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Supplementary appendix

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Supplement to: Prospective Studies Collaboration and Asia Pacific Cohort Studies Collaboration. Sex-specific relevance of diabetes to occlusive vascular and other mortality: a collaborative meta-analysis of individual data from 980 793 adults from 68 prospective studies. *Lancet Diabetes Endocrinol* 2018; published online May 8. http://dx.doi.org/10.1016/S2213-8587(18)30079-2.

Sex differences in diabetes-associated mortality: Meta-analysis of 20,000 occlusive vascular deaths in 1 million adults

Supplementary Appendix, Table of Contents

Webtable 1: Study characteristics

	Median year of screening	No. participants	No. occlusive vascular deaths	Men, %	Mean age (years) at: Screening	Mean age (years) at: Occlusive vascular death	Diabetes, %	Mean (SD): BMI, kg/m^2	Mean (SD): SBP, mmHg	Mean (SD): DBP, mmHg	Mean (SD): Total cholesterol, mmol/L	Mean (SD): HDL cholesterol, mmol/L	Current smoker, %
Europe													
Belgian Inter-university Research on Nutrition & Health (BIRNH)	1983	10027	131	52	48	70	2.0	25.9 (4.0)	134 (19)	81 (12)	6.1 (1.2)	1.4 (0.4)	---
British Regional Heart Study (BRHS)	1979	7347	443	100	50	62	1.2	25.5 (3.2)	145 (21)	82 (13)	6.3 (1.0)	---	41
British United Provident Association (BUPA)	1981	5235	95	100	46	62	0.9	25.0 (2.7)	130 (16)	82 (11)	6.2 (1.2)	1.3 (0.4)	21
Caerphilly and Speedwell	1981	1750	99	100	52	61	1.7	26.0 (3.5)	140 (18)	88 (12)	5.7 (1.1)	1.1 (0.3)	44
CB project	1977	48652	239	48	39	51	0.8	24.6 (3.4)	130 (17)	79 (11)	5.4 (1.1)	---	52
Centre d'Investigations Preventives et Cliniques (IPC)	1977	179090	381	57	41	62	5.9	23.8 (3.4)	131 (14)	80 (10)	5.6 (1.1)	---	30
Copenhagen City Heart Study	1977	12575	519	45	52	69	1.7	25.1 (4.1)	137 (22)	83 (12)	6.1 (1.2)	1.5 (0.4)	59
Finish Mobile Clinic Survey	---	39098	3522	54	41	69	1.5	25.2 (3.8)	142 (23)	80 (14)	6.6 (1.4)	---	34
FINRISK	1983	37009	1853	48	43	63	2.5	26.1 (4.2)	143 (21)	87 (12)	6.4 (1.3)	1.4 (0.4)	31
Glostrup Population Studies	1969	9031	185	50	48	70	2.0	24.8 (4.0)	127 (19)	79 (11)	6.1 (1.2)	1.5 (0.4)	52
Gothenburg Prospective Study of Women	1963	1400	69	0	47	70	0.8	24.0 (3.7)	133 (22)	85 (11)	6.8 (1.2)	---	41
Israeli Ischaemic Heart Disease Study	---	9687	942	100	49	67	5.5	25.7 (3.3)	135 (20)	84 (11)	5.4 (1.0)	0.9 (0.2)	51
Norwegian Counties Study	1975	46738	908	50	42	54	0.6	24.9 (3.6)	134 (17)	83 (11)	6.3 (1.3)	---	42
Northwick Park Heart Study (NPHS)	1973	3034	125	71	46	67	0.0	24.9 (3.2)	138 (22)	85 (14)	6.0 (1.2)	---	38
Oslo	1970	15683	762	100	45	57	0.9	24.7 (2.9)	136 (16)	87 (11)	6.9 (1.3)	---	46
Paris Prospective Study	1982	7455	212	100	47	64	2.7	25.9 (3.3)	141 (21)	80 (14)	5.8 (1.1)	---	74
Prospective Cardiovascular Munster Study (PROCAM)	1983	13578	101	76	47	58	4.5	26.0 (3.4)	131 (19)	85 (11)	5.8 (1.1)	1.3 (0.4)	30
Renfrew/Paisley	1975	10202	835	45	54	67	1.1	25.6 (3.8)	148 (23)	85 (13)	6.1 (1.1)	---	51
Scottish Heart Health Study (SHHS)	1986	11117	170	50	49	59	1.3	25.7 (4.0)	132 (20)	82 (12)	6.4 (1.3)	1.5 (0.4)	36
Caerphilly and Speedwell	1980	1786	101	100	54	64	1.5	25.5 (3.1)	138 (22)	86 (13)	5.9 (1.2)	1.1 (0.4)	38
Tromso	1979	14339	102	52	36	54	0.4	23.7 (3.2)	126 (15)	81 (10)	5.9 (1.2)	1.6 (0.5)	---
United Kingdom Heart Disease Prevention Project (UKHDPP)	1971	8724	1033	100	49	65	1.1	25.4 (3.2)	139 (19)	84 (12)	5.6 (1.0)	---	51
Whitehall	1968	18144	1340	100	52	64	0.9	24.7 (3.0)	136 (21)	85 (14)	5.1 (1.2)	---	42
West Scotland	1971	5079	533	86	47	64	0.6	25.0 (3.2)	134 (17)	83 (10)	5.8 (1.0)	---	56
Subtotal	**1980**	**516780**	**14700**	**61**	**43**	**65**	**3.0**	**24.7 (3.6)**	**134 (19)**	**82 (12)**	**5.9 (1.3)**	**1.4 (0.4)**	**38**

	Median year of screening	No. participants	No. occlusive vascular deaths	Men, %	Mean age (years) at: Screening	Mean age (years) at: Occulsive vascular death	Diabetes, %	Mean (SD): BMI, kg/m^2	Mean (SD): SBP, mmHg	Mean (SD): DBP, mmHg	Mean (SD): LDL cholesterol, mmol/L	Mean (SD): HDL cholesterol, mmol/L	Current smoker, %
North America/Australasia													
Atherosclerosis Risk in Communities (ARIC)	1988	14484	130	44	54	61	6.7	27.5 (5.1)	121 (19)	74 (11)	5.5 (1.1)	1.3 (0.4)	26
Australian Longitudinal Study of Aging	1992	883	37	49	76	82	7.6	25.9 (4.0)	149 (22)	80 (11)	5.9 (1.2)	1.3 (0.4)	9
The Australian Risk Factor Prevalence Study	1989	7705	50	49	45	66	1.7	25.5 (4.2)	126 (18)	79 (11)	5.6 (1.1)	1.3 (0.4)	23
Busselton Health Study	1972	2736	161	47	41	76	1.4	24.5 (3.7)	130 (20)	74 (13)	5.7 (1.3)	1.5 (0.4)	30
Cardiovascular Health Study	1989	4339	90	40	72	79	9.7	26.4 (4.6)	136 (21)	70 (11)	5.6 (1.0)	1.4 (0.4)	12
Charleston	1961	1964	407	45	49	72	3.0	25.4 (4.8)	145 (29)	86 (12)	6.1 (1.3)	---	47
Fletcher Challenge	1993	8338	75	73	47	69	2.7	26.7 (4.1)	127 (17)	78 (11)	5.5 (1.1)	---	22
Framingham Heart Study	1951	2948	438	48	43	70	1.3	25.5 (4.2)	138 (24)	86 (13)	5.7 (1.1)	---	63
Honolulu Heart Program	1967	7137	511	100	54	73	25.4	23.9 (3.1)	133 (21)	82 (12)	5.6 (1.0)	---	45
Melbourne Collaborative Cohort	1993	38980	221	40	54	67	4.9	26.8 (4.4)	137 (20)	77 (12)	5.5 (1.1)	---	11
Minnesota Heart Survey	1986	6146	27	47	47	66	4.5	26.8 (4.9)	122 (17)	75 (11)	5.3 (1.0)	1.3 (0.4)	28
Newcastle	1989	3060	24	49	53	67	2.5	27.0 (4.6)	133 (20)	79 (11)	5.8 (1.1)	1.3 (0.4)	19
First National Health & Nutrition Examination Survey Epidemiologic Follow-up Study (NHEFS)	1972	9721	894	39	49	75	5.2	25.6 (4.9)	135 (24)	83 (13)	5.7 (1.3)	---	37
Perth	1983	8691	121	53	46	69	1.8	25.2 (3.9)	130 (20)	81 (11)	5.8 (1.2)	1.4 (0.4)	---
Puerto Rico Health Heart Program	1973	4624	451	45	55	78	3.8	24.5 (3.5)	131 (23)	79 (11)	5.4 (1.0)	---	26
Tecumseh	1960	3335	424	49	47	70	9.4	25.8 (4.6)	139 (22)	84 (12)	5.4 (1.0)	---	---
US Health Professionals Follow-up Study	1986	21594	140	100	54	66	3.2	25.4 (3.1)	129 (13)	81 (7)	5.2 (0.9)	---	9
US Nurses' Health Study (NHS II)	1988	46038	80	0	55	64	4.6	25.6 (4.8)	126 (13)	79 (9)	5.3 (1.2)	---	16
Subtotal	**1988**	**192723**	**4281**	**43**	**53**	**72**	**5.2**	**26.0 (4.4)**	**130 (19)**	**79 (11)**	**5.5 (1.1)**	**1.3 (0.4)**	**18**

	Median year of screening	No. participants	No. occlusive vascular deaths	Men, %	Mean age (years) at: Screening	Mean age (years) at: Occlusive vascular death	Diabetes, %	Mean (SD): BMI, kg/m^2	Mean (SD): SBP, mmHg	Mean (SD): DBP, mmHg	Mean (SD): Total cholesterol, mmol/L	Mean (SD): HDL cholesterol, mmol/L	Current smoker, %
Asia													
Aito Town	1981	1560	10	44	51	70	2.6	22.6 (3.0)	136 (21)	79 (13)	4.6 (0.9)	1.4 (0.4)	19
Akabane	1985	1803	13	44	54	67	2.4	22.5 (3.0)	125 (19)	74 (12)	5.0 (0.9)	1.2 (0.3)	28
Anzhen 2	1992	4139	1	49	47	50	10.7	24.0 (3.3)	122 (18)	78 (11)	4.7 (0.9)	1.4 (0.4)	21
Beijing Ageing	1992	1390	0	51	69	.	26.5	23.2 (3.9)	141 (25)	81 (13)	4.3 (1.0)	1.5 (0.6)	32
Civil Serivce Workers	1991	9147	2	67	47	56	1.7	22.5 (2.7)	126 (18)	75 (11)	5.2 (0.9)	1.4 (0.4)	38
Electricity Generating Authority of Thailand (EGAT)	1985	3488	28	77	43	53	2.8	23.1 (3.1)	121 (16)	75 (11)	5.8 (1.1)	1.2 (0.3)	43
Fangshan Cohorts	1992	806	0	33	47	.	6.7	25.0 (3.7)	133 (25)	79 (12)	4.6 (1.1)	1.4 (0.4)	39
Guangzhou Occupational Cohort	1991	1847	2	71	45	64	8.4	22.8 (2.9)	115 (16)	76 (10)	5.5 (1.3)	1.3 (0.4)	46
Hong Kong	1991	123	2	48	77	87	13.0	22.4 (3.6)	148 (21)	80 (12)	5.4 (0.9)	1.6 (0.5)	18
Ikawa	1977	2098	31	44	52	72	1.2	23.6 (3.2)	137 (22)	83 (12)	4.7 (0.8)	---	31
Japan Railways	1978	24708	32	100	43	54	1.9	22.8 (2.7)	129 (17)	81 (12)	4.6 (0.9)	---	65
Korean Medical Insurance Corporation (KMIC)	1992	183349	164	63	44	51	7.2	23.0 (2.5)	122 (15)	80 (10)	5.0 (0.9)	---	9
Kounan	1991	1031	7	45	53	72	11.9	21.9 (2.9)	130 (19)	78 (11)	4.9 (0.9)	1.6 (0.4)	31
Kyowa	1983	4099	25	43	54	69	4.3	23.5 (3.3)	137 (20)	81 (12)	4.9 (1.0)	---	33
Miyama	1989	408	0	38	59	.	2.5	22.3 (3.0)	129 (23)	77 (12)	5.1 (0.9)	1.3 (0.3)	24
Noichi	1976	2179	32	37	54	72	5.0	22.9 (3.2)	136 (21)	80 (12)	4.8 (0.9)	---	26
Ohasama	1992	1787	4	35	58	78	9.5	23.3 (3.1)	127 (17)	72 (12)	5.0 (0.9)	1.4 (0.4)	21
Saitama	1987	3429	43	38	54	76	1.7	22.4 (2.9)	135 (20)	80 (12)	5.0 (1.0)	---	29
Shibata	1977	2223	133	43	56	78	1.1	22.4 (3.0)	130 (21)	78 (12)	4.6 (1.2)	---	33
Shigaraki Town	1993	3301	5	41	57	78	6.8	22.5 (3.0)	132 (19)	78 (12)	5.0 (0.9)	1.4 (0.4)	29
Shirakawa	1977	4394	74	46	49	69	0.9	21.5 (2.7)	127 (22)	77 (13)	4.7 (0.9)	---	35
Singapore Heart & Thyroid	1984	2152	24	50	41	66	10.8	23.6 (4.3)	123 (21)	76 (12)	5.9 (1.2)	0.9 (0.4)	22
Singapore National Health Survey 1992 (NHS92)	1992	2495	20	48	43	59	11.9	23.7 (4.1)	121 (19)	71 (12)	5.5 (1.0)	1.2 (0.3)	18
Tanno/Soubetsu	1977	1972	30	47	51	65	7.0	23.6 (3.2)	133 (20)	83 (10)	4.9 (1.0)	---	38
Two Township Study in Taiwan (CVDFACTS)	1991	4736	17	45	50	70	2.8	23.8 (3.3)	120 (19)	76 (11)	5.0 (1.2)	1.2 (0.4)	22
Yunnan Tin Miner	1992	2626	6	96	54	67	0.5	21.9 (2.9)	122 (21)	80 (13)	4.3 (0.8)	1.4 (0.4)	69
Subtotal	**1992**	**271290**	**705**	**64**	**45**	**66**	**6.2**	**23.0 (2.7)**	**124 (17)**	**79 (11)**	**4.9 (0.9)**	**1.3 (0.4)**	**20**
Total	**1985**	**980793**	**19686**	**58**	**46**	**66**	**4.3**	**24.5 (3.7)**	**131 (19)**	**81 (11)**	**5.5 (1.2)**	**1.4 (0.4)**	**29**

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Webtable 2: Baseline chatacteristics of men and women with and without diabetes at study recruitment

	Men		Women	
	Diabetes	**No diabetes**	**Diabetes**	**No diabetes**
No. participants	28 450	540 075	14 001	398 267
Mean (SD)				
Age, years	50.2 (9.8)	45.5 (9.8)	51.0 (11.1)	45.5 (8.4)
SBP, mmHg	134.6 (17.4)	132.5 (17.3)	132.3 (18.1)	127.5 (14.9)
DBP, mmHg	83.9 (11.2)	82.2 (11.1)	79.7 (11.0)	78.0 (9.6)
BMI, kg/m²	25.0 (3.2)	24.6 (3.2)	26.0 (4.1)	24.1 (2.8)
Total cholesterol, mmol/L	5.5 (1.2)	5.6 (1.2)	5.5 (1.2)	5.5 (1.0)
Smoking habit, %				
Current cigarette	27.0	35.5	14.7	18.9
Other*	50.1	40.3	24.7	22.9
Never	22.9	24.2	60.7	58.2
No. participants with measured HDL cholesterol	3767	92 870	2832	68 872
Total cholesterol, mmol/L	5.5 (1.2)	5.7 (1.2)	5.6 (1.2)	5.7 (1.0)
HDL cholesterol, mmol/L	1.2 (0.4)	1.2 (0.4)	1.3 (0.4)	1.5 (0.3)
Total cholesterol/ HDL ratio	5.3 (1.9)	4.9 (1.9)	4.6 (1.4)	4 (1.6)

Estimates are standardised for baseline age and study

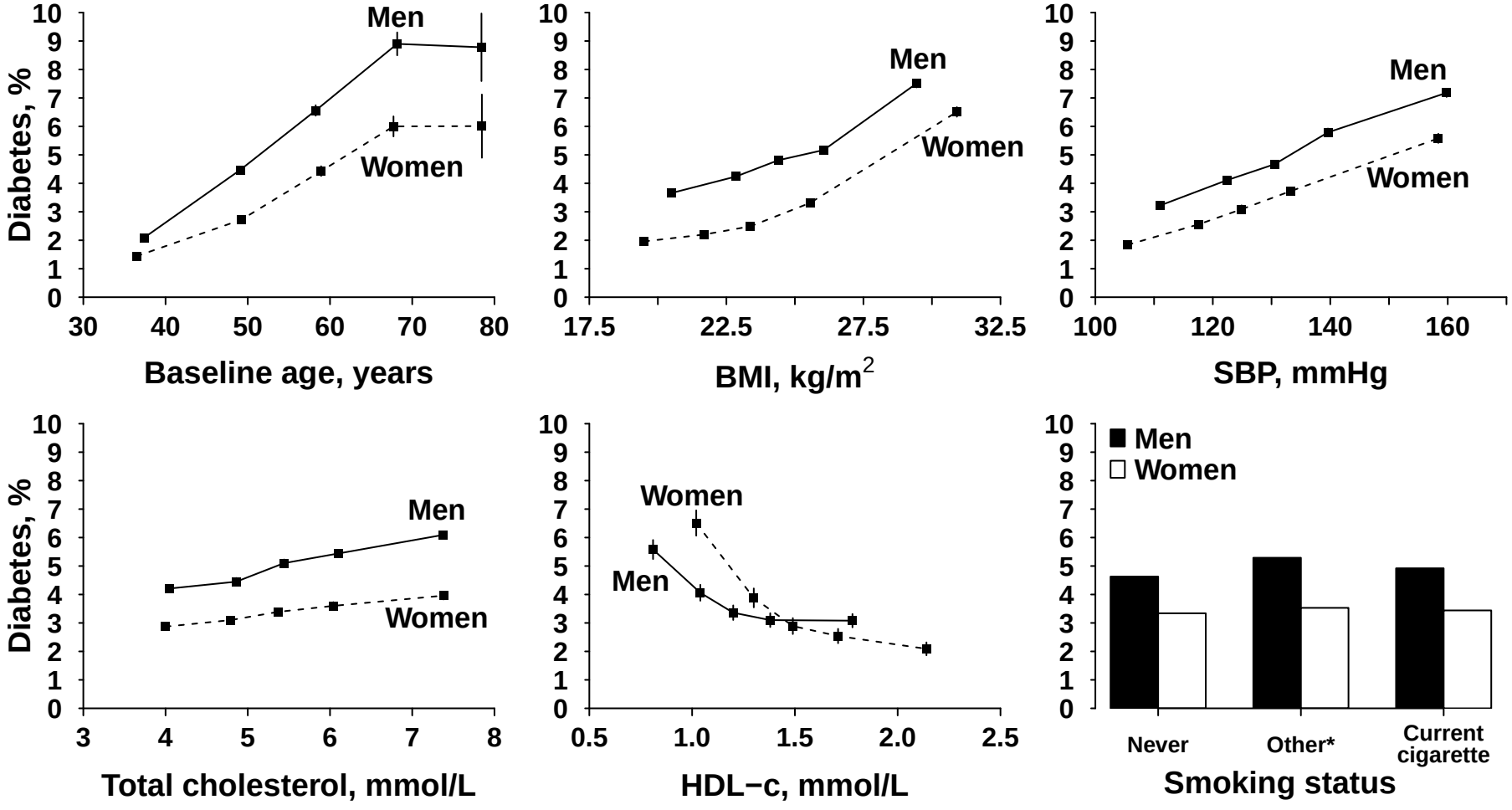
* "Other“ includes ex-smoker of any type of tobacco, smoking status not known (not recorded or not able to reliably distinguish between never, ex or current), or current smoker of other types of tobacco (n=23 475; 7.2%)

Web table 3: Relevance of: (a) total cholesterol; (b) SBP; and (c) BMI to occlusive vascular mortality at ages 35-89 years, by sex and diabetes at study recruitment

		RR (95% CI)
Cholesterol (per mmol/L)		
Men	Diabetes	1.56 (1.37-1.76)
	No diabetes	1.56 (1.44-1.69)
Women	Diabetes	1.36 (1.19-1.56)
	No diabetes	1.24 (1.10-1.39)
SBP (per 20 mmHg)		
Men	Diabetes	1.54 (1.38-1.71)
	No diabetes	1.82 (1.68-1.97)
Women	Diabetes	1.45 (1.12-1.88)
	No diabetes	1.92 (1.81-2.03)
BMI (per 5 kg/m^2)		
Men	Diabetes	1.35 (1.26-1.44)
	No diabetes	1.38 (1.28-1.48)
Women	Diabetes	1.24 (1.15-1.34)
	No diabetes	1.21 (1.13-1.31)

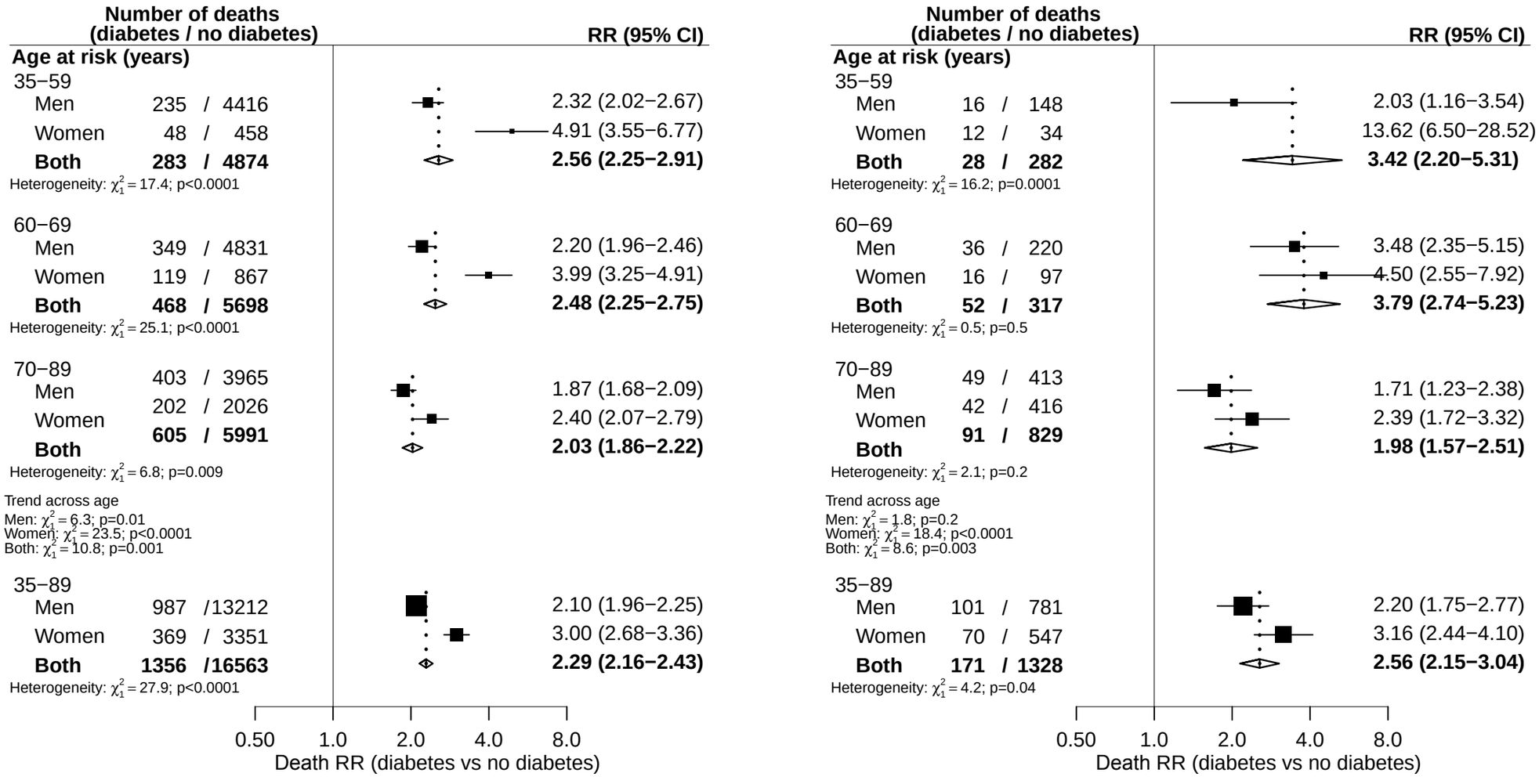
RR=death rate ratio; CI=confidence interval. SBP=Systolic blood pressure; BMI=Body-mass index. Analyses are adjusted for age at risk, study, smoking and, where appropriate, total cholesterol, SBP, DBP and BMI. Usual total cholesterol and SBP refer to the long-term average level of that risk factor. Regression dilution ratios of 0·65 for total cholesterol and 0·67 for SBP were calculated by regressing serial measurements from 175,000 participants with at least one re-measurement a few years later, on baseline levels of these risk factors. No adjustment was applied for BMI, since one single measurement at baseline was highly correlated with long-term BMI. Analyses exclude those with prior ischaemic heart disease or stroke diagnosed by a doctor, and those with missing covariate data. Occlusive vascular mortality includes death from ischaemic heart disease (ICD-9 410-414), ischaemic stroke (ICD-9 433-434) or other atherosclerotic diseases (ICD-9 440, 443, 445) as the underlying cause.

Webfigure 1: Sex−specific prevalence of diabetes at study recruitment by baseline characteristics



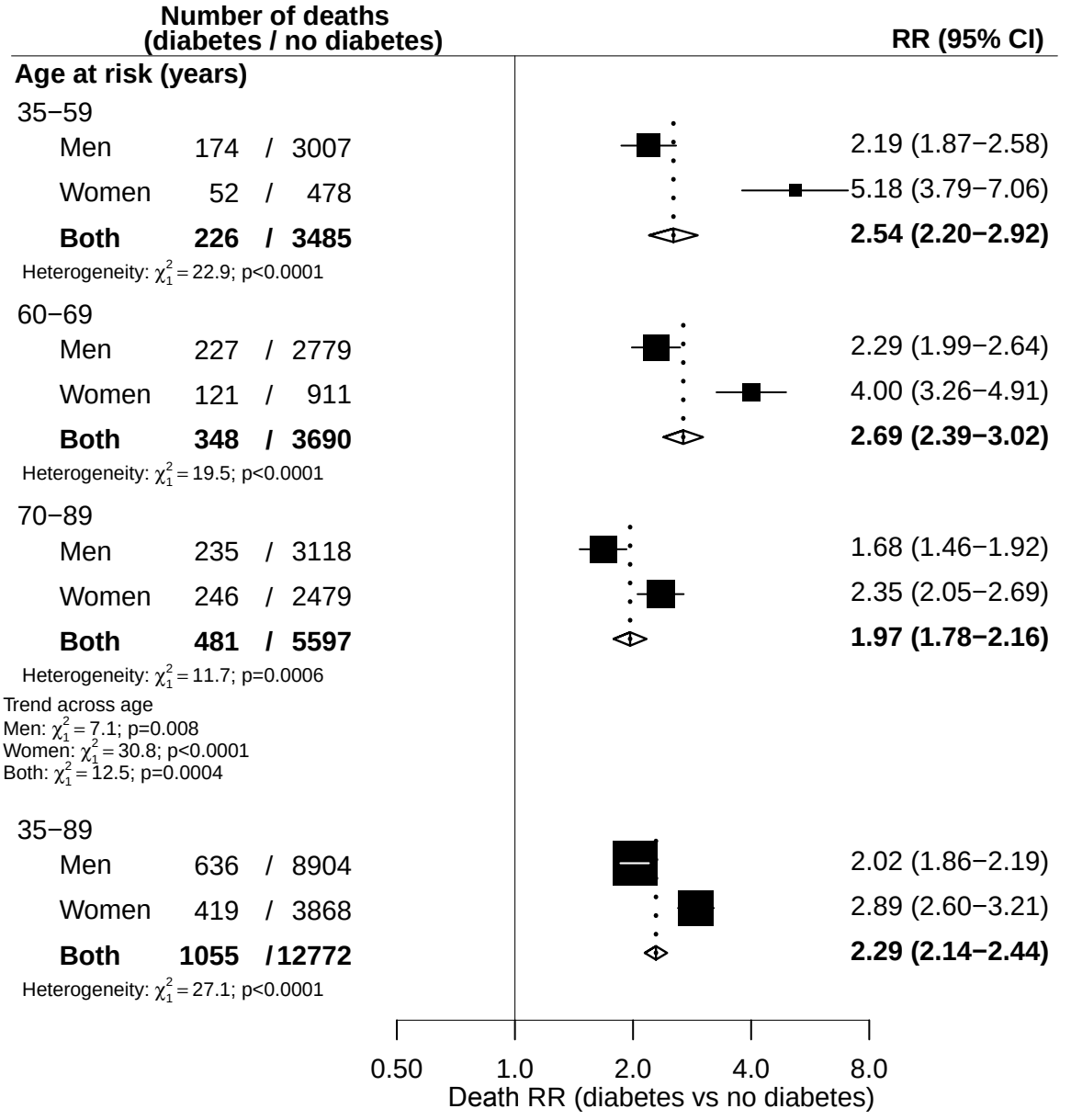
BMI=body−mass index; SBP=systolic blood pressure; HDL−c=high density lipoprotein cholesterol. *includes former smokers, smokers of non−cigarette tobacco, and people with smoking status not known.
Analyses adjusted for baseline age, cohort and smoking (where appropriate). Associations of diabetes with total cholesterol and SBP are additionally adjusted for BMI.
For the subset of 168,341 participants with HDL−c available, the overall prevalence of diabetes at recruitment was 4.1% in both men and women.

Webfigure 2: Age and sex−specific relevance of diabetes at study recruitment to IHD and ischaemic stroke mortality



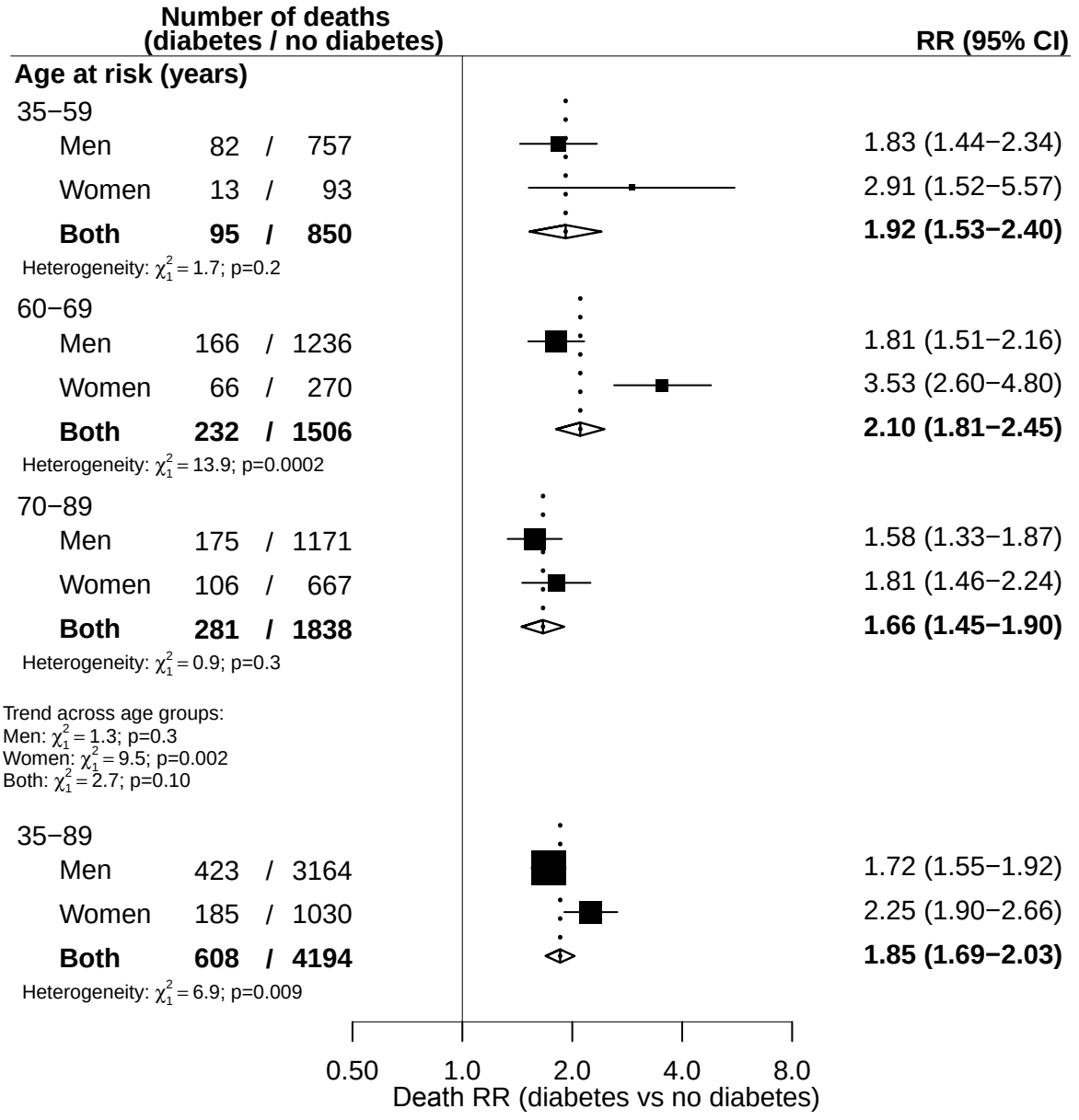
RR=rate ratio; CI=Confidence Interval. Analyses are adjusted for age at risk, BMI, SBP, DBP, total cholesterol, smoking ("never" smoked any type of tobacco regularly, "current cigarette" smoker, and "former and other", including ex−smoker of any type of tobacco, current smoker of other types of tobacco, or smoking status not known) and study, and exclude people with prior ischaemic heart disease or stroke diagnosed by a doctor, or with missing covariate data. Each diamond represents the inverse variance−weighted average of the two estimates above it. Ischaemic heart disease includes (ICD−9 410−414) and ischaemic stroke includes (ICD−9 433−434).

Webfigure 3: Age and sex−specific relevance of diabetes at study recruitment to occlusive vascular mortality (limited to studies that included both men and women)



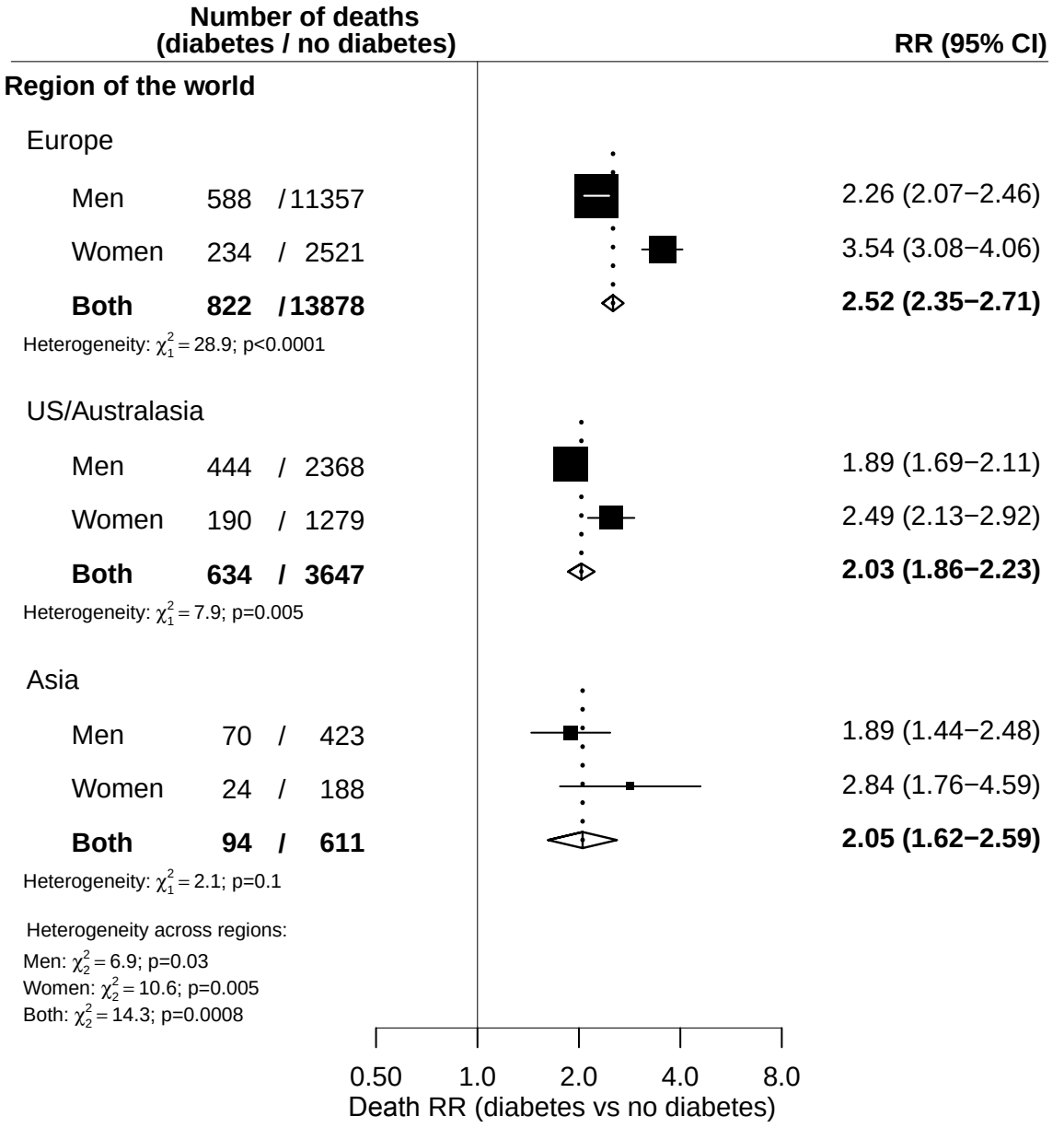
RR=rate ratio; CI=confidence interval. Analyses are adjusted for age at risk, BMI, SBP, DBP, total cholesterol, smoking ("never" smoked any type of tobacco regularly, "current cigarette" smoker, and "former and other", including ex−smoker of any type of tobacco, current smoker of other types of tobacco, or smoking status not known), and study, and exclude people with prior ischaemic heart disease or stroke diagnosed by a doctor, or with missing covariate data. Each diamond represents the inverse variance−weighted average of the two estimates above it. Occlusive vascular mortality includes death from ischaemic heart disease (ICD−9 410−414), ischaemic stroke (ICD−9 433−434) or other atherosclerotic diseases (ICD−9 440, 443, 445) as the underlying cause.

Webfigure 4: Relevance of diabetes at study recruitment to occlusive vascular mortality, by age and sex in those with prior IHD or stroke



RR=rate ratio; CI=confidence interval. Analyses are adjusted for age at risk, BMI, SBP, DBP, total cholesterol, smoking ("never" smoked any type of tobacco regularly, "current cigarette", smoker; and "former and other", including ex−smoker of any type of tobacco, current smoker of other types of tobacco, or smoking status not known) and study, and exclude people without prior ischaemic heart disease or stroke diagnosed by a doctor, or with missing covariate data. Each diamond represents the inverse variance−weighted average of the two estimates above it. Occlusive vascular mortality includes death from ischaemic heart disease (ICD−9 410−414), ischaemic stroke (ICD−9 433−434) or other atherosclerotic diseases (ICD−9 440, 443, 445) as the underlying cause.

Webfigure 5: Relevance of diabetes at study recruitment to occlusive vascular mortality at ages 35−89, by sex and region



RR=rate ratio; CI=confidence interval. Analyses are adjusted for age at risk, BMI, SBP, DBP, total cholesterol, smoking ("never" smoked any type of tobacco regularly, "current cigarette", smoker; and "former and other", including ex−smoker of any type of tobacco, current smoker of other types of tobacco, or smoking status not known) and study, and exclude people with prior ischaemic heart disease or stroke diagnosed by a doctor, or with missing covariate data. Each diamond represents the inverse variance−weighted average of the two estimates above it. Occlusive vascular mortality includes death from ischaemic heart disease (ICD−9 410−414), ischaemic stroke (ICD−9 433−434) or other atherosclerotic diseases (ICD−9 440, 443, 445) as the underlying cause.