

Sex and Time Trends in Cardiovascular Disease Incidence and Mortality: the Framingham Heart Study, 1950–1989

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Variations in cardiovascular disease mortality between sexes, over time, and across regions point to population differences in the biologic, behavioral, and environmental factors influencing cardiovascular health. The authors examined 20-year trends in risk factors, incidence, and mortality among women and men in Framingham, Massachusetts, who were members of the Framingham Heart Study and aged 50–59 years in 1950, 1960, and 1970. The incidence declined 21% between the female cohorts ($p < 0.01$ for trend) with the greatest decline occurring between the 1950 and 1960 cohorts. The 20-year incidence declined only 6% between the male cohorts despite an 18% decline ($p < 0.05$ for trend) during the first 10 years of follow-up. Cardiovascular disease mortality declined 59% between the female cohorts and 53% between the male cohorts (both $p < 0.001$ for trend). The largest mortality declines occurred between the 1950 and 1960 female cohorts during the second 10 years of follow-up and between the 1960 and 1970 male cohorts during both follow-up periods. Obesity, hypercholesterolemia, and high blood pressure were significantly lower at baseline and 10 years later in the 1970 female cohort compared with the 1950 cohort (all $p < 0.001$). Smoking and high blood pressure were significantly lower at baseline and 10 years later in the 1970 male cohort compared with the 1950 cohort (both $p < 0.001$). More than half of the 51% decline in coronary heart disease mortality observed in women between 1950 and 1989 and one third to one half of the 44% decline observed in men could be attributed to improvements in risk factors in the 1970 cohorts. *Am J Epidemiol* 1996;143:338–50.

cardiovascular diseases; incidence; mortality; risk factors; sex

Cardiovascular disease mortality, essentially death from coronary heart disease and stroke, has declined more than 40 percent since 1960 for men and women in the United States. While the decline in stroke mortality began as early as 1915 (1), the decline in coronary mortality has varied in the time of onset and magnitude between sexes (2, 3), across geographic regions (2–4), and, to a lesser extent, between age groups (2). There was more regional variation in the onset time for women than for men with the decline occurring between 1958 and 1975 for white women and between 1968 and 1975 for white men (2, 5). There were also sex differences in the magnitude of the decline with women, at the national level, experiencing a larger decline than did men (3, 5).

These variations in the mortality decline point to causal factors (such as primary prevention efforts, medical care for the diagnosis and treatment of cardiovascular disease, and trends in the population distribution of risk factors) that vary across regions, sexes, and age groups. The Framingham Heart Study offers a unique opportunity to study the interplay of secular trends in biologic, behavioral, and environmental factors within a free-living, stable population. Previously, we reported a 60 percent decline in cardiovascular disease mortality and a 19 percent decline in incidence after 10 years of follow-up of men in 1970 compared with similarly aged men in 1950 (6). The purpose of the present study was to describe sex and time differences in 20-year cardiovascular disease incidence and mortality among women and men in the Framingham Study and to relate these to secular trends and sex differences in cardiovascular risk factors.

MATERIALS AND METHODS

The Framingham Heart Study is a prospective epidemiologic study of cardiovascular disease following a two-thirds population sample of the residents of Framingham, Massachusetts (7). The original cohort of 5,209 were aged 28–62 years when assembled in

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1948 and included 55 percent women. The sampling methods, response rates, and follow-up examination procedures have been described extensively (7–9). Information on newly developed cardiovascular disease and on risk factors was obtained through standard biennial examinations consisting of an interview, physical examination, and laboratory tests. Information on all cardiovascular disease events, hospitalizations, and deaths occurring between examinations was obtained through daily hospital and death surveillance.

Study population

This report focuses on 20-year event rates among three successive cohorts of 50- to 59-year-old women and men free of cardiovascular disease at baseline. This age group was chosen because it was well represented in the Framingham Study at three points in time bridging the decline in cardiovascular mortality: 1950, 1960, and 1970. There were 757 women and 618 men who were 50–59 years old as of the baseline, January 1, 1950 (the 1950 cohorts), 816 women and 586 men 50–59 years old as of January 1, 1960 (the 1960 cohorts), and 834 women and 598 men 50–59 years old as of January 1, 1970 (the 1970 cohorts).

Risk factor data

The methods of risk factor measurement and laboratory analysis have been described elsewhere (10). Data on current cigarette smoking, high blood pressure, diabetes mellitus, hypercholesterolemia, and obesity are presented here. High blood pressure was defined as systolic blood pressure ≥ 160 mmHg and/or diastolic blood pressure ≥ 95 mmHg. The criteria for diabetes mellitus were an abnormal glucose tolerance test, at least two examinations with a casual blood glucose of ≥ 150 mg/100 ml, or under treatment for diabetes. Obesity was defined as weight ≥ 120 percent of the US average for sex, age, and height (10, 11). Hypercholesterolemia was defined as total cholesterol ≥ 240 mg/dl (≥ 6.206 mmol/liter). In the 1970s, plasma cholesterol measurements were substituted for serum cholesterol. Since plasma cholesterol values have been shown to be systematically lower than those from serum (12), plasma values were inflated by 3 percent (13).

Subjects in the Framingham Study are examined every 2 years; however, it often takes longer than 2 years to examine all subjects. Since more than one examination cycle may be in progress at one time, risk factor data were taken from the examination that a cohort member attended nearest to his/her cohort's baseline (regardless of examination cycle) and within 2.5 years of baseline. If data were missing on a risk

factor, they were taken from the examination identified for the subject as being the next closest to baseline as long as it took place within 2.5 years of baseline. This process was repeated to obtain risk factor data for the beginning of the second 10 years of follow-up (i.e., for January 1, 1960, for the 1950 cohorts; January 1, 1970, for the 1960 cohorts; January 1, 1980, for the 1970 cohorts).

Morbidity and mortality data

The original objectives of the Framingham Study included determining the occurrence of those manifestations of cardiovascular disease that led to death from coronary heart disease and stroke. These manifestations were coronary heart disease (myocardial infarction, angina, sudden and nonsudden coronary death, and coronary insufficiency), stroke, and other cardiovascular disease (transient ischemic attacks, congestive heart failure, intermittent claudication, and other cardiovascular death). Throughout the Framingham Study, cardiovascular events have been dated and assigned a diagnosis based on medical record review and standard criteria for each outcome (10) consistently applied at regular meetings of a panel of physicians.

The diagnostic criteria used by the Framingham Study have changed little since its inception. The criterion for myocardial infarction has been the presence of Q-waves not previously seen on the electrocardiogram (7). More recently, medical records have contained data on a number of cardiac enzymes. However, subjects diagnosed only on the basis of enzyme studies and history, without diagnostic electrocardiographic changes, have been kept in a special category. In 1956, a recorded increase in serum aspartate transaminase and a history of prolonged ischemic chest pain were accepted as evidence of myocardial infarction. Later, in 1962, serum lactate dehydrogenase was included in the criteria. In the early 1980s, data on creatine kinase and its isoenzymes were included in the medical review procedures. Although the clinical criteria for stroke have not changed, computed tomographic scans have been available since 1978 to aid in classifying stroke according to mechanism.

Statistical methods

The trends in risk factors, incidence, and mortality over the cohorts were analyzed with the difference between the 1950 and 1970 cohorts being used as the primary comparison. The linear regression for trend (14), the General Linear Models procedure (15), was used to analyze continuous variables. For dichotomous variables, the Mantel-Haenszel test for trend was used (16). The Kaplan-Meier incidence and mortality rates

were calculated (17) and tested using the z statistic (15). Survival curves (the LIFETEST procedure) (15) were used to describe the distribution of incidence and mortality over time. The log rank test was used to test the equality of the survival curves across cohorts (17). A significance level of $p < 0.05$ was used to test hypotheses, and all significance tests were two tailed. The contribution of risk factor trends to changes in the 10-year risk of coronary heart disease mortality was estimated using two models developed by Leaverton et al. (18) using the Framingham population and the National Health and Nutrition Examination Survey Epidemiologic Follow-up Study population.

RESULTS

Sex and cohort differences in incidence, mortality, and risk factors

Sex and cohort differences in the 20-year cardiovascular disease incidence and mortality trends are shown

in table 1. There existed a 21 percent decline in incidence between the 1950 and 1970 female cohorts ($p < 0.01$ for trend) and an insignificant 6 percent decline between the male cohorts. The majority of the female decline occurred between the 1950 and 1960 cohorts (19 percent, $p < 0.01$) followed by a smaller decline (2 percent) between the 1960 and 1970 cohorts. Reductions in the incidence of coronary heart disease (20 percent, $p < 0.05$ for trend) and of stroke (51 percent, $p < 0.05$ for trend) contributed to the overall decline. Cardiovascular disease mortality declined more than 50 percent between the 1950 and 1970 male and female cohorts (both $p < 0.001$ for trend). The greatest reduction for women occurred between the 1950 and 1960 cohorts (37 percent, $p < 0.01$), while for men, it occurred between the 1960 and 1970 cohorts (45 percent, $p < 0.001$).

Among women, the 59 percent decline in mortality was led by an 84 percent reduction in death from

TABLE 1. Cumulative cardiovascular disease incidence and mortality during 20 years of follow-up for women and men aged 50–59 years at baseline, the Framingham Heart Study, 1950–1989

Endpoint	1950 cohort		Test for difference in rates between adjoining cohorts†	1960 cohort		Test for difference in rates between adjoining cohorts	1970 cohort		% of change between 1950 and 1970 cohorts
	Kaplan-Meier rate/1,000 persons‡	No of cases		Kaplan-Meier rate/1,000 persons	No of cases		Kaplan-Meier rate/1,000 persons	No of cases	
<i>Women§</i>									
Cardiovascular disease incidence	372	267	**	301	223		294	224	-21**,
Coronary heart disease	218	145		184	127		175	126	-20*
Stroke	82	48	*	47	29		40	26	-51*
Other cardiovascular disease¶	125	74		101	67		109	72	-13
Cardiovascular disease mortality	147	103	**	92	66	*	60	44	-59***
Coronary heart disease	69	46		54	38		34	25	-51**
Stroke	29	19		18	12		18	13	-38
Other cardiovascular disease#	57	38	**	22	16	*	9	6	-84***
All-cause mortality	248	185		213	167		205	164	-17††
<i>Men‡‡</i>									
Cardiovascular disease incidence	510	294		510	274		478	257	-6
Coronary heart disease	354	184		357	174		346	172	-2.3
Stroke	79	32		79	31		80	30	1.3
Other cardiovascular disease	176	78		172	69		132	55	-25
Cardiovascular disease mortality	249	140		215	114	***	118	59	-53***
Coronary heart disease	161	88		145	74	**	90	46	-44***
Stroke	34	16		37	18		22	9	-35
Other cardiovascular disease	71	36		47	22	***	9	4	-87***
All-cause mortality	388	238		370	214		319	181	-18***

† Test for difference in rates between adjoining cohorts * $p < 0.05$, ** $p < 0.01$; *** $p < 0.001$

‡ Kaplan-Meier rates in the subcategories will not equal the total because of censoring (see J F Lawless Statistical models and methods for lifetable data New York John Wiley & Sons, Inc, 1982) (17)

§ Women 1950 cohort ($n = 757$); 1960 cohort ($n = 816$), 1970 cohort ($n = 834$).

|| Test for trend * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

¶ Other cardiovascular disease includes isolated transient ischemic attacks, congestive heart failure, intermittent claudication, and death from cardiovascular disease (other than coronary disease or stroke) as the first cardiovascular event.

Mortality from cardiovascular disease other than coronary heart disease or stroke.

†† Test for trend. $p = 0.054$.

‡‡ Men 1950 cohort ($n = 618$), 1960 cohort ($n = 586$), 1970 cohort ($n = 598$)

cardiovascular disease other than stroke ($p < 0.001$ for trend) followed by a 51 percent reduction in coronary heart disease mortality ($p < 0.01$ for trend). A 38 percent decline in stroke mortality also contributed to the overall decline; however the sample was too small to detect significance. The 53 percent decline in mortality in men was led by a 44 percent reduction in coronary heart disease mortality followed by an 87 percent reduction in death from cardiovascular disease other than coronary heart disease or stroke (both $p < 0.001$ for trend). The major portion of both of these reductions occurred between the 1960 and 1970 cohorts. The sample was again too small to detect the significance of the 35 percent decline in stroke mortality.

Table 2 displays the mix of diagnoses among the incident cases of coronary heart disease in each cohort. Among the female cohorts, the incidence of each diagnostic category of coronary heart disease declined except for myocardial infarction. Twenty-eight percent of all incident cases of coronary heart disease were diagnosed as myocardial infarction in the 1950 and 1960 cohorts compared with 40 percent in the 1970 cohort ($p < 0.05$ by the chi-square test). While the incidence of myocardial infarction fell between the

1950 and 1960 cohorts and then rose 37 percent between the 1960 and 1970 cohorts, the proportion of Q-wave infarctions in each cohort remained constant at 87–89 percent ($p > 0.50$ by the chi-square test). There was no significant change in any diagnostic category of coronary heart disease among the male cohorts.

Table 3 compares the trends in incidence and mortality during the two 10-year follow-up periods of each cohort. Among women, the 21 percent decline in 20-year incidence was made up of an 11 percent decline during the first 10 years of follow-up and a 31 percent decline during the second 10 years ($p < 0.01$ for trend). The major decline (26 percent, $p < 0.01$) occurred between the 1950 and 1960 cohorts during the second 10 years of follow-up, i.e., between 1960–1969 and 1970–1979.

More than one half of the mortality decline among women occurred during the second 10 years of follow-up (64 percent, $p < 0.001$ for trend). This decline was made up of a 42 percent reduction between the 1950 and 1960 cohorts ($p < 0.01$) followed by a 36 percent reduction between the 1960 and 1970 cohorts ($p < 0.05$). A reduction in mortality from cardiovascular disease other than coronary heart dis-

TABLE 2. Incident cases of coronary heart disease during 20 years of follow-up for women and men aged 50–59 years at baseline, the Framingham Heart Study, 1950–1989

Endpoint	1950 cohort		1960 cohort		1970 cohort	
	Kaplan-Meier rate/1,000 persons*	No of cases	Kaplan-Meier rate/1,000 persons	No. of cases	Kaplan-Meier rate/1,000 persons	No of cases
<i>Women†</i>						
Coronary heart disease	218	145	184	127	175	126
Myocardial infarction	61	35	51	33	70	46‡
Q-wave	52	32	46	29	61	40
Sudden death (<1 hour)	14	8	20	12	3	2
Non-sudden death	4	2	4	3	0	0
Angina pectoris	138	91	99	66	107	75
Coronary insufficiency	16	9	21	13	4	3
<i>Men§</i>						
Coronary heart disease	354	184	357	174	346	172
Myocardial infarction	191	85	199	86	195	87
Q-wave	172	77	171	73	161	71
Sudden death (<1 hour)	35	14	36	16	25	10
Non-sudden death	5	2	9	4	11	3
Angina pectoris	160	79	137	60	148	63
Coronary insufficiency	10	4	22	8	12	5

* Kaplan-Meier rates in the subcategories will not equal the total because of censoring (see J. F. Lawless Statistical models and methods for lifetable data. New York: John Wiley & Sons, Inc, 1982) (17).

† Women: 1950 cohort ($n = 757$); 1960 cohort ($n = 816$); 1970 cohort ($n = 834$).

‡ $p = 0.05$ (by chi-square test) for the difference between cohorts in the proportion of incident cases diagnosed as myocardial infarction. All trends are nonsignificant at $p \geq 0.10$.

§ Men: 1950 cohort ($n = 618$); 1960 cohort ($n = 586$); 1970 cohort ($n = 598$).

|| $p < 0.05$ (by chi-square test) for the difference between cohorts in the proportion of Q-wave infarctions.

TABLE 3. Cardiovascular disease incidence and mortality during 20 years of follow-up (the first 10 years among women and men aged 50–59 years vs. the second 10 years among women and men aged 60–69 years), the Framingham Heart Study, 1950–1989

Endpoint	1950 cohort		Test for difference in rates between adjoining cohorts†	1960 cohort		Test for difference in rates between adjoining cohorts	1970 cohort		% of change between 1950 and 1970 cohorts
	Kaplan-Meier rate/1,000 persons‡	No. of cases		Kaplan-Meier rate/1,000 persons	No. of cases		Kaplan-Meier rate/1,000 persons	No. of cases	
<i>Women§</i>									
Cardiovascular disease incidence									
First 10 years	162	120		140	109		144	116	-11
Second 10 years	252	147	**	187	114		175	108	-31**,
Cardiovascular disease mortality									
First 10 years	33	24		25	19		18	14	-46
Second 10 years	118	79	**	69	47	*	43	30	-64***
Coronary heart disease mortality									
First 10 years	14	10		12	9		13	10	-7
Second 10 years	56	36		43	29	*	22	15	-61**
Stroke mortality									
First 10 years	7	5		1	1		5	4	—¶
Second 10 years	22	14		17	11		13	9	-41
Other cardiovascular disease mortality#									
First 10 years	12	9		12	9			0	—
Second 10 years	45	29	***	11	7		9	6	-80***
<i>Men††</i>									
Cardiovascular disease incidence									
First 10 years	262	158		233	132		216	124	-18*
Second 10 years	335	136		361	142		334	133	-0.3
Cardiovascular disease mortality									
First 10 years	87	52		78	44	***	30	17	-66***
Second 10 years	178	88		149	70	**	90	42	-49***
Coronary heart disease mortality									
First 10 years	56	33		54	30	*	30	17	-46*
Second 10 years	111	55		96	44		62	29	-44**
Stroke mortality									
First 10 years	9	5		7	4		0		—
Second 10 years	25	11		30	14		22	9	-12
Other cardiovascular disease mortality									
First 10 years	24	14		18	10		0		—
Second 10 years	49	22		29	12	*	9	4	-82***

† Test for difference in rates between adjoining cohorts. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

‡ Kaplan-Meier rates in the subcategories will not equal the total because of censoring (see J. F. Lawless. Statistical models and methods for lifetable data. New York: John Wiley & Sons, Inc, 1982) (17).

§ Women: 1950 cohort, first 10 years ($n = 757$) versus second 10 years ($n = 667$); 1960 cohort, first 10 years ($n = 816$) versus second 10 years ($n = 680$); 1970 cohort, first 10 years ($n = 834$) versus second 10 years ($n = 742$).

|| Test for trend * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

¶ —, percentage of change not calculated because of small sample size

Mortality from cardiovascular disease other than coronary heart disease or stroke.

†† Men: 1950 cohort, first 10 years ($n = 818$) versus second 10 years ($n = 510$); 1960 cohort, first 10 years ($n = 586$) versus second 10 years ($n = 486$); 1970 cohort, first 10 years ($n = 598$) versus second 10 years ($n = 509$)

ease and stroke led the decline between the 1950 and 1960 cohorts, while a reduction in coronary heart disease mortality led the decline between the 1960 and 1970 cohorts.

Although there was no significant decline in the 20-year incidence of cardiovascular disease among the male cohorts, there was a significant 18 percent decline during the first 10 years of follow-up ($p < 0.05$ for trend) followed by a 0.3 percent decline during the

second 10 years. Cardiovascular disease mortality declined in both follow-up periods: 66 percent during the first 10 years and 49 percent during the second 10 years (both $p < 0.001$ for trend). Gains during each 10-year period were due to significant mortality reductions that occurred between the 1960 and 1970 cohorts.

Figures 1–4 graphically depict these sex, time, and cohort differences in cardiovascular disease incidence

and mortality. The survival curves for 20-year cardiovascular disease incidence were significantly different for women in the three cohorts (figure 1, $p = 0.003$ by log-rank test) with the greatest difference occurring during the second 10 years of follow-up of the 1950 and 1960 cohorts. The survival curves for 20-year cardiovascular mortality were also significantly different (figure 2, $p < 0.0001$ by log-rank test). Again, the greatest difference occurred during the second 10 years of follow-up of the 1950 and 1960 cohorts.

The survival curves for 20-year cardiovascular disease incidence were not significantly different for the three male cohorts (figure 3, $p = 0.36$ by log-rank test). However, the differences in survival curves for cardiovascular disease mortality were significant (figure 4, $p < 0.0001$ by log-rank test) with the greatest difference occurring between the 1960 and 1970 cohorts during both 10-year follow-up periods.

Table 4 presents the prevalence of risk factors at the baseline of each cohort and 10 years later (i.e., at the beginning of the second 10-year follow-up period for each cohort). Women in the 1970 cohort showed significantly better risk factor profiles at the start of each 10-year follow-up period when compared with women in the 1950 cohort, except for cigarette smoking and diabetes mellitus. The prevalence of cigarette smoking at baseline increased by 20 percent between the 1950 and 1970 cohorts ($p < 0.001$ for trend). At the start of the second 10 years of follow-up, smoking continued to be higher in the 1970 female cohort compared with the 1950 cohort ($p < 0.001$ for trend); however, it was reduced by 14 percent from what it had been at baseline (31 percent compared with 45 percent). The prevalence of diabetes mellitus was significantly higher at

the baseline of the 1970 cohort compared with that of the 1950 cohort. At the start of the second 10 years of follow-up, it was still higher for women in the 1970 cohort, but the difference was not significant.

The prevalences of obesity, hypercholesterolemia, and high blood pressure were significantly lower at baseline and 10 years later for women in the 1970 cohort compared with the 1950 cohort. The prevalence of high blood pressure fell from 32 percent at baseline in the 1950 cohort to 12 percent in the 1970 cohort ($p < 0.001$ for trend). At the start of the second 10 years of follow-up, the difference was even greater, falling from 35 percent in the 1950 female cohort to 9 percent in the 1970 cohort. While the use of antihypertension medication rose significantly to 11 percent at the baseline of the 1970 cohort ($p < 0.001$ for trend), at the start of the second 10 years of follow-up, its use doubled between the 1950 and 1970 cohorts (from 17 percent to 33 percent).

The prevalence of cigarette smoking and high blood pressure improved significantly between men in the 1950 and 1970 cohorts. Improvements were found at baseline and 10 years later. Cigarette smoking declined from 56 percent at the baseline of the 1950 cohort to 44 percent in the 1970 cohort ($p < 0.001$ for trend) and continued to decline in the 1970 cohort to 26 percent at the start of the second 10 years of follow-up ($p < 0.001$ for trend). The prevalence of high blood pressure at baseline decreased from 26 percent in the 1950 cohort to 16 percent in the 1970 cohort ($p < 0.001$ for trend). The prevalence continued to be lower among men in the 1970 cohort at the start of the second 10 years of follow-up (10 percent). The use of antihypertension medication was low

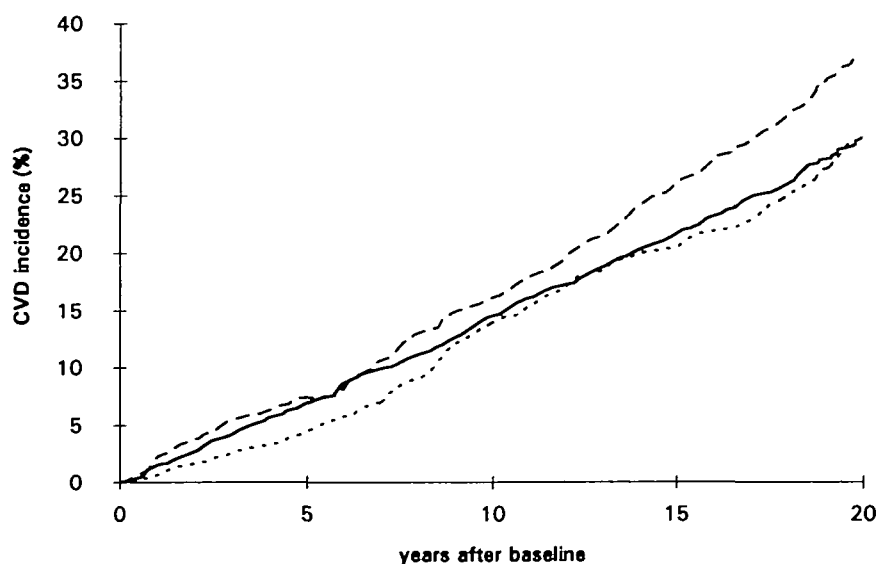


FIGURE 1. Twenty-year cardiovascular disease (CVD) incidence in the 1950, 1960, and 1970 female cohorts, Framingham Heart Study. Dashed line, 1950 cohort; dotted line, 1960 cohort; solid line, 1970 cohort.

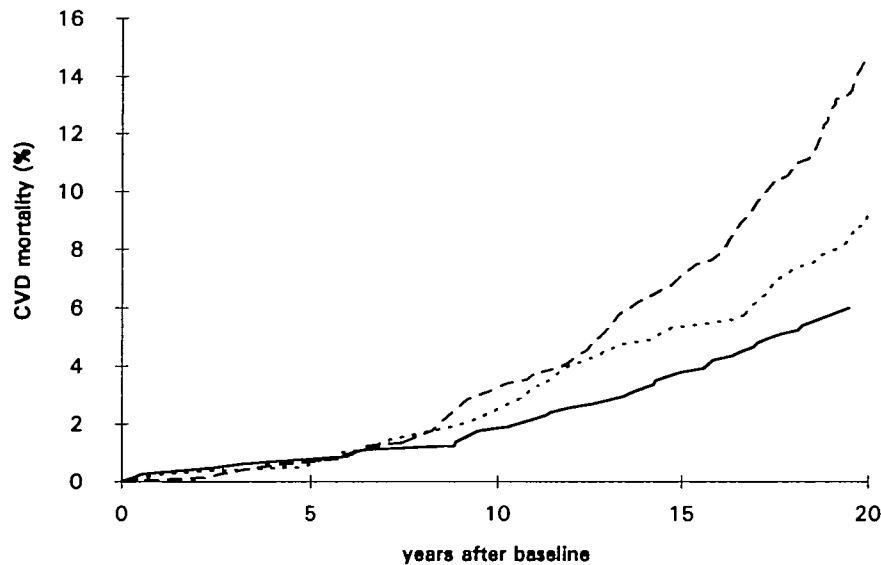


FIGURE 2. Twenty-year cardiovascular disease (CVD) mortality in the 1950, 1960, and 1970 female cohorts, Framingham Heart Study. Dashed line, 1950 cohort; dotted line, 1960 cohort; solid line, 1970 cohort.

among men at the baseline of each cohort. However, at the start of the second 10-year period, use tripled from 10 percent of hypertensives in the 1950 male cohort to 29 percent in the 1970 cohort.

The prevalence of obesity at baseline rose significantly between men in the 1950 and 1970 cohorts ($p < 0.05$ for trend). There was also an increase between the cohorts at the start of the second 10 years, but it was not significant. While there was no significant difference in the prevalence of hypercholesterolemia at the baseline of the cohorts, at the start of the second 10 years of follow-up, prevalence declined

from 48 percent in the 1950 cohort to 37 percent in the 1970 cohort ($p < 0.01$ for trend).

Estimated contribution of risk factor trends to the decline in coronary heart disease mortality

We used two models (18) to ascertain the contribution of these trends in risk factors to the declines in coronary heart disease mortality observed between 1950 and 1989 among women and men in this study. The baseline risk factor levels were used in conjunction with sex-specific logistic regression coefficients

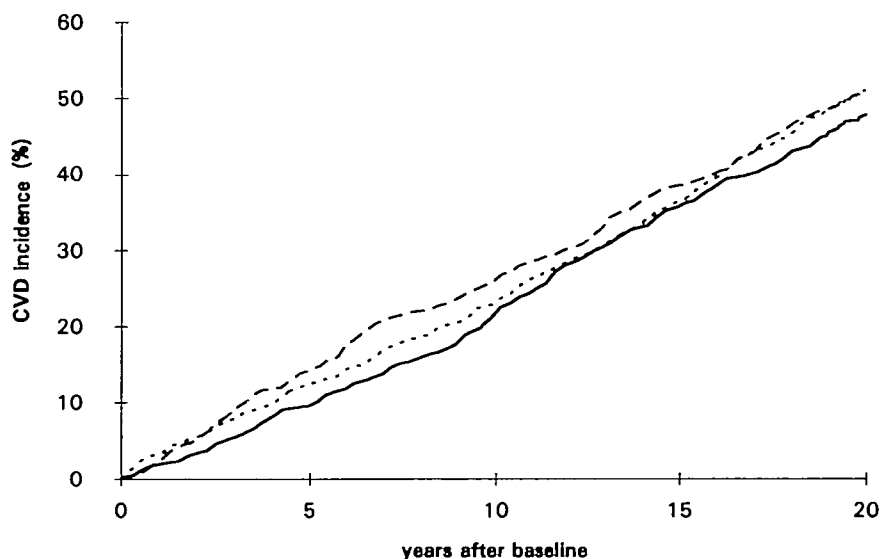


FIGURE 3. Twenty-year cardiovascular disease (CVD) incidence in the 1950, 1960, and 1970 male cohorts, Framingham Heart Study. Dashed line, 1950 cohort; dotted line, 1960 cohort; solid line, 1970 cohort.

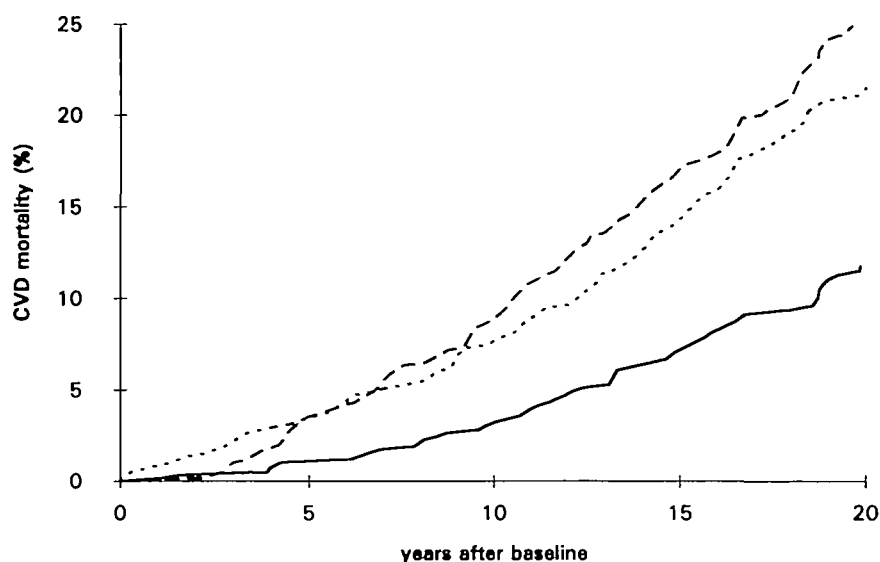


FIGURE 4. Twenty-year cardiovascular disease (CVD) mortality in the 1950, 1960, and 1970 male cohorts, Framingham Heart Study. Dashed line, 1950 cohort; dotted line, 1960 cohort, solid line, 1970 cohort.

to compute a predicted probability of death from coronary heart disease for members of the 1950, 1960, and 1970 cohorts. These probabilities were summed to produce a predicted 10-year mortality rate for each cohort. The rates were compared, and a "predicted decline" between 1950–1959 and 1970–1979 was calculated. A similar procedure was used (only with risk factors from the start of the second 10 years of follow-up) to predict the decline between 1960–1969 and 1980–1989. Table 5 presents the results.

The Framingham risk model and the National Health and Nutrition Examination Survey Epidemiologic Follow-up Study model predicted similar results. The models predicted a 27–32 percent reduction in mortality during the first 10 years of the follow-up of women in the 1970 cohort compared with the 1950 cohort and a 29–32 percent reduction during the second 10 years. All of the 7 percent decline in coronary heart disease mortality observed in the first 10 years and more than half of the 61 percent decline observed in the second 10 years could be attributed to improvements in risk factors between women in the 1950 and 1970 cohorts.

For men in this study, the models predicted a 15–17 percent mortality reduction during the first 10 years of follow-up of the 1950 and 1970 cohorts and a 20–22 percent reduction during the second 10 years. Improvements in the risk factors between men in the 1950 and 1970 cohorts could account for approximately one third of the 46 percent decline in coronary heart disease mortality observed during the first 10 years of follow-up and approximately half of the 44 percent decline observed during the second 10 years.

DISCUSSION

Variations in the decline in cardiovascular mortality by sex, time, and region underscore the multiple factors contributing to the manifestation of cardiovascular disease. While men are more genetically susceptible than women, they share with women the same biologic markers of risk: high blood pressure, hypercholesterolemia, and diabetes mellitus (19). Behavioral and environmental factors, such as cigarette smoking, hypertension control, dietary habits, availability and use of medical care resources, and socioeconomic forces within a community, can raise or lower the risk associated with these genetic and biologic factors. Together, these factors contribute to changes in the incidence and case-fatality rates that, in turn, determine the extent of population declines in mortality.

Sex differences in incidence trends

Pell and Fayerweather (20) reported a 28 percent decline in the incidence of acute myocardial infarction among male DuPont employees between 1960 and 1970. There was no trend for women employees. The incidence of coronary heart disease declined 11 percent for men and increased 9 percent for women in Rochester, Minnesota, between 1965–1969 and 1979–1982 (21). The incidence of myocardial infarction declined 20 percent for men and increased 17 percent for women. Goldberg et al. (22) reported a 10 percent increase in acute myocardial infarction between 1975 and 1981 among men and women in the Worcester Heart Attack Study. This increase was accompanied by a 21 percent reduction in Q-wave infarctions. Over

TABLE 4. Prevalence of risk factors at baseline of each cohort and 10 years later, the Framingham Heart Study, 1950-1989

Cohort	Mean age (years)		Cigarette smoking (%)		Pack-years†		Obesity (%)‡		Body mass index (weight (kg)/height (m) ²)		Hypercholesterolemia (%)§	
	Baseline	10 years later	Baseline	10 years later	Baseline	10 years later	Baseline	10 years later	Baseline	10 years later	Baseline	10 years later
1950	54 (3)††	64 (3)	25	25	10 (11)	3 (9)	62	55	27.1	27.0	57	70
1960	54 (3)	64 (3)	36	24	16 (13)	7 (14)	47	48	25.6	26.3	65	60
1970	55 (3)*	65 (3)	45***	31***	25 (15)***	11 (19)***	44***	49	25.5***	26.6	47***	55***
					Women#							
					Men‡‡							
1950	54 (3)	64 (3)	56	47	34 (21)	21 (27)	49	50	26.0	26.0	34	48
1960	55 (3)	64 (3)	53	33	37 (21)	17 (28)	54	51	26.0	26.5	48	39
1970	54 (3)	64 (3)	44***	26***	42 (20)***	14 (27)***	58*	56	26.7***	27.3***	36	37**
					Systolic blood pressure (mmHg)		Diastolic blood pressure (mmHg)		Hypertension medication (%)¶		Diabetes mellitus (%)¶¶	
					Baseline	10 years later	Baseline	10 years later	Baseline	10 years later	Baseline	10 years later
1950	252 (47)	268 (46)	32	35	153 (30)	152 (28)	91 (14)	87 (14)	0	17	2.9	5.7
1960	258 (43)	253 (43)	20	26	138 (24)	144 (23)	84 (13)	81 (12)	11	21	2.2	9
1970	241 (42)***	248 (42)***	12***	9***	131 (20)***	135 (19)***	80 (11)***	77 (9)***	11***	33***	5.9**	7.4
					Women							
					Men							
1950	226 (42)	238 (42)	26	24	143 (24)	142 (26)	88 (14)	84 (13)	0	10	3.7	6.3
1960	240 (39)	225 (41)	18	23	135 (21)	142 (21)	85 (12)	82 (11)	4	13	3.4	14.4
1970	227 (40)	227 (39)***	16***	10***	135 (20)***	137 (19)***	83 (11)***	80 (10)***	7***	29***	6.1*	10*

* p < 0.05; ** p < 0.01; *** p < 0.001 (test for trend).

† Pack-years defined as (number of cigarettes per day x number of years smoking)/20

‡ Weight ≥ 120% of the US mean for sex, age, and height (Metropolitan Life Insurance data).

§ Total cholesterol ≥ 240 mg/dl (≥ 6.206 mmol/liter); 1970 data adjusted by 3% to account for the use of plasma rather than serum cholesterol.

¶ Systolic blood pressure ≥ 160 mmHg or diastolic blood pressure ≥ 95 mmHg (or both).

¶¶ Under treatment for diabetes, abnormal glucose tolerance test, or at least two examinations with a casual blood glucose determination of at least 150 mg/100 ml. # Women: 1950 cohort, baseline (n = 715), 10 years later (n = 667); 1960 cohort, baseline (n = 786), 10 years later (n = 680); 1970 cohort, baseline (n = 750), 10 years later (n = 742).

†† Numbers in parentheses, standard deviation.

‡‡ Men: 1950 cohort, baseline (n = 598), 10 years later (n = 598); 1960 cohort, baseline (n = 510); 1970 cohort, baseline (n = 572), 10 years later (n = 486); 1970 cohort, baseline (n = 561), 10 years later (n = 509).

TABLE 5. Percentage of observed decline in coronary heart disease mortality "attributable" to risk factor changes, the Framingham Heart Study, 1950-1989

Predictive model by period	Observed decline (%)	Predicted decline (%)*	Observed change attributable to risk factor change (%)
<i>Women</i>			
Framingham risk model†			
1950-1959 to 1970-1979	-7	-32	100
1960-1969 to 1980-1989	-61	-32	53
NHEFS‡			
1950-1959 to 1970-1979	-7	-26	100
1960-1969 to 1980-1989	-61	-29	48
<i>Men</i>			
Framingham risk model			
1950-1959 to 1970-1979	-46	-17	37
1960-1969 to 1980-1989	-44	-20	46
NHEFS			
1950-1959 to 1970-1979	-46	-15	33
1960-1969 to 1980-1989	-44	-22	50

* Risk factors (age, systolic blood pressure, smoking, total cholesterol, and diabetes mellitus) for each cohort member were entered into the sex-specific logistic regression model from each study to compute a predicted probability of coronary heart disease death in 10 years.

† Framingham risk model for coronary heart disease mortality (P. E. Leaverton et al J Chronic Dis 1987;40:775-84) (18).

‡ NHEFS, National Health and Nutrition Examination Survey I Epidemiologic Follow-up Study risk model for coronary heart disease mortality (18).

Potential bias introduced by changes in disease detection

Changes in diagnostic practices over time are a potential source of bias in long-term studies of disease incidence and mortality. The Framingham Heart Study has tried to protect itself from this bias by keeping case ascertainment methods constant and by consistently applying event criteria that have changed little since the start of the Study in 1948. However, with the increased use of cardiac enzymes to diagnose myocardial infarction and the introduction of computed tomographic scans to diagnose stroke, the quality and quantity of information available to the practicing physician have changed. The increased diagnostic sensitivity afforded by the routine availability of computed tomographic scans in the late 1970s could have increased the detection of milder strokes and may have contributed to the decline in stroke severity reported by Wolf et al. (24).

Cardiac enzymes may increase the sensitivity of the diagnosis of myocardial infarction (25), thereby influencing trends in incidence and mortality. However, we found no evidence that the increased use of cardiac enzymes explained the rise in incidence of myocardial infarction among women in the 1970 cohort. Diagnoses were based on electrocardiographic changes in more than 87 percent of the cases in each cohort, while diagnoses were based on enzymes and history, without electrocardiographic changes, in 6 percent of the cases in the 1950 cohort, 12 percent in the 1960 cohort, and only 4 percent of the cases in the 1970 cohort. There was no reduction in the incidence of Q-wave infarction across the cohorts that would indicate less severe disease. Among the male cohorts, however, there was increased use of enzymes (6) and a reduced incidence of Q-wave infarctions. Thus, if there was increased detection of smaller or less severe infarctions, it may have occurred among the men but not the women in this study. This would be consistent with published reports of sex bias in the use of new diagnostic and therapeutic technologies (26).

Sex and time differences in mortality

The time of onset and magnitude of the decline in coronary heart disease mortality have varied by sex (2, 4, 5). In most regions of the country, the decline occurred between 1968 and 1975 in men, while it occurred between 1958 and 1975 in women (5). Nationally, the decline was greater for women (30 percent) than for men (26 percent) (3). Among women, the mortality decline occurred in both the acute and chronic components of coronary heart disease, while in men, the decline was concentrated in the acute component (3).

the entire period 1975-1984, there was a 27 percent decline in myocardial infarction (23).

In the present study, the incidence of cardiovascular disease over 20 years of follow-up declined 21 percent among women. The greatest decline occurred between the 1950 and 1960 female cohorts because of the reduced incidence of both coronary heart disease and stroke. The decline in incidence of stroke among women in the Framingham Study has been reported by Wolf et al. (24); however, this is the first report of a decline in coronary heart disease among women in that study. Reduced incidence was associated with declines in sudden death, angina pectoris, and coronary insufficiency as well as increased incidence of myocardial infarction in the 1970 cohort. Among men, the 20-year incidence of cardiovascular disease declined only 6 percent. Previously (6), we reported an 18 percent decline after 10 years of follow-up. This was followed by a 0.3 percent decline during the second 10-year period. The incidence of coronary heart disease and of myocardial infarction changed little in men between 1950 and 1989.

The DuPont study found that 24-hour and 30-day case fatality rates declined 30 percent during the period 1969–1983 (20). Case fatality in the Worcester Heart Attack Study decreased 32 percent between 1975 and 1984 with out-of-hospital deaths from coronary heart disease falling 44 percent (23). These survival gains have not just been short term. The Minnesota Heart Study (27) reported a 35 percent increase in long-term (4-year) survival from myocardial infarction for men and a 27 percent increase for women between 1970 and 1980. Seventy percent of the male improvement and all of the female improvement were due to lower in-hospital mortality.

In the present study, 20-year cardiovascular disease mortality declined 59 percent between the 1950 and 1970 female cohorts and 53 percent between the male cohorts. There were sex differences in the timing of the largest mortality decline and in the type of disease leading the decline. Among women, more than one half of the decline in mortality occurred during the second 10 years of follow-up. The decline between the 1950 and 1960 cohorts was led by reduced mortality from other cardiovascular disease, while the majority of the decline in coronary heart disease mortality occurred later, between the 1960 and 1970 female cohorts. Among men, cardiovascular disease mortality declined 66 percent during the first 10 years of follow-up (6) and another 49 percent during the second 10 years. There were declines in coronary heart disease mortality of over 40 percent during both follow-up periods. In both cases, the major mortality reductions occurred between the 1960 and 1970 cohorts.

Compressed mortality

Studies of the decline in cardiovascular mortality have given rise to the issue of compressed morbidity and mortality (28–30). At issue is whether the mortality decline indicates a real gain in healthy life or whether death is merely delayed or shifted to another cause. On the basis of the present analyses, it cannot be determined whether the small 20-year decline in incidence among men reflects increased detection of disease, a delay and compression of morbidity, or a real reduction in disease. However, the analyses do indicate that cardiovascular mortality among men and women was not delayed or shifted to other causes. Cardiovascular mortality declined 46 percent or more for men and women in each of the 10-year follow-up periods. All-cause mortality over 20 years (table 1) declined 17 percent across the female cohorts ($p = 0.054$ for trend) and 18 percent across the male cohorts ($p < 0.001$ for trend).

Risk factor trends

Risk factors have improved nationally. The National Center for Health Statistics reported that both systolic blood pressure and serum cholesterol levels improved for men and women between 1960 and 1980 (31–33). The decline in serum cholesterol has continued through 1991 with more than half occurring in the period 1974–1991 (34). The Minnesota Heart Survey (35) reported decreases in systolic and diastolic blood pressure and serum cholesterol among men and women between 1980–1982 and 1985–1987, and the Minnesota Heart Health Program reported secular trends in risk factors between 1980 and 1990 (36). Systolic blood pressure declined 6.3 mmHg, and cholesterol declined 9 mg/dl among men and women, while smoking decreased 11.3 percent among men.

In the present study, we found secular trends and sex differences in the prevalence of biologic and behavioral risk factors across the cohorts. Improvements in baseline risk factor levels were observed between the 1950 and 1970 cohorts, and these improvements continued 10 years later. Systolic and diastolic blood pressure decreased significantly across the male and female cohorts as did the prevalence of high blood pressure. While the prevalence of high blood pressure was similar in women and men in each cohort, the use of antihypertension medication among men lagged behind such use among women until the second follow-up period of the 1970 cohort (i.e., 1980–1989). The prevalence of hypercholesterolemia declined by 10 percent or more between women in the 1950 and 1970 cohorts but was consistently higher than prevalence in men. Cigarette smoking decreased during each follow-up period of the male cohorts in 1960 and 1970, apparently reflecting the impact of the Surgeon General's report in 1965. Increased smoking among women in these cohorts, on the other hand, appears to indicate a lack of concern about this threat to women's health. The prevalence of obesity decreased as smoking increased between the 1950 and 1970 female cohorts, and obesity rose with the decreased prevalence of smoking between the male cohorts. These opposite trends found between men and women in this study appear to reflect the inverse correlation of obesity with smoking. The Minnesota Heart Survey also reported an increased body mass index with a decreased prevalence of smoking (35).

There is strong evidence that secular trends in risk factors have contributed to the decline in cardiovascular and coronary mortality (6, 35). Walker (37) was among the first to note that the first decline in age-specific coronary heart disease mortality was accompanied by a decline in cigarette smoking and in dietary risk factors along with more effective treatment of

hypertension. Goldman and Cook (38) estimated that risk factor changes accounted for 54 percent of the 21 percent decline in ischemic heart disease mortality between 1968 and 1976. Improvements in risk factors explained between 16 and 46 percent of the decline in coronary heart disease mortality among men and between 19 and 100 percent of the decline among women that occurred in 1973–1987 in Minnesota (35). In this study, we estimate that secular trends in risk factors could account for 50 percent or more of the decline in coronary mortality observed between 1950 and 1989 among women and for 33–50 percent of the decline observed among men.

The search for causes of the decline in mortality has focused on the relative contribution of changes in incidence and changes in case fatality rates. It has been assumed that reduced incidence would be due to primary prevention through improved risk factors, while reduced case fatality rates would point to the increased use of medical interventions (20, 22). However, the issues are far more complex. Risk factors play an important role in the natural history of cardiovascular disease affecting both its incidence and its prognosis (39). Medical interventions, on the other hand, can influence the incidence, presentation, and case fatality rates (40). Further studies are needed to evaluate sex and time differences in the relative contribution of risk factors and of the use of medical interventions to changes in the incidence and case fatality rates.

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