



Forty-year change in coronary heart disease mortality among working aged men and women in Eastern Finland: the role of primary prevention and risk factor reduction

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4 women in Eastern Finland: the role of primary prevention and risk factor reduction
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Abstract

Objectives: To estimate the extent to which changes in the main cardiovascular risk factors (smoking prevalence, and serum cholesterol and systolic blood pressure levels) at the population explain the 40 year decline in coronary heart disease (CHD) mortality among working aged men and women.

Design: Predicted change in CHD mortality was estimated by 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 CHD mortality were obtained from the National Causes of Death Register.

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 of main cardiovascular risk factors through population-based primary prevention

Main outcome measures: Predicted and observed age standardized CHD mortality

Results: From the early seventies (1969-1972) to 2012 CHD mortality decreased among men aged 35 to 64 years by 82% (from 643 to 118 per 100,000). Among women the decline was 84% (from 114 to 17 per 100,000). During the same time period, the levels of major cardiovascular risk factors, smoking prevalence, serum total cholesterol and systolic blood pressure declined remarkably, except a small increase in serum cholesterol levels between 2007 and 2012. During the first ten years, changes in these three risk factors explained nearly all of the observed mortality reduction. Since the mid-1980s, the observed reduction in mortality has been larger than predicted. In the last ten years about two thirds of the CHD mortality reduction was explained by changes in risk factors and one third by other factors.

Conclusion: Population based primary prevention and reduction in the levels of major risk factors are crucial in lowering of disease burden and mortality due to CHD. An additional gain can be achieved by secondary prevention among high risk individuals and by treatment of acute events.

What this paper adds

Section 1: What is already known on this subject

Tobacco smoking, high serum cholesterol and high blood pressure are the main classical risk factors for CHD. Age-standardised CHD mortality has been declining in many western countries but is increasing in many developing countries and countries in transition. Relatively little is known, as to how much primary prevention and changes in risk factors can explain the changes in CHD mortality.

Section 2: What this study adds

Reduction of the levels of major risk factors is crucial in lowering of disease burden and mortality due to CHD in the population. An additional but smaller gain can be achieved by secondary prevention among high risk individuals and by treatment of acute events.

Introduction

Even though mortality from coronary heart disease (CHD) and other cardiovascular diseases (CVD) has been decreasing in many countries, particularly in western industrialized countries, in the last decades, they are still the most common causes of death in the world [1]. Furthermore, CVD mortality is increasing in many developing countries and countries in transition. Of the total of 54.9 million deaths in the world in 2013, 17.3 million (31%) were due to CVDs. Globally CVD is the most common cause of death in all World Health Organization (WHO) regions except in the African region. CHD is the most common CVD in Europe, Americas and Australia, whereas cerebrovascular diseases are more important in many Asian countries.

CHD epidemic started in the United States in the 1930s and spread into the Western European countries after the Second World War [2]. In Finland, CHD mortality started to increase in the 1950s associated with increasing standard of living and changes in diet and other lifestyles. In the late 1960s, CHD mortality in Finland was the highest in the world, and mortality was particularly high among the working aged men in Eastern Finland, especially in the Province of North Karelia.

Data on the causes of CHD and other CVD started to accumulate in 1940s and 1950s. Large epidemiological studies, such as the British Medical Doctors Study, the Framingham Study and the Seven Countries Study, could identify a few behavioral and biological factors associated with the CHD risk [3-5]. The roles of tobacco smoking, high serum cholesterol and high blood pressure in the development of CHD were relatively well established already in the 1960s, and since then their importance and causal relationship with the CHD incidence and mortality have been confirmed in a large number of observational epidemiological studies and clinical trials [6-8]. Also dietary factors contributing to high cholesterol and high blood pressure levels, high intake of saturated fat and salt (sodium chloride), have been known already for decades [9,10].

The North Karelia Project, first community-based CVD prevention project in the world, was launched in 1972. The main aim of the project was to reduce the extremely high CHD mortality among the working aged men in the province by reducing the levels of the three main cardiovascular risk factors [11]. Main emphasis was put on behavioral change through community action and participation, supported by screening of high risk individuals and medical treatment [12]. Systematic population-based risk factor monitoring was developed as part of the project and since 1972 risk factor surveys have been conducted every five years. The last, ninth consecutive, health examination survey was conducted in 2012 [13]. Positive development in risk factor levels started fairly soon after the start of the project, first in North Karelia, and later on in other parts of Finland. Also CHD mortality started to decline.

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3 Twenty years ago, in 1994, we reported the role of the risk factor change in CHD mortality reduction from
4 1972 to 1992 in the same population [14]. Our finding was that about three quarters of the mortality
5 reduction was explained by the changes in the three classical cardiovascular risk factors. In the last twenty
6 years, cardiovascular risk factor patterns, secondary prevention practices and treatment of acute events
7 have markedly changed in Finland and in other developed countries [13,15]. The aim of the present study is
8 to analyze the role of primary prevention and risk factor changes in forty-year (1972-2012) CHD mortality
9 trends among working aged men and women in Eastern Finland, and whether the role of the three main
10 risk factors in explaining CHD mortality trend has changed in the last twenty years.
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19 **Material and methods**

20 Participants

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22 The study population consists of participants of nine independent population-based surveys. The first
23 cardiovascular risk factor survey was conducted in the provinces of North Karelia and Kuopio in Eastern
24 Finland in 1972 as part of the North Karelia Project. Since then, the levels of behavioral and biological risk
25 factors have been continuously monitored every five years and the last risk factor survey was conducted in
26 2012 [13].
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33 For each survey year a random sample was drawn from the national population register. In 1972 and 1977
34 the sample was 6.6% of the population born during 1913-1947. Since 1982 an age, sex and study area
35 stratified random sample was taken from the population aged 25 to 64 years according to the WHO
36 MONICA Project protocol [16]. A total of 34,525 men and women aged 30 to 59 years, which is the
37 common age range of all nine surveys, participated in the risk factor surveys. In the first surveys,
38 participation rate was high, over 90% but declined in the later surveys being 64% in the last survey.
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44 Ethical approval has been obtained according to the commonly required research procedures and Finnish
45 legislation during each survey. The three last surveys were approved by the Coordinating Ethics Committee
46 of the Helsinki and Uusimaa Hospital District. From 1997 onwards a written informed consent has been
47 obtained from each participant. The study has been conducted according to the World Medical Association
48 Declaration of Helsinki on ethical principles for medical research.
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Risk factor measurements

In each survey year, data collection included (1) a self-administered questionnaire filled in at home, checked and, if needed, completed at the study site, (2) physical measurements at the study site done by trained study nurses and (3) blood samples for laboratory analyses. During the whole forty year period, collection of risk factor data was done following the same standardized 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 standardized measuring technique. Blood pressure was measured from the right arm of the subject after a five minute rest. Serum cholesterol analyses were done in the same central laboratory in the National Institute for Health and Welfare (formerly National Public Health institute). Due 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 center in Prague and the last three 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

CHD 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 CHD mortality were obtained from the National Causes of Death Register. During the follow-up, 1014 (830 in men and 173 in women) CHD deaths were observed. The probability of death in the logistic regression model was $1/(1+\exp(13.0-0.102 \times \text{age}-0.818 \times \text{smoking}-0.016 \times \text{systolic blood pressure}-0.368 \times \text{cholesterol}))$ for men and $1/(1+\exp(16.22-0.119 \times \text{age}-1.06 \times \text{smoking}-0.022 \times \text{systolic blood pressure}-0.330 \times \text{cholesterol}))$ for women. All terms were significant at 0.001 level. The original model included both systolic and diastolic blood pressure. In stepwise analysis systolic pressure was selected in the final model.

Average probability of CHD death for each five-year period from 1972 to 2012 was calculated by including the mean level of the measured risk factors in the logistic regression functions. The relative importance of

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3 each risk factor was estimated separately by changing the logistic regression function value of only that risk
4 factor and keeping the other risk factors unchanged at the 1972 level. The predicted percentage change in
5 CHD mortality compared with the 1972 level was then calculated for each survey period. Confidence
6 interval for the predicted mortality change was calculated by taking into account the standard errors of the
7 risk factor level in each survey and the standard errors of parameters' estimates in the logistic regression
8 function.
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12 13 Observed mortality

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16 Data on the forty-year trend in CHD mortality in the study area were obtained from the National Causes of
17 Death Register for men and women aged 35-64 years. The following ICD codes were classified as CHD
18 deaths: ICD 8 and 9 410-414, and ICD 10 I20-I25. Annual mortality rates were standardized for age in five
19 year age groups using the baseline (1972) population structure as a standard population. The percentage
20 decline in observed CHD mortality was calculated using the mean of 1969-1972 mortality as baseline.
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27 **Results**

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30 From the baseline level at the early seventies (1969-1972) to 2012 CHD mortality decreased from 643 to
31 118 per 100,000 among working aged men (aged 35 to 64 years) and from 114 to 17 per 100,000 among
32 working aged women (Figure 1). The decrease was 82% in men and 84% in women (Table 1).
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36 During the same time period, from 1972 to 2012, marked changes were observed also in the levels of risk
37 factors (table 2). Smoking prevalence decreased from 52.6% to 29.3% among men. Among women smoking
38 was rare in the 1970s, only 11.4% of women were smokers. The proportion increased up to 22.4% in 2002
39 and declined then slightly being 19.4% in 2012. In both genders, serum total cholesterol declined
40 remarkably during the first 35 years of the study but a small increase was observed between 2007 and
41 2012. In 1972, the mean serum cholesterol level was 6.8 mmol/l in men and 6.7 mmol/l in women, and in
42 2012 the levels were 5.4 mmol/l and 5.3 mmol/l, respectively. Mean systolic blood pressure also declined
43 remarkably from 147.1 mmHg to 135.9 mmHg in men and 149.2 to 129.1 mmHg in women.
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50 During the first ten years, changes in smoking prevalence, and serum cholesterol and systolic blood
51 pressure levels explained nearly all of the observed mortality reduction (Figures 2 and 3). Between 1982
52 and 2002, the observed CHD mortality decline was faster than predicted. In the last ten years trends in
53 observed and predicted mortality have been quite similar. In the 1990s about three quarters (in 1992 75%
54 in men and 76% in women), and in the last ten years about two thirds (in 2012 69% in men and 66% in
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women) of the CHD mortality reduction was explained by changes in the analyzed three risk factors. In men, reduction in serum cholesterol levels explained most of the mortality decline. In women, mortality reduction was equally explained by reductions in serum cholesterol and systolic blood pressure levels.

Discussion

In the 1970s, reduction in risk factors explained practically all of the observed reduction in CHD mortality, in the 1980s the observed mortality started to decline faster than the mortality estimates predicted by the risk factor changes. In the 1990s risk factors explained about three quarters of mortality reduction, and in the last ten years still about two thirds. Changes in serum cholesterol levels explained most of the CHD mortality reduction in men, whereas changes in serum cholesterol and systolic blood pressure levels were equally important in women. The remaining one third of mortality reduction may be explained by three major groups of factors: (1) change in other primary risk factors, which were not included in our analysis, such as changes in diet and physical activity, (2) improvement in secondary prevention and (3) improvement in the treatment of acute cardiac events

Smoking used to be very common among men in Finland and some two thirds of men were smokers in the 1950s. Smoking prevalence started to go down among men in the 1960s and in the 1970s and 1980s the decreasing trend accelerated due to active anti-smoking campaigns and legislation. Among women, smoking was not part of the culture in Eastern Finland, and the prevalence of smoking used to be low, but it started to increase in the 1980s and 1990s due to urbanization and change in the culture. Among women the increase of smoking prevalence levelled off in the 1990s and in the last ten years prevalence of smoking has been decreasing also in women. The first comprehensive tobacco law was introduced in Finland in 1976, and since then the law has been revised several times [18]. Currently the smoking prevalence in Finland is one of the lowest in Europe. The official target according to the latest amendment of the tobacco law is smoke-free Finland (defined as smoking prevalence below 2%) by 2040.

In the early 1970s, serum cholesterol levels in eastern Finland were extremely high, the average was nearly seven mmol/l and over 90% of the middle-aged population had serum cholesterol higher than five mmol/l, the recommended upper limit in current international guidelines [19, 20]. Thus, a population-based strategy to move the whole cholesterol distribution towards the lower levels was the only way to go. The role of fat content in the diet as the determinant of serum cholesterol levels, the relationship of polyunsaturated and saturated fat intake, was known already in the 1960s [9]. Due to high consumption of fatty milk products and butter, which were core components in traditional diet and also the main

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3 agricultural products in the area, saturated fat intake used to be very high. On the other hand, forty years
4 ago vegetable oils were hardly known and vegetable consumption was low in Eastern Finland. Even though
5 the promotion of dietary change was challenging, major changes were observed.
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9 Main dietary changes were the change from fatty milk to low-fat and skimmed milk, a huge reduction in
10 butter consumption, from nearly 20 kg to less than 5 kg per capita per year, and a marked increase in the
11 use of vegetables and vegetable oils [21,22]. In parallel with dietary changes, serum cholesterol levels
12 started to decline. Based on nutritional data collected at the same time with cholesterol measurements, at
13 population level over 80% of cholesterol lowering is explained by dietary changes and only less than 20% by
14 pharmaceutical drug (statins) treatment of high cholesterol [23]. Paradoxically, reduction of serum
15 cholesterol levels was fastest in the 1970s and 1980s, at the time when pharmaceutical drug treatment of
16 high serum cholesterol was minimal, and the decrease levelled off in the 1990s when drug treatment
17 became more common. In the 2012 survey, 18 % of participants (21% of men and 15% of women) were
18 using statins.
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26 In the last five years, both reported intake of saturated fat and dietary cholesterol, and measured
27 cholesterol levels increased slightly. Actually, the measured cholesterol change was nearly the same as
28 calculated from the dietary data by using the classical Hegsted equation [24]. The reason for the
29 unfavorable dietary change and cholesterol increase might be the boom of low carbohydrate (and high fat)
30 diet in Finland during the last risk factor survey in 2012. How permanent this change is will be seen in the
31 next risk factor survey in 2017.
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37 Also mean blood pressure levels were very high in eastern Finland in the early 1970s. In the lowering of
38 blood pressure, a combined strategy of lifestyle change, mainly reduction of high salt intake, and screening
39 and pharmaceutical drug treatment were applied [25]. The average salt intake declined by one third, from
40 14 grams in men and 10 grams in women in the 1970s to 8.9 and 6.5 grams in 2012, respectively [26].
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42 Obesity was not particularly common in eastern Finland forty years ago but it became a major health
43 problem later on [13]. Both systolic and diastolic blood pressures declined first thirty years, and systolic
44 pressure has continued its decline since then, but in diastolic pressure the reduction levelled off in the
45 1990s and a small increase has been observed in the last ten years. This difference in trends may be due to
46 the difference in systolic and diastolic blood pressure pathophysiology: systolic pressure is mainly
47 determined by arteriosclerosis and stiffness of large arteries whereas diastolic pressure depends more on
48 obesity and peripheral resistance [27, 28].
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56 In the 1970s and early 1980s, practically the whole observed CHD mortality reduction was explained by
57 reduction of the risk factors. The trend lines started to separate in the middle of the 1980s and the
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3 observed mortality reduction was faster than predicted. In the last ten years the trends in predicted and
4 observed mortality reduction have been quite similar and about two thirds of the mortality reduction is
5 explained by changes in risk factors and one third by other factors. These findings fit quite well with the
6 development of secondary prevention and treatment practices in the last decades. In the 1980s new
7 secondary prevention guidelines were introduced including active drug treatment with aspirin, beta-
8 blockers, ACE inhibitors and later on statins [29]. Also invasive cardiology expanded. Even though the first
9 coronary bypass operation was conducted in Finland in 1973 the number of operations was small until the
10 end of 1980s. Percutaneous coronary interventions (PCI) were started in the early 1990s. The number of
11 PCI procedures five folded in ten years between 1994 and 2004. Accordingly, case fatality of acute CHD
12 events reduced by one third between 1994 and 2004 and the decline has continued [30, 31]. Among CHD
13 patients aged 30 years or more (self-reported previous myocardial infarct or coronary heart disease) age-
14 standardised prevalence of revascularization procedures (bypass operation or PCI) was 54 % in men and 34
15 % in women in 2011, compared to 33 % and 12 % in 2000 [32].

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25 In addition to the three classical risk factors, a few other factors, such as physical inactivity, obesity, and
26 elevated blood glucose level and diabetes as their consequence, have been identified as major causes for
27 CHD [33, 34]. Even though a large number of other factors, including sensitive C-reactive protein (CRP) and
28 other markers of low grade inflammation, hemostatic factors, vitamin and flavonoid intake and other
29 dietary factors, and amount and quality of sleep, have been shown to be associated with the risk of CHD,
30 final evidence on their causal role in the development of CHDs is still lacking [35]. Family history of CHD and
31 a number of genetic markers are associated with CHD risk but the role of hereditary factors in the
32 development of CHD and particularly in diseases prevention is largely open [36]. Genetic background of the
33 population has not changed markedly during the last forty years and cannot explain the dramatic decrease
34 in CHD mortality.

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The role of risk factor changes and treatments in CHD mortality have been analyzed in many countries
using the IMPACT-model approach developed in United Kingdom [37, 38]. The model takes into account
population level changes in main risk factors, and the most effective treatments including lipid and blood
pressure lowering drugs both in primary and secondary prevention, treatments in acute events and
rehabilitation. Reduction in CHD mortality attributable to risk factors and treatments vary based on the
time period, baseline situation in risk factor levels and treatments, and observed changes in risk factors and
treatment practices. In countries, where the decline in risk factors have been significant during the
observation period the majority of the mortality decline has been attributable to risk factor reduction. For
example in Sweden 77% of the mortality decline between 1986 and 2002 was attributable to risk factor
reductions [39]. On the other hand, in Turkey 47% and in Portugal 50% of mortality decrease between 1995

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3 and 2008 was attributed to changes in treatment protocols, mainly related to initial treatments after an
4 acute myocardial infarction and improvement of antihypertensive medication [40, 41].
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7 The main strengths of our study are the long and systematic population-based risk factor monitoring using
8 the same standardized protocol over four decades and a practically complete mortality data. The main
9 limitation is the decreasing participation rate in the risk factor surveys. Even though the 60% participation
10 rate in large health examination surveys is still relatively good in international comparison, we know that
11 the risk factor levels among non-participants are somewhat higher than among the participants [42].
12 Therefore, our model may overestimate the importance of the risk factor change in the last couple of
13 decades. On the other hand, our predictive model is based on single measurements of the risk factors being
14 prone to random measurement error which diminishes the strength of the true association between the
15 measured risk factor and the endpoint, and as a consequence underestimates the importance of risk factor
16 change in CHD mortality reduction [43].
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24 In conclusion, even though secondary prevention and treatment protocols have markedly developed in the
25 last decades, primary prevention and reduction of the levels of main classical cardiovascular risk factors
26 should still be considered as the main strategy to reduce disease burden and mortality due to CHD. This is
27 in accordance with the current WHO non-communicable disease action plan, which stresses the role of
28 population-based approach in prevention and control of cardiovascular and other non-communicable
29 diseases [44]. An additional mortality reduction can be achieved through secondary prevention by
30 screening and treating high risk individuals, and by improved treatment of acute cardiac events.
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Figure 1. : Age-standardised CHD mortality 1969-2012, men and women 35-64 years
(per 100 000, logarithmic scale)

Figure 2. Predicted and observed reduction in CHD mortality 1972-2012, men 35-64 years

Figure 3. Predicted and observed reduction in CHD mortality 1972-2012, women 35-64 years

Confidential: For Review Only

Table 1. Observed and by the risk factor change predicted CHD mortality decline among men and women aged 35 to 64 years in Eastern Finland

Year	Observed CHD mortality decline (%) *	Predicted CHD mortality decline (%) **				Proportion of the predicted CHD mortality decline from the observed mortality decline (%)
		Smoking alone	Systolic blood pressure alone	Serum cholesterol level alone	All three risk factors together	
Men						
1969-72 (baseline)	0	0	0	0	0	
1977	17	4.6 (0.5-8.8)	4.4 (0.3-8.6)	8.4 (4.2-12.5)	16.5 (12.3-20.7)	97
1982	25	8.3 (3.1-13.4)	2.5 (-2.7-7.6)	16.6 (11.5-21.8)	25.4 (20.3-30.6)	101
1987	38	9.1 (3.3-14.9)	4.7 (-1.1-10.5)	17.4 (11.6-23.2)	28.5 (22.7-34.3)	75
1992	55	11.7 (4.8-18.7)	9.4 (2.4-16.4)	26.4 (19.4-33.3)	41.3 (34.3-48.2)	75
1997	67	14.2 (7.3-21.0)	12.0 (5.2-18.9)	31.6 (24.7-38.4)	48.5 (41.7-55.4)	72
2002	75	11.7 (4.5-18.9)	14.2 (7.0-21.3)	34.0 (26.8-41.2)	50.2 (43.0-57.4)	67
2007	78	14.9 (6.9-22.9)	13.1 (5.2-21.1)	39.8 (31.8-47.8)	55.7 (47.7-63.7)	71
2012	82	16.9 (8.4-25.3)	15.9 (7.4-24.4)	37.8 (29.3-46.3)	56.8 (48.3-65.3)	69

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Women						
1969-72 (baseline)	0	0	0	0	0	
1977	28	-1.4 (-5.4-2.6)	15.5 (11.5-19.5)	10.9 (6.9-14.9)	23.7 (19.6-27.7)	85
1982	41	-5.3 (-10.5- -0.1)	15.4 (10.2-20.6)	19.3 (14.1-24.5)	28.1 (22.9-33.3)	68
1987	45	-6.4 (-12.0 - -0.9)	21.6 (16.0-27.2)	22.4 (16.-27.9)	35.5 (29.7-40.8)	79
1992	59	-11.0 (-17.7- -4.3)	27.5 (20.7-34.2)	31.3 (24.5-38.0)	44.7 (37.9-51.4)	76
1997	72	-7.0 (-13.6- -0.5)	30.6 (24.1-37.1)	31.4 (24.8-37.9)	49.0 (42.5-55.6)	68
2002	77	-12.2 (-19.0- -5.5)	31.6 (25.2-38.6)	35.9 (29.2-42.6)	51.5 (44.3-57.7)	67
2007	79	-11.7 (-19.3- -4.1)	31.3 (23.6-38.9)	39.4 (31.8-47.0)	53.5 (45.9-61.1)	68
2012	84	-8.8 (-16.7- -0.9)	35.7 (27.8-43.6)	36.6 (28.7-44.5)	55.7 (47.8-63.6)	66

*Five year means, **Predicted decline in CHD mortality based on risk factor changes during each five year period

Table 2. Cardiovascular risk factor levels among men and women aged 30 to 59 years in eastern Finland from 1972 to 2012

Year	Men			Women		
	Smoking (%)	Serum cholesterol (mmol/L)	Systolic blood pressure (mmHg)	Smoking (%)	Serum cholesterol (mmol/L)	Systolic blood pressure (mmHg)
1972	52.6 (51.2-54.1)	6.77 (6.73-6.81)	147.1 (146.5-147.7)	11.4 (10.5-12.3)	6.69 (6.65-6.72)	149.2 (148.5-149.9)
1979	46.6 (45.2-48.1)	6.52 (6.49-6.56)	144.2 (143.6-144.7)	12.7 (11.8-13.7)	6.34 (6.30-6.38)	141.6 (140.9-142.2)
1982	41.7 (39.6-43.8)	6.26 (6.21-6.31)	145.5 (144.7-146.3)	16.3 (14.7-17.9)	6.04 (5.98-6.09)	141.6 (140.7-142.5)
1987	40.5 (38.0-42.9)	6.23 (6.17-6.29)	144.0 (143.1-144.9)	17.3 (15.5-19.2)	5.92 (5.86-5.98)	138.1 (137.2-139.1)
1992	36.8 (33.7-39.8)	5.91 (5.84-5.98)	140.7 (139.5-141.8)	21.3 (18.8-23.8)	5.55 (5.48-5.61)	134.6 (133.3-135.9)
1997	33.3 (30.3-36.2)	5.70 (5.64-7.77)	138.8 (137.7-139.9)	17.9 (15.6-20.1)	5.54 (5.48-5.60)	132.6 (131.5-133.7)
2002	36.9 (33.7-40.0)	5.60 (5.53-5.68)	137.2 (136.0-138.4)	22.4 (19.8-24.9)	5.33 (5.28-5.39)	131.8 (130.5-133.09)
2007	32.2 (28.7-35.7)	5.35 (5.27-5.42)	138.0 (136.7-139.3)	21.9 (19.0-24.9)	5.16 (5.10-5.23)	132.2 (130.8-133.6)
2012	29.3 (25.6-32.9)	5.44 (5.35-5.52)	135.9 (134.5-137.2)	19.4 (16.5-22.3)	5.30 (5.23-5.37)	129.1 (127.9-130.4)

Figure 1: Age-standardised CHD mortality 1969-2012, men and women 35-64 years (per 100 000, logarithmic scale)

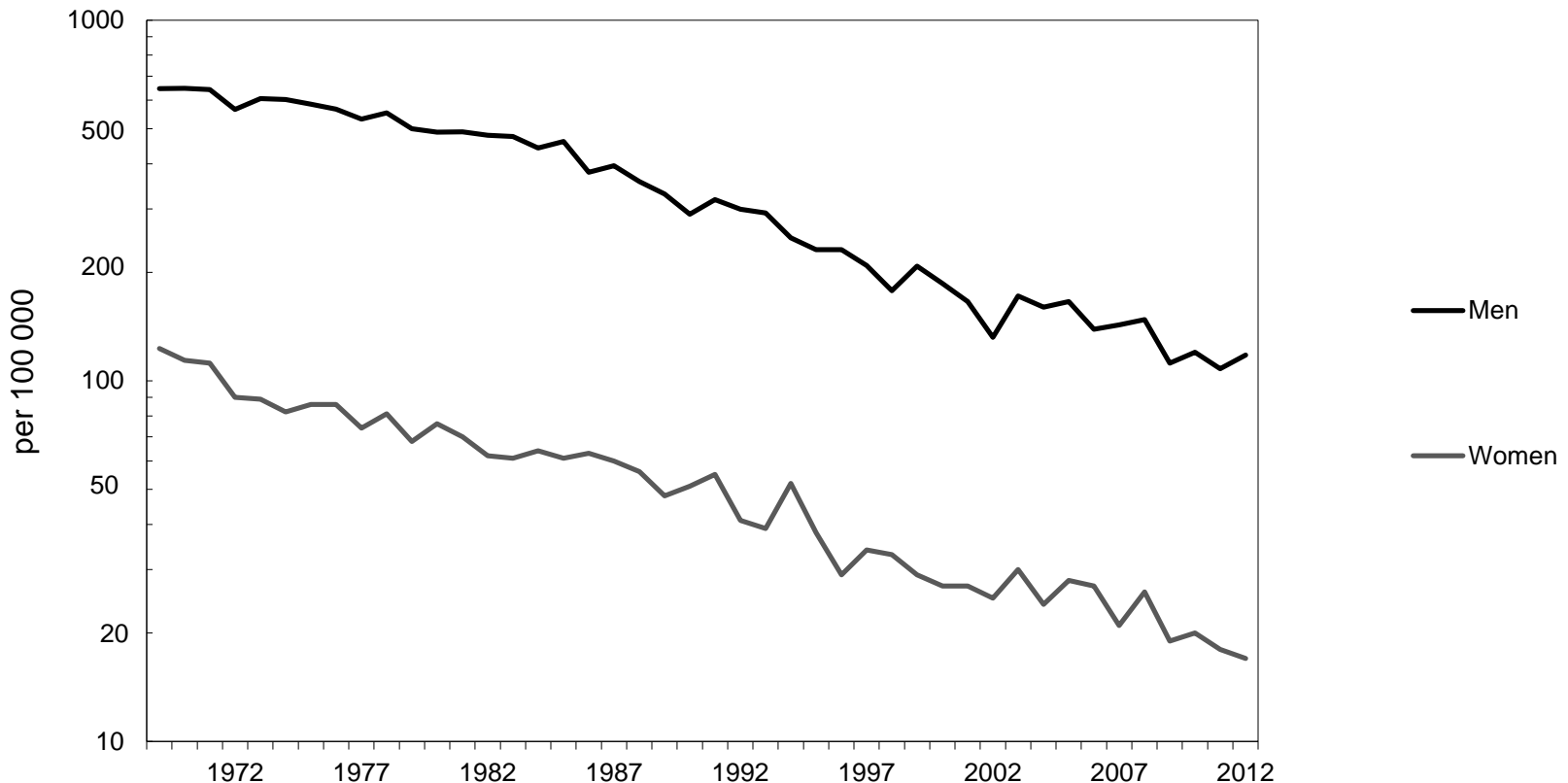


Figure 2: Predicted and observed reduction in CHD mortality 1972-2012, men 35-64 years

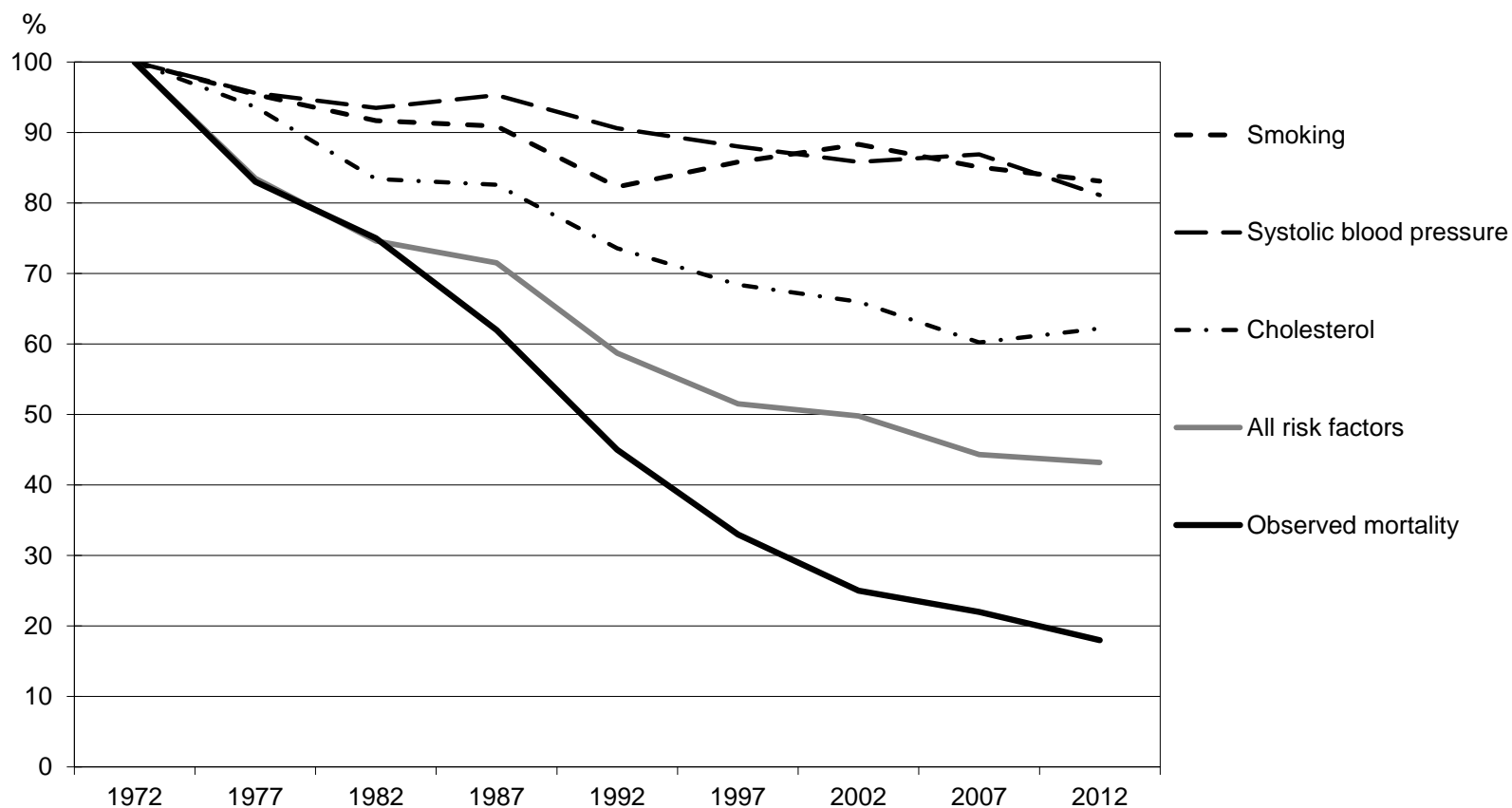


Figure 3: Predicted and observed reduction in CHD mortality 1972-2012, women 35-64 years

