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How Much of the Recent Decline in the Incidence of Myocardial Infarction in British Men Can Be Explained by Changes in Cardiovascular Risk Factors?:

Evidence From a Prospective Population-Based Study

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Abstract

Background—The incidence of myocardial infarction (MI) in Britain has fallen markedly in recent years. Few studies have investigated the extent to which this decline can be explained by concurrent changes in major cardiovascular risk factors.

Methods and Results—The British Regional Heart Study examined changes in cardiovascular risk factors and MI incidence over 25 years from 1978 in a cohort of 7735 men. During this time, the age-adjusted hazard of MI decreased by 3.8% (95% confidence interval 2.6% to 5.0%) per annum, which corresponds to a 62% decline over the 25 years. At the same time, after adjustment for age, cigarette smoking prevalence, mean systolic blood pressure, and mean non–high-density lipoprotein (HDL) cholesterol decreased, whereas mean HDL cholesterol, mean body mass index, and physical activity levels rose. No significant change occurred in alcohol consumption. The fall in cigarette smoking explained the greatest part of the decline in MI incidence (23%), followed by changes in blood pressure (13%), HDL cholesterol (12%), and non-HDL cholesterol (10%). In combination, 46% (approximate 95% confidence interval 23% to 164%) of the decline in MI could be explained by these risk factor changes. Physical activity and alcohol consumption had little influence, whereas the increase in body mass index would have produced a rise in MI risk.

Conclusions—Modest favorable changes in the major cardiovascular risk factors appear to have contributed to considerable reductions in MI incidence. This highlights the potential value of population-wide measures to reduce exposure to these risk factors in the prevention of coronary heart disease.

Keywords

myocardial infarction; risk factors; population; epidemiology; prevention

Cardiovascular disease, particularly coronary heart disease (CHD), remains the leading cause of death in the United Kingdom[1]; however, death rates from CHD have declined appreciably in the United Kingdom in recent years (by 44% between 1994 and 2004).[1] An

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understanding of the reasons for the decline may help to inform future efforts to reduce CHD, both in the United Kingdom and in other locations.

Previous studies have suggested that declines in CHD mortality mainly reflect declines in CHD incidence due to population-wide changes in risk factors rather than improved survival of patients who already have CHD.[2,3] Studies using the IMPACT model[2] suggested that population-wide risk factor change contributed ≈60% of the decline in CHD mortality that occurred in Scotland between 1975 and 1994[2] and ≈58% of the CHD mortality decline in England and Wales between 1981 and 2000.[3]

Although a small number of studies have been able to examine the contribution of changes in risk factors, both individually and in combination, to changes in incidence, most have been based on aggregate data. Very few studies have been able to examine the influence of risk factor changes on CHD incidence within a single population.[4] The aim of the present analysis was therefore to investigate recent trends in the incidence of myocardial infarction (MI), the dominant manifestation of CHD, and to examine to what extent changes in incidence may be attributable to observed changes in established cardiovascular risk factors. We used data from the prospective British Regional Heart Study,[5] in which information on time trends in risk factors and CHD incidence is available and in which a marked decline in CHD incidence has already been demonstrated.[6] In the present report, we have examined the relationship between changes in risk factors and changes in MI incidence over a period of 25 years.

Methods

The British Regional Heart Study

The British Regional Heart study, described elsewhere,[5] is a prospective study of cardiovascular disease in a socially and geographically representative cohort of middle-aged men in Britain. A total of 7735 men, aged 40 to 59 years when recruited, were selected from 24 general physician practices across Britain by random sampling, stratified by general physician practice and 5-year age group, over a recruitment period from 1978 to 1980. The men were followed up for 25 years to 2004 for all-cause mortality through the National Health Service (United Kingdom) central registers and for cardiovascular morbidity by regular (every 2 years) reviews of general physician records. Follow-up has been maintained for >99% of surviving men throughout this period.

Principal Outcome

The principal outcome was a first MI (fatal or nonfatal). Diagnosis of fatal MI was based on deaths with CHD as the underlying cause, including sudden death of presumed cardiac origin (International Classification of Diseases, Ninth Revision, codes 410 to 414). Nonfatal MI was diagnosed in accordance with criteria used in the MONICA (MONItoring trends and determinants in CArdiovascular disease) study of the World Health Organization.[7]

Assessment of Risk Factors

Men completed an interviewer-administered questionnaire at baseline (1978 to 1980) and self-administered questionnaires at 5, 13, 17, and 20 years after recruitment, answering identical questions each time about cigarette smoking, weekly alcohol intake, physical activity (except at the fifth-year questionnaire), and body weight. From the information given, men were categorized at each questionnaire time point as “current,” “ex,” or “never” smokers. The men’s alcohol consumption was categorized as “never,” “occasionally,” “light,” “moderate,” and “heavy.”[8] Answers to questions relating to recreational activities, regular walking and cycling, and sporting activity were combined to give each man a

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physical activity score. Men were grouped into 6 categories based on their score: “inactive,” “occasional,” “light,” “moderate,” “moderately vigorous,” and “vigorous.” This score has been detailed and validated previously.[9]

Body weight, height, systolic blood pressure, total cholesterol, and high-density lipoprotein (HDL) cholesterol were measured at physical examinations at baseline and after 20 years of follow-up. Systolic blood pressure was measured at baseline with the London School of Hygiene and Tropical Medicine sphygmomanometer and at 20 years with the Dinamap 1846SX vital signs monitor (Critikon Inc, Tampa, Fla). On both occasions, the mean of 2 successive readings, adjusted for observer variation, was used. The 20-year measurements were adjusted for the overestimation of systolic blood pressure by the Dinamap 1846 identified in earlier studies.[10] Blood samples (nonfasting at baseline, fasting at 20 years) were analyzed for serum total cholesterol by a modified Liebermann-Burchard method on a Technicon SMA 12/60 analyzer (Technicon Instruments, Tarrytown, NY) at baseline and with a Hitachi 747 automated analyzer (Roche Diagnostics, Indianapolis, Ind) at 20 years. HDL cholesterol was measured by the Liebermann-Burchard method or enzymatic procedures after precipitation with magnesium phosphotungstate. The assays were cross-calibrated by remeasuring a small number of residual baseline samples for total and HDL cholesterol levels with the assay techniques applied at the 20-year examination. In 47 subjects, the mean within-person difference in total cholesterol (remeasured minus baseline) was 0.072 (SD 0.718) mmol/L (P=0.5 from a paired t test for the difference). The mean within-person difference in HDL cholesterol (remeasured minus baseline) was 0.067 (SD 0.552) mmol/L (P=0.4). Because the differences were not significantly different from zero and were based on samples stored for almost 20 years, these differences have not been taken into account in the main analyses. Non-HDL cholesterol was computed as the difference between the total and HDL cholesterol levels. At baseline and 20 years, body mass index (BMI) was calculated directly from height and weight measurements taken at the physical examinations. At the times of the other questionnaires, the self-reported weight was used, and height was estimated by linear interpolation between the baseline and 20-year measurements. The validity of self-reported weight was checked by comparing the weight measured at 20 years with self-reported weight that was also obtained at 20 years. The self-reported weights at the other time points were corrected by the mean difference between the 2 weights (the self-reported weight was a mean of 0.643 kg lower than the measured value).

Statistical Analyses

Incidence rates of first MI per 1000 person-years for each 5-year age group and for each 5-year calendar time period from baseline were computed. With use of the repeated data on smoking status from each follow-up questionnaire, the age-adjusted change in the prevalence of cigarette smoking over 20 years from baseline was estimated from logistic regression of the smoking status of each man at each questionnaire time point (dichotomized into “current” and “not current” cigarette smoker) on calendar time, with age included as a covariate. Generalized estimating equations (GEEs) with robust standard errors were used for the regression to take account of dependency between individual men’s repeated measures. Age-adjusted estimates of the changes in the odds of being at least moderately physically active and the odds of being a regular drinker over time were obtained in the same way. Similarly, linear regressions with GEEs of each continuous variable (BMI, systolic blood pressure, HDL cholesterol, and non-HDL cholesterol) in turn on calendar time, with age as a covariate, were used to give estimates of the age-adjusted mean changes in these variables over 20 years.

The availability of exact dates of MI enabled use of Cox proportional hazards regression to estimate the yearly change in the hazard of MI over the follow-up period. Survival times were censored at death or June 15, 2004 (the latest date that follow-up data on morbidity and

mortality were available), whichever came sooner. Age was used as the underlying time scale, with date of birth as a time origin and age at entry to the study as a delayed entry time to take account of left truncation. Use of an age time scale, as well as automatic adjustment for age,[11] permitted calendar time to be entered into the model as a covariate so that the change in the hazard of MI with calendar time could be estimated. Schoenfeld residuals were used to test the proportional hazards assumption.[12]

The extent to which the changes in each of the risk factors statistically explained the change in MI hazard was estimated by the expression $(\beta_0-\beta_1)/\beta_0$, where β_0 is the coefficient of calendar time in the Cox regression model with just calendar time as a covariate, and β_1 is the coefficient of calendar time in a Cox regression model with additional adjustment for the risk factors added to the model as time-dependent covariates.[13] Bias-corrected bootstrap resampling was used to give an approximate 95% confidence interval (CI) for this estimate.[14] For time-dependent covariates, the level of the covariate was updated at the date of each questionnaire/examination. This corresponds to looking at the effect of the current risk factor level at each questionnaire time point on survival from MI in the time following this questionnaire, up until the time of the next questionnaire. Physical activity, alcohol consumption, and cigarette smoking were entered into models as categorical class variables. The physical activity category at 5 years of follow-up was imputed as the median of the category at baseline and the category at 13 years, rounded to the nearest integer, with the categories ordered from “inactive” up to “vigorous.” BMI, blood pressure, non-HDL cholesterol, and HDL cholesterol were continuous. Because data on blood pressure, non-HDL cholesterol, and HDL cholesterol were only available at baseline and 20 years, to eliminate bias, all models incorporating these variables included only follow-up data from baseline until 5 years and then from 20 years to 25 years. In the above expression, coefficients of calendar time from these models were compared with the coefficient from a separate unadjusted model that also used these restricted follow-up data.

Subjects Included in Analysis

All study men were included except those who had had an MI before baseline. Men who had an MI during follow-up were excluded from the analyses of MI incidence after the time of their event. These men were also excluded after the time of their event from the GEE regression analyses of changes in risk factors so that the changes in the risk factors estimated from the GEE analyses corresponded to pre-MI changes that influence the trend in the hazard of a first MI. Only men alive and present at the 20-year follow-up could contribute to the GEE analyses of changes in blood pressure and cholesterol (data at 2 or more time points were needed for each man to be included). Men with angina (either at baseline or during follow up) were retained for analysis unless they also developed MI.

The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

Results

Trends in the Incidence of Major CHD

Of the 7735 men recruited, 952 initially reported a definite or possible MI before entry into the study and so were excluded from the analysis. Of the remaining 6783 men (included men shown in Table 1), 1255 were recorded as having a first MI over 140 423 person-years of follow-up, which yielded an overall event rate of 8.94 events per 1000 person-years (95% CI 8.46 to 9.45). Within 5-year age groups, first-MI incidence rates tended to decrease over time (Table 2). From Cox regression, after adjustment for age, the hazard rate of MI fell by 3.8% (95% CI 2.6% to 5.0%, $P<0.001$) per annum, which corresponds to a fall of 62% over

the 25-year follow-up period to 2004. No evidence was present of departure from the proportional hazards assumption of the Cox regression.

Trends in Cardiovascular Risk Factors

A clear decrease took place over time in the proportion of men who were cigarette smokers, both within 5-year age groups and overall (Table 3). The age-adjusted odds of being a current cigarette smoker declined by 73% (95% CI 68% to 78%, $P<0.001$) between baseline and the 20-year follow-up. No significant evidence existed of a change over this time period in the proportion of men who drank regularly ($P=0.2$). Physical activity levels increased slightly, with the age-adjusted odds of being at least moderately active at 20-year follow-up being 1.91 (95% CI 1.62 to 2.24, $P<0.001$) times that at baseline. Over the 20-year period, age-adjusted mean BMI increased by 1.89 kg/m^2 (95% CI 1.61 to 2.18 kg/m^2, $P<0.001$). Age-adjusted mean systolic blood pressure fell by 6.6 mm Hg (95% CI 4.3 to 8.9 mm Hg, $P<0.001$). Age-adjusted mean HDL cholesterol levels increased by 0.16 mmol/L (95% CI 0.13 to 0.20 mmol/L, $P<0.001$), and non-HDL cholesterol levels fell by 0.28 mmol/L (95% CI 0.16 to 0.40 mmol/L, $P<0.001$).

Analysis of Relation of Trends in Risk Factors to Trends in MI Incidence

Estimates of the proportions of the decline in the hazard of a first MI over time attributable to each risk factor change are presented in Table 4. The largest single contribution was that of the fall in cigarette smoking, which alone statistically explained 23% (approximate 95% CI 15% to 34%) of the observed 62% decline in the hazard of MI over the 25 years from baseline. The change in systolic blood pressure explained 13% (approximate 95% CI 6% to 54%) of the decline in hazard, the change in HDL cholesterol explained 12% (approximate 95% CI 5% to 42%), and the change in non-HDL cholesterol explained 10% (approximate 95% CI 4% to 32%). Physical activity explained a borderline significant part of the decline (5%, approximate 95% CI 0% to 11%). Alcohol consumption had little impact (1% explained). The change in BMI was adverse (−7% of the decline in MI explained) and would have been expected to lead to an increase rather than a decline in the hazard of MI over time.

Taken together, the 4 factors that singly accounted for statistically significant reductions in MI hazard (cigarette smoking, systolic blood pressure, non-HDL cholesterol, and HDL cholesterol) could explain 46% (approximate 95% CI 23% to 164%) of the decline. The interpretation of the CI, with an upper bound >100%, is that the data are consistent (at the 95% confidence level) with the risk factors explaining at worst 23% of the decline in the hazard of MI and at best an even greater decline than that observed. The addition of physical activity and alcohol intake made little difference to this estimate (44%, approximate 95% CI 22% to 149%).

The effect of adjustment for the (nonsignificant) laboratory measurement differences in blood lipid measurements described in Methods would be to reduce the mean 20-year increase in the HDL cholesterol level from 0.16 to 0.10 mmol/L, while leaving the decrease in non-HDL cholesterol levels unchanged at 0.28 mmol/L. On this basis, the contribution of HDL cholesterol to the observed decline in MI hazard would be reduced from 12% to 7% (approximate 95% CI 3% to 29%), whereas that of non-HDL cholesterol levels would remain unchanged at 10%. The overall combined contribution of the 4 major risk factors (smoking, blood pressure, non-HDL cholesterol, HDL cholesterol, and physical activity) would be reduced from 46% to 43%.

Discussion

The age-adjusted hazard of first MI in this large cohort of middle-aged British men has more than halved, falling by 62% over 25 years since 1978. Forty-six percent of this decrease in MI hazard could be explained by a combination of changes in the major risk factors over this time: a fall in the number of cigarette smokers (most powerful of all), a decrease in the mean systolic blood pressure of the cohort, an increase in mean HDL cholesterol, and a decrease in mean non-HDL cholesterol. Physical activity and alcohol consumption had relatively little impact. The change in BMI was counterproductive and would have been expected to lead to an increase rather than a decline in the incidence of MI.

Few studies have looked directly at how changes in risk factors in a cohort correspond to changes in MI incidence, and just 1 other study, by Hu et al,[4] used individual data (US Nurses Health Study). In that study, which did not measure blood pressure or blood lipids, decreased smoking prevalence accounted in isolation for 42% of the decline in CHD, changes in diet (particularly a decrease in saturated fat and an increase in fiber) accounted for 52%, and an increase in postmenopausal hormone use accounted for 29%. In the presence of an adverse change in BMI, 68% of the decline in incidence could be explained by combined changes in smoking, diet, and postmenopausal hormone use. The larger percentage of 68% of the decline explained by the risk factors may reflect the quality of exposure assessment and the influence of diet on a range of risk factors, including blood pressure and cholesterol. Estimates of the protective effect of hormone replacement therapy can be discounted in light of more recent evidence that postmenopausal hormone use increases CHD risk,[15] which would bring the combined percentage explained closer to the present estimate. The World Heath Organization MONICA Project, based on aggregate data, suggested that cigarette smoking, systolic blood pressure, and total cholesterol together explained ≈38% of the variation in coronary event rates from the mid-1980s to the mid-1990s in men in 27 different populations.[16] The individual contribution of cigarette smoking was 20%, that of total cholesterol was 19%, and that of systolic blood pressure was 6%, figures broadly consistent with the present findings. Two previous investigations have used aggregate data to examine the influence of risk factors on the decline in CHD in the United Kingdom. The IMPACT project, which examined the determinants of the CHD mortality decline in England between 1981 and 2000, found that 58% of the decline could be accounted for by major risk factor changes, with the decline in cigarette smoking accounting for 48% and changes in blood pressure and total cholesterol accounting for 10% each.[3] Similar proportions were observed in Scotland (60% for all major factors, 36% for cigarette smoking, and 6% each for blood pressure and total cholesterol).[2] These percentages correspond well with the present results; the slightly larger contribution of smoking found from IMPACT possibly reflect the fact that CHD mortality rather than incidence was the outcome of interest. None of these studies examined the contribution of HDL cholesterol.

Strengths and Weaknesses

The present study cohort is socially and geographically representative of British men, with the exception of ethnic minority groups. Its representativeness is substantiated by observations that the trends in MI incidence closely mirror those found in other studies on similar UK populations and trends in CHD mortality.[1] Moreover, the trends seen in risk factors in the present cohort are consistent with routine data for the United Kingdom reported in the Health Survey for England[17] and the Office for National Statistics General Household Survey.[18] Response rates and follow-up rates were excellent throughout the entire follow-up period. The analysis was based on risk factor changes and events in the same population of individuals; risk factor changes (particularly for health behaviors) were recorded frequently and by identical methods of ascertainment on each occasion. First MI

was used as the primary outcome because it is the dominant manifestation of CHD with serious short- and long-term prognostic implications. In addition, the use of consistent diagnostic criteria for MI throughout the follow-up period in the present study means that the estimate of the change in incidence of MI cannot be confused with changes in diagnostic criteria over time.

The study has certain limitations. First, the overall statistical power and precision of the analysis were limited, and CIs were therefore wide. Second, the analyses of changes in risk factors were necessarily based on attendees rather than the entire study population. Although this could have introduced response and survival biases, mean differences in blood pressure and cigarette smoking levels between attendees and nonattendees were small[19] compared with overall changes over time, which indicates that the selection was unlikely to have had a dramatic influence on the observed trends. The limited (2 point) data on blood pressure and cholesterol necessitated restriction of the follow-up time to the first 5 years and the last 5 years only to analyze the contribution of these risk factors. The effect of the use of this restricted data set on the results was investigated by comparing estimates of the contribution of smoking, alcohol consumption, and physical activity computed with these restricted data with the reported estimates for these risk factors computed from the full data set. In all cases, the contributions estimated from the limited data set (17% for smoking, 0.2% for alcohol, and 2% for physical activity) were smaller than the estimates from the full data set. This suggests that use of these limited data may have led to underestimation of the contributions of blood pressure and cholesterol. The effects of regression dilution, which could influence both the extent of risk factor changes over time and the estimates of risk factor associations with MI risk, also were not taken into account; these could influence estimates of risk factor contributions in either direction. Analyses were based on the assumption that the effects of changes in risk factors on CHD outcomes occur within the time between consecutive questionnaires (≈5 years). This could lead to underestimation of the effects of a risk factor change, if a lag time is present of >5 years before the benefits of a risk factor change are realized; however, evidence exists that substantial benefits from smoking cessation, changes in blood lipids, and changes in blood pressure are realized within 5 years.[20–22] Although we have considered several major cardiovascular risk factors, changes in novel risk markers,[23] not measured longitudinally in the present study population, could also be important. Diabetes mellitus, which has been increasing in prevalence and could not therefore account for the observed decline in CHD risk, was not included in the present analyses.

Implications of the Results

The results suggest that changes in major CHD risk factors have accounted for approximately half of the reduction in MI observed. The largest contribution has come from the decline in cigarette smoking, followed by the modest changes in non-HDL cholesterol, HDL cholesterol, and systolic blood pressure, with a smaller, borderline-significant contribution from physical activity. An increase in mean HDL cholesterol levels has had a role in the fall in MI incidence, in addition to and distinct from the changes in non-HDL cholesterol levels. In the analyses presented here, we have not distinguished between improvements in risk factors (particularly blood pressure and blood lipids) due to lifestyle changes and those due to medical treatment. Preliminary investigations suggest that a considerable proportion of the secular decline in systolic blood pressure is due to medical treatment (received by ≈35% of participants during the study period); in contrast, lipid-lowering treatment (taken by only 7% of participants) contributed little to the decline in non-HDL cholesterol and made no contribution to the increase in HDL cholesterol. According to the results, an appreciable proportion of the decline in MI incidence remains unexplained. It remains possible that this unexplained decline is also accounted for by risk factor changes

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(which would reflect imprecision in the analysis); however, the decline could also reflect the role of the increasing availability of early treatment, particularly revascularization, for angina (especially unstable angina). The potential impact of changes in early treatment on CHD incidence will be examined in a separate report. The rise in population BMI during the past 25 years in the United Kingdom has almost certainly reduced the scale of the decline in CHD that has occurred, although its effects have been outweighed by the favorable changes in cigarette smoking, blood lipids, and blood pressure. The potential for further reductions in CHD in the UK population through cigarette smoking is constrained by the already low remaining cigarette smoking prevalence; however, the changes in blood pressure and particularly in blood lipids that have occurred so far are very modest. Population-wide changes in these factors, particularly through population-wide dietary changes, still have considerable potential for further reductions in CHD risk.

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References

1. Allender, S.; Peto, V.; Scarborough, P.; Raynor, M. British Heart Foundation statistics database: coronary heart disease statistics. 2006 editionAvailable at: www.heartstats.org Accessed January 15, 2007
2. Capewell S, Morrison CE, McMurray JJ. Contribution of modern cardiovascular treatment and risk factor changes to the decline in coronary heart disease mortality in Scotland between 1975 and 1994. Heart. 1999; 81:380–386. [PubMed: 10092564]
3. Unal B, Critchley JA, Capewell S. Explaining the decline in coronary heart disease mortality in England and Wales between 1981 and 2000. Circulation. 2004; 109:1101–1107. [PubMed: 14993137]
4. Hu FB, Stampfer MJ, Manson JE, Grodstein F, Colditz GA, Speizer FE, Willett WC. Trends in the incidence of coronary heart disease and changes in diet and lifestyle in women. N Engl J Med. 2000; 343:530–537. [PubMed: 10954760]
5. Walker M, Whincup PH, Shaper AG. The British Regional Heart Study 1975–2004. Int J Epidemiol. 2004; 33:1185–1192. [PubMed: 15319395]
6. Lampe FC, Morris RW, Walker M, Shaper AG, Whincup PH. Trends in rates of different forms of diagnosed coronary heart disease, 1978 to 2000: prospective, population based study of British men. BMJ. 2005; 330:1046–1050. [PubMed: 15879388]
7. Tunstall-Pedoe H, Kuulasmaa K, Amouyel P, Arveiler D, Rajakangas AM, Pajak A. Myocardial infarction and coronary deaths in the World Health Organization MONICA Project: registration procedures, event rates, and case-fatality rates in 38 populations from 21 countries in four continents. Circulation. 1994; 90:583–612. [PubMed: 8026046]
8. Wannamethee SG, Shaper AG. Taking up regular drinking in middle age: effect on major coronary heart disease events and mortality. Heart. 2002; 87:32–36. [PubMed: 11751661]
9. Shaper AG, Wannamethee G, Weatherall R. Physical activity and ischaemic heart disease in middle-aged British men. Br Heart J. 1991; 66:384–394. [PubMed: 1747302]
10. Whincup PH, Bruce NG, Cook DG, Shaper AG. The Dinamap 1846SX automated blood pressure recorder: comparison with the Hawksley random zero sphygmomanometer under field conditions. J Epidemiol Community Health. 1992; 46:164–169. [PubMed: 1583434]
11. Thiebaut AC, Benichou J. Choice of time-scale in Cox's model analysis of epidemiologic cohort data: a simulation study. Stat Med. 2004; 23:3803–3820. [PubMed: 15580597]

12. Schoenfeld D. Partial residuals for the proportional hazards regression model. Biometrika. 1982; 69:239–241.
13. Freedman LS, Graubard BI, Schatzkin A. Statistical validation of intermediate endpoints for chronic diseases. Stat Med. 1992; 11:167–178. [PubMed: 1579756]
14. Efron, B.; Tibshirani, RJ. An Introduction to the Bootstrap. Chapman & Hall; London, England: 1993.
15. Teede HJ. The menopause and HRT: hormone replacement therapy, cardiovascular and cerebrovascular disease. Best Pract Res Clin Endocrinol Metab. 2003; 17:73–90. [PubMed: 12763513]
16. Kuulasmaa K, Tunstall-Pedoe H, Dobson A, Fortmann S, Sans S, Tolonen H, Evans A, Ferrario M, Tuomilehto J, for the WHO MONICA Project. Estimation of contribution of changes in classic risk factors to trends in coronary-event rates across the WHO MONICA Project populations. Lancet. 2000; 355:675–687. [PubMed: 10703799]
17. Department of Health. Health Survey for England 2004. Available at: http://www.dh.gov.uk/en/Publicationsandstatistics/Surveys/HealthSurveyForEngland/index.htm Accessed June 1, 2006
18. Office for National Statistics. 2004 General Household Survey. Available at: http://www.statistics.gov.uk/ssd/surveys/general_household_survey.asp Accessed June 1, 2006
19. Thomas MC, Walker M, Lennon LT, Thomson AG, Lampe FC, Shaper AG. Non-attendance at re-examination 20 years after screening in the British Regional Heart Study. J Public Health Med. 2002; 24:285–291. [PubMed: 12546205]
20. Dobson AJ, Alexander HM, Heller RF, Lloyd DM. How soon after quitting smoking does risk of heart attack decline? J Clin Epidemiol. 1991; 44:1247–1253. [PubMed: 1941018]
21. Law MR, Wald NJ, Thompson SG. By how much and how quickly does reduction in serum cholesterol concentration lower risk of ischaemic heart disease? BMJ. 1994; 308:367–372. [PubMed: 8043072]
22. Boutitie F, Gueyffier F, Pocock SJ, Boissel JP. Assessing treatment-time interaction in clinical trials with time to event data: a meta-analysis of hypertension trials. Stat Med. 1998; 17:2883–2903. [PubMed: 9921608]
23. Critchley JA, Capewell S. Prospective cohort studies of coronary heart disease in the UK: a systematic review of past, present and planned studies. J Cardiovasc Risk. 2003; 10:111–119. [PubMed: 12668908]

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CLINICAL PERSPECTIVE

The incidence of myocardial infarction (MI) in Britain has been falling since the 1970s. We have estimated that after adjustment for age, the incidence of first MI declined by 62% from 1979 to 2004 in a representative cohort of middle-aged British men. Few studies have investigated the contribution of changes in major cardiovascular risk factors to the decline in MI. Combining data on risk factor changes with data on MI incidence, we found that approximately half of the decline in MI incidence in this cohort of men could be explained by favorable population-wide time trends in cigarette smoking, systolic blood pressure, high-density lipoprotein (HDL) cholesterol, and non-HDL cholesterol together. A large fall in cigarette smoking prevalence explained the greatest single part of the decline (23%), followed by a fall in mean systolic blood pressure (13%), a rise in HDL cholesterol (12%), and a fall in non-HDL cholesterol (10%); however, these contributions may be underestimated owing to imprecision. A marked increase in mean body mass index is likely to have limited the extent of the decline. The results indicate that population-wide changes in risk factors have considerable potential for reducing MI incidence in the United Kingdom and in other locations. In the United Kingdom, although the future impact of smoking changes may be limited by the already low smoking prevalence, the potential benefits of further reductions in population systolic blood pressure and blood lipid levels, by a combination of dietary and drug management, are still considerable.

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Table 1

Overall Response Rate and No. of Men Participating in the Study by Age and Follow-Up Time, Excluding Those Reporting a Previous MI at Baseline

	Overall Response Rate,* All Men, %	No. of Men Included in This Study by Age Group, y								
		40–44	45–49	50–54	55–59	60–64	65–69	70–74	75–79	All Men, n
Baseline (1978–1980)	…	1708	1696	1676	1703	…	…	…	…	6783
5 years (1983–1985)	98	…	1639	1633	1594	1569	…	…	…	6435
13 years (1992)	91	…	…	399	1474	1382	1255	827	…	5337
17 years (1996)	88	…	…	…	660	1369	1227	1045	468	4769
20 years (1998–2000)	77	…	…	…	…	1199	1122	917	643	3881

*Overall response rate=proportion of men still alive at the time of the follow-up questionnaire who responded to the questionnaire.

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Table 2

Rates of Incidence of a First MI per 1000 Person-Years by Age and Follow-Up Time After Initial Screening

Follow-Up Time, y	Age Groups, y								
	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75–79	80–84
0–5	1.94 (0.97–3.89)	3.63 (2.55–5.16)	6.42 (4.90–8.40)	7.83 (6.12–10.03)	11.16 (8.36–14.89)	…	…	…	…
5–10	…	2.22 (1.16–4.28)	6.30 (4.80–8.27)	7.29 (5.62–9.45)	11.51 (9.30–14.23)	15.53 (11.95–20.18)	…	…	…
10–15	…	…	7.94 (5.58–11.29)	4.82 (3.51–6.62)	11.17 (8.97–13.91)	11.26 (8.95–14.16)	14.86 (11.10–19.90)	…	…
15–20	…	…	…	5.09 (3.25–7.98)	6.34 (4.77–8.44)	9.11 (7.06–11.76)	17.08 (13.96–20.91)	17.25 (12.70–23.43)	…
20–25	…	…	…	…	5.08 (3.20–8.06)	9.26 (7.25–11.83)	12.28 (9.73–15.50)	18.22 (14.61–22.72)	21.41 (15.45–29.69)

Data are expressed as incident rates per 100 person-years (95% CI) unless otherwise indicated. Trends in incidence over time can be seen by looking down each age-group column.

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Table 3

Smoking, Alcohol Consumption, Physical Activity, and BMI by Age Group and Follow-Up Time

	Age Group, y							
	40–44	**45–49**	**50–54**	**55–59**	**60–64**	**65–69**	**70–74**	**75–79**
No. (%) of current smokers								
Baseline	626 (36.7)	703 (41.6)	731 (43.7)	687 (40.4)	…	…	…	…
5 y	…	479 (29.6)	535 (33.2)	533 (33.9)	460 (29.9)	…	…	…
13 y	…	…	88 (22.2)	279 (19.0)	280 (20.3)	236 (18.9)	131 (15.9)	…
17 y	…	…	…	104 (15.9)	206 (15.3)	196 (16.2)	149 (14.4)	51 (11.1)
20 y	…	…	…	…	157 (13.1)	151 (13.5)	116 (12.7)	57 (8.9)
No. (%) of regular drinkers								
Baseline	1229 (72.0)	1213 (71.6)	1162 (69.4)	1173 (69.0)	…	…	…	…
5 y	…	1049 (64.9)	1023 (63.1)	885 (56.3)	908 (59.2)	…	…	…
13 y	…	…	250 (65.8)	904 (64.1)	742 (57.1)	667 (55.6)	437 (55.6)	…
17 y	…	…	…	424 (67.1)	885 (67.4)	697 (59.5)	577 (58.6)	250 (55.8)
20 y	…	…	…	…	789 (67.0)	723 (65.5)	516 (57.8)	359 (57.5)
No. (%) of men with at least moderate physical activity *								
Baseline	768 (45.4)	675 (40.3)	583 (35.2)	555 (33.2)	…	…	…	…
5 y	…	…	…	…	…	…	…	…
13 y	…	…	169 (43.3)	659 (45.8)	587 (44.2)	500 (44.4)	297 (39.5)	…
17 y	…	…	…	268 (42.4)	548 (41.7)	482 (42.1)	325 (35.2)	126 (30.6)
20 y	…	…	…	…	590 (50.7)	556 (50.9)	405 (46.1)	228 (37.4)
Mean BMI, kg/m^2 (SD)								
Baseline	25.3 (3.1)	25.4 (3.1)	25.6 (3.2)	25.4 (3.2)	…	…	…	…
5 y	…	26.1 (3.3)	26.1 (3.2)	26.2 (3.2)	26.1 (3.2)	…	…	…
13 y	…	…	26.9 (3.6)	26.7 (3.5)	26.5 (3.3)	26.5 (3.3)	26.2 (3.3)	…
17 y	…	…	…	27.2 (3.5)	27.1 (3.9)	26.9 (3.5)	26.5 (3.6)	26.1 (3.3)
20 y	…	…	…	…	27.3 (3.8)	27.1 (3.7)	26.8 (3.7)	26.2 (3.5)

* Corresponds to men judged to have moderate, moderately vigorous, or vigorous activity levels (as opposed to inactive, occasional, or light).

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Table 4

Fall in the Hazard of a First MI per Annum and Over 25 Years and Percentage of This Fall Explained by Risk Factors From Cox Regression Analyses With Time-Dependent Covariates

Cox Model	Risk Factors Adjusted for	Coefficient for Calendar Time, β	Fall in Hazard of MI per Annum, % (95% CI)	P	Corresponding Fall in Hazard Over 25 y, %*	% of Observed Decline in Hazard Explained by Risk Factor(s)†, (95% CI)
No adjustment for risk factors						
A	No adjustment	−0.0385	3.78 (2.6 to 5.0)	<0.001	61.8	…
A2	No adjustment, restricted follow-up (first 5 y and last 5 y only)‡	−0.0492	4.80 (1.4 to 8.1)	0.007	70.8	…
Adjustment for individual risk factors, compared with model A		…	…	…	…	…
B	Smoking (current/ex/never)	−0.0297	2.93 (1.7 to 4.1)	<0.001	52.4	22.9 (15.2 to 34.0)
C	Physical activity (inactive/occasional/light/ moderate/moderately vigorous/vigorous)	−0.0365	3.59 (2.4 to 4.8)	<0.001	59.9	5.2 (0.3 to 10.7)
D	Alcohol consumption (never/occasional/light/moderate/ heavy)	−0.0381	3.74 (2.5 to 4.9)	<0.001	61.4	1.1 (−1.8 to 4.5)
E	BMI, kg/m^2 (continuous)	−0.0413	4.04 (2.8 to 5.2)	<0.001	64.4	−7.1 (−13 to −3.1)
Adjustment for individual risk factors, compared with model A2		…	…	…	…	…
F	HDL cholesterol, mmol/L (continuous)	−0.0432	4.22 (0.8 to 7.6)	0.02	66.0	12.3 (5.1 to 42.3)
G	Non-HDL cholesterol, mmol/L (continuous)	−0.0445	4.36 (0.9 to 7.7)	0.01	67.2	9.5 (4.2 to 31.5)
H	Systolic blood pressure, mm Hg (continuous)	−0.0426	4.17 (0.7 to 7.5)	0.02	65.5	13.4 (5.5 to 53.9)
Adjustment for combinations of risk factors, compared with model A2		…	…	…	…	…
J	Smoking, HDL cholesterol, non-HDL cholesterol, systolic blood pressure	−0.0265	2.62 (−1.0 to 6.1)	0.2	48.5	46.1 (22.9 to 163.6)
K	Smoking, HDL cholesterol,	−0.0275	2.71 (−0.9 to 6.2)	0.1	49.7	44.1 (21.7 to 149.1)

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Cox Model	Risk Factors Adjusted for	Coefficient for Calendar Time, β	Fall in Hazard of MI per Annum, % (95% CI)	P	Corresponding Fall in Hazard Over 25 y, %*	% of Observed Decline in Hazard Explained by Risk Factor(s)†, (95% CI)
	non-HDL cholesterol, systolic blood pressure, physical activity, alcohol					

*Corresponding fall in hazard over 25 years=100%×[1−exp(β×25)].

†For smoking, alcohol, physical activity, and BMI, percentage of the observed decline in hazard over 25 years explained by the risk factor=100%×($\beta_0-\beta_1$)/β_0 where β_0 is the coefficient for calendar time in the model with adjustment only for age (model A), and β_1 is the coefficient for calendar time in the model with additional adjustment for the risk factor. For systolic blood pressure, HDL cholesterol, non-HDL cholesterol, and all risk factors combined, β_0 is the coefficient for calendar time in the restricted model only with adjustment for age (model A2), and β_1 is the coefficient in the model with additional adjustment for the risk factor(s).

‡Separate unadjusted model with restricted follow-up data to enable a valid comparison with models that incorporated blood pressure and cholesterol, because data on these variables were only available at limited time points.