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Modelling the decreasing coronary heart disease mortality in Sweden between 1986 and 2002

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Aims Coronary heart disease (CHD) mortality rates have been falling in Sweden since the 1980s. We used the previously validated IMPACT CHD model to examine how much of the mortality decrease in Sweden between 1986 and 2002 could be attributed to medical and surgical treatments, and how much to changes in cardiovascular risk factors.

Methods and results The IMPACT mortality model was used to combine and analyse data on uptake and effectiveness of cardiological treatments and risk factor trends in Sweden. The main data sources were official statistics, national quality of care registers, published trials and meta-analyses, and national population surveys. Between 1986 and 2002, CHD mortality rates in Sweden decreased by 53.4% in men and 52.0% in women aged 25–84 years. This resulted in 13 180 fewer deaths in 2002. Approximately 36% of this decrease was attributed to treatments in individuals and 55% to population risk factor reductions. Adverse trends were seen for diabetes and overweight.

Conclusion More than half of the substantial CHD mortality decrease in Sweden between 1986 and 2002 was attributable to reductions in major risk factors, mainly a large decrease in total serum cholesterol. These findings emphasize the value of a comprehensive strategy that promotes primary prevention and evidence-based medical treatments, especially secondary prevention.

Keywords Coronary disease • Mortality • Risk factors • Treatment • Registries • Sweden

Introduction

During the last few decades, there has been a decrease in coronary heart disease (CHD) mortality in Sweden similar to that in several other western high-income countries.[1] However, CHD remains the most common cause of death in Sweden and other western regions.[2–4]

The decreasing trends in CHD mortality can be partly explained by the changes in major cardiovascular risk factors including total cholesterol, smoking, and blood pressure levels. These favourable changes have, however, been offset by increasing overweight and obesity.[5–9] In addition, the uptake of medical and surgical treatments has been rapid, with increasing use of effective therapies, such as thrombolysis, β-blockers, aspirin, ACE-inhibitors, statins, percutaneous coronary intervention (PCI), and coronary artery bypass surgery (CABG).[10,11]

Because CHD remains the single largest cause of death in Western populations, researchers have used models of various degrees of complexity to try to explain the observed decline in CHD mortality. Combining data on major risk factors in the population (cholesterol, blood pressure, smoking, diabetes, obesity, and physical inactivity) with data on medical treatment and interventions has been used in epidemiological models to simplify and help explain a complex reality.[12] The majority of the models consistently suggest that risk factor improvements explain more of the mortality decline than treatments, ranging from 44% in the USA to 72% in Finland.[13–19]

Sweden has a long-standing tradition of administrative registries, a public health system with national coverage, and individual Personal Identification Numbers (PIN) codes for all citizens. Using the PIN code, the Hospital Discharge Register and national quality registries can be linked to cause-specific mortality data. In

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addition, national and local cardiovascular population surveys provide high-quality epidemiology data, suitable for advanced model-building in explaining trends in CHD mortality. In the present investigation, we used these data to examine how much of the large Swedish CHD mortality decrease between 1986 and 2002 could be attributed to 'evidence-based' medical and surgical treatments, and how much could be explained by changes in major cardiovascular risk factors.

Methods

Mortality model

To investigate how changes in risk factors and medical treatments have affected the decreasing mortality rates in CHD among Swedish men and women 25–84 years of age, we used an updated version of the IMPACT mortality model. This model, previously described in detail elsewhere[14,15,17,18,20] was further developed and refined for Sweden. The model includes the major population risk factors: smoking, total cholesterol, systolic blood pressure, body mass index (BMI), diabetes, and physical inactivity (*Table 1*). It also includes a comprehensive coverage of all standard evidence-based medical and surgical treatments used for CHD (*Table 2*).

Data sources used to construct the Swedish model are shown in *Table 3* and use aggregated data from registers kept by the Official Statistics of Sweden and the National Board of Health and Welfare, Swedish Quality of Care Registers (RIKS-HIA, SCAAR), cardiovascular and other population studies (MONICA, INTERGENE Study, the Prospective Population Study of Women in Goteborg, the AMORIS Study). Effects of interventions were estimated from multicentre studies of cardiovascular interventions.

Data from other sources were used only in rare instances. When more than one data sources was available, we used the one we considered to be the most representative. For maximum representation, we pooled survey data from different parts of Sweden. Detailed information on the IMPACT model and data sources for the Swedish analyses are provided in the Supplementary material online, *Appendix, Tables S1–S10*, available at *European Heart Journal* online.

Deaths prevented or postponed in 2002

Total population and age distribution data for Sweden in 1986 and 2002 were obtained from the National Board of Health and Welfare. The number of CHD deaths by age and sex in 1986 and 2002 were obtained from the Cause of Death Register, administered by the National Board of Health and Welfare (Supplementary material online, *Appendix, Table S2*). We calculated the number of CHD deaths expected in 2002 if the CHD mortality rates in 1986 had persisted, by multiplying the age-specific mortality rates for 1986 by the population for each 10-year age stratum in the year 2002 (thus accounting for the increasing life expectancy of the population). Subtracting the number of deaths observed in 2002 from the number expected, then yielded the fall in the number of CHD deaths (prevented or postponed) in 2002, which the model needed to explain.

Mortality reductions attributable to Treatments

The prevalence of CHD by diagnosis [acute myocardial infarction (AMI) and unstable angina UAP] was obtained from the Swedish Hospital Discharge Register. Case-fatality rates, and the risk reduction due to treatment, all stratified by age, sex, and diagnosis, were calculated by linking to the Swedish Death Register (Supplementary material online, *Appendix, Tables S2–S6*). The number of deaths prevented or postponed by each intervention in each group of CHD patients in the year 2002 (*Table 2*) was calculated by multiplying the number of people in each diagnostic group by the proportion of those patients who received a particular treatment, by the case-fatality rate over 1 year, and by the relative reduction in 1-year case-fatality by the administered treatment.[14,18]

For example, in Sweden 2002, ~2755 men aged 55–64 were hospitalized with AMI (*Table 4*). Some 87% were prescribed aspirin, with an expected mortality reduction of 15%.[21] The expected age-specific 1-year case-fatality rate was ~4.9%. The number of deaths prevented or postponed for at least a year by the use of aspirin among men aged 55–64 were then calculated as:

$$2755 \times 0.87 \times 0.15 \times 0.049 = 18$$

Several adjustments were made to these basic analyses. While most of the therapeutic measures studied were not in use in 1986, this was not true for all treatments (e.g. CABG surgery for stable angina pectoris). In such cases, the number of deaths prevented or postponed as a result of the therapy as used in 1986 was calculated and subtracted from the figure for 2002, to calculate the net benefit.

In the Model, we only included those actually referred to CABG or PCI, therefore counted as 100% in *Table 2*. In the original IMPACT Model, PCI effectiveness was based on the earlier studies by Yusuf *et al.*,[22] Pocock *et al.*,[23] and Bucher *et al.*[24] indicating equivalence between PCI and CABG. These results are now outdated by more recent evidence from the large COURAGE trial,[25] and the newly published meta-analysis by Cecil *et al.*[26] Accordingly, we estimated the effectiveness of PCI in patients with stable angina to zero in the Swedish IMPACT Model.

We assumed that compliance, the proportion of treated patients actually taking therapeutically effective levels of medication, was 100% among hospital patients, 70% among symptomatic community patients, and 50% among asymptomatic community patients.[27,28] To avoid double counting of patients treated, we identified potential overlaps between different groups of patients and made appropriate adjustments (Supplementary material online, *Appendix, Table S10*). To address the potential effect on relative reduction in case-fatality rate for individual patients receiving multiple treatments, we used the Mant and Hicks cumulative relative benefit approach.[29–31]

Relative benefit=1 − [(1-relative reduction in case-fatality rate for treatment A) × (1 − relative reduction in case-fatality rate for treatment B) × ⋯ × (1 − relative reduction in case-fatality rate for treatment *N*).

Mortality reductions attributable to changes in risk factors

Two approaches were used to calculate the numbers of deaths prevented or postponed as a result of changes in risk factors. (i) We used a *regression approach* for systolic blood pressure, cholesterol, and BMI. The number of deaths prevented or postponed as a result of the change in the prevalence or mean of value for each of these risk factors (*Table 1*) was estimated as the product of three variables: the number of CHD deaths observed in 1986 (the base year), the subsequent reduction in that risk factor and the regression coefficient quantifying the change in mortality from CHD per unit of absolute change in the risk factor (Supplementary material online, *Appendix, Table S4*). For example, in 1986, there were 570 CHD deaths among 471 039 women aged 55–64 years of age. Between 1986 and 2002, the mean systolic blood pressure in this group decreased by 2.4 mmHg. The largest meta-analysis showed an estimated age- and

Table 1 **Deaths from coronary heart disease prevented or postponed as a result of changes in population risk factors in Sweden 1986–2002**

Risk factor[a]	Absolute level of risk factor[b]		Changes in risk factor		Beta regression coefficient for change in mortality rates	Relative risk	Deaths prevented or postponed					
							Number of deaths			Percent of total reduction		
	1986	2002	Absolute change	Relative change (%)			Best estimate[c]	Minimum estimate[c]	Maximum estimate[c]	Best estimate[c]	Minimum estimate[c]	Maximum estimate[c]
Total cholesterol, mmol/L	6.15 (6.14–6.16)[d]	5.51 (5.47–5.55)[d]	−0.64	−10.4			5210	4400	6390	39.5	33.4	48.5
Men					−0.633							
Women					−0.517							
Smoking prevalence, %	28.9 (27.5–30.3)[d]	18.6 (17.1–20.1)[d]	−10.3	−55.4			1195	955	2575	9.1	7.2	19.5
Men						2.52						
Women						2.14						
Systolic blood pressure, mmHg	133.8 (133.2–134.4)[d]	131.2 (130.6–131.9)[d]	−2.6	−1.9			900	740	1145	6.8	5.6	8.7
Men					−0.032							
Women					−0.040							
Physical inactivity, %	16.0 (14.8–16.8)[d]	11.5 (10.5–12.7)[d]	4.3	−27.3			790	75	1800	6.0	0.6	13.6
Men						1.27						
Women						1.33						
BMI, kg/m^2	24.3 (23.1–25.4)[d]	25.4 (23.8–27.0)[d]	+1.1	4.7			−265	−150	−415	−2.0	−1.1	−3.1
Men					0.065							
Women					0.062							
Diabetes prevalence, %	2.7 (2.2–3.2)[d]	3.8 (3.1–4.5)[d]	+1.1	40.7			−630	−325	−1005	−4.8	−2.5	−7.6
Men						2.66						
Women						3.53						
Total risk factors							7200	5695	10490	54.6	43.2	79.6

[a]Numbers of deaths prevented or postponed were rounded to nearest 0 or 5. Total adult (age 25–84) population in 1986 was 5 565 255.
[b]Sourced from Official Statistics of Sweden (smoking prevalence, physical inactivity, BMI and diabetes), the AMORIS Study (cholesterol 1986) and the MONICA Project (GOT and Northern Sweden), the Study of men born 1913, the Population Study of Women in Gothenburg, INTERGENE Study (blood pressure and cholesterol). Units are percent change in mortality rate per unit of risk factor as shown in column one. Additional details of data sources are described in the Supplementary material online, *Appendix*.
[c]Minimum estimate 0.8 of best estimate, maximum estimate 1.2 of best estimate.
[d]Figures in parentheses denote 95% CI.

Table 2 Estimated deaths prevented or postponed by medical or surgical treatments in Sweden in 2002

Treatments	Number of eligible patients	Patients receiving treatment (%)	Relative risk reduction (%)	Mean case-fatality (%)	Absolute risk reduction	Deaths prevented or postponed					
						No. of deaths			Percentage of total reduction		
						Best estimate[a]	Minimum estimate[a]	Maximum estimate[a]	Best estimate[a]	Minimum estimate[a]	Maximum estimate[a]
Acute myocardial infarction	20 955	—	—	0.117	—	745	470	1495	5.7	3.5	11.3[b]
Resuscitation in the community	3965	39	0.05	0.117	0.019	70	15	50	0.5	0.1	0.4
Resuscitation in the hospital	800	100	0.32	0.117	0.320	230	165	615	1.8	1.2	4.7
Thrombolysis	20 955	18	0.22	0.117	0.022	70	45	140	0.5	0.3	1.1
Aspirin	20 955	81	0.15	0.117	0.018	260	155	475	2.0	1.2	3.6
β-Blocker	20 955	85	0.04	0.117	0.005	75	45	145	0.6	0.3	1.1
ACE-inhibitor	20 955	51	0.07	0.117	0.008	80	65	100	0.6	0.5	0.8
Primary angioplasty	20 955	8	0.31	0.117	0.029	40	25	90	0.3	0.2	0.7
Primary CABG	20 955	0	0.20	0.117	0.023	0	0	5	0.0[c]	0.0[c]	0.1
Treatments in 1986 subtracted						−80	−45	−125	−0.6	−0.3	−1.0
Unstable angina	17 290			0.067		225	155	500	1.7[b]	1.2[b]	3.8[b]
Aspirin and heparin		56	0.33	0.067	0.021	165	120	325	1.2	1.0	2.6
Aspirin alone		35	0.15	0.067	0.010	45	20	140	0.4	0.2	1.2
Glycoprotein IIB/IIIA antagonists		10	0.09	0.067	0.006	5	5	10	0.1	0.1	0.1
CABG		1	0.43	0.067	0.027	0	0	5	0.0[c]	0.0[c]	0.0[c]
Angioplasty		4	0.32	0.067	0.020	10	10	20	0.1	0.1	0.2
Secondary-prevention after myocardial infarction	99 815			0.079		1175	640	3 010	8.9[b]	4.9	22.8
Aspirin		77	0.15	0.079	0.009	270	130	680	2.1	1.0	5.2
β-Blocker		56	0.23	0.079	0.018	330	195	840	2.5	1.5	6.4
ACE-inhibitor		37	0.20	0.079	0.018	220	105	545	1.7	0.8	4.1
Statin		49	0.22	0.079	0.017	245	135	585	1.9	1.0	4.4
Warfarin		7	0.22	0.079	0.017	40	25	110	0.3	0.2	0.8
Rehabilitation		18	0.26	0.079	0.018	70	50	250	0.5	0.4	1.9
Secondary-prevention after CABG or PCI	41 950			0.034		430	260	1065	3.3	2.0	8.1[b]
Aspirin		78	0.15	0.034	0.005	110	50	240	0.8	0.4	1.8
β-Blocker		66	0.23	0.034	0.007	90	40	295	0.7	0.3	2.2
ACE-inhibitor		43	0.20	0.034	0.007	60	60	90	0.5	0.4	0.7
Statin		58	0.22	0.034	0.009	105	60	260	0.8	0.5	2.0

Continued

Table 2 *Continued*

Treatments	Number of eligible patients	Patients receiving treatment (%)	Relative risk reduction (%)	Mean case-fatality (%)	Absolute risk reduction	Deaths prevented or postponed					
						No. of deaths			Percentage of total reduction		
						Best estimate[a]	Minimum estimate[a]	Maximum estimate[a]	Best estimate[a]	Minimum estimate[a]	Maximum estimate[a]
Warfarin		8	0.22	0.034	0.005	10	5	30	0.1	0.0	0.2
Rehabilitation		37	0.26	0.034	0.008	55	45	150	0.4	0.4	1.1
Treatments in secondary-prevention 1986 subtracted						−10	−5	−20			
Chronic angina	132 215					535	435	1045	4.0	3.3	7.9
CABG 1994 to 2002	76 790	100	0.22	0.036	0.007	390	365	775	2.9	2.8	5.9
With CABG in 1986 subtracted						−35	−25	−55	−0.3	−0.2	−0.4
Angioplasty, 1994–2002	23 740	100	0	0.060	0	0	0	0	0	0	0
Aspirin in the community	158 530	27	0.15	0.012	0.002	40	30	60	0.3	0.2	0.4
Statins in the community	158 530	74	0.22	0.012	0.003	140	65	265	1.1	0.5	2.0
Heart failure with hospital admission	7030			0.209		365	190	805	2.8	1.5	6.1
ACE-inhibitor		48	0.20	0.209	0.049	100	50	240	0.8	0.4	1.8
β-Blocker		39	0.35	0.209	0.073	115	55	290	0.9	0.4	2.2
Spironolactone		10	0.30	0.209	0.063	25	15	65	0.2	0.1	0.5
Aspirin		51	0.15	0.209	0.029	70	30	125	0.5	0.3	1.0
Statins		35	0.22	0.209	0.016	55	40	85	0.4	0.3	0.6
Heart failure in the community	46 095			0.061		550	390	885	4.1[b]	2.9	6.7[b]
ACE-inhibitor		48	0.20	0.061	0.009	120	95	145	0.9	0.7	1.1
β-Blocker		49	0.35	0.061	0.021	210	175	265	1.6	1.3	2.0
Spironolactone		10	0.30	0.061	0.019	25	20	40	0.2	0.2	0.3
Aspirin		51	0.15	0.061	0.009	130	70	350	1.0	0.5	2.6
Statin		35	0.22	0.061	0.014	65	30	85	0.5	0.2	0.6
Hypertension treatments	1 488 900	59	0.13	0.010	0.001	575	245	955	4.4	1.8	7.3
Statins for lipid reduction (primary-prevention)	3 922 480	6	0.30	0.007	0.001	200	70	550	1.5	0.5	4.2
Total treatments						4790	2850	10 290	36.3[b]	21.6	78.2

Numbers of eligible patients and category totals of deaths prevented or postponed were rounded to nearest 0 or 5, totals may therefore not always sum exactly.
ACE, angiotensin-converting enzyme; AMI, acute myocardial infarction; CABG, coronary artery bypass graft surgery; CPR, cardiopulmonary resuscitation; GP, glycoprotein; PCI, percutaneous coronary intervention (with or without stent); UAP, unstable angina. Additional details of data sources are described in the Supplementary material online, *Appendix*.
[a]Minimum estimate 0.8 of best estimate, maximum estimate 1.2 of best estimate.
[b]Subject to rounding error.
[c]CABG < 0.0.

Table 3 Main Data Sources for the Parameters Used in the Swedish IMPACT Model 1986 and 2002 (For detailed information see Supplementary material online, *Appendix*)

	1986	2002
Population, deaths, CHD Mortality	The National Board of Health and Welfare	The National Board of Health and Welfare
Number of patients admitted yearly: MI, AP, HF	The Hospital Discharge Register	The Hospital Discharge Register
Number of patients treated with		
CABG	The Hospital Discharge Register	Swedish Quality Registry for General Thoracic Surgery, the Hospital Discharge Register
PCI	The Hospital Discharge Register	The Hospital Discharge Register, SCAAR.
Cardiopulmonary resuscitation in the community	Assume zero	Swedish Cardiac Arrest Registry
AMI, UAP	Assume zero	RIKS-HIA
Secondary-prevention following AMI	Assume zero	EUROASPIRE,[40] RIKS-HIA
Secondary-prevention following CABG or PCI	Assume zero	EUROASPIRE[40]
Congestive heart failure	Assume zero	IMPROVEMENT[41], OBS-CHF[41]
Treatment for chronic angina	Assume zero	EUROASPIRE[40]
Community angina pectoris: total	MONICA Got and Northern Sweden	INTERGENE Study 2001–2004
Community Chronic heart failure		
Prevalence	Assume same 1986 as 2002[42]	The Hospital Discharge Register 2003
Medication (ACE-inhibitors, β-blockers, Spironolactone)	Assume zero	IMPROVEMENT[43]
Medication (aspirin, statins)	Assume zero	OBS-CHF[41]
Hypertension		
Prevalence	MONICA GOT and Northern Sweden	INTERGENE Study
Treated (%)	MONICA GOT and Northern Sweden	INTERGENE Study and MONICA Northern Sweden
Statins for primary-prevention		INTERGENE Study
Population risk factor prevalence		
Current smoking, Physical activity, Obesity (BMI), Diabetes	ULF, the Official Statistics of Sweden	ULF, the Official Statistics of Sweden
Systolic blood pressure	MONICA GOT and Northern Sweden	MONICA Northern Sweden and INTERGENE Study, the Prospective Population Study of Women in Goteborg.
Cholesterol	The AMORIS Study[9]	MONICA GOT and Northern Sweden, INTERGENE Study

sex-specific reduction in mortality of 50% for every 20 mmHg reduction in systolic blood pressure, generating a logarithmic coefficient of -0.035.[32] The number of deaths prevented or postponed as a result of this change was then estimated as:

$$\begin{aligned}\text{Number of deaths} &= [1 - \exp(\text{coefficient} \times \text{change})] \\ &\quad \times \text{deaths in1986} \\ &= [1 - \exp(-0.035 \times 2.4)] \times 570 = 46.\end{aligned}$$

(ii) A *population-attributable risk fraction approach* was used to determine the impact of changing prevalence of smoking, diabetes, and physical inactivity. The population-attributable risk fraction was calculated conventionally as $[P \times (\text{RR-1})]/[1 + P \times (\text{RR} - 1)]$, where P is the prevalence of the risk factor (Supplementary material online, *Appendix, Table S4*) and RR is the relative risk for CHD mortality associated with that risk factor (Supplementary material online, *Appendix, Table S8*). The number of deaths prevented or postponed was then estimated as the number of deaths from CHD in 1986 (the base year) multiplied by the difference between the population-attributable risk fraction in 1986 and that in 2002 (*Table 1*).

For example, the prevalence of diabetes in men aged 65–74 years increased from 6.1% in 1986 to 9.5% in 2002. Given a relative risk of 1.93, the population-attributable risk fraction increased from 0.054 to 0.081. Additional deaths in 2002 attributable to an increased prevalence of diabetes were therefore calculated as follows:[14,15,20,32]

$$\begin{aligned}&\text{Deaths from coronary heart disease in 1986} \\ &= 4790 \times (0.081 - 0.054) = 129.\end{aligned}$$

Because independent regression coefficients and relative risks for each risk factor were taken from multivariate analyses, we assumed that there was no further synergy between the treatment and risk factor sections of the model or among the major risk factors.

The numbers of deaths prevented or postponed as a result of risk factor changes were systematically quantified for each specific patient group to account for potential differences in effect. Lag times between the changes in the risk factor rate and event rate were not

Table 4 Example of a multi-way sensitivity analysis for men*

	Patient numbers[†] *a*	Treatment uptake[‡] *b*	Relative mortality reduction[§] *c* (%)	1 year case-fatality[†] *d* (%)	Deaths prevented or postponed ($a \times b \times c \times d$)
Best estimate	2755	0.87	15	4.9	18
Minimum estimate	2205	0.70	11	3.9	7
Maximum estimate	3305	0.99	19	5.9	37

*In Sweden in 2002, about 2755 men aged 55–64 was hospitalized with AMI, of whom approximately 87% were given aspirin. Aspirin use reduces case-fatality rate by ~15%. The underlying 1-year case-fatality rate in these men was approximately 4.9%. The calculated number of deaths prevented or postponed was ~18. A multi-way sensitivity analysis was then performed. Lower and upper bounds for each parameter were estimated using either 95% CIs where available or, failing that, using calculated bounds of plus or minus 20% (treatment uptake however was capped at 99%). Multiplying all lower-bound estimates together yielded the lower-bound estimate of deaths prevented or postponed, and multiplying all upper-bound estimates together yielded the upper-bound estimate of deaths prevented or postponed.
[†]Hospital Discharge Register Centre for Epidemiology (the EPC), the National Board of Health and Welfare.
[‡]The Register of Information and Knowledge about Swedish Heart Intensive Care Admissions (RIKS-HIA), 2002.
[§]Antithrombotic Trialists' Coalition (2002). Lower and upper 95% CI from Antithrombotic Trialists' Collaboration. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. *BMJ* 2002;**324:**71–86.

modelled; it was assumed that these lag times would be relatively unimportant over a period of two decades.[18,33,34]

Comparison of estimated with observed mortality changes

The model estimates for the total number of deaths prevented or postponed by each treatment and for each risk factor change were rounded to the nearest multiple of five deaths (e.g. 696 became 695). All of these figures were then summed and compared with the observed changes in mortality for men and women in each age group. Any shortfall in the overall model estimate was then presumed to be attributable either to inaccuracies in our model estimates or to other, unmeasured risk factors.[14,16,18,32]

Sensitivity analyses

All the above assumptions and variables were tested in a multi-way sensitivity analysis using the analysis of extremes method.[14,19,32] For each variable in the model, we assigned a lower value and an upper value, using 95% confidence intervals (CIs) when available and otherwise using ±20% (for the number of patients, use of treatment, and compliance). For example, for aspirin treatment in men aged 55–64 years hospitalized with AMI, the best estimate was 18 deaths prevented or postponed. The minimum estimate from the multi-way sensitivity analysis was seven and maximum estimate was 37 (*Table 4*).

Methods for calculating 95% confidence interval for weighted mean

The CI estimation is based on the standard deviation of the samples and their size, which gives us the standard error (or variance) of the sample mean. Multiplying the standard error of the mean with the 1.96 provides an estimate of half of the 95% CI. When a weighted mean was used to give the mean for the whole population based on subsamples, the corresponding standard error was estimated accordingly as a weighted summation based on the standard errors of the subsamples. This procedure was used for data from AMORIS Study[9] and MONICA Study. Data from the ULF, the Official Statistics of Sweden, had the half 95% CI already estimated.

Results

Between 1986 and 2002, CHD mortality rates in Sweden decreased by 53.4% in men and 52.0% in women aged 25–84 years. The age-adjusted CHD rates per 100 000 population fell from 544.1 to 253.4 among men 25–84 years and from 291.5 to 140.0 among women aged 25–84 years. In 1986, there were 23 060 deaths among this age group recorded as due to CHDs, according to the *International Classification of Diseases*, 9th Revision (codes 410–414). In 2002, a total of 11 850 such deaths were recorded, according to the *International Classification of Diseases*, 10th Revision (codes I20–I25). Yet, had these death rates from 1986 persisted in 2002, another 11 210 deaths would have occurred, which translates to a total of 13 180 CHD deaths postponed or prevented, when taking the increasing numbers in the population into account. During the same period all-cause mortality per 100 000 declined from 1482.6 in 1986 to 1082.5 in 2002 in men and from 1018.6 to 832.4 in women. The proportion of deaths related to CHD decreased from 36.7% and 28.6% in 1986 to 23.4% and 16.8% 2002 in men and women, respectively.

Approximately 11 985 of the 13 180 decrease in number of deaths could be explained using the Swedish IMPACT model. The agreement between the estimated and observed mortality decreases for men and women in each age group was generally good. Overall, the model accounted for 90.9% of the total mortality decrease in Sweden between 1986 and 2002. The remaining 9.1% was attributed to changes in other, unmeasured factors.

Figure 1 shows comparison of model estimated and observed reductions in deaths from CHD in Sweden between 1986 and 2002, stratified by age and sex.

Major cardiovascular risk factors

Changes in the major cardiovascular risk factors together account for ~7200 fewer deaths (minimum estimate, 5695; maximum, 10 490) (*Table 1*). This corresponds to some 55% of the total mortality decrease between 1986 and 2002.

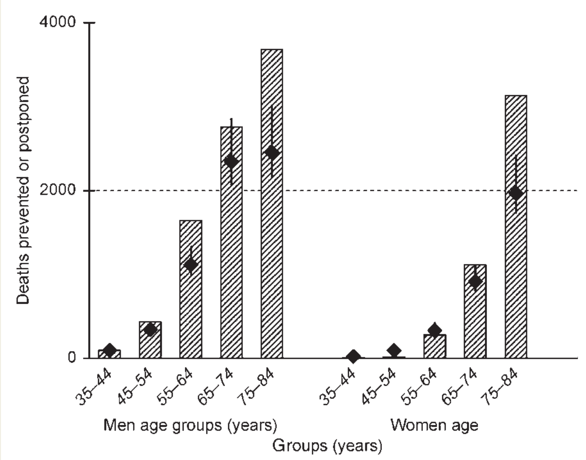

Figure 1 Comparison of Model Estimated and Observed Reductions in Deaths from CHD in Sweden between 1986 and 2002, Stratified by Age and Sex The bars show the observed deaths in each age group, with diamonds being the best-model estimate, and vertical lines the extreme minimum and maximum estimates in the sensitivity analysis.

The largest reduction in deaths was explained by substantial reductions in total cholesterol levels, from 6.15 mmol/L in 1986 to 5.51 mmol/L in 2002, a total net effect decrease of 0.64 mmol/L, or 10.4%; explaining ∼39% of the mortality reduction. This was followed by 1195 fewer deaths attributable to decreased smoking prevalence (from 28.9% in 1986 to 18.6% in 2002) and 900 fewer deaths attributable to a decrease in blood pressure by 2.6 mmHg. There was also a decrease in physical inactivity with trends towards more organized exercise and higher activity level, especially in older people (*Table 1*).

Adverse trends were seen with respect to the proportion of population who were overweight or obese, with increasing mean BMI from 24.3 to 25.4. The prevalence in diabetes increased from 2.7% to 3.8% from 1986 to 2002. In total, these adverse trends in overweight and diabetes generated ∼895 additional CHD deaths (*Table 1*).

Medical and surgical treatments

Medical and surgical treatments together prevented or postponed ∼4790 deaths (minimum estimate, 2850; maximum estimate, 10 290) (*Table 2*) related to CHD. These effects together explained ∼36.3% of the mortality reduction. The largest reduction came from the use of secondary-prevention medications or rehabilitation after AMI (8.9%). The mortality decreases attributable to hospital and community treatments for heart failure and initial treatment for AMI and UAP were about the same size (6.9% and 7.4%, respectively). For AMI, ∼745 deaths were prevented or postponed by immediate treatments; the largest contributions came from aspirin, cardiopulmonary resuscitation, ACE-inhibitors, β-blockers, and thrombolysis. Smaller proportions were explained by treatment for hypertension (4.4%) and chronic angina (4.0%). Revascularization for chronic angina and statins for primary-prevention contributed relatively small reductions, 2.6% and 1.5%, respectively. Coronary artery bypass surgery and angioplasty in connection with AMI or UAP accounted for ∼1% of deaths prevented or postponed (*Table 2*).

Proportional contributions to the decrease in deaths

Figure 2 demonstrates the results of the sensitivity analysis. The proportional contributions of specific treatments and risk factor changes to the overall decrease in CHD mortality in Sweden between 1986 and 2002 remained relatively consistent. Thus, all initial treatments for AMI and UAP together accounted for ∼970 fewer deaths, representing 7.4% of the total decrease of 11 985 deaths. The minimum estimated contribution was 625 fewer deaths (4.7%), and the maximum was 1995 (15.1%) (*Table 2*). The contribution of treatment for AMI and UAP was consistently smaller than that for secondary-prevention treatments irrespectively of whether best, minimum or maximum estimates were compared.

Discussion

CHD mortality rates in Sweden declined by more than half between 1986 and 2002. The largest contributor to the decrease was the reduction in major risk factors, accounting for ∼7200 fewer deaths (out of 13 180), primarily a large (0.64 mmol/L) decrease in total cholesterol. The substantial reduction in population total cholesterol level from 6.15 to 5.51 mmol/L, from 1986 to 2002, explained almost 40% of the decrease in CHD mortality. Most of these large cholesterol decrease are probably attributable to changes in diet.[5] Almost 10% of the mortality reduction came from a decline in smoking prevalence.

However, adverse trends were also seen. There were divergent data for physical activity with trends towards more organized exercise and higher activity level in older people (∼27%) but less regular daily activity.[5] Furthermore, the BMI, from 24.3 to 25.4 and increase in diabetes prevalence from 2.7 to 3.8% accounted for ∼900 extra deaths in 2002. Half of all men over 45 years in Sweden are currently overweight or obese, with increasing rates amongst the youngest. This means that the full effect of this increase in body weight on CHD mortality rates will not yet be fully realized.

Previous studies using the IMPACT methodology have all consistently shown a greater contribution from reduction in population risk factor levels than from treatments.[15,17,19] Sweden has a slightly different risk factor pattern with lower smoking rates but instead a fairly extensive use of moist snuff, as well as a comparatively low prevalence of diabetes and obesity. In contrast, there were marked reductions in mean levels of serum cholesterol. These differences offer an opportunity to investigate how decreasing serum cholesterol in a community with low and decreasing smoking rates might influence future CHD mortality rates.

Cardiology treatments developed rapidly during the period of study (1986–2002). Approximately 36% of the Swedish mortality decrease was attributable to the combined effects of modern

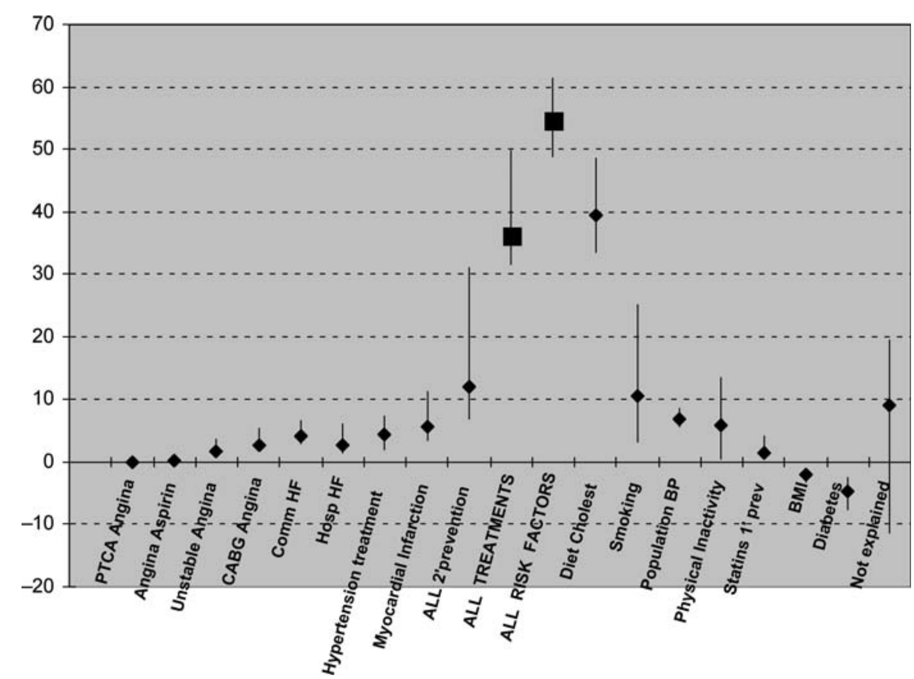

Figure 2 The proportional contributions of specific treatments and risk factor changes to the overall decrease in CHD mortality in Sweden between 1986 and 2002. The bars show the observed deaths in each age group, with diamonds being the best-model estimate, and vertical lines the extreme minimum and maximum estimates in the sensitivity analysis.

cardiological treatments. Thrombolysis accounted for only a small proportion of the deaths prevented by initial treatments for AMI, compared with aspirin and cardiopulmonary resuscitation. Revascularization from CABG surgery and angioplasty for AMI and UAP together accounted for $<1\%$ of the reduction in mortality, vs. 5% in the US model.[16] This comparatively low contribution could partly reflect the lower rates of angioplasty in acute coronary syndromes in Sweden, compared with other industrialized countries (www.heartstats.org). Moreover, the meta-analysis used in the US model relates to earlier studies of CABG before the efficacy of medical treatments was recognized. Therefore, it is likely to be an overestimation of potential benefits even if allowing for better surgical techniques. In addition, the MASS-II study, which compared medical therapy for multivessel CAD with PCI and CABG showed no difference in death rates between the groups, implying that the lowest possible effect of CABG could potentially be zero.[35] Heart failure treatment in the community accounted for a slightly higher number of deaths prevented or postponed compared with hospital treatment for heart failure.

Irrespective of whether best minimum or maximum estimates were used, the largest contribution from medical treatment came from secondary prevention. The foremost medications being β-blockers and aspirin followed by statins and ACE-inhibitors.

Modelling studies have a number of potential strengths. The best models can transparently integrate and simultaneously consider huge amounts of data from many sources. Explicit assumptions can then be tested by sensitivity analyses.[18] However, modelling studies also have limitations. In the present study, ~10% of the decreased mortality remains unexplained, which could be due to factors not included in the model. For example, the IMPACT model does not include data on socioeconomic status. Since low socioeconomic status is an independent risk factor for CHD in men and women, socioeconomic changes could be a contributory cause to the observed decrease in CHD mortality.[36,37] Further, models are dependent on the variable extent and quality of data available on CHD risk factor trends and treatment uptakes. Even so, population data and hospital discharge registries in Sweden are particularly good and cover almost 100%. Data from RIKS-HIA cover more than 90% of Swedish hospitals. Since Sweden has almost no private hospitals and no private CCU, the data probably reflect the majority of the Swedish population. This, together with a long tradition of upholding registries and national population surveys, should minimize the problem of making assumptions on less reliable data.

The Model included only those aged 25–84 years because of very limited data in older groups. In addition, the model fit was poorer in the youngest and oldest aged women, explaining less of the observed decrease in CHD mortality in these age groups compared with men. Elderly patients and women have been shown to be under-represented in many clinical trials and surveys in cardiovascular heart disease.[38] We also assumed that effectiveness in the population equalled efficacy in randomized trials. Our treatment benefits may therefore be slightly overestimated. The lower agreement of observed with expected deaths in women is partly due to less data but perhaps also because women develop coronary artery disease later than men.[39] This highlights the need for future work with respect to gender differences and differences between younger and older ages.

In conclusion, more than half of the recent substantial CHD mortality decrease in Sweden was attributable to population reductions in major risk factors, chiefly serum cholesterol, with some 36% attributable to medical therapies. All ages up to 84 were included and the results are thus likely to be applicable to the entire Swedish population. Comprehensive strategies to reduce CHD should therefore actively promote primary prevention as well as maximizing the population coverage of effective treatments.

Supplementary material

Supplementary material is available at *European Heart Journal* online.

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