Heart Disease, Cancer, and Stroke Mortality Trends And Their Interrelations

An International Perspective

Thomas J. Thom, BA; Frederick H. Epstein, MD, FRCP

Background Changes in mortality from heart disease, cancer, and stroke over recent decades in many countries have received much attention. However, comprehensive and concurrent analyses of these trends and their effect on total mortality have been lacking. Moreover, the extent to which the trends for one disease may relate to those for another disease is unknown. Concordance of trends for major diseases would suggest that they have common causes and thus may be responsive to the same preventive measures.

Methods and Results Age-adjusted death rates for total mortality and mortality from heart disease, stroke, lung cancer, and cancer other than lung cancer were obtained for the years 1950 to 1987 in 27 countries by sex and ages 35 to 74 years from the World Health Organization statistical reports. Concordance of mortality trends was assessed for ages 35 to 74 between 1950 and 1983 through visual inspection and semi-quantitative measurements of percentage change over time. The epidemic increase in heart disease mortality ended in the 1960s or 1970s in most industrialized countries; death rates often declined very steeply. Stroke mortality also changed from an increase to a decline or from a modest to a steep decline in the 1960s or 1970s. Lung cancer mortality slopes generally changed from a steep increase to either a modest increase, a flat trend, or a decline; the changes in slope are lagging behind those for heart disease and stroke. These improvements influenced trends for total mortality. Cancer other than lung cancer trends are less distinct than those for the three other causes of mortality. Yet, testing them for concordance with heart disease trends reveals that they are mostly concordant on a time-lag analysis that assumes that heart disease responds more rapidly to a change in lifestyle or environment than cancer. Trends for heart disease and lung cancer in men also tend to be concordant on time-lag analysis. Heart disease and stroke trends have become more concordant with time.

Conclusions Trends for mortality from heart disease, stroke, lung cancer, and, less distinctly, cancer other than lung cancer, tend to be similar in different countries, leading to a corresponding similarity in total mortality trends. An analysis of trends for pairs of diseases within countries indicates a tendency toward concordance of trends, suggesting the existence of common causes amenable to the same preventive measures. This analysis of international mortality trends is intended to stimulate further research along these lines, as a guide to preventive and therapeutic action. (Circulation. 1994;90:574-582.)

Key Words • cancer • cerebrovascular disorders • heart diseases • mortality

Over the past 20 years, death rates for heart disease and stroke declined substantially in most industrialized countries, and, at least in younger men, mortality increases for lung cancer may have been reversed in some countries.1,2 In the United States, the decline in mortality for heart disease, particularly coronary heart disease, was accompanied by a fall in death rates for total mortality and most other major causes of death, except for lung cancer during the earliest part of the period.3 In contrast to the great attention given to the changing heart disease mortality trends, both nationally4 and internationally,5 parallel developments, at least in the United States, with regard to other major causes of death have not attracted a comparable amount of interest. The current analyses present a simultaneous view of the secular mortality trends between 1950 and 1987 for heart disease, stroke, lung cancer, cancer other than lung cancer, and total mortality in the United States and 26 other countries (1) to permit a comprehensive comparison of the secular mortality trends for the major components of total mortality within and between countries and (2) to search for concordance in mortality trends between these diseases. Concordance would suggest common causes for two or more diseases so that measures to prevent coronary heart disease also might protect against other major chronic diseases. The present report is based on an extensive monograph published under the aegis of the National Heart, Lung, and Blood Institute, National Institutes of Health,6 available without charge from Thomas Thom, Epidemiology and Biometry Program, National Heart, Lung, and Blood Institute, Bethesda, MD, 20892, USA. The aim is to provide a baseline from which further research might be pursued to relate mortality trends to trends in risk factors and medical care.

Methods

Mortality statistics in this study consist of death rates for the years 1950 to 1987 reported to the World Health Organization or calculated from Reference 6 by 27 countries for total mortality and four cause-of-death groups. Selection of countries was made according to data availability and presumed validity. To minimize problems with data comparability across countries, the analysis was confined to a core of developed and industrialized countries presumed to have the most reliable
and valid mortality statistics on chronic diseases. Death rates are age adjusted; adjustment factors are given elsewhere. They are graphed in the figure for each country by sex for ages 35 to 74 years for eight time periods from 1950 to 1954 to 1984 to 1987. Data for the open-ended age group 75 and over were not included because of a lack of reliability for intercountry comparison, especially with respect to diagnostic accuracy. The four causes of death are (1) heart disease, which includes hypertension and diseases of the heart except rheumatic fever and rheumatic heart disease; (2) cerebrovascular diseases, which are referred to as "stroke"; (3) lung cancer, which is separated from total cancer; and (4) all cancers except lung cancer. Statistical variation around death rates in the figures is quite small and therefore was not included. Computations were made of standard errors of selected age-adjusted death rates based on the method described by Chiang. The largest relative standard error, 8%, is for the death rate for lung cancer in Northern Ireland women for the time period 1950 to 1954; the rate is 10.9 per 100 000 population, and the standard error is 0.9 per 100 000 population. By comparison, the rate for lung cancer in that period in French women is 8.1 with a standard error of 0.1, about 1% relative standard error.

Codes of the International Classification of Diseases (ICD) for these causes of death, the age-adjustment factors used for rates for ages 35 to 74, and data limitations and documentation are given in Reference 6. Graphs presented in this paper summarize the entire age range of 35 to 74 years, whereas Reference 6 presents trends for specific age groups. Although Reference 6 includes mortality trends from ischemic (coronary) heart disease, they are not described here; there are differences in steepness of declines, in when they began, and in relative ranking of countries for coronary heart disease compared with total heart disease. Instead, mortality from heart disease as defined here is described because of its better intercountry comparability with respect to accuracy of cause of death statistics and its consistency across revisions of the ICD. Reference 6 does not include other major causes of death because of concerns about their accuracy and intercountry comparability. Present analyses focus on the age groups 45 to 64 and 65 to 74 years where numbers of deaths are generally large enough for rates to be stable, and age adjustment of rates (within ages 45 to 64) is of minor influence on intercountry comparability.

Methods to assess whether mortality trends for pairs of diseases are concordant or discordant in direction are described in detail elsewhere. For the purpose of the present report, selected results of the visual method of trend assessment are presented. This method is based on cumulative percent change charts which show, for each country, the trends in heart disease, stroke, and cancer mortality; pairs of trend lines were compared visually to determine whether they were concordant or discordant in direction. These charts were also used for the analysis of trends that takes into account a time lag, by comparing trends for heart disease during the first half of the period with those for the other conditions during the second half. Death rates for the period 1984 to 1987 were not included in the analysis because they were not completely available as the analysis was being developed. A semiquantiative method, which was not used for the analyses presented here, measured concordance and discordance based on comparisons of percent change in death rates for two diseases between successive time periods from 1950 to 1954 to 1979 to 1983 for each country, as explained elsewhere. Major concordance or discordance is defined by a mortality change of 3% or more for both diseases in the same or opposite direction in the time interval; minor changes are defined by a change of 3% or more for one and less than 3% for the other disease. Results found by this method confirmed results based on the visual assessment.

Results

Overall Mortality Trends

Mortality trends from 1950 to 1987 for many countries show some striking changes. The epidemic increase in heart disease mortality, particularly in men, ended in the 1960s or 1970s in most industrialized countries; in a number of them, death rates are now declining markedly. During the same time period, especially in men, the slope of the trend line for stroke mortality has likewise shown downward changes in many countries. The upward trend in lung cancer mortality has generally slowed, flattened, or reversed. The time period when the improvements began varied by country but coincided rather closely for heart disease, stroke, and total mortality within many countries, with improvement in lung cancer mortality mostly lagging behind. The trends, along with those for mortality from cancer other than lung cancer, are shown in detail for the 27 countries in the figure.

Total Mortality Trends

The age-adjusted death rates for total mortality declined by at least 15% in men and women during the period from 1965 to 1969 to 1984 to 1987 in 16 of the 27 countries. Many declines are much greater than 20%. The large decline follows an upward or flat trend or a moderate decline. The contribution to that decline in total mortality since 1965 to 1969 made by declines in mortality from heart disease and stroke was ≥75% in Australia, Canada, New Zealand, and the United States. Israel and Norway would belong in that group except that total mortality had declined <20% in men. During the period, total mortality declined substantially in Austria, Belgium, England/Wales, Finland, France, the Federal Republic of Germany (West), Italy, Japan, Portugal, Scotland, Spain, and Switzerland, but the contribution made by declines in heart disease and stroke was generally closer to 50% than 75%.

The total mortality trends in Japan deserve special emphasis. In 1950 to 1954, the total death rate in Japan was highest among the 27 countries in women and, next to Finland, second highest in men. By 1984 to 1987, Japan had the lowest total death rates of any country in men and women. Although heart disease and stroke mortality declined markedly in Japanese men and women during the entire period, only about one third of the decline in total mortality resulted from a decline in these two diseases. Two thirds of the decline came from various noncardiovascular and noncancer causes of death and was achieved mostly in the 1950s and 1960s. Between 1965 to 1969 and 1984 to 1987, when the age-adjusted death rate for total mortality declined over 40% in men and women, more than one half of that decline was attributed to heart disease and stroke.

Heart Disease Mortality Trends

In men, mortality from heart disease, as defined under "Methods," in 21 countries changed from an increasing or flat trend to a decline, and in Japan and France the trend was steadily downward about 30% throughout the period. The marked changes in trends began first in Canada, the United States, and possibly in Switzerland. Declines began in the late 1960s in Belgium, Denmark, Finland, and Italy, and in the early...
Other than lung cancer, in 7 countries by sex, ages 30-74 years, 1964-94.

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<tr>
<th>Country</th>
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**Codes for Periods**

- A: 1950-54
- B: 1955-59
- C: 1960-64
- D: 1965-69
- E: 1970-74
- F: 1975-78
- G: 1975-83
- H: 1984-87

- Total
- Heart Disease
- Stroke
- Lung Cancer
- Cancer, Other than Lung
1970s in England/Wales, Israel, Norway, Portugal, and Scotland. Declines were relatively late in starting in Austria, the Federal Republic of Germany, Ireland, the Netherlands, Northern Ireland, Spain, and Sweden. Increases rather than declines are seen in Czechoslovakia, Hungary, Poland, and Yugoslavia. Declines from peak rates were more than 35% in Australia, Canada, and the United States and less than 10% in Ireland, Norway, and the Federal Republic of Germany.

In women, declines in heart disease mortality occurred in all countries except Czechoslovakia, Poland, and Yugoslavia. Declines began earlier, generally in the 1950s, and more gradually in women than they did in men, and generally the declines were larger. Sometime during the overall period there was a noticeable change in direction from flat to downward or from modestly to steeply downward in heart disease mortality in women in Australia, Belgium, Denmark, Finland, Israel, Italy, Norway, New Zealand, and the United States.

**Stroke Mortality Trends**

In most countries, the death rates for stroke in both men and women declined very steeply, especially in the latter half of the period 1950 to 1987. In men, a change from an increasing or flat trend in stroke mortality to a declining trend is seen in Austria, Belgium, Finland, Ireland, Japan, Norway, New Zealand, and Portugal. A change from a modest to a steep decline is seen in Australia, Canada, France, Israel, the Netherlands, Northern Ireland, Scotland, Spain, Switzerland, and the United States. In Denmark, England/Wales, the Federal Republic of Germany, Italy, and Sweden, stroke mortality was downward throughout the period with little discernible change in slope. Throughout the entire period, stroke mortality increased in Poland and Yugoslavia, increased irregularly in Hungary, and leveled off after an increase in Czechoslovakia. In women, there also was a noticeable improvement in the slope of the trend line for stroke mortality in most of the countries where downward trends occurred in men, and the timing of the change was generally similar to that in men. The major difference is that in women the change was almost always from a modest to a steep decline. Only Belgium and the Eastern European countries experienced an increase in the earlier part of the period 1950 to 1987.

**Lung Cancer Mortality Trends**

In the earlier part of the period 1950 to 1987, lung cancer mortality in men and women increased, generally very steeply, in all countries. In men, the most common pattern was for that increase to slow, flatten, or turn to a decline, seen in all countries except Hungary, Poland, Portugal, Spain, and Yugoslavia. Actual turn-arounds to declining trends are clearly seen in England/Wales, Finland, New Zealand, and Scotland. In women, flattening of the earlier increasing trends are seen clearly only in Australia, Ireland, Israel, Japan, and New Zealand, with Spain showing a decline. Possible ameliorating of the increasing trend is seen in England/Wales, Northern Ireland, Poland, and the United States. In most countries the slope in recent years is less favorable for women than for men.

**Mortality Trends for All Cancers Except Lung Cancer**

Changes in mortality from all cancers except lung cancer have generally been modest over the period 1950 to 1987 in all 27 countries. There are no striking improvements in mortality in the second part of the period compared with the first part in any country. Also, unlike lung cancer, heart disease, or stroke, there is almost no correspondence among countries with respect to trend patterns in men compared with trends in women. Thus, only in Finland, Switzerland, and the United States is the trend downward and only in Yugoslavia upward throughout the period in both sexes. Mortality tended to decline, though mostly in women, in Austria, Belgium, Canada, Denmark, France, the Federal Republic of Germany, Japan, the Netherlands, Spain, and Sweden.

**Interrelations of Trends**

The second aim of this report addresses the hypothesis that different chronic diseases share common causes and may thus be responsive to similar preventive and treatment measures. One method to test this hypothesis is to measure the extent of concordance in mortality trend for pairs of diseases among a group of countries. In these analyses, a contemporary comparison of the trends might not be appropriate because mortality from one disease may take a longer time to change in response to changes in causative factors than would another disease. Therefore, both contemporary and time-lag analyses were done. The various methods to measure concordance were described elsewhere. Some of the results are described below. Concordance is measured by country from 1950 to 1983 in age groups 45 to 64 and 65 to 74 years for selected pairs of diseases.

Contemporary analysis of mortality in men aged 45 to 64 years among 23 countries for which complete data are available showed that 13 had trends for heart disease (HD) that were concordant in slope with trends for cancer other than lung cancer (OCA) during the first half of the period 1950 to 1983 (Table). The number increased to 18 countries during the second half of the period. There was concordance in as many as 21 of the 23 countries shown for the time-lag analysis, where HD trends in the first half of the period 1950 to 1983 were compared with the OCA trends of the second half of the period, with the assumption that factors affecting both HD and OCA (eg, smoking and nutrition) will take longer to affect cancer than HD. The lag time of about 15 years was chosen empirically to compare two approximately equal periods of observation but also because it is plausible in terms of estimating the likely incubation periods of HD and cancer. For older men, concordance is seen in 14 countries in both periods for contemporary analysis, increasing to 19 countries in time-lag analysis. For women of all ages, concordance is high both in contemporary and time-lag analysis.

Given the established common risk factor of cigarette smoking for both HD and lung cancer and the likely earlier impact of this factor on HD than on lung cancer, only time-lag analysis appears appropriate (Table). It shows a high degree of concordance between mortality trends for these two causes of death in men but a very low degree of concordance in women, expected in view...
Concordance of Mortality Trends Among Countries For Pairs of Causes of Death During Two Time Periods

<table>
<thead>
<tr>
<th>Diseases</th>
<th>Time Periods</th>
<th>Countries With Concordant Trends/ All Countries</th>
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<td>Men</td>
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<td>Age, y</td>
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<td>Heart disease vs cancer other than lung</td>
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<td>Time-lag analysis*</td>
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<td>Heart disease vs lung cancer</td>
<td>Time-lag analysis*</td>
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<td>Heart disease vs stroke</td>
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*Time-lag analysis: comparing heart disease mortality during time period I with mortality during time period II from (a) cancer other than lung cancer and (b) lung cancer.

Note that the total number of countries in the three disease categories are not the same because the number of countries with data needed for the time-lag analysis was not the same for the three pairs of diseases.

of the wide divergence of the trends of the two diseases in women and different smoking patterns in men and women over time (Table).

If we consider that the decline in mortality from HD began much later than did the decline for stroke in most countries, we still see an increasing tendency for a high degree of concordance between trends for these two causes of death over the period 1950 to 1983 (Table). This result is more striking in men than women, because the decline for heart disease generally began later in men than it did in women.

For stroke and OCA (not shown), there is a tendency toward increasing concordance over the period 1950 to 1983 among the countries in both men and women. It is difficult to construct a hypothesis of shared causes between the two disease categories, but links to nutritional factors, smoking, and alcohol must be considered.

Mortality from stroke and lung cancer (not shown) have been in opposite directions over the period 1950 to 1987 in most countries. This lack of concordance is not surprising given that the common factor, cigarette smoking, is a much stronger risk factor for lung cancer than for stroke, and the two diseases appear to have little else in common with respect to causal factors. There is no appreciable degree of either concordance or discordance among time trends for lung cancer and other cancers. This is in accordance with expectation because the steep increases in lung cancer mortality in most countries have not been observed for any other types of cancers.

Discussion

Following the mortality trends since the mid-1960s or 1970s shows that there were marked declines in total mortality and mortality from HD and stroke and decreases in the upward slope of the trend line for lung cancer in most industrialized countries. In many countries the timing of the improvements in HD and stroke mortality coincided reasonably well with the improvements in total mortality, while the slowing or reversal of the increase for lung cancer occurred later. Declines for HD and stroke were very steep in a number of countries. These patterns were present in both sexes, but changes were seen more clearly in men, as described in detail elsewhere.

Limitations of cause-of-death statistics and their uncertain intercountry comparability complicate explanation of time trends. In comparing countries, our major limitation is that the statistics are cross-sectional mortality tabulations based on the underlying causes of death as selected according to ICD codes and rules that are not consistently applied across countries. Credibility of these statistics is, however, enhanced by the occurrence of similar patterns in so many countries, especially the extraordinarily large declines for HD and stroke and their evident impact on total mortality. These results strongly support the conclusion that some forces of change in the prevention and treatment of these and related chronic diseases are at work. They argue against the contention that much of the mortality decline for HD and stroke resulted from a shift to cancer or other causes of death.

The concerns about diagnostic accuracy in these statistics are minimized by inclusion of only broad cause-of-death groups for analysis. Thus, comparability across countries and time is improved but at the cost of diagnostic specificity within the HD and cancer categories. Mortality of specific diagnostic subgroups that may differ differently internationally are merged, diluting the impact of factors that may affect the specific diagnostic subgroups differentially. This applies particularly to the description of time trends for OCA and in the analysis of interrelations between this cause of death group and HD (another broad group) or stroke. OCA is a very heterogeneous group, combining types of cancer differing widely in the balance between exogenous factors, such as diet, and endogenous factors, such as hormones, as well as the effects of these factors on the initiating and promoting phases of cancerogenesis. Looking for concordance with mortality from other diseases was a calculated risk, which, however, turned out to be worth taking. However, the descriptions of
trends and interrelations and the conclusions drawn are probably not as pronounced as might have been the case with more diagnostic-specific disease categories.

The concept that two or more chronic diseases share one or more causes has implications for their prevention and treatment. There are several lines of evidence for the existence of links between some of these diseases.8,9 One piece of evidence would come from the concordance of secular mortality trends. In addition to demonstrating the mere existence of common causes, we must define them to enable the institution of preventive measures. Among lifestyles, nutritional factors are of key importance. Specifically, there are various links between dietary constituents and HD, stroke, and cancer.10-16 Other connections with lifestyle are provided particularly by the detrimental effect of smoking and the protective effect of physical activity.17 Psychosocial factors and social class affect health by simultaneously influencing a multiplicity of chronic disorders.18-20 The biological environment, in terms of infective and immunological processes, and the physical environment harbor in all likelihood pathogenic mechanisms common for a number of diseases. Last, but not least, the international secular trends that have been described are no doubt affected by differences in patterns of medical care.21

The analyses for concordance and discordance of trends are limited to ages 45 to 74 years and the time period 1950 to 1983 since the extension to ages 35 to 44 years and the inclusion of time period 1984 to 1987 were not part of the original plan when this work began. Likewise, we had not anticipated that contemporary comparison would not suffice and that a time lag had to be taken into account. The choice of a time lag of approximately 15 years, dividing the entire observation period from 1950 to 1983 into two halves, was both convenient and plausible. The incubation period of coronary HD has been estimated to be about 10 years22 but, in a community setting, it may be shorter, because a prevention program initiated in 1972 coincided with a significant decline in mortality between 1969 and 1979.23 By contrast, the decline in cancer mortality lagged behind by about 10 years, starting around 1980.23 On the basis of this one study, the time lag between coronary HD and cancer, including in this case lung cancer, would be of the order of 10 years. For lung cancer and smoking, the latency period has been estimated to be at least 20 years.24 Factors associated with migration affect colorectal cancer mortality 20 to 30 years later.25 In Chinese Americans, it takes 20 or more years until a significant effect of saturated fat consumption on colorectal cancer incidence can be shown.26 These various data would seem to be compatible with the original "informed guess" that, on exposure to a common cause, cancer will respond somewhere around 15 years later than coronary HD.

Future work will require the design of more accurate and innovative methods for the measurement of long-term mortality trends. There is also a need to experiment with different time-lag periods between exposure to changes in lifestyle or environmental factors and their impact on disease manifestations to find which of them provides the best fit. It should also be taken into account that concordance of trends evolve and increase with time, as other methods of analysis, not shown here, suggest.6

This report and Reference 6 are intended to stimulate expansion of intercountry analyses directed at explanatory hypotheses of the remarkable time trend changes in mortality and of the emerging evidence that coronary HD and other chronic diseases share common underlying and preventable causes. The impact of the prevention of these causes might thus extend well beyond the prevention of coronary HD. An international perspective of mortality trends is essential because explanatory evidence from single countries alone cannot be sufficiently convincing, and because inter-country comparisons will give each country a measure of the success of its preventive and therapeutic strategies toward controlling the major causes of death.

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