Decline in US Stroke Mortality in the Era Before Antihypertensive Therapy

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Background and Purpose: This study was done to determine if reported declines in stroke mortality in the era before antihypertensive therapy are artifactual.

Methods: This study involved analyses of national and state vital statistics data using adjusted and specific rates.

Results: Adoption of the third revision of the International List of Causes of Death in 1921 produced an abrupt 6.6% decrease in stroke mortality rates, but otherwise, changes in disease classification systems had little effect on stroke mortality rates. Adoption of the second revision of the joint-cause manual produced a 9.2% drop in stroke death rates, but other revisions of the joint-cause selection rules had little effect. While rates for the expanding group of states in the death registration area progressively declined, rates for fixed component areas remained constant until around 1925 and then declined. Reselection of the underlying cause from aggregate multiple cause data for 1917, 1925, and 1940 using uniform selection rules confirmed a decline after 1925. Correlation analyses of rates of change for stroke and heart disease rates did not support a shift in diagnosis to explain the divergent trends.

Conclusions: The apparent decline in stroke mortality rates before 1925 is an artifact of changes in disease classification systems, joint-cause selection rules, and nonrandom incorporation of states with different mortality rates into the expanding registration area. The decline after 1925 could not be explained by changes in coding systems or joint-cause selection rules or by a shift in diagnosis from stroke to heart disease. (Stroke. 1993;24:1382-1388.)

Key Words • cerebrovascular disorders • epidemiology • mortality

United States stroke mortality rates have been declining since at least 1900,1-3 but the reasons for this decline have remained obscure. Temporal changes in recognized stroke risk factors are insufficient to explain the decline.4,5 Antihypertensive therapy first became available in the 1950s, and it was not until the 1960s and 1970s that large-scale public health campaigns were mounted to deal with the high prevalence of untreated hypertension in the United States.2 The subsequent acceleration in the rate of decline of stroke mortality was initially attributed to the improved recognition and treatment of hypertension.5 However, more recent studies have questioned the magnitude of the contribution of antihypertensive treatment to the decline in stroke mortality5,7-9; in particular, Bonita and Beaglehole4 have suggested that hypertension can account for at most 25% of the decline in US stroke mortality from 1970 to 1980.

Particularly in the era before antihypertensive therapy, it remains to be established whether the reported declines represent a real change in stroke mortality or were at least partly an artifact of changing diagnostic and reporting practices. If the reported decline in stroke mortality rates is real or if the trend can be corrected to adjust for identified bias, temporal changes in stroke mortality could be meaningfully compared with temporal changes in potential contributing factors, such as changing dietary patterns or the changing frequency of cigarette smoking.

This study evaluates the effect of various potential biases on the decline of stroke mortality in the era before antihypertensive therapy.

Materials and Methods

The number of deaths due to stroke and each stroke type by state, race, gender, and age were obtained from volumes of Mortality Statistics for 1900 through 1936 and from volumes of Vital Statistics of the United States for 1937 through 1948. During the period from 1900 through 1948, five revisions of the International List of Causes of Death (ICD) were used in the United States: ICD-1, 1900 through 1909; ICD-2, 1910 through 1920; ICD-3, 1921 through 1929; ICD-4, 1930 through 1938; and ICD-5, 1939 through 1948. The ICD revision in effect in the United States and the corresponding rubrics for stroke are shown in Table 1.10-15

Population data by state, race, gender, and age were obtained from published tabulations of the population enumerated as of April 1 in the decennial censuses of 1900 through 1950.16-20 Population estimates for intercensal years were obtained by linear interpolation.

Age-adjusted mortality rates were computed by the direct method, that is, by applying the age-specific death
rates for stroke to the standard population distributed by age. The reference population used was the total United States population enumerated as of April 1, 1940. Age-adjusted stroke mortality rates for 1900 through 1933 were calculated for the total and white populations of the expanding group of states in the death registration area (DRA). Rates also were calculated for fixed geographic areas: the death registration states of 1900 for 1900 through 1933, the death registration states of 1910 for 1910 through 1933, and the death registration states of 1920 for 1920 through 1933. In calculating rates for the white populations, the following states were excluded for some years because these states did not tabulate deaths by race and because the percentage of nonwhites in these states was greater than 10%: Washington, DC, 1900 through 1905; Delaware, 1919 through 1933; Arizona, 1926 through 1933; and New Mexico, 1929 through 1933. For those states that did not tabulate deaths by race and that had fewer than 10% nonwhites in their populations, the total population was considered as white.

For most years, the US Bureau of the Census coded only the underlying cause of death selected from each death certificate; however, for 1917, 1925, 1936, and 1940, the Bureau of the Census specially coded the underlying (or principal) cause of death and one associated (or contributory) cause of death.21-24 For the years 1917, 1925, and 1940, the Bureau of the Census published cross-tabulations of underlying and associated causes of death.21-24 For each of these years, the underlying cause was selected using different selection rules.25-27 More than one cause of death was reported on 35% of death certificates in 1917, compared with 44% in 1925 and 55% in 1940;24 of certificates assigned to stroke, an even higher percentage had other conditions reported: 49% in 1917, 54% in 1925, and 69% in 1940.21-23

To evaluate the effect in changing joint-cause selection rules, the underlying cause of death was reselected from the cross-tabulated data for 1917 and 192521,22 according to the 1939 edition of the Manual of Joint Causes of Death,27 which was used in the original coding for 1940. The International List titles for 1917 and 1925 were transferred to the corresponding title used in 1940 (1938 revision of the International List) using the Classification of Terms and Comparability of Titles Through Five Revisions of the International List of Causes of Death.30 In some cases, the categories to be recoded included multiple entities, some preferred to stroke in the assignment of the underlying cause of death and some not preferred. In the case of such ambiguities, all deaths in the category were coded in both ways, producing a range in the recoded data. The percentage change in the number of deaths from stroke in 1917 and 1925 was used to calculate an estimate of the range of age-adjusted stroke mortality rates for those years, assuming the percentage of cases recoded was the same for all age groups.

During the period from 1940 through 1948, the DRA for the coterminous United States was complete, and there were no changes in coding systems or joint-cause selection rules. To evaluate whether some of the decline in stroke in this period was due to a shift in diagnosis or a shift in attribution of cause of death, age-adjusted mortality rates for stroke (ICD-5 rubric 83) and heart disease (ICD-5 rubrics 90 through 95) were calculated by state, race, gender, and year of death. The average rate of change of these rates was assessed by state for each race-gender group using linear regression. Analysis of residuals was used to identify violations of the assumptions of either linearity or homogeneity of variance.

### Results

Age-adjusted stroke mortality rates declined by 41.7%, from 134.23/100 000 population per year in 1900 to 78.20/100 000 population per year in 1948 (Fig 1). Declines occurred within the period of each revision of the ICD and were most precipitous during ICD-4 and ICD-5. Percentage declines for each ICD period are as follows: ICD-1, 6.5%; ICD-2, 3.6%; ICD-3, 2.9%; ICD-4, 16.3%; and ICD-5, 12.7%. Declines also occurred within the period of each revision of the joint-cause selection rules.

The trends were not consistent for the various stroke types. Most stroke deaths from 1900 through 1948 were attributed to cerebral hemorrhage or effusion; rates for this diagnostic category actually increased from 1900 through 1916 and then declined. Almost all of the modest decline in overall stroke mortality rates in the first two decades of this century occurred as a result of a more precipitous decline in deaths from "hemiplegia and other paralysis of unspecified origin." Because the magnitude of the decline in this nonspecific category was greater than collective increases in other stroke categories, the decline resulted from either a true decline in deaths attributable to this category or, more likely, a shift to more specific conditions, including nonstroke categories. Although cerebral embolism and thrombosis represented only a small proportion of stroke diagnoses, rates for these conditions actually increased over the period.

With changes in ICD coding systems or joint-cause selection rules, there were generally minor discontinuities in trends, which did not explain the overall decline (Fig 1). Two significant discontinuities occurred with sudden drops in rates upon adoption of ICD-3 in 1921 (a decrease of 6.6%) and application of the second

### Table 1. Rubrics for Stroke by Revision of International List of Causes of Death (ICD)

<table>
<thead>
<tr>
<th>Title name in ICD-5</th>
<th>Rubrics by ICD revision</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebral hemorrhage or effusion</td>
<td>83a</td>
</tr>
<tr>
<td>Cerebral embolism and thrombosis</td>
<td>83b</td>
</tr>
<tr>
<td>Cerebral softening</td>
<td>83c</td>
</tr>
<tr>
<td>Hemiplegia and other paralysis of unspecified origin</td>
<td>83d</td>
</tr>
</tbody>
</table>

*Includes noncerebral embolism and thrombosis.
Fig 1. Graph shows adjusted mortality rates for stroke and stroke types in US death registration states from 1900 through 1948. --- Indicates total stroke; ..., cerebral hemorrhage or effusion; ..., hemiplegia and other paralysis; ..., cerebral embolism and thrombosis; and ..., cerebral softening. For 1900 through 1920, rates are adjusted by age to total US population enumerated April 1, 1940. For 1921 through 1948, rates are adjusted by age, race, and gender. Five revisions of the International List of Causes of Death (ICD) were used to classify causes of death from 1900 through 1948; the period of each ICD revision is separated by solid vertical lines. Four revisions of the joint-cause manual (JCM) were used to select underlying cause of death from among all causes listed on death certificate; period of each JCM revision is separated by interrupted vertical lines. Abrupt decreases in rates are evident with introduction of ICD-3 in 1921 and adoption of JCM-2 in 1925.

Fig 2. Maps indicate annual age-adjusted stroke mortality rates for whites for 1900, 1910, 1920, and 1933. Areas were not included (unshaded) if they were either not in the death registration area or did not report deaths by race. States included in 1900 were all in the northeastern United States. Rates for these states were very high and remained relatively constant through at least 1920. States with lower rates were added after 1900, producing a spurious decline in stroke mortality rates.

death in 1921 was adjusted by additional revisions to the International List through 1948. Indicates five revisions of the International List of Causes of Death (ICD) were used to classify causes of death from 1900 through 1948; the period of each ICD revision is separated by solid vertical lines. Four revisions of the joint-cause manual (JCM) were used to select underlying cause of death from among all causes listed on death certificate; period of each JCM revision is separated by interrupted vertical lines. Abrupt decreases in rates are evident with introduction of ICD-3 in 1921 and adoption of JCM-2 in 1925.

Age-adjusted stroke mortality rates for whites were mapped by state for the years 1900, 1910, 1920, and 1933 (Fig 2). In 1900, the DRA included 10 states in the East North Central, Middle Atlantic, and New England census divisions; age-adjusted annual stroke mortality rates ranged from 116.91/100 000 population in Michigan to 164.76/100 000 population in New Jersey. By 1910, 21 states were included in the DRA, scattered across all census divisions except the three divisions in the South; stroke mortality rates ranged from 80.05 in Minnesota to 162.51 in New Jersey. States in the DRA in 1900 had approximately the same stroke mortality rates in 1910. Of the 11 states added to the DRA from 1900 through 1910, 4 had comparable rates to those in the 1900 DRA, and 7 had lower rates. By 1920, the DRA included 34 states representing all census divisions except the West South Central division; rates ranged from 84.26 in Mississippi to 150.61 in New Jersey. States in the DRA in 1910 had approximately the same rates in 1920, but many of the added states again had low rates. In 1933, the DRA included the entire contiguous United States, although 3 states (Arizona, Delaware, and New Mexico) had large populations of nonwhites and did not tabulate deaths by race; rates ranged from 68.24 in Utah to 118.78 in South Carolina. From 1920 through 1933, rates declined considerably in all states but particularly in the Northeast, shifting the distribution of excess stroke mortality southward.

Because stroke mortality rates differed across states, the nonrandom entry of states into the DRA confounded national estimates. While age-adjusted rates for the expanding group of death registration states erratically but progressively declined, rates for fixed component areas remained comparatively constant until
around 1925 and then declined (Fig 3). After 1925 the declines were greatest in the originally high-rate areas, so that by 1933 the age-adjusted rates for the United States and for the death registration states of 1900, 1910, 1920 were almost identical (Fig 3).

Over the years 1917, 1925, and 1940, estimated age-adjusted mortality rates declined in parallel for stroke as the underlying or contributing cause of death, for stroke as the underlying cause of death, and for stroke as the only listed cause of death (Fig 4). Reselection of the underlying cause of death for these years using uniform selection rules (1939 joint-cause manual) produced fairly wide ranges of recoded deaths and estimated rates for 1917 and 1925 (Table 2 and Fig 4). For both of these years, the range of recoded stroke deaths and estimated rates included the original estimates. For the interval from 1925 through 1940, the recoded data support a decline in stroke mortality rates because even the lower end of the range of estimated rates in 1925 is greater than the rate for 1940.

Comparison of average annual rates of change for stroke and heart disease mortality rates by state did not support a shift in diagnosis to explain the divergent trends. Indeed, at a state level, the trends were not consistently divergent. For white men, rates increased for both conditions in 4 states, increased for heart disease and decreased for stroke in 30 (in 3, the decline in stroke was more than the increase in heart disease), and decreased for both conditions in 15. For white women, rates increased for both conditions in 3 states, increased for heart disease and decreased for stroke in 6 (in 4, the decline in stroke was more than the increase in heart disease), increased for stroke and decreased for heart disease in 3, and decreased for both conditions in 37. For nonwhite men, rates increased for both conditions in 9 states, increased for heart disease and decreased for stroke in 8 (in 4, the decline in stroke was more than the increase in heart disease), increased for

stroke and decreased for heart disease in 8, and decreased for both conditions in 24. For nonwhite women, rates increased for both conditions in 7 states, increased for heart disease and decreased for stroke in 6 (in 2, the decline in stroke was more than the increase in heart disease), increased for stroke and decreased for heart disease in 11, and decreased for both conditions in 25.

Correlation analyses of state rates also did not support a shift in diagnosis to explain the divergent national trends in stroke and heart disease mortality rates. If a shift in diagnosis is the explanation for divergent trends, average annual rates of change for the two conditions should be negatively correlated. Instead, rates of change for stroke and heart disease rates are positively correlated for whites in the interval from 1940 through 1948: white men, $r = .32, P = .02$; white women, $r = .39, P < .01$.

Rates of change are not significantly associated for nonwhites: nonwhite men, $r = .14, P = \text{NS}$ (outlier Vermont excluded); nonwhite women, $r = .04, P = \text{NS}$ (outlier Vermont excluded). Changes for nonwhites in Vermont were extreme in this interval and not consistent across gender: Rates decreased markedly for stroke and increased markedly for heart disease in men but increased markedly for both conditions in women.

**Discussion**

Some of the apparent decline in US stroke mortality rates before the advent of antihypertensive therapy is
Table 2. Underlying Cause of Death* in Persons Dying With Stroke Using Original Coding and Recoding With 1939 Joint-Cause Manual: United States Death Registration States, 1917, 1925, and 1940

<table>
<thead>
<tr>
<th>Underlying cause of death among persons dying with stroke</th>
<th>1917</th>
<th>1925</th>
<th>1940</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deaths (%)</td>
<td>Recoded deaths (%)</td>
<td>Deaths (%)</td>
<td>Recoded deaths (%)</td>
</tr>
<tr>
<td>Stroke</td>
<td>71,456 (81.6) 45,689-74,897 (52.1-85.5)</td>
<td>92,984 (78.0) 85,051-113,268 (71.3-95.0)</td>
<td>119,753 (66.3)</td>
</tr>
<tr>
<td>Cerebral hemorrhage or effusion</td>
<td>62,417 (71.2) 38,086-61,855 (43.5-70.6)</td>
<td>72,177 (69.3) 75,261-97,912 (63.1-82.1)</td>
<td>105,210 (58.2)</td>
</tr>
<tr>
<td>Cerebral embolism or thrombosis</td>
<td>2,706 (3.1) 2,792-5,298 (3.2-6.0)</td>
<td>3,668 (3.1) 3,693-6,298 (3.1-5.3)</td>
<td>10,240 (5.7)</td>
</tr>
<tr>
<td>Cerebral softening, hemiplegia, or paralysis of unspecified origin</td>
<td>6,333 (7.2) 4,811-7,744 (5.5-8.8)</td>
<td>6,665 (5.6) 6,097-9,058 (5.1-7.6)</td>
<td>4,303 (2.4)</td>
</tr>
<tr>
<td>Diseases of the circulatory system</td>
<td>4,807 (5.5) 564-23,084 (0.6-26.3)</td>
<td>9,926 (8.3) 677-10,850 (0.6-9.1)</td>
<td>30,469 (16.9)</td>
</tr>
<tr>
<td>Diseases of the genitourinary system</td>
<td>3,321 (3.8) 6,280-7,707 (7.2-7.7)</td>
<td>8,991 (7.5) 15,989-9,894 (0.0-8.3)</td>
<td>11,801 (6.5)</td>
</tr>
<tr>
<td>Other</td>
<td>8,028 (9.2) 5,871-12,132 (6.7-13.8)</td>
<td>7,344 (6.2) 5,285-13,450 (4.4-11.3)</td>
<td>18,619 (10.3)</td>
</tr>
<tr>
<td>Total</td>
<td>87,612</td>
<td>87,612</td>
<td>119,245</td>
</tr>
</tbody>
</table>

*Only conditions that accounted for 5% or more of deaths in at least one of the study years are listed individually.

Artificial. Indeed, the entire reported decline in stroke mortality rates before 1925 can be explained by the combination of changes in disease classification systems, joint-cause selection rules, and geographic coverage of death certification. The decline after 1925 cannot be attributed to these factors and does not apparently result from a shift in diagnosis from stroke to heart disease. Other possible causes of artificial mortality trends—such as changes in recognition and reporting of individual diseases, changes in the accuracy of reporting of age at death, and errors in the enumeration of the populations—either cannot be easily studied retrospectively or are unlikely to account for the generally steady and marked decline in stroke mortality rates over half a century.

Changes in the cause-of-death classification system produced only one marked discontinuity in stroke mortality trends during the interval from 1900 through 1948. The abrupt 6.6% decrease in stroke death rates with the introduction of ICD-3 in 1921 was of comparable magnitude to the net 8.7% decrease in age-adjusted stroke death rates over the previous 20 years. While stroke types were not accurately diagnosed in this period, changes in coding systems preferentially affected some stroke categories and were then reflected in overall stroke rates. The introduction of ICD-3 affected rates for cerebral hemorrhage as well as cerebral embolism and thrombosis. ICD-2 rubric 64 ("cerebral hemorrhage, apoplexy") included several nonstroke terms that were transferred to nonstroke rubrics in ICD-3: "alcoholic edema of brain," "alcoholic wet brain," and "wet brain" were transferred to ICD-3 rubric 66 ("alcoholism"); "atheroma of brain" and "cerebral atheroma" were transferred to ICD-3 rubric 91b ("atherosclerosis"); and "hemorrhagic pachymeningitis" was transferred to ICD-3 rubric 71a ("simple meningitis").

Adoption of the other ICD revisions during the period from 1900 through 1948—ICD-2, ICD-4, and ICD-5—produced no marked breaks in continuity of stroke mortality trends, although considerable changes were made in the stroke list titles for ICD-2 and ICD-5. To measure the net effect of the ICD-5 revision, the US Bureau of the Census dually coded all reported deaths for the year 1940 using both ICD-5 and ICD-4. As anticipated from examination of stroke trends, the net effect of the ICD-5 revision was minimal: 119,753 stroke deaths were coded with ICD-5 compared with 120,306 coded with ICD-4, a net decrease of less than 0.5%. Changes for each stroke type were also small: −0.3% for cerebral hemorrhage, −2.4% for cerebral embolism and thrombosis, −0.7% for hemiplegia and other paralysis, and +2.3% for cerebral softening.

The confused process of blindly transferring a disease to a rubric was preferred to carefully transferring a disease to a rubric. The introduction of ICD-3 to the death certificate. The first revision of the International List incorporated a vague set of rules for joint-cause selection, which produced arbitrary and inconsistent coding. To improve the selection procedures, the Index of Joint Causes of Death was published in 1914. In the 1914 manual each individual term was given a "weight"; unfortunately, this manual did not include all combinations of joint causes of death that appeared on certificates, so registrars were still forced to make arbitrary selections of the underlying cause of death. A second edition, The Manual of Joint Causes of Death, was published in 1926. In the 1925 and later manuals, any term listed under a joint-cause subdivision has the same "weight" as other terms included under that subdivision. Further changes in assignment were made in the third edition in 1933, and very minor changes were made in the fourth edition in 1939.

A large break in continuity in stroke mortality trends—a decrease of 9.2%—occurred with institution of the new joint-cause selection rules in 1925, whereas the revisions of selection rules in 1914, 1933, and 1939 had little apparent effect on overall stroke rates. With the 1925 revision, the terms under ICD-3 rubric 74a ("cerebral hemorrhage") were given less weight in selection of the underlying cause than conditions frequently reported in combination with cerebral hemor-
rhage, particularly diseases of the heart and chronic nephritis.25,26,30

Reselection of the underlying cause of death from aggregate joint-cause tabulations for 1917, 1925, and 1940 using uniform selection rules produced wide ranges of recorded deaths and estimated rates for 1917 and 1925. Nevertheless, for the interval from 1925 through 1940, the recoded data support a decline in stroke mortality rates because even the lower end of the range of estimated rates in 1925 is greater than the estimated rate for 1940. In addition, estimated age-adjusted stroke mortality rates also declined from 1925 through 1940 for stroke listed as any cause of death and for stroke listed as the only cause of death.

Although changes in classification systems and joint-cause selection rules contributed to the apparent decline in stroke mortality rates before the advent of antihypertensive therapy, the major discontinuities associated with these factors occurred before 1925. Other factors must be involved because stroke rates continued to decline from 1925 through 1948 and because declines in stroke mortality rates occurred within the period of each of the first five revisions of the ICD and within the period of each of the four editions of the joint-cause selection manual.

One additional important factor involved in the apparent decline was a changing geographic area for death registration. In the early twentieth century, national estimates of mortality rates were based on deaths in the DRA. Admission of states and cities to the DRA required at least 90% completeness of death registration, use of standard death certificates, and acceptable state registration laws.32 The DRA, which included only 10 states and the District of Columbia in 1900, expanded to the entire coterminous United States by 1933.32 Before about 1925, the DRA was not representative of the United States population as a whole: The early states were mainly northeastern states with predominately white populations. Because stroke mortality rates differed across states, the nondistribution of states into the DRA confounded national estimates. When changes in the geographic area of death certification are taken into account (by examining trends in stroke mortality rates for fixed geographic areas within the expanding DRA), no decline in rates is evident until after 1925, when rates precipitously decline for the DRA and for each of the component areas.

It has been suggested that some decline in stroke mortality rates may be due to a shift in diagnosis from stroke to heart disease.2,6 Indeed, national mortality trends for stroke and heart disease were divergent before the 1960s: Rates for heart disease increased, whereas rates for stroke declined. However, comparison of average annual rates of change for stroke and heart disease mortality rates by state from 1940 through 1948 did not support a shift in diagnosis to explain the divergent trends. Indeed, except for white men, trends were more often consistent than divergent for stroke and heart disease mortality rates. In addition, rates of change for stroke and heart disease mortality rates were positively correlated for white men and for white women but not associated for blacks; if a shift in diagnosis was responsible for the divergent national trends, average annual rates of change at a state level should have been negatively correlated, but they were not. An analysis by Moriyama and colleagues2 of changes in these conditions from 1949 through 1951 to 1959 through 1961 also failed to identify evidence to support a major shift in diagnoses from stroke to heart disease.

The causes for the decline in stroke mortality rates after 1925 are unknown, but the decline from this point cannot readily be attributed to artifacts. If the marked decline in stroke mortality rates from 1925 through 1948 is not artifactual, the decline in stroke mortality rates began decades before the decline in ischemic heart disease mortality rates23,31-37 and decades before any known declines in the prevalence or severity of recognized stroke risk factors, including hypertension and cigarette smoking.38-44

Acknowledgments

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http://stroke.ahajournals.org/content/24/9/1382