SPECIAL ARTICLE

Explaining the Decrease in U.S. Deaths from Coronary Disease, 1980–2000

Earl S. Ford, M.D., M.P.H., Umed A. Ajani, M.B., B.S., M.P.H., Janet B. Croft, Ph.D., Julia A. Critchley, D.Phil., M.Sc., Darwin R. Labarthe, M.D., M.P.H., Ph.D., Thomas E. Kottke, M.D., Wayne H. Giles, M.D., M.S., and Simon Capewell, M.D.

ABSTRACT

BACKGROUND

Mortality from coronary heart disease in the United States has decreased substantially in recent decades. We conducted a study to determine how much of this decrease could be explained by the use of medical and surgical treatments as opposed to changes in cardiovascular risk factors.

METHODS

We applied a previously validated statistical model, IMPACT, to data on the use and effectiveness of specific cardiac treatments and on changes in risk factors between 1980 and 2000 among U.S. adults 25 to 84 years old. The difference between the observed and expected number of deaths from coronary heart disease in 2000 was distributed among the treatments and risk factors included in the analyses.

RESULTS

From 1980 through 2000, the age-adjusted death rate for coronary heart disease fell from 542.9 to 266.8 deaths per 100,000 population among men and from 263.3 to 134.4 deaths per 100,000 population among women, resulting in 341,745 fewer deaths from coronary heart disease in 2000. Approximately 47% of this decrease was attributed to treatments, including secondary preventive therapies after myocardial infarction or revascularization (11%), initial treatments for acute myocardial infarction or unstable angina (10%), treatments for heart failure (9%), revascularization for chronic angina (5%), and other therapies (12%). Approximately 44% was attributed to changes in risk factors, including reductions in total cholesterol (24%), systolic blood pressure (20%), smoking prevalence (12%), and physical inactivity (5%), although these reductions were partially offset by increases in the body-mass index and the prevalence of diabetes, which accounted for an increased number of deaths (8% and 10%, respectively).

CONCLUSIONS

Approximately half the decline in U.S. deaths from coronary heart disease from 1980 through 2000 may be attributable to reductions in major risk factors and approximately half to evidence-based medical therapies.

From the Division of Adult and Community Health (E.S.F., U.A.A., W.H.G.) and the Division for Heart Disease and Stroke Prevention (J.B.C., D.R.L.), National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta; the Institute of Health and Society, Newcastle University, Newcastle upon Tyne (J.A.C.), and the Division of Public Health, University of Liverpool, Liverpool (S.C.) — both in the United Kingdom; and HealthPartners Research Foundation, Minneapolis (T.E.K.). Address reprint requests to Dr. Capewell at the Division of Public Health, University of Liverpool, Whelan Building, Quadrangle, Liverpool L69 3GB, United Kingdom, or at capewell@liverpool.ac.uk.

N Engl J Med 2007;356:2388-98.
Copyright © 2007 Massachusetts Medical Society.

Downloaded from www.nejm.org at UPF on October 22, 2008 .
Copyright © 2007 Massachusetts Medical Society. All rights reserved.

Rates of death from coronary heart disease in the United States underwent profound secular changes during the 20th century.[1,2] After peaking around 1968, age-adjusted rates were cut in half. Two factors may have contributed to this decline.

First, there have been substantial decreases in the prevalence of some major cardiovascular risk factors, including smoking, elevated total cholesterol, and high blood pressure.[3-8] However, the prevalence of both obesity and diabetes has increased alarmingly.[9-11]

Second, there has been a revolution in the treatments for established coronary heart disease, with major breakthroughs in evidence-based therapies, including the use of thrombolysis, coronary-artery bypass grafting (CABG), coronary angioplasty and stents, and angiotensin-converting–enzyme (ACE) inhibitors and statins.

The annual direct and indirect costs for coronary heart disease were $142.5 billion in 2006, and they continue to rise.[12] Determining the respective contributions of prevention and therapy to the declines in mortality from coronary heart disease is therefore becoming increasingly important, for the purposes of both understanding past trends and planning future strategies. Estimates of the contribution from reductions in risk factors before 1990 have ranged from 50 to 54% in the United States[13,14] and from 44 to 76% in other industrialized countries.[15-22] However, to our knowledge, no U.S. studies have considered the dramatic changes since 1990 or have attempted to quantify the relative contributions of specific therapies and trends in risk factors. We therefore applied a model that has been used successfully in several other countries to examine trends in U.S. deaths from coronary heart disease between 1980 and 2000.

METHODS

MORTALITY MODEL AND DATA SOURCES

To examine the contributions of various factors to the changes in rates of death from coronary heart disease among U.S. adults 25 to 84 years of age, we used an updated version of the IMPACT mortality model, which was previously validated in Europe, New Zealand, and China.[18-23] This model has been described in detail elsewhere.[18,19,23,24] It incorporates major population risk factors for coronary heart disease (smoking, high blood pressure, elevated total cholesterol, obesity, diabetes, and physical inactivity) and all usual medical and surgical treatments for coronary heart disease.

Wherever possible, data sources specific to the U.S. population were used to construct the U.S. model. When more than one data source was available, we chose the source that we considered to be most representative, least biased, and most up-to-date. Detailed information on the IMPACT model and data sources for the U.S. analysis is provided in the Supplementary Appendix, available with the full text of this article at www.nejm.org.

DEATHS PREVENTED OR POSTPONED

Data on the total U.S. population and age distribution in 1980 and 2000 were obtained from the U.S. Census Bureau. Deaths according to age and sex and mortality rates associated with coronary heart disease in 1980 and 2000 were obtained from the National Vital Statistics System of the National Center for Health Statistics. We calculated the number of deaths from coronary heart disease that would have been expected in 2000 if the mortality rates in 1980 had remained unchanged by multiplying the age-specific mortality rates for 1980 by the population for each 10-year age stratum in the year 2000 (thus accounting for the aging of the population). Subtracting the number of deaths observed in 2000 from the number expected then yielded the drop in the number of deaths (prevented or postponed) in 2000 that the model would have to explain.

TREATMENTS AND MORTALITY REDUCTIONS

The prevalence of coronary heart disease by diagnosis, the estimated frequency of use of specific treatments, the case fatality rate by diagnosis, and the risk reduction due to treatment, all stratified by age and sex, were obtained from published sources (Tables 2 through 5 in the Supplementary Appendix). The number of deaths prevented or postponed as a result of each intervention in each group of patients in the year 2000 (Table 1) 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 a period of 1 year, and by the relative reduction in the 1-year case fatality rate that was accounted for by the treatment.[19,20] For example, in the United States in 2000, approximately 102,280 men between the

Downloaded from www.nejm.org at UPF on October 22, 2008 .
Copyright © 2007 Massachusetts Medical Society. All rights reserved.

Table 1. Estimated Deaths Prevented or Postponed by Medical or Surgical Treatments in the United States in 2000.*

Treatment	No. of Eligible Patients	Patients Receiving Treatment	Relative Risk Reduction	Mean Case Fatality Rate	Absolute Risk Reduction	Deaths Prevented or Postponed					
						Best Estimate	Minimum Estimate	Maximum Estimate	Best Estimate	Minimum Estimate	Maximum Estimate
			percent				*no. of deaths*		*percent of total reduction*		
Acute myocardial infarction	670,715	—	—	0.094	—	21,570	9,045	37,720	6.3	2.6	11.0
Resuscitation in the community	204,330	43	0.05	0.094	0.050	4,435	2,205	7,450	1.3	0.6	2.2
Resuscitation in the hospital	13,415	100	0.33	0.094	0.342	4,095	1,050	5,660	1.2	0.3	1.7
Thrombolysis	670,715	20	0.24	0.094	0.019	2,410	1,260	4,250	0.7	0.4	1.2
Aspirin	670,715	84	0.15	0.094	0.014	7,735	3,960	13,265	2.3	1.2	3.9
Beta-blocker	670,715	7	0.31	0.094	0.025	340	–505	2,130	0.3	–0.1	0.6
ACE inhibitor	670,715	16	0.04	0.094	0.004	805	160	1,995	0.1	0.0	0.6
Primary angioplasty	670,715	21	0.07	0.094	0.007	1,070	560	1,900	0.2	0.2	0.6
Primary CABG	670,715	8	0.39	0.094	0.037	1,925	1,035	3,495	0.6	0.3	1.0
Treatments in 1980 subtracted						–1,245	–680	–2,415	–0.4	–0.2	–0.7
Unstable angina	665,260			0.065		13,575	6,960	23,490	4.0	2.0	6.9
Aspirin and heparin		60	0.33	0.065	0.021	6,350	3,250	10,975	1.9	1.0	3.2
Aspirin alone		17	0.15	0.065	0.010	790	410	1,385	0.2	0.1	0.4
Glycoprotein IIb/IIIa antagonists and clopidogrel		21	0.09	0.065	0.006	595	310	1,040	0.2	0.1	0.3
CABG		20	0.43	0.065	0.028	2,760	1,415	4,765	0.8	0.4	1.4
Angioplasty		30	0.32	0.065	0.021	3,080	1,575	5,320	0.9	0.5	1.6
Secondary prevention after myocardial infarction	2,866,965			0.057		28,565	12,255	62,030	8.4	3.6	18.2
Aspirin		38	0.15	0.057	0.007	5,135	2,285	11,560	1.5	0.7	3.4
Beta-blocker		29	0.23	0.057	0.012	6,750	2,765	13,995	2.0	0.8	4.1
ACE inhibitor		26	0.20	0.057	0.010	5,155	2,125	10,745	1.5	0.6	3.1
Statin		36	0.22	0.057	0.011	4,700	2,175	11,000	1.4	0.6	3.2
Warfarin		9	0.22	0.057	0.012	2,175	870	4,395	0.6	0.3	1.3
Rehabilitation		21	0.26	0.057	0.012	4,650	2,040	10,330	1.4	0.6	3.0

Downloaded from www.nejm.org at UPF on October 22, 2008 .
Copyright © 2007 Massachusetts Medical Society. All rights reserved.

Secondary prevention after CABG or PTCA	1,948,660			0.019		7,435	3,070	15,535	2.2	0.9	4.6
Aspirin		40	0.15	0.019	0.003	1,310	555	2,800	0.4	0.2	0.8
Beta-blocker		33	0.23	0.019	0.004	1,460	595	3,010	0.4	0.2	0.9
ACE inhibitor		26	0.20	0.019	0.004	1,010	410	2,080	0.3	0.1	0.6
Statin		38	0.22	0.019	0.004	1,550	665	3,365	0.5	0.2	1.0
Warfarin		9	0.22	0.019	0.004	450	180	915	0.1	0.1	0.3
Rehabilitation		32	0.26	0.019	0.004	1,655	665	3,360	0.5	0.2	1.0
Secondary-prevention treatments in 1980 subtracted						–195					
Chronic angina	4,987,375			0.015		17,730	5,595	40,950	5.2	1.6	12.0
CABG, 1990 to 2000	2,356,695	100	0.36	0.020	0.005	14,365	6,720	34,180	4.2	2.0	10.0
With CABG in 1980 subtracted						–3,065	–1,960	–4,410	–0.9	–0.6	–1.3
Angioplasty, 1990 to 2000	22,059,760	100	0.13	0.019	0.002	4,390	0	6,960	1.3	0.0	2.0
Aspirin in the community	2,119,495	24	0.15	0.011	0.001	1,060	435	2,195	0.3	0.1	0.6
Statins in the community	2,119,495	39	0.23	0.011	0.002	980	400	2,030	0.3	0.1	0.6
Heart failure with hospital admission	258,745			0.237		11,735	4,945	25,030	3.4	1.4	7.3
ACE inhibitor		43	0.20	0.237	0.047	3,130	1,375	6,960	0.9	0.4	2.0
Beta-blocker		31	0.35	0.237	0.082	4,300	1,750	8,850	1.3	0.5	2.6
Spironolactone		7	0.30	0.237	0.071	825	330	1,665	0.2	0.1	0.5
Aspirin		30	0.15	0.237	0.035	1,700	715	3,615	0.5	0.2	1.1
Statins		28	0.23	0.237	0.055	1,785	780	3,940	0.5	0.2	1.2
Heart failure in the community	1,876,405			0.063		18,500	7,735	39,170	5.4	2.3	11.5
ACE inhibitor		48	0.20	0.063	0.009	3,375	1,550	7,845	1.0	0.5	2.3
Beta-blocker		30	0.35	0.063	0.022	7,180	2,940	14,885	2.1	0.9	4.4
Spironolactone		8	0.28	0.063	0.024	1,685	690	3,500	0.5	0.2	1.0
Aspirin		30	0.15	0.063	0.009	3,105	1,265	6,405	0.9	0.4	1.9
Statin		30	0.23	0.063	0.015	3,150	1,290	6,535	0.9	0.4	1.9
Hypertension	54,353,660	58	0.13	0.008	0.001	23,845	1,945	68,370	7.0	0.6	20.0
Statins for lipid reduction (primary prevention)†	96,384,630	20	0.29	0.004	0.001	16,580	6,515	35,100	4.9	1.9	10.3
Total treatments						159,330	58,065	347,395	46.6	19.2	94.3

* Percentages may not sum to 100 because of rounding. Data sources are described in the Supplementary Appendix. CABG denotes coronary-artery bypass grafting, AMI acute myocardial infarction, ACE angiotensin-converting enzyme, and PTCA percutaneous transluminal coronary angioplasty (with or without stenting).

† The number of deaths prevented or postponed includes 475 that were prevented or postponed owing to treatment with gemfibrozil and niacin for primary prevention of hyperlipidemia.

Downloaded from www.nejm.org at UPF on October 22, 2008 .
Copyright © 2007 Massachusetts Medical Society. All rights reserved.

ages of 55 and 64 years were hospitalized with acute myocardial infarction. Some 84% were given aspirin, with an expected mortality reduction of 15%.[25] The expected age-specific, 1-year case fatality rate was approximately 5.4%.[26] The number of deaths prevented or postponed for at least a year by the use of aspirin among men in this age group was then calculated as $102{,}280 \times 0.84 \times 0.15 \times 0.054 = 696$.

Several adjustments were made to these basic analyses. Although most of the therapeutic measures studied were not in use in 1980, in some cases such use was already substantial (e.g., CABG for stable angina pectoris). In such cases, the number of deaths prevented or postponed as a result of the therapy as used in 1980 was calculated and subtracted from the number of deaths for 2000 to calculate the net benefit. We assumed that compliance — the proportion of treated patients actually taking therapeutically effective levels of medication — was 100% among hospitalized patients, 70% among symptomatic patients in the community, and 50% among asymptomatic patients in the community.[19,24,27,28] To avoid double counting of patients treated, we identified potential overlaps between different groups of patients and made appropriate adjustments (Table 9 in the Supplementary Appendix). For example, heart failure develops within 1 year after acute myocardial infarction in approximately one quarter of survivors, and approximately half the patients undergoing CABG have had a previous myocardial infarction.[19,24] To address the potential effect on the relative reduction in the case fatality rate for individual patients receiving multiple treatments, we used the Mant and Hicks cumulative-relative-benefit approach[29]:

$$\text{relative benefit} = 1 - (1 - \text{relative reduction in case fatality rate for treatment A}) \times (1 - \text{relative reduction in case fatality rate for treatment B}) \times \ldots \times (1 - \text{relative reduction in case fatality rate for treatment N}).$$

RISK FACTORS AND MORTALITY REDUCTIONS

Two approaches were used to calculate the numbers of deaths prevented or postponed as a result of changes in risk factors. We used a regression approach for systolic blood pressure, cholesterol, and body-mass index. The number of deaths prevented or postponed as a result of the change in the prevalence of or mean value for each of these risk factors (Table 2) was estimated as the product of three variables: the number of deaths from coronary heart disease in 1980 (the base year), the subsequent reduction in that risk factor (Table 2 in the Supplementary Appendix), and the regression coefficient quantifying the change in mortality from coronary heart disease per unit of absolute change in the risk factor (Table 6 in the Supplementary Appendix). For example, in 1980, there were 26,352 deaths from coronary heart disease among 12,629,000 women who were 55 to 64 years of age. The mean systolic blood pressure in this group decreased by 3.09 mm Hg between 1980 and 2000. The largest meta-analysis showed an estimated age- and sex-specific reduction in mortality of 50% for every reduction of 20 mm Hg in systolic pressure, yielding a logarithmic (ln) coefficient of −0.035.[33]

The number of deaths prevented or postponed as a result of this change was then estimated as follows:

$$\text{number of deaths} = (1 - e^{(\text{coefficient} \times \text{change})}) \times \text{deaths in 1980} = (1 - e^{(-0.035 \times 3.09)}) \times 26{,}352 = 2701.$$

The population-attributable risk fraction was used to determine the effect of changes in the prevalence of smoking, diabetes, and physical inactivity. The population-attributable risk fraction was calculated conventionally as $[P \times (RR-1)] \div [(1+P) \times (RR-1)]$, where P is the prevalence of the risk factor (Table 2 in the Supplementary Appendix) and RR is the relative risk of death from coronary heart disease associated with that risk factor (Table 7 in the Supplementary Appendix). The number of deaths prevented or postponed was then estimated as the number of deaths from coronary heart disease in 1980 (the base year) multiplied by the difference between the population-attributable risk fraction in 1980 and that in 2000 (Table 2). For example, the prevalence of diabetes among men 65 to 74 years of age increased from 14.5% in 1980 to 20.7% in 2000. Given a relative risk of 1.93, the population-attributable risk fraction increased from 0.119 to 0.161. Additional deaths from coronary heart disease in 2000 that were attributable to an increased prevalence of diabetes were therefore calculated as follows[18,19,23,24]:

$$\text{deaths from coronary heart disease in 1980} = (123{,}055) \times (0.161 - 0.119) = 5168.$$

Because independent regression coefficients and relative risks for each risk factor were obtained from multivariate analyses, we assumed

Downloaded from www.nejm.org at UPF on October 22, 2008 .
Copyright © 2007 Massachusetts Medical Society. All rights reserved.

Table 2. Deaths from Coronary Heart Disease That Were Prevented or Postponed as a Result of Changes in Population Risk Factors in the United States, 1980 to 2000.*

Risk Factor†	Absolute Level of Risk Factor‡		Change in Risk Factor		Beta Regression Coefficient for Change in Mortality Rate§	Relative Risk	Deaths Prevented or Postponed					
	1980	2000	Absolute Change	Relative Change (%)			Best Estimate	Minimum Estimate	Maximum Estimate	Best Estimate	Minimum Estimate	Maximum Estimate
							no. of deaths			*percent of total reduction*		
Smoking prevalence (%)	36.3	24.6	−11.7	−32.2			39,925	34,955	52,435	11.7	10.2	15.3
Men						2.52						
Women						2.14						
Systolic blood pressure (mm Hg)	129.0	123.9	−5.1	−4.0			68,800	53,730	105,060	20.1	15.7	30.7
Men					−0.0334							
Women					−0.0413							
Total cholesterol (mmol/liter)	5.67	5.33	−0.34	−6.1			82,830	58,455	95,570	24.2	17.1	28.0
Men					−0.9458							
Women					−0.9121							
Physical inactivity (%)	29.6	27.3	−2.3	−7.8	—		17,445	8,340	29,035	5.1	2.4	8.5
Men						1.27						
Women						1.33						
BMI	25.6	28.2	+2.6	10.1			−25,905	−14,430	−40,405	−7.6	−4.2	−11.8
Men					0.0297							
Women					0.0297							
Diabetes prevalence (%)	6.5	9.4	+2.9	44.2	—		−33,465	−23,885	−43,330	−9.8	−7.0	−12.7
Men						1.93						
Women						2.59						
Total risk factors							149,635	117,165	198,360	43.8	34.3	58.0

* Percentages may not sum to 100 because of rounding. BMI denotes body-mass index (the weight in kilograms divided by the square of the height in meters). To convert the values for cholesterol to milligrams per deciliter, divide by 0.02586. Data sources are described in the Supplementary Appendix.

† The total adult population in 1980 was 177,745,055. For systolic pressure, the numbers of deaths exclude patients receiving treatment for hypertension, and for total cholesterol, the numbers exclude patients receiving statins.

‡ Data are from the National Center for Health Statistics,[30,31] except for data on physical inactivity, which are from the Behavioral Risk Factor Surveillance System.[32]

§ The change in the mortality rate per unit of measurement for the risk factor is shown.

Downloaded from www.nejm.org at UPF on October 22, 2008 .
Copyright © 2007 Massachusetts Medical Society. All rights reserved.

that there was no further synergy between the treatment and risk-factor sections of the model or among the major risk factors.

The number of deaths prevented or postponed as a result of changes in risk factors was systematically quantified for each specific patient group to account for potential differences in effect. Lag times between the change in the risk-factor rate and the change in the event rate were not modeled; it was assumed that these lag times would be relatively unimportant over a period of two decades.[20,23,34,35]

COMPARISON OF ESTIMATED AND 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 5 (e.g., 696 became 695). All 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 calculated estimates or to other, unmeasured risk factors.[19,20,24]

SENSITIVITY ANALYSES

We tested all the above assumptions and variables in a multiple-way sensitivity analysis, using the analysis-of-extremes method.[19,20,24,36] For each variable in the model, we assigned a lower value and an upper value, using 95% confidence intervals when available and otherwise using ±20% (for the number of patients, use of treatment, and compliance). For example, for aspirin treatment in men 55 to 64 years of age who were hospitalized with acute myocardial infarction, the best estimate was 696 deaths prevented or postponed. The minimum estimate from the multiple-way sensitivity analysis was 259, and the maximum estimate was 1501 (Table 3).

RESULTS

From 1980 to 2000, the age-adjusted rate of coronary heart disease fell from 542.9 to 266.8 cases per 100,000 population among men aged 25 to 84 years and from 263.3 to 134.4 among women aged 25 to 84 years. In 1980, a total of 462,984 deaths among people in this age group were recorded as due to coronary heart disease, according to the *International Classification of Diseases, 9th Revision* (codes 410–414 and 429.2).[41] In 2000, a total of 337,658 such deaths were recorded, according to the *International Classification of Diseases, 10th Revision* (codes I20–I25).[42] However, had the age-specific death rates from 1980 remained in 2000, an additional 341,745 deaths from coronary heart disease would have occurred.

The U.S. IMPACT model explained approximately 308,965 (90%) of this decrease in the number of deaths from coronary heart disease. Under the assumptions of the sensitivity analysis,

Table 3. Example of a Multiple-Way Sensitivity Analysis.*

Estimate	No. of Patients (a)†	Proportion Receiving Treatment (b)‡	Relative Mortality Reduction (c)‡	1-Year Case Fatality Rate (d)‡	No. of Deaths Prevented or Postponed (a×b×c×d)
			percent		
Best	102,280	0.84	15	5.4	696
Minimum	81,824	0.67	11	4.3	259
Maximum	122,736	0.99	19	6.5	1501

* In the United States in 2000, about 102,280 men aged 55 to 64 years were hospitalized with acute myocardial infarction, of whom approximately 84% were given aspirin. Aspirin use reduced the case fatality rate by approximately 15%. The underlying 1-year case fatality rate in these men was approximately 5.4%. The calculated number of deaths prevented or postponed was approximately 696. A multiple-way sensitivity analysis was then performed. Lower and upper bounds for each variable were estimated with use of 95% confidence intervals, when available, or failing that, with use of calculated bounds of ±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.

† Numbers of patients are from the National Hospital Discharge Survey[37] and the Medical Expenditure Panel Survey.[38]

‡ Treatment data are from Rogers et al.,[39] data on mortality reduction are from the Antithrombotic Trialists' Collaboration,[40] and case fatality rates are from Capewell et al.[26]

Downloaded from www.nejm.org at UPF on October 22, 2008 .
Copyright © 2007 Massachusetts Medical Society. All rights reserved.

the minimum and maximum numbers of deaths from coronary heart disease that were explained were 175,230 (51%) and 545,755 (160%). The agreement between the number of estimated deaths and the number of observed deaths was reasonably good for men across all groups and for women under the age of 75 years (Fig. 1). Changes in medical treatments accounted for approximately 47% and risk-factor changes accounted for approximately 44% of the decrease in deaths (Tables 1 and 2).

MEDICAL AND SURGICAL TREATMENTS

Approximately 159,330 of the deaths from coronary heart disease that were prevented or postponed were attributable to medical therapies (minimum estimate, 58,065; maximum estimate, 347,395) (Table 1). The largest reductions in deaths came from the use of secondary-prevention medications or rehabilitation after acute myocardial infarction or after revascularization (a total reduction of approximately 35,800 deaths) and from the use of initial treatments for acute myocardial infarction or unstable angina (approximately 35,145 deaths), followed by treatments for heart failure and hypertension, statin therapy for primary prevention, and treatments for chronic angina. The use of revascularization for chronic angina resulted in a reduction of approximately 15,690 deaths in 2000, as compared with deaths in 1980, or approximately 5% of the total.

RISK FACTORS

Approximately 149,635 fewer deaths from coronary heart disease were attributable to changes in risk factors (minimum estimate, 117,165; maximum estimate, 198,360) (Table 2). Decreases in the total cholesterol concentration (by 0.34 mmol per liter), systolic blood pressure (by 5.1 mm Hg), and smoking prevalence (by 11.7%) were estimated to have prevented or postponed approximately 82,830, 68,800, and 39,925 deaths, respectively. The 2.3% decrease in physical inactivity prevented or postponed approximately 17,445 deaths. In contrast, the increase in the body-mass index (the weight in kilograms divided by the square of the height in meters) of 2.6 and the 2.9% increase in the prevalence of diabetes resulted in approximately 25,905 and 33,465 additional deaths overall, respectively (Table 2).

PROPORTIONAL CONTRIBUTIONS TO THE DECREASE IN DEATHS

Sensitivity analyses showed that the proportional contributions of specific treatments and risk-factor changes to the overall reduction in deaths from coronary heart disease in 2000 were relatively consistent (Tables 1 and 2). Thus, all initial treatments for acute myocardial infarction together accounted for approximately 21,570 fewer deaths, representing 6.3% of the total decrease of 341,745 deaths. The minimum estimated contribution was 9045 fewer deaths (2.6%), and the maximum was 37,720 (11.0%). The contribution of treatments for acute myocardial infarction therefore remained consistently smaller than that of secondary prevention or therapies for heart failure, irrespective of whether best, minimum, or maximum estimates were compared (Table 1).

DISCUSSION

The burden of coronary heart disease in the United States remains enormous, even though associated mortality rates fell by more than 40% between 1980 and 2000. These two decades saw rapid growth in costly medical technology and pharmaceutical treatments for coronary heart disease, as well as substantial public health efforts to reduce

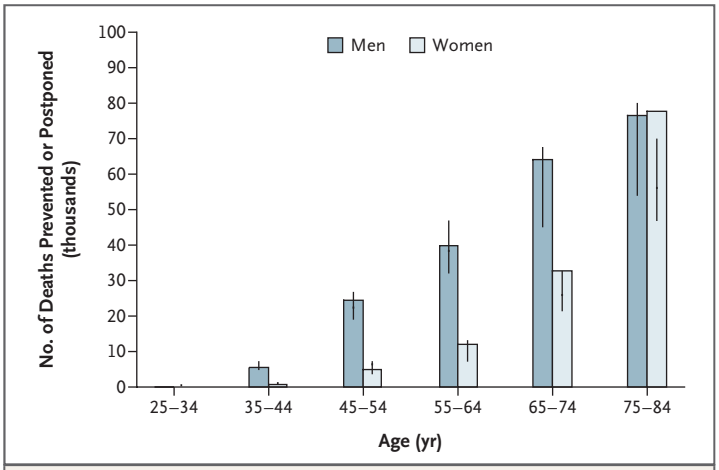

Figure 1. Estimated and Observed Reductions in Deaths from Coronary Heart Disease in the United States between 1980 and 2000, Stratified According to Age and Sex.

The bars show the observed decrease in deaths in each age group, and the vertical lines the extreme minimum and maximum estimates in the sensitivity analysis.

Downloaded from www.nejm.org at UPF on October 22, 2008 .
Copyright © 2007 Massachusetts Medical Society. All rights reserved.

the prevalence of major cardiovascular risk factors. Establishing the relative contributions of these two approaches is therefore of considerable importance. We found that reductions in major risk factors probably accounted for approximately half the decrease in deaths from coronary heart disease, as in most other industrialized countries studied.[15-22] Earlier U.S. studies likewise suggested a contribution of approximately 54% of the reduction in deaths between 1968 and 1976[14] and approximately 50% between 1980 and 1990.[13]

Irrespective of the assumptions used, we found that the largest contributions from medical therapies consistently came from secondary prevention, followed by treatments for acute coronary syndromes, then heart failure. Revascularization by means of CABG or angioplasty for stable or unstable disease together accounted for approximately 7% of the overall drop in deaths from coronary heart disease, a finding that is consistent with the results of previous studies in the United States[43] and elsewhere.[19-22,44]

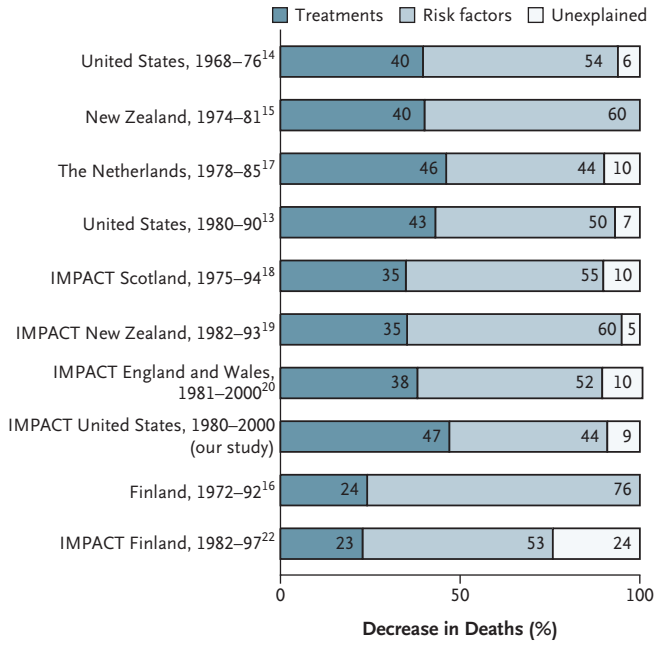

Figure 2. Percentage of the Decrease in Deaths from Coronary Heart Disease Attributed to Treatments and Risk-Factor Changes in Our Study Population and in Other Populations.

In the New Zealand study, 1974 to 1981 (Beaglehole[15]), the analysis focused on specific treatments and inferred contribution from risk factors. In the Finland study, 1972 to 1992 (Vartiainen et al.[16]), the analysis focused on risk factors and inferred contribution from treatments.

Although most of the changes in treatments and risk factors between 1980 and 2000 led to reductions in deaths from coronary heart disease, two major exceptions are noteworthy. Our analysis estimated that increases in the body-mass index accounted overall for about 26,000 additional deaths from coronary heart disease in 2000 and increases in the prevalence of diabetes for about 33,500 additional deaths; both figures are consistent with the results of other recent studies.[45,46] Efforts to address these two risk factors should therefore receive particular attention in future measures to improve the public health.[10,11]

Modeling studies have a number of potential strengths, including the ability to transparently integrate and simultaneously consider huge amounts of data from many sources and then test explicit assumptions by means of sensitivity analyses. Our analysis of extremes suggested that the proportional contributions to the overall reductions in deaths from specific treatments and risk-factor changes remained reasonably consistent, irrespective of whether best, minimum, or maximum estimates were considered (Tables 1 and 2). This was reassuring, as was the general consistency with the results of most studies performed elsewhere (Fig. 2).[15-17,19,20]

However, all modeling analyses should be interpreted with appropriate caution. All require the gathering of data from numerous sources, each with recognized limitations. We sometimes had to use data from studies that might have been limited by geographic, ethnic, or selection bias or by the need to extrapolate to older age groups. Risk estimates were not necessarily fully independent of each other. Furthermore, most interactions were averaged across broad groups. We therefore made the explicit assumptions detailed in the Supplementary Appendix. Furthermore, we analyzed only the estimated reduction in deaths from coronary heart disease, not life-years gained or improvement in the quality of life.[47] Analyses of these changes are warranted, as well as comparisons among racial and ethnic groups and economic analyses.

The estimates of changes in risk factors remain imprecise. Furthermore, we did not explicitly consider the effect of lag times; however, they may be relatively unimportant over a 20-year period.[20,23,33,35] Although major efforts were made to address overlaps, residual double counting of some individual patients remains possible. We

Downloaded from www.nejm.org at UPF on October 22, 2008 .
Copyright © 2007 Massachusetts Medical Society. All rights reserved.

also assumed that, after adjustments for reduced dosing and imperfect compliance, the efficacy of treatments in randomized, controlled trials could be generalized to usual clinical practice.[48,49] Both assumptions may have potentially overestimated the true treatment effect.

In conclusion, our analyses suggest that approximately half the recent decrease in deaths from coronary heart disease in the United States may be attributable to reductions in major risk factors and approximately half to evidence-based medical therapies. Future strategies for preventing and treating coronary heart disease should therefore be comprehensive, maximizing the coverage of effective treatments and actively promoting population-based prevention by reducing risk factors.

No potential conflict of interest relevant to this article was reported.

The findings and conclusions in this article are those of the authors and do not represent the views of the Centers for Disease Control and Prevention.

REFERENCES

1. Rosamond W, Flegal K, Friday G, et al. Heart disease and stroke statistics — 2007 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation 2007;115:e69-e171. [Erratum, Circulation 2007;115:e172].
2. Morbidity and mortality: 2004 chart book on cardiovascular, lung, and blood diseases. Bethesda, MD: National Heart, Lung, and Blood Institute, 2004. (Accessed May 11, 2007, at http://www.nhlbi.nih.gov/resources/docs/cht-book.htm.)
3. Centers for Disease Control and Prevention. Percentage of adults who were current, former, or never smokers, overall and by sex, race, Hispanic origin, age, and education status: National Health Interview Surveys, selected years — United States, 1965–2004. (Accessed May 11, 2007, at http://www.cdc.gov/tobacco/data_statistics/tables/adult/table_2.htm.)
4. Hajjar I, Kotchen TA. Trends in prevalence, awareness, treatment, and control of hypertension in the United States, 1988-2000. JAMA 2003;290:199-206.
5. Burt VL, Cutler JA, Higgins M, et al. Trends in the prevalence, awareness, treatment, and control of hypertension in the adult US population: data from the Health Examination Surveys, 1960 to 1991. Hypertension 1995;26:60-9. [Erratum, Hypertension 1996;27:1192.]
6. Johnson CL, Rifkind BM, Sempos CT, et al. Declining serum total cholesterol levels among US adults: the National Health and Nutrition Examination Surveys. JAMA 1993;269:3002-8.
7. Ford ES, Mokdad AH, Giles WH, Mensah GA. Serum total cholesterol concentrations and awareness, treatment, and control of hypercholesterolemia among US adults: findings from the National Health and Nutrition Examination Survey, 1999 to 2000. Circulation 2003;107:2185-9.
8. Prevalence of no leisure-time physical activity — 35 states and the District of Columbia, 1988–2002. MMWR Morb Mortal Wkly Rep 2004;53:82-6.
9. Hedley AA, Ogden CL, Johnson CL, Carroll MD, Curtin LR, Flegal KM. Prevalence of overweight and obesity among US children, adolescents, and adults, 1999-2002. JAMA 2004;291:2847-50.
10. Harris MI, Hadden WC, Knowler WC, Bennett PH. Prevalence of diabetes and impaired glucose tolerance and plasma glucose levels in U.S. population aged 20-74 yr. Diabetes 1987;36:523-34.
11. Harris MI, Flegal KM, Cowie CC, et al. Prevalence of diabetes, impaired fasting glucose, and impaired glucose tolerance in U.S. adults: the Third National Health and Nutrition Examination Survey, 1988-1994. Diabetes Care 1998;21:518-24.
12. Thom T, Haase N, Rosamond W, et al. Heart disease and stroke statistics — 2006 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation 2006;113:e85-e151. [Errata, Circulation 2006;113:e696, 114:e630.]
13. Hunink MG, Goldman L, Tosteson AN, et al. The recent decline in mortality from coronary heart disease, 1980-1990: the effect of secular trends in risk factors and treatment. JAMA 1997;277:535-42.
14. Goldman L, Cook EF. The decline in ischemic heart disease mortality rates: an analysis of the comparative effects of medical interventions and changes in lifestyle. Ann Intern Med 1984;101:825-36.
15. Beaglehole R. Medical management and the decline in mortality from coronary heart disease. Br Med J (Clin Res Ed) 1986;292:33-5.
16. Vartiainen E, Puska P, Pekkanen J, Tuomilehto J, Jousilahti P. Changes in risk factors explain changes in mortality from ischaemic heart disease in Finland. BMJ 1994;309:23-7.
17. Bots ML, Grobbee DE. Decline of coronary heart disease mortality in the Netherlands from 1978 to 1985: contribution of medical care and changes over time in presence of major cardiovascular risk factors. J Cardiovasc Risk 1996;3:271-6.
18. Capewell S, Morrison CE, McMurray JJ. Contribution of modern cardiovascular treatment and risk factor changes to the decline in coronary heart disease mortality in Scotland between 1975 and 1994. Heart 1999;81:380-6.
19. Capewell S, Beaglehole R, Seddon M, McMurray J. Explanation for the decline in coronary heart disease mortality rates in Auckland, New Zealand, between 1982 and 1993. Circulation 2000;102:1511-6.
20. Unal B, Critchley JA, Capewell S. Explaining the decline in coronary heart disease mortality in England and Wales, 1981-2000. Circulation 2004;109:1101-7.
21. *Idem.* Modelling the decline in coronary heart disease deaths in England and Wales, 1981-2000: comparing contributions from primary prevention and secondary prevention. BMJ 2005;331:614.
22. Laatikainen T, Critchley J, Vartiainen E, Salomaa V, Ketonen M, Capewell S. Explaining the decline in coronary heart disease mortality in Finland between 1982 and 1997. Am J Epidemiol 2005;162:764-73.
23. Critchley J, Liu J, Zhao D, Wei W, Capewell S. Explaining the increase in coronary heart disease mortality in Beijing between 1984 and 1999. Circulation 2004;110:1236-44.
24. Ural B, Critchley J, Capewell S. IMPACT, a validated, comprehensive coronary heart disease model. Liverpool, United Kingdom: University of Liverpool, 2006. (Accessed May 11, 2007, at http://www.liv.ac.uk/PublicHealth/sc/bua/impact.html.)
25. Ryan R, Majeed A. Prevalence of ischaemic heart disease and its management with statins and aspirin in general practice in England and Wales, 1994-98. Health Stat Q 2001;12:34-9.
26. Capewell S, Livingston BM, MacIntyre K, et al. Trends in case-fatality in 117 718 patients admitted with acute myocardial infarction in Scotland. Eur Heart J 2000;21:1833-40.
27. Butler J, Arbogast PG, BeLue R, et al. Outpatient adherence to beta-blocker therapy after acute myocardial infarction. J Am Coll Cardiol 2002;40:1589-95.
28. Nichol MB, Venturini F, Sung JC. A critical evaluation of the methodology of the literature on medication compliance. Ann Pharmacother 1999;33:531-40.
29. Mant J, Hicks N. Detecting differences in quality of care: the sensitivity of measures of process and outcome in treating acute myocardial infarction. BMJ 1995;311:793-6.

Downloaded from www.nejm.org at UPF on October 22, 2008 .
Copyright © 2007 Massachusetts Medical Society. All rights reserved.

30. National Center for Health Statistics. Plan and operation of the second National Health and Nutrition Examination Survey 1976-80. Programs and collection procedures, series 1, no. 15. Hyattsville, MD: National Center for Health Statistics, 1981. (DHHS publication no. (PHS) 81-1317).
31. *Idem*. NHANES 1999-2000. (Accessed May 11, 2007, at http://www.cdc.gov/nchs/about/major/nhanes/NHANES99_00.htm.)
32. Mokdad AH, Stroup DF, Giles WH. Public health surveillance for behavioral risk factors in a changing environment: recommendations from the Behavioral Risk Factor Surveillance Team. MMWR Recomm Rep 2003;52(RR-9):1-12.
33. Lewington S, Clarke R, Qizilbash N, Peto R, Collins R. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. Lancet 2002;360:1903-13. [Erratum, Lancet 2003;361:1060.]
34. Critchley JA, Capewell S. Mortality risk reduction associated with smoking cessation in patients with coronary heart disease: a systematic review. JAMA 2003;290:86-97.
35. Law MR, Wald NJ, Thompson SG. By how much and how quickly does reduction in serum cholesterol concentration lower risk of ischaemic heart disease? BMJ 1994;308:367-72.
36. Briggs A, Sculpher M, Buxton M. Uncertainty in the economic evaluation of health care technologies: the role of sensitivity analysis. Health Econ 1994;3:95-104.
37. Design and operation of the National Hospital Discharge Survey: 1988 redesign. Programs and collection procedures, series 1, no. 39. Hyattsville, MD: National Center for Health Statistics, 2000. (DHHS publication no. (PHS) 2001-1315.)
38. The Medical Expenditure Panel Survey. Rockville, MD: Agency for Healthcare Research and Quality. (Accessed May 11, 2007, at http://www.meps.ahrq.gov/mepsweb.)
39. Rogers WJ, Canto JG, Lambrew CT, et al. Temporal trends in the treatment of over 1.5 million patients with myocardial infarction in the U.S. from 1990 through 1999: the National Registry of Myocardial Infarction 1, 2 and 3. J Am Coll Cardiol 2000;36:2056-63.
40. Antithrombotic Trialists' Collaboration. Collaborative meta-analysis of randomized trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. BMJ 2002;324:71-86.
41. Department of Health and Human Services. International classification of diseases, 9th revision, clinical modification: ICD-9-CM. Washington, DC. Department of Health and Human Services, 1980. (DHHS publication no. (PHS) 80-1260.)
42. International statistical classification of diseases and related health problems, 10th rev., ICD-10. Geneva: World Health Organization, 1992.
43. Doliszny KM, Luepker RV, Burke GL, Pryor DB, Blackburn H. Estimated contribution of coronary artery bypass graft surgery to the decline in coronary heart disease mortality: the Minnesota Heart Survey. J Am Coll Cardiol 1994;24:95-103.
44. Cooper K, Davies R, Roderick P, Chase D, Raftery J. The development of a simulation model of the treatment of coronary heart disease. Health Care Manag Sci 2002;5:259-67.
45. Flegal KM, Graubard BI, Williamson DF, Gail MH. Excess deaths associated with underweight, overweight, and obesity. JAMA 2005;293:1861-7.
46. Olshansky SJ, Passaro DJ, Hershow RC, et al. A potential decline in life expectancy in the United States in the 21st century. N Engl J Med 2005;352:1138-45.
47. Unal B, Critchley JA, Fidan D, Capewell S. Life-years gained from modern cardiological treatments and population risk factor changes in England and Wales, 1981-2000. Am J Public Health 2005;95:103-8.
48. McAlister FA. Relative treatment effects are consistent across the spectrum of underlying risks . . . usually. Int J Epidemiol 2002;31:76-7.
49. Hippisley-Cox J, Coupland C. Effect of combinations of drugs on all cause mortality in patients with ischaemic heart disease: nested case-control analysis. BMJ 2005;330:1059-63. [Erratum, BMJ 2006;332:912.]

Copyright © 2007 Massachusetts Medical Society.

FULL TEXT OF ALL *JOURNAL* ARTICLES ON THE WORLD WIDE WEB

Access to the complete text of the *Journal* on the Internet is free to all subscribers. To use this Web site, subscribers should go to the *Journal*'s home page (**www.nejm.org**) and register by entering their names and subscriber numbers as they appear on their mailing labels. After this one-time registration, subscribers can use their passwords to log on for electronic access to the entire *Journal* from any computer that is connected to the Internet. Features include a library of all issues since January 1993 and abstracts since January 1975, a full-text search capacity, and a personal archive for saving articles and search results of interest. All articles can be printed in a format that is virtually identical to that of the typeset pages. Beginning 6 months after publication, the full text of all Original Articles and Special Articles is available free to nonsubscribers who have completed a brief registration.

Downloaded from www.nejm.org at UPF on October 22, 2008 .
Copyright © 2007 Massachusetts Medical Society. All rights reserved.