

40-Year CHD Mortality Trends and the Role of Risk Factors in Mortality Decline

The North Karelia Project Experience



Pekka Jousilahti*, Tiina Laatikainen[†], Veikko Salomaa*, Arto Pietilä*, Erkki Vartiainen*, Pekka Puska*
Helsinki and Kuopio, Finland

ABSTRACT

In the 1960s and early 1970s, coronary heart disease (CHD) mortality in Finland was the highest in the world, and within Finland, mortality was particularly high in the eastern part of the country. The North Karelia Project, the first large community-based cardiovascular diseases prevention program was established in 1972 to reduce the extremely high CHD mortality through behavioral change and reduction of the main cardiovascular disease risk factors among the whole population of North Karelia, the easternmost province of Finland. During the 40-year period from 1972 to 2012, smoking prevalence, serum total cholesterol, and systolic blood pressure declined markedly, except a small increase in serum cholesterol levels between 2007 and 2012. From the early 1970s to 2012, CHD mortality decreased by 82% (from 643 to 118 per 100,000) among working-age (35 to 64 years) men. Among working-age women, the decline was 84% (from 114 to 17 per 100,000). During the first 10 years, changes in these 3 target risk factors explained nearly all of the observed mortality reduction. Since the mid-1980s, the observed reduction in mortality has been larger than the predicted reduction. In the early 1970s, premature CHD mortality (35 to 74 years) was about 37% higher among Eastern Finnish men and 23% higher among Eastern Finnish women, compared with men and women in Southwestern Finland. During the last 40 years, premature CHD mortality declined markedly in both areas, but the decline was larger in Eastern Finland and the mortality gap between the two areas nearly disappeared.

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. The CHD epidemic started in the United States in the 1930s and spread into the Western European countries after the Second World War [2]. Data on the causes of CHD started to accumulate in the 1940s and 1950s. Large epidemiological studies, such as the British Medical Doctors Study, the Framingham Heart Study, and the Seven Countries Study, identified a few behavioral and biological factors associated with the CHD risk, particularly tobacco smoking, high serum cholesterol, and high blood pressure [3–5]. Since then, their importance and causal relationship with the CHD risk 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, such as high intake of saturated fat and salt (sodium chloride), have been known already for decades [9,10].

CHD mortality started to increase in Finland in the 1950s and was associated with improving standard of living and changes in diet and other lifestyles. In the late 1960s, CHD

mortality in Finland was the highest in the world [2], and mortality was particularly high among the working-age men in the eastern part of the country. The North Karelia Project, the 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 working-age men by reducing the levels of the 3 main CVD 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 5 years [13].

Twenty years ago, we analyzed, for the first time, the role of primary prevention and risk factor changes in CHD mortality reduction among working-age (25 to 64 years) men and women in Eastern Finland [14]. We present the most recent analyses covering 4 decades from the early 1970s to 2012 [15]. Furthermore, we describe premature CHD mortality (ages 35 to 74 years) trends in Eastern and Southwestern Finland during the last 40 years.

STUDY POPULATION, DATA COLLECTION, AND ANALYSIS

The National FINRISK study consists of 9 independent population-based surveys conducted for the first time in 1972.

The authors report no relationships that could be construed as a conflict of interest.

From the *National Institute for Health and Welfare, Department of Health, Helsinki, Finland; and the †University of Eastern Finland, Kuopio, Finland. Correspondence: P. Jousilahti (pekka.jousilahti@thl.fi).

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Since then, the levels of behavioral and biological risk factors have been continuously monitored every 5 years and the last risk factor survey was conducted in 2012 [13]. In 1972 and 1977, the study covered 2 provinces in Eastern Finland, North Karelia and Kuopio. The Turku-Loimaa region in Southwestern Finland was included in the survey in 1982. Later on, in order to improve national representativeness, the study area was expanded also to the Helsinki-Vantaa region in Southern Finland and Oulu province in Northern Finland. 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 from 1913 to 1947. Since 1982, an age-, sex-, and study area–stratified random sample was taken from the population 25 to 64 years of age according to the World Health Organization (WHO) MONICA (Multinational Monitoring of Trends and Determinants in Cardiovascular Disease) project protocol [16].

In the first surveys, participation rate was high, over 90% but declined in the later surveys and was 64% in the last survey [13]. The analysis on the role of risk factor change on CHD mortality reduction in Eastern Finland includes 34,525 men and women ages 30 to 59 years (which was the common age range in all surveys) participating in the risk factor surveys between 1972 and 2012 in the North Karelia and Kuopio provinces and having complete data on all needed risk factors.

In each survey year, data collection included a self-administered questionnaire filled out at home, physical measurements at the study site done by trained study nurses, and blood samples for laboratory analyses. During the entire 40-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. Nonsmokers were those who had never smoked regularly, and those smokers who had stopped smoking at least 6 months before the survey. At the study site, blood pressure was measured from the right arm of the subject after a 5-min rest using mercury sphygmomanometers. 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]. Systematic measurement errors due to changes in laboratory methods and reagents in different study years have been corrected on the basis of the quality control analyses [13].

CHD mortality was predicted using a logistic regression model. Statistical methods are described in detail in our recent publication [15]. The model included the following risk factors: age, smoking status, serum total cholesterol, and systolic blood pressure. Average probability of CHD death for each 5-year period from 1972 to 2012 was calculated by including the mean level of the measured risk factors in the logistic regression functions. The predicted percentage change

in CHD mortality compared with the 1972 level was then calculated for each survey period.

Data on CHD mortality were obtained from the National Causes of Death Register through computerized register linkage by using the unique personal identification number assigned for every permanent resident of Finland. The following *International Classification of Diseases (ICD)* codes (8th to 10th revisions) were classified as CHD deaths: *ICD-8* and *ICD-9* 410 to 414, and *ICD-10* I20 to I25. Mortality rates were standardized for age in 5-year age groups using the baseline (1972) population structure as a standard population (analysis on the role of risk factors on CHD mortality decline in Eastern Finland) and European Standard population (CHD mortality trends in Eastern and Southwestern Finland).

Ethical approval has been obtained according to the commonly required research procedures and Finnish legislation during each survey. The 3 last surveys were approved by the Coordinating Ethics Committee of the Helsinki and Uusimaa Hospital District. From 1997 onward, written informed consent has been obtained from each participant. The study has been conducted according to the World Medical Association Declaration of Helsinki on ethical principles for medical research.

ROLE OF RISK FACTOR CHANGES IN CHD MORTALITY DECLINE AMONG WORKING-AGE POPULATION IN EASTERN FINLAND

During the 40-year period, from 1972 to 2012, the levels of all 3 risk factors declined markedly, except smoking among women (Table 1).

From the baseline level in the early 1970s to 2012, CHD mortality decreased from 643 to 118 per 100,000 among working-age (ages 35 to 64 years) men and from 114 to 17 per 100,000 among working-age women (Fig. 1). The decrease was 82% in men and 84% in women (Table 2).

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

TRENDS IN PREMATURE CHD MORTALITY IN EASTERN AND SOUTHWESTERN FINLAND

In the early 1970s, premature CHD mortality in Eastern Finland was about 37% higher in men and 23% higher in

TABLE 1. CVD risk factor levels among men and women in eastern Finland from 1972 to 2012

Year	Men			Women		
	Smoking (%)	Serum cholesterol (mmol/l)	Systolic blood pressure (mm Hg)	Smoking (%)	Serum cholesterol (mmol/l)	Systolic blood pressure (mm Hg)
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)

CVD, cardiovascular disease.

women, compared with the in southwestern part of the country. Figs. 4 and 5 show the age-adjusted CHD mortality among men and women ages 35 to 74 years in Eastern and Southwestern Finland from 1973 to 2013. During the 4 decades, premature CHD mortality declined markedly in both areas, but the decline was larger in Eastern Finland. In Eastern Finland, age-adjusted mortality reduced from 858 to 163 per 100,000 among men, and from 202 to 34 per 100,000 among women. In Southwestern Finland, the decline was from 585 to 135 and from 140 to 29 per 100,000, respectively. The average annual decline was 4.4% ($p < 0.001$) in men and 4.9% ($p < 0.001$) in women in Eastern Finland and 4.2% ($p < 0.001$) in men and 4.8% ($p < 0.001$) in women in Southwestern Finland. At the end of the survey period, differences in premature CHD mortality between Eastern and Southwestern Finland had nearly disappeared.

DISCUSSION

This and numerous other publications of the North Karelia Project have shown the great reductions in cardiovascular

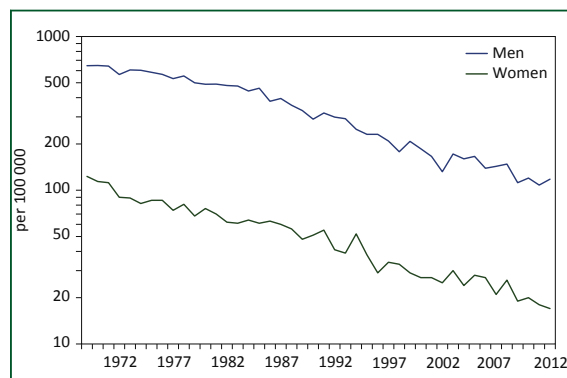
death rates in North Karelia since the start of the North Karelia Project in 1972, and later on also in other parts in Finland. The project was started to reduce the high rates of CVD by population-wide prevention, based on, at that time, relatively new scientific information on the likely causal risk factors: serum cholesterol; blood pressure; and smoking.

In the 1970s, reduction in risk factors explained practically all of the observed reduction in CHD mortality among the working-age population in Eastern Finland. 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 10 years, still about two-thirds. The remaining one-third of mortality reduction may be explained by 3 major groups of factors: 1) changes in other primary risk factors, which were not included in our analysis, such as diet and physical activity; 2) improvement in secondary prevention; and 3) improvement in the treatment of acute cardiac events. Furthermore, difference in premature CHD mortality

TABLE 2. Observed and predicted mortality decline (%) among men and women in eastern Finland from 1972 to 2012

Year	Men		Women	
	Observed*	Predicted [†]	Observed*	Predicted [†]
1969 to 1972 (baseline)	0	0	0	0
1977	17	16.5 (12.3–20.7)	28	23.7 (19.6–27.7)
1982	25	25.4 (20.3–30.6)	41	28.1 (22.9–33.3)
1987	38	28.5 (22.7–34.39)	45	35.5 (29.7–40.8)
1992	55	41.3 (34.3–48.2)	59	44.7 (37.9–51.4)
1997	67	48.5 (41.7–55.4)	72	49.0 (42.5–55.6)
2002	75	50.2 (43.0–57.4)	77	51.5 (44.3–57.7)
2007	78	55.7 (47.7–63.7)	79	53.5 (45.9–61.1)
2012	82	56.8 (48.3–65.3)	84	55.7 (47.8–63.6)

*5-year means.
[†]Predicted decline in coronary heart disease mortality based on risk factor changes during each 5-year period.

**FIGURE 1.** Age-standardized CHD mortality from 1969 to 2012 in Eastern Finland, men and women 35 to 64 years (per 100,000, logarithmic scale). CHD, coronary heart disease.

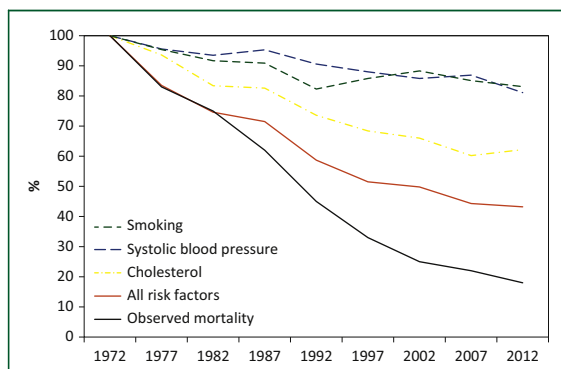


FIGURE 2. Predicted and observed reduction in CHD mortality from 1972 to 2012 in Eastern Finland, men 35 to 64 years. CHD, coronary heart disease.

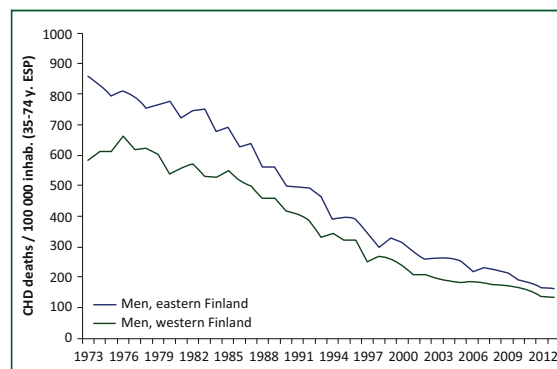


FIGURE 4. Age-standardized CHD mortality from 1973 to 2013 in Eastern and Southwestern Finland, men 35 to 74 years. CHD, coronary heart disease.

between Eastern and Southwestern Finland nearly disappeared during the 4 decades.

In addition to the 3 classical risk factors, a few other factors, such as physical inactivity, obesity, and elevated blood glucose, and diabetes as their consequence, have been identified as major causes for CHD [18,19]. The role of alcohol consumption in CHD risk is controversial; very modest drinking may reduce the risk, but heavy and binge drinking are most likely harmful [20]. Physical inactivity and obesity were not particularly common in Eastern Finland in the 1970s, but they have become evident health problems later on. Physical activity in work and travel to and from work has decreased, whereas leisure time physical activity has continuously increased during the last decades [21]. Mean body mass index and prevalence of obesity started to increase in the late 1970s, but the increase levelled off during the last 5 years [13]. Including body mass index in the predictive model did not affect the results markedly, most probably because the effect of obesity on CHD risk is largely mediated through its effect on blood pressure.

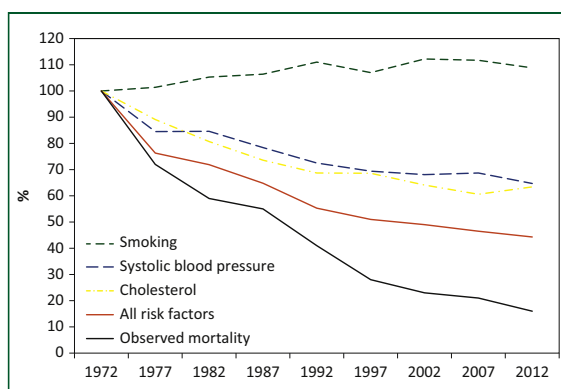


FIGURE 3. Predicted and observed reduction in CHD mortality from 1972 to 2012 in Eastern Finland, women 35 to 64 years. CHD, coronary heart disease.

Since the mid-1980s, with the development of secondary prevention and treatment practices, their impact on mortality reduction has grown. In the 1980s, new secondary prevention guidelines were introduced including active drug treatment with aspirin, beta-blockers, angiotensin-converting enzyme inhibitors, and, later, statins [22]. Invasive cardiology grew in the 1980s and percutaneous coronary interventions were introduced in the early 1990s. The number of percutaneous coronary interventions procedures rose 5-fold in 10 years between 1994 and 2004. Accordingly, case fatality of acute CHD events were reduced by one-third between 1994 and 2004 and the decline has continued [23,24]. Our findings are also in line with the earlier IMPACT model analysis on the roles of primary and secondary prevention and treatment of acute events on CHD mortality decline in Finland [25].

The results also show that the reduction in serum cholesterol level seems to explain major part of the decline. This together with the decline in blood pressure indicates that the general dietary changes were of overwhelming importance in the mortality decline. For serum cholesterol, the impact of drug treatment during this period was still marginal, and for blood pressure, the reduction in salt was important, in addition to drug treatment.

The difference in CHD mortality between Eastern and Southwestern Finland was recognized for the first time in the 1940s [26]. In our analysis on the premature CHD mortality trends, mortality in Eastern Finland was about one-third higher in men and one-quarter higher in women, compared with southwestern Finland. During the 4 decades, the mortality gap between the 2 areas practically disappeared. Because we do not have comparable risk factor data from both areas during the whole period, we cannot analyze the effect of risk factor change on CHD mortality change in southwestern Finland directly. When southwestern Finland was included in the Finnish risk factor monitoring system, the levels of main risk factors were higher in Eastern Finland, except female smoking,

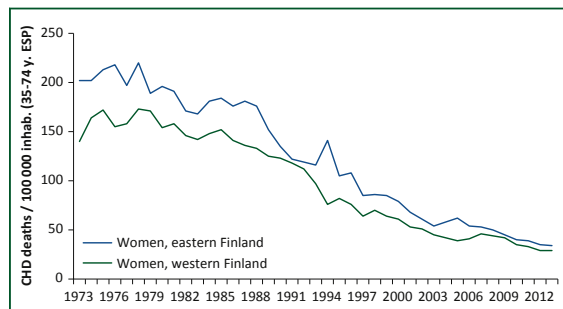


FIGURE 5. Age-standardized CHD mortality from 1973 to 2013 in Eastern and Southwestern Finland, women 35 to 74 years. CHD, coronary heart disease.

compared with in Southwestern Finland [13]. Since then, the levels of risk factors have declined in both areas.

Family history of CHD and a number of genetic markers are associated with CHD risk, but the role of hereditary factors in the prevention of CHD is still largely open [27]. Because genetic factors of a fairly stable population do not change much during 40 years, they cannot explain the dramatic decrease in CHD mortality in Eastern Finland. However, genetic factors may have a role in the CHD mortality difference between Eastern and Southwestern Finland. Recent genetic research has shown that the genetic backgrounds of the populations of Eastern and Southwestern Finland are markedly different [28]. We have also shown before that the parental history of premature CHD, a surrogate marker of genetic risk, is an independent risk factor for myocardial infarction, and also explains part of the disease's risk difference between Eastern and Southwestern Finland [29,30].

The main strength of our study is the long and systematic population-based risk factor monitoring using the same standardized protocol over 4 decades in Eastern Finland and practically complete mortality data. Unfortunately, we do not have comparable risk factor data from Southwestern Finland from the same period. A limitation is the decreasing participation rate and possible measurement error in risk factor surveys. Even though the 60% participation rate in large health examination surveys is still fairly good in international comparison, we know that the risk factor levels among nonparticipants are somewhat higher than among the participants [31]. Therefore, our model may overestimate the importance of the risk factor change in the last couple of decades. On the other hand, our predictive model is 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 consequently underestimates the importance of risk factor change in CHD mortality reduction [32]. Because we assessed the smoking status only at the baseline, and we were not able to update it during the follow-up, our model

most probably underestimated the role of smoking in the CHD mortality decline [33].

SUMMARY

In conclusion, even though secondary prevention and treatment protocols have markedly developed in the last decades, primary prevention and reduction of the levels of main classical CVD risk factors should still be considered as the main strategy to reduce disease burden and mortality due to CHD. This is the most cost-effective and sustainable approach to improving national heart health—and is also in accordance with the current WHO noncommunicable disease action plan [34]. An additional mortality reduction can be achieved by secondary prevention and by improved treatment of acute cardiac events.

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