Primary prevention and risk factor reduction in coronary heart disease mortality among working aged men and women in eastern Finland over 40 years: population based observational study

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ABSTRACT

OBJECTIVE
To estimate how much changes in the main risk factors of cardiovascular disease (smoking prevalence, serum cholesterol, and systolic blood pressure) can explain the reduction in coronary heart disease mortality observed among working aged men and women in eastern Finland.

DESIGN
Population based observational study.

SETTING
Eastern Finland.

PARTICIPANTS
34 525 men and women aged 30-59 years who participated in the national FINRISK studies between 1972 and 2012.

INTERVENTIONS
Change in main cardiovascular risk factors through population based primary prevention.

MAIN OUTCOME MEASURES
Predicted and observed age standardised mortality due to coronary heart disease. Predicted change was estimated with a logistic regression model using risk factor data collected in nine consecutive, population based, risk factor surveys conducted every five years since 1972. Data on observed mortality were obtained from the National Causes of Death Register.

RESULTS
During the 40 year study period, levels of the three major cardiovascular risk factors decreased except for a small increase in serum cholesterol levels between 2007 and 2012. From years 1969-1972 to 2012, coronary heart disease mortality decreased by 82% (from 643 to 118 deaths per 100 000 people) and 84% (114 to 17)

among men and women aged 35-64 years, respectively. During the first 10 years of the study, changes in these three target risk factors contributed to nearly all of the observed mortality reduction. Since the mid-1980s, the observed reduction in mortality has been larger than predicted. In the last 10 years of the study, about two thirds (69% in men and 66% in women) of the reduction could be explained by changes in the three main risk factors, and the remaining third by other factors.

CONCLUSION
Reductions in disease burden and mortality due to coronary heart disease can be achieved through the use of population based primary prevention programmes. Secondary prevention among high risk individuals and treatment of acute events of coronary heart disease could confer additional benefit.

WHAT IS ALREADY KNOWN ON THIS TOPIC

Tobacco smoking, high serum cholesterol, and high blood pressure are the main classical risk factors for coronary heart disease

Age standardised mortality from the disease has been declining in many Western countries, but is increasing in many developing countries and countries in transition

It is not known how much primary prevention and changes in these three risk factors can explain the changes observed in coronary heart disease mortality

WHAT THIS STUDY ADDS

Risk factor reduction at the population level is an effective way of reducing coronary heart disease mortality

Secondary prevention among high risk individuals and treatment of acute events of coronary heart disease could confer additional benefit

Introduction

Although mortality from coronary heart disease and other cardiovascular diseases has been decreasing in many countries (particularly in Western industrialised countries), in the past few decades, these diseases are still the most common causes of death in the world. Furthermore, cardiovascular mortality is increasing in many developing countries and countries in transition. Of 54.9 million deaths occurring worldwide in 2013, 17.3 million (31%) were due to cardiovascular diseases. Globally, cardiovascular disease is the most common cause of death in all World Health Organization regions except in the African region. Coronary heart disease is the most common cardiovascular disease in Europe, the Americas, and Australia, whereas cerebrovascular diseases are more important in many Asian countries.[1]

The coronary heart disease epidemic started in the United States in the 1930s and spread to western European countries after the second world war.[2] Data on the causes of coronary heart disease started to accumulate in the 1940s and 1950s. Large epidemiological studies, such as the British Medical Doctors Study, Framingham Study, and Seven Countries Study, could identify a few behavioural and biological factors associated with the risk of coronary heart disease, particularly tobacco smoking, high serum cholesterol, and high blood pressure.[3-5] Since then, the factors' importance and causal association with risk of coronary heart disease have been confirmed in many observational epidemiological studies and clinical trials.[6-8] Furthermore, dietary factors contributing to high levels of cholesterol and blood pressure, high intake of saturated fat and salt (sodium chloride), have been known already for decades.[9 10]

Mortality from coronary heart disease started to increase in Finland in the 1950s, associated with an increasing standard of living and changes in diet and other lifestyles. In the late 1960s, this mortality in Finland was the highest in the world, and was particularly high among working aged men in the eastern part of the country. The North Karelia Project, a community based project aimed at preventing cardiovascular disease, was launched in 1972. The main aim of the project was to reduce the extremely high mortality from coronary heart disease among working aged men by reducing the levels of the three main cardiovascular risk factors.[11] The project focused on behavioural change through community action and participation, supported by screening of high risk individuals and medical treatment.[12] Systematic monitoring of risk factors in the population was developed as part of the project, and since 1972, risk factor surveys have been conducted every five years.[13]

In 1994, we reported the role of risk factor changes in the reduction of coronary heart disease mortality from 1972 to 1992 among working aged men and women in eastern Finland.[14] In the past 20 years, cardiovascular risk factor patterns, secondary prevention practices, and treatment of acute events have markedly changed.[13 15] The aim of the present study was to analyse the role of primary prevention and risk factor changes in trends of coronary heart disease mortality over 40 years (1972-2012), in the same population as the 1994 study. We also aimed to determine whether the role of the three main cardiovascular risk factors had changed in contributing to trends in coronary heart disease mortality over the past 20 years.

Methods

Participants

The study population consisted of participants of the National FINRISK Study, nine independent population based surveys conducted in the provinces of North Karelia and Kuopio in eastern Finland, starting from 1972. Since then, the levels of behavioural and biological risk factors have been continuously monitored every five years, and the most recent risk factor survey was conducted in 2012.[13]

For each survey year, a random sample was drawn from the national population register. In 1972 and 1977, the sample was 6.6% of the population born during 1913-47. Since 1982, a random sample stratified by age, sex, and study area was taken from the population aged 25-64 years according to the WHO MONICA Project protocol.[16] A total of 34 525 men and women aged 30-59 years—which was the common age range of all nine surveys—were included in the present analysis. In the first surveys, participation rate was high (>90%) but decreased in the later surveys (64% in the last survey).

Ethical approval had been obtained according to the commonly required research procedures and Finnish legislation during each survey. The three last surveys were approved by the coordinating ethics committee of the Helsinki and Uusimaa Hospital District. From 1997 onwards, a written informed consent has been obtained from each participant. The study had been conducted according to the World Medical Association Declaration of Helsinki on ethical principles for medical research.

Risk factor measurements

In each survey year, data collection included:

- A self-administered questionnaire filled in at home, checked, and (if needed) completed at the study site
- Physical measurements at the study site done by trained study nurses
- Blood samples for laboratory analyses.

During the whole 40 year period, collection of risk factor data was done following the same standardised core protocol.[13]

Smoking was assessed with a standard set of questions in the study questionnaire. Non-smokers were those who had never smoked regularly, and those smokers who had stopped smoking at least six months before the survey. At the study site, blood pressure was measured using mercury sphygmomanometers. Before the survey, all nurses who did blood pressure measurements received a four day training to ensure a standardised measuring technique. Blood pressure was measured from the right arm of the patient after a five minute rest.

Serum cholesterol analyses were done in the same central laboratory at the National Institute for Health and Welfare (formerly National Public Health institute). Owing to changes in laboratory technology during the 40 year period, several methods were used for determining serum cholesterol levels. Methods, instruments, and reagents for cholesterol measurement and the quality analysis data have been described elsewhere.[17] The laboratory has taken part in international quality assurance systems, first with the WHO laboratory reference centre in Prague and the three most recent surveys with the Center for Disease Control and Prevention in Atlanta. Based on the quality analysis, systematic measurement errors due to changes in laboratory methods and reagents in different study years have been corrected.[13]

Mortality prediction

Coronary heart disease mortality was predicted using a logistic regression model based on a 15 year follow-up of 14 536 men and 15 278 women who participated in the risk factor surveys between 1972 and 1997. Age, serum total cholesterol, and systolic blood pressure were included into the model as continuous variables and smoking status as a dichotomous variable. Data on coronary heart disease mortality were obtained from the National Causes of Death Register. During follow-up, 1003 deaths (830 in men and 173 in women) from coronary heart disease were observed. The probability of death in the logistic regression model was $1 \div (1 + \exp(13.0 - (0.102 \times age) - (0.818 \times smoking) - (0.016 \times systolic\ blood\ pressure) - (0.368 \times cholesterol)))$ for men and $1 \div (1 + \exp(16.22 - (0.119 \times age) - (1.06 \times smoking) - (0.022 \times systolic\ blood\ pressure) - (0.330 \times cholesterol)))$ for women. All terms were significant at the

0.001 level. The original model included both systolic and diastolic blood pressure. In a stepwise analysis, systolic pressure was selected in the final model.

We calculated the average probability of coronary heart disease death for each five year period from 1972 to 2012 by including the mean levels of the measured risk factors in the logistic regression functions. The relative importance of each risk factor was estimated separately by changing the logistic regression function value of only that risk factor and keeping the other risk factors unchanged at the 1972 level. The predicted percentage change in coronary heart disease mortality compared with the 1972 level was then calculated for each survey period. We calculated confidence intervals for the predicted mortality change by taking into account the standard errors of parameters' estimates in the logistic regression function.

Observed mortality
We obtained data on the 40 year trend in coronary heart disease mortality in the study area from the National Causes of Death Register for men and women aged 35-64 years. The following codes were classified as deaths from coronary heart disease: 410-414 from ICD-8 (international classification of diseases, 8th revision) and ICD-9, and I20-I25 from ICD-10. We standardised annual mortality rates for age in five year age groups using the baseline population structure (at year 1972) as a standard population. The percentage decline in observed mortality from coronary heart disease was calculated by use of the mean mortality during years 1969-72 as baseline.

Patient involvement
No patients were involved in setting the research question or the outcome measures, nor were they involved in developing plans for recruitment, design, or implementation of the study. No patients were asked to advise on interpretation or writing up of results. There are no plans to disseminate the results of the research to study participants or the relevant patient community.

Results
During the 40 year period from 1972 to 2012, we saw marked changes in the levels of cardiovascular risk factors (table 1). Smoking prevalence fell from 53% to 29% among men. Smoking was rare among women in the 1970s, when only 11% of women were smokers. The proportion increased to 22% in 2002 and declined slightly to 19% in 2012. In both sexes, serum total cholesterol declined remarkably during the first 35 years of the study, but increased slightly between 2007 and 2012. In 1972, mean serum cholesterol was 6.8 mmol/L in men and 6.7 mmol/L in women; in 2012, corresponding levels were 5.4 mmol/L and 5.3 mmol/L, respectively. Mean systolic blood pressure also decreased considerably from 147.1 to 135.9 mm Hg in men and 149.2 to 129.1 mm Hg in women.

From the baseline level in 1969-1972 to 2012, coronary heart disease mortality decreased from 643 to 118 deaths per 100 000 working aged men (age 35-64 years) and from 114 to 17 deaths per 100 000 working aged women (fig 1). The reduction was 82% in men and 84% in women (table 2).

During the first 10 years of the study, changes in smoking prevalence, serum cholesterol, and systolic blood pressure contributed to nearly all of the reduction in observed coronary heart disease mortality (figs 2 and 3). Between 1982 and 2002, the observed reduction in mortality was faster than predicted. In the last 10 years, trends in observed and predicted mortality have been relatively similar. In the 1990s, about three quarters (75% in men and 76% in women in 1992), and in the last 10 years of the study about two thirds (69% in men and 66% in women in 2012) of the mortality reduction could be explained by changes in the three cardiovascular risk factors. In men, the reduction in serum cholesterol levels contributed to most of the mortality decline. In women, reductions in serum cholesterol and systolic blood pressure levels contributed equally to the mortality reduction.

Discussion
Principal findings
In the 1970s, reduction in levels of the three main cardiovascular risk factors contributed to nearly all of the observed reduction in coronary heart disease mortality. But in the 1980s, the observed mortality started to decline faster than the mortality estimates predicted by risk factor changes. In the 1990s, levels of the three risk factors contributed to about three quarters of the reduction in coronary heart disease mortality; in the last 10

Table 1 | Levels of three main risk factors for cardiovascular disease among men and women aged 30-59 years in eastern Finland from 1972 to 2012

Survey year	Men				Women			
	No	Smoking prevalence (%)	Serum cholesterol (mmol/L)	Systolic blood pressure (mm Hg)	No	Smoking prevalence (%)	Serum cholesterol (mmol/L)	Systolic blood pressure (mm Hg)
1972	4462	52.6 (51.2 to 54.1)	6.77 (6.73 to 6.81)	147.1 (146.5 to 147.7)	4804	11.4 (10.5 to 12.3)	6.69 (6.65 to 6.72)	149.2 (148.5 to 149.9)
1979	4436	46.6 (45.2 to 48.1)	6.52 (6.49 to 6.56)	144.2 (143.6 to 144.7)	4659	12.7 (11.8 to 13.7)	6.34 (6.30 to 6.38)	141.6 (140.9 to 142.2)
1982	2144	41.7 (39.6 to 43.8)	6.26 (6.21 to 6.31)	145.5 (144.7 to 146.3)	2005	16.3 (14.7 to 17.9)	6.04 (5.98 to 6.09)	141.6 (140.7 to 142.5)
1987	1528	40.5 (38.0 to 42.9)	6.23 (6.17 to 6.29)	144.0 (143.1 to 144.9)	1672	17.3 (15.5 to 19.2)	5.92 (5.86 to 5.98)	138.1 (137.2 to 139.1)
1992	962	36.8 (33.7 to 39.8)	5.91 (5.84 to 5.98)	140.7 (139.5 to 141.8)	1031	21.3 (18.8 to 23.8)	5.55 (5.48 to 5.61)	134.6 (133.3 to 135.9)
1997	1004	33.3 (30.3 to 36.2)	5.70 (5.64 to 7.77)	138.8 (137.7 to 139.9)	1107	17.9 (15.6 to 20.1)	5.54 (5.48 to 5.60)	132.6 (131.5 to 133.7)
2002	895	36.9 (33.7 to 40.0)	5.60 (5.53 to 5.68)	137.2 (136.0 to 138.4)	1036	22.4 (19.8 to 24.9)	5.33 (5.28 to 5.39)	131.8 (130.5 to 133.0)
2007	699	32.2 (28.7 to 35.7)	5.35 (5.27 to 5.42)	138.0 (136.7 to 139.3)	770	21.9 (19.0 to 24.9)	5.16 (5.10 to 5.23)	132.2 (130.8 to 133.6)
2012	605	29.3 (25.6 to 32.9)	5.44 (5.35 to 5.52)	135.9 (134.5 to 137.2)	706	19.4 (16.5 to 22.3)	5.30 (5.23 to 5.37)	129.1 (127.9 to 130.4)

Data are prevalence (95% confidence interval) or mean (95% confidence interval) unless stated otherwise.
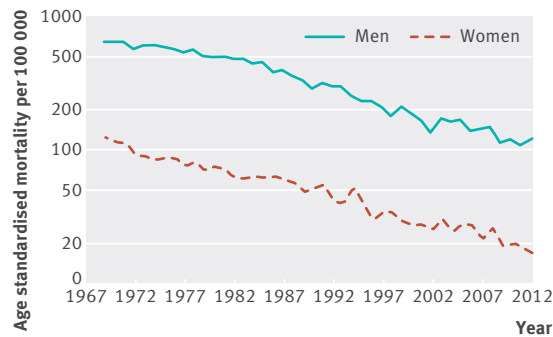
Fig 1 | Age standardised mortality from coronary heart disease in 1969-2012 (logarithmic scale), for working aged men and women (age 35-64 years) in eastern Finland

years of the study, this proportion went down to about two thirds. In men, changes in serum cholesterol levels contributed to most of the reduction in mortality, whereas changes in serum cholesterol and systolic blood pressure were equally important in mortality for women. The remaining one third of mortality reduction might be explained by three other major factors: changes in other primary risk factors not included in our analysis, such as diet and physical activity; improved secondary prevention; and improved treatment of acute cardiac events.

Population based primary prevention

Smoking was common among men in Finland, and two thirds of men were smokers in the 1950s. Smoking prevalence began to decline among men in the 1960s and 1970s, and in the 1980s the decreasing trend accelerated owing to active anti-smoking campaigns and legislation. Among women, smoking was not part of the culture in eastern Finland, and the prevalence of smoking was low. Smoking prevalence in women started to increase in the 1980s and 1990s owing to urbanisation and change in the culture. This increase levelled off in the 1990s, and in the last 10 years of the study, the prevalence of smoking among women has also fallen. The first comprehensive tobacco law was introduced in Finland in 1976, and the law has since been revised several times.[18] The smoking prevalence in Finland is currently one of the lowest in Europe. According to the latest amendment of the tobacco law, a smoke-free Finland (defined as smoking prevalence below 5%) is the target to be achieved by 2040.

In the early 1970s, serum cholesterol levels in eastern Finland were extremely high. The average level was nearly 7 mmol/L; and over 90% of the middle aged population had levels higher than 5 mmol/L, the recommended upper limit in current international guidelines.[19 20] Thus, a population based strategy to reduce the entire cholesterol distribution was the most effective way to advance prevention of coronary heart disease. The role of fat content in the diet in determining serum cholesterol levels (that is, the association between polyunsaturated and saturated fat intake) was known already in the 1960s.[9] Owing to the high consumption of fatty milk products and butter, which were core components in traditional diet and also the main agricultural products in the area, saturated fat intake was high. On the other hand, vegetable oils were hardly known 40 years ago, and vegetable consumption was low in eastern Finland.

Table 2 | Observed and predicted reduction in coronary heart disease mortality among working aged men and women (age 35-64 years) in eastern Finland

Survey year	Observed reduction (%)*	Predicted reduction (%; 95% CI)†				Proportion of predicted reduction from observed reduction (%)
		Smoking only	Systolic blood pressure only	Serum cholesterol level only	All risk factors combined	
Men						
1969-72‡	0	0	0	0	0	—
1977	17	4.6 (0.5 to 8.8)	4.4 (0.3 to 8.6)	8.4 (4.2 to 12.5)	16.5 (12.3 to 20.7)	97
1982	25	8.3 (3.1 to 13.4)	2.5 (−2.7 to 7.6)	16.6 (11.5 to 21.8)	25.4 (20.3 to 30.6)	101
1987	38	9.1 (3.3 to 14.9)	4.7 (−1.1 to 10.5)	17.4 (11.6 to 23.2)	28.5 (22.7 to 34.3)	75
1992	55	11.7 (4.8 to 18.7)	9.4 (2.4 to 16.4)	26.4 (19.4 to 33.3)	41.3 (34.3 to 48.2)	75
1997	67	14.2 (7.3 to 21.0)	12.0 (5.2 to 18.9)	31.6 (24.7 to 38.4)	48.5 (41.7 to 55.4)	72
2002	75	11.7 (4.5 to 18.9)	14.2 (7.0 to 21.3)	34.0 (26.8 to 41.2)	50.2 (43.0 to 57.4)	67
2007	78	14.9 (6.9 to 22.9)	13.1 (5.2 to 21.1)	39.8 (31.8 to 47.8)	55.7 (47.7 to 63.7)	71
2012	82	16.9 (8.4 to 25.3)	15.9 (7.4 to 24.4)	37.8 (29.3 to 46.3)	56.8 (48.3 to 65.3)	69
Women						
1969-72‡	0	0	0	0	0	—
1977	28	−1.4 (−5.4 to 2.6)	15.5 (11.5 to 19.5)	10.9 (6.9 to 14.9)	23.7 (19.6 to 27.7)	85
1982	41	−5.3 (−10.5 to −0.1)	15.4 (10.2 to 20.6)	19.3 (14.1 to 24.5)	28.1 (22.9 to 33.3)	68
1987	45	−6.4 (−12.0 to −0.1)	21.6 (16.0 to 27.2)	22.4 (16. to 27.9)	35.5 (29.7 to 40.8)	79
1992	59	−11.0 (−17.7 to −4.3)	27.5 (20.7 to 34.2)	31.3 (24.5 to 38.0)	44.7 (37.9 to 51.4)	76
1997	72	−7.0 (−13.6 to −0.5)	30.6 (24.1 to 37.1)	31.4 (24.8 to 37.9)	49.0 (42.5 to 55.6)	68
2002	77	−12.2 (−19.0 to −5.5)	31.6 (25.2 to 38.6)	35.9 (29.2 to 42.6)	51.5 (44.3 to 57.7)	67
2007	79	−11.7 (−19.3 to −4.1)	31.3 (23.6 to 38.9)	39.4 (31.8 to 47.0)	53.5 (45.9 to 61.1)	68
2012	84	−8.8 (−16.7 to −0.9)	35.7 (27.8 to 43.6)	36.6 (28.7 to 44.5)	55.7 (47.8 to 63.6)	66

*Five year means.
†Predicted reduction in coronary heart disease mortality based on risk factor changes during each five year period.
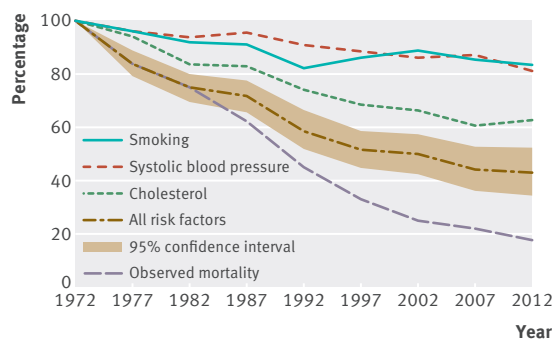‡Baseline period.

Fig 2 | Predicted and observed reduction (%) in coronary heart disease mortality in men aged 35-64 years, 1972-2012
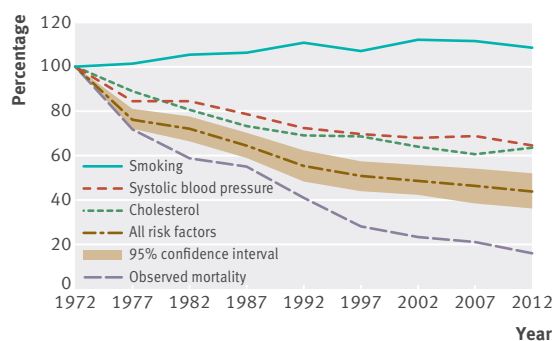

Fig 3 | Predicted and observed reduction (%) in coronary heart disease mortality in women aged 35-64 years, 1972-2012

Although the promotion of dietary change was challenging, major changes were observed. These included the transition from consumption of fatty milk to low fat and skimmed milk; a substantial reduction in butter consumption, from nearly 20 kg to less than 5 kg per capita per year; and a marked increase in the use of vegetables and vegetable oils.[21][22] In parallel with dietary changes, serum cholesterol levels started to decline. Based on nutritional data collected at the same time as cholesterol measurements, at population level over 80% of the cholesterol lowering could be explained by dietary changes, and only less than 20% by the use of drugs (statins) to treat high cholesterol.[23] Paradoxically, reduction of serum cholesterol was the fastest in the 1970s and 1980s, when pharmaceutical drug treatment for high serum cholesterol levels was minimal, and the reduction levelled off in the 1990s as drug treatment became more common. In the 2012 survey, 18% of participants (21% of men and 15% of women) were using statins.

In the last five years of the study, both the reported intake of saturated fat and dietary cholesterol and measured cholesterol levels increased slightly. In fact, the measured cholesterol change was nearly the same as that calculated from the dietary data by use of the classical Hegsted equation.[24] The unfavourable dietary change and cholesterol increase might be due to the increased popularity of low carbohydrate (and high fat) diets in Finland during the last risk factor survey in 2012. How permanent this change is will be seen in the next risk factor survey in 2017.

Furthermore, mean blood pressure levels were very high in eastern Finland in the early 1970s. On the lowering of blood pressure, a combined strategy of lifestyle change was applied (mainly reduction of high salt intake, and use of screening and pharmaceutical drug treatment).[25] The average salt intake declined by a third, from 14 g in men and 10 g in women in the 1970s to 8.9 g and 6.5 g in 2007, respectively.[26] In the present study, we observed a small increase in salt intake in the last five years. Both systolic and diastolic blood pressures decreased in the first 30 years, and systolic pressure has continued to decrease since then. However, the reduction in diastolic pressure levelled off in the 1990s, with a small increase observed in the last 10 years. This difference in trends could be due to the difference in systolic and diastolic blood pressure pathophysiology. Systolic pressure is mainly determined by the stiffness of large arteries, whereas diastolic pressure depends more on the peripheral resistance.[27][28]

In addition to the three main cardiovascular risk factors, other factors such as physical inactivity, obesity, and elevated blood glucose—and diabetes as their consequence—have been identified as major causes for coronary heart disease.[29][30] The role of alcohol drinking in risk of coronary heart disease is controversial: very modest drinking could reduce the risk but heavy and binge drinking are probably harmful.[31] Physical inactivity and obesity were not particularly common in eastern Finland in the 1970s but they become evident health problems later on.

Physical activity at work and travel to and from work has decreased whereas physical activity during leisure time has continuously increased in recent decades.[32] However, the objective measurement of total physical activity is complicated in large population based studies. Mean body mass index and prevalence of obesity started to increase in the late 1970s but the increase levelled off during the last five years of the study.[13] Inclusion of body mass index in the predictive model did not affect the results markedly, probably because the effect of obesity on coronary heart disease risk is largely mediated through its effect on blood pressure. We do not have comparable data on the changes in diabetes prevalence during the survey period. Self-reported data are not reliable because diagnostic activity to detect diabetes in healthcare, and also international diagnostic criteria for diabetes, have changed in recent decades. Total alcohol consumption has about doubled in Finland in the past four decades; therefore, the prevalence of harmful drinking has probably increased.[33]

Role of secondary prevention, treatment, and other factors

In the 1970s and early 1980s, nearly the entire observed reduction in coronary heart disease mortality could be explained by reduction in the levels of the three main cardiovascular risk factors. The predicted and observed trend lines started to separate in the mid-1980s, and the observed reduction in mortality was faster than predicted. In the last 10 years of the study, the trends in predicted and observed reduction of mortality were

similar, and about two thirds of the observed reduction could be explained by changes in the three main risk factors and the remaining third by other factors.

These findings accord with the development of secondary prevention and treatment practices in the past decades. In the 1980s, new guidelines on secondary prevention were introduced, including active drug treatment with aspirin, β blockers, angiotensin converting enzyme inhibitors, and statins.[34] Invasive cardiology also expanded in the late 1980s. Use of percutaneous coronary interventions began in the early 1990s; the number of these procedures rose fivefold between 1994 and 2004. Accordingly, case fatality of acute events of coronary heart disease fell by a third between 1994 and 2004, and the decline has since continued.[35 36] Among patients with coronary heart disease aged 30 years or older (self-reported previous myocardial infarct or coronary heart disease), age standardised prevalence of revascularisation procedures (bypass operation or percutaneous coronary intervention) was 54% in men and 34% in women in 2011, compared with 33% and 12% in 2000, respectively.[37] However, because we do not have individual level data on secondary prevention and treatment, we can only indirectly estimate the role of secondary prevention on mortality.

Sensitive C reactive protein and other markers of low grade inflammation, haemostatic factors, vitamin and flavonoid intake and other dietary factors, amount and quality of sleep, and depression and social deprivation have been shown to be associated with the risk of coronary heart disease. However, final evidence on their role in the development of coronary heart diseases is still lacking.[38] Family history and a number of genetic markers are associated with risk of coronary heart disease, but the role of hereditary factors in disease prevention is largely open.[39] Genetic background of the population has not changed during the past 40 years and cannot explain the substantial decrease in coronary heart disease mortality.

Comparison with other studies
The role of risk factor changes and treatments in coronary heart disease mortality has been analysed in many countries, using the IMPACT model approach developed in the United Kingdom.[40 41] The IMPACT model takes into account population level changes in the main risk factors and the most effective treatments in coronary heart disease. These treatments include lipid and blood pressure lowering drugs in both primary and secondary prevention, treatments in acute events, and rehabilitation. The reduction in coronary heart disease mortality attributable to risk factors and treatments vary depending on the time period, risk factor levels and treatments at baseline, and observed changes in risk factors and treatment practices, as well as the age group of patients. In countries where the decline in risk factors has been considerable during the observation period, most of the mortality decline has been attributable to risk factor reduction. In IMPACT studies conducted in different countries (such as Sweden, Turkey, Portugal, and USA), the proportion of mortality decline

attributed to treatment and secondary prevention varied between a quarter and a half.[42-45]

Strengths and limitations
The main strengths of our study were the long and systematic monitoring of population based risk factors, which used the same standardised protocol over four decades and a practically complete set of mortality data. To our knowledge, risk factor monitoring in eastern Finland is the longest continuous system for population based risk factor monitoring in the world. Even though individual verification of the cause of death is not possible in large population studies, validation studies have shown that the reliability of diagnosis in the Finnish Causes of Death Register is good.[46]

The main limitations of the study were related to the decreasing participation rate and potential measurement error in risk factor surveys. Although a 60% participation rate in large health examination surveys is still fairly good in international comparison, the risk factor levels among non-participants in the present study may have been higher than among participants.[47] Therefore, our model could have overestimated the importance of the risk factor change in the last two decades of the study. On the other hand, our predictive model was based on single measurements of the risk factors being prone to random measurement error, which diminishes the strength of the true association between the measured risk factor and the endpoint, and therefore could underestimate the importance of risk factor change in reductions in coronary heart disease mortality.[48] Because we assessed the smoking status at baseline only, and we were not able to update smoking status during follow-up, our model most likely underestimated the role of smoking in the reduction of coronary heart disease mortality.[49]

Although saturated fat (and trans fat) intake, intake of dietary cholesterol, and drug treatment are the main determinants of serum cholesterol levels, the observed change in serum cholesterol most probably reflects other dietary changes as well. Similarly, reduced salt intake might be associated with other healthy lifestyle changes. Therefore, the estimated effect of the change in serum cholesterol and blood pressure could include unmeasured confounding caused by the change in other dietary factors. Finally, although pharmaceutical treatment reduces serum cholesterol and blood pressure effectively, it is unlikely to completely reverse the atherosclerosis developed before the start of treatment.

Conclusions and policy implications
Although secondary prevention and treatment protocols have markedly developed in recent decades, primary prevention and reduction in levels of the main classical factors contributing to cardiovascular risk should still be considered as the main strategy to reduce disease burden and mortality due to coronary heart disease. This is in accordance with the current WHO action plan on non-communicable diseases, which stresses the role of a population based approach in prevention and control of cardiovascular and other

non-communicable diseases.[50] Secondary prevention among high risk individuals and treatment of acute events of coronary heart disease could confer additional benefit.

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