Temporal Trends in Coronary Heart Disease Mortality and Sudden Cardiac Death From 1950 to 1999

The Framingham Heart Study

Caroline S. Fox, MD, MPH; Jane C. Evans, DSc; Martin G. Larson, ScD; William B. Kannel, MD, MPH; Daniel Levy, MD

Background—Throughout the past 50 years, heart disease has been the leading cause of death in the United States. Although declines in coronary heart disease (CHD) mortality have been noted, there is still uncertainty about the magnitude of the decline and whether the trend is similar for sudden cardiac death (SCD).

Methods and Results—We examined temporal trends in SCD and nonsudden CHD death in the Framingham Heart Study original and offspring cohorts from 1950 to 1999. SCD was defined as a death attributed to CHD with preceding symptoms that lasted less than 1 hour; all deaths were adjudicated by a physician panel. Log-linear Poisson regression was used to estimate CHD mortality and SCD risk ratios (RRs); RRs were adjusted for age and gender. There were 811 CHD deaths: 453 nonsudden and 358 SCDs. Ninety-one (20%) of nonsudden CHD deaths and 173 (48%) of SCDs were in subjects free of antecedent CHD. From 1950–1969 to 1990–1999, overall CHD death rates decreased by 59% (95% CI 47% to 68%, \( P_{\text{trend}} < 0.001 \)). Nonsudden CHD death decreased by 64% (95% CI 50% to 74%, \( P_{\text{trend}} < 0.001 \)), and SCD rates decreased by 49% (95% CI 28% to 64%, \( P_{\text{trend}} < 0.001 \)). These trends were seen in men and women, in subjects with and without a prior history of CHD, and in smokers and nonsmokers.

Conclusions—The risks of SCD and nonsudden CHD mortality have decreased by 49% to 64% over the past 50 years. These trends were evident in subjects with and without heart disease, which suggests important contributions of primary and secondary prevention to the decreasing risk of CHD death and SCD. (Circulation. 2004;110:522-527.)

Key Words: coronary disease ■ death, sudden ■ epidemiology ■ prevention

Throughout the past 50 years, heart disease has been the leading cause of death in the United States. Despite substantial declines, coronary heart disease (CHD) still accounts for nearly 700,000 deaths per year in the United States, and sudden cardiac death (SCD) accounts for almost half of all CHD deaths, constituting the largest component of CHD mortality. SCD is often the first and only manifestation of CHD, highlighting the importance of primary prevention efforts.

Whereas marked reductions have been documented in CHD mortality and out-of-hospital CHD death, most of the data describing trends in CHD mortality and SCD are based on relatively short-term follow-up, and classification of death is often made with death certificates. Lack of uniformity in death certificate designation of cause of death and changes in International Classification of Disease coding limit the accuracy of estimates of long-term trends in CHD death and SCD. Although out-of-hospital CHD death by death certificate is often used as a proxy for SCD, it has been shown to overestimate SCD. Because the location of death is a critical component in defining out-of-hospital CHD death, and because coding of location of death on the death certificate has changed recently, trends in out-of-hospital CHD death based on death certificates cannot be assessed accurately in the long term.

Most trend analyses of SCD and nonsudden CHD death have focused on narrow windows of time to avoid these methodological issues. Thus, the magnitude of the decline in mortality over the long term is not known. The Framingham Heart Study provides a unique setting in which long-term trends in CHD death and SCD can be studied. In addition to 50 years of observational data, all deaths have been ascertained uniformly and adjudicated by a physician panel, which eliminates reliance on death certificates as a means of designating cause of death.

Methods

Cases of CHD death were identified during the entirety of follow-up of Framingham Heart Study participants. Beginning in 1948, 5209...
men and women aged 28 to 62 years were enrolled in the study. Offspring and spouses of offspring or the original cohort were enrolled in the study starting in 1971. Selection criteria and study design have been described. The standard clinic examination included an interview, a physical examination, and laboratory tests. Cardiovascular events, including all hospitalizations and deaths, were documented throughout follow-up by daily hospital and death surveillance. The study sample consisted of all original and offspring cohort participants who had a nonsudden CHD death or a sudden cardiac death from 1950 through 1999. Deaths were examined in relation to whether subjects had preexisting CHD or congestive heart failure (CHF).

A panel of 3 physicians reviewed each cardiovascular event according to preestablished criteria. CHD death included both nonsudden deaths due to CHD (ie, >1 hour after onset of symptoms) and SCD. SCD was defined as a CHD death that occurred within 1 hour of the onset of symptoms and that had no other probable cause of death suggested by the medical record; the definition of SCD has not changed since the inception of the study. Each death underwent an internal review that attempted to determine the duration of symptoms, if any, before death. Hospital records, primary medical doctor records, and next-of-kin interviews were routinely sought to determine the timing of symptoms before death. Subjects found dead in bed were not considered SCD cases when the interval between the time the subject was witnessed to be alive and symptom free and the time found dead in bed could not be determined with certainty to be less than 1 hour. Subjects who experienced out-of-hospital cardiac arrest and were resuscitated were not included in the primary analyses because this information was not routinely collected in the early 1990s. Previous CHD included a history of angina, coronary insufficiency (unstable angina with ischemic ECG changes), and recognized myocardial infarction. Criteria for CHF have been published. Subjects with a systolic blood pressure ≥140 mm Hg or a diastolic blood pressure ≥90 mm Hg (average of 2 readings taken by the examining physician) or who were taking antihypertensive medication were defined as hypertensive. Lipid measures included total cholesterol. Smoking status was defined as current smoking (yes/no). Body mass index was defined as weight (kilograms) divided by the square of height (meters). Diabetes was diagnosed by either a fasting plasma glucose ≥126 mg/dL, a nonfasting plasma glucose ≥200 mg/dL, or treatment with either insulin or an oral hypoglycemic agent. Recognized cardiac disease was used (PROC GENMOD in SAS). Likelihood ratio statistics were used to test the null hypothesis that the rates of CHD death, nonsudden CHD death, and SCD were identical in all time periods. This 2-decade period was selected to be the referent group because of relatively small numbers of events in either decade alone. Age- and gender-adjusted incidence rates of CHD death, nonsudden CHD death, and SCD (per 100 000 person-years of observation) were calculated for each time period; Poisson regression was used (PROC GENMOD in SAS). Likelihood ratio statistics were used to test the null hypothesis that the rates of CHD death, nonsudden CHD death, and SCD were identical in all time periods. We estimated RR and 95% CIs for each subsequent decade compared with 1950 to 1969; RR were adjusted for age and gender. Decade-specific RRs were first calculated for the overall sample. Prespecified subgroup analyses were conducted to examine whether the time period effects differed by (1) prior history of CHD or CHF (yes/no) and (2) gender (male versus female). Stratification by current smoking status (yes/no) was additionally examined. CHD and CHF were included together to identify participants with preexisting heart disease, to explore differences with regard to primary and secondary prevention (ie, declines in participants without a prior history of CHD or CHF suggest effects of primary prevention, whereas declines in participants with a prior history of CHD or CHF may be attributable to secondary prevention). Trend analyses across the 4 time periods were performed. In secondary analyses, we incorporated resuscitated SCDs from the 1990s (n = 12) and compared this RR to data from the 1950 to 1969 time period.

To reduce the influence of aging in the closed cohort in this study and to ensure that the age distributions across all decades overlapped, we restricted our analysis to subjects between ages 40 and 79 years. This age range was represented in all decades.

Results

From 1950 to 1999, there were 811 deaths attributed to CHD (571 men, 240 women); 453 (56%) were nonsudden CHD deaths (298 men, 155 women), and 358 (44%) were SCD events (273 men, 85 women). The characteristics of subjects at the time of death by time period are presented in Table 1. Twenty percent of nonsudden CHD deaths (91/453) and approximately half of the SCDs (173/358) occurred in subjects without a clinical history of CHD or CHF. In 1950 to 1969, the age- and gender-adjusted incidence rates for CHD death, nonsudden CHD death, and SCD (per 100 000 person-years of follow-up) were 470, 284, and 185, respectively, and decreased thereafter (Figure).

Overall, CHD death decreased by 59% from 1950–1969 to 1990–1999. There was a 64% decline in nonsudden CHD death from 1950–1969 to 1990–1999 (Table 2). In subjects without a prior history of CHD or CHF, the risk of nonsudden CHD death was 74% lower in 1990 to 1999, whereas in subjects with a prior history of CHD or CHF, the risk was 62% lower than in the referent period. The risk of nonsudden CHD death declined by 63% in men and by 66% in women. Nonsmokers experienced steeper declines than smokers (61% versus 44%).

The risk of SCD was 49% lower in 1990 to 1999 compared with 1950 to 1969 (Table 3). In subjects without a prior history of CHD or CHF, the SCD risk was 39% lower in 1990 to 1999, whereas in subjects with a prior history of CHD or CHF, the risk was 57% lower than in the referent period. The declines in men and women were almost equal (49% versus 47%). Smokers experienced steeper declines than nonsmokers (47% versus 33%).

We repeated analyses of trend after including 12 cases from 1990 to 1999 of participants who were resuscitated after a cardiovascular collapse and survived ≥1 hour. These 12 cases would likely have resulted in SCD were it not for attempted resuscitation. The RR for SCD in 1990 to 1999 compared with 1950 to 1969 was 0.62 (95% CI 0.45 to 0.86).
Risk factor profiles, by decade, for nonsudden CHD death, SCD, and the overall Framingham Heart Study sample are shown in Table 4. Mean systolic blood pressure, total cholesterol, and the prevalence of smoking declined over the time periods studied.

**Discussion**

The risks of SCD and nonsudden CHD mortality in the Framingham Heart Study have decreased by 49% to 64% since 1950 to 1969. These trends were evident in subjects with prior heart disease and in those without, which suggests important contributions of both primary and secondary prevention to the declines in CHD death and SCD.

The present study has advantages over most prior studies that have relied on death certificate ascertainment of CHD death and that used out-of-hospital CHD death as a proxy for SCD. Death certificates have been shown to overestimate CHD death by as much as 24%, and validation studies have shown that out-of-hospital CHD death assigned by death certificates overestimates SCD. Furthermore, this overestimation is markedly worse when more stringent definitions of SCD are used. Although vital statistics data and death certificates are accessible and inexpensive sources for classifying deaths in large epidemiological studies, their use may overestimate and misclassify CHD death and SCD. Reliance on death certificate data as a means of approximating CHD mortality and SCD will be accurate only if the proportion of false-positive classifications is known and remains constant over time.

To better understand the components of these observed declines in CHD death and SCD, we stratified cases in the present study by presence or absence of antecedent clinical heart disease. Subjects with preexisting CHD and CHF are at a significantly increased risk of CHD death and SCD; preexisting heart failure confers a 5-fold increased risk in SCD compared with the general population. By highlighting CHD death and SCD in subjects with and without known heart disease, we sought to explore differences with regard to primary and secondary prevention. Declines in CHD death and SCD rates in subjects without a prior clinical history of heart disease suggest beneficial contributions of primary prevention, whereas reductions in subjects with prior heart disease may reflect secondary prevention effects. Risk reduction estimates based on published literature have estimated that more than half of the decline in CHD mortality between 1968 and 1976 was attributable to lifestyle changes.

**TABLE 1. Characteristics of Subjects at the Time of Death**

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<tbody>
<tr>
<td>Total CHD deaths, n</td>
<td>286</td>
<td>241</td>
<td>193</td>
<td>91</td>
</tr>
<tr>
<td>Age, y</td>
<td>62±8</td>
<td>68±8</td>
<td>69±8</td>
<td>71±8</td>
</tr>
<tr>
<td>Male, %</td>
<td>72</td>
<td>65</td>
<td>74</td>
<td>73</td>
</tr>
<tr>
<td>Prior CHD or CHF, %</td>
<td>62</td>
<td>67</td>
<td>75</td>
<td>70</td>
</tr>
<tr>
<td>Nonsudden CHD</td>
<td>156</td>
<td>139</td>
<td>113</td>
<td>45</td>
</tr>
<tr>
<td>deaths, n</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>63±8</td>
<td>68±8</td>
<td>69±8</td>
<td>72±8</td>
</tr>
<tr>
<td>Male, %</td>
<td>66</td>
<td>63</td>
<td>68</td>
<td>69</td>
</tr>
<tr>
<td>Prior CHD or CHF, %</td>
<td>69</td>
<td>82</td>
<td>88</td>
<td>91</td>
</tr>
<tr>
<td>Total SCD, n</td>
<td>130</td>
<td>102</td>
<td>80</td>
<td>46</td>
</tr>
<tr>
<td>Age, y</td>
<td>61±8</td>
<td>68±8</td>
<td>67±8</td>
<td>70±8</td>
</tr>
<tr>
<td>Male, %</td>
<td>80</td>
<td>68</td>
<td>81</td>
<td>76</td>
</tr>
<tr>
<td>Prior CHD or CHF, %</td>
<td>53</td>
<td>47</td>
<td>56</td>
<td>50</td>
</tr>
</tbody>
</table>

**TABLE 2. RRs and 95% CIs for Nonsudden CHD Death by Decade of Interest**

<table>
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<tbody>
<tr>
<td>Overall</td>
<td>1.0</td>
<td>0.84 (0.67–1.07)</td>
<td>0.63 (0.49–0.81)</td>
<td>0.36 (0.26–0.50)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>By gender</td>
<td></td>
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</tr>
<tr>
<td>Male</td>
<td>1.0</td>
<td>0.84 (0.63–1.13)</td>
<td>0.68 (0.50–0.93)</td>
<td>0.37 (0.24–0.56)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Female</td>
<td>1.0</td>
<td>0.83 (0.56–1.24)</td>
<td>0.54 (0.35–0.83)</td>
<td>0.34 (0.19–0.61)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CHD/CHF status</td>
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<tr>
<td>No CHD/CHF</td>
<td>1.0</td>
<td>0.68 (0.42–1.11)</td>
<td>0.39 (0.22–0.69)</td>
<td>0.26 (0.12–0.58)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Prior history</td>
<td>1.0</td>
<td>0.88 (0.67–1.16)</td>
<td>0.69 (0.52–0.92)</td>
<td>0.38 (0.26–0.57)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Smoking status</td>
<td></td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Current smoker</td>
<td>1.0</td>
<td>0.85 (0.57–1.25)</td>
<td>0.66 (0.43–1.02)</td>
<td>0.56 (0.31–1.03)</td>
<td>&lt;0.02</td>
</tr>
<tr>
<td>Current nonsmoker</td>
<td>1.0</td>
<td>0.83 (0.60–1.14)</td>
<td>0.63 (0.45–0.88)</td>
<td>0.39 (0.25–0.59)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*RRs are adjusted for age, gender, and an age–gender interaction term, except for the gender-specific analyses, which were only adjusted for age.*
risk factor profile data in the present study demonstrate declines in mean systolic blood pressure, cholesterol, and smoking over time. The present analysis looking at trends in nonsudden CHD death and SCD among subjects currently versus not currently smoking demonstrates significant declines in both groups. Increased use of aspirin, β-adrenergic receptor blockers, ACE inhibitors, and lipid-lowering therapy in patients with chronic CHD, greater use of antiplatelet and thrombolytic treatment, and coronary revascularization are believed to be responsible for reductions in acute myocardial infarction mortality and CHD death.

Improvements in early defibrillation by automated external defibrillators (AEDs) also may have contributed to the observed decline in risk of CHD death and SCD. AEDs were first developed in the 1970s and used clinically beginning in 1979. Prehospital interventions, including rapid defibrillation by advanced and basic life support providers, also have been shown to improve survival after cardiac arrest. Additionally, the implantation of defibrillators in patients at high risk for ventricular tachyarrhythmias may improve survival of such patients; however, widespread use of these devices did not begin until the late 1990s, and they are unlikely to have contributed to the declines observed in the present study.

Nearly 20% of all nonsudden CHD deaths and nearly half of all SCDs occurred in subjects without a prior history of heart disease, which implies that interventions targeted only at high-risk subjects with CHD or CHF will have no effect on a large proportion of individuals at risk for SCD. In addition to secondary prevention, further population-based primary interventions are needed to sustain declines in CHD death and SCD.

Framingham trends in CHD death and SCD parallel nationwide declines in CHD mortality, which suggests that the present results may be generalized outside of this community-based sample. Furthermore, SCD trends in the present study are consistent with prior studies that have shown a decline in out-of-hospital CHD death.

This investigation has advantages over prior studies that have examined trends in CHD death and out-of-hospital CHD death. All deaths were adjudicated by an experienced physician panel using hospital records, primary medical doctor records, and next-of-kin interviews. Death certificates, which have been shown to overestimate CHD death and SCD, were not used to establish cause of death. SCD trend data in the present study are particularly notable because the diagnosis of SCD in the Framingham Heart Study has been unaffected by definitional changes over the past 50 years. This can be viewed in contrast to uncertainty with regard to long-term trends in acute myocardial infarction, primarily due to the introduction of more sensitive biomarkers that have dramatically affected clinical diagnosis. Lastly, we were able to examine CHD death and SCD trends by the presence or absence of clinical heart disease.

Although the long-standing nature of the Framingham Heart Study makes it an ideal setting in which to examine long-term trends in cardiovascular mortality, some limitations exist. Our study sample is not nationally representative, nor is it ethnically diverse. However, the relations of risk factors to CHD outcomes observed in Framingham have recently been validated in 6 ethnically and geographically diverse cohorts and were found to be applicable in other populations. Furthermore, trends in CHD mortality in Framingham are very similar to previously reported national data, which suggests that our results may be generalized outside of this community. We were unable to assess trends in subjects aged 80 years and older owing to sparse data for this age group in the earliest time period of the study. Although we observed sizable declines in CHD mortality and SCD, the study was underpowered to determine whether the slopes of the declines differed. We used a conservative 1-hour definition of SCD; unwitnessed deaths were not included in our definition, unless the death occurred within 1 hour of the subject having been last observed to be alive and free of symptoms. Similarly, we were unable to include SCD that may have occurred among those found dead in bed. It has been shown that up to 60% of all out-of hospital cardiac deaths are witnessed. An older, single person living at home is more likely to have an unwitnessed death, and the aging of the cohort in the present study presents the possibility for an increasing number of unwitnessed deaths. We were unable to assess the overall impact of defibrillation on SCD, because we began systematically collecting information on resuscitated SCD in the early 1990s. However, we were able to perform a secondary analysis that included cases of resuscita-
tated SCD in the 1990s. The RR changed from 0.51 to 0.62, which suggests that some but not all of the decline in SCD can be attributed to resuscitated deaths.

The present data show that the overall risks of SCD and nonsudden CHD death have decreased by 49% to 64% since 1950. These trends were evident in subjects with and in those without clinically apparent heart disease, which suggests important contributions of both primary and secondary prevention to the decreasing risk of CHD death.

Acknowledgments
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References


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