.76%	6.89%	256	140	435	15.87	7.60	32.66
	1995	8.26%	5.09%	12.12%	507	283	843			
	2000	10.08%	6.24%	14.60%	712	398	1173			
	2005	9.17%	5.65%	13.28%	675	372	1161			
	2010	8.10%	4.95%	11.86%	617	329	1101			
	2015	7.64%	4.68%	11.18%	669	338	1285			
Eastern Europe and Central Asia	1990	0.06%	0.03%	0.09%	15	9	23	10.92	6.47	16.73
	1995	0.12%	0.07%	0.19%	44	26	68			
	2000	0.30%	0.18%	0.45%	108	64	166			
	2005	0.49%	0.29%	0.74%	184	109	281			
	2010	0.67%	0.40%	1.02%	206	122	317			
	2015	1.00%	0.59%	1.51%	299	177	458			
Latin America and the Caribbean	1990	0.32%	0.18%	0.49%	38	22	60	1.89	1.10	2.98
	1995	0.48%	0.28%	0.75%	61	35	96			
	2000	0.55%	0.32%	0.86%	71	41	111			
	2005	0.56%	0.33%	0.87%	74	43	115			

	2010	0.56%	0.32%	0.87%	78	45	123			
	2015	0.56%	0.33%	0.86%	87	51	138			
Middle East and North Africa	1990	0.01%	0.01%	0.03%	1	0	2	0.53	0.28	0.95
	1995	0.03%	0.02%	0.07%	3	1	5			
	2000	0.07%	0.04%	0.12%	6	3	10			
	2005	0.10%	0.06%	0.16%	9	5	15			
	2010	0.12%	0.07%	0.19%	12	7	20			
	2015	0.13%	0.07%	0.23%	15	8	27			
West and Central Africa	1990	1.76%	0.95%	2.96%	84	41	161	4.66	2.10	9.88
	1995	3.02%	1.72%	4.84%	159	82	283			
	2000	3.70%	2.17%	5.78%	226	121	398			
	2005	3.40%	1.99%	5.28%	224	119	403			
	2010	2.88%	1.68%	4.54%	204	104	387			
	2015	2.51%	1.45%	3.93%	205	95	418			
Western & Central Europe and North America	1990	0.26%	0.15%	0.39%	116	69	178	0.70	0.41	1.07
	1995	0.28%	0.17%	0.44%	124	73	192			
	2000	0.34%	0.20%	0.53%	136	80	211			
	2005	0.37%	0.22%	0.56%	132	77	203			
	2010	0.39%	0.23%	0.59%	126	74	194			
	2015	0.40%	0.24%	0.61%	134	79	206			

Supplementary table 10: Population attributable fraction (95% CI) and HIV attributable cardiovascular DALY's in all patients stratified by country (using HIV prevalence data for all age groups [age >15 years] for 2016 and cardiovascular burden data [CVD DALY] for 2015)

			Population attributable fraction, (%)			
Country ISO code	**Country**	**Total CVD DALYs per 100,000 persons**	**CE**	**LL**	**UL**	**HIV attributable CVD Burden in DALYs per 100,000 persons**
AFG	Afghanistan	19223.17	0.05	0.02	0.11	9.77 (3.78- 22.19)
AGO	Angola	6678.37	2.37	1.28	3.95	157.96 (53.59- 451.65)
ALB	Albania	4645.48	0.07	0.03	0.14	3.13 (1.28- 6.73)
ARG	Argentina	2858.93	0.39	0.23	0.60	11.14 (6.60- 17.10)
ARM	Armenia	5753.21	0.18	0.10	0.30	10.42 (5.74- 17.13)
AUS	Australia	1508.33	0.16	0.10	0.25	2.46 (1.44- 3.79)
AUT	Austria	1774.93	0.12	0.07	0.20	2.22 (1.26- 3.54)
AZE	Azerbaijan	7474.42	0.16	0.09	0.27	11.94 (6.36- 20.38)
BDI	Burundi	4776.43	1.25	0.72	1.97	59.05 (28.91- 113.62)
BEL	Belgium	1656.79	0.31	0.18	0.47	5.11 (3.03- 7.78)
BEN	Benin	5857.37	1.22	0.69	1.98	71.34 (33.26- 146.69)
BFA	Burkina Faso	4592.73	1.02	0.59	1.61	46.86 (23.54- 88.50)
BGD	Bangladesh	6529.98	0.01	0.01	0.01	0.58 (0.34- 0.93)
BGR	Bulgaria	6151.96	0.06	0.03	0.09	3.49 (2.03- 5.51)
BIH	Bosnia and Herzegovina	3269.54	0.01	0.01	0.02	0.43 (0.25- 0.67)
BLR	Belarus	9145.68	0.53	0.31	0.84	48.23 (27.88- 76.68)
BLZ	Belize	3903.80	1.62	0.96	2.48	63.15 (37.21- 97.04)
BMH	The Bahamas	3440.30	2.99	1.78	4.51	102.90 (61.02- 157.75)

BOL	Bolivia	3226.96	0.27	0.14	0.47	8.54 (4.36- 15.60)
BRA	Brazil	3513.53	0.60	0.33	1.01	21.19 (11.63- 35.51)
BRB	Barbados	2729.17	1.33	0.79	2.01	36.28 (21.44- 55.77)
BRN	Brunei	2909.18	0.01	0.00	0.02	0.30 (0.13- 0.61)
BTN	Bhutan	4059.12	0.88	0.22	2.48	35.76 (8.78- 104.19)
BWA	Botswana	5558.03	20.61	13.32	28.38	1131.66 (420.55-3026.26)
CAF	Central African Republic	8968.68	4.01	2.39	6.10	359.55 (167.70- 727.42)
CAN	Canada	1572.11	0.30	0.18	0.46	4.70 (2.76- 7.16)
CHE	Switzerland	1233.71	0.28	0.17	0.44	3.47 (2.04- 5.40)
CHL	Chile	1934.76	0.26	0.14	0.45	5.05 (2.67- 8.61)
CHN	China	4113.85	0.09	0.04	0.17	3.67 (1.77- 6.90)
CIV	Cote d'Ivoire	6093.99	3.49	2.08	5.32	212.75 (107.77- 400.01)
CMR	Cameroon	5358.95	4.79	2.87	7.23	256.37 (126.97- 488.80)
COD	Democratic Republic of the Congo	5108.56	0.96	0.54	1.54	48.96 (23.85- 95.69)
COG	Congo	6597.92	2.93	1.74	4.51	192.65 (97.30- 368.94)
COL	Colombia	2398.17	0.46	0.27	0.70	11.07 (6.52- 16.86)
CPV	Cape Verde	3997.88	1.02	0.59	1.61	40.64 (23.03- 65.92)
CRI	Costa Rica	1806.10	0.31	0.19	0.48	5.62 (3.34- 8.72)
CUB	Cuba	3174.66	0.26	0.16	0.40	8.28 (4.92- 12.82)
CYP	Cyprus	1840.70	0.10	0.06	0.15	1.78 (1.05- 2.76)
CZE	Czech Republic	3418.80	0.05	0.03	0.08	1.86 (1.10- 2.85)
DEU	Germany	1905.37	0.15	0.09	0.23	2.85 (1.69- 4.38)

DJI	Djibouti	4897.61	1.69	0.92	2.87	81.91 (35.35- 181.85)
DNK	Denmark	1688.54	0.16	0.10	0.25	2.78 (1.64- 4.26)
DOM	Dominican Republic	4246.33	1.10	0.61	1.80	46.60 (26.01- 76.65)
DZA	Algeria	3961.81	0.03	0.02	0.06	1.38 (0.77- 2.25)
ECU	Ecuador	2405.90	0.29	0.16	0.46	6.92 (3.95- 11.17)
EGY	Egypt	6798.63	0.02	0.01	0.04	1.52 (0.74- 2.88)
ERI	Eritrea	5960.88	0.74	0.42	1.20	44.16 (18.93- 96.75)
ESP	Spain	1335.60	0.45	0.26	0.70	5.95 (3.46- 9.33)
EST	Estonia	3593.64	0.64	0.38	0.97	22.98 (13.41- 35.11)
ETH	Ethiopia	4695.61	1.25	0.73	1.95	58.46 (29.70- 108.72)
FIN	Finland	2125.43	0.10	0.06	0.15	2.03 (1.20- 3.14)
FJI	Fiji	7940.55	0.14	0.08	0.25	11.47 (6.04- 20.14)
FRA	France	1240.94	0.41	0.25	0.63	5.13 (3.06- 7.87)
GAB	Gabon	4533.40	4.08	2.43	6.28	185.02 (94.14- 338.34)
GBR	United Kingdom	1817.83	0.25	0.15	0.38	4.55 (2.69- 6.97)
GEO	Georgia	7363.06	0.34	0.20	0.55	25.38 (14.45- 41.22)
GHA	Ghana	5696.14	1.80	1.05	2.78	101.75 (48.33- 203.48)
GIN	Guinea	5821.53	1.72	1.02	2.67	100.21 (51.84- 181.83)
GMB	The Gambia	4251.49	1.98	1.15	3.09	84.10 (44.25- 146.69)
GNB	Guinea-Bissau	6956.55	3.71	2.20	5.65	254.67 (87.95- 738.68)
GNQ	Equatorial Guinea	4568.86	5.16	3.13	7.72	232.21 (91.74- 586.20)
GRC	Greece	2714.53	0.20	0.12	0.31	5.52 (3.27- 8.43)
GTM	Guatemala	2501.26	0.61	0.32	1.05	15.16 (7.97- 26.58)

GUY	Guyana	7533.43	1.58	0.94	2.40	118.86 (69.92- 182.94)
HND	Honduras	5395.95	0.42	0.24	0.65	22.36 (12.58- 37.04)
HRV	Croatia	3780.20	0.06	0.03	0.09	2.14 (1.25- 3.34)
HTI	Haiti	7314.48	1.95	1.13	3.06	141.98 (79.38- 233.49)
HUN	Hungary	4014.95	0.06	0.04	0.10	2.46 (1.43- 3.87)
IDN	Indonesia	6496.89	0.43	0.25	0.66	27.59 (15.73- 44.42)
IND	India	5818.48	0.27	0.15	0.42	15.44 (8.91- 24.67)
IRL	Ireland	1803.77	0.23	0.10	0.45	4.12 (1.86- 8.19)
IRN	Iran	5478.20	0.16	0.08	0.29	8.46 (4.12- 15.86)
ISL	Iceland	1539.78	0.18	0.11	0.29	2.83 (1.64- 4.46)
ISR	Israel	1378.31	0.18	0.10	0.27	2.42 (1.42- 3.71)
ITA	Italy	1535.91	0.31	0.18	0.48	4.76 (2.81- 7.33)
JAM	Jamaica	3175.66	1.59	0.93	2.45	50.38 (29.27- 79.03)
JPN	Japan	1350.42	0.03	0.02	0.04	0.35 (0.20- 0.55)
KAZ	Kazakhstan	8512.02	0.20	0.12	0.32	17.39 (10.10- 27.42)
KEN	Kenya	2723.56	6.05	3.57	9.16	164.12 (95.75- 257.17)
KGZ	Kyrgyzstan	9377.04	0.23	0.13	0.37	21.24 (12.11- 34.40)
KHM	Cambodia	6475.74	0.74	0.43	1.12	47.68 (27.70- 74.92)
LAO	Laos	6710.65	0.27	0.16	0.41	17.85 (10.25- 28.40)
LBN	Lebanon	3635.77	0.06	0.04	0.10	2.24 (1.24- 3.75)
LBR	Liberia	4529.63	1.18	0.68	1.88	53.31 (27.27- 97.59)
LKA	Sri Lanka	3430.10	0.03	0.02	0.06	1.07 (0.54- 1.98)
LSO	Lesotho	8158.75	20.35	13.10	28.19	1651.21 (846.33-3071.57)

LTU	Lithuania	5052.77	0.10	0.06	0.16	5.20 (3.06- 7.99)
LUX	Luxembourg	1424.52	0.39	0.22	0.66	5.58 (3.06- 9.36)
LVA	Latvia	5436.91	0.49	0.29	0.75	26.51 (15.66- 40.91)
MAR	Morocco	3673.49	0.11	0.07	0.18	4.14 (2.32- 6.97)
MDA	Moldova	6840.05	0.59	0.35	0.92	40.47 (23.64- 62.99)
MDG	Madagascar	6824.90	0.36	0.21	0.58	24.66 (12.05- 48.26)
MDV	Maldives	2616.55	0.01	0.01	0.02	0.36 (0.20- 0.59)
MEX	Mexico	2428.54	0.25	0.15	0.39	6.13 (3.64- 9.36)
MKD	Macedonia	5295.64	0.01	0.00	0.02	0.30 (0.06- 0.92)
MLI	Mali	4716.07	1.42	0.82	2.21	66.53 (32.76- 123.41)
MMR	Myanmar	4701.60	0.68	0.40	1.05	31.93 (16.86- 56.76)
MNG	Mongolia	10490.64	0.02	0.01	0.04	2.43 (1.37- 3.97)
MOZ	Mozambique	5432.77	10.70	6.45	16.10	583.13 (281.09-1131.12)
MRT	Mauritania	3626.74	0.58	0.29	1.07	21.20 (9.27- 45.10)
MUS	Mauritius	4131.08	0.89	0.52	1.42	37.02 (21.56- 58.45)
MWI	Malawi	3454.43	9.86	6.10	14.29	339.27 (174.53- 624.37)
MYS	Malaysia	4620.04	0.46	0.27	0.71	21.12 (12.22- 33.37)
NAM	Namibia	4245.25	13.70	8.54	19.46	577.53 (306.94-1042.73)
NER	Niger	4457.03	0.50	0.30	0.78	22.23 (11.27- 41.53)
NGA	Nigeria	2867.20	3.38	1.91	5.43	95.94 (48.92- 183.83)
NIC	Nicaragua	2404.71	0.29	0.16	0.48	6.93 (3.77- 11.74)
NLD	Netherlands	1472.99	0.22	0.13	0.34	3.28 (1.94- 5.03)
NOR	Norway	1505.35	0.12	0.07	0.19	1.88 (1.11- 2.90)

NPL	Nepal	4629.62	0.23	0.13	0.36	10.72 (5.93- 17.94)
NZL	New Zealand	1747.10	0.12	0.07	0.18	2.03 (1.20- 3.12)
PAK	Pakistan	8755.75	0.11	0.06	0.19	9.29 (4.79- 16.59)
PAN	Panama	2255.05	0.69	0.41	1.05	15.57 (9.17- 24.05)
PER	Peru	1604.15	0.35	0.20	0.55	5.53 (3.16- 8.83)
PHL	Philippines	6045.88	0.11	0.04	0.24	6.79 (2.69- 14.84)
PNG	Papua New Guinea	9930.48	0.89	0.53	1.34	87.73 (45.60- 157.48)
POL	Poland	3551.80	0.10	0.06	0.15	3.51 (2.07- 5.39)
PRK	North Korea	5733.23	0.02	0.01	0.03	0.90 (0.46- 1.63)
PRT	Portugal	1764.79	0.49	0.29	0.75	8.61 (5.09- 13.23)
PRY	Paraguay	4023.08	0.46	0.24	0.81	18.46 (9.48- 33.01)
QAT	Qatar	2615.09	0.06	0.04	0.09	1.55 (0.88- 2.50)
ROU	Romania	5582.02	0.10	0.06	0.15	5.33 (3.13- 8.21)
RUS	Russia	7718.85	1.11	0.66	1.68	85.93 (51.20- 130.40)
RWA	Rwanda	3760.68	3.44	2.04	5.20	129.21 (64.09- 242.77)
SEN	Senegal	5236.53	0.57	0.33	0.91	29.41 (14.04- 60.84)
SGP	Singapore	1812.26	0.14	0.08	0.21	2.53 (1.48- 3.89)
SLB	Solomon Islands	10832.15	0.53	0.28	0.90	56.77 (26.72- 112.28)
SLE	Sierra Leone	5968.33	1.42	0.83	2.22	84.89 (43.93- 153.46)
SLV	El Salvador	2578.69	0.52	0.31	0.81	13.49 (7.96- 21.10)
SRB	Serbia	4799.36	0.08	0.04	0.12	3.67 (2.13- 5.70)
SSD	South Sudan	5018.56	2.46	1.30	4.26	122.61 (41.66- 358.99)
SUR	Suriname	4605.28	1.08	0.63	1.68	49.75 (28.75- 78.74)

SVK	Slovakia	4047.02	0.03	0.02	0.06	1.29 (0.67- 2.25)
SVN	Slovenia	1901.68	0.06	0.03	0.09	1.06 (0.62- 1.68)
SWE	Sweden	1785.40	0.15	0.09	0.23	2.68 (1.57- 4.11)
SWZ	Swaziland	7304.29	24.45	16.08	33.14	1764.56 (854.35-3534.00)
TCD	Chad	5269.87	2.36	1.35	3.74	124.15 (56.71- 256.63)
TGO	Togo	5520.49	2.73	1.61	4.17	150.36 (78.23- 274.43)
THA	Thailand	2708.62	0.94	0.56	1.44	25.37 (14.78- 40.20)
TJK	Tajikistan	7289.50	0.34	0.19	0.54	24.55 (13.84- 39.71)
TLS	Timor-Leste	4440.79	0.10	0.04	0.22	4.47 (1.73- 9.90)
TTO	Trinidad and Tobago	4682.47	1.16	0.69	1.76	54.27 (32.39- 82.69)
TUR	Turkey	2583.92	0.04	0.02	0.07	1.09 (0.63- 1.75)
TZA	Tanzania	4048.33	5.25	3.16	7.88	210.14 (103.36- 410.45)
UGA	Uganda	4486.21	7.69	4.70	11.32	344.21 (172.42- 643.48)
UKR	Ukraine	8748.90	0.66	0.39	1.02	57.54 (33.78- 89.58)
URY	Uruguay	2515.58	0.43	0.25	0.67	10.89 (6.35- 16.93)
USA	United States	2224.96	0.61	0.36	0.93	13.63 (8.01- 20.78)
UZB	Uzbekistan	8120.58	0.18	0.10	0.31	14.83 (7.92- 25.39)
VEN	Venezuela	3611.64	0.55	0.33	0.84	19.98 (11.75- 30.91)
VNM	Vietnam	3901.48	0.42	0.24	0.64	16.21 (9.19- 26.43)
ZAF	South Africa	4243.50	16.99	10.83	23.71	721.69 (455.53-1025.78)
ZMB	Zambia	6249.67	13.31	8.31	18.95	825.18 (460.42-1398.95)
ZWE	Zimbabwe	3867.22	14.74	9.23	20.88	567.82 (302.16-1016.55)

Supplementary table 11: Population attributable fraction (95% CI) for HIV (using prevalence data for 2015 in the 15-49 year age group) compared to other cardiovascular risk factors

Location	Ambient particulate matter pollution[1]	High total cholesterol[2]	High body-mass index[3]	High fasting plasma glucose[4]	Household air pollution from solid fuels[5]	Smoking[6]	Alcohol use[7]	HIV
Swaziland	0.00 (0.00- 0.00)	14.52 (10.82-18.75)	32.26 (24.45-40.27)	12.60 (9.95-15.99)	15.96 (10.65-21.41)	8.60 (4.93-12.75)	3.11 (2.31- 3.88)	24.95 (16.48-33.60)
Lesotho	10.74 (8.89-12.82)	9.35 (6.10-13.37)	26.09 (18.23-34.08)	7.79 (5.98-10.29)	15.10 (10.42-20.16)	14.32 (7.69-21.53)	3.39 (2.23- 4.52)	20.76 (13.45-28.59)
Botswana	10.27 (8.46-12.37)	17.49 (13.31-21.79)	28.02 (21.01-35.55)	12.51 (9.90-15.91)	10.49 (4.74-17.03)	15.69 (12.54-19.36)	3.89 (2.53- 5.14)	20.43 (13.23-28.12)
South Africa	11.62 (10.03-13.13)	18.67 (15.16-22.97)	30.98 (25.39-36.45)	15.60 (12.64-19.50)	4.20 (2.93- 5.71)	15.94 (14.08-17.90)	4.35 (3.47- 5.06)	18.27 (11.69-25.29)
Zimbabwe	8.37 (6.71-10.09)	11.38 (8.31-14.86)	15.29 (9.79-21.12)	8.71 (6.49-11.87)	13.79 (9.93-17.84)	10.52 (7.06-14.46)	2.05 (1.43- 2.76)	14.54 (9.16-20.75)
Namibia	10.65 (8.81-12.73)	18.50 (14.73-23.13)	20.02 (14.29-26.21)	11.04 (8.61-14.21)	14.91 (11.01-19.33)	18.09 (14.65-21.80)	0.00 (0.00- 0.00)	13.43 (8.37-19.10)
Zambia	11.31 (9.59-13.00)	13.22 (9.80-17.35)	19.59 (13.10-26.75)	7.99 (6.09-10.25)	19.69 (15.62-23.88)	15.19 (11.34-19.35)	0.00 (0.00- 0.00)	13.00 (8.18-18.52)
Mozambique	8.70 (6.97-10.52)	13.08 (10.07-16.62)	17.67 (11.42-25.29)	0.00 (0.00- 0.00)	19.28 (14.80-23.72)	15.21 (10.62-19.93)	1.55 (0.78- 2.32)	10.95 (6.53-16.57)
Malawi	9.22 (7.38-11.03)	13.25 (9.83-17.33)	12.92 (7.39-18.65)	4.80 (3.52- 6.59)	18.33 (13.90-22.73)	12.15 (8.62-16.54)	1.20 (0.87- 1.56)	9.54 (5.86-13.94)
Uganda	12.41 (10.48-14.30)	6.37 (4.10- 9.15)	13.73 (7.75-20.58)	2.60 (1.86- 3.55)	18.10 (14.03-22.19)	9.04 (6.48-12.16)	5.69 (4.22- 7.35)	7.65 (4.66-11.25)
Kenya	8.29 (6.94- 9.65)	8.24 (6.02-10.94)	19.12 (13.26-25.17)	6.45 (4.91- 8.46)	17.23 (13.45-21.08)	11.34 (9.55-13.41)	2.44 (1.61- 3.24)	6.42 (3.86- 9.73)
Tanzania	9.71 (7.97-11.59)	16.38 (13.04-20.28)	14.48 (8.50-21.46)	7.40 (5.58- 9.74)	18.95 (14.33-23.80)	11.63 (7.76-17.05)	3.71 (2.74- 4.66)	5.16 (3.10- 7.71)
Cameroon	15.26 (12.79-17.83)	8.82 (5.77-12.45)	24.12 (17.31-31.70)	6.68 (5.08- 8.85)	17.84 (13.07-22.86)	7.47 (4.96-10.67)	3.86 (2.93- 5.03)	4.91 (2.94- 7.40)
Cote dvoire	11.49 (9.56-13.66)	13.50 (9.95-17.51)	18.39 (11.73-25.59)	9.22 (6.91-12.08)	20.28 (15.65-25.19)	10.43 (6.76-14.47)	1.68 (0.93- 2.39)	3.51 (2.08- 5.39)
Nigeria	11.86 (9.91-13.87)	14.68 (11.33-18.60)	19.10 (13.44-25.52)	8.82 (6.61-11.45)	15.88 (11.73-20.70)	5.94 (4.48- 7.82)	0.00 (0.00- 0.00)	3.14 (1.75- 5.09)
Angola	11.29 (8.73-14.31)	11.89 (8.46-16.16)	20.02 (12.80-28.52)	8.85 (6.62-11.93)	15.46 (10.27-21.62)	8.66 (6.60-11.54)	2.79 (1.04- 4.65)	2.49 (1.36- 4.18)
Chad	12.15 (9.51-14.82)	10.19 (6.95-14.19)	19.66 (12.93-26.73)	9.89 (7.31-13.04)	19.82 (14.99-24.95)	8.49 (5.52-12.81)	2.00 (1.24- 2.83)	2.36 (1.33- 3.79)
Ghana	12.14 (10.04-14.16)	11.24 (7.49-15.33)	24.30 (16.91-33.00)	12.81 (10.04-16.44)	20.96 (16.65-25.78)	5.67 (3.57- 8.57)	2.26 (1.26- 3.41)	1.84 (1.07- 2.87)
Burundi	11.77 (9.27-13.96)	9.23 (6.31-12.64)	6.25 (2.73-11.07)	5.00 (3.64- 6.69)	19.67 (14.53-24.63)	7.33 (4.86-10.77)	4.63 (3.57- 6.08)	1.15 (0.66- 1.85)

Democratic Republic of the Congo	12.24 (9.98-14.43)	11.07 (7.78-14.80)	11.04 (6.30-16.64)	7.05 (5.23- 9.40)	20.08 (15.16-24.94)	8.95 (5.64-12.75)	0.99 (-0.21- 2.28)	0.96 (0.55- 1.55)

Definitions of risk factors

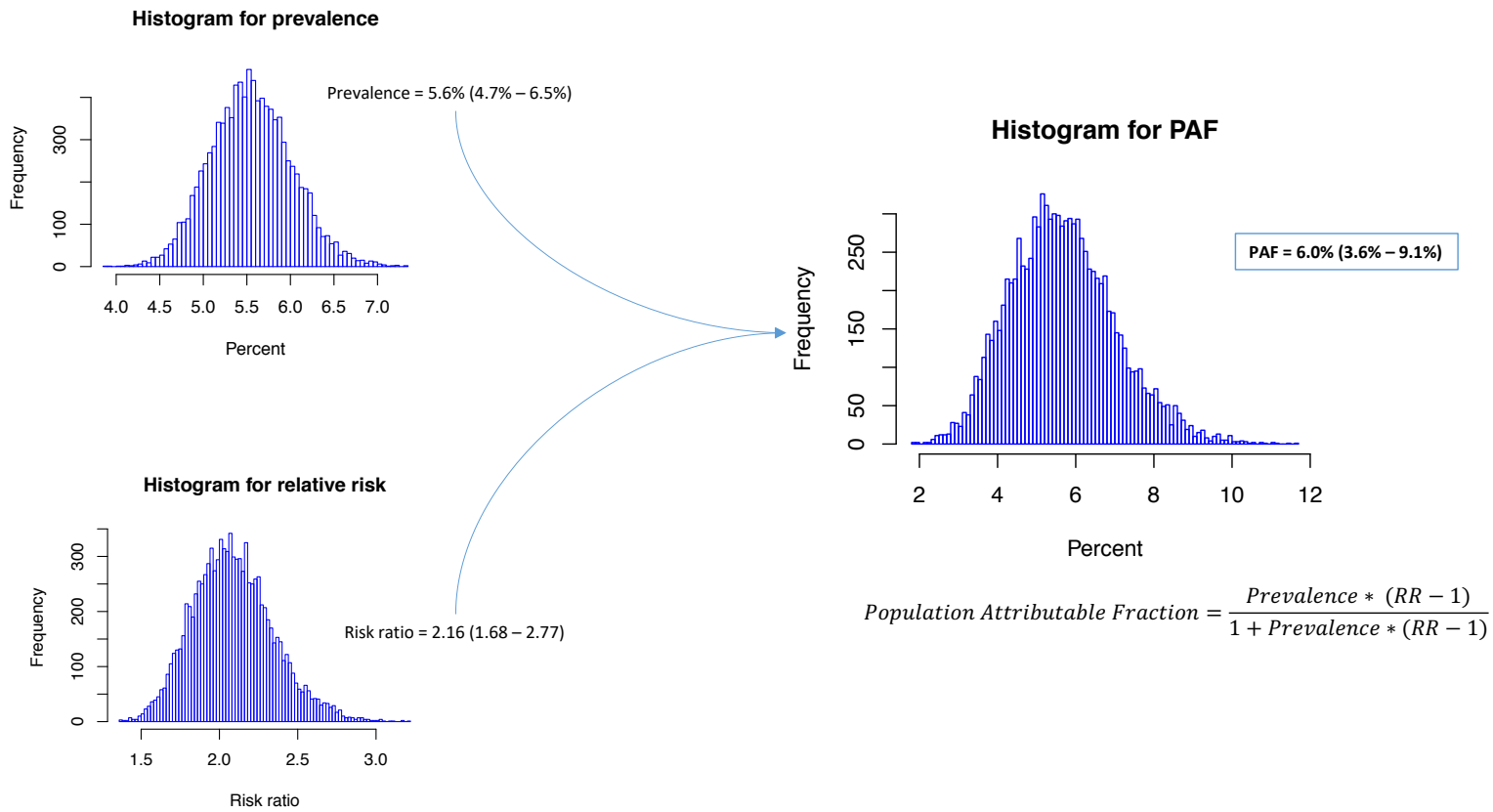
1. Ambient concentration of particles with an aerodynamic diameter smaller than 2·5 µm at levels greater than 5.8-8.8 µg/m3
2. Total cholesterol greater than 3.8-4.0 mmol/L
3. Body mass index higher than 21.0-23·0 kg/m²
4. Fasting plasma higher than 4.9-5.3 mmol/L*
5. Household air pollution from solid fuels
6. Any tobacco smoking
7. Any alcohol consumption

Supplement figures

Supplementary figure 1A

Kenya

Illustration for deriving population attributable fraction (PAF)

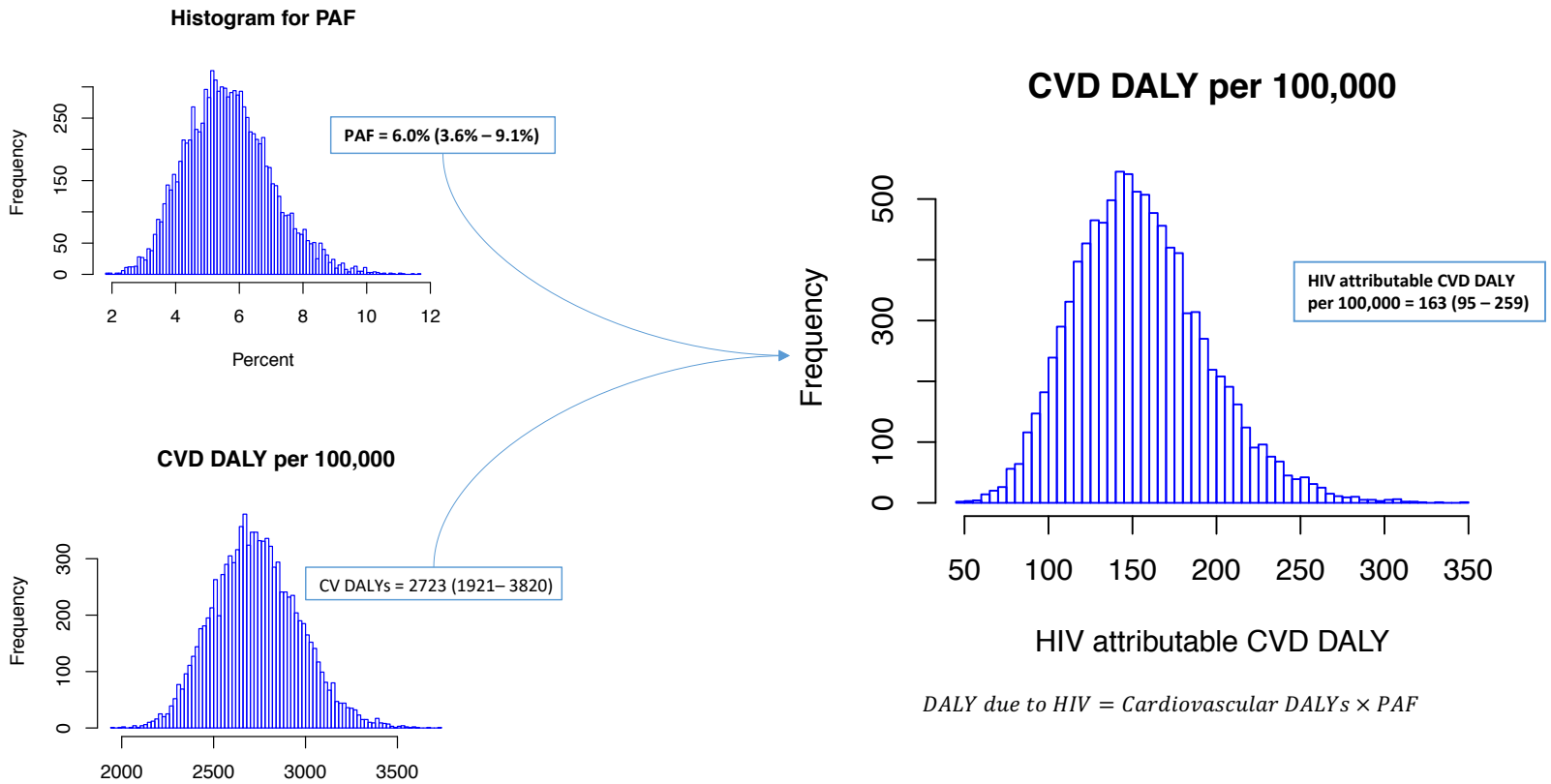


$$Population\ Attributable\ Fraction = \frac{Prevalence * (RR - 1)}{1 + Prevalence * (RR - 1)}$$

Supplementary figure 1B

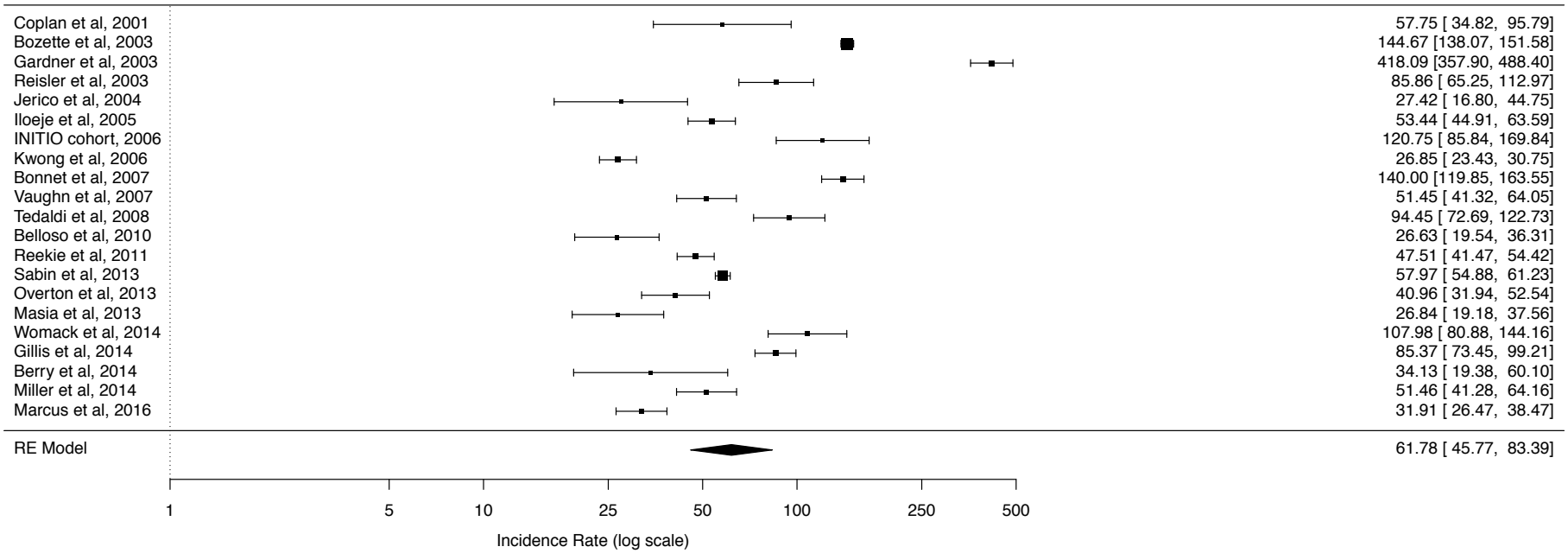
Kenya

Illustration for deriving HIV attributable CVD disability adjusted life years (DALYs) per 100,000 persons

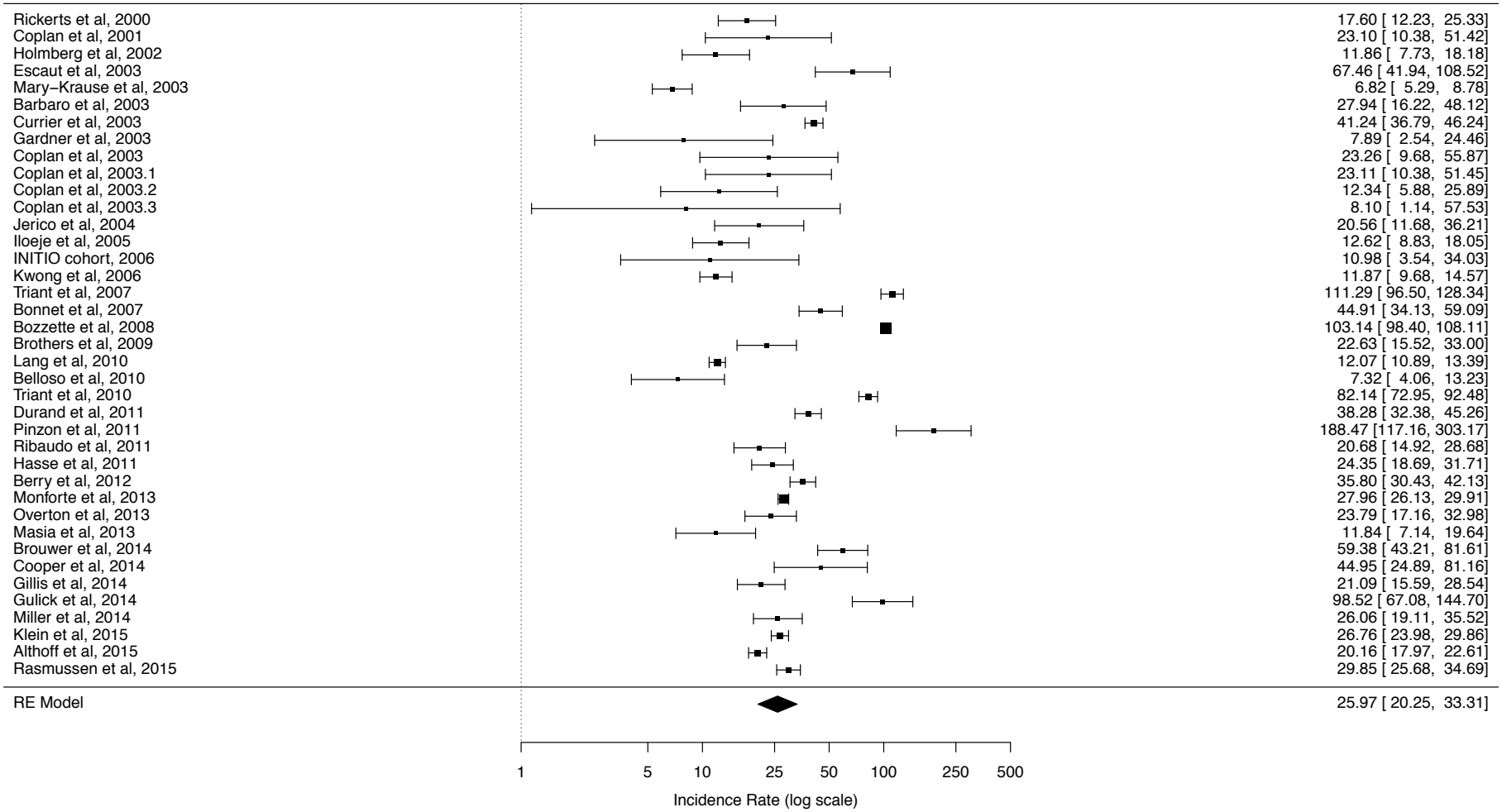


$$DALY\ due\ to\ HIV = Cardiovascular\ DALYs \times PAF$$

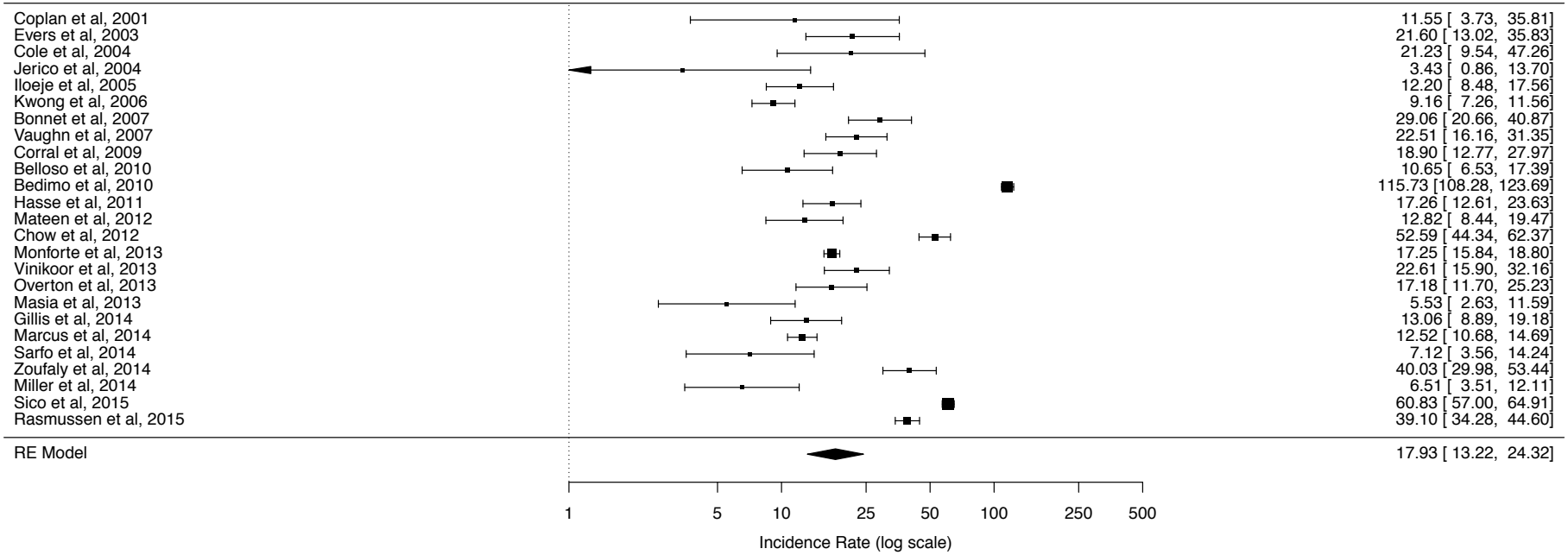
Supplementary figure 2A: Pooled estimate of incident cardiovascular disease



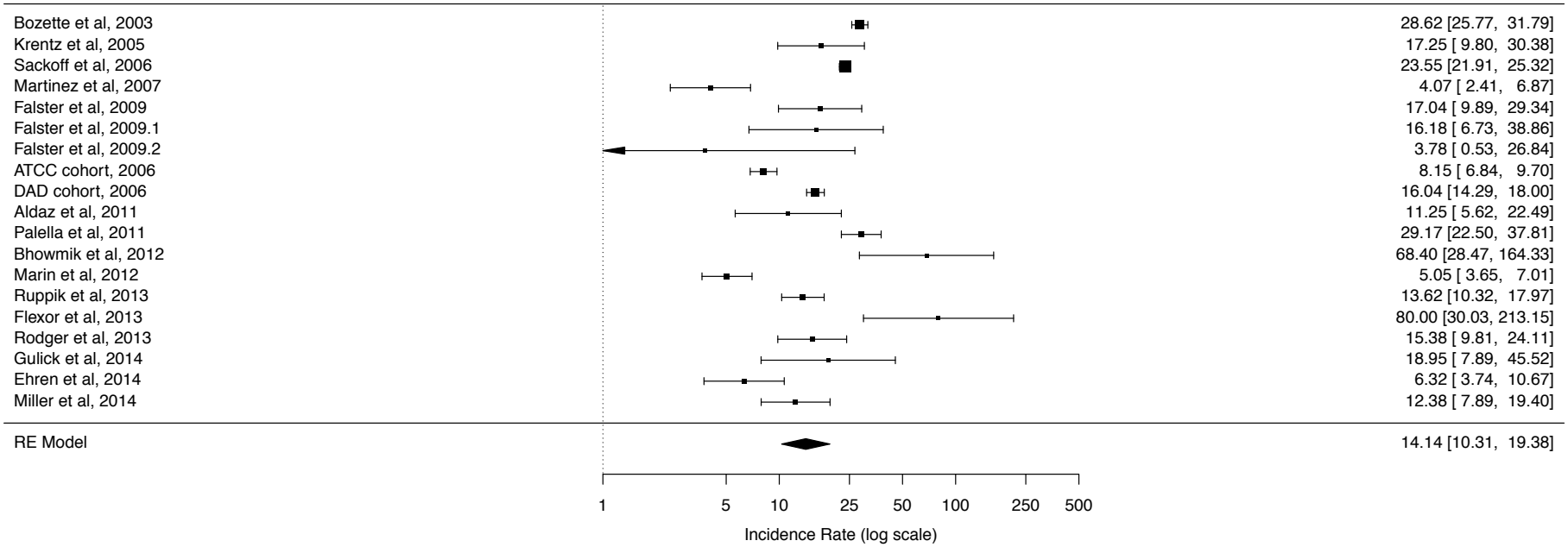
Supplementary figure 2B: Pooled estimate of incident myocardial infarction



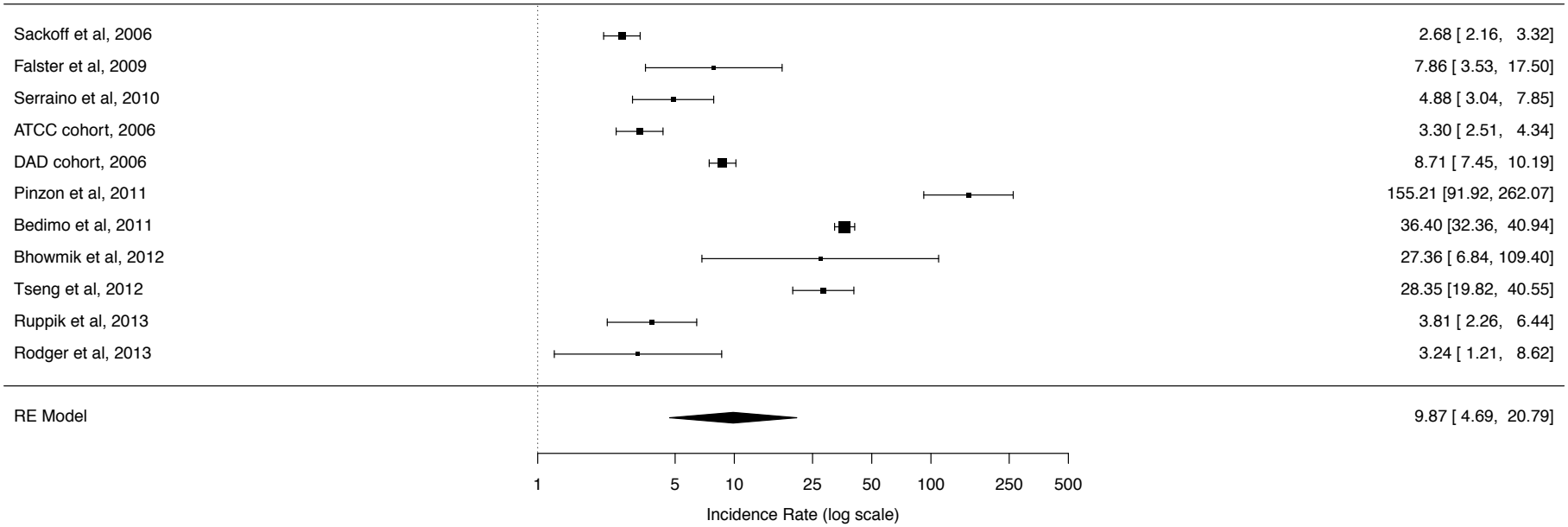
Supplementary figure 2C: Pooled estimate of incident stroke



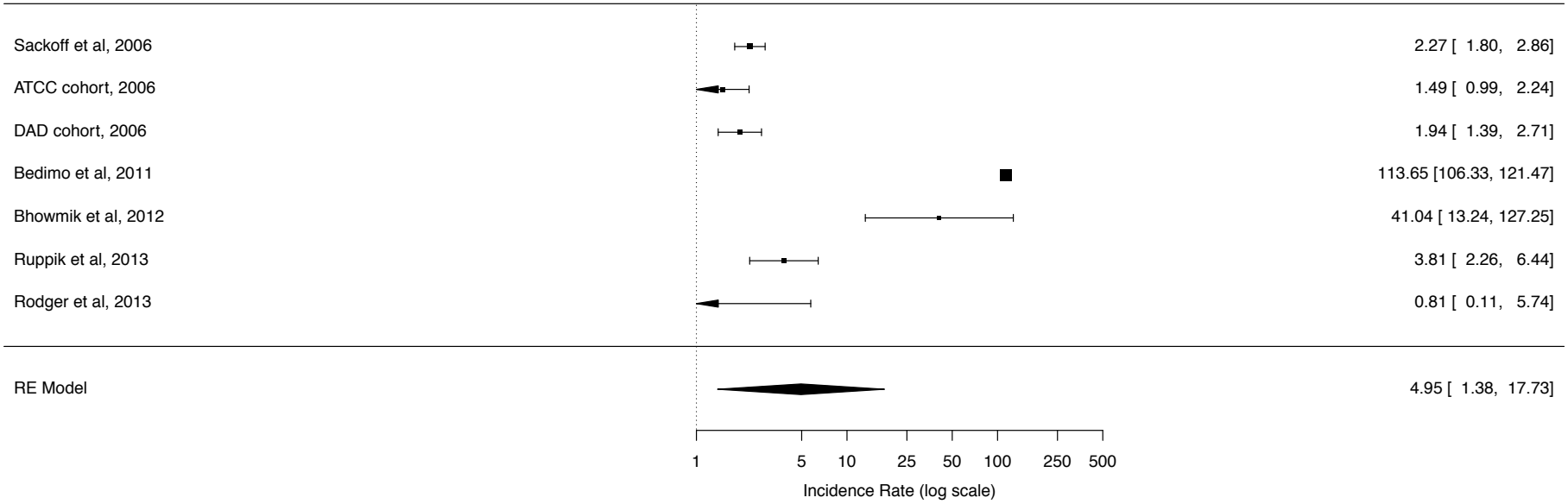
Supplementary figure 2D: Pooled estimate of incident mortality from cardiovascular disease



Supplementary figure 2E: Pooled estimate of incident mortality from myocardial infarction

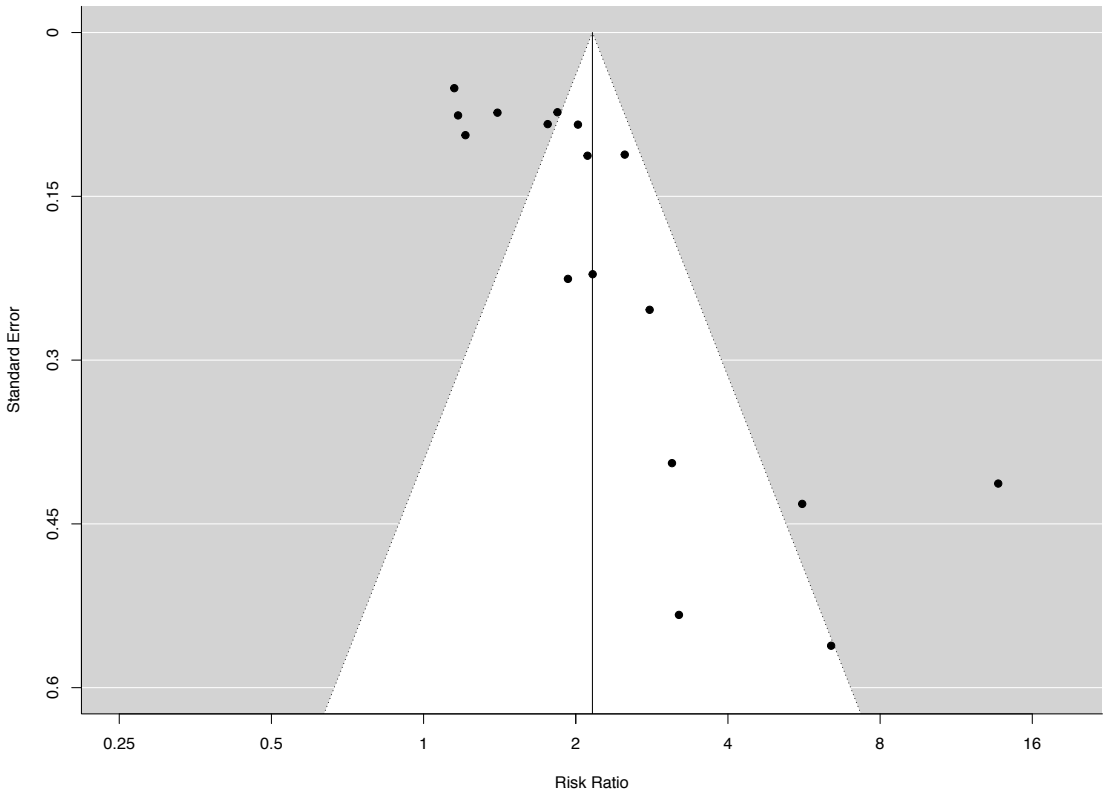


Supplementary figure 2F: Pooled estimate of incident mortality from stroke

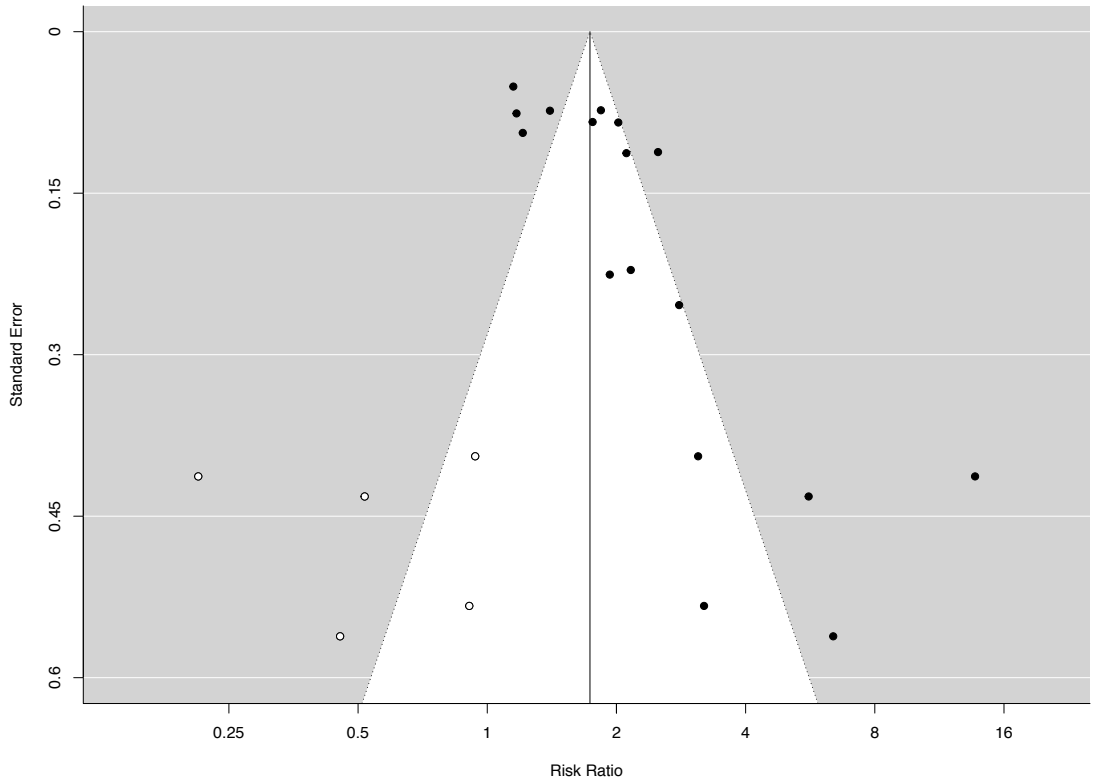


Supplementary figure 3: Funnel plot for the risk ratio showing before (a) and after (b) imputation for small study bias using the 'trim and fill' method. Solid line represents the risk ratio. Solid filled dots in (a) and (b) represent individual study estimates and unfilled dots in (b) represent imputed studies using the trim and fill method

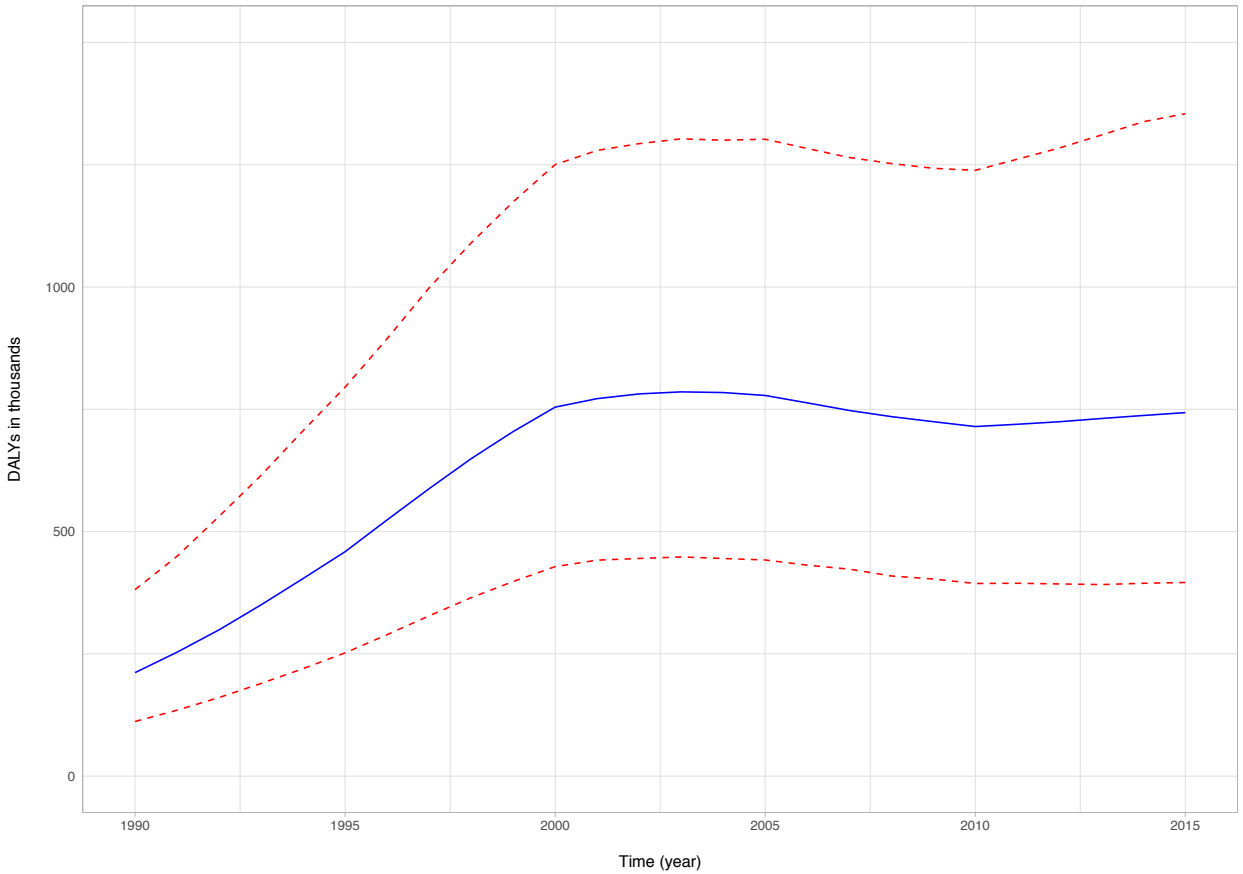
a) Funnel plot for studies providing estimates for the pooled risk ratio



b) Funnel plot for studies providing estimates for the pooled risk ratio (filled black) and imputed studies (unfilled) using the trim and fill method



Supplementary figure 4: Temporal change in the disability-adjusted life years (DALYs) of HIV associated cardiovascular disease in 20 of 21 UNAIDS priority countries



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