Lifetime and 10-year risks of cardiovascular mortality in relation to risk factors in middle and old age: 50-year follow-up of the Whitehall study of London Civil Servants

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Summary (n=293)

Background: Cardiovascular mortality (CVD) declined substantially in the United Kingdom in recent decades, but the continued relevance of conventional risk factors for (~~prediction of~~) CVD mortality risk throughout the life-course is uncertain. We conducted a study to compare the 10-year risks and lifetime risk of CVD mortality associated with conventional risk factors in middle and old age.

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Methods: The Whitehall study was a prospective study of 19,019 male London civil servants (mean age 52 years) when enrolled in 1967-1970 and followed-up for 50 years for cause-specific mortality. In 1997, 7044 (83%) survivors (mean age 77 years) were resurveyed. The 10-year and lifetime risks of CVD mortality were estimated by levels of CVD risk factors recorded in middle-age and old-age, respectively.

Results: By July 2020, 97% died (22%, 51% and 80% before age 70, 80 and 90 years, respectively) and 7446 of 18404 deaths (40%) were from CVD. The 10-year and lifetime risks of CVD death increased linearly with higher levels of CVD risk factors recorded in middle-age and in old-age. Individuals in the top versus bottom (95% vs 5%) of CVD risk scores in middle age had a 10.3% (95% confidence interval 7.2-13.4) vs 0.6% (0.1-1.2) 10-year risk of CVD mortality, a 61.4% (59.4-65.3) vs 31.3% (24.1-34.5) lifetime risk of CVD mortality and a 12-year difference in life expectancy from age 50 years. The corresponding differences in old-age were 11.0% (4.4-17.5) vs 0.8% (0.0-2.2) for 10-year risk and 42.1% (28.2-50.0) vs 30.3% (6.0-38.0) for lifetime risk of CVD mortality and a 6-year difference in life expectancy from age 70 years.

Conclusions: Conventional risk factors remained strongly (predictive) associated with CVD mortality and life expectancy through the life-course. The findings highlight the relevance of estimation of lifetime risks of CVD and 10-year risks of CVD for primary prevention of CVD.

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Research in context

Evidence before this study

- Reductions in cigarette smoking and levels of other CVD risk factors have resulted in major improvements in life expectancy in the United Kingdom (UK) in recent decades.
- Higher proportions of individuals are surviving beyond age 80 years, prompting questions about the continued relevance of CVD risk factors throughout the life-course.

Added value of this study

- Among 19019 men who enrolled in the Whitehall study in 1967-1970, 97% died before 1 July 2020 (97%) and 22%, 51% and 80% of these deaths occurred before age 70, 80 and 90 years, respectively.
- The 10-year risks of CVD death varied over 10-fold between 5% and 95% of total CVD risk scores in middle age and in old age, but the corresponding differences in lifetime risks of CVD differed by 2-fold (31% vs 61%) in middle age and 1.4-fold (30% vs 42%) in old age.

Implications of all the available evidence

- Higher levels of CVD risk factors were associated with higher 10-year risks of CVD and lifetime risks of CVD in middle age and in old age.
- Differences in CVD risk scores (5% vs 95%) were also associated with 12-year differences in life expectancy from age 50 and 6-year differences in life expectancy from age 70 years.
- The improved survival in many countries now highlights the importance of estimation of lifetime risks of CVD in addition to 10-year risks of CVD for primary prevention of CVD.

Introduction

Cardiovascular diseases (CVD) account for about 20 million deaths annually worldwide and 200,000 deaths in the United Kingdom (UK).[1] Previous population-based prospective studies have highlighted the importance of cigarette smoking, systolic blood pressure (SBP), total cholesterol and diabetes as major modifiable risk factors for CVD.[2] The Framingham study conducted in the United States, reported that higher levels of these risk factors, and their combinations were linearly and positively associated with higher risks of CVD prompting estimation of "total" CVD risk scores in healthy adults to predict risk of subsequent CVD outcomes. [3-5] The Whitehall study of 19,019 civil servants enrolled in 1967-1970 was the first long-term prospective study to estimate the combined effects of these risk factors for CVD mortality in the United Kingdom (UK). It showed that most CVD deaths occurred in individuals with only moderate rather than extreme elevations of individual CVD risk factors.[6-9]

The findings of these and other prospective studies of the combined effects of major modifiable CVD risk factors on CVD outcomes have guided public health policies on "high-risk" and "population approaches" for primary prevention of CVD.[10,11] However, subsequent studies have acknowledged the limitations of reliance on 10-year risks of CVD[12] and advocated inclusion of lifetime risks of CVD[13-15] and life expectancy (including CVD and non-CVD deaths) in addition to estimation of 10-year risks of CVD to guide clinical decisions on the use of drug treatments for primary prevention of CVD.[15]

Widespread cessation of cigarette smoking, improvements in diet and increased use of lipid-lowering and blood pressure-lowering medication in the UK population have resulted in substantial reductions in age-standardised CVD mortality and increases in life expectancy in the UK.[16] Moreover, the proportions of deaths occurring before age 70 years in UK men have declined from about 30% to 10%, and life expectancy was increased by about 10 years between 1970 and 2020. Thus, substantial changes in levels of CVD risk factors within the UK population in recent decades have prompted questions about the continued relevance of measurement of CVD risk factors in middle or old age for prediction of CVD mortality in old age. Hence, assessment of risk prediction for primary prevention of CVD may require prediction of lifetime risks of CVD in addition to 10-year risks of CVD mortality at periodic intervals throughout the life-course in middle and old age.

The Whitehall study measured CVD risk factors in a population sample of middle-aged men (mean age 52 years) in 1970 and re-surveyed survivors in old age (mean age 77 years) at about 25 years after enrolment.[17-20] We conducted a study using the 50-year follow-up of these study participants to (i) compare levels of CVD risk factors within individuals in middle and old age and estimate their associations with CVD mortality; and (ii) to contrast the 10-year risks of CVD mortality, lifetime risks of CVD mortality and life expectancy in relation to CVD risk factors recorded in middle and old age; and (iii) to estimate the 10-year risks of CVD mortality and lifetime risks of CVD mortality and life expectancy associated with extreme levels of CVD risk scores throughout the life-course until very old age.

Methods

Study population and baseline examination

Data were collected from 19,019 men, aged 40-69 years who were working in the Civil Service in London when first examined between September 1967 and January 1970. Participants completed a questionnaire on medical history, symptoms of major diseases, smoking habits, employment grade and marital status. All participants underwent a physical examination to record their height, weight and blood pressure, and had electrocardiography and lung function tests recorded. A trained nurse measured blood pressure once in the left arm with a London School of Hygiene sphygmomanometer.

Blood samples were collected from the earlobe into 2 mm glass tubing. Blood total cholesterol concentration was measured by a ferrocyanide reduction method. All participants (except those with self-reported diabetes) had blood glucose measured two hours after drinking a dextrose drink. Individuals with a glucose concentration of 11.1 mmol/L or greater were classified as having screen detected diabetes.

Resurvey of survivors in 1997

Among survivors in 1997, a resurvey of all surviving 8537 participants was conducted during 1997-1998. About one month prior to writing to study participants who were not known to be dead in 1997, their vital status was checked with the Office of National Statistics. Surviving study participants were resurveyed using a postal questionnaire that collected data on medical history, smoking habits, alcohol consumption, employment details and current medication. Individuals with a diagnosis of heart attack, angina or stroke were defined as having prior CVD. Following completion of a study questionnaire, a blood collection kit was sent to all responders and they were asked to attend their general practice. The enclosed instructions asked the general practitioner to measure the study participant's blood pressure after 5 minutes in a seated position on two occasions, with a minimum interval of 1 minute between each reading. A blood sample of 10 ml was collected into a vacutainer (containing EDTA) provided, and the whole blood sample was sent to the study laboratory in a pre-paid transport tube and protective plastic envelope provided. Blood total cholesterol, LDL-cholesterol (LDL-C) and HDL-cholesterol (HDL-C) were measured using a Beckman auto-analyser at the Wolfson Laboratory at University of Oxford.

Ascertainment of cause-specific mortality at follow-up

Participants were linked by their unique identification number to national mortality registers from the date of baseline examination onwards. The date of death and causes of death were obtained initially from the Office for National Statistics and subsequently after 2018 from National Health Service (NHS) Digital which classified causes of deaths using International Classification of Diseases [ICD], 9th and 10th revisions for all deaths occurring up until 30 June 2020. CVD mortality was coded using ICD-10 codes I00-I99 or R96 as the underlying causes of death (Table S1) prior to 30 June 2018, University of Oxford held identifiable records on causes of death provided by Office of National Statistics. After June 2018, the original death data were destroyed and replaced by pseudonymised mortality data on deaths linked to participant records provided by NHS Digital under a Section 251 support.

Ethics and Governance

The Whitehall resurvey was a collaborative study between the Universities of Oxford, University College London, and the London School of Hygiene and Tropical

Medicine, respectively. The study procedures for the resurvey and follow-up for vital status were also approved by the Ethics Committees for University of Oxford, University College London and London School of Hygiene and Tropical Medicine. Sharing of these data was limited between the Universities of Oxford, University College London and London School of Hygiene and Tropical Medicine, respectively.

Statistical analyses

To minimize risks of reverse causality, all analyses of associations of CVD risk factors with mortality outcomes were restricted to individuals with no self-reported history of stroke or heart attack at the baseline and a subset with no prior CVD at resurvey. After successfully confirming the proportional hazards assumption, Cox proportional hazards models were used to estimate the age- and smoking-adjusted hazard ratios (HRs) of CVD mortality associated with individual CVD risk factors and with combinations of CVD risk factors. These hazard ratios and their 95% confidence intervals (CI) of CVD mortality were estimated for categories of CVD risk factors (smoking, systolic blood pressure, or total cholesterol) at baseline, by incremental levels of such risk factors (current cigarette smoking vs non-smokers) and elevated SBP ≥140 mmHg (or blood pressure-lowering treatment) and elevated cholesterol (≥5.0 mmol/L), respectively. Likewise, HRs were estimated for levels of CVD risk factors at resurvey, but were also calculated for levels of HDL-C and LDL-C, respectively, in addition to total cholesterol. In old age, the HRs (95% CI) of CVD in relation to CVD risk factors combined included current smoking, SBP (≥140 mmHg) and HDL-C <1.0 mmol/L instead of total cholesterol (≥5 mmol/L) (as HDL-C was more strongly related with CVD mortality than total cholesterol in old age).

By using standard lifetable methods, the age-specific mortality rates were used to estimate life expectancy from age 50 years (defined as the number of years one is expected to live having survived to age 50 years), and separately from age 70 years (defined as the number of years one is expected to live having survived to age 70 years). Subsequently, we estimated 10-year risks of CVD mortality, lifetime risks of CVD mortality, and life expectancy for fifths and extreme 5th percentiles (5% and 95% percentiles) of CVD risk score for CVD mortality based on combinations of the three risk factors recorded at age 50 years and age 70 years, respectively. In addition, from survival curves starting at ages 50 and 70 years, we estimated differences in the median survival for individuals with extreme 5% percentiles of CVD risk scores.

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

A schematic representation of the study design and number of study participants examined at baseline and resurvey and deaths during the 50 year follow-up is provided in Figure S1. Among the 19,019 participants at baseline, 10,482 (55%) died before the resurvey. Overall, 7044 of 8537 (83%) surviving participants, participated in the resurvey and responded to a questionnaire in 1997-1998. Among the 7034 men with valid questionnaire responses, 5419 men (77%) also provided data on blood pressure and blood lipids at resurvey and 4061 (75%) of these individuals with complete data had no prior history of CVD at resurvey. The primary analyses of cause-specific mortality in relation to levels of CVD risk factors in old age were restricted to 18,089 (95%) participants aged 50 years or greater at baseline and 3554 of these participants with no prior history of heart attack or stroke (CVD) at resurvey.

Table 1 shows the distribution of CVD risk factors in all participants at baseline (mean age 52 years) and all participants at resurvey (mean age 77 years) and the subset (mean age 77 years) with no prior history of CVD at resurvey. Mean levels of CVD risk factors differed substantially between middle and old age. The prevalence of current cigarette smoking declined from 43.1% in 1970 to 12.3% in all participants in 1997 and 13.6% in those with no prior CVD at resurvey. The mean (SD) levels of SBP increased from 136 (21) in 1970 to 145 (20) mmHg in all participants and the subset without prior CVD in 1997. Mean levels of total cholesterol also increased from 5.1 (1.2), to 5.1 (1.0) and 5.5 (1.0) mmol/L in the corresponding groups, respectively. In contrast, mean levels of BMI remained stable between middle and old age.

Table 2 shows that among all men in middle age with no prior CVD at baseline, 43% were current smokers, 39% had mean levels of SBP ≥140 mmHg and 50.6% had mean levels of total cholesterol ≥5 mmol/L. Overall, 17% had none of these three CVD risk factors, 42% had at least one factor, 33% had two and only 8% had all three CVD risk factors. **Table 3** shows that the proportions with SBP ≥140 mmHg in old-age increased to 66% and those with elevated levels of total cholesterol ≥5 mmol/L increased to 71% and those with low HDL-C (<1 mol/L) were 41%. Overall, 18% had no CVD risk factors, 48% had one CVD risk factor, 30% had two and 4% had three CVD risk factors, respectively.

Figure 1 shows the overall survival from age 50 years by levels of CVD risk scores. Among men aged 50 years, 22% died before age 70 years, 51% died before 80 years, and 86% died before aged 90 years. The percentage survival differed substantially by levels of CVD risk scores recorded at baseline. **Figure 1** shows that the median difference in survival was 14 years between those in the top vs bottom 5% (95th vs 5th percentiles) of CVD scores in middle age. Moreover, differences in overall survival by corresponding levels of CVD risk factors persisted beyond age 80 years to 90 years, respectively. Among survivors at age 70 years, about 61% and 17% were still alive at age 80 and 90 years, respectively. The median difference in survival from age 70 years was 8 years for those with CVD risk scores between 5% and 95% percentiles for CVD risk scores measured in middle age.

Table S1 shows the distribution of major causes of deaths by age at death and demonstrated that the proportion of deaths due to CVD declined with increasing age. Overall, the proportion of all deaths due to CVD declined from 51.9%, 47.9%, 43.1% and 41.9% at age <70, 70-79, 80-89, 90+ years, respectively. Likewise, the proportion of deaths due to ischaemic heart disease (IHD) declined from 34.9%, 30.3%, 21.6% and 26.5% at age <70, 70-79, 80-89, 90+ years. In contrast, the proportion of deaths due to stroke increased from 5.4%, 8.8%, 11.5% and 9.2% in the corresponding age groups, respectively.

Table 2 shows the numbers of CVD deaths, 10-year risks of CVD death, lifetime risks of CVD deaths and life expectancy by levels of CVD risk factors recorded at baseline. Current smoking was associated with 3-fold higher 10-year risks of CVD mortality and a 6.3 year difference in life expectancy. Higher levels of SBP were linearly and positively associated with higher risks of CVD mortality and lower life expectancy, respectively. Likewise, higher levels of total cholesterol were associated with higher 10-year risks and lifetime risks of CVD mortality. Analysis of combinations of these CVD risk factors recorded in middle age demonstrated that risk of CVD mortality were linearly and positively associated with higher levels of combinations of these risk factors. Individuals with all three CVD risk factors vs none had 8.5-fold higher 10-year risks of CVD death (8.5% vs 1%), a 1.5-fold higher lifetime risks of CVD death (54.3% vs 36.9%) and a 10-year difference in life expectancy.

Table 3 shows the distribution of CVD deaths, 10-year risks of CVD mortality, lifetime risks of CVD mortality and life expectancy by levels of CVD risk factors recorded in old age. Since total cholesterol was a weak predictor of CVD deaths in old age and low HDL-C was a stronger predictor of CVD death, low HDL-C levels were substituted for high total cholesterol levels when estimating CVD risk scores in old age. Most of CVD deaths in old age also occurred in individuals with only one or two CVD risk factors. Consistent with the patterns in middle age, the 10-year risks and lifetime risks of CVD death increased linearly and positively with increasing numbers of CVD risk factors recorded in old age. The differences in 10-year risks of CVD mortality between men with all three vs none of these CVD risk factors were 3-fold (10.9% vs 3.8%), but lifetime risks also differed 1.35-fold (36.6% vs 27.8%) and life expectancy differed by 2 years, respectively.

Table 4 shows the 10-year and lifetime risks of CVD mortality and life expectancy by fifths of CVD risk scores or by extreme 5% (95% vs 5%) when estimated in middle and old age, respectively. Higher levels of CVD risk scores were also linearly and positively associated with higher 10-year risks of CVD death and lifetime risks of CVD death in middle and old age and were inversely associated with life expectancy from age 50 years and 70 years, respectively. Individuals in the top versus bottom

(95% vs 5% percentiles) of CVD risk scores in middle-age had 10% vs 1% 10-year risk of CVD death and 61% vs 31% lifetime risk of CVD mortality. The corresponding differences in old age were 11% vs 1% for 10-year and 42% vs 30% for lifetime risks of CVD mortality. Likewise, differences in life expectancy between those with CVD risk scores at 95% vs 5% were 12 years in middle age and 6 years in old age, respectively.

Discussion

The 50-year follow-up of 19,019 male civil servants demonstrated that despite substantial improvements in life expectancy, conventional CVD risk factors recorded in middle and in old age remained strongly predictive of 10-year risks and lifetime risks of CVD throughout the life-course. About half of the population survived beyond age 80 years, but higher levels of conventional CVD risk factors remained strongly predictive of CVD mortality and life expectancy until very old age. Overall, two-thirds of men with the lowest levels of CVD risk scores at age 50 years survived to 80 years, and one quarter survived to 90 years, compared with only one-fifth or one twentieth of those with highest levels of CVD risk scores. Despite a 75% reduction in the prevalence of current cigarette smoking, and a 10% increase in mean levels of SBP and total cholesterol between 1970 and 1997, CVD risk scores estimated in middle age still predicted about a 1.5-fold difference in lifetime risks of CVD death from age 50 years and about 1.4-fold difference in lifetime risks of CVD death from age 70 years.

Estimation of 10-year risks of CVD is widely used to guide decisions on use of LDL-lowering or blood pressure-lowering drug treatment for primary prevention of CVD.

The present study demonstrated that substantial differences in CVD risk factors were associated with modest differences in 10-year risks of CVD mortality in individuals, but the magnitude of differences in lifetime risks of CVD mortality were much greater. Thus, middle-aged individuals with moderate elevations of CVD risk scores had moderate differences in 10-year risks of CVD mortality but could still have substantial lifetime risks of CVD death. Hence, in the absence of elevated 10-year risk of CVD mortality, decisions on the initiation of drug treatment should consider lifetime risks of CVD in addition to 10-year risks of CVD mortality.

The Whitehall study was initiated at the peak of the epidemic of CVD mortality in the UK in 1970 to assess the relevance of conventional CVD risk factors for prediction of CVD mortality in a sample of the UK male population. The resurvey of surviving participants in this study was initiated in 1997 to assess the continued relevance of conventional risk factors for prediction of CVD mortality in very old age. The Whitehall study had several unique features, including being the first large prospective study of conventional CVD risk factors recorded in middle-aged men in the UK, with prolonged follow-up for 50 years, resurvey of levels of CVD risk factors in surviving participants in old age and having almost complete mortality (97% of men died) data for the present analyses. However, the study also had several limitations, including absence of any data on non-fatal CVD outcomes, no data on women, no data on different ethnic groups and analysis being limited to an employed cohort of civil servants. Moreover, the present analyses did not assess any differences of lifetime risks or 10-year risk of CVD mortality by employment grade.

The present 50-year follow-up analysis confirms the continued importance of conventional CVD risk factors for CVD mortality that were reported in the first decade of the follow-up of Whitehall Study population. The initial results of this study prompted Rose to advocate both a “population strategy” (to alter lifestyle, environment and physiological determinants to reduce CVD risk factors) and a “high-risk strategy” (to prescribe medication for high-risk individuals) to reduce levels of CVD risk factors. Moreover, the results of the present analyses highlight the importance of “population strategies” in addition to “high-risk” strategies to reduce mean levels or proportions with these risk factors for avoidance of CVD before age 70 years and greater absolute benefits for the much larger number of deaths occurring after age 70 years. The results also suggest that treatment decisions relying on 10-year risks of CVD for primary prevention of CVD could result in substantial proportions of the population being under-treated. Men with CVD risk scores in the top vs bottom (95% vs ≤5%) of CVD risk scores had 12 years less life expectancy from age 50 years and 6 years less life expectancy from age 70 years, respectively.

The findings of the Whitehall study are consistent with results of similar prospective studies conducted in other populations. A meta-analysis of 18 cohort studies of lifetime risks of CVD involving 257,384 men and women reported that the lifetime risks of non-fatal and fatal CVD outcomes at age 45, 55, 65 and 75 years by levels of CVD risk scores found similar gradients in lifetime risks of CVD outcomes by levels of CVD risk factors.[22] The Framingham study estimated lifetime risks between 1960-1980, 1980-1999, and 2000-2019, and the graded associations with higher levels of CVD risk factors were broadly comparable with those reported in the present study.

Likewise, meta-analyses of randomised trials of statin therapy in the Cholesterol Treatment Trialists' Collaboration,[27,28] or of blood pressure-lowering treatment in the Blood Pressure Lowering Treatment Trialists' Collaboration both advocated that treatment decision should be based on absolute risks of CVD rather than arbitrary levels of individual risk factors for initiation of medication for primary prevention of CVD. The current guidelines of the European Society of Cardiology[29] advocate complete cessation of tobacco smoking, promotion of a healthy diet low in saturated fat, with a focus on vegetables, fruit, promotion of moderate physical activity, reduction in levels of adiposity, and maintenance of levels of blood pressure below 140/90 mmHg and levels of LDL-C <3 mmol/L (<116 mg/dL) and triglycerides <1.7 mmol/L, and HBA_1C <7%, respectively. Most expert groups in USA, UK and other European countries also advocate that drug treatment to reduce levels of LDL-C or SBP or both should be considered for individuals at high 10-year risk of CVD.[24,25,29,30]

The present report advocates a greater use of lifetime risks of CVD death in addition to the 10-year risks of CVD death, perhaps when used in a stepped approach to consider lifetime risks of CVD in men (and women), particularly in those without high levels of 10-year risks of CVD mortality. The results suggest that premature deaths from CVD could be largely avoidable by lowering levels of a few major modifiable CVD risk factors, not only among people aged 50 years or older, but also among people aged 75 years or older. Thus, differences in levels in CVD risk scores achieved by feasible changes in conventional CVD risk factors (≥95% vs ≤5%) predict lifetime risks of CVD mortality for 2 in every 3 men at high-risk vs only 1 in 3 men in low-risk in middle age and 12 year gain in life expectancy from age 50 years, or almost 6 years gain from age 70 years or older if they could change from high to low risk of CVD. Further research is required to assess if these findings can be extrapolated to women, people from different socioeconomic groups or from different ethnic backgrounds.

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Figure legends

Figure 1: Survival from age 50 and 70 years by levels of CVD risk scores at baseline in the 50 year follow-up of the Whitehall study.

Table 1: Distribution of CVD risk factors in all participants at entry in middle-age and in survivors in old age.

Mean (SD) or n%	All participants at baseline	Survivors at resurvey	Survivors at resurvey and no prior CVD
No. of participants	19019	7044	5166
Age, years	52.0 (6.7)	77.2 (5.1)	76.9 (5.0)
Cigarette smoker			
Current-smoker, n (%)	7918a (43.1%)	803 (12.3%)	654 (13.6%)
Ex-smoker, n (%)	6934 (37.8%)	3731 (57.0%)	2605 (54.1%)
Never-smoker, n (%)	3502 (19.1%)	2011 (30.7%)	1558 (32.3%)
Clinical measures			
Systolic blood pressure, mmHg,	136.4 (21.2)	144.9 (20.2)	145.5 (20.0)
Diastolic blood pressure, mmHg	84.1 (13.8)	80.1 (10.8)	80.7 (10.7)
Body Mass Index, kg/m^2	24.7 (3.0)	24.6 (3.1)	24.6 (3.1)
Blood lipids			
Total cholesterol, mmol/L	5.10 (1.21)	5.51 (1.01)	5.54 (1.01)
LDL-cholesterol, mmol/L	-	3.10 (0.90)	3.10 (0.90)
HDL-cholesterol, mmol/L	-	1.10 (0.38)	1.12 (0.39)

[a] 665 pipe and cigar smokers were excluded in analyses of cigarette smokers in this table.

Table 2: Absolute risks of CVD mortality and life expectancy in relation to risk factors and risk factor combinations at baseline

	No. of participants (%)	No. of CVD deaths[a]	10-year risk[b] of CVD death (95% CI), %	Lifetime risk[b] of CVD death (95% CI), %	Life expectancy[b] (95% CI), yrs
Risk factors					
Smoking					
Never smokers	3464 (19.1)	1457	1.6 (1.1, 2.1)	44.3 (40.0, 46.0)	32.6 (32.2, 32.9)
Ex-smokers	6852 (37.8)	2943	2.4 (1.9, 2.8)	44.7 (42.1, 45.9)	30.9 (30.7, 31.2)
Current smokers [c]	7829 (43.1)	3261	4.9 (4.3, 5.5)	43.5 (40.9, 44.7)	26.3 (26.1, 26.6)
Systolic blood pressure (mmHg)					
<120	3924 (20.9)	1349	2.0 (1.5, 2.5)	35.9 (31.9, 37.5)	31.1 (30.8, 31.5)
120 – 139	7615 (40.5)	3018	2.6 (2.1, 2.9)	41.5 (38.8, 42.7)	30.4 (30.1, 30.7)
140 – 159	4797 (25.5)	2238	3.8 (3.1, 4.5)	48.5 (45.4, 50.0)	28.2 (27.9, 28.6)
≥ 160	2459 (13.1)	1341	8.3 (6.7, 9.9)	57.1 (53.8, 59.2)	24.8 (24.2, 25.4)
Cholesterol (mmol/L)					
<5.0	8911 (49.2)	3471	2.4 (2.0, 2.8)	40.9 (39.3, 42.0)	30.0 (29.7, 30.2)
5.0 – 5.9	5442 (30.1)	2373	3.5 (2.9, 4.1)	45.3 (42.3, 46.7)	29.4 (29.1, 29.7)
≥ 6.0	3748 (20.7)	1824	4.7 (3.9, 5.5)	50.5 (47.3, 52.2)	28.2 (27.8, 28.6)
Number of risk factors [d]					
None	2970 (17.0)	1034	1.0 (0.6, 1.4)	36.9 (32.5, 38.7)	33.4 (33.0, 33.8)
One	7262 (41.6)	2938	2.3 (1.9, 2.7)	42.2 (39.4, 43.4)	30.3 (30.1, 30.6)
Two	5790 (33.2)	2670	5.0 (4.1, 5.6)	47.9 (45.3, 49.3)	27.0 (26.7, 27.3)
Three	1442 (8.3)	751	8.5 (6.5, 10.5)	54.3 (49.9, 57.1)	23.6 (22.9, 24.3)

[a] Number of CVD deaths over 50-year follow-up from baseline
[b] 10-year risk, lifetime risk and life expectancy are for men aged 50 years.
[c] Current cigarette smokers only, current pipe and cigar smokers were excluded
[d] Risk factors are current smoking, systolic blood pressure ≥140 mmHg and cholesterol ≥5.0 mmol/L.

Table 3: Absolute risks of CVD mortality and life expectancy in relation to risk factors and risk factor combinations at resurvey in the subset with no prior CVD at resurvey

	No. of participants	No. of CVD deaths[a]	10-year risk[b] of CVD death (95% CI), %	Lifetime risk[b] of CVD death (95% CI), %	Life expectancy[b] (95% CI), years
Risk factors					
Smoking					
Never smoker	1557 (32.4)	491	6.2 (4.5, 7.7)	33.6 (27.1, 36.1)	17.5 (17.0, 18.0)
Ex-smoker	2590 (54.1)	798	6.3 (4.7, 7.9)	31.8 (27.4, 33.9)	15.9 (15.5, 16.4)
Current smoker	649 (13.5)	220	8.8 (5.2, 12.3)	34.9 (26.4, 39.1)	14.7 (14.0, 15.5)
Systolic blood pressure (mmHg)					
<120	275 (6.9)	73	2.1 (0.0, 4.1)	27.3 (10.3, 32.9)	17.2 (16.1, 18.4)
120 – 139	1067 (27.3)	306	5.6 (3.7, 7.4)	30.5 (23.3, 33.5)	17.6 (17.0, 18.1)
140 – 159	1461 (37.0)	465	5.0 (3.3, 6.7)	33.0 (27.5, 35.6)	16.9 (16.4, 17.5)
≥ 160	1138 (28.8)	406	6.0 (4.0, 8.0)	36.9 (29.8, 40.0)	16.4 (15.7, 17.1)
Total Cholesterol (mmol/L)					
<5.0	1174 (29.2)	360	4.9 (2.8, 7.0)	30.9 (24.1, 34.0)	16.3 (15.6, 16.9)
5.0 – 5.9	1607 (39.9)	526	5.5 (3.9, 7.1)	33.9 (27.8, 36.4)	16.9 (16.4, 17.4)
≥ 6.0	1244 (30.9)	393	5.5 (3.8, 7.1)	34.0 (27.9, 36.9)	17.7 (17.2, 18.2)
HDL- Cholesterol (mmol/L)					
<1.0	1632 (41.4)	532	6.6 (4.9, 8.2)	35.2 (28.8, 37.7)	17.0 (16.5, 17.5)
1.0 – 1.39	1445 (36.4)	460	4.5 (2.9, 6.0)	32.8 (27.0, 35.4)	17.0 (16.4, 17.5)
≥ 1.4	884 (22.2)	263	3.8 (2.0, 5.7)	35.2 (28.8, 37.7)	17.1 (16.4, 17.8)
LDL- Cholesterol (mmol/L)					
<3.0	1247 (31.5)	358	4.4 (2.4, 6.3)	29.0 (21.9, 31.9)	16.6 (16.0, 17.2)
3.0 – 3.9	1896 (47.9)	633	5.2 (4.1, 6.9)	34.8 (29.6, 37.1)	17.0 (16.4, 17.5)
≥ 4.0	818 (20.6)	264	5.6 (3.5, 7.6)	34.9 (28.0, 38.4)	17.7 (17.1, 18.3)
Number of risk factors[c]					
None	638 (18.0)	169	3.8 (1.6, 5.9)	27.8 (18.9, 31.6)	17.0 (16.5, 17.5)
One	1725 (48.4)	545	4.2 (2.8, 5.5)	32.4 (26.5, 34.8)	16.6 (15.9, 17.2)
Two	1060 (29.9)	340	6.1 (4.0, 8.2)	34.3 (27.4, 37.4)	16.8 (15.6, 18.0)
Three	131 (3.7)	58	10.9 (3.9, 17.7)	37.6 (27.4, 46.3)	15.1 (13.9, 16.2)

[a] Number of CVD deaths over 25-year follow-up from resurvey

[b] 10-year risk, lifetime risk and life expectancy are for men aged 70 years.

[c] Risk factors are current smoking, systolic blood pressure ≥140 mmHg and HDL-cholesterol <1.0 mmol/L

Table 4: Absolute risks of CVD mortality and life expectancy by levels of cardiovascular risk scores at age 50 and 70 years.

	No. of participants	No. of CVD Deaths	10-year risk of CVD death (95% CI), %	Lifetime risk of CVD death[c] (95% CI), %	Life expectancy (95% CI), yrs
Risk scores at age 50[a]					
1 (lowest fifth)	3623	1247	1.4 (0.9, 1.8)	36.3 (32.3, 39.7)	33.1 (32.7, 33.5)
2	3612	1384	1.5 (1.0, 1.9)	40.0 (36.0, 41.7)	31.2 (30.9, 31.6)
3	3631	1486	2.2 (1.6, 2.7)	42.6 (38.8, 44.3)	29.9 (29.5, 30.3)
4	3510	1659	5.1 (4.2, 6.0)	48.1 (44.8, 49.8)	27.7 (27.3, 28.2)
5 (highest fifth)	3613	1888	7.7 (6.4, 9.9)	54.5 (51.3, 56.2)	24.2 (23.7, 24.6)
Lowest 5%	906	270	0.6 (0.1, 1.2)	31.3 (24.1, 34.5)	34.3 (33.6, 35.0)
Middle 90%	16280	6855	3.1 (2.8, 3.5)	44.0 (42.2, 44.8)	29.5 (29.3, 29.7)
Highest 5%	903	539	10.3 (7.2, 13.4)	61.4 (59.4, 65.3)	21.7 (20.7, 22.6)
Risk scores at age 70[b]					
1 (lowest fifth)	709	202	2.9 (1.3, 4.4)	30.6 (20.9, 34.4)	18.8 (18.1, 19.4)
2	712	196	6.5 (3.9, 8.8)	28.6 (18.1, 32.2)	16.6 (15.8, 17.4)
3	712	221	5.2 (2.5, 7.8)	32.8 (25.7, 36.7)	16.9 (16.1, 17.7)
4	710	230	4.5 (2.2, 6.8)	33.6 (24.8, 37.5)	16.9 (16.1, 17.6)
5 (highest fifth)	711	263	6.3 (3.6, 9.0)	38.4 (31.1, 42.3)	16.1 (15.3, 16.8)
Lowest 5%	176	48	0.8 (0.0, 2.2)	30.3 (6.0, 38.0)	20.4 (19.5, 21.3)
Middle 90%	3200	991	5.0 (3.9, 6.0)	32.3 (28.3, 34.1)	16.9 (16.6, 17.3)
Highest 5%	178	73	11.0 (4.4, 17.5)	42.1 (28.2, 50.0)	14.8 (13.1, 16.4)

[a] Risk scores at age 50 years were based on systolic blood pressure, total cholesterol and smoking.
[b] Risk scores at age 70 years were based on systolic blood pressure, HDL-cholesterol and smoking.
[c] Risk scores were computed for CVD deaths over the entire follow-up from baseline and resurvey, respectively.

Figure 1: Survival from age 50 and 70 years by levels of CVD risk scores at baseline in the 50 year follow-up of the Whitehall study.