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Original Research

Myocardial infarction and death findings from a 22-year follow-up of a cohort of 980 employed Swedish men

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ABSTRACT

Objectives: In this article, we present death and myocardial infarction (MI) incidences over 22 years in relation to possible risk factors and their explanatory value.
Study design: In 1993, 980 middle-aged Swedish men in an automotive industry were surveyed at a health checkup as part of the Renault-Volvo Coeur project. The Swedish cohort was revisited in 2015.
Methods: In 2015, incident MIs were identified using postal questionnaires, hospital records, and the Swedish national MI and death registers. The statistical results were given as odds ratios (ORs) and pseudo-R^2 (PR^2), showing the proportion of variation in risk explained by logistic models.
Results: One hundred and four deaths (4.6 per 1000 person-years) and 89 first MIs (4.2 per 1000 person-years) were identified. The Framingham risk index showed the strongest association with MI (OR = 23; 95% confidence interval [CI] = 5.42, 96.9), comparing the fifth quintile with the first. The all-cause death showed an OR of 3.2 (95% CI = 1.65, 6.08), with a suggested U-shape over quintiles. The percentages of PR^2 for MI and death were 8.8% and 6.6%, respectively. All risk factors together explained 22% of the variation in risk of MI. Comparing mortality in men living alone with those married yielded an OR of 3.78, which was found to be statistically significant. The corresponding OR for MI was not significant.
Conclusions: Traditional risk factors were confirmed but explained a modest proportion of the risk variation.

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Introduction

Cardiovascular disease (CVD) is a main cause of death in Europe, contributing almost half of all deaths.[1] In 2015, the life expectancies at birth for Swedish and French men were 82.2 and 82.3 years, respectively.[2] The Framingham Heart Study, started in 1947, introduced the concept of risk factors.[3] Strong correlations between death or myocardial infarction (MI) and lifestyle as well as contextual risk factors at the national level were observed in the Seven Countries Study.[4,5] The MONICA collaboration studied MI and coronary death epidemiology in 21 countries. The annual age-standardized coronary event rates of MI in men for the period 1985–1987 were lower in Toulouse, France (240 per 100,000), than in Gothenburg, Sweden (406 per 100,000).[6]

Tunstall-Pedoe[7] claimed that French men consumed more fat (e.g., cheese) and wine than men in the northern European countries such as Sweden but exhibited lower MI rates. This seemingly contradictory finding was called the French paradox[8] and inspired the Coeur project, a joint medical research project between two automotive companies, one in Sweden and one in France, started in 1992. The hypothesis was that the differences in environmental risk factors, dietary habits, hereditary factors, and individual risk factors between the two populations can explain the paradox.

In 1993, baseline data were collected from 1000 randomly selected men aged 45–50 years from each enterprise.[9] The coronary heart disese (CHD) risks in the two groups, as estimated by the Framingham risk index (FRI),[9,10] were similar. In 1998, all participants in France and Sweden were again summoned for a renewed assessment of cardiovascular risk factors, now including questions on general well-being and work-related stress. Employees living alone had more risk factors for CHD pertaining to lifestyle and social networking than divorced or married/cohabiting men. The proportion of men living alone was significantly higher in Sweden (24%) than in France (10%).[11]

In 2015, 22 years after the baseline, the cumulative incidences of cardiovascular end points and deaths in the Swedish cohort were estimated, and statistical associations with potential risk factors as measured at baseline in 1993 were studied.

The general objective of this article is to study overall mortality and cardiovascular morbidity in a cohort of middle-aged men employed in the Swedish automotive industry who were followed up from 1993 to 2015, specifically, to estimate incidences of death and MI and to estimate statistical associations between death, MI, and explanatory variables from the 1993 survey.

Methods

The baseline survey in 1993

The Swedish baseline survey in 1993 collected complete data from 980 of 1000 randomly selected men aged 45–50 years in four different factories of a Swedish automotive manufacturer using a self-administered questionnaire on demographic, social, health, lifestyle, and working conditions as well as laboratory examinations. The following baseline variables were used for the present article: age; married/single/divorced; manual (blue-collar)/clerical (white-collar) work; number of children; smoking status; education: basic, high school, university; systolic blood pressure in mmHg; diastolic blood pressure in mmHg; pulse rate in beats/min; total serum cholesterol; serum high-density lipoprotein cholesterol (HDL-C) in mmol/L; serum triglycerides (TGs) in mmol/L, diabetes mellitus; left ventricular hypertrophy; FRI; blood glucose in mmol/L; alcohol intake in g/week; height in cm; weight in kg; body mass index (BMI) in kg/m^2; sagittal abdominal diameter in cm; and waist-hip ratio. Standardization of blood pressure, anthropometric measurements, and laboratory tests have been detailed elsewhere.[9]

The 22-year follow-up

In 2015, a follow-up survey of 896 men (excluding 104 men reported to have died) was conducted using mailed questionnaires, largely including the same variables as used in the baseline. Seventy-six percent of them responded. Complete information in both surveys was available for 672 men.

The survey contained information reminding of the participant's involvement in the Coeur project and the aim of the follow-up as well as questions about any occurrences of heart disease and stroke that they had suffered as well as consent to sign that hospital-based information could be collected if necessary. The survey was mailed in August 2015. A reminder was sent four weeks later.

Each response from the subjects was coded into a secure SPSS file (IBM Corp., Armonk, NY). The baseline Coeur data set, originally in SAS software, and the follow-up data set were merged. The software used for the present analyses was Stata version 15 (StataCorp LC, College Station, TX).

End point information from registers

In February 2016, the Swedish death registry was contacted to identify who out of our 1000 participants had died. To validate the self-reported information about MI received from the responders and other sources, we used hospital records and the Swedish national myocardial infarction registry (Swedeheart). This registry also provided information about heart attacks in the non-responders in the 2015 survey.[12] To define MI, we used the code 410 of the International Classification of Diseases Ninth Revision and codes I21–I23 of the Tenth Revision.[13]

Statistical analysis

Conventional statistical characteristics were used to describe the distribution of variables totally and for the following three subgroups: (1) those who participated in the follow-up survey of 2015; (2) those who did not participate in the follow-up survey of 2015 and are still alive; and (3) those who had died.

Estimated Nelson-Aalen curves were used to describe the distribution over age for deaths and MI occurrences.[14]

The basic tools for the analysis of associations between risk factors and outcomes were logistic regression models.

Goodness of fit and explanatory capacity were studied using McFadden pseudo-R^2 (PR^2).[15]

Results

Table 1 shows baseline characteristics for selected variables by the aforementioned defined subgroups.

The proportion of blue-collar (manual) workers was slightly higher, and the proportion of married/cohabiting men was lower in 2015 non-responders than in responders. The participants who died had significantly a higher FRI at baseline than others.

Mortality

The 104 deaths correspond to an estimated death rate of 4.8 per 1000 person-years (95% confidence interval [CI]: 3.8–5.8). Twenty-six participants (25%) had died from MI. The results of the analysis of death for key continuous variables are shown in Table 2.

The estimated FRI showed the highest PR^2, that is, it gave the best explanation of risk variation. The blood pressure variables, pulse rate, and the BMI showed similar results. The three anthropometric variables showed trends toward higher death rates in the highest quintiles. For total alcohol consumption, there was a weak and not statistically significant trend of decreasing death rates with increasing alcohol consumption.

Myocardial infarction

The results for MI in Table 3 are organized in the same way as those for deaths in Table 2. Altogether, 89 men had their first MI during the 22-year follow-up. The overall estimate of first-time MI was 4.2 per 1000 person-years (95% CI: 3.4–5.0). The FRI showed the highest PR^2, and the results for other variables were similar to those for death risk. In addition, however, there was a statistically significant decreased MI risk for increasing the HDL-to-total cholesterol ratio. There was also a weak trend of increased risk with increased level of TGs.

Table 4 shows the results for categorical variables. The results for death risk and MI risk appear to be similar. The highest odds ratio (OR) and the highest PR^2 were seen for the dichotomous variable smoking (yes or no). The associations for MI risk were generally weaker than those for death risk. There are statistically significant positive associations (increased risk) between death and both smoking and manual labor, and negative associations with death (decreased risk) were seen for married or cohabiting men, high level of education, number of children, and partners working outside the home. Diabetes was associated with increased mortality risk and risk of MI.

Table 1 – Characteristics of the distributions of selected variables for the cohort of 980 employed middle-aged men with complete baseline information from 1993.

Variable	Total	Participants answering the questionnaire in 2015	Living participants not answering the questionnaire in 2015	Participants reported deceased
Participants with baseline data (n)	980	672	208	100
Age (years)	47.7 (1.48)	47.7 (1.46)	47.6 (1.50)	47.8 (1.52)
Blue-collar workers (%) [95% CI]	39 [35–43]	34 [30–39]	47 [39–57]	58 [44–74]
University education (%) [95% CI]	24 [21–27]	25 [21–29]	25 [19–32]	14 [8–23]
Married or cohabitant (%) [95% CI]	76 [71–82]	81 [74–88]	70 [60–82]	58 [44–74]
Noisy work environment (%)	1.95 (0.20)	1.96 (0.01)	1.95 (0.20)	1.91 (0.27)
Systolic blood pressure (mmHg)	117 (14.7)	116 (13.6)	118 (15.4)	124 (18.4)
Diastolic blood pressure (mmHg)	75 (11.8)	74 (11.3)	76 (12.3)	79 (13.7)
Pulse rate (beats per minute)	63.4 (9.64)	62.5 (9.20)	64.4 (9.85)	67.6 (10.8)
Cholesterol (mmol/l)	6.0 (1.01)	5.9 (1.00)	6.0 (1.06)	6.0 (1.03)
High-density lipoprotein (mmol/l)	1.2 (0.29)	1.2 (0.30)	1.2 (0.29)	1.2 (0.27)
Triglycerides (mmol/l)	1.5 (0.92)	1.5 (0.84)	1.6 (1.04)	1.8 (1.15)
Glycemia (mmol/l)	5.5 (1.02)	5.4 (1.02)	5.5 (0.81)	5.8 (1.32)
BMI (kg/m^2)	25.6 (3.35)	25.3 (3.17)	26.1 (3.32)	26.7 (4.24)
Waist-hip ratio	0.93 (0.06)	0.93 (0.05)	0.94 (0.06)	0.95 (0.06)
Sagittal abd. diam./height	11.3 (1.6)	11.2 (1.5)	11.6 (1.7)	11.9 (1.8)
Percentage daily smokers [95% CI]	28 [25–31]	24 [20–28]	32 [25–40]	49 [37–64]
Average alcohol consumption/g/week	51.9	52.5	53.1	46.2
Framingham risk index	0.091 (0.058)	0.084 (0.056)	0.094 (0.060)	0.132 (0.081)
Diabetes at baseline (%)	1.3	0.8	1.4	3.8
Hypertension at baseline (%)	10	8	18	22
Heart attack in family (%)	23	23	22	27
Number of heart attacks before baseline			1	2
Number of persons with at least one MI	89 (9%)	45 (6.7%)	18 (8.7%)	26 (26%)

Numeric variables are described with means and standard deviations in brackets. Percentages are shown for the dichotomous variables.
CI, confidence interval; BMI, body mass index; Sagittal abd. diam, sagittal abdominal diameter; MI, myocardial infarction.

Table 2 – Estimated cumulative all-cause death rates (104 persons) per 100 persons after the 22-year follow-up of the 1993 cohort of 1000 employed middle-aged men by quintile of key variables.

Quintile	Framingham risk index	Systolic blood pressure	Diastolic blood pressure	Pulse rate
1st	7.7	6.2	7.1	6.57
2nd	3.8	8.5	7.0	6.74
3rd	4.4	6.9	11.2	7.91
4th	12	11.1	9.0	12.30
5th	20.9	18.6	17.0	18.64
OR, 5th to 1st [95% CI]	3.17 [1.65; 6.08]	3.43 [1.78; 6.60]	2.68 [1.39; 5.15]	3.26 [1.66; 6.42]
P-value	0.001	0.000	0.003	0.001
Pseudo-R^2 (%)	6.6	3.1	2.1	3.1
Quintile	Total cholesterol	HDL cholesterol/total cholesterol	Triglyceride	Glycemia
1st	10.3	13.1	7.1	8.3
2nd	6.7	11.0	9.2	7.7
3rd	12.1	8.2	9.5	7.1
4th	9.3	7.7	10.7	11.1
5th	11.5	8.8	13.6	17.0
OR, 5th to 1st [95% CI]	1.12 [0.59; 2.14]	0.63 [0.48; 1.24]	2.03 [1.02; 4.03]	2.27 [1.19; 4.31]
P-value	0.717	0.27	0.041	0.012
Pseudo-R^2 (%)	0.65	0.71	0.75	2.0
Quintile	BMI	Sagital. abd. diam./height	Waist-hip ratio	Alcohol
1st	7.7	7.1	6.6	14.0
2nd	7.4	7.7	6.8	10.4
3rd	7.3	9.2	9.4	10.4
4th	12.6	10.7	8.1	6.8
5th	15.6	16.4	19.9	8.4
OR, 5th to 1st [95% CI]	2.22 [1.15; 4.28]	2.57 [1.32; 5.02]	3.51 [1.80; 6.84]	0.56 [0.30; 1.05]
P-value	0.017	0.005	0.000	0.074
Pseudo-R^2 (%)	1.9	2.4	3.6	1.1

Odds ratio (OR) means comparisons between the highest and lowest quintiles.
HDL, high-density lipoprotein; CI, confidence interval; BMI, body mass index; Sagittal abd. Diam., sagittal abdominal diameter.

Fig. 1 shows the cumulative incidence of death by marital and smoking status. The strongest increase of cumulative incidence over age is seen for smokers with low education.

There was a negative association between the number of children and the risk of death. This was basically due to the fact that those with no children at home showed a higher estimated risk than others.

Estimated incidences of MI by age during the observation period 1993–2015

Fig. 2 shows the increased cumulative incidences of MI by age.

There was no trend observed regarding MI risk and different numbers of children.

A significant negative association between MI risk and HDL-C was seen. HDL-C also had the highest PR^2 for MI (1.9%) among the blood lipids tested, and the waist-hip ratio had the highest PR^2 among the anthropometric indices (2.5%). Note the high OR for diabetes, 8.02 for death and 9.34 for MI.

The patterns of OR basically remained the same in multiple analyses. ORs, as expected, moved closer to unity, and some lost their statistical significance. Investigation of colinearity was undertaken. The percentage of PR^2 for multiple models including all variables for MI merely reached 22%.

Discussion

The official death rates in Swedish males aged 50 years in 2015 were 6.4 per 1000 person-years.[16] The estimated death rate in this study was 4.8 per 1000 person-years. Hence, the mortality among the workers included was comparatively low, which is likely a consequence of the severely ill and disabled being excluded from employment the healthy worker effect.[17] However, the FRI was the best predictor of risk of MI in this study, explaining only 5.3% of the total risk variation for MI and 4.2% of the risk variation for all-cause death. Multiple models including all variables for MI that merely reached 22% explained variation. QRISK2 and the use of biomarkers and ankle-brachial index may replace the FRI to obtain a better explanation.[18–22] The improved version proposed by De Ruijter et al.[20] increases the area under the curve for a receiver operating characteristic (ROC) analysis from 0.53 to 0.65, a substantial increase but still at a modest level. In a Swedish study of men aged 45–73 years in the city of Malmö, the risk score based on smoking, hypertension, diabetes, and obesity explained 38–58% of the variation between city areas, but this analysis is made at an aggregated, not individual, level.[23] Much higher explanatory power is natural for aggregated information where the individual risk variation is not influencing.

Table 3 – Estimated cumulative incidence of myocardial infarction (89 persons) after 22-year follow-up of the 1993 cohort of employed middle-aged men by quintile of key variables.

Quintile	Framingham risk index	Systolic blood pressure	Diastolic blood pressure	Pulse rate
1st	1.1	5.8	7.1	8.6
2nd	5.5	9.9	7.0	5.7
3rd	7.1	8.6	8.6	7.4
4th	12.6	6.4	10.0	7.5
5th	20.3	14.4	12.1	15.8
OR, 5th to 1st [95% CI]	23.0 [5.42; 96.9]	2.72 [1.36; 5.44]	1.79 [0.90; 3.58]	2.00 [1.05; 3.79]
P-value	0.000	0.005	0.095	0.034
Pseudo-R^2 (%)	8.8	1.9	0.7	2.2
Quintile	Total cholesterol	HDL cholesterol/total cholesterol	Triglycerides	Glycemia
1st	6.2	17.5	6.1	8.8
2nd	5.7	11.5	6.7	6.1
3rd	11.6	8.2	10.5	4.6
4th	7.7	5.0	8.0	11.1
5th	13.6	4.4	13.6	13.8
OR, 5th to 1st [95% CI]	2.37 [1.16; 4.86]	0.21 [0.10; 0.48]	2.40 [1.17; 4.91]	1.65 [0.86; 3.17]
P-value	0.018	0.000	0.016	0.133
Pseudo-R^2 (%)	1.9	2.9	1.5	2.6
Quintile	BMI	Sagittal abd diam./height.	Waist-hip ratio	Alcohol
1st	6.7	3.0	3.0	7.2
2nd	4.2	10.3	6.8	13.0
3rd	4.7	6.1	10.8	7.6
4th	14.1	11.2	9.1	7.3
5th	14.1	13.8	14.7	9.9
OR, 5th to 1st [95% CI]	2.29 [1.14; 4.58]	5.10 [2.05; 12.7]	5.46 [2.21; 3.5]	1.42 [0.72; 2.82]
P-value	0.019	0.000	0.000	0.312
Pseudo-R^2 (%)	4.2	2.3	3.4	0.9

Odds ratio (OR) means comparisons between the highest and lowest quintiles.
HDL, high-density lipoprotein; CI, 95% confidence interval; BMI, body mass index; Sagittal abd. Diam., sagittal abdominal diameter.

The explanatory capacity of risk factors may also be influenced by change in health behavior over the 22 years studied. Smoking was a comparatively strong predictor of MI and of cumulative all-cause death (Fig. 1). Marriage had an association with death, possibly reflecting a protection.[24–27] There was a general reduction of smoking over the observed time at the national Swedish level, from 13.1% in 2008–2009 to 10.6% in 2014–2016, probably paralleled in our cohort.[28]

An important finding was a negative correlation between the level of education and the incidence of MI confirming the effect observed in the major 52 countries INTERHEART study by Rosengren et al.,[30] in 2009, and Hu et al.,[29] in 2010, that claimed that globally, the strongest socioeconomic predictor of acute MI risk was low education, most pronounced in high-income countries.

Marital status was associated with all-cause mortality, but the association with MI did not reach statistical significance. In the INTERHEART study, being single was consistently associated with increased risk of MI.[30] Previous studies such as the Framingham offspring study have shown that a number of factors may be involved.[27] Married men were found to have a cardiovascular risk less than half that of unmarried men, and women who 'self-silenced' during arguments had four times the cardiovascular risk of women who did not. In a cohort of 3365 middle-aged men in the Netherlands who were followed up for up to 10 years, the relative risk of all-cause mortality in unmarried men (as compared with married men) was 2.3.[25]

With 90% of French men being married or having a companion (as compared with 76% of Swedish men), this finding is inconsistent with our hypothesis for the French paradox of MI in our cohort. However, all-cause mortality was higher in unmarried participants, which agrees with our findings. This may be due to the key role of spouses in an individual's informal health support network, including better dietary habits in married men.[31]

Manual workers compared with clerical workers bore an increased risk of MI and death, and this result is consistent with previous research, where 7083 middle-aged men in Gothenburg were followed up for 12 years.[32]

The French paradox 'Autres pays, autres moeurs' and evaluation of some theories concerning its cause was the basis of this study.[8] We found that there were no significant FRI differences between the Swedish and French cohorts at the baseline. A national difference in carotid thickness was detected, which may still be a contributory factor to the national differences in MI.[33] Unfortunately, we were unable to follow up the French cohort after 22 years. We found no association with alcohol, or wine specifically, in the Swedish cohort, and we are therefore unable to confirm earlier theories of a J-shaped association with MI. However, self-reported wine drinkers had an OR of 0.42 compared with others with regard to the death rate. In a review of moderate alcohol consumption and the risk of CHD, Rimm et al found support for benefits of alcohol linked to CHD primarily to the alcohol content and not to other components of each drink. Their

Table 4 – Estimates of cumulative deaths rate and incidences of myocardial infarction (MI) as related to selected dichotomous variables

Characteristic	Death				MI			
	Rate	OR	95% CI	Pse. R^2 (%)	Rate	OR	95% CI	Pse. R^2 (%)
Smoking status								
Smoker = 1	18.2	2.97	1.95; 4.54	3.9	16.8	3.25	2.08; 5.09	4.5
Non-smoker = 0	7.0				5.8			
Type of work								
Manual work = 1	15.0	2.32	1.54; 3.54	2,4	11.3	1.64	1.05; 2.55	0.8
Other = 0	7.6				7.3			
Education								
High education = 1	5.9	0.38	0.21; 0.70	1.8	5.1	0.44	0.23; 0.86	0.5
Middle education = 1	8.2	0.54	0.33; 0.87	1.1	9.1	0.83	0.51; 1.36	1.1
Low education = 0	14.1				10.7			
Marital status								
Single = 1	23.7	3.78	2.27; 6.31	3.0	8.7	1.12	0.57; 2.20	0.0
Married = 0	7.6				9.7			
Divorced = 1	13.2	1.86	1.03; 3.36	0.2	8.7	1.05	0.54; 2.06	0.0
Married = 0	7.6				9.1			
Wife works outside home								
Yes = 1	7.6	0.44	0.26; 0.64	2.3	8.1	0.88	0.50; 1.58	0.0
No = 0	16.8				9.1			
Diabetes								
Yes = 1	46.1	8.02	2.64; 24.4	1.8	46.1	9.34	3.07; 28.5	2.2
No = 0	9.6				8.4			
Family heart attack								
Yes = 1	11.8	1.24	0.78; 1.99	0.4	10.9	1.37	0.84; 2.24	0.8
No = 0	9.7				8.2			
Family diabetes								
Yes = 1	13.7	1.49	0.86; 2.59	0.3	9.9	1.16	0.62; 2.16	0.0
No = 0	9.6				8.6			

All estimates are given as number of outcomes per 100 (%) of baseline population. Odds ratio (OR) means comparisons between the highest and the lowest quintiles.
MI, myocardial infarction; CI, confidence interval; Pse. R2; pseudo-R^2.

thought of a possible mechanism pointed to a positive association between alcohol and HDL-C because high concentration of HDL-C is associated with a lower risk of CHD.[34] Keys[5] offered conclusions in line with the results from our research. The design of this 22-year follow-up of MI and death did not involve the French cohort; thus, no conclusions can be drawn on potential differences of end points. Wilhelmsen et al. followed up a cohort similar to ours: men born in 1913, until their hundredth birthday. These workers found a significant association between long survival and non-smoking,

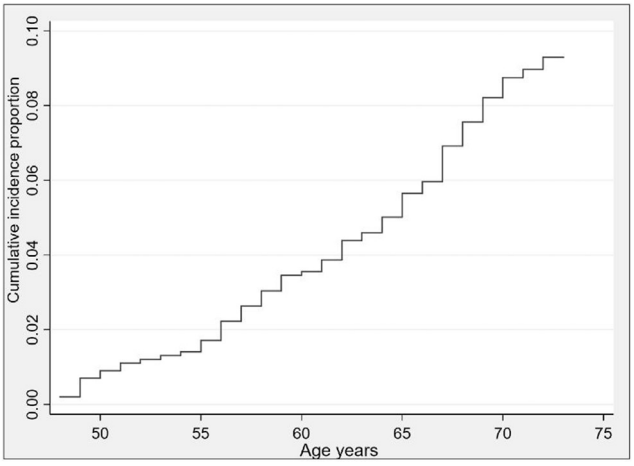

Fig. 1 – Estimated cumulative incidences of death by age during the observation period 1993–2015 for subgroups defined by marital status and smoking status.

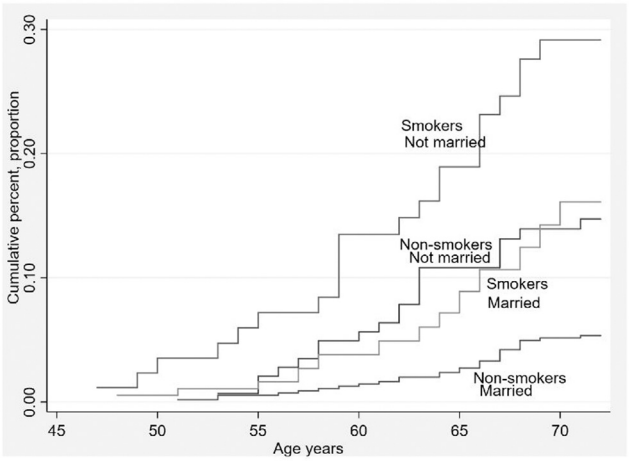

Fig. 2 – Estimated cumulative incidences of MI by age during the observation period 1993–2015. MI, myocardial infarction.

high social class, high physical working capacity, and high age of the mother at death.[35] This further confirms our findings of increased risk of all-cause death with smoking and with low education.

In summary, while the risk factors studied were associated with risk of coronary heart disease, they explained merely 22% of all such events. Moreover, the FRI did not show a linear relationship but rather a J-shaped relationship to risk.

Risk, variation in risk, and confounding

The risk of death or MI for an individual person is an abstract characteristic that cannot be directly observed or measured. In a defined group of people, the individuals have different risks, together forming a distribution that is conditioned by a large number of factors. We can obtain estimates of the mean risk for a group by counting the number of events and relate this to an appropriate denominator. Another important objective is to find factors that create the total risk variation.

To find out if and how a specific binary outcome is statistically associated with some explanatory variable(s), we most often use generalized linear regression (GLR) models, where the results are given as estimated risk differences, risk ratios, or ORs, presented with CIs and *P*-values.

Another question concerns how much of the total risk variation within a study group can be 'explained' by the variation of specific explanatory variable(s). For the GLR, it is not possible to use the traditional R^2 value as in linear regression. A number of approaches to so-called PR^2 have been proposed based either on the likelihood of estimated models or on the individual risks as predicted by a model.[15]

Risk ratios and ORs are almost invariably presented for studies together with judgments of statistical significance. The *P*-values have often become central, despite the fact that they only reflect the importance of random variation and provide rather poor information about an association not least because they are also dependent on the sample size and the number of end points. Estimates of explanatory power are not often published. Quite often, in the study of chronic disease such as CVD, highly statistically significant associations appear mainly because of large sample sizes.

Simple and multiple regression models, confounding, and adjustment

In a simple regression model, we see the relation between one explanatory variable and the risk as it is in reality, that is, possibly influenced by confounding variables. In multiple models, we adjust with respect to other explanatory variables assuming that these are fixed, which is of course almost always unrealistic in practice. The policy in this article has been to first and foremost present results from the simple analysis, pointing to multiple analyses when there is certain interest in doing so.

Conclusion

Most associations between risk of death or MI and explanatory variables found in this study confirm earlier results. No association was, however, particularly strong, in the sense that it explained a large part of the risk variation. A multiple model for CHD including all independent variables explained merely 22% of the individual risk variation.

Author statements

Acknowledgments

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Ethical approval

The Research Ethics Committee of Gothenburg University approved the study protocol on February 11, 1993, and the Swedish Data Inspection Board approved on January 26, 1993. This protocol also specified follow-up of end points.

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Competing interests

None declared.

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Appendix A. Supplementary data

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