THE LANCET

Supplementary webappendix

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Supplement to: The Emerging Risk Factors Collaboration. Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies. *Lancet* 2010; **375:** 2215–2222.

Web Extra Material

Diabetes mellitus, fasting glucose, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies

The Emerging Risk Factors Collaboration

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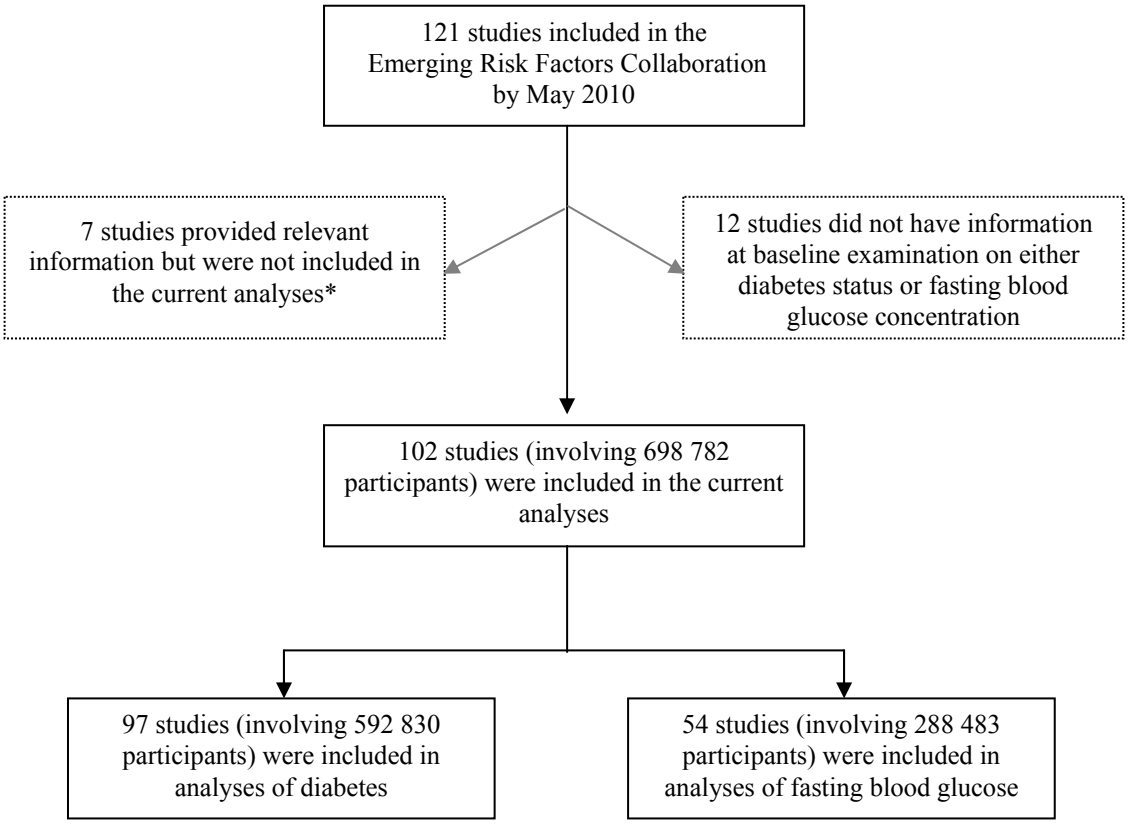
eFigure 1 **Flow diagram showing steps involved in study selection for the current analysis.**

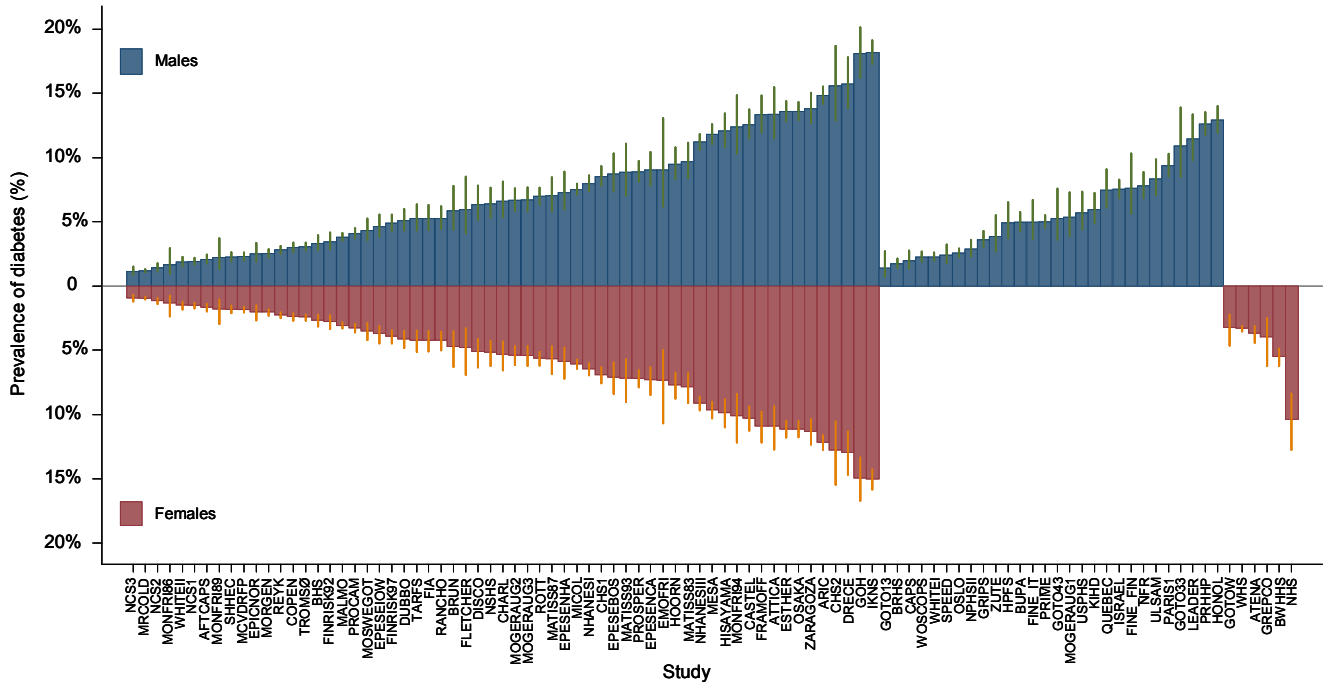


To be eligible for inclusion in the Emerging Risk Factors Collaboration (ERFC), prospective studies (reported variously as observational cohort studies, trials, or analyses of nested case-control or case-cohort subsets) had: (1) data available from baseline measurements of at least one of the relevant markers assessed; (2) at least 1 year of follow-up; (3) participants not selected on the basis of having previous cardiovascular diseases; and (4) information on cause-specific mortality and/or major cardiovascular morbidity collected during follow-up. Studies were prioritized for inclusion if they were known to have recorded at least 20 000 person years at risk. Most eligible studies were identified in previously published meta-analyses, with additional studies identified through updated computer-assisted literature searches of databases, scanning of reference lists, hand-searching of relevant journals and correspondence with authors of relevant reports. Further details of the ERFC (including search strategies, contributing studies, data provision and management, and other characteristics) have been reported previously (*Eur J Epidemiol. 2007;22:839-869*).

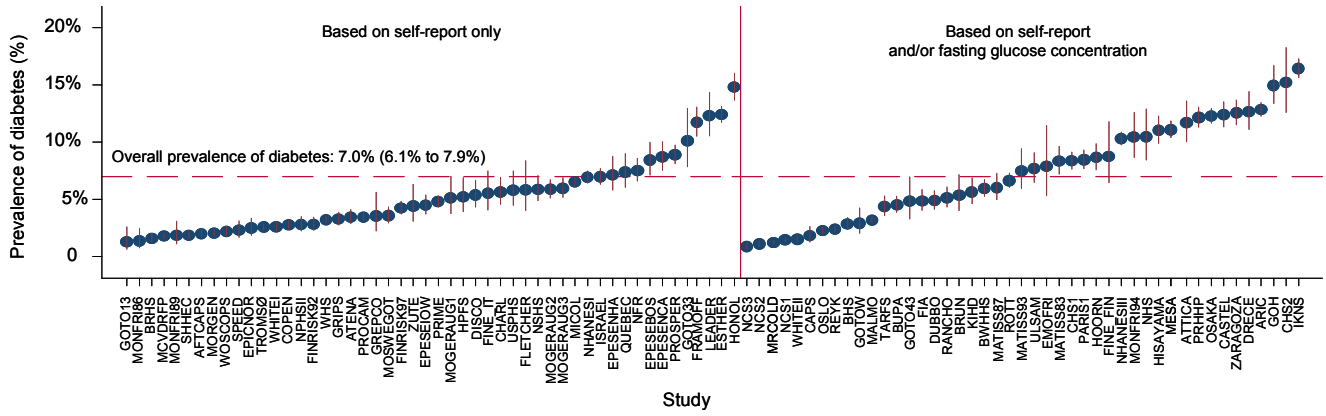
* None of the participants in GLOSTRUP and USPHS2 had a history of diabetes at baseline, and fasting glucose information was not provided. All of the participants with relevant information in NORTH KARELIA and PREVEND had a history of diabetes, and fasting glucose information was not provided. Data from EAS, LASA and WHI-HaBPS had not been fully harmonised by the ERFC coordinating centre at the time analyses were conducted.

eFigure 2 Prevalence of diabetes at the initial survey in 592 830 participants in 97 studies

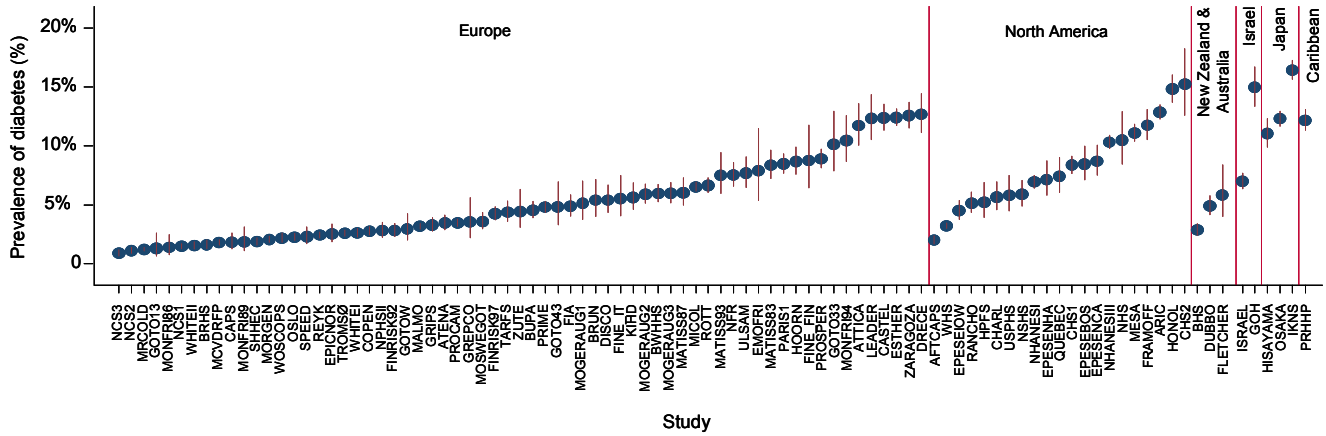
A Age-adjusted prevalence of diabetes, by sex



B Age- and sex-adjusted prevalence of diabetes, by study-specific definition of history of diabetes

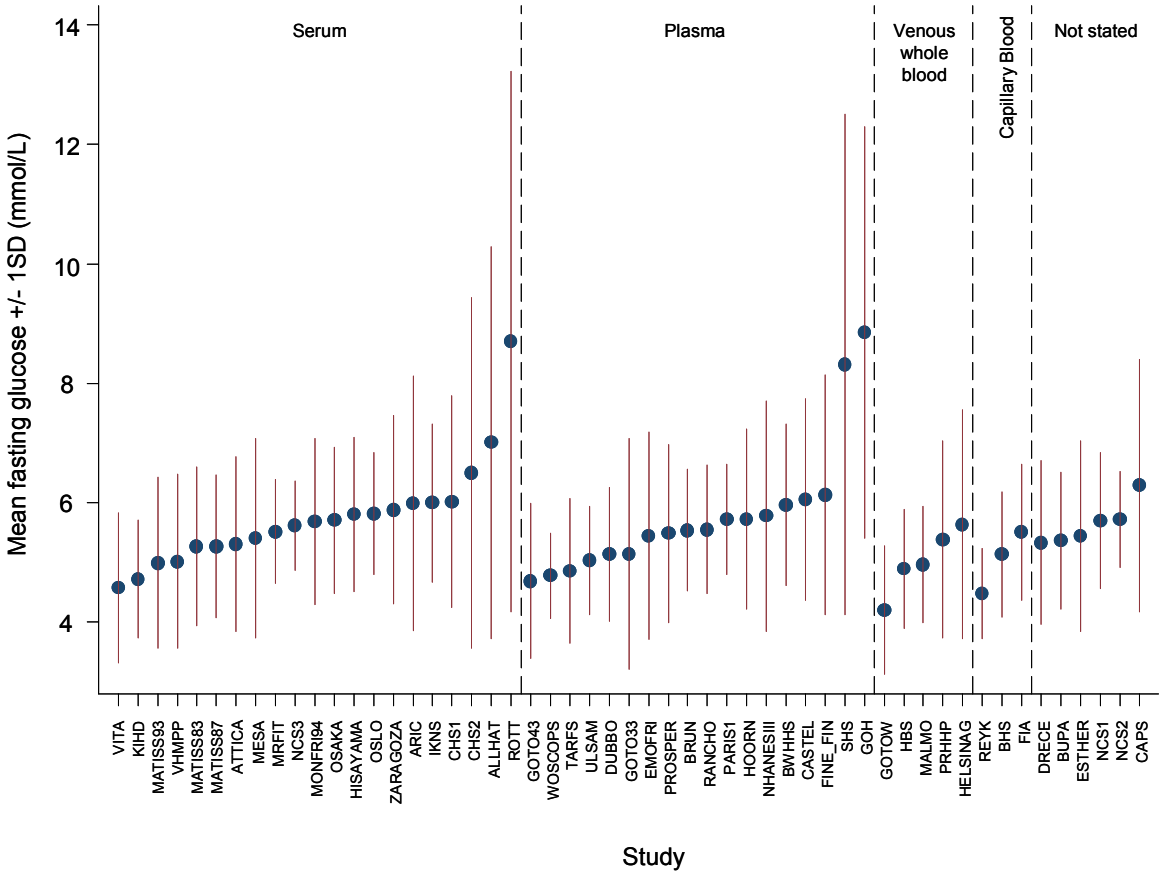


C Age- and sex-adjusted prevalence of diabetes, by geographical region

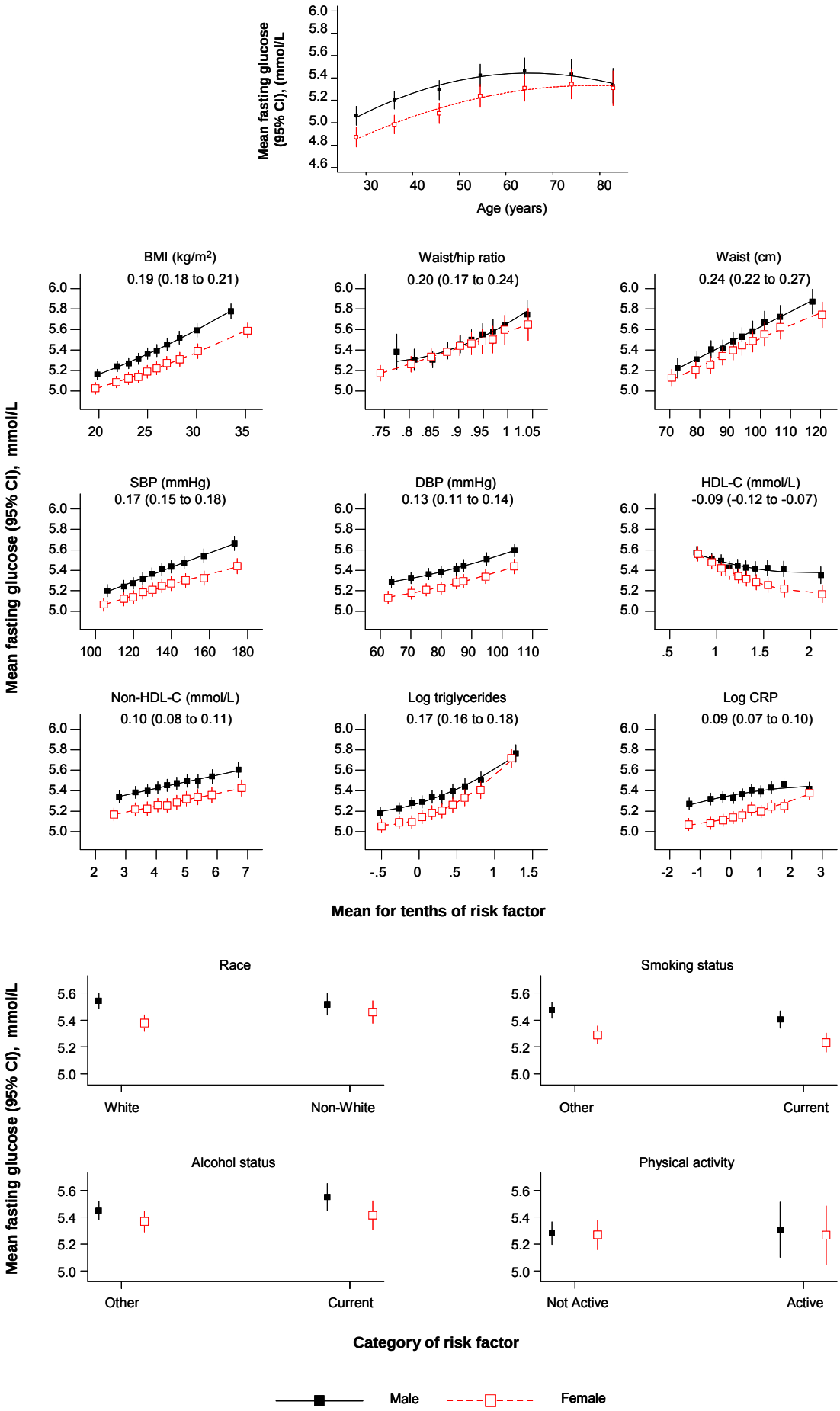


People were classified as having diabetes based on self-report or fasting glucose ≥7 mmol/L. Prevalence was adjusted to age 60. Two studies (ALLHAT and SHS) with adjusted prevalence of diabetes higher than 20% are not presented in this figure.

eFigure 3 Mean fasting glucose concentration at baseline by type of blood sample

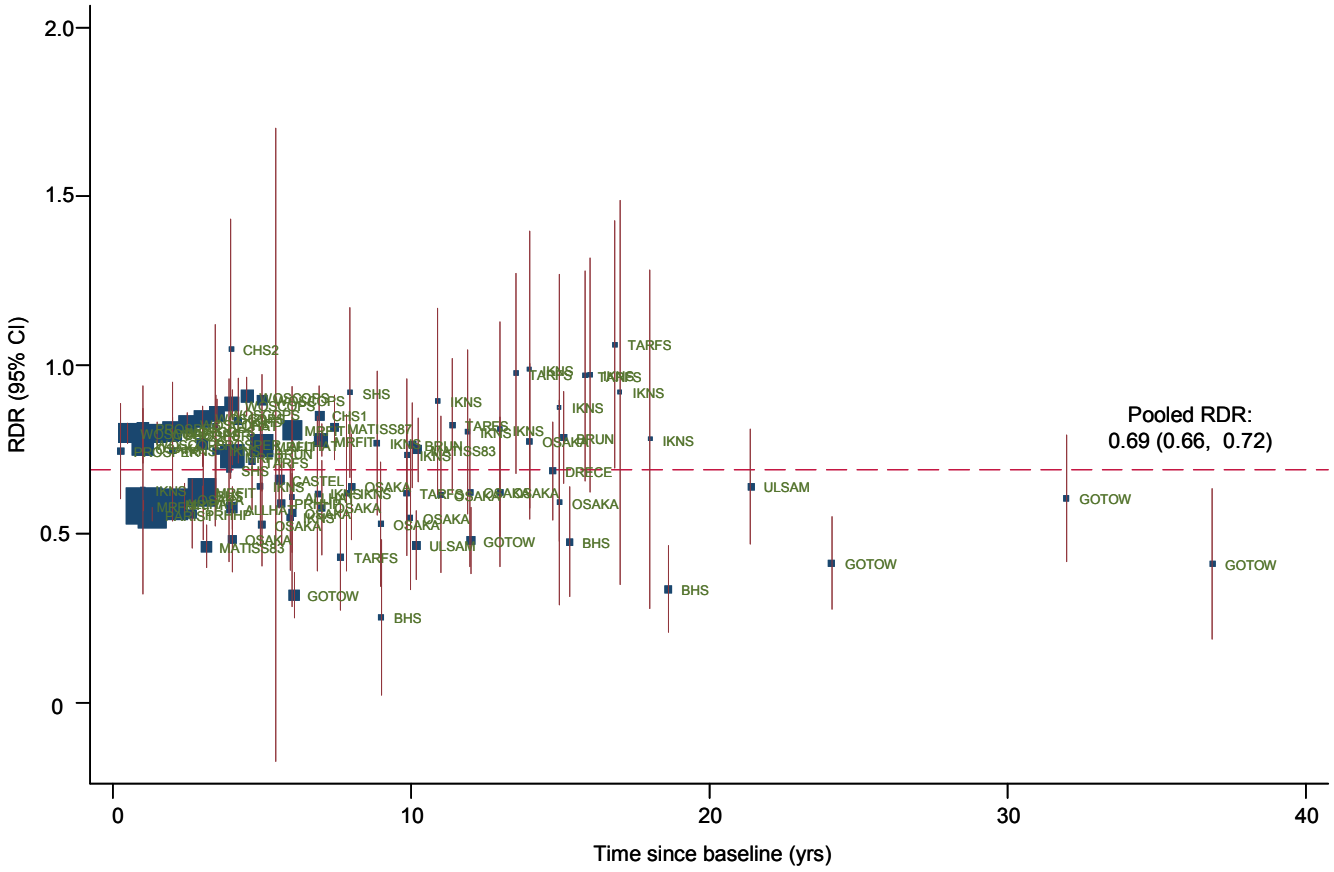


eFigure 4 **Cross-sectional correlates of fasting glucose concentration in people without known diabetes at baseline**



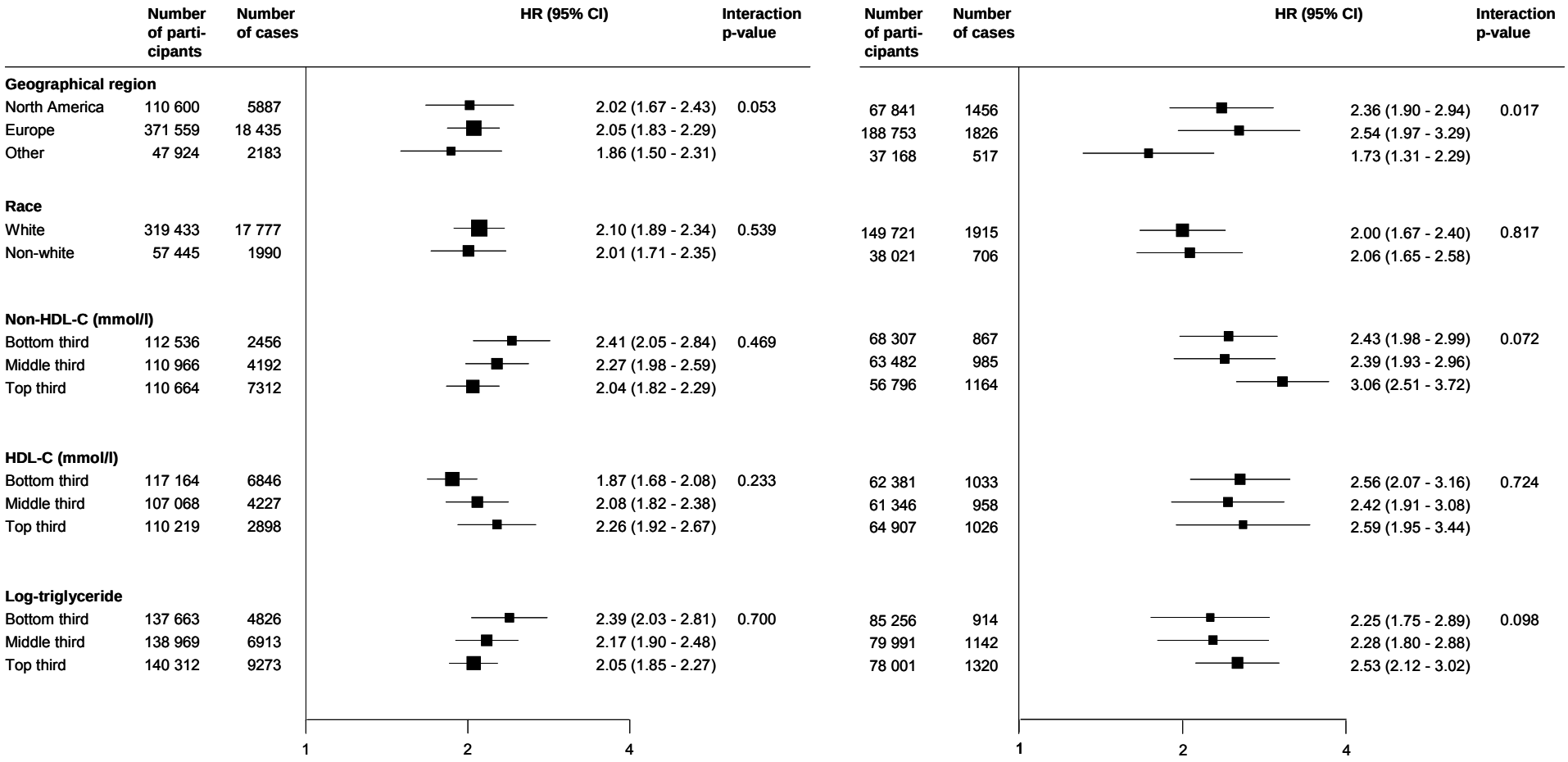
For all correlates except age, response means are adjusted to age 60. For continuous risk markers, values presented are the Pearson's correlation coefficient (95% CI) for the association between the risk marker and fasting glucose concentration in men and women combined.

eFigure 5 **Age- and sex-adjusted regression dilution ratios for fasting glucose measurements in people without known history of diabetes at baseline**



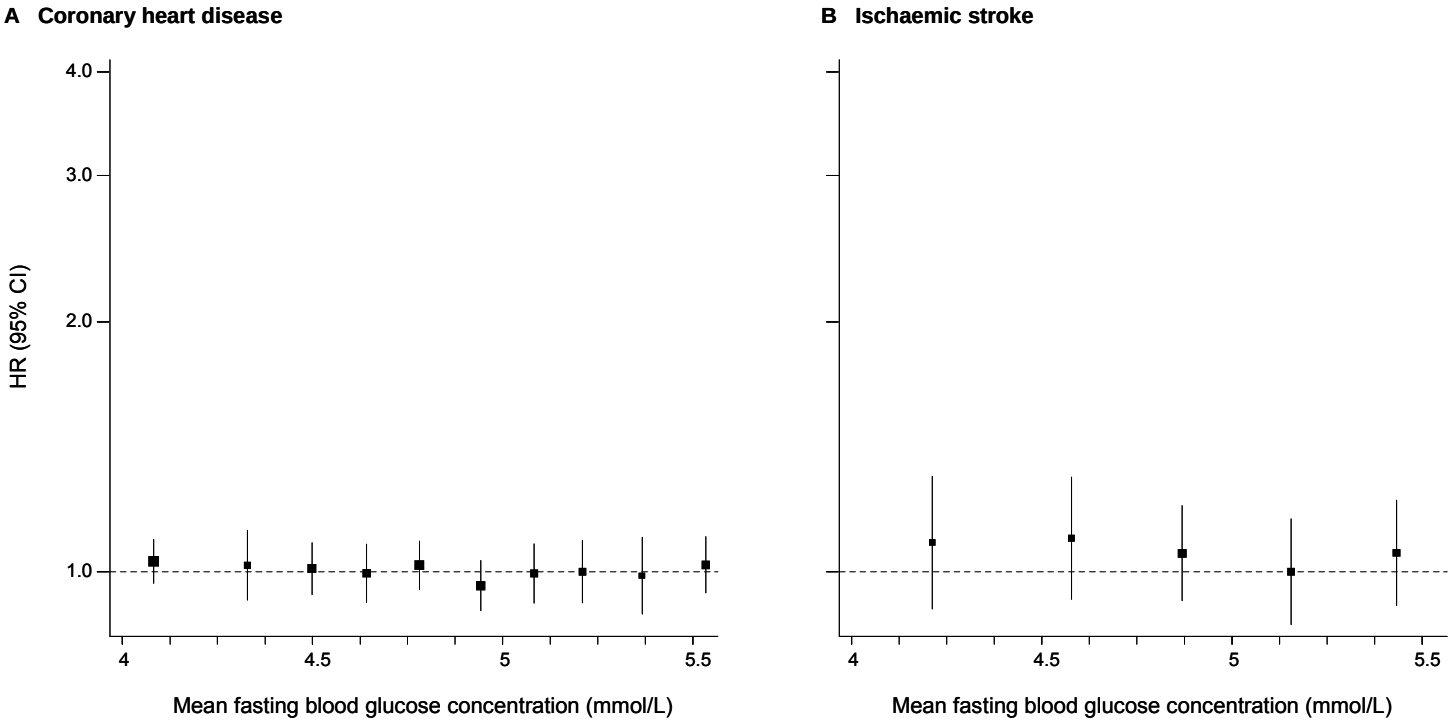
Analyses were based on 201 814 repeat (re-survey) measurements from 65 223 participants with information on fasting glucose concentration from more than one survey. For each re-survey, studies with fewer than 50 participants were excluded. In people with known diabetes at baseline, the pooled RDR was 0.49 (0.44 - 0.54).

eFigure 6 **Hazard ratios for coronary heart disease and ischaemic stroke in people with diabetes at baseline compared with people without diabetes, by additional characteristics**



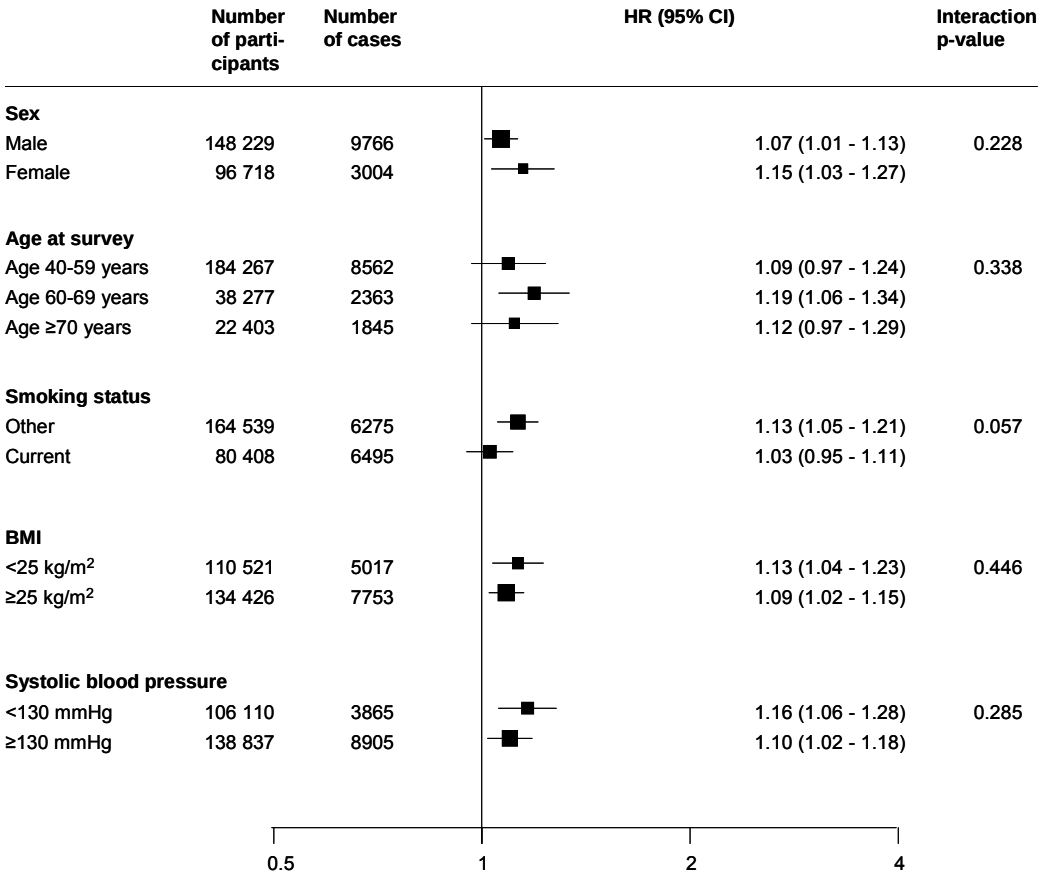
People were classified as having diabetes based on self-report or fasting glucose ≥7 mmol/L. Regression analyses were stratified, where appropriate, by sex and trial group, and adjusted for age, smoking status, BMI and systolic blood pressure. Studies with fewer than 11 cases of an outcome were excluded from the analysis of that outcome. P-values for interaction were calculated from analyses using continuous variables where appropriate. Sizes of data markers are proportional to the inverse of the variance of the hazard ratios. Non-HDL-C: Bottom, middle and top third defined as <3.83, 3.83 to <4.83, and ≥4.83 mmol/L with mean values of 3.17, 4.33, and 5.72 mmol/L respectively. HDL-C: Bottom, middle and top third defined as <1.14, 1.15 to <1.45, and ≥1.45 mmol/L with mean values of 0.96, 1.29, and 1.79 mmol/L respectively. Log-triglycerides: bottom, middle and top third defined as <0.07, 0.08 to <0.52, and ≥0.52 with mean values of -0.24, 0.29, and 0.91 respectively. There was no significant association between overall or sex-specific prevalence of diabetes and risk of coronary heart disease or ischaemic stroke (linear meta-regression P>0.1 for each).

eFigure 7 Hazard ratios for coronary heart disease and ischaemic stroke by baseline fasting glucose concentration between 3.9 and 5.6 mmol/L, in participants without known diabetes at baseline



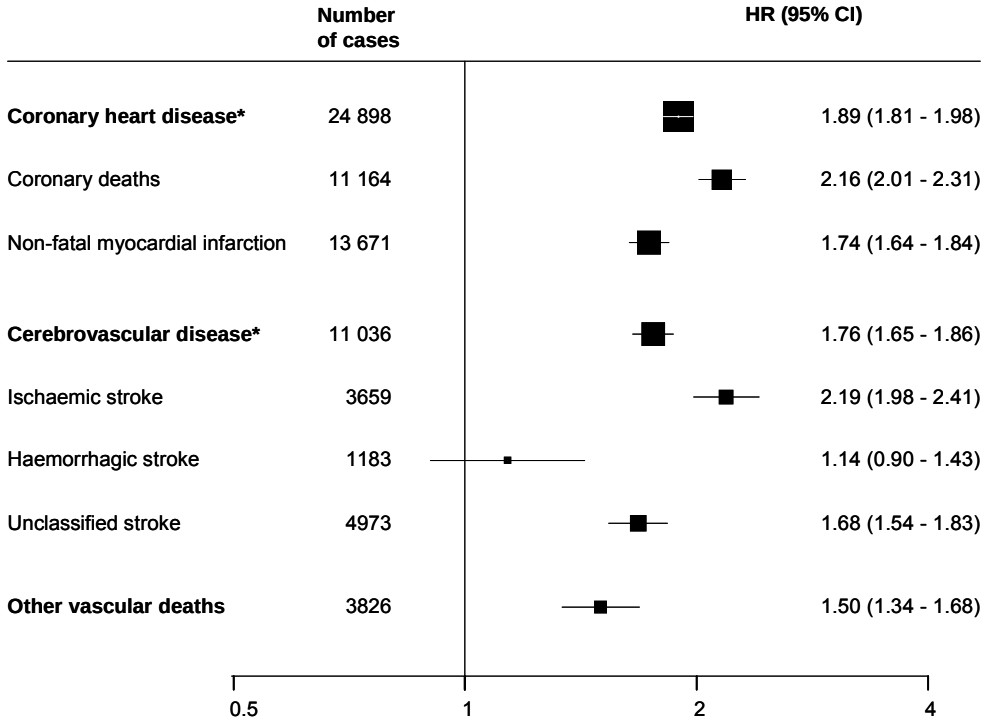
Analyses were based on 179 659 participants (9479 cases) for CHD and 124 414 participants (967 cases) for ischaemic stroke. Participants were classified into tenths of fasting glucose for CHD and fifths for ischaemic stroke. Hazard ratios are plotted against the mean fasting glucose in each group. Reference groups are: the 8th quantile for CHD and the 4th quantile for stroke (ie, the quantile that contains the overall mean). Regression analyses were stratified, where appropriate, by sex and trial group, and adjusted for age, smoking status, BMI and systolic blood pressure. Studies with fewer than 11 cases of an outcome (with fasting glucose between 3.9 and 5.6 mmol/L) were excluded from analysis of that outcome. Sizes of data markers are proportional to the inverse of the variance of the hazard ratios.

eFigure 8 **Hazard ratios for coronary heart disease in people with impaired fasting glucose, by individual-level characteristics**



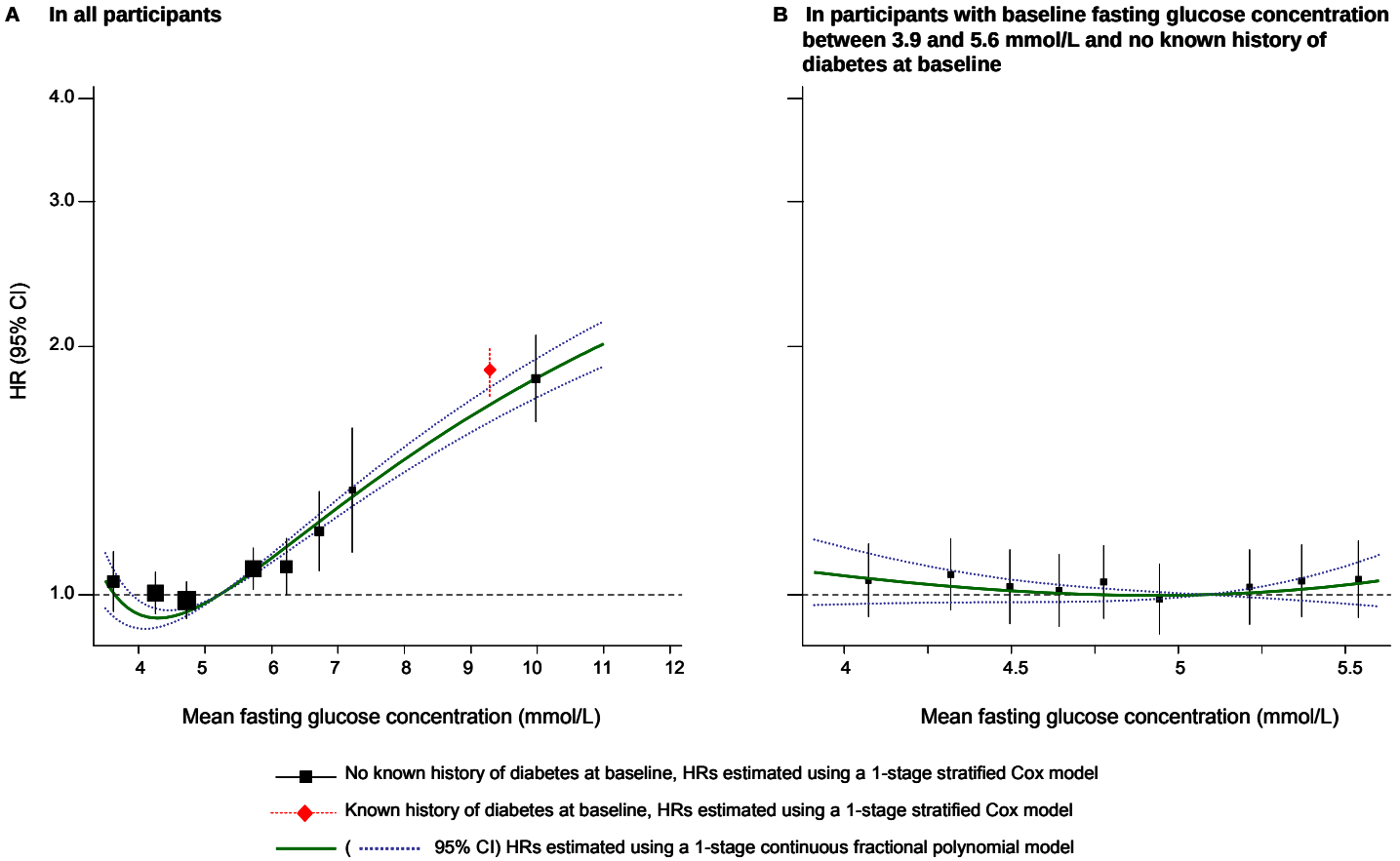
Impaired fasting glucose was defined as those without known diabetes at baseline and fasting glucose values between 5.6 and 6.99 mmol/L (according to ADA criteria). HRs were calculated in reference to people with fasting glucose values below 5.6mmol/L. Regression analyses were stratified, where appropriate, by sex and trial group, and adjusted for age, smoking status, BMI and systolic blood pressure. Studies with fewer than 11 coronary heart disease cases were excluded from analysis. P-values for interaction were calculated from analyses using continuous variables where appropriate. Sizes of data markers are proportional to the inverse of the variance of the hazard ratios. Numbers of participants and cases include people with impaired fasting glucose and those in the reference group.

eFigure 9 **Hazard ratios for vascular outcomes in people with diabetes at baseline compared with people without diabetes, using 1-stage ("fixed-effect") regression models**



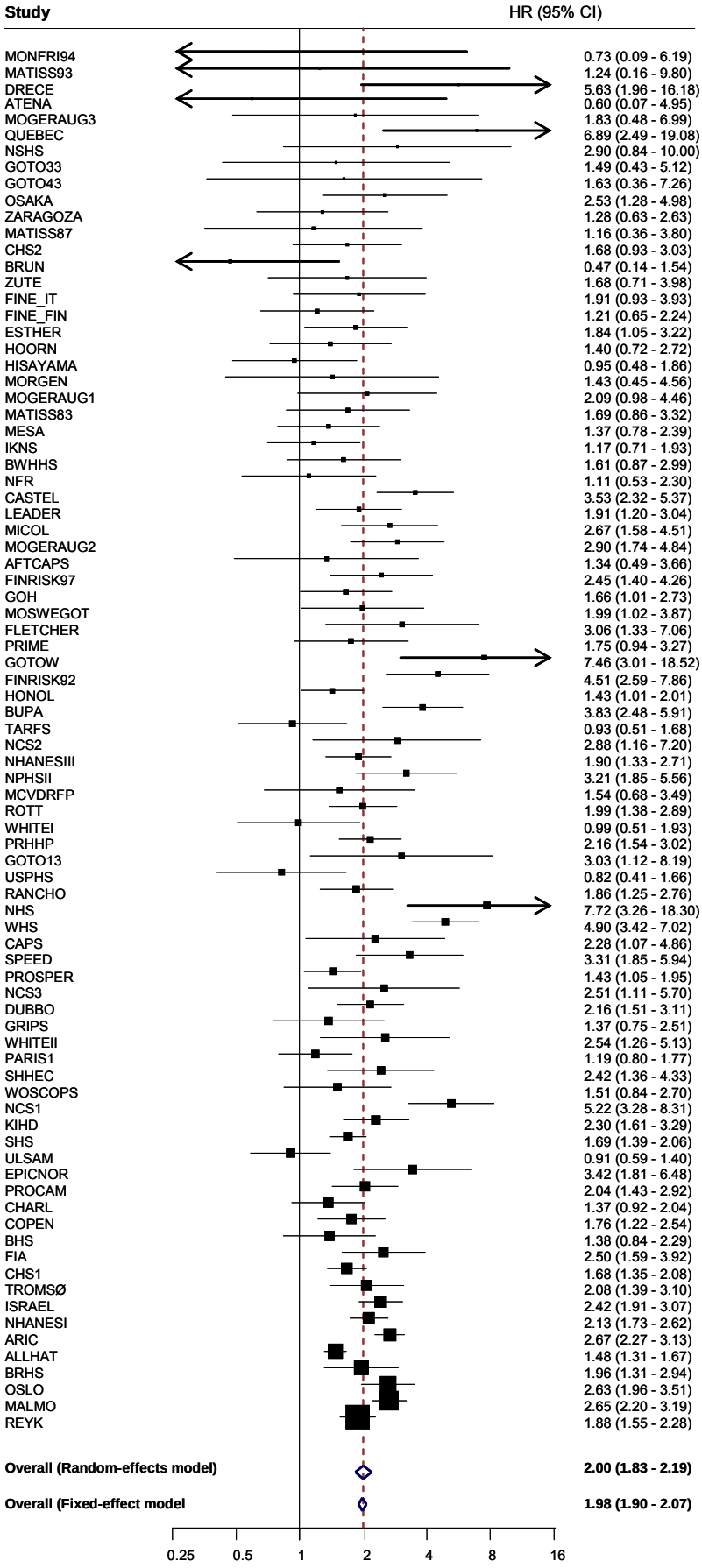
Analyses were based on up to 524 422 participants from up to 82 studies. People were classified as having diabetes based on self-report or fasting glucose ≥7 mmol/L. Regression analyses were stratified, where appropriate, by sex and trial group, and adjusted for age, smoking status, BMI and systolic blood pressure. Studies with fewer than 11 cases of an outcome were excluded from the analysis of that outcome. Sizes of data markers are proportional to the inverse of the variance of the hazard ratios.
*Includes both fatal and non-fatal events

eFigure 10 Hazard ratios for coronary heart disease by baseline fasting glucose concentration using 1-stage ("fixed effect") and continuous regression models



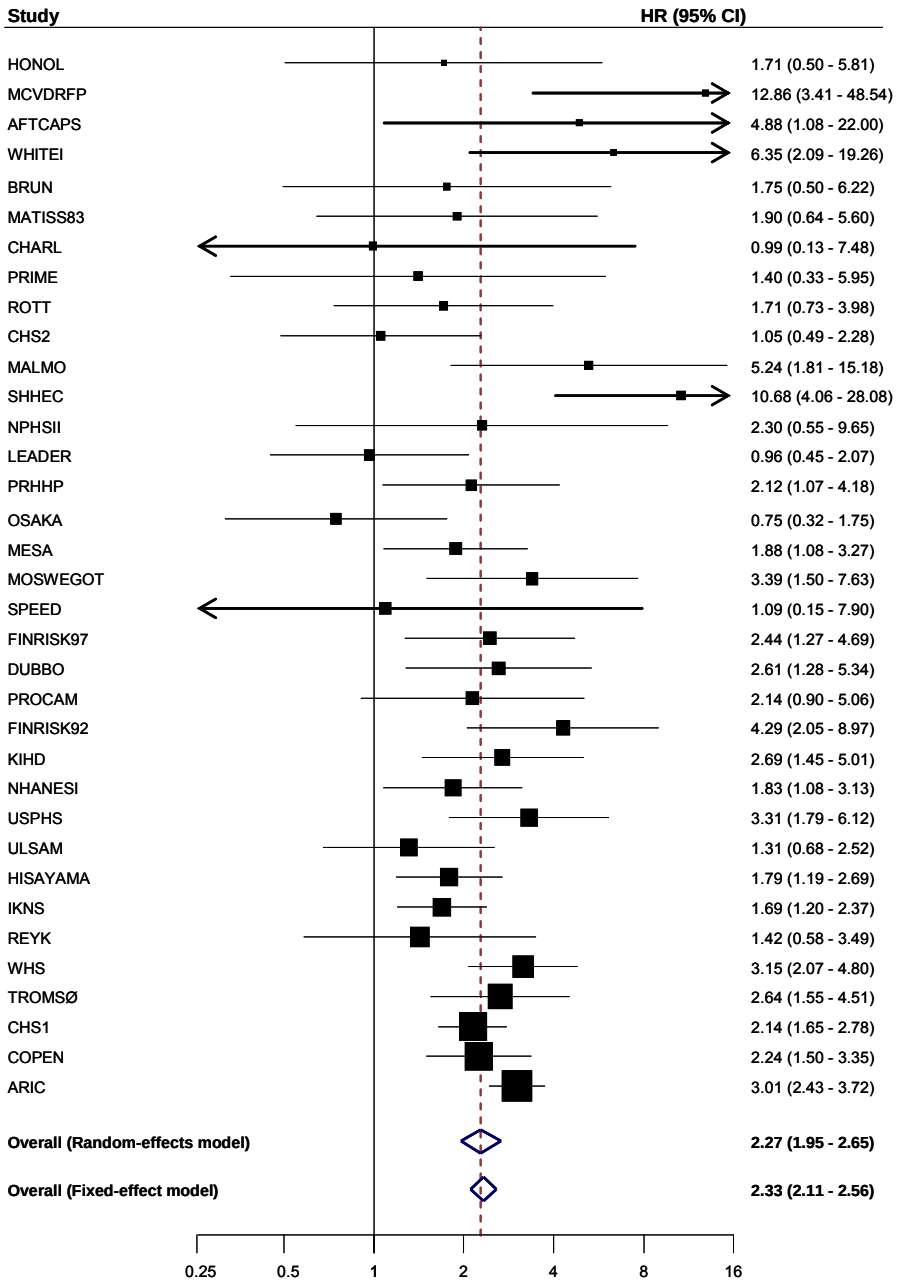
Regression analyses were stratified, where appropriate, by sex and trial group, and adjusted for age, smoking status, BMI and systolic blood pressure. Studies with fewer than 11 CHD cases and all case-control studies were excluded. Sizes of data markers are proportional to the inverse of the variance of the hazard ratios. Analyses in (a) were based on 276 964 participants (14 458 cases). Participants with fasting glucose values in the top and bottom 0.2% were excluded. Participants without known diabetes at baseline are classified into groups of fasting glucose: <4, 4-4.5, 4.5-5, 5-5.5, 5.5-6, 6-6.5, 6.5-7, 7-7.5 and >7.5 mmol/L. The reference group is defined as those without known diabetes with glucose values between 5 – 5.5 mmol/L. Analyses in (b) were based on 178 164 participants (9263 cases). Participants are classified into tenths of fasting glucose. The reference group is the 7th quantile.

eFigure 11 (a) **Study-specific hazard ratios for coronary heart disease in people with diabetes at baseline compared with people without diabetes**



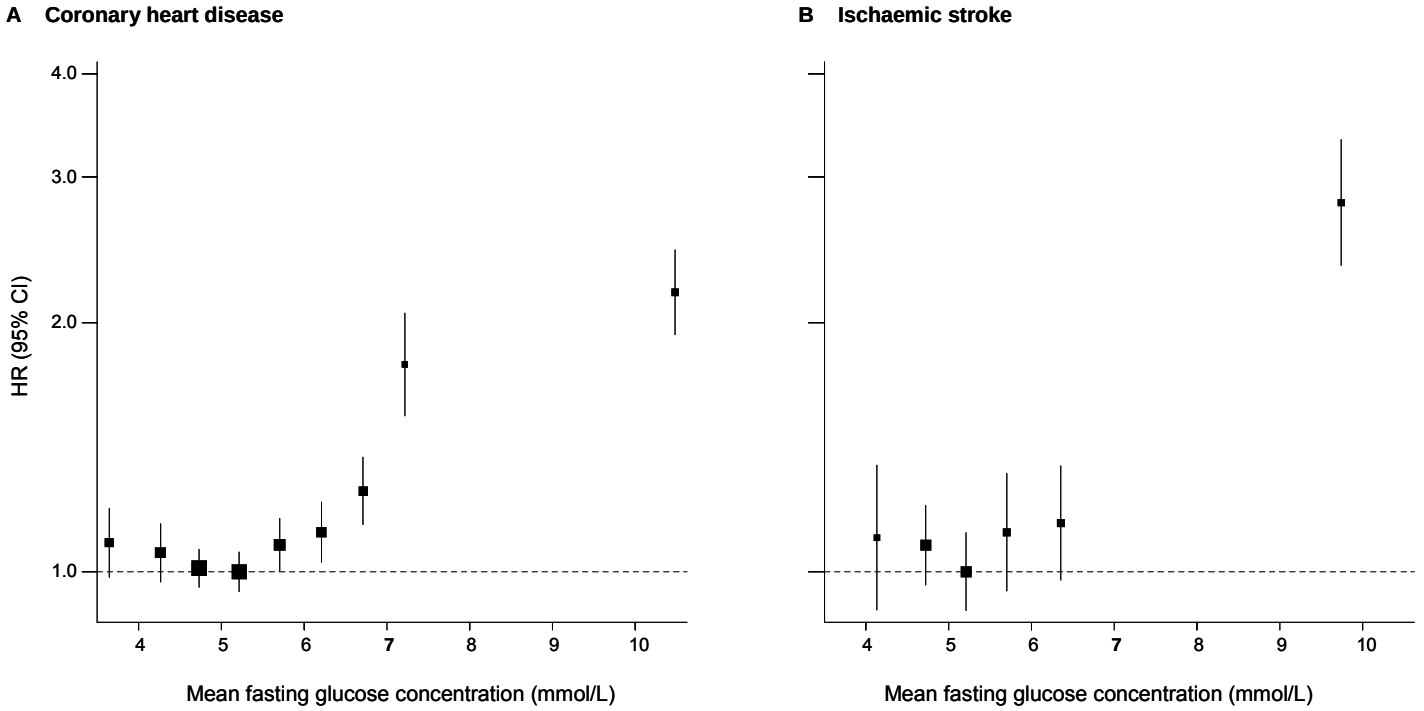
Regression analyses were stratified, where appropriate, by sex and trial group, and adjusted for age, smoking status, BMI and systolic blood pressure. Studies are ordered (top to bottom) by increasing number of CHD cases. Studies with fewer than 11 CHD cases were excluded from analysis. Sizes of data markers are proportional to the inverse of the variance of the hazard ratios.

eFigure 11 (b) **Study-specific hazard ratios for ischaemic stroke in people with diabetes at baseline compared with people without diabetes**



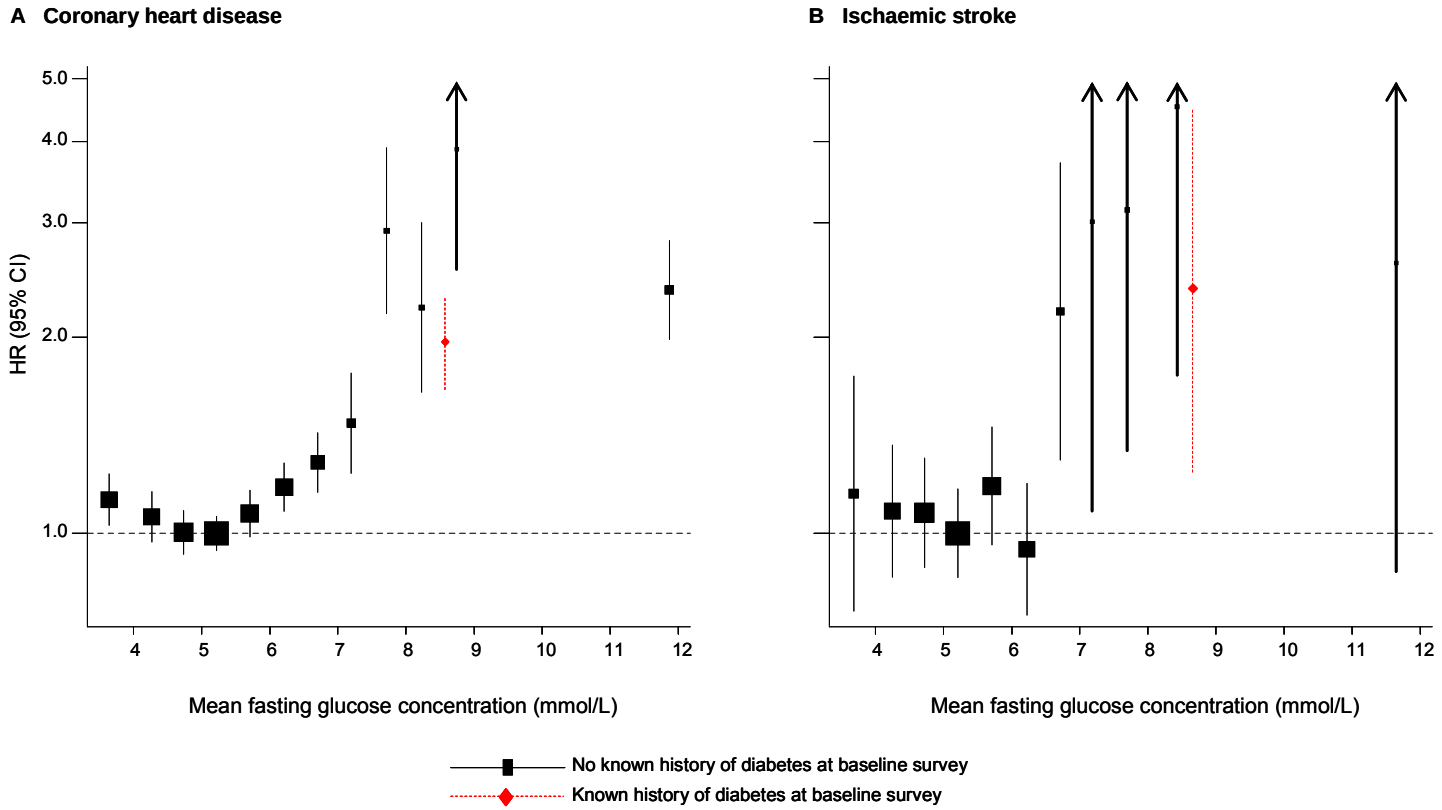
Regression analyses were stratified, where appropriate, by sex and trial group, and adjusted for age, smoking status, BMI and systolic blood pressure. Studies are ordered (top to bottom) by increasing number of ischaemic stroke cases. Studies with fewer than 11 ischaemic stroke cases were excluded from analysis. Sizes of data markers are proportional to the inverse of the variance of the hazard ratios.

eFigure 12 Hazard ratios for coronary heart disease and ischaemic stroke by baseline fasting glucose concentration, ignoring known history of diabetes at baseline



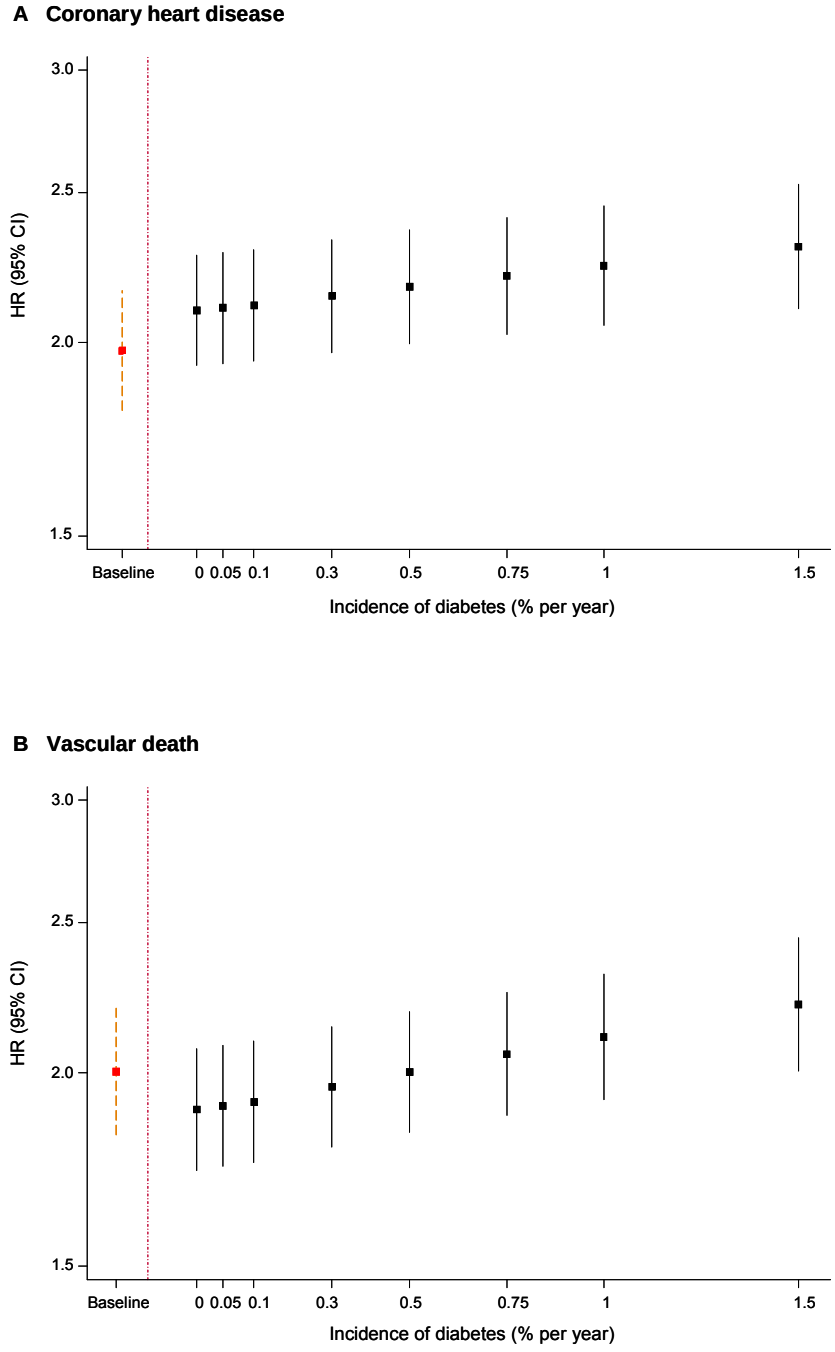
Analyses were based on 279 290 participants (14 814 cases) for CHD and 175 542 participants (1754 cases) for ischaemic stroke. Participants are classified into groups of fasting glucose (coronary heart disease: <4, 4-4.5, 4.5-5, 5-5.5, 5.5-6, 6-6.5, 6.5-7, 7-7.5 and >7.5 mmol/L; ischaemic stroke: <4.5, 4.5-5, 5-5.5, 5.5-6, 6-7, and >7 mmol/L). Hazard ratios are plotted against the mean fasting glucose in each group. The reference group for both outcomes is 5-5.5 mmol/L. Regression analyses were stratified, where appropriate, by sex and trial group, and adjusted for age, smoking status, BMI and systolic blood pressure. Studies with fewer than 11 cases of an outcome were excluded from analysis of that outcome. Sizes of data markers are proportional to the inverse of the variance of the hazard ratios.

eFigure 13 **Hazard ratios for coronary heart disease and ischaemic stroke by baseline fasting glucose concentration, including categories in the range 7-9 mmol/L**



Analyses were based on 279 290 participants (14 814 cases) for CHD and 175 542 participants (1754 cases) for ischaemic stroke. People were classified as having diabetes based on self-report or fasting glucose ≥7 mmol/L. Participants without known diabetes at baseline are classified into groups of fasting glucose (coronary heart disease: <4, 4-4.5, 4.5-5, 5-5.5, 5.5-6, 6-6.5, 6.5-7, 7-7.5, 7.5-8, 8-8.5, 8.5-9 and >9 mmol/L; ischaemic stroke: <4.5, 4.5-5, 5-5.5, 5.5-6, 6-6.5, 6.5-7, 7-7.5, 7.5-8, 8-8.5, 8.5-9 and >9 mmol/L). Hazard ratios are plotted against the mean fasting glucose in each group. The reference group for both outcomes is 5-5.5 mmol/L. Regression analyses were stratified, where appropriate, by sex and trial group, and adjusted for age, smoking status, BMI and systolic blood pressure. Studies with fewer than 11 cases of an outcome were excluded from analysis of that outcome. Sizes of data markers are proportional to the inverse of the variance of the hazard ratios.

eFigure 14 Hazard ratios for coronary heart disease and vascular death in people with diabetes compared with people without diabetes, allowing for time-dependent diabetes status



Analyses were based on 524 422 participants (24 898 cases) for CHD and 501 166 participants (23 706 cases) for vascular deaths. HRs were estimated using a two-stage approach where study-specific HRs were calculated then pooled across studies by random-effects meta-analyses. In the first stage, regression analyses were stratified, where appropriate, by sex and trial group, and adjusted for age, smoking status, BMI and systolic blood pressure. In the baseline analyses (indicated by red markers) diabetes status was defined only according to the baseline measurement. In the other analyses, diabetes status was modelled as a time dependent continuous variable to represent the probability of having diabetes (range between 0 and 1). Multiple records were used for each participant when available. Up to 428 241 repeat measurements from 179 054 participants contributed to the analyses. Diabetes status was assessed at baseline and reassessed at each re-survey. People were classified as having diabetes based on self-report or fasting glucose ≥7 mmol/L. Participants classified as having diabetes kept diabetes status of 1 until time of event. For participants with no known diabetes, the probability of having diabetes was calculated according to the incident rates of diabetes (% per year) based on the cumulative exponential distribution. Case-control and studies with fewer than 11 cases of an outcome were excluded from analysis of that outcome. Sizes of data markers are proportional to the inverse of the variance of the hazard ratios.

eTable 1. Characteristics of the 102 individual studies included in analyses.

Study abbreviation	Location	Population source	Sampling method	No. of participants	Mean (SD) age at survey	Number (%) Male	Number (%) with diabetes at baseline	Mean (SD) fasting glucose (mmol/L) at baseline
Cohort studies								
ARIC	USA	Households	Random	14590	54 (6)	6297 (43)	1589 (11)	6.0 (2.1)
ATENA	Italy	Volunteers	Random	4752	50 (7)	0 (0)	118 (2)	-
ATTICA	Greece	General population	Random	1601	51 (11)	822 (51)	147 (9)	5.3 (1.5)
BHS	Australia	Electoral rolls	Complete	6221	45 (16)	2940 (47)	122 (2)	5.1 (1.1)
BRHS	UK	GP/Health service lists	Random	6810	50 (6)	6810 (100)	77 (1)	-
BRUN	Italy	Population register	Random	817	58 (11)	398 (49)	44 (5)	5.5 (1.0)
BUPA	UK	GP/Health service lists	Complete	20884	47 (8)	20884 (100)	159 (1)	5.4 (1.1)
BWHHS	UK	General population	Random	3030	68 (5)	0 (0)	245 (8)	6.0 (1.4)
CAPS	UK	Electoral rolls	Random	2161	52 (5)	2161 (100)	30 (1)	6.3 (2.1)
CASTEL	Italy	Screening	Complete	2534	73 (5)	963 (38)	484 (19)	6.1 (1.7)
CHARL	USA	Households	Random	1945	50 (11)	866 (45)	83 (4)	-
CHS1	USA	Medicare lists	Random	3872	72 (5)	1483 (38)	495 (13)	6.0 (1.8)
CHS2	USA	Medicare lists	Random	473	72 (5)	178 (38)	104 (22)	6.5 (2.9)
COPEN	Denmark	General population	Random	8414	58 (15)	3587 (43)	247 (3)	-
DISCO	Italy	NR	NR	1932	50 (11)	846 (44)	79 (4)	-
DRECE	Spain	General population	Random	2860	41 (11)	1384 (48)	192 (7)	5.3 (1.4)
DUBBO	Australia	Electoral rolls	Complete	2061	68 (7)	866 (42)	139 (7)	5.1 (1.1)
EMOFRI	Italy	General population	Random	360	55 (6)	176 (49)	24 (7)	5.4 (1.7)
EPESEBOS	USA	General population	Complete	1033	72 (5)	353 (34)	131 (13)	-
EPESEIOW	USA	General population	Complete	1588	73 (5)	511 (32)	115 (7)	-
EPESENCA	USA	General population	Random	1348	72 (5)	448 (33)	177 (13)	-
EPESENHA	USA	General population	Random	814	73 (6)	302 (37)	92 (11)	-
ESTHER	Germany	GP listings	Complete	8042	62 (7)	3394 (42)	1055 (13)	5.4 (1.6)
FINE_FIN	Finland	NR	NR	279	77 (5)	279 (100)	42 (15)	6.1 (2.0)
FINE_IT	Italy	Survivors of an existing cohort	Complete	475	73 (5)	475 (100)	41 (9)	-
FINRISK92	Finland	General population	Random	5263	46 (10)	2438 (46)	96 (2)	-
FINRISK97	Finland	General population	Random	6328	51 (11)	3138 (50)	213 (3)	-
FRAMOFF	USA	Offspring or spouse to Framingham heart study participants	Complete	2854	54 (10)	1269 (44)	291 (10)	-
GOH	Israel	General population	Random	2772	44 (9)	1380 (50)	255 (9)	8.8 (3.4)
GOTO13	Sweden	General population	Complete	766	54 (0)	766 (100)	8 (1)	-

Study abbreviation	Location	Population source	Sampling method	No. of participants	Mean (SD) age at survey	Number (%) Male	Number (%) with diabetes at baseline	Mean (SD) fasting glucose (mmol/L) at baseline
GOTO33	Sweden	General population	Complete	733	51 (0)	733 (100)	54 (7)	5.1 (1.9)
GOTO43	Sweden	General population	Complete	773	50 (0)	773 (100)	26 (3)	4.7 (1.3)
GOTOW	Sweden	General population	Random	1455	47 (7)	0 (0)	27 (2)	4.2 (1.1)
GREPCO	Italy	NR	NR	815	44 (8)	0 (0)	17 (2)	-
GRIPS	Germany	Occupational	Complete	5786	48 (5)	5786 (100)	124 (2)	-
HBS	Finland	Occupational	Complete	1142	60 (4)	1142 (100)	19 (2)	4.9 (1.0)
HELSINAG	Finland	Population register	Random	527	79 (4)	131 (25)	0 (0)	5.6 (1.9)
HISAYAMA	Japan	General population	Complete	2576	59 (12)	1087 (42)	295 (11)	5.8 (1.3)
HONOL	USA	GP/Health service lists	Complete	2571	78 (4)	2571 (100)	651 (25)	-
HOORN	Netherlands	General population	Random	2230	61 (7)	983 (44)	207 (9)	5.7 (1.5)
IKNS	Japan	General population	Complete	8043	58 (10)	3300 (41)	1305 (16)	6.0 (1.3)
ISRAEL	Israel	Occupational	Occupational	7838	49 (7)	7838 (100)	384 (5)	-
KIHD	Finland	General population	Random	2068	53 (5)	2068 (100)	91 (4)	4.7 (1.0)
MALMO	Sweden	Screening	Random	32495	46 (7)	21923 (67)	630 (2)	5.0 (1.0)
MATISS83	Italy	Electoral rolls	Random	2557	51 (10)	1197 (47)	168 (7)	5.3 (1.3)
MATISS87	Italy	Electoral rolls	Random	2113	52 (9)	933 (44)	101 (5)	5.3 (1.2)
MATISS93	Italy	Electoral rolls	Random	1211	49 (9)	588 (49)	66 (5)	5.0 (1.4)
MCVDRFP	Netherlands	General population	Random	23111	42 (10)	10704 (46)	231 (1)	-
MESA	USA	General population	Random	6760	62 (10)	3186 (47)	844 (12)	5.4 (1.7)
MICOL	Italy	Electoral rolls	NR	23196	51 (10)	12810 (55)	1149 (5)	-
MOGERAUG1	Germany	General population	Random	874	54 (6)	874 (100)	37 (4)	-
MOGERAUG2	Germany	General population	Random	4025	53 (12)	1974 (49)	200 (5)	-
MOGERAUG3	Germany	General population	Random	3398	55 (11)	1676 (49)	183 (5)	-
MONFRI86	Italy	NR	NR	1138	49 (9)	556 (49)	11 (1)	-
MONFRI89	Italy	NR	NR	1105	48 (8)	545 (49)	14 (1)	-
MONFRI94	Italy	Electoral rolls	Random	1296	49 (8)	632 (49)	96 (7)	5.7 (1.4)
MORGEN	Netherlands	General population	Random	17739	46 (9)	8063 (45)	226 (1)	-
MOSWEGOT	Sweden	General population	Random	4157	47 (11)	1972 (47)	99 (2)	-
MRCOLD	UK	GP/Health service lists	Random	10521	80 (4)	3937 (37)	271 (3)	-
NCS1	Norway	General population	Complete	24238	42 (4)	11943 (49)	189 (1)	5.7 (1.1)
NCS2	Norway	General population	Complete	13106	42 (4)	6684 (51)	76 (1)	5.7 (0.8)
NCS3	Norway	General population	Complete	10179	42 (4)	5283 (52)	47 (0)	5.6 (0.7)
NFR	Italy	NR	NR	3133	55 (5)	3133 (100)	202 (6)	-

Study abbreviation	Location	Population source	Sampling method	No. of participants	Mean (SD) age at survey	Number (%) Male	Number (%) with diabetes at baseline	Mean (SD) fasting glucose (mmol/L) at baseline
NHANESI	USA	General population	Cluster	11621	49 (15)	4617 (40)	631 (5)	-
NHANESIII	USA	General population	Cluster	12566	54 (16)	5801 (46)	1226 (10)	5.8 (1.9)
NPHSII	UK	GP/Health service lists	Complete	2968	57 (3)	2968 (100)	74 (2)	-
NSHS	Canada	General population	Random	1944	54 (16)	932 (48)	108 (6)	-
OSAKA	Japan	General population or occupational	Complete	12307	52 (10)	8335 (68)	1231 (10)	5.7 (1.2)
OSLO	Norway	General population	Complete & random	17392	44 (6)	17392 (100)	221 (1)	5.8 (1.0)
PARIS1	France	Occupational	Complete	7079	47 (2)	7079 (100)	385 (5)	5.7 (0.9)
PRHHP	Caribbean	General population	Complete	6350	54 (6)	6350 (100)	644 (10)	5.4 (1.7)
PRIME	France/NI	General population	Quota	9582	55 (3)	9582 (100)	385 (4)	-
PROCAM	Germany	Occupational	Complete	20218	44 (10)	14648 (72)	414 (2)	-
QUEBEC	Canada	General population	Random	1307	57 (7)	1307 (100)	90 (7)	-
RANCHO	USA	Households	Complete	1806	68 (11)	744 (41)	133 (7)	5.5 (1.1)
REYK	Iceland	General population	Complete	16840	52 (9)	8060 (48)	322 (2)	4.5 (0.8)
ROTT	Netherlands	General population	Complete	4823	68 (8)	1824 (38)	432 (9)	8.7 (4.5)
SHHEC	UK	GP/Health service lists	Random	10966	49 (7)	5398 (49)	143 (1)	-
SHS	USA	General population	Complete	4131	56 (8)	1614 (39)	2032 (49)	8.3 (4.2)
SPEED	UK	GP/Health service lists	Complete	2126	55 (4)	2126 (100)	41 (2)	-
TARFS	Turkey	Households	Random	3535	43 (13)	1760 (50)	95 (3)	4.9 (1.2)
TROMSØ	Norway	Households	Complete	22568	44 (15)	10597 (47)	380 (2)	-
ULSAM	Sweden	General population	Complete	2280	50 (1)	2280 (100)	122 (5)	5.0 (0.9)
VHMPP	Austria	Health check-up	Complete	66395	49 (13)	32195 (48)	0 (0)	5.0 (1.5)
VITA	Italy	Census lists	Random	9031	51 (8)	4055 (45)	0 (0)	4.6 (1.3)
WHITEI	UK	Occupational	Complete	4013	76 (5)	4013 (100)	191 (5)	-
WHITEII	UK	Occupational	Complete	10191	45 (6)	6802 (67)	92 (1)	6.2 (-)
WHS	USA	Occupational	Complete	28022	55 (7)	0 (0)	770 (3)	-
ZARAGOZA	Spain	GP/Health service lists	Complete	3662	58 (12)	1528 (42)	465 (13)	5.9 (1.6)
ZUTE	Netherlands	General population	Random	390	76 (4)	390 (100)	30 (8)	-
Case-control studies								
USPHS	USA	Occupational	Complete	934	60 (9)	934 (100)	56 (6)	-
EPICNOR	UK	GP/Health service lists	Complete	1422	66 (8)	966 (68)	46 (3)	-
FIA	Sweden	General population	Random	2624	54 (7)	2116 (81)	106 (4)	5.5 (1.1)
FLETCHER	New Zealand	Occupational, electoral rolls	Complete & random	477	57 (12)	405 (85)	27 (6)	-
HPFS	USA	Occupational	Random	736	65 (8)	736 (100)	47 (6)	-

Study abbreviation	Location	Population source	Sampling method	No. of participants	Mean (SD) age at survey	Number (%) Male	Number (%) with diabetes at baseline	Mean (SD) fasting glucose (mmol/L) at baseline
NHS	USA	Occupational	Random	717	60 (6)	0 (0)	77 (11)	-
Clinical trials								
AFTCAPS	USA	Screening	Complete	6577	58 (7)	5587 (85)	127 (2)	-
ALLHAT	USA/Canada/Puerto Rico/US Virgin Islands	General population	NR	28146	66 (8)	13806 (49)	12049 (43)	7.0 (3.3)
LEADER	UK	GP listings	Complete	941	68 (9)	941 (100)	152 (16)	-
MRFIT	USA	Screening	Complete	12840	47 (6)	12840 (100)	425 (3)	5.5 (0.9)
PROSPER	Scotland/Ireland/ Netherlands	Screening	Complete	3253	75 (3)	1350 (42)	477 (15)	5.5 (1.5)
WOSCOPS	UK	Screening	Complete	6214	55 (6)	6214 (100)	115 (2)	4.8 (0.7)
Studies with information on history of diabetes at baseline*								
TOTAL (97 studies)				**592830**	**52 (13)**	**332664 (56)**	**38851 (7)**	**5.5 (2.0)**
Studies with information on fasting glucose concentration†								
TOTAL (54 studies)				**288483**	**53 (12)**	**172425 (60)**	**22434 (8)**	**5.4 (1.8)**
All studies								
TOTAL (102 studies)				**698782**	**52 (13)**	**398731 (57)**	**39295 (6)**	**5.4 (1.8)**

*2 studies provided data on previous history of diabetes but were not included in the analyses of diabetes because none of the participants (MRFIT) and all of the participants with history of diabetes information (HBS) had diabetes. 3 studies (HELSINAG, VITA and VHMPP) did not provide data on previous history of diabetes.
†48 studies did not provide information on fasting glucose concentration.

eTable 2 Definitions of outcomes assessed in the current report

Outcome	ICD version	
	ICD-9	**ICD-10**
Myocardial infarction	410, 412	I21, I22
Coronary heart disease	410-414	I20–I25
Ischaemic stroke	433, 434	I63
Haemorrhagic stroke	431	I61
Unclassified stroke*	436	I64
Other cerebrovascular disease	430, 432, 435, 437, 438	F01, I60, I62, I65-I69
Other cardiovascular outcomes	093, 391, 393-405, 415-417, 420-429, 440-444, 446-453, 458, 459, 745-747, 798	G45, I01, I05-I15, I20, I26-I28, I30-I52, I70-I82, I87,I95, I97-I99, Q20-Q28, R96

Corresponding ICD-6, 7 or 8 codes were used for studies that recorded outcomes using earlier ICD versions.
*Unclassified stroke was defined by the ICD codes stated, or as strokes not specified as ischaemic or haemorrhagic by study-specific codes.

eTable 3 Baseline characteristics of participants with information on self-reported diabetes status (with or without supplementary information on fasting glucose)

	Overall summary statistics		
	No of studies	No of participants	Mean (SD) or %
Diabetes status	97	592 830	
Definite	97	38 851	7%
Other	97	553 979	93%
Non-lipid markers			
Age at survey (yrs)	97	592 830	52 (13)
Fasting glucose (mmol/L)	46	182 704	5.6 (1.8)
BMI (kg/m^2)	93	564 889	26 (4)
Waist-to-hip ratio	37	137 552	0.89 (0.08)
Waist (cm)	39	138 225	90 (12)
SBP (mmHg)	92	563 287	136 (19)
DBP (mmHg)	92	564 874	82 (11)
Lipid markers			
Total cholesterol (mmol/L)	91	549 935	5.80 (1.10)
Non-HDL-C (mmol/L)	78	359 519	4.48 (1.12)
HDL-C (mmol/L)	78	359 844	1.34 (0.38)
Log triglycerides	77	440 829	0.32 (0.52)
Apo B (g/L)	27	110 309	1.08 (0.28)
Apo AI (g/L)	26	112 931	1.46 (0.27)
Inflammatory markers			
Log-CRP	40	116 926	0.66 (1.11)
Fibrinogen (g/L)	40	178 774	3.23 (0.71)
Categorical variables			
Sex	97	592 830	
Male	91	332 664	56%
Female	69	260 166	44%
Race	74	417 422	
Non-white	26	61 510	15%
White	68	355 912	85%
Geographical region	97	592 830	
North America	23	1362 88	23%
Europe	65	407 933	69%
Australia	2	8248	1%
New Zealand	1	477	<0.5%
Israel	2	10 610	2%
Japan	3	22 926	4%
Caribbean	1	6348	1%
Smoking status	97	578 291	
Current	97	196 840	34%
Other	97	381 451	66%
Alcohol status	74	411 109	
Current	67	254 896	62%
Other	72	156 213	38%

*2 studies provided data on history of diabetes but were not included in the analyses of diabetes because none of the participants (MRFIT) and all of the participants with history of diabetes information (HBS) had diabetes. A further 93 093 participants had information on fasting glucose concentration at baseline, but no information on self-reported diabetes status.

eTable 4 Summary of vascular outcomes recorded.

Study	No. of partici-pants	Median follow-up (5th & 95th percentiles)	All CVD events	All CVD deaths	All CHD	All CHD deaths	All MI	MI (non-fatal)	MI deaths	All CBVD events	Ischaem. stroke	Ischaem. stroke deaths	Ischaem. stroke (non-fatal)	Haemo-rrhagic stroke	Unclass-ified stroke	Unclass-ified stroke deaths	Unclass-ified stroke (non-fatal)	Other vascular deaths	All-cause mortality
Cohort studies																			
ARIC	14590	14.0 (5.0 to 15.7)	1642	427	876	200	797	676	121	563	454	2	452	56	16	16	0	110	1501
ATENA	4752	6.7 (5.2 to 8.1)	30	9	18	1	18	17	1	4	1	0	1	2	0	0	0	6	40
ATTICA	1601	5.0 (5.0 to 5.0)	30	30	0	0	0	0	0	0	0	0	0	0	0	0	0	0	50
BHS	6221	25.0 (7.1 to 33.2)	957	957	537	537	361	0	361	223	22	22	0	21	147	147	0	120	2045
BRHS	6810	24.5 (4.7 to 25.4)	1858	776	1215	541	1037	674	363	516	7	7	0	13	475	67	408	85	1960
BRUN	817	15.3 (3.9 to 15.5)	101	56	54	31	42	23	19	40	24	9	15	15	0	0	0	7	180
BUPA	20884	23.7 (11.3 to 26.7)	1505	1505	1012	1012	612	0	612	254	31	31	0	37	145	145	0	164	3543
BWHHS	3030	7.3 (3.1 to 8.4)	220	34	99	14	85	85	0	102	0	0	0	1	101	0	101	11	258
CAPS	2161	13.0 (4.0 to 13.0)	295	155	254	114	214	140	74	19	3	3	0	4	9	9	0	15	348
CASTEL	2534	11.2 (2.3 to 14.0)	533	533	97	97	97	0	97	109	0	0	0	0	109	109	0	327	1143
CHARL	1945	23.8 (3.5 to 40.0)	921	575	509	293	356	216	140	251	29	29	0	35	173	43	130	87	1192
CHS1	3872	12.1 (2.0 to 12.9)	1115	271	593	213	593	380	213	466	367	0	367	62	37	2	35	0	1072
CHS2	473	9.1 (1.5 to 9.5)	109	27	54	21	54	33	21	49	40	0	40	5	4	0	4	0	92
COPEN	8414	13.1 (2.4 to 14.9)	1467	396	544	51	493	493	0	628	387	3	384	74	136	23	113	159	1814
DISCO	1932	5.5 (5.5 to 9.5)	12	12	9	9	5	0	5	3	1	1	0	1	1	1	0	0	29
DRECE	2860	16.4 (15.5 to 16.6)	31	31	16	16	8	0	8	6	0	0	0	1	4	4	0	5	140
DUBBO	2061	14.1 (1.8 to 14.9)	541	135	284	63	221	221	0	191	76	0	76	19	87	0	87	43	488
EMOFRI	360	6.8 (6.5 to 7.2)	8	4	2	0	2	2	0	3	2	0	2	1	0	0	0	3	9
EPESEBOS	1033	10.4 (6.4 to 10.9)	190	67	81	20	73	61	12	62	48	0	48	9	3	0	3	41	149
EPESEIOW	1588	10.8 (6.8 to 11.1)	287	122	101	38	82	63	19	117	47	1	46	8	58	12	46	50	266
EPESENCA	1348	10.4 (6.5 to 10.9)	241	79	100	32	82	68	14	100	61	1	60	8	30	4	26	35	196
EPESENHA	814	10.5 (6.3 to 10.8)	179	86	55	7	52	48	4	47	32	0	32	3	12	2	10	60	146
ESTHER	8042	5.0 (2.0 to 5.9)	211	22	78	11	76	67	9	129	3	3	0	1	124	2	122	2	100
FINE_FIN	279	6.8 (0.9 to 10.0)	112	63	71	38	49	33	16	29	8	8	0	1	16	0	16	8	150
FINE_IT	475	9.6 (1.8 to 21.4)	218	150	68	50	48	18	30	106	4	4	0	5	86	36	50	32	343
FINRISK92	5263	11.8 (7.1 to 11.9)	295	60	150	31	134	119	15	123	83	0	83	36	0	0	0	15	244
FINRISK97	6328	6.8 (6.0 to 6.9)	220	58	107	33	93	74	19	93	73	0	73	19	0	0	0	15	208
FRAMOFF	2854	12.0 (4.7 to 14.4)	125	5	83	4	79	79	0	41	36	0	36	5	0	0	0	0	111
GOH	2772	35.0 (14.4 to 36.0)	268	268	121	121	75	0	75	60	2	2	0	5	27	27	0	58	1025
GOTO13	766	23.4 (5.0 to 30.5)	373	43	216	2	216	214	2	117	0	0	0	1	116	0	116	32	253
GOTO33	733	12.8 (5.8 to 13.1)	44	22	27	13	23	14	9	8	0	0	0	0	8	0	8	4	81

Study	No. of partic-ipants	Median follow-up (5th & 95th percentiles)	All CVD events	All CVD deaths	All CHD	All CHD deaths	All MI	MI (non-fatal)	MI deaths	All CBVD events	Ischaem. stroke	Ischaem. stroke deaths	Ischaem. stroke (non-fatal)	Haemo-rrhagic stroke	Unclass-ified stroke	Unclass-ified stroke deaths	Unclass-ified stroke (non-fatal)	Other vascular deaths	All-cause mortality
GOTO43	773	10.0 (7.9 to 10.7)	42	4	28	1	28	27	1	12	9	1	8	1	1	0	1	1	25
GOTOW	1455	32.2 (8.9 to 32.7)	369	131	148	54	148	94	54	179	0	0	0	0	179	35	144	0	408
GREPCO	815	7.9 (7.7 to 8.9)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	5
GRIPS	5786	9.8 (4.8 to 10.0)	449	47	299	0	299	299	0	103	0	0	0	0	103	0	103	43	225
HBS	1142	20.5 (6.0 to 20.5)	113	113	75	75	0	0	0	24	0	0	0	0	24	24	0	0	359
HELSINAG	527	8.3 (1.7 to 11.0)	135	135	56	56	39	0	39	53	28	28	0	3	4	4	0	17	310
HISAYAMA	2576	14.0 (3.2 to 14.0)	356	76	77	10	70	67	3	220	148	1	147	49	0	0	0	27	387
HONOL	2571	6.2 (1.4 to 7.6)	318	113	157	42	146	115	31	135	13	13	0	40	75	4	71	15	569
HOORN	2230	8.8 (3.7 to 9.9)	172	70	73	13	72	60	12	53	3	3	0	4	46	4	42	44	213
IKNS	8043	11.1 (5.1 to 18.6)	495	154	84	47	78	37	41	344	158	21	137	71	90	1	89	63	760
ISRAEL	7838	23.3 (7.9 to 23.9)	1001	1001	733	733	0	0	0	268	0	0	0	0	268	268	0	0	2573
KIHD	2068	20.1 (2.9 to 24.1)	588	61	406	17	399	389	10	153	111	8	103	35	3	0	3	12	348
MALMO	32495	18.2 (7.9 to 22.6)	2418	1185	2047	814	1686	1233	453	144	36	36	0	49	17	17	0	94	3290
MATISS83	2557	18.6 (6.4 to 19.5)	334	195	82	36	75	46	29	99	26	0	26	10	57	2	55	136	410
MATISS87	2113	15.6 (7.0 to 16.2)	175	95	46	24	44	22	22	58	9	0	9	8	39	0	39	67	208
MATISS93	1211	8.3 (6.8 to 9.3)	32	14	14	3	14	11	3	7	1	0	1	2	3	0	3	11	30
MCVDRFP	23111	16.8 (13.6 to 18.9)	454	454	196	196	158	0	158	96	15	15	0	31	32	32	0	86	1770
MESA	6760	4.8 (2.5 to 5.2)	172	21	83	14	69	69	0	83	67	0	67	13	2	1	1	0	143
MICOL	23196	5.9 (4.7 to 7.1)	168	168	120	120	68	0	68	36	7	7	0	3	22	22	0	5	579
MOGERAUG1	874	12.9 (3.6 to 13.4)	108	61	79	32	73	47	26	5	0	0	0	2	2	2	0	19	126
MOGERAUG2	4025	7.9 (2.3 to 8.4)	130	67	105	42	97	63	34	7	1	1	0	1	3	3	0	14	203
MOGERAUG3	3398	3.0 (1.8 to 3.6)	38	27	19	8	17	11	6	5	2	2	0	1	2	2	0	9	59
MONFRI86	1138	16.7 (6.2 to 16.9)	84	49	24	6	24	18	6	17	8	0	8	3	5	0	5	42	133
MONFRI89	1105	13.6 (6.7 to 13.7)	63	35	19	4	19	15	4	14	6	0	6	4	4	1	3	28	79
MONFRI94	1296	8.5 (7.0 to 8.8)	40	13	11	0	11	11	0	17	6	0	6	7	2	0	2	11	40
MORGEN	17739	10.8 (8.5 to 13.1)	150	150	77	77	61	0	61	25	4	4	0	10	4	4	0	24	590
MOSWEGOT	4157	12.9 (7.6 to 18.6)	280	67	143	39	133	104	29	117	66	3	63	17	15	1	14	12	235
MRCOLD	10521	8.5 (1.1 to 11.7)	2766	2766	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6556
NCS1	24238	16.1 (14.4 to 16.7)	553	553	378	378	287	0	287	67	9	9	0	17	12	12	0	84	1448
NCS2	13106	17.3 (15.5 to 17.8)	282	282	195	195	154	0	154	27	2	2	0	6	6	6	0	40	815
NCS3	10179	18.2 (12.1 to 18.8)	474	474	292	292	217	0	217	88	8	8	0	25	24	24	0	73	1011
NFR	3133	10.2 (6.1 to 11.2)	127	127	93	93	63	0	63	27	2	2	0	9	11	11	0	5	340
NHANESI	11621	18.4 (4.7 to 21.0)	1939	1211	1034	655	740	379	361	547	152	36	116	55	290	100	190	189	2747
NHANESIII	12566	8.8 (3.4 to 11.8)	883	883	487	487	185	0	185	176	0	0	0	0	176	176	0	111	2086

Study	No. of partici-pants	Median follow-up (5th & 95th percentiles)	All CVD events	All CVD deaths	All CHD	All CHD deaths	All MI	MI (non-fatal)	MI deaths	All CBVD events	Ischaem. stroke	Ischaem. stroke deaths	Ischaem. stroke (non-fatal)	Haemo-rrhagic stroke	Unclass-ified stroke	Unclass-ified stroke deaths	Unclass-ified stroke (non-fatal)	Other vascular deaths	All-cause mortality
NPHSII	2968	8.3 (3.4 to 10.4)	298	57	195	20	192	175	17	73	39	0	39	7	20	3	17	28	203
NSHS	1944	9.6 (3.3 to 10.0)	109	56	37	37	23	0	23	58	1	1	0	1	55	2	53	14	56
OSAKA	12307	10.2 (3.9 to 18.8)	268	108	43	16	37	27	10	148	60	11	49	27	45	0	45	72	637
OSLO	17392	29.5 (10.9 to 30.5)	2638	2638	1617	1617	1101	0	1101	384	57	57	0	80	172	172	0	443	5944
PARIS1	7079	22.9 (7.6 to 26.1)	603	603	341	341	0	0	0	100	0	0	0	0	100	100	0	0	2083
PRHHP	6350	8.3 (5.1 to 12.0)	384	245	213	88	176	125	51	84	54	43	11	20	5	5	0	64	597
PRIME	9582	5.2 (5.0 to 7.3)	208	37	146	17	141	129	12	42	33	0	33	6	3	0	3	17	185
PROCAM	20218	9.9 (3.9 to 18.9)	742	302	486	119	428	367	61	106	77	9	68	22	7	7	0	136	1000
QUEBEC	1307	5.3 (3.5 to 5.6)	55	13	35	2	35	33	2	9	0	0	0	0	9	0	9	7	51
RANCHO	1806	14.1 (2.0 to 18.1)	515	115	225	3	223	222	1	188	0	0	0	1	178	0	178	41	498
REYK	16840	24.7 (6.3 to 37.1)	4559	2526	3263	1230	2900	2033	867	769	183	183	0	162	244	244	0	344	6717
ROTT	4823	12.0 (3.0 to 14.2)	670	455	250	35	245	215	30	146	39	39	0	23	64	64	0	165	1431
SHHEC	10966	10.0 (6.9 to 10.0)	520	127	364	98	334	266	68	132	37	0	37	12	63	0	63	13	529
SHS	4131	12.4 (2.0 to 14.3)	784	310	449	147	370	302	68	216	8	8	0	10	192	20	172	61	1157
SPEED	2126	16.7 (3.3 to 18.2)	354	195	253	155	232	98	134	77	66	5	61	2	5	5	0	17	478
TARFS	3535	15.6 (4.9 to 18.0)	348	286	243	189	79	54	25	65	1	1	0	0	64	56	8	28	532
TROMSØ	22568	18.8 (5.1 to 19.3)	2138	344	1143	154	1095	989	106	829	610	1	609	101	64	16	48	121	1422
ULSAM	2280	27.9 (6.5 to 35.9)	995	251	592	146	515	446	69	316	195	2	193	56	41	3	38	51	855
VHMPP	66395	9.9 (1.3 to 13.7)	1191	1191	647	647	289	0	289	239	26	26	0	40	133	133	0	139	2568
VITA	9031	3.3 (1.7 to 5.3)	66	21	38	8	37	30	7	19	15	0	15	2	1	1	0	7	87
WHITEI	4013	8.2 (2.0 to 8.4)	471	471	217	217	96	0	96	140	20	20	0	14	73	73	0	85	1234
WHITEII	10191	12.4 (4.8 to 14.1)	346	93	315	62	292	253	39	10	2	2	0	2	4	4	0	10	328
WHS	28022	10.2 (8.4 to 10.8)	622	96	249	10	243	239	4	291	244	0	244	26	2	0	2	53	642
ZARAGOZA	3662	5.1 (4.0 to 5.1)	127	37	59	21	59	38	21	68	16	16	0	0	52	0	52	0	39
ZUTE	390	8.6 (1.1 to 10.1)	124	56	57	20	51	37	14	39	1	1	0	1	34	3	31	25	160
Case-control studies																			
USPHS	934	-	0	0	244	22	244	221	22	0	153	5	147	0	0	0	0	0	0
EPICNOR	1422	7.1 (2.2 to 9.3)	0	0	480	223	261	257	4	0	0	0	0	0	0	0	0	0	0
FIA	2624	4.0 (0.5 to 9.3)	0	0	600	135	600	465	135	0	0	0	0	0	0	0	0	0	0
FLETCHER	477	5.5 (1.8 to 6.4)	0	0	144	0	0	0	0	0	0	0	0	0	0	0	0	0	0
HPFS	736	6.0 (1.2 to 6.0)	0	0	218	32	197	186	11	0	0	0	0	0	0	0	0	0	0
NHS	717	8.0 (1.4 to 8.8)	0	0	239	27	239	212	27	0	0	0	0	0	0	0	0	0	0
Clinical trials																			
AFTCAPS	6577	5.1 (4.3 to 6.7)	190	26	146	4	146	142	4	23	22	0	22	0	1	1	0	12	57

Study	No. of partic-ipants	Median follow-up (5th & 95th percentiles)	All CVD events	All CVD deaths	All CHD	All CHD deaths	All MI	MI (non-fatal)	MI deaths	All CBVD events	Ischaem. stroke	Ischaem. stroke deaths	Ischaem. stroke (non-fatal)	Haemo-rrhagic stroke	Unclass-ified stroke	Unclass-ified stroke deaths	Unclass-ified stroke (non-fatal)	Other vascular deaths	All-cause mortality
ALLHAT	28146	4.4 (0.8 to 6.7)	1669	6	1126	5	1126	1121	5	543	0	0	0	0	543	1	542	0	11
LEADER	941	4.2 (0.8 to 6.2)	182	95	99	63	79	36	43	67	52	7	45	3	12	6	6	11	184
MRFIT	12840	6.9 (4.4 to 7.8)	896	256	767	184	711	583	128	80	5	5	0	4	61	4	57	26	484
PROSPER	3253	3.2 (1.1 to 3.8)	395	88	266	65	201	201	0	115	0	0	0	0	115	9	106	0	243
WOSCOPS	6214	4.8 (2.9 to 6.0)	452	80	371	71	300	300	0	72	0	0	0	0	72	0	72	0	185
Studies with information on history of diabetes at baseline*																			
TOTAL (97 studies)	592830	11.1 (3.2 to 25.9)	49086	25989	28856	12598	23247	16113	7133	12471	4649	681	3967	1466	5522	2044	3478	4438	72100
Studies with information on fasting glucose concentration†																			
TOTAL (54 studies)	288483	10.5 (2.1 to 26.1)	23862	11659	15120	6289	12371	8831	3540	5755	1924	399	1525	684	2670	987	1683	1921	31882
All studies																			
TOTAL (102 studies)	698782	10.8 (2.8 to 25.6)	52765	28964	31288	14406	24848	16737	8110	13113	4754	768	3985	1546	5879	2337	3542	4766	78853

CVD indicates cardiovascular disease; CBVD cerebrovascular disease.

*2 studies provided data on history of diabetes but were not included in the analyses of diabetes because none of the participants (MRFIT) and all of the participants with history of diabetes information (HBS) had diabetes. 3 studies (HELSINAG, VITA and VHMPP) did not provide data on history of diabetes.

†48 studies did not provide information on fasting glucose concentration.

eTable 5 **Hazard ratios for coronary heart disease in people with diabetes compared with people without diabetes, progressively adjusted for baseline levels of several risk factors.**

(a) Adjusted for conventional risk factors.

	Data from studies with complete information on sex, age, smoking, BMI, SBP, HDL-C, non-HDL-C and triglycerides				
With adjustment for ...	**HR (95% CI)**	**χ^2**	**Q statistic (df)**	**P for heterogeneity between studies**	**I^2 (95% CI)**
			264 353 participants; 11 848 cases		
Age	2.06 (1.82, 2.34)	127	206 (60)	<0.0001	71(62-78)
Plus smoking	2.10 (1.85, 2.39)	134	202 (60)	<0.0001	70(62-77)
Plus BMI	2.00 (1.78, 2.25)	131	173 (60)	<0.0001	65(55-74)
Plus SBP	1.91 (1.70, 2.14)	119	163 (60)	<0.0001	63(52-72)
Plus non-HDL-C	1.93 (1.71, 2.16)	123	163 (60)	<0.0001	63(51-72)
Plus HDL-C	1.87 (1.67, 2.09)	119	149 (60)	<0.0001	60(47-70)
Plus log-triglycerides	1.87 (1.67, 2.09)	120	146 (60)	<0.0001	59(45-69)

(b) Adjusted for conventional risk factors and apolipoproteins.

	Data from studies with complete information on sex, age, smoking, BMI, SBP, HDL-C, non-HDL-C and triglycerides				
With adjustment for ...	**HR (95% CI)**	**χ^2**	**Q statistic (df)**	**P for heterogeneity between studies**	**I^2 (95% CI)**
			87 702 participants; 4998		
Age	2.42 (1.91, 3.08)	53	116 (21)	<0.0001	82(74-88)
Plus smoking	2.47 (1.95, 3.13)	57	111 (21)	<0.0001	81(72-87)
Plus BMI	2.29 (1.82, 2.87)	51	98 (21)	<0.0001	78(68-86)
Plus SBP	2.16 (1.73, 2.70)	46	92 (21)	<0.0001	77(66-85)
Plus Apo-B	**2.19 (1.77, 2.71)**	**53**	**82 (21)**	**<0.0001**	**74(61-83)**
Plus Apo-A1	**2.11 (1.71, 2.61)**	**48**	**81 (21)**	**<0.0001**	**74(60-83)**
Plus log-triglycerides	2.08 (1.69, 2.55)	48	75 (21)	<0.0001	72(57-82)

(c) Adjusted for conventional risk factors and waist-to-hip ratio (WHR).

	Data from studies with complete information on sex, age, smoking, BMI, SBP, HDL-C, non-HDL-C and triglycerides				
With adjustment for ...	**HR (95% CI)**	**χ^2**	**Q statistic (df)**	**P for heterogeneity between studies**	**I^2 (95% CI)**
			90 335 participants; 4552 cases		
Age	2.07 (1.76, 2.45)	75	59 (23)	<0.0001	61(39-75)
Plus smoking	2.12 (1.80, 2.51)	78	60 (23)	<0.0001	61(40-75)
Plus WHR	**1.99 (1.72, 2.31)**	**85**	**45 (23)**	**0.0038**	**49(18-68)**
Plus SBP	1.87 (1.62, 2.17)	71	44 (23)	0.0049	48(16-68)
Plus non-HDL-C	1.88 (1.62, 2.18)	68	46 (23)	0.0029	50(20-69)
Plus HDL-C	1.81 (1.57, 2.09)	66	42 (23)	0.0088	45(12-66)
Plus log-triglycerides	1.83 (1.59, 2.12)	68	41 (23)	0.0109	44(10-66)

(d) Adjusted for other vascular risk factors.

With adjustment for ...	**No. of participants**	**No. of events**	**HR (95% CI)**	**Wald χ^2**
Conventional risk factors	129 569	6139	2.00 (1.69, 2.37)	64.7
Plus fibrinogen	129 569	6139	1.95 (1.65, 2.29)	63.6
Conventional risk factors	80 563	4631	1.93 (1.61, 2.32)	50.2
Plus log-CRP	80 563	4631	1.90 (1.59, 2.28)	49.4
Conventional risk factors	144 998	7541	1.81 (1.57, 2.09)	64.8
Plus eGFR	144 998	7541	1.81 (1.57, 2.10)	64.4
Conventional risk factors	96 524	5641	1.65 (1.45, 1.90)	53.1
Plus fasting glucose	96 524	5641	1.54 (1.35, 1.75)	42.4

Conventional risk factors included age, smoking status, BMI, systolic blood pressure, non-HDL-C, HDL-C and log triglycerides. Studies with fewer than 11 events for an outcome were excluded from the analysis of that outcome. All regression analyses were stratified, where appropriate, by sex and trial group.

eTable 6 **Change in metrics of vascular disease risk prediction upon addition of history of diabetes or fasting glucose concentration to a reference model containing conventional risk factors**

Covariate added to reference model	Increment in C-index (95% CI)	Net reclassification improvement (95% CI)	Integrated discrimination improvement (95% CI)
Diabetes	0.0081 (0.0065, 0.0098) P<0.0001	0.0584 (0.0461, 0.0708) P<0.0001	0.0065(0.0052, 0.0078) P<0.0001
IFG in people without diabetes	0.0000 (-0.0000, 0.0001) P=0.243	-0.0050 (-0.0012, 0.0020) P=0.180	0.00001 (0.000006, 0.000013) P<0.0001
Fasting glucose‡ in people without diabetes	0.0002 (-0.0002, 0.0007) P=0.256	-0.0018 (-0.0080, 0.0044) P=0.571	0.0004 (0.0001, 0.0007) P=0.015

Vascular disease was defined as first-ever fatal or non-fatal coronary heart disease or cerebrovascular outcome. The reference model with conventional risk factors (stratified by sex) included age, smoking status, systolic blood pressure, total cholesterol and HDL cholesterol. People were classified as having diabetes based on self-report or fasting glucose ≥7 mmol/L. Impaired fasting glucose (IFG) was defined by ADA criteria (5.6-7 mmol/L)

‡ To accommodate for a non-linear association, fasting glucose concentration was entered as a categorical variable (categories: <4, 4-4.5, 4.5-5, 5-5.5, 5.5-6, 6-6.5 and 6.5-7 mmol/L)

Assessments of the C-index were restricted to 112 913 participants (9973 cases) with information on both history of diabetes and fasting glucose concentration. Of these, 94 268 participants (7860 cases) did not have diabetes at baseline (and contributed to the analyses of fasting glucose). Assessments of net reclassification improvement and integrated discrimination improvement were restricted to 36 093 participants (3865 cases) with information on both history of diabetes and fasting glucose concentration and followed up for at least 10 years. Of these, 31 821 participants (2952 cases) did not have diabetes at baseline and contributed to the analyses of fasting glucose. Only studies recording both fatal and non-fatal events contributed to the reclassification analyses.

eTable 7 Hazard ratios for coronary heart disease and ischaemic stroke in people with diabetes at baseline compared with people without diabetes, progressively adjusted for usual levels of conventional risk factors

With adjustment for ...	Data from studies with complete information on sex, age, smoking, BMI, SBP, HDL-C, non-HDL-C and triglycerides				
	HR (95% CI)	**χ^2**	**Q statistic (df)**	**P for heterogeneity between studies**	**I^2 (95% CI)**
Coronary heart disease	*264 353 participants; 11 848*				
Age	2.06 (1.82, 2.34)	126.7	206 (60)	<0.0001	71 (62-77)
Plus smoking	2.06 (1.82, 2.34)	125.7	206 (60)	<0.0001	71 (62-78)
Plus BMI	2.01 (1.78, 2.27)	127.1	185 (60)	<0.0001	68 (58-75)
Plus SBP	1.87 (1.66, 2.09)	114.4	160 (60)	<0.0001	62 (50-71)
Plus non-HDL-C	1.93 (1.72, 2.17)	124.1	162 (60)	<0.0001	63 (51-72)
Plus HDL-C	1.84 (1.65, 2.05)	117.9	143 (60)	<0.0001	58 (44-68)
Plus log-triglycerides	1.83 (1.64, 2.04)	116.3	139 (60)	<0.0001	57 (42-68)
Ischaemic stroke	*157 315 participants; 2858 cases*				
Age	2.56 (2.15, 3.05)	112.4	47 (25)	0.0047	47 (16-66)
Plus smoking	2.58 (2.16, 3.09)	108.5	49 (25)	0.0025	49 (20-68)
Plus BMI	2.51 (2.12, 2.96)	116.8	43 (25)	0.0150	41 (7-63)
Plus SBP	2.22 (1.90, 2.59)	101.1	37 (25)	0.0542	33 (0-58)
Plus non-HDL-C	2.23 (1.91, 2.60)	102.1	37 (25)	0.0572	33 (0-58)
Plus HDL-C	2.19 (1.89, 2.53)	108.6	34 (25)	0.1158	26 (0-54)
Plus log-triglycerides	2.18 (1.89, 2.52)	113.8	32 (25)	0.1579	22 (0-52)

Note: Studies with fewer than 11 events for an outcome were excluded from the analysis of that outcome. All regression analyses were stratified, where appropriate, by sex and trial group.

eTable 8 Population attributable fraction for vascular death associated with diabetes

Prevalence of diabetes among cases	Population attributable fraction (95% CI)
11.5% (observed)	5.3% (4.6%, 5.9%)
Hypothetical examples	
20%	10.8% (10%, 11.7%)
40%	21.7% (19.9%, 23.4%)

The observed diabetes prevalence among cases of 11.5% (10.0% - 12.9%) corresponds to diabetes prevalence in the general population of 7.0% (6.1% - 7.9%). Regression analyses were stratified, where appropriate, by sex and trial group, and adjusted for age, smoking status, BMI and systolic blood pressure.
Overall population attributable fractions (PAF) presented were calculated by random effects meta-analysis of study specific PAFs. Study specific PAFs were calculated using the formula: **PAF = Pe * (RR-1) / RR**, where Pe is the exposure prevalence among cases and RR is the relative risk.

eTable 9 **Population attributable fraction for vascular death associated with diabetes, after making allowances for misclassification in diabetes status**

	Prevalence of diabetes among cases		
	10%	**20%**	**30%**
Baseline	5.0% (4.5%, 5.5%)	10.0% (9.0%, 10.9%)	15.0 % (13.5%, 16.4%)
Incident rate of diabetes (% per year)			
0%	4.7% (4.2%, 5.2%)	9.4% (8.4%, 10.3%)	14.2% (12.7%, 15.5%)
0.1%	4.8% (4.3%, 5.2%)	9.6% (8.6%, 10.5%)	14.3% (12.9%, 15.7%)
0.3%	4.9% (4.4%, 5.3%)	9.8% (8.8%, 10.7%)	14.7% (13.2%, 16.0%)
0.5%	5.0% (4.5%, 5.4%)	10.0% (9.1%, 10.9%)	15% (13.6%, 16.3%)
1%	5.3% (4.8%, 5.7%)	10.5% (9.6%, 11.4%)	15.8% (14.4%, 17.0%)
1.5%	5.5% (5.0%, 5.9%)	11.0% (10%, 11.8%)	16.5% (15%, 17.7%)

Analyses used HRs estimated from analyses of time dependent diabetes status described in eFigure 13.

eAppendix 1. List of studies' acronyms

AFTCAPS, Air Force/Texas Coronary Atherosclerosis Prevention Study
ALLHAT, Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial
ARIC, Atherosclerosis Risk in Communities Study
ATENA, cohort of Progetto CUORE
ATTICA, ATTICA Study
BHS, Busselton Health Study
BRHS, British Regional Heart Study
BRUN, Bruneck Study
BUPA, BUPA Study
BWHHS, British Women's Heart and Health Study
CaPS, Caerphilly Prospective Study
CASTEL, Cardiovascular Study in the Elderly
CHARL, Charleston Heart Study
CHS-1, cohort of Cardiovascular Health Study (CHS)
CHS-2, cohort of Cardiovascular Health Study (CHS)
COPEN, Copenhagen City Heart Study
CUORE, Progetto CUORE
DISCO, District of Sezze Chronic Disease Control Programme, cohort of Risk Factors and Life Expectancy Pooling Project (RIFLE)
DRECE, Diet and Risk of Cardiovascular Disease in Spain
DUBBO, Dubbo Study of the Elderly
EMOFRI, cohort of Progetto CUORE
EPESEBOS, The Established Populations for the Epidemiologic Study of the Elderly Studies, Boston
EPESEIOW, The Established Populations for the Epidemiologic Study of the Elderly Studies, Iowa
EPESENCA, The Established Populations for the Epidemiologic Study of the Elderly Studies, North Carolina
EPESENHA, The Established Populations for the Epidemiologic Study of the Elderly Studies, New Haven
EPICNOR, EPIC Norfolk Study
ESTHER, Epidemiologische Studie zu Chancen der Verhütung, Früherkennung und Therapie chronischer Erkrankungen in der älteren Bevölkerung
FIA, First myocardial infarction in Northern Sweden
FINE-FIN, Finland, Italy and Netherlands Elderly Study - Finland cohort
FINE-IT, Finland, Italy and Netherlands Elderly Study – Italian cohort
FINRISK-92, Finrisk Cohort 1992
FINRISK-97, Finrisk Cohort 1997
FLETCHER, Fletcher Challenge Blood Study
FRAMOFF, Framingham Offspring Study
GLOSTRUP, Glostrup Study
GOH, The Glucose Intolerance, Obesity and Hypertension Study
GOTO13, Göteborg 1913 Study
GOTO33, Göteborg 1933 Study
GOTO43, Göteborg 1943 Study
GOTOW, Population Study of Women in Gothenburg, Sweden
GREPCO, cohort of Risk Factors and Life Expectancy Pooling Project (RIFLE)
GRIPS, Göttingen Risk Incidence and Prevalence Study
HBS, Helsinki Businessmen Study
HELSINAG, Helsinki Aging Study
HISAYAMA, Hisayama Study
HONOL, Honolulu Heart Program
HOORN, Hoorn Study
HPFS, Health Professionals Follow-up Study
IKNS, Ikawa, Kyowa, and Noichi Study
ISRAEL, Israeli Ischaemic Heart Disease Study
KIHD, Kuopio Ischaemic Heart Disease Study
LASA, Longitudinal Aging Study Amsterdam
LEADER, Lower Extremity Arterial Disease Event Reduction Trial
MALMO, Malmö Preventative Project
MATISS-83, cohort of Progetto CUORE
MATISS-87, cohort of Progetto CUORE
MATISS-93, cohort of Progetto CUORE
MCVDRFP, Monitoring of CVD Risk Factors Project
MESA, Multi-ethnic Study of Atherosclerosis
MICOL, cohort of Risk Factors and Life Expectancy Pooling Project (RIFLE)
MOGERAUG1, MONICA/KORA Augsburg Surveys S1

MOGERAUG2, MONICA/KORA Augsburg Surveys S2
MOGERAUG3, MONICA/KORA Augsburg Surveys S3
MONFRI-86, cohort of Progetto CUORE
MONFRI-89, cohort of Progetto CUORE
MONFRI-94, cohort of Progetto CUORE
MORGEN, Monitoring Project on Chronic Disease Risk Factors
MOSWEGOT, MONICA Göteborg Study
MRCOLD, MRC Study of Older People
MRFIT, Multiple Risk Factor Intervention Trial 1
NCS 1, 2 and 3, Norwegian Counties Studies
NFR, cohort of Risk Factors and Life Expectancy Pooling Project (RIFLE)
NHANES I, First National Health and Nutrition Examination Survey
NHANES III, Third National Health and Nutrition Examination Survey
NHS, Nurses' Health Study
NORTH KARELIA, North Karelia Project
NPHSII, Northwick Park Heart Study II
NSHS, Nova Scotia Health Survey
OSAKA, Osaka Study
OSLO, Oslo Study
PARIS1, Paris Prospective Study I
PREVEND, Prevention of Renal and Vascular Endstage Disease Study
PRHHP, Puerto Rico Heart Health Program
PRIME, Prospective Epidemiological Study of Myocardial Infarction
PROCAM, Prospective Cardiovascular Münster Study
PROSPER, Prospective Study of Pravastatin in the Elderly at Risk
QUEBEC, Quebec Cardiovascular Study
RANCHO, Rancho Bernardo Study
REYK, Reykjavik Study
RIFLE, Risk Factors and Life Expectancy Pooling Project
ROTT, The Rotterdam Study
SHHEC, Scottish Heart Health Extended Cohort
SHS, Strong Heart Study
SPEED, Speedwell Study
TARFS, Turkish Adult Risk Factor Study
TROMSØ, Tromsø Study
ULSAM, Uppsala Longitudinal Study of Adult Men
USPHS, U.S. Physicians Health Study
USPHS2, U.S Physicians Health Study 2
VHMPP, Vorarlberg Health Monitoring and Promotion Programme
VITA, Vicenza Thrombophilia and Athrosclerosis Project
WHI-HaBPS, Women's Health Initiative – Hormones and Biomarkers Preventing Stroke Study
WHITE I, Whitehall I Study
WHITE II, Whitehall II Study
WHS, Womens Health Study
WOSCOPS, West of Scotland Coronary Prevention Study
ZARAGOZA, Zaragosa study
ZUTE, Zutphen Elderly Study

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