Epidemiology

Secular Trends in Deaths From Cardiovascular Diseases
A 25-Year Community Study

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Background—Although age-adjusted cardiovascular disease (CVD) mortality has declined over the past decades, controversies remain about whether this trend was similar across locations of death and disease categories and about the existence of age and sex disparities.

Methods and Results—We examined CVD mortality trends in Olmsted County, Minnesota, between 1979 and 2003 using the categories defined by the American Heart Association, including coronary heart disease (CHD), non-CHD diseases of the heart, and noncardiac circulatory diseases. Data on demographics, cause, and location of death of all 6378 residents who died of CVD were analyzed. Although decreases in the age-adjusted rates occurred in all groups, the magnitude of the decline varied widely. Lesser annual declines were noted in out-of-hospital than in-hospital deaths (1.8% versus 4.8%; \( P < 0.001 \)), in older than in younger persons (1.5% at age \( \geq 85 \) years versus 3.9% for those \( \leq 74 \) years of age; \( P < 0.001 \)), and in women relative to men (2.5% versus 3.3%; \( P = 0.007 \)). Furthermore, although CHD showed a marked annual decrease (3.3%), more modest decrements were found for non-CHD diseases of the heart (2.1%) and noncardiac circulatory diseases (2.4%) (\( P = 0.02 \) and \( P = 0.04 \) for the comparison with CHD decline, respectively).

Conclusions—Over the past 25 years, CVD mortality declined markedly in the community, but there were large disparities in the magnitude of the decline, resulting in a shift in the distribution toward out-of-hospital and non-CHD deaths. Further reduction in CVD mortality will require strategies directed at elderly persons and women, in whom out-of-hospital rates have improved only minimally. (Circulation. 2006;113:2285-2292.)

Key Words: cardiovascular diseases ■ epidemiology ■ mortality ■ population ■ prevention

Although age-adjusted cardiovascular disease (CVD) mortality has declined over the past decades, several important controversies remain with regard to this trend. First, conflicting results have been obtained on the decline according to location of death, with some \(^4-8\) but not all \(^9,10\) studies reporting a steeper decline in in-hospital than in out-of-hospital mortality. Nevertheless, because most studies did not include persons \( > 74 \) years of age, the age past which most cardiac deaths occur, \(^7,8\) the interpretation of these findings is uncertain.

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Second, conflicting evidence has been reported with regard to age and sex disparities in the magnitude of the decline. A few community studies have noted slower decreases in women \(^10,11\) and the elderly, \(^7\) but these findings have not been supported by others. \(^4-6,9\) Again, because many of these studies do not include elderly persons \(^4,5,9,10\) and others lack statistical power to detect age and sex interactions, \(^6,10\) an important variation in trends could have been missed.

Third, recent classification used by the American Heart Association divides CVD into 3 categories: coronary heart disease (CHD), diseases of the heart, and diseases of the circulatory system. \(^1\) Whereas trends in CHD mortality have been the focus of many studies, \(^4-10,12,13\) the other categories have rarely been investigated. Because these include heart failure and stroke, for which attenuations in the decline have been documented recently, \(^3,14-16\) it is important to examine whether the magnitude of the decline applied equally to all categories of CVD.

Prior studies in Olmsted County, Minnesota, have suggested that improved case fatality rates, \(^17\) reduced myocardial infarction (MI) severity, \(^18\) and decreasing MI recurrence rates \(^19\) may have played a greater role in overall mortality decline than did changing CHD incidence rates. \(^17,20\) However, because diverging trends across age groups and sex for MI incidence and survival, \(^17\) anatomic coronary disease prevalence, \(^21\) and cardiac death \(^7,11\) had been noted by the mid-1990s, it is unknown to what extent these patterns affected subsequent mortality in an aging population.

Thus, the present study was undertaken to examine trends in CVD mortality in Olmsted County over 25 years,
between 1979 and 2003. Specifically, we assessed variations according to location of death, age, sex, and specific CVD categories.

**Methods**

**Study Setting**

The population of Olmsted County is served by a largely unified medical care system that has accumulated comprehensive clinical records over an extensive period. Olmsted County (2000 census population, 124,277) is 144 km southeast of Minneapolis and St Paul, with 70% of its population residing in Rochester, the centrally located county seat. In 2000, 90% of all residents were white and 11% were 65 years of age. The Olmsted population is largely middle class, with 91% of adults having graduated from high school. Except for a higher proportion being employed in the healthcare industry, the population characteristics are similar to those of US whites.

Epidemiological research in Olmsted County is feasible because the city and county are relatively isolated from other urban centers, and nearly all medical care is delivered to local residents by a handful of providers. The Mayo Medical Center and the Olmsted Medical Group and its affiliated Olmsted Community Hospital provide comprehensive care for the region in every clinical discipline. The epidemiological potential of this situation is enhanced by the fact that each provider uses a unit medical record system through which all data collected for an individual are assembled in one place. The unit records of each provider in the county are available for use. These medical records are easily retrievable because the Mayo Clinic has maintained since the early 1900s extensive indexes based on clinical and histological diagnoses and surgical and billable procedures. The Rochester Epidemiology Project has developed a similar index for the records of other providers of medical care to local residents. This indexing system includes death certificates for Olmsted County residents. The result is a linkage of medical records from essentially all sources of medical care available to and used by the Olmsted County population. All aspects of the study were approved by the appropriate institutional review boards.

**Death Enumeration and Coding**

We searched death certificate data obtained from the Minnesota Department of Health to identify individuals ≥25 years of age who were listed as residents of Olmsted County at the time of death. Information on date of birth, date of death, sex, underlying cause of death, and site of death was collected. The *International Classification of Diseases, Clinical Modification* (ICD-CM), was used to classify deaths. The 9th version was used for the years 1979 through 1998 and the 10th thereafter. Since the late 1960s, all death certificates issued in Minnesota have described the location of death as coded by the Minnesota Department of Health. We defined out-of-hospital deaths as those taking place outside of short-term-care or long-term-care hospitals, including deaths occurring in emergency departments, private homes, public places, nursing or boarding-care homes, and infirmaries, as well as deaths among persons declared dead on arrival at a hospital. In-hospital deaths were those coded as occurring in short-term–care or long-term–care hospitals.

The procedures used in Olmsted County for completion of death certificates are different from those used in most other places. The coroner (chief medical examiner) or a pathologist member of the staff of the Mayo Clinic completes the death certificate for almost every Olmsted County resident who dies under the care of a Mayo Clinic physician, regardless of whether an autopsy is performed. When an autopsy is performed, its findings take precedence over clinical information. The autopsy rate is 30%, higher than the national average of 15%.

**Statistical Analyses**

We adapted the classification used by the AHA to produce a set of mutually exclusive CVD categories, including CHD, non-CHD diseases of the heart, and noncardiac circulatory diseases (Table 1). The underlying cause of death was used for all analyses.

Age-, sex-, and year-specific mortality rates were calculated for each CVD category. The denominators were determined by Olmsted County population census data for 1970, 1980, 1990, and 2000, with linear interpolation for the intercensal years and extrapolation after 2000. These rates were directly standardized to the age and sex distributions of the 2000 US population.

Poisson regression models were used to assess temporal trends in CVD mortality rates overall and by selected categories. Specific counts for each calendar year, age (using midpoints of 10-year intervals), sex, and location of death (ie, in and out of hospital) were used as the units of observation. Calendar year and successive age intervals were entered as continuous variables, with their quadratic terms tested and rejected. The logarithm of the count was modeled with the logarithm of the year-, age-, and sex-specific population size as the offset using the SAS GENMOD procedure. Annual percentage change and an overall relative risk (RR) for the entire study period in specific groups and categories were estimated through stratified analyses. Comparisons of temporal trends across locations of death, age, sex, and CVD categories were performed by including the 2-way interaction term of each variable with year, separately, after adjustment for all main effects. The 3-way interaction terms year by location by age and year by location by sex were used to examine differential age and sex trends according to location and were evaluated on the basis of fully interacted 2-way models. Model goodness of fit was assessed, and there was no evidence of overdispersion or autocorrelation.

The contribution (in percentage) of each specific CVD category to the total age- and sex-adjusted decline was estimated from this formula: \( 100 \times \frac{(dM/dM)}{dM} \), where \( dM \) is specific adjusted mortality rate in 1979 through 1985 minus specific adjusted mortality.
Results

Over the 25-year period covered by the study, 6378 CVD deaths were recorded, including 57% CHD, 18% non-CHD diseases of the heart, and 25% noncardiac circulatory diseases. Of all CVD deaths, 54% occurred in women and 69% in persons ≥75 years of age (39% in persons ≥85 years of age). The most frequent causes of death were CHD and stroke, accounting for 57% and 19% of all CVD deaths, respectively (Table 2). Heart failure, which is included in the “other forms of heart disease” group, was recorded as the underlying cause of death in an additional 4% of the cases.

From the period 1979 through 1983 to the period 1999 through 2003, the average ±SD age at CVD death increased from 76±13 to 80±14 years (P<0.001), as did the proportion of decedents ≥85 years of age (39% in persons ≥85 years of age). The most frequent causes of death were CHD and stroke, accounting for 57% and 19% of all CVD deaths, respectively (Table 2). Heart failure, which is included in the “other forms of heart disease” group, was recorded as the underlying cause of death in an additional 4% of the cases.

Within out-of-hospital deaths, similar trends were observed in nursing homes (the site of death for 45% of out-of-hospital decedents) and in other sites (respective annual declines, 2.0% and 1.6%; P=0.39).

Trends by Age and Sex

The decline in CVD mortality differed markedly according to age. Although an overall reduction occurred for all ages, its magnitude was greater in younger than in older persons (P<0.001 for the year-by-age interaction). Indeed, the aver-
age yearly decline in CVD mortality was 3.9% (95% CI, 3.3 to 4.5) for persons <75 years of age, 3.4% (95% CI, 2.8 to 4.0) for those 75 to 84 years of age, and 1.5% (95% CI, 0.9 to 2.0) for those ≥85 years of age (Figure 2). Over the 25 years of the study, this equates to RRs for fatal CVD of 0.38 (95% CI, 0.33 to 0.44), 0.44 (95% CI, 0.38 to 0.50), and 0.70 (95% CI, 0.61 to 0.80) for the 3 age groups, respectively, in 2003 versus 1979 (Figure 3).

Furthermore, as indicated by the significance of the 3-way interaction year by location by age (P<0.001), trends across age groups differed between in-hospital deaths (annual declines, 5.6% [95% CI, 4.7 to 6.5]) in those <75 years of age, 4.7% [95% CI, 3.8 to 5.6] in those 75 to 84 years of age, and 3.6% [95% CI, 2.5 to 4.6] in those ≥85 years of age) and out-of-hospital rates (annual declines, 2.8% [95% CI, 2.0 to 3.5], 2.5% [95% CI, 1.7 to 3.3], and 0.8% [95% CI, 0.1 to 1.4], for the respective 3 age groups). This corresponds to RRs in 2003, as compared with 1979, of 0.25 (95% CI, 0.20 to 0.32), 0.32 (95% CI, 0.25 to 0.40), and 0.42 (95% CI, 0.32 to 0.54) in in-hospital and 0.51 (95% CI, 0.42 to 0.62), 0.55 (95% CI, 0.45 to 0.66), and 0.84 (95% CI, 0.72 to 0.98) in out-of-hospital CVD deaths, respectively (Figure 3).

Large sex disparities also were observed. Although the age-adjusted CVD mortality was higher among men, this gap diminished over time as a result of a steeper downward trend in men than in women (P=0.007 for the year-by-sex interaction). Indeed, the annual decline in men was 3.3% (95% CI, 2.8 to 3.8), as compared with 2.5% (95% CI, 2.0 to 3.0) in women, and the RRs of CVD mortality in 2003 versus 1979 were 0.45 (95% CI, 0.40 to 0.50) in men and 0.54 (95% CI, 0.49 to 0.61) in women (Figure 3).

Furthermore, although trends in the age-adjusted in-hospital deaths were similar across sexes (annual decline, 4.8%; 95% CI, 4.0 to 5.6), the decline in out-of-hospital deaths was greater for men (annual decline, 2.4%; 95% CI, 1.7 to 3.0) than for women (annual decline, 1.4%; 95% CI, 0.8 to 2.0) (P<0.001 for the year-by-location-by-sex interaction). As shown in Figure 3, over the 25 years of the study, this corresponds to an RR of 0.31 (95% CI, 0.25 to 0.38) in both sexes for in-hospital death, as compared with 0.56 (95% CI, 0.49 to 0.66) among men and 0.71 (95% CI, 0.62 to 0.82) among women for out-of-hospital CVD death.

Trends Across CVD Categories
Trends have differed across CVD categories. The age- and sex-adjusted CHD mortality decreased markedly over time (annual decline, 3.3%; 95% CI, 2.8 to 3.7), contrasting with more modest decreases in non-CHD diseases of the heart (annual decline, 2.1%; 95% CI, 1.3 to 2.9; P=0.02 for the comparison with CHD trend) and noncardiac circulatory diseases (annual decline, 2.4%; 95% CI, 1.8 to 3.1; P=0.04 for the comparison with CHD trend). In the latest 5 years, the distribution of CVD deaths was 55% CHD, 18% non-CHD diseases of the heart, and 27% noncardiac circulatory diseases, as compared with 59%, 16%, and 25%, respectively, in the initial 5 years (Figure 4). Of the total decline in CVD mortality over the study period, 64% was attributable to decreasing CHD, 22% to decreasing noncardiac circulatory diseases, and 14% to declining non-CHD diseases of the heart.

Discussion

Summary of Findings
Over the past 25 years in the geographically defined population of Olmsted County, the age- and sex-adjusted mortality from CVD declined steadily. This favorable trend was observed in all CVD categories, for both in- and out-of-hospital locations, and across all demographic groups examined.
Although these findings are encouraging, sizable variations in the magnitude of these declines were found: Out-of-hospital declined less than in-hospital; slower decrements occurred in the elderly and in women; and CHD mortality decreased more rapidly than did other CVD categories. The sex disparities were driven by diverging trends in out-of-hospital deaths. Overall, despite a high proportion of CVD deaths occurring outside the hospital, the contribution of the decline in out-of-hospital rates to the total decline in CVD mortality was relatively modest, whereas much greater contribution was made through in-hospital reduction. These data indicate that declining trends were clustered mostly in the hospital setting and among younger subjects and men. Furthermore, the distribution of CVD deaths has shifted toward non-CHD causes.

Overall Decline in CVD Mortality

Mortality trends in the Olmsted County population are similar to those measured in other cohorts. Indeed, we report here a 50% decline in CVD mortality between 1979 and 2003, which is commensurate with the 52% decline in heart disease observed in the total US population between 1970 and 20023 and similarly congruent with the 64% and 70% decline in CHD mortality reported in the Framingham Heart Study6 and in the Minnesota Heart Study4 over similar time periods.

In the context of this decline, a controversy still exists as to the relative contributions of primary prevention, acute cardiac care, and secondary prevention. Although reports from the Framingham Heart Study have emphasized the role of temporal reduction in CVD risk factors,6,25 community surveillance data from the Minnesota Heart Study4 and the Atherosclerosis Risk in Communities Study12 have attributed the decline largely to improvements in acute cardiac care and secondary prevention after MI. However, neither of these studies included persons >74 years of age, which limits their ability to detect age- and sex-specific trends.

In accord with the other community surveillance studies, reports from Olmsted County have indicated secular improvements in several aspects related to the management and survival of coronary patients,17–19,26 whereas no major decline has been shown in the overall incidence of CHD.17,20 However, all of the trends examined in this community, without exception, have differed by age and sex, indicating the need for specific assessment.

Specific Trends in Olmsted County

Trends by Location of Death

A marked discrepancy in the magnitude of CVD decline was found with regard to location of death in that in-hospital deaths declined more rapidly than out-of-hospital deaths. Within the latter setting, trends found in nursing homes were similar to those in other sites. Previous reports on this issue yielded discrepant results, in part because of differences in study populations5,9 and the inclusion or exclusion of elderly persons.4–10 As demonstrated by the present data, inclusion of all age groups in such analyses is crucial because data indicated a differential rate reduction by age.

Reduction in length of hospital stay for MI27 and improved survival of patients with CHD who formerly might have died in the hospital17 could have contributed to this shift in the location of deaths. On the other hand, a more rapid admission to hospital after symptom onset has been shown over time,28 which may balance the effect of the shortened hospital stay.

It has been argued that time trends in out-of-hospital mortality likely reflect the success of prevention strategies, whereas trends in in-hospital mortality are more closely related to acute medical care and early treatment.4,8,13 The encouraging decline in the proportion of CVD deaths occurring in hospital may therefore reflect the improvements in emergency services and in patient treatment.19,26,28 However, the increased proportion of out-of-
hospital deaths indicates a need for public health initiatives toward prevention, early recognition of cardiac symptoms and signs, and access to emergency cardiac care.8

Trends by Age and Sex
Conflicting findings have been published with regard to the existence of age and sex disparities in CVD mortality trends,4-7,9-11 but many of these studies did not include elderly persons, which hinders their ability to detect such variations. The present data indicate that older persons and women benefit the least from the decline in CVD mortality and that the disparities in trends apply mainly to out-of-hospital deaths. The driving forces of these diverging declines are complex, likely multifactorial, and may themselves have evolved over time. Prior studies in Olmsted County have shown that, over time, the incidence of MI and the prevalence of atherosclerosis decreased in men but remained stable or even increased slightly in women and elderly persons.17,20,21 Among patients with MI, survival benefits were clustered in younger ages and men.17 The increase in MI incidence among women and older persons suggests that primary prevention has been less effective in these groups. This is supported by data on differential trends in risk factor prevalence with increasing age.29 However, because most of the age and sex disparities pertain to out-of-hospital deaths and given that more than half of out-of-hospital decedents have antecedent coronary disease,6,7,9 secondary prevention (or lack of) also might contribute largely to the disparities in trends. Indeed, according to recent studies of the Olmsted County population, traditional risk factors at the time of MI are more prevalent and confer a higher risk for recurrent ischemic events in women than in men.30 Furthermore, women and older patients are less likely to participate in secondary prevention programs after MI.31

Studies have shown that women with MI wait longer than men after the onset of symptoms to seek care.32,33 Lack of awareness, more ambiguous MI signs and symptoms, and social isolation may contribute to delays.32,34 These factors may be involved in the lesser temporal decline in out-of-hospital CVD death rates among women.

Finally, although studies have suggested that men and younger MI patients tend to be treated more aggressively, particularly with reperfusion therapy and cardiac catheterization,26,35-37 this may not be the primary explanation for the diverging trends shown in our study because in-hospital death trends have been relatively homogeneous across age groups and similar in men and women. Furthermore, sex disparities in the management of MI appear to have remained constant over time and thus are unlikely to confound the observed temporal trends.37

Trends Across CVD Categories
CHD has declined more rapidly than non-CHD diseases of the heart and noncardiac circulatory diseases. Improved survival after MI may have contributed to the diverging trends across CVD categories because the risk of stroke and heart failure is substantially increased in MI survivors.38,39 However, this hypothesis was not fully supported by a recent study that failed to explain the observed slowing of the stroke mortality rate decline during the 1990s by the prolonged survival of CHD patients.15 Thus, other possible explanations, including less successful prevention and treatment for the non-CHD causes, should be considered.

Implications
The disparities in the magnitude of the decline in CVD mortality presented in this study delineate opportunities for prevention and interventions. First, the lesser decline in non-CHD categories underscores the fact that the healthcare community should be increasingly prepared to address entities other than acute coronary disease. Second, because persons dying of CVD do so increasingly out of the hospital, clinical and public health efforts should be directed at prevention. To this end, it is important to emphasize that prevention should apply not only to primary but also to secondary prevention because about half of out-of-hospital CVD decedents have a history of coronary disease.5-7,8 Finally, the burden of fatal CVD has shifted to elderly persons and women, which defines the population toward whom these initiatives should be primarily targeted. It should be underscored that in the very elderly, interventions may revolve around end-of-life issues in the setting of chronic CVD rather than aggressive acute care.

Potential Limitations
Although the population of Olmsted County is becoming more diverse, during the study period, it consisted primarily of US whites. Nevertheless, trends in CVD mortality in this population seem to parallel national data,3,1 which suggests that these data may be generalized outside of this community.

The reliance on death certificates may introduce bias. On the other hand, death certificates are the only data source currently available to assess population trends in CVD mortality, provided that the accuracy remains relatively constant over time. To this end, a validation study performed in Olmsted County has found a similar accuracy of death certificate data for out-of-hospital CHD, typically considered more challenging than in-hospital events,40 throughout the 1980s and 1990s.23 In addition, our analyses are restricted to broad disease categories for which death certificate data are more accurate than for specific diseases.41

Conclusions
In this community over the past 25 years, CVD mortality declined steadily, but the magnitude of the decline differed greatly, with less improvement among elderly persons and women. Furthermore, the proportion of persons dying out of hospital and from non-CHD causes has increased, thus changing the face of CVD deaths. Prevention strategies should be directed toward the out-of-hospital setting, with increased focus on non-CHD causes, while targeting elderly persons and women.

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Disclosures

None.

References

CLINICAL PERSPECTIVE

Despite the dramatic decline in age-adjusted mortality from cardiovascular disease (CVD) in the United States over the past few decades, it is uncertain whether this decline was distributed uniformly across locations of death, age, sex, and CVD categories as defined by the American Heart Association (ie, coronary heart disease [CHD], diseases of the heart, and diseases of the circulatory system). We examined mortality trends in the population of Olmsted County (Minnesota) between 1979 and 2003, during which time 6378 residents died of CVD. Over the 25-year period, CVD mortality rates declined steadily overall and across all locations of death, age groups, sex, and CVD categories examined. Although overall CVD mortality declined by 50%, large variations in the magnitude of the decline were detected. Out-of-hospital deaths declined less than in-hospital deaths; slower decrements occurred in the elderly and in women; and CHD decreased more rapidly than did other CVD categories. Thus, declining trends were clustered mostly in the hospital setting, among younger subjects, and among men, and the distribution of CVD deaths has shifted toward non-CHD causes. To maintain the decline in CVD mortality, prevention strategies should be directed toward the out-of-hospital setting, with increased focus on non-CHD causes while targeting elderly persons and women.
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