The Development of Sex Differences in Cardiovascular Disease Mortality: A Historical Perspective

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Objectives. Little is known about why males have higher cardiovascular disease (CVD) mortality rates than do females. An important factor that has hampered efforts in this regard is the lack of clarity about whether male excess mortality from CVD has existed throughout history. To answer this question, an investigation was conducted of trends in CVD mortality differences between the sexes from the time when data first became available until the present, including the full range of age groups.

Methods. Mortality statistics for CVD in England and Wales from 1861 through 1992 and in the United States from 1900 through 1991 were used. Results. Three stages in the relationship between male and female CVD mortality were found: (1) An early stage of equal male and female mortality, (2) a stage of the appearance of sex differences in mortality, and (3) a stage with consistently present male excess mortality.

Conclusion. Male excess mortality from CVD has not always been present in the historical record. Further research is needed to elucidate the causes of this excess mortality. (Am J Public Health. 1998;88:1348–1353)

Data and Methods

Mortality statistics for CVD in England and Wales were used for the years 1861, 1871, 1881, 1891, 1901, 1911–1914, 1921, 1922, 1925, 1931, 1934, 1936, 1937, 1940, 1943–1971, and 1973–1992 for the age groups <1, 1–4, 5–14, 15–24, 25–34, 35–44, 45–54, 55–64, 65–74, and 75+ years. Data came from a number of sources. For the years since 1952, these data were available from official statistical issues. Before 1952, deaths from CVD were distributed among different subdivisions, which were different for different revisions of the ICD codes. To obtain death rates for CVD it was necessary to combine these subdivisions into one figure for each year. Such work had been conducted by Preston et al. for the years 1861, 1871, 1881, 1891, 1901, 1911, 1921, 1931, 1940, and 1951. To obtain data in intermediate years, we conducted the same work for the years 1912–1914, 1922, 1925, 1936–1937, and 1943–1950. Deaths from different subdivisions were combined into a single figure for the total number of deaths from CVD on the basis of guidelines from an

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official statistical issue\textsuperscript{20} in which various subdivisions of CVD for each revision of \textit{ICD} were delineated. Death rates were calculated as $m_i = M_i / \delta_i$, where $M_i$ represents the number of deaths from CVD in the age group $x$ during 1 year and $\delta_i$ represents the population in the age group $x$ during the same year.

Death rates from CVD in the United States for the periods 1900–1952 and 1958–1991 for the age groups <1, 1–4, 5–14, 15–24, 25–34, 35–44, 45–54, 55–64, 65–74, 75–84, and 85+ years were obtained from official sources.\textsuperscript{22} Death rates from all causes in the United States for the period 1900–1991 for the age groups 35–44, 45–54, 55–64, and 65–74 were obtained from two relevant sources.\textsuperscript{21,22} Death rates from various components of CVD in the United States in 1986 were examined. Although complete US coverage for mortality in all states was not obtained until 1933, the death rates for the expanding registration states are generally considered to approximate complete national rates.\textsuperscript{5} CVD was defined in terms of the \textit{ICD} codes over the various revisions.\textsuperscript{15,18,20,21} (Additional materials related to the methodology used may be obtained from the authors on request.)

**Results**

Figure 1 compares the CVD mortality trends for males and females for the period 1861–1992 in England and Wales. There were close similarities in mortality levels and trends over the entire period for males and females in the 4 age groups younger than 25 years and in the age group 75+ years. However, in the middle age groups (from 25 to 74 years), the long-term trends of male mortality differ significantly from those of female mortality. Until the 1920s, male and female mortality in the middle age groups changed concordantly and there was no evidence of a significant disparity between the sexes: male and female mortalities did not differ by more than 33% for the age groups between 25 and 74 years. However, beginning in the 1920s, a sharp divergence in trends occurred: the mortality of males increased, while that of females continued to decrease. As a result, male mortality in the middle age groups began to sharply surpass female mortality. Thus, male excess mortality appeared only in the beginning of the 1920s and was characteristic only of the middle age groups. Sex differences stabilized by the late 1960s. There is no evidence that changes in the \textit{ICD} codes affected mortality trends to a large extent, because there are no major shifts at the time points when \textit{ICD} changes were implemented. It is interesting to note the spikes of CVD mortality in young males (ages 15–24 and 25–35) at the time of World Wars I and II.

To investigate whether the trends noted above were characteristic of the United States as well as of England and Wales, we compared the CVD mortality trends for males and females for the period 1900 through 1991 in the United States (Figure 2). In general, the basic patterns were the same. For the middle age groups, there was an early stage with no apparent male excess mortality from CVD: male and female mortalities did not differ by more than 22% for the age groups between 25 and 74 years in the period before the 1920s. The second stage (from the 1920s to the 1960s) was characterized by intensively increasing male excess mortality from CVD. The third stage (the 1960s to the present) was characterized by a consistently present male excess mortality from CVD and stabilization of the magnitude of the sex differences.

These stages are depicted in clearer detail in Figure 3, which represents male:female mortality ratios in the United States from 1900 through 1991 for 11 age groups for CVD and 5 age groups for general mortality. The first stage (i.e. from the time data were first available until the 1920s) was characterized by an equality of male and female CVD mortality. Male excess mortality began to appear in the second stage (from the 1920s until the 1960s). The third stage (from the 1960s to the present) was one in which male excess mortality stabilized at a certain level and even showed a slight decrease. Remarkable similarities exist between trends in male excess mortality from CVD and trends from all causes.

The age dependency of male excess mortality for various subdivisions of CVD in the United States in 1986 is shown in Figure 4. Ischemic heart disease (IHD) is the major component responsible for excess male
CVD mortality. The disparity between male and female mortality from IHD is twice as high as that for CVD in the middle age groups. The category "all other forms of heart disease" is also characterized by disparity between the sexes. This is not the case for cerebrovascular disease. Hypertensive heart disease mortality is higher in males than in females before age 75; the reverse is found after age 75.

Discussion

These results underscore the fact that it was not until the 1920s that male excess mortality from CVD appeared. Is this phenomenon a real one or a spurious trend resulting from changes in ICD coding, diagnostic practices, or some other bias? The primary source of error is probably in the diagnosis and coding of cause of death. An important diagnostic factor affecting trends in cause-specific mortality has been the declining proportion of deaths attributed to ill-defined and unknown causes (including senility). Between 1848 and 1872 in England and Wales, 49.2% of all male deaths in the age group older than 65 years were attributed to vague diagnoses, while in 1956 and 1957 this percentage was only 2.9%. CVD was especially affected by this artifact, as more than 40% of ill-defined conditions were actually CVD. The apparent increase in CVD mortality in the age group older than 75 years in England and Wales, and in the United States before the middle of the 20th century, is probably artificial and due to the effect described above. However, sex differences in CVD mortality are unlikely to be affected, inasmuch as death certification practices were the same for both sexes and this effect is important only in the age group older than 65 years, whereas sex differences in mortality appear in younger age groups.

Moriyama et al. found that 15.1% of CVD deaths in the United States were classified incorrectly in 1960. However, the majority of these misclassifications fell within the broad division of CVD—fewer than 1% of the cases classified as CVD were not in fact some type of CVD, a percentage not substantial enough to seriously affect trends in CVD. It is widely acknowledged that inaccurate or inconsistent diagnosis and coding of cause of death can be substantially overcome by broad categories of causes of death. Conclusions derived from the analysis of sex ratios are even more robust with respect to this source of error, since changes in terminology and diagnostic methods tend to affect both sexes equally.

The period under investigation comprises 9 revisions of the ICD code. It is widely accepted that ICD changes manifest themselves in a discontinuity of trends resulting from the change from one ICD system to another. Figures 1 through 3 show that male excess mortality appeared as a steady year-by-year trend within several adjacent revisions, not as major shifts at the time points corresponding to the ICD changes. Therefore, the rise in male excess mortality does not seem to be the result of changes in ICD classifications.

The appearance of male excess mortality from CVD was closely correlated with the appearance of male excess mortality from all causes, as shown in Figure 3. In fact, the correlation is nearly perfect for ages older than 45. This observation limits the possibility that this phenomenon is a spurious trend resulting from changes in classification or diagnostic practices. It also suggests that historical trends in the male-to-female mortality ratio for deaths from all causes are largely due to changes in male and female CVD mortality patterns.

We conclude that the appearance of a sex disparity in CVD mortality is most probably a real phenomenon. This contradicts the view that males are inherently more vulnerable to CVD than females. Rather, it suggests that factors disproportionately affecting males and females began entering industrialized societies in the 1920s, giving rise to male excess mortality. When the influence of these factors stabilized, male excess mortality stopped rising and the trends in CVD mortality of both sexes became concordant again. This time point manifested as a downturn in male mortality trends, because male mortality
started to follow the same decreasing trend as female mortality during this century. This observation may be valuable, because the latest downturn in CVD mortality, starting with the 1960s, is not currently well explained and is viewed as being caused by a multitude of factors operating in each country (e.g., changes in lifestyle, disease detection, and control and treatment of CVD).12-26

IHD is the main component responsible for male excess mortality from CVD. Sex differences in mortality from IHD are approximately double those found in mortality from CVD as a whole. An increasing trend in mortality due to IHD was mentioned by Halliday and Anderson14 for England and Wales for the period 1931 through 1971 in social classes I and V. Moriyama et al.5 found a similar effect for the United States during the period 1940 through 1960. Other CVD components also reveal rising sex disparities in mortality, but these disparities are quantitatively much smaller than that for IHD. Moriyama et al.5 analyzed trends in various CVD components for the period 1914 through 1960. Male-female differences in death rates were slightly increased for hypertensive heart disease and cerebrovascular disease. The category “all other forms of heart disease” is also characterized by male excess mortality. The above-cited increasing trends in sex differences in the main CVD components make it unlikely that the trends in sex differences in CVD are due to changes in the relative importance of causes of death with large vs small sex differentials. Instead, the reason for male excess mortality from CVD may best be understood by considering the etiology of IHD. In addition, historical trends in male and female CVD mortality are best examined from an analysis of the entire category of CVD, because (1) the accuracy of mortality data for the entire category is one or two orders of magnitude higher than that for specific components; (2) the subdivision of CVD into different components may be artificial and arbitrary, while the CVD category is naturally distinctive from other categories in most cases; and (3) different CVD components are related, for example, IHD is influenced by hypertension.

To date, there have been many hypotheses to explain male excess mortality from CVD. Here we review these hypotheses in relation to the patterns observed in the present study.

One class of hypotheses underlines the importance of fundamental biological differences between the sexes, as illustrated in Madigan’s classic work.11 Some investigators have hypothesized a protective effect of female sex hormones or a destructive effect of male ones.22,25,27-29 There are also hypotheses positing a protective influence of menstrual blood loss25,28 and hypotheses implicating the different proportions of type A personalities among males and females.25,28,30 Inasmuch as male excess mortality from CVD appeared only in certain periods, these hypotheses do not seem to explain this effect (although they may explain some of the intermediate mechanisms).

A second class of hypotheses proposes a protective effect of the female lifestyle. These include the hypothesis of a more favorable female diet,25,28 and more female attention to personal health.25,28 These hypotheses are not consistent with the mortality trends in the period of rising male excess mortality. As Figures 1 and 2 show, the sex differences in CVD mortality occurred because of unfavorable tendencies in male mortality and not because of favorable tendencies in female mortality, as would be the case if differences in mortality were due to improvements in female lifestyles.

Others have suggested that the different social roles of the sexes affect their respective mortality rates,25,28 with particular emphasis on the fact that males tend to be employed in more dangerous, harmful, and difficult occupations. However, it is unlikely that this situation appeared only in the 1920s. Moreover, the second part of the 20th century is characterized by increasing attention to the prevention of occupational hazards.

Of particular interest is the well-known hypothesis connecting the male excess in CVD mortality with a higher prevalence of cigarette smoking among males.22,25,27,28 It has been shown that cigarette smoking increases CVD mortality.21-23,31-33 Male smokers between the ages of 45 and 64 have a 90% higher CVD death rate than male nonsmokers.34 in
25 US states, and 37.5% of US males and 29.5% of US females smoked in 1978.34 Sex differences in smoking in England and Wales were less: 45% of males and 42% of females smoked in 1976.35 These differences were larger in earlier years. In 1948 in England and Wales, the prevalence of cigarette smoking was 65% in males and 41% in females.35

One prospective study of more than 1 million men and women (representing almost all segments of the US population) contains age- and sex-specific death rates for IHD (the main subdivision of CVD and the chief CVD subdivision responsible for sex differences in CVD mortality) for smokers and nonsmokers. If the cigarette smoking hypothesis is true, then the sex ratio for CVD deaths among nonsmokers should be around 1. The sex ratios for mortality from IHD for nonsmokers aged 45–54, 55–64, 65–74, and 75–84 years are 4.55, 3.33, 2.14, and 1.59, respectively. The ratios for cigarette smokers are 6.39, 3.62, 2.15, and 1.64. Nonsmoking males also have a much higher mortality rate than nonsmoking females. So, in spite of the fact that cigarette smoking is a well-established risk factor for CVD and apparently contributes to the sex disparity in CVD, it is unlikely to be the principal cause of the sex differences found. A similar conclusion was suggested on the basis of opposite trends in sex ratios in IHD mortality and sex ratios in cigarette smoking during the 1950s and 1960s.25 At the same time, changes in sex ratios in cigarette smoking are expected to influence male excess mortality from CVD. Recent small-scale declines in male excess mortality from CVD are likely to be the result of a decline in sex differences in cigarette smoking.

At present, many consider a multivariate explanation to be the most plausible.23,27 Wingard3 examined the sex mortality differential (in total mortality) in relation to 10 demographic and behavioral factors. Johnson37 attempted to explain the sex differential in IHD by controlling for 6 of the most important known clinical risk factors: serum cholesterol, systolic blood pressure, diastolic blood pressure, left-ventricular hypertrophy, cigarette smoking, and glucose intolerance. Both studies concluded that the sex differences in IHD cannot be explained by the joint effect of the factors studied.

Thus, neither the traditional single-factor hypotheses nor the multivariate approach seem to adequately explain male excess mortality from CVD. It is likely that the main cause of this phenomenon is not presently known. We believe that the analysis of secular trends in sex differences in CVD in different countries is a useful tool to help identify this cause (or causes). Hypotheses should be screened for their concordance with the regularities of male and female secular trends in CVD. A key strategy is to identify factors possibly responsible for the male–female disparity in CVD, which began affecting industrialized societies in the 1920s and stabilized by the 1960s.

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