

Webappendix (with webtables 1-6 and webfigures 1-11): study selection, data collection and statistical methods

Study selection criteria

As described previously,^{1,2} collaboration was sought in 1996 between the investigators of each of the prospective cohort studies with more than 5000 person-years of follow-up in which data on blood pressure, blood cholesterol, date of birth (or age) and sex had all been recorded on enrolment (the baseline visit) and, in subsequent follow-up, the cause and date of death (or age at death) had been routinely sought for all individual participants. Relevant studies were identified through computer searches of MEDLINE and EMBASE, by hand-searches of meeting abstracts and by personal communication with investigators. To minimise the effects of reverse causality (whereby established disease could change the blood cholesterol levels), studies were excluded if they had selected participants on the basis of a positive history of stroke or heart disease (as defined in their study), and individuals from contributing studies were excluded from the present analyses if they were recorded as having such a history at baseline (although a few studies had not recorded information on previous vascular disease).

Data collection

Cause-specific mortality was sought in the greatest detail available, using a 3-digit International Classification of Diseases coding (ICD-6 to ICD-10, depending on the study). In most studies the cause of death was initially taken from the death certificate, but in many studies confirmation was then sought from medical records, autopsy findings or other sources. Vascular causes are categorised as before,¹ and the ICD-9 codes for the endpoints in this report are shown in webtable 1.

The present meta-analysis is of the relevance to various types of vascular mortality, in different circumstances, of total, HDL, non-HDL (total minus HDL) and the ratio of total to HDL (total/HDL) cholesterol, after allowance for regression dilution (webtables 2-4). Non-HDL cholesterol was used rather than LDL cholesterol because information on LDL cholesterol was available for only about 5% of the participants, and even fewer had both a direct measurement of LDL cholesterol and long follow-up. (Non-HDL cholesterol may, however, not be a good surrogate for LDL cholesterol when triglyceride levels are high.) Information was sought not only on baseline levels of blood cholesterol but also on cholesterol levels measured at any subsequent follow-up, to help correct for regression dilution:³ see below for details.

Webtable 5 summarises the characteristics of the included studies. Some studies collected samples after fasting (24 studies; 393 678 individuals) and others did not (34 studies; 419 471 individuals, plus the MRFIT study with 347 681 men). Most collected serum (47 studies; 715 398 individuals, plus MRFIT) but a few collected plasma (11 studies; 97 751 individuals). Three studies, all of US health professionals (79 188 individuals), used only self-reported cholesterol levels. The methods used for blood pressure measurement have been reported previously.² In most studies, weight and height were measured by field workers at enrolment, but they were self-reported in the three studies of US health professionals.⁴⁻⁶ Body mass index (BMI) was defined as weight in kilograms divided by the square of height in metres. Smoking was self-reported at enrolment and, in these populations, it is likely that those who were lifelong non-smokers at baseline would have continued not to smoke, but many who smoked might not have been lifelong cigarette smokers or might have stopped soon after enrolment (in both cases limiting their risk).

Statistical methods

95% confidence intervals (CIs) and two-sided p-values are used. The main analyses of IHD were age-specific, with five groups of age at risk (40-49, 50-59, 60-69, 70-79, 80-89 years) for analyses of total cholesterol, and three groups (40-59, 60-69, 70-89 years) for the smaller numbers with data on HDL or non-HDL cholesterol (ignoring the few deaths outside the age range 40-89). For the main analyses of other vascular outcomes, some of these age groups were merged for statistical stability. People with no follow-up at ages 40-89 were wholly excluded (even from webtable 5). To avoid a few potentially untrustworthy extreme values unduly influencing the results, people with baseline measurements of total cholesterol exceeding 12 mmol/L, HDL cholesterol exceeding 3.5 mmol/L or total/HDL cholesterol exceeding 12 were also excluded from all the main analyses (and also from webtable 5; the only exception was that webtable 4 and webfigure 1 include those whose only reason for exclusion was a high baseline cholesterol).

Sensitivity analyses—To exclude any major effects of prevalent disease on blood cholesterol (“reverse causality”), people who already had any record at baseline of prior vascular disease were excluded from all analyses. As a further check on this, several of the analyses were repeated after excluding all deaths and person-years within the first 5 years of follow-up. Sensitivity analyses were also performed to see whether any heterogeneity in the results between studies could be explained by differences in the methods used to assess cholesterol (serum or plasma; fasting or non-fasting), year of baseline survey or cause of death ascertainment. To investigate whether extreme results from individual studies biased the estimated hazard ratios from the meta-analysis, studies that contributed most to the heterogeneity were successively excluded until the p-values for heterogeneity among the remaining studies were greater than 0.1.

Regression analyses—Hazard ratios (HR) and confidence intervals (CI) for the associations between cause-specific mortality and cholesterol levels were estimated by Cox regression, adjusted for age (within whatever range of age at risk was being considered), sex and study. Adjustments for age at risk were made by inserting a term that allowed the hazard ratio in each age range to be estimated as the geometric mean of the hazard ratios in each half-decade that contributed to that range. The analyses were stratified for sex and study. Additional analyses were stratified for cigarette smoking at baseline (three levels: current cigarette smoker; never smoked any form of tobacco regularly; and other, including unknown) and adjusted for baseline systolic blood pressure (SBP) as a continuous variable.

In the main IHD analyses, participants were divided by the baseline measurements into six categories of total cholesterol (<4.5, 4.5-, 5.5-, 6.5-, 7.5-, 8.5-12 mmol/L) or four categories of HDL cholesterol (<1, 1-, 1.25-, 1.5-3.5 mmol/L), non-HDL cholesterol (<4, 4-, 5-, ≥6 mmol/L) and total/HDL cholesterol (<4.25, 4.25-, 5.5-, 6.75-12), and the hazard ratios in these categories were plotted against the estimated mean usual value, rather than the mean measured value,² in each category (webtables 2-4).

For age-specific IHD analyses, participants were additionally divided into five periods of age at risk as well as the six total cholesterol categories, yielding 30 groups; or three periods of age at risk and four HDL-related categories, yielding 12 groups. For SBP-specific subgroup analyses, participants were divided into three SBP groups and six total cholesterol categories, yielding 18 different groups. To determine the strength of an association (eg, the log hazard ratio per 1 mmol/L lower usual total cholesterol) in any particular subgroup, the inverse-variance-weighted least-squares straight line through the log mortality rates in that subgroup was fitted.² To allow direct comparisons of the strengths of different associations, hazard ratios are presented for differences of 1.0 mmol/L for total and non-HDL cholesterol, 0.33 mmol/L for HDL cholesterol and 1.33 for

total/HDL cholesterol, which in these studies are in approximate proportions to the standard deviations (sd) of the measured values of these factors.

The relative abilities of measurements of different cholesterol indices to predict subsequent mortality from IHD were assessed using the baseline measurements of those indices (not corrected for regression dilution). The “informativeness” of each index was defined (for a given endpoint in a given set of individuals) to be proportional to the χ^2 statistic (twice the change in the log-likelihood) upon adding that index into a regression model containing just age at baseline, sex and study.⁷ Hence, this χ^2 statistic is larger for indices that are more informative. When comparing the predictive abilities of total and HDL cholesterol (and variables derived from them), the χ^2 statistics were calculated only for those people who had complete data on both. (Note that if the relative risks produced by two different risk factors [eg, smoking and cholesterol] are independent of each other, the χ^2 statistic on fitting both will be approximately the sum of the χ^2 statistics on fitting each separately.)

Floating absolute risks—The hazard ratios are presented as floating absolute risks.^{8,9} This does not alter their values, but ascribes an appropriate variance to the log of the hazard ratio for each group, including even the reference group with hazard ratio 1 (rather than having one group arbitrarily chosen to have a relative risk of 1 with no associated variation). This allows the values to be compared informatively (ie, with known variance) between any pair of exposure categories, rather than only between each exposure category and the arbitrarily chosen reference category.

Regression dilution—Assessment of the relationships between prolonged differences in “usual” (ie, long-term average) cholesterol levels and IHD mortality requires correction for the regression dilution bias,³ which is caused by the combined effects of measurement errors, short-term biological variability (including both transient fluctuations and any diurnal or seasonal variation), and longer-term within-person differences in lipid levels (which may occur for several reasons, including changes in physical activity, diet, treatment or disease status). Such fluctuations make the uncorrected associations with cholesterol levels measured at a single baseline visit underestimate the true associations of risk with usual cholesterol levels. To estimate the usual values some years after the baseline survey in each of the 6 baseline categories of total cholesterol, the means of the measured values in each of those 6 categories were shrunk towards the overall mean, M , by a factor, R . If the mean of the measured values in a particular category is m , then the mean of the usual values in that category is taken to be $M + R(m - M)$. The shrinkage factor is called the regression dilution ratio, and is about two-thirds for each variable (0.65, 0.73, 0.70 and 0.68, respectively, for total, HDL, non-HDL and total/HDL cholesterol: webtables 2 and 3). Hence, the range of usual cholesterol values from the lowest to the highest cholesterol category is only about two-thirds as great as the range of measured values. Because of this, graphs of risk versus usual cholesterol are, appropriately, about 50% steeper than uncorrected graphs of risk versus measured cholesterol would have been.

A total of 40 313 individuals had a non-outlier baseline measurement of total and HDL cholesterol and then a remeasurement of both. Taking only the first remeasurement in each of them (which was at a mean of 4.2 years after baseline), webtable 2 shows the self-correlation r and the mean change d between these pairs of measurements, and, in categories defined only by the baseline measurement, shows the mean baseline value and mean resurvey value. For each variable, the regression dilution ratio, R , was taken to be an appropriate correlation coefficient from webtable 2, and the effects of using these are shown in webtable 3. (For details, see webtable footnotes: webtable 2 gives the actual resurvey values and webtable 3 gives the estimated usual values that were used in the main analyses.) Comparison of webtables 2 and 3 shows that if any of the variables is divided into only four major categories then the mean baseline measurement is approximately linearly related to the mean remeasurement. Hence, shrinkage by a constant factor is approximately correct.

Webappendix references

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- Webtable 1. Vascular endpoints and their ICD-9 codes.**
- Webtable 2. Mean baseline values and mean resurvey values for the first resurvey (mean 4.2 years later), in categories defined by baseline measurement.**
40 000 individuals with non-outlier baseline measurements of total and HDL cholesterol and with a remeasurement of both.
- Webtable 3. Mean baseline values and estimated usual values ~7 years later for total cholesterol, or ~4 years later for HDL-related variables, in categories defined by baseline measurement.**
892 000 individuals with non-outlier baseline total cholesterol and 154 000 with non-outlier total and HDL cholesterol values at baseline.
- Webtable 4. Total cholesterol (mmol/L) resurvey data: mean baseline and first resurvey values among all participants with at least one resurvey.**
Baseline measurements of 175 000 individuals with baseline measurement of total cholesterol and with a remeasurement.
- Webtable 5. Study characteristics.**
- Webtable 6. Effect of additional adjustment for baseline SBP and baseline smoking status.**
Age-specific hazard ratios for 1 mmol/L lower usual total cholesterol.
- Webfigure 1. IHD mortality (33 853 deaths) in categories defined only by the baseline cholesterol measurement versus: (a) mean of baseline values in each group; and (b) mean of first resurvey values in each group (approximating mean usual values).**
Conventions as in figure 1. The number just above a vertical CI is the hazard ratio, and the number just below it is the number of deaths. Mean baseline values in each category are from all 892 000 eligible participants (plus those who would have been eligible except for having a baseline cholesterol measurement >12 mmol/L). Mean resurvey values in each category are from the 175 000 participants in webtable 4 (but with the lowest category <3.5 mmol/L at baseline, and the highest two categories 9.5-12 and >12 mmol/L). Results for those with baseline cholesterol measurement >12 mmol/L are not used in the main analyses, but are plotted here. For this category, the horizontal 95% CI indicates the uncertainty of the usual cholesterol level (estimated from those with resurvey values in webtable 4).
- Webfigure 2. IHD mortality (33 744 deaths) versus usual total cholesterol, by region. Age-specific hazard ratios for 1 mmol/L lower usual total cholesterol.**
Conventions as in figure 1. Tests for heterogeneity are between Europe and USA/Australia only.

Webfigure 3. PSC and MRFIT study: IHD mortality (54 987 deaths) versus usual total cholesterol. Age- and sex-specific hazard ratios for 1 mmol/L lower usual total cholesterol.

Conventions as in figure 1. Diamonds are inverse-variance-weighted means of PSC and MRFIT log hazard ratios.

Webfigure 4. IHD mortality (33 744 deaths) versus usual total cholesterol: (a) SBP-specific associations; and (b) SBP-specific hazard ratios for 1 mmol/L lower usual total cholesterol.

Conventions as in figure 1. Age at death is mean age at IHD death.

Webfigure 5. IHD mortality (3020 deaths) versus usual: (a) HDL cholesterol; (b) non-HDL cholesterol; and (c) total/HDL cholesterol. Age- and sex-specific hazard ratios for given differences.

Conventions as in figure 1.

Webfigure 6. IHD mortality (3020 deaths) versus: (a) usual HDL cholesterol by baseline measurement of non-HDL cholesterol; and (b) usual non-HDL cholesterol by baseline measurement of HDL cholesterol.

Conventions as in figure 1.

Webfigure 7. PSC and MRFIT study: stroke mortality (15 259 deaths) versus usual total cholesterol. Age- and sex-specific hazard ratios for 1 mmol/L lower usual total cholesterol.

Conventions as in figure 1 and webfigure 3.

Webfigure 8. PSC and MRFIT study: stroke subtype mortality versus usual total cholesterol.

Conventions as in figure 1 and webfigure 1.

Webfigure 9. Vascular mortality from causes other than IHD or stroke (9855 deaths) versus usual total cholesterol: (a) age-specific associations; and (b) age- and sex-specific hazard ratios for 1 mmol/L lower usual total cholesterol.

Conventions as in figure 1.

Webfigure 10. PSC and MRFIT study: other vascular mortality (19 258 deaths) versus usual total cholesterol. Age- and sex-specific hazard ratios for 1 mmol/L lower usual total cholesterol.

Conventions as in figure 1 and webfigure 3.

Webfigure 11. Other vascular mortality (1032 deaths) versus usual: (a) HDL cholesterol; (b) non-HDL cholesterol; and (c) total/HDL cholesterol. Age-specific associations.

Conventions as in figure 3. HR denotes the hazard ratio per 1.33 lower total/HDL cholesterol.

Webtable 1: Vascular endpoints and their ICD-9 codes¹

Endpoint	ICD-9
All vascular	390-459, 798
Ischaemic heart disease (IHD)	410-414
Total stroke	430-438
Subarachnoid haemorrhage (SAH)	430
Haemorrhagic stroke	431-432
Ischaemic stroke	433-434
Unknown type ²	435-438
Other vascular ³	390-459 (less 410-414, 430-438), 798
Non-vascular ⁴	All other, excluding unknown (780-797, 799)

¹ Not all studies provided ICD-9 codes. When other ICD versions or study's own codes were provided these were grouped accordingly to give the required endpoints.

² Transient ischaemic attacks (ICD-9 code 435) were assumed to be coding errors (by definition) and were included with "unknown" type of stroke.

³ Sudden deaths were included with other vascular deaths.

⁴ The non-vascular deaths exclude about 16 000 deaths from unknown causes that were classified as non-vascular deaths in a previous report.²

Webtable 2: Mean baseline values and mean resurvey values for the first resurvey (mean 4.2 years years later), in categories defined by baseline measurement

40 000 individuals with non-outlier baseline measurements of total and HDL cholesterol and with a remeasurement of both

Variable (with <i>r</i> =self-correlation, <i>d</i> =mean change)	Baseline categories (mmol/L)	Number of people	Mean (mmol/L)	
			Baseline	Resurvey
Total cholesterol (<i>r</i> =0.68, <i>d</i> =-0.037)	<4.5	6450	4.05	4.49
	4.5-<5.5	13 697	5.03	5.17
	5.5-<6.5	12 642	5.94	5.81
	6.5-<7.5	5436	6.91	6.46
	7.5-<8.5	1619	7.87	6.96
	8.5-12	469	9.21	7.62*
	All	40 313	5.57	5.54
	Difference, highest vs lowest			5.17
HDL cholesterol (<i>r</i> =0.73, <i>d</i> =-0.032)	<1.0	10 509	0.86	0.94
	1.0-<1.25	10 755	1.13	1.14
	1.25-<1.5	8467	1.37	1.31
	1.5-3.5	10 582	1.82	1.65
	All	40 313	1.29	1.26
	Difference, highest vs lowest			0.96
Non-HDL cholesterol (<i>r</i> =0.70, <i>d</i> =-0.006)	<4.0	17 114	3.28	3.57
	4.0-<5.0	13 340	4.47	4.44
	5.0-<6.0	6893	5.41	5.09
	≥6.0	2966	6.66	5.79
	All	40 313	4.28	4.28
	Difference, highest vs lowest			3.38
Total/HDL cholesterol (<i>r</i> =0.68, <i>d</i> =0.072)	<4.25	18 059	3.35	3.72
	4.25-<5.5	10 830	4.82	4.97
	5.5-<6.75	6636	6.01	5.87
	6.75-12	4788	7.90	6.96
	All	40 313	4.73	4.80
	Difference, highest vs lowest			4.54

40 000 with remeasurement of both HDL and total cholesterol:

A total of 40 313 had non-outlier baseline measurements of both total and HDL mmol/L cholesterol and at least one remeasurement (outlier: total > 12, HDL > 3.5 or total/HDL > 12). All measurements and remeasurements are first adjusted for age at baseline, sex and study.

r = correlation coefficient, resurvey vs baseline. The standard error for each *r* is about 0.0025, ie, $(1-r^2)/\sqrt{40\ 313}$.

d = change in mean, resurvey minus baseline

* Standard error (SE) 0.04; all other resurvey SEs are small (<0.02).

175 000 with remeasurement of total cholesterol (irrespective of whether HDL cholesterol was ever measured):

A total of 175 349 had a non-outlier (ie, ≤ 12) baseline measurement of total cholesterol and at least one remeasurement.

After adjustment for age at baseline, sex and study the correlation between this baseline measurement and the first remeasurement (mean 4.6 years later) was *r* = 0.68 (as for the 40 313 individuals with HDL cholesterol in this table), and the baseline and resurvey mean values were 5.53 and 5.58 mmol/L.

37 000 with double remeasurement of total cholesterol:

A total of 37 050 had a non-outlier (ie, ≤ 12) baseline measurement of total cholesterol and at least two remeasurements.

Taking this baseline measurement, the first remeasurement <4.5 years (mean 2.4 years) after baseline and, second, the first remeasurement ≥ 4.5 years (mean 6.2 years) after baseline, and adjusting all three for age at baseline, sex and study, the baseline, first and second mean values (and their standard deviations) were 5.56 (1.08), 5.51 (1.06) and 5.58 (1.05) mmol/L, and the partial correlation coefficients were *r* = 0.70 (baseline vs first, mean 2.4 years apart), *r* = 0.67 (first vs second, mean 3.8 years apart) and *r* = 0.65 (baseline vs second, mean 6.2 years apart). Taking this trend in the self-correlation coefficients together with the value of *r* = 0.68 for the 175 349 remeasurements at a mean of 4.6 years after baseline, we estimated that the self-correlation for remeasurements of total cholesterol ~7 years apart would be 0.65 (0.03 less than the *r* at 4.2 or 4.6 years) and that the difference in the mean would be 7/4.2 times the difference, *d*, at 4.2 years.

Webtable 3: Mean baseline values and estimated usual values ~7 years later for total cholesterol, or ~4 years later for HDL-related variables, in categories defined by baseline measurement

892 000 individuals with non-outlier total cholesterol and 154 000 with non-outlier HDL and total cholesterol values at baseline.

Variable	Baseline categories (mmol/L)	Number of people	Mean (mmol/L)	
			Baseline	Usual
Total cholesterol	<4.5	142 305	4.04	4.58
	4.5-<5.5	253 668	5.06	5.24
	5.5-<6.5	264 514	5.98	5.84
	6.5-<7.5	154 757	6.93	6.46
	7.5-<8.5	54 674	7.88	7.08
	8.5-12	22 419	9.15	7.90
	All	892 337	5.77	5.71
	Difference, highest vs lowest		5.11	3.32
HDL cholesterol	<1.0	26 915	0.87	0.98
	1.0-<1.25	39 596	1.14	1.17
	1.25-<1.5	36 081	1.37	1.34
	1.5-3.5	51 206	1.82	1.67
	All	153 798	1.37	1.34
		Difference, highest vs lowest		0.95
Non-HDL cholesterol	<4.0	58 911	3.29	3.63
	4.0-<5.0	48 612	4.47	4.45
	5.0-<6.0	30 183	5.41	5.11
	≥6.0	16 092	6.71	6.02
	All	153 798	4.43	4.43
	Difference, highest vs lowest		3.42	2.39
Total/HDL cholesterol	<4.25	73 901	3.35	3.82
	4.25-<5.5	41 327	4.80	4.80
	5.5-<6.75	22 986	5.99	5.62
	6.75-12	15 584	7.87	6.89
	All	153 798	4.59	4.66
	Difference, highest vs lowest		4.52	3.07

Baseline values are adjusted for age at baseline, sex and study.

For the 3020 with a baseline measurement of **HDL cholesterol** who died of IHD, the mean time to death was 8.2 years (5.7, 8.2 and 9.9 years respectively for deaths at ages 40-59, 60-69 and 70-89), and the usual cholesterol ~4 years after baseline is used in the main analysis. For each of the three HDL-related variables, the usual value ~4 years after baseline (ie, a mean of ~4 years before death) is used for all age groups. Calculation of this involves the category-specific baseline means and the overall mean in this table (webtable 3), and the self-correlation r and change d for the 40 313 remeasurements ~4 years apart in webtable 2. The category-specific means are shrunk towards the overall mean by multiplication by r , and d is then added.

For the 33 744 with a baseline measurement of **total cholesterol** who died of IHD, the mean time to death was 11.9 years (6.4, 8.8, 11.1, 13.3 and 14.6 years, respectively, for deaths at ages 40-49, 50-59, 60-69, 70-79 and 80-89), and the usual total cholesterol ~7 years after baseline is used for all groups, calculated as for the HDL-related variables but using ($r - 0.03$) and ($7d/4.2$), as in the footnotes to webtable 2.

Webtable 4: Total cholesterol (mmol/L) resurvey data: mean baseline and first resurvey values among all participants with at least one resurvey

Baseline measurements of 175 000 individuals with baseline measurement of total cholesterol and with a remeasurement

Range (mmol/L)	No. with a resurvey	Mean years to resurvey	Baseline Mean	Resurvey mean (se)
0.5-<2.5 ¹	168	4.5	2.15	3.71 (0.082)
2.5-<3.5	4944	4.6	3.20	3.91 (0.011)
3.5-<4.5	29 909	4.6	4.10	4.50 (0.004)
4.5-<5.5	56 364	4.6	5.02	5.22 (0.003)
5.5-<6.5	49 543	4.6	5.96	5.92 (0.004)
6.5-<7.5	23 701	4.7	6.92	6.60 (0.006)
7.5-<8.5	7982	4.8	7.89	7.22 (0.011)
8.5-<9.5	2056	5.2	8.87	7.79 (0.027)
9.5-<10.5	502	5.3	9.90	8.38 (0.079)
10.5-12.0	180	5.2	11.01	8.62 (0.145)
>12.0 ²	74	5.5	14.21	8.74 (0.336)

¹ No individuals had a baseline cholesterol measurement < 0.5 mmol/L

² Individuals with baseline cholesterol measurements > 12 mmol/L were excluded from the main analyses, but their IHD hazard is plotted in webfigure 1

Webtable 5: Study characteristics

Study; as in list of collaborators (and year screening began)	Sample ¹		All participants ²					Participants with a measurement of HDL cholesterol ³					
	Fasting/non-fasting	Serum/plasma	Number analysed	Baseline total cholesterol (mmol/L)	Mean age at death	No. of vascular deaths	Mean years to death	Number analysed	Baseline total cholesterol (mmol/L)	Baseline HDL cholesterol (mmol/L)	Mean age at death	No. of vascular deaths	Mean years to death
Europe (32) & Israel (1)													
BIRNH (1980), Belgium	N	S	9380	6.1	69	312	5.1	9303	6.1	1.4	69	310	5.1
BRHS (1978), UK	N	S	7352	6.3	62	575	9.0						
BUPA (1975), UK	F	S	21 074	6.3	65	928	10.4	8777	6.2	1.3	62	278	8.8
Caerphilly (1979), UK	F	P	1768	5.7	62	116	7.8	1764	5.7	1.1	62	116	7.8
CB project (1974), NL	N	S	48 345	5.4	52	375	9.4						
Copenhagen (1976), DK	N	P	13 230	6.1	70	873	6.3	1524	6.0	1.5	71	97	6.2
Finrisk (1972), Finland	F	S	36 070	6.5	63	2415	10.8	13 602	6.2	1.4	62	471	6.5
Finnish Mobile Clinic (1966)	F	S	43 867	6.4	70	4710	13.0						
FLEMENGHO (1985), Belgium	N	S	851	6.0	76	39	3.9	570	6.1	1.3	77	36	3.9
Glostrup (1977), DK	F	S	8750	6.2	70	292	5.5	8730	6.2	1.5	70	291	5.5
Gothenburg Women (1968), Sweden	F	S	1402	6.8	70	094	18.2						
Israeli IHD (1963)	N	S	9665	5.4	68	1540	14.8	6376	5.4	1.0	68	1022	14.9
Midspan (1970), UK	F	P	6558	5.8	65	896	13.4						
Norwegian Counties (~1975)	N	S	47 745	6.3	55	1352	10.5						
NPHS (1972), UK	N	S	3048	6.0	67	182	11.1						
OG-Rome (1979), Italy	F	S	3165	5.5	63	133	5.4	2939	5.6	1.2	63	127	5.5
Oslo (1972), Norway	N	S	15 790	6.9	57	941	10.8						
Paris (1967), France	F	S	7462	5.8	63	595	14.4						
IPC-Paris (1978), France	F	S	159 929	5.6	64	792	8.1						
PROCAM (1978), Germany	F	S	13 544	5.8	57	121	3.8	13 544	5.8	1.3	57	121	3.8
Renfrew/Paisley (1972), UK	N	P	11 114	6.1	67	1279	10.3						
SC (Seven countries) Croatia (1958)	N	S	1291	5.0	69	301	16.5						
SC Finland (1959)	N	S	1510	6.7	86	431	15.0						
SC Greece (1960)	N	S	1130	5.3	70	158	17.6						
SC Italy (1960)	N	S	2285	5.3	67	398	15.3						
SC Netherlands (1960)	N	S	782	6.1	68	190	15.9						
SC Serbia (1962)	N	S	963	4.3	69	247	17.0						
SHHS (1984), UK	N	S	10 962	6.4	59	257	5.1	10 508	6.4	1.5	59	236	5.1
Speedwell (1979), UK	F	P	1745	5.8	64	129	7.8	1702	5.8	1.1	64	128	7.9
Tromso (1979), Norway	N	S	11 458	6.1	55	121	6.7	11 449	6.1	1.6	55	121	6.7
UK HDPP (1971)	N	P	13 143	5.6	66	1794	13.0						
Varmland (~1963), Sweden	N	S	95 871	6.5	74	20 228	12.7						
Whitehall (1967), UK	F	P	18 150	5.1	64	1771	8.3						
SUBTOTAL			629 399	6.0	69	44 585	12.0	90 788	6.0	1.4	65	3354	8.9
USA (18) & Australia (2)													
ARIC (1986), USA	F	P	14 566	5.5	61	247	3.6	14 565	5.5	1.4	61	247	3.6
Busselton (1966), Australia	F	S	5912	5.8	76	758	14.6	3901	5.9	1.5	78	285	9.2
Charleston (1960), USA	F	S	2048	6.1	72	669	17.3						
Evans County (1960), USA	N	S	2918	5.4	76	226	23.1						
Framingham (1949), USA	N	S	3053	5.7	71	728	23.1						
Honolulu (1965), USA	N	S	7548	5.6	73	879	16.1						
LRC (1972), USA	F	P	7954	5.8	70	502	9.7	7913	5.8	1.3	70	502	9.7
MHHP (1980), USA	N	S	11 825	5.5	68	200	4.3	11 523	5.5	1.3	69	192	4.3
MHS (1981), USA	N	S	5132	5.4	68	45	3.0	5122	5.4	1.3	68	45	3.0
NHEFS (1971), USA	N	S	12 458	5.7	75	1672	10.4						
Perth (1979), Australia	F	S	8374	5.8	69	181	8.8	5321	5.7	1.4	68	76	7.1
CHS (1989), USA	F	P	4473	5.6	79	156	2.2	4470	5.6	1.4	79	156	2.2
Puerto Rico HHP (1965)	N	S	9121	5.2	65	675	7.1						
Rancho Bernardo (1971), USA	F	P	5050	5.5	79	752	10.9						
Tecumseh (1959), USA	N	S	3999	5.3	71	701	13.9						
Health Professionals (1986), USA	U	U	21 946	5.2	66	208	2.6						
Nurses' Health (1988), USA	U	U	49 533	5.3	64	152	2.5						
Physicians' Health (1981), USA	U	U	7709	5.5	70	237	6.3						
SUBTOTAL			183 619	5.5	72	8988	12.3	52 815	5.6	1.3	71	1503	6.8
Japan (8) and China (2)													
Seven Cities China (1986),	F	S	7082	4.9	67	048	1.8	6655	4.9	1.4	67	43	1.7
Ikawa (1975), Japan	N	S	2124	4.7	70	112	10.4						
Japan Railway (1973)	N	S	45 812	4.6	53	508	5.2						
Kyowa (1981), Japan	N	S	4213	4.9	68	067	6.3						
Noichi (1975), Japan	N	S	2199	4.9	72	135	10.6						
Ohasama (1990), Japan	F	S	2340	5.1	70	16	2.1	235	5.0	1.3			
Saitama (1986), Japan	F	S	3379	5.0	73	67	4.1	3305	5.0	2.0	73	66	4.1
SC (Seven Countries) Japan (1958)	N	S	913	4.3	70	148	16.1						
Shanghai (1972), China	F	S	9016	4.2	67	372	10.3						
Shibata (1977), Japan	N	S	2241	4.6	77	216	7.9						
SUBTOTAL			79 319	4.6	65	1689	8.3	10 195	4.9	1.6	71	109	3.2
TOTAL			892 337	5.8	69	55 262	11.9	153 798	5.8	1.4	67	4966	8
MRFIT (1975), USA ⁴			347 681	5.8	66	34 242	16.7						

¹ Type of blood sample: F=fasting; N=non-fasting; S=serum; P=plasma; U=unknown (total cholesterol self-reported; any HDL cholesterol measurements not available to this collaboration).

² Individuals with no history of vascular disease at baseline; complete data on age, sex, total cholesterol, SBP and DBP; and known vital status at the end of follow-up. Excludes participants with no follow-up in the age range 40-89 years or with an outlier baseline total cholesterol (> 12 mmol/L).

³ As for footnote 2 but with non-outlier data also available for HDL cholesterol (outlier: total > 12, HDL > 3.5 or total/HDL > 12).

⁴ The MRFIT prospective study (of screenees for the Multiple Risk Factor Intervention Trial) was not included in the main PSC analyses but was analysed in parallel.

Webtable 6: Effects of additional adjustment for baseline SBP and baseline smoking status

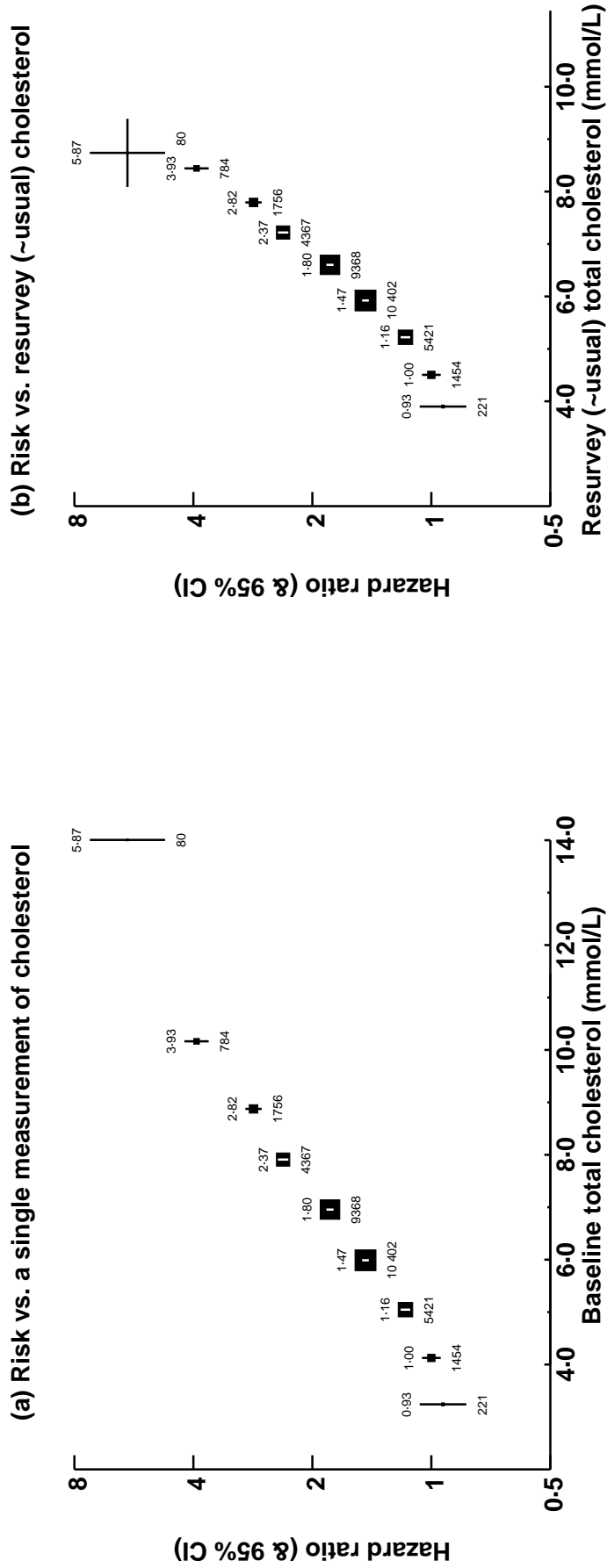
Age-specific hazard ratios for 1 mmol/L lower usual total cholesterol

Disease	Age at risk	No. of deaths	HR (& 95%CI) adjusted for		
			Age, sex & study ¹	+ SBP	+ SBP + smoking
IHD	80-89	5626	0.85 (0.82-0.89)	0.87 (0.83-0.90)	0.87 (0.83-0.90)
	70-79	10829	0.82 (0.80-0.85)	0.84 (0.81-0.86)	0.84 (0.81-0.86)
	60-69	10419	0.72 (0.69-0.74)	0.74 (0.72-0.76)	0.74 (0.72-0.76)
	50-59	5561	0.58 (0.56-0.61)	0.61 (0.59-0.63)	0.62 (0.60-0.65)
	40-49	1309	0.44 (0.42-0.48)	0.47 (0.44-0.50)	0.49 (0.46-0.52)
Total stroke	80-89	2632	1.06 (1.00-1.13)	1.08 (1.01-1.15)	1.07 (1.00-1.14)
	70-79	4311	1.04 (0.99-1.09)	1.07 (1.02-1.12)	1.07 (1.01-1.12)
	60-69	2938	1.02 (0.97-1.08)	1.08 (1.02-1.14)	1.08 (1.02-1.14)
	40-59	1782	0.90 (0.84-0.97)	1.00 (0.93-1.08)	1.02 (0.94-1.09)
Haemorrhagic stroke	80-89	422	1.06 (0.90-1.25)	1.08 (0.92-1.28)	1.07 (0.91-1.26)
	70-79	915	1.18 (1.06-1.31)	1.20 (1.08-1.33)	1.20 (1.08-1.34)
	60-69	743	1.09 (0.97-1.23)	1.14 (1.02-1.29)	1.14 (1.02-1.28)
	40-59	620	0.92 (0.81-1.04)	1.02 (0.90-1.15)	1.02 (0.90-1.16)
Ischaemic stroke	80-89	519	1.09 (0.95-1.26)	1.12 (0.97-1.28)	1.11 (0.96-1.27)
	70-79	850	1.06 (0.95-1.17)	1.09 (0.98-1.21)	1.09 (0.98-1.20)
	60-69	540	0.89 (0.79-1.01)	0.94 (0.83-1.06)	0.94 (0.83-1.06)
	40-59	225	0.73 (0.61-0.87)	0.80 (0.66-0.96)	0.82 (0.68-0.98)
SAH	80-89	33	0.93 (0.52-1.67)	0.93 (0.52-1.66)	0.94 (0.52-1.69)
	70-79	108	0.97 (0.72-1.31)	0.99 (0.74-1.34)	0.98 (0.73-1.33)
	60-69	273	1.17 (0.98-1.41)	1.23 (1.02-1.47)	1.23 (1.02-1.47)
	40-59	455	1.01 (0.88-1.17)	1.10 (0.95-1.27)	1.13 (0.98-1.31)
Unknown/ unclassified stroke	80-89	1658	1.06 (0.97-1.15)	1.06 (0.98-1.16)	1.06 (0.98-1.15)
	70-79	2438	0.99 (0.92-1.05)	1.02 (0.95-1.09)	1.01 (0.95-1.08)
	60-69	1382	1.02 (0.94-1.11)	1.09 (1.00-1.18)	1.09 (1.00-1.18)
	40-59	482	0.89 (0.77-1.03)	1.00 (0.87-1.16)	1.01 (0.87-1.17)

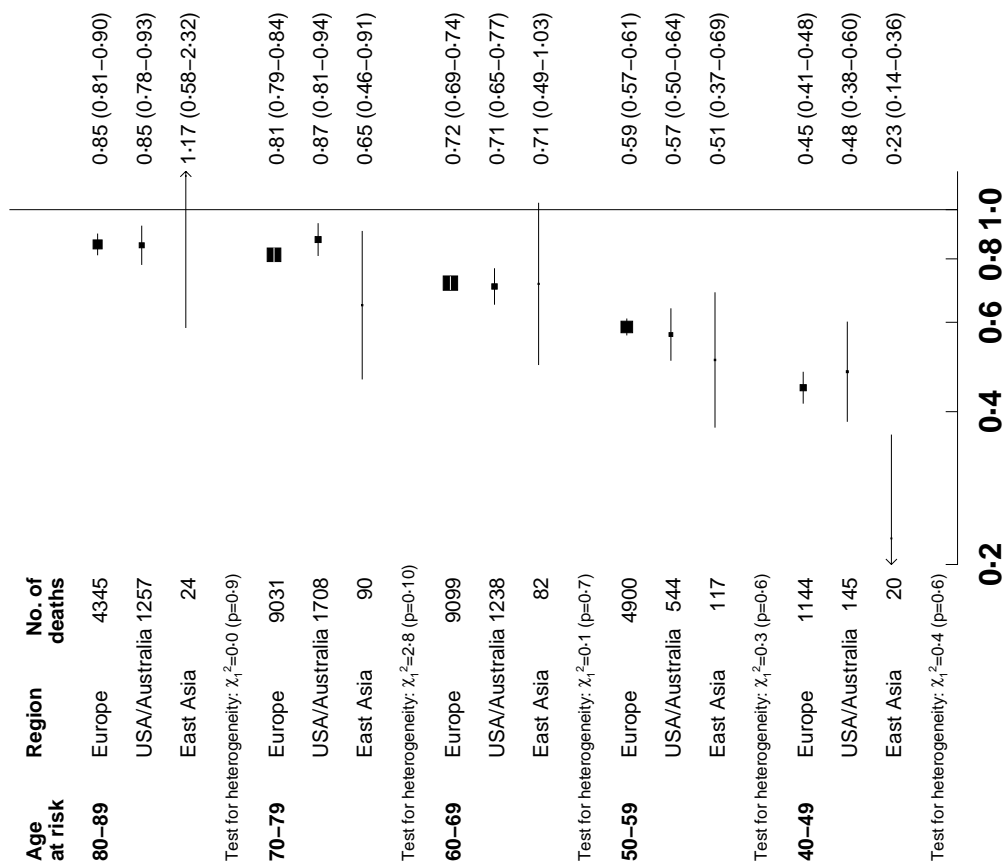
¹ As in figures 1 & 4

Webfigure 1: IHD mortality (33 853 deaths) in categories defined only by the baseline cholesterol measurement versus:

(a) mean of baseline values in each group; and (b) mean of first resurvey values in each group (approximating mean usual values)

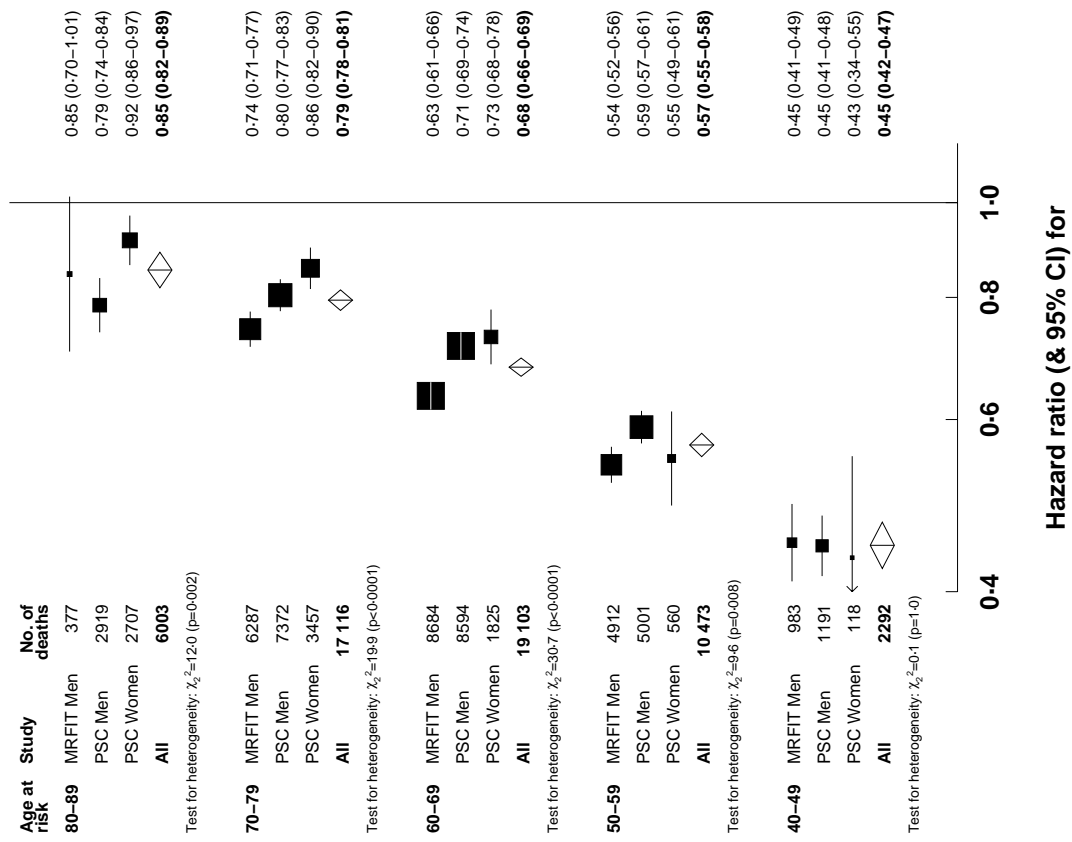


Webfigure 2: IHD mortality (33 744 deaths) versus usual total cholesterol, by region
 Age-specific hazard ratios for 1 mmol/L lower usual total cholesterol



**Hazard ratio (& 95% CI) for
 1 mmol/L lower usual total cholesterol**

Webfigure 3: PSC and MRFIT study: IHD mortality (54 987 deaths) versus usual total cholesterol
Age- and sex-specific hazard ratios for 1 mmol/L lower usual total cholesterol

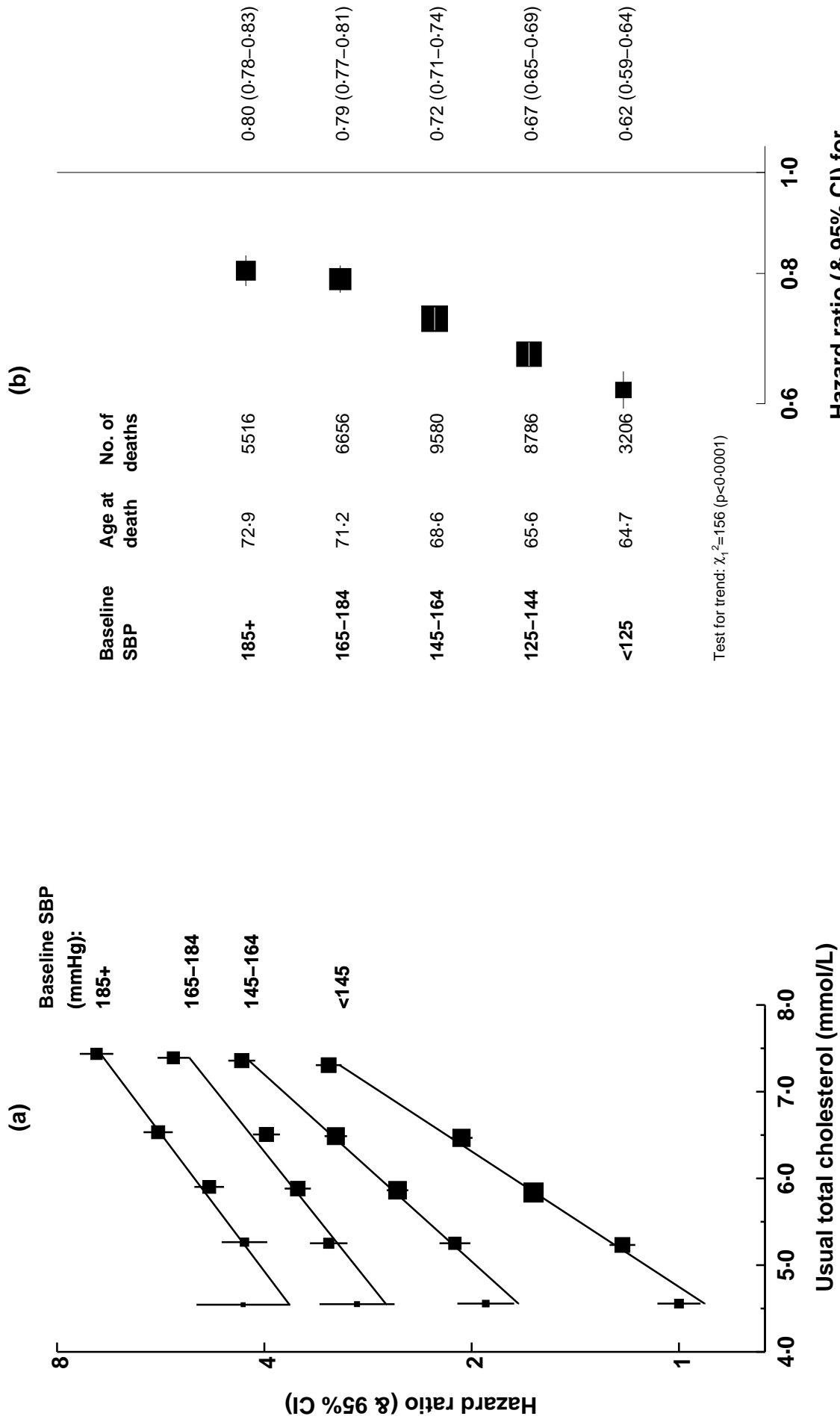


Hazard ratio (& 95% CI) for
1 mmol/L lower usual total cholesterol

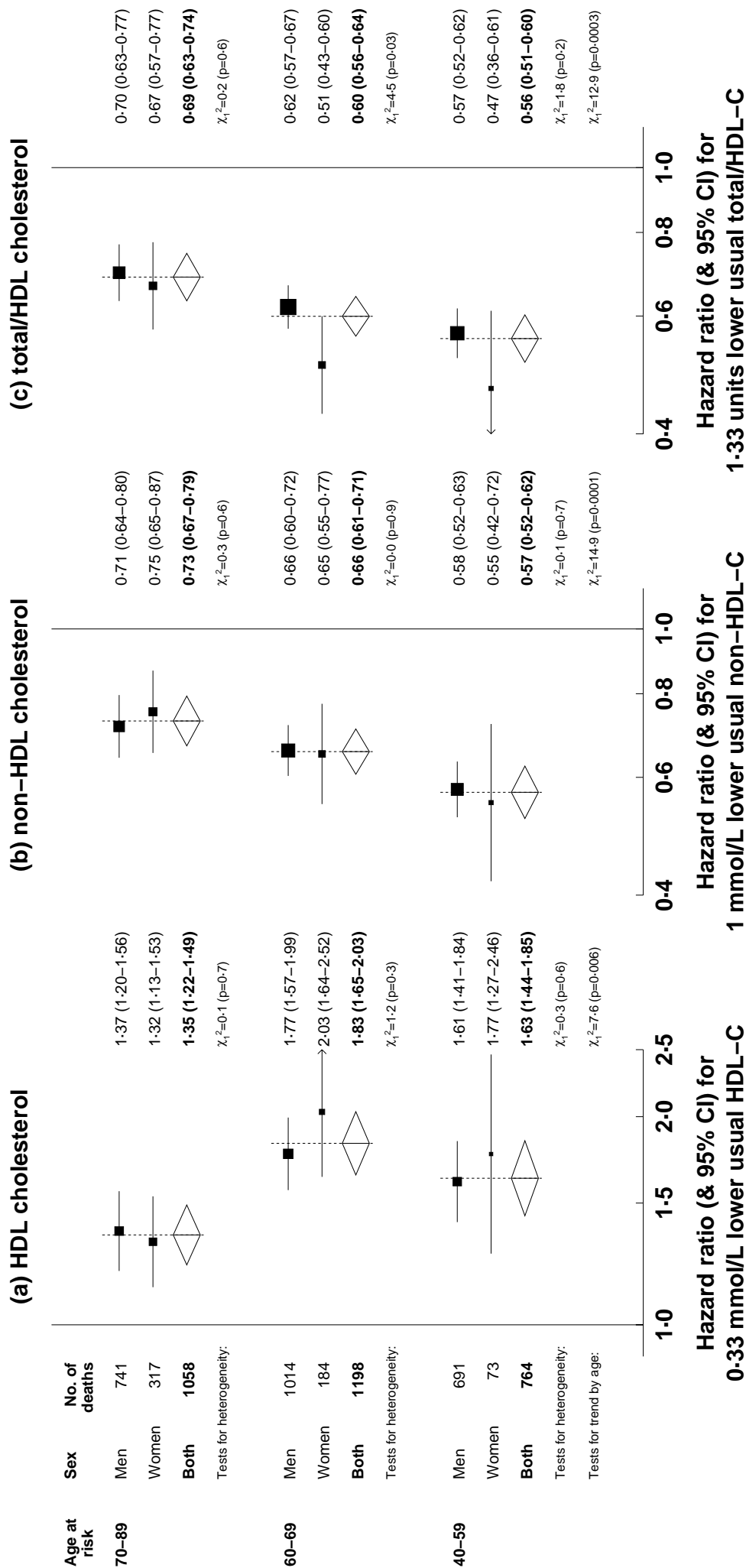
Webfigure 4: IHD mortality (33 744 deaths) versus usual total cholesterol:

(a) SBP-specific associations; and

(b) SBP-specific hazard ratios for 1 mmol/L lower usual total cholesterol



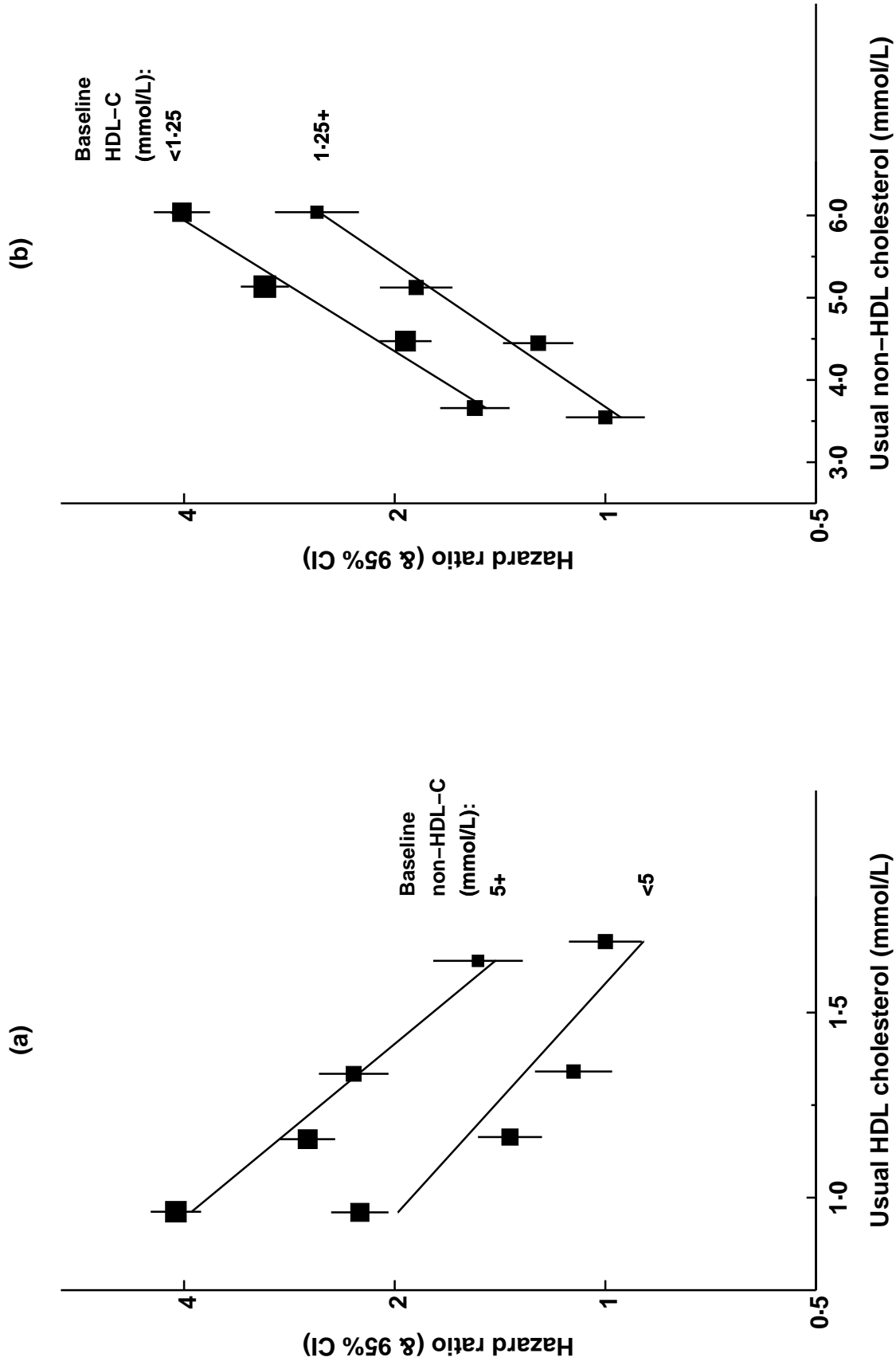
Webfigure 5. IHD mortality (3020 deaths) versus usual:
(a) HDL cholesterol; (b) non-HDL cholesterol; and (c) total/HDL cholesterol
 Age- and sex-specific hazard ratios for given differences



Webfigure 6: IHD mortality (3020 deaths) versus:

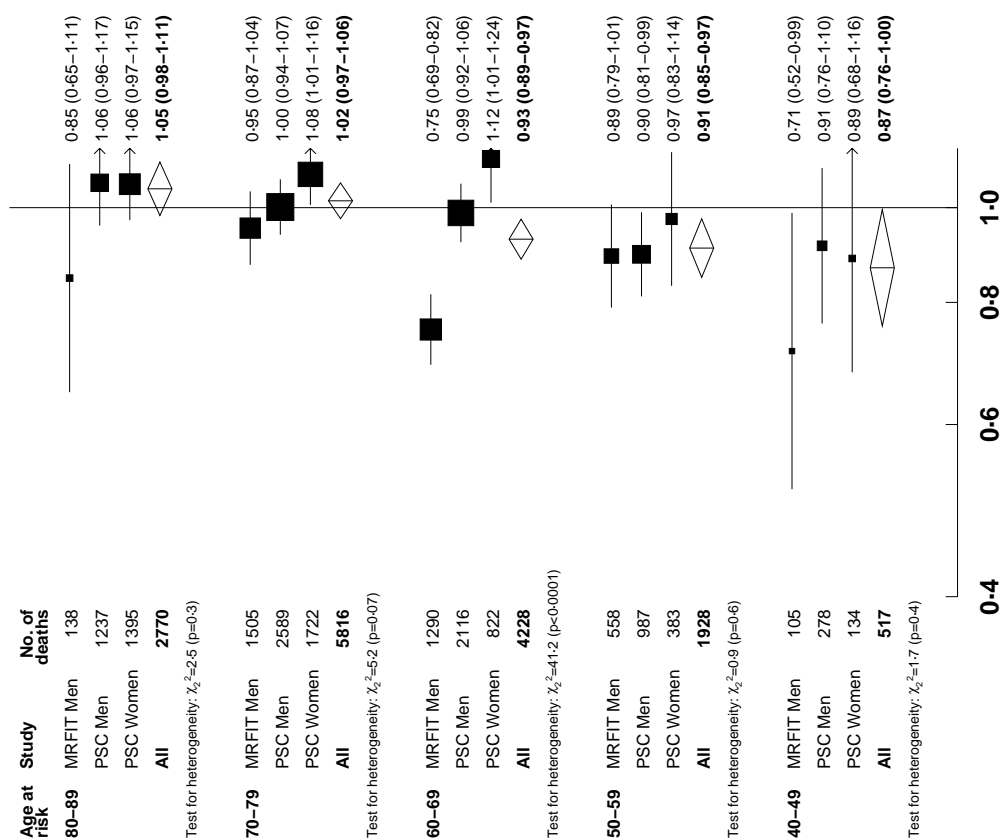
(a) usual HDL cholesterol by baseline measurement of non-HDL cholesterol; and

(b) usual non-HDL cholesterol by baseline measurement of HDL cholesterol



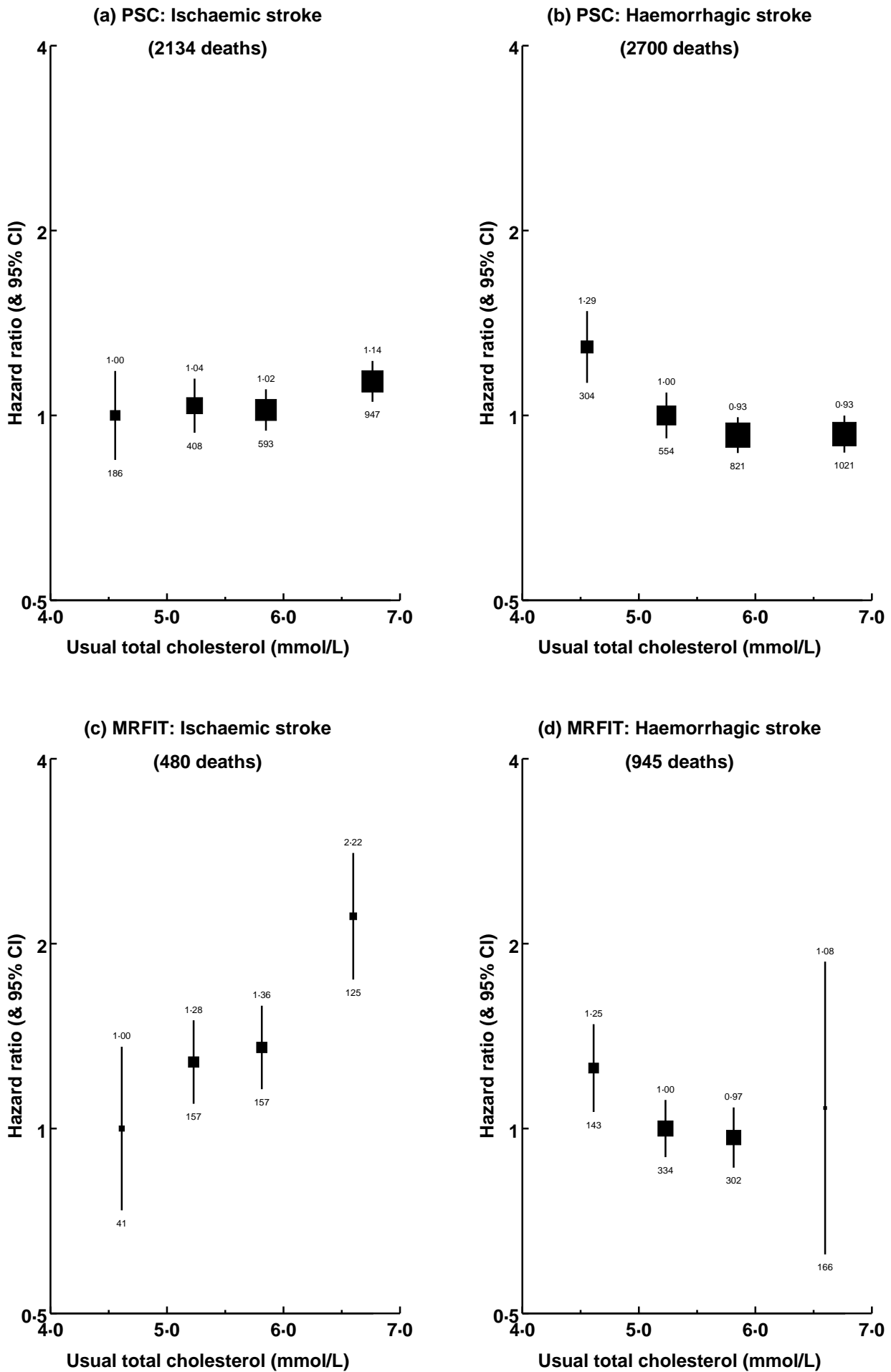
Webfigure 7: PSC and MRFIT study: stroke mortality (15 259 deaths) versus usual total cholesterol

Age- and sex-specific hazard ratios for 1 mmol/L lower usual total cholesterol



Hazard ratio (& 95% CI) for
1 mmol/L lower usual total cholesterol

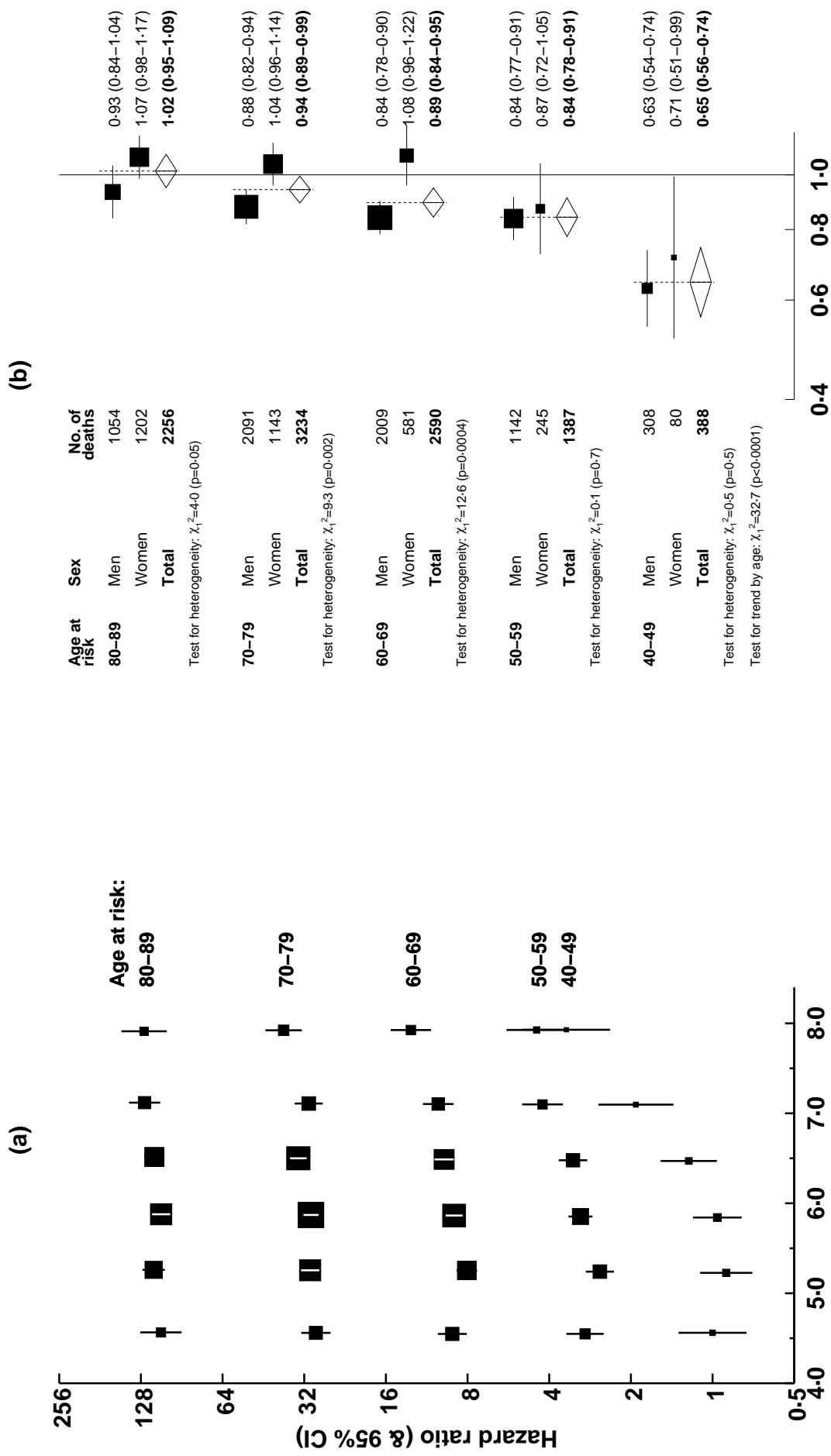
Webfigure 8: PSC and MRFIT study: stroke subtype mortality versus usual total cholesterol



Webfigure 9: Vascular mortality from causes other than IHD or stroke (9855 deaths) versus usual total cholesterol:

(a) age-specific associations; and

(b) age- and sex-specific hazard ratios for 1 mmol/L lower usual total cholesterol



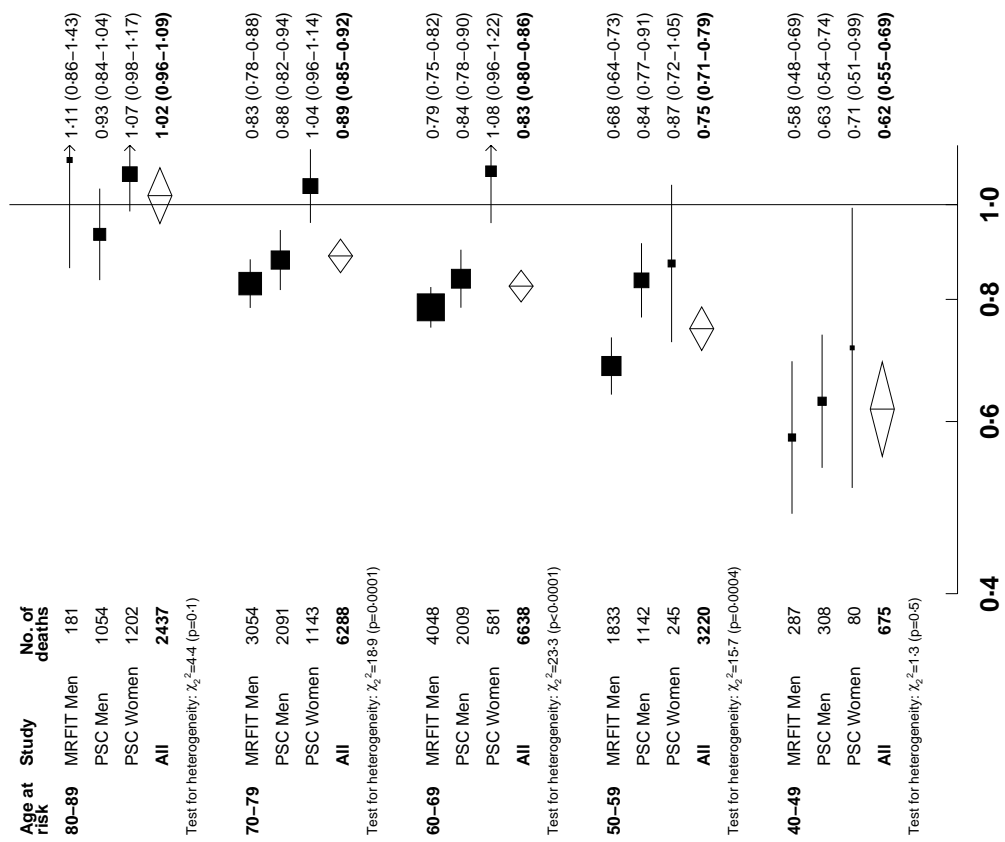
Usual total cholesterol (mmol/L)

Hazard ratio (& 95% CI) for

1 mmol/l lower usual total cholesterol

Webfigure 10: PSC and MRFIT study: other vascular mortality (19 258 deaths) versus usual total cholesterol

Age- and sex-specific hazard ratios for 1 mmol/L lower usual total cholesterol



Hazard ratio (& 95% CI) for
1 mmol/L lower usual total cholesterol

**Webfigure 11: Other vascular mortality (1032 deaths) versus usual:
 (a) HDL cholesterol; (b) non-HDL cholesterol; and (c) total/HDL cholesterol**
 Age-specific associations

