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**Therapeutic Milestone: Stroke Declines From the Second to the Third Leading Organ- and Disease-Specific Cause of Death in the United States**

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# Therapeutic Milestone

## Stroke Declines From the Second to the Third Leading Organ- and Disease-Specific Cause of Death in the United States

Amytis Towfighi, MD; Bruce Ovbiagele, MD, MS; Jeffrey L. Saver, MD

**Background and Purpose**—Stroke mortality rates declined for much of the second half of the 20th century, but recent trends and their relation to other organ- and disease-specific causes of death have not been characterized.

**Methods**—Using the National Center for Health Statistics mortality data, leading organ- and disease-specific causes of death were assessed for the most recent 10-year period (1996 to 2005) in the United States with a specific focus on stroke deaths.

**Results**—Age-adjusted stroke death rates declined by 25.4%; as a result, lung cancer (which only declined by 9.2%) surpassed stroke as the second leading cause of death in 2003. Despite a 31.9% decline in age-adjusted ischemic heart disease death rates, it remains the leading cause of death. Stroke is now the fifth leading cause of death in men and the fourth leading cause of death in whites but remains the second leading cause of death in women and blacks.

**Conclusions**—With stroke death rates decreasing substantially in the United States from 1996 to 2005, stroke moved from the second to the third leading organ- and disease-specific cause of death. Women and blacks may warrant attention for targeted stroke prevention and treatment because they continue to have disproportionately high stroke death rates. (*Stroke*. 2010;41:499-503.)

**Key Words:** cause of death ■ deaths ■ mortality ■ stroke

Stroke mortality rates have decreased in the United States since the 1920s.<sup>1</sup> Although stroke mortality rates decreased by 1%/year among whites from 1920 through the 1960s, the decline was much less pronounced among non-whites.<sup>1</sup> The rate of decline in both blacks and whites accelerated in the 1970s, likely due to improved hypertension control, but slowed in the 1980s and may have stopped in the 1990s.<sup>2</sup>

Little is known about recent trends in stroke mortality and how these compare with other organ- and disease process-specific causes of death. This study was undertaken to evaluate trends in the top 5 organ- and disease-specific causes of death in the United States from 1996 to 2005 with a specific focus on trends in stroke death rates.

### Methods

Number of deaths, crude death rates, and age-adjusted death rates in the United States for the most recent 10-year period (1996 to 2005) were obtained from the National Vital Statistics System of the Centers for Disease Control and Prevention's National Center for Health Statistics. The National Center for Health Statistics compiles a national database of information reported on death certificates in 50 states and the District of Columbia. More than 99% of deaths are believed to be registered.<sup>3</sup> Information is initially completed by funeral directors, physicians, medical examiners, and coroners and subsequently filed in state registration offices.

Death rates were based on populations enumerated as of April 1 for census years and estimated as of July 1 for all other years.<sup>3</sup> The base population for age-adjusted death rates was changed in 1999 when the Year 2000 Age Standard was instituted<sup>4</sup>; therefore, to compare age-adjusted death rates from 1996 to 2005, we adjusted the 1996 to 1998 death rates to the Year 2000 Age Standard. We used the usual 11-age strata of: <1, 1 to 4, 5 to 14, 15 to 24, 25 to 34, 35 to 44, 45 to 54, 55 to 64, 65 to 74, 75 to 84, and ≥85 years. For a given year, the overall age-adjusted rate =  $\sum P_i r_i$  in which  $P_i$  is the proportion of the 2000 US population in the  $i^{\text{th}}$  age stratum ( $i=1 \dots 11$ ) and  $r_i$  is the age-specific rate in the  $i^{\text{th}}$  stratum for the year in question;  $\sum P_i=1$ .

Causes-of-death statistics were classified in accordance with the International Statistical Classification of Diseases and Related Health Problems, Ninth and Tenth Revisions (ICD-9 for 1996 to 1998 and ICD-10 for 1999 to 2005).

For this analysis, combined organ-specific and disease process-specific causes of death were analyzed. Consequently, for vascular diseases, ischemic heart disease, stroke, and peripheral vascular disease were analyzed separately and for cancer, lung cancer, breast cancer, colon cancer, and so on were analyzed separately. The National Center for Health Statistics does not separate trauma/accidents into organ-specific components; therefore, this was the only category analyzed at the disease-process, multiorgan level.

The 5 leading organ- and disease-specific causes of death in the general population were: "ischemic heart disease" (ICD-9 codes 410 to 414, 429.2; ICD-10 codes I20 to I25), "malignant neoplasms of the trachea, bronchus, and lung" (ICD-9 code I62; ICD-10 codes C33 to C34), "cerebrovascular diseases" (ICD-9 codes 430 to 434, 436 to

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**Table. Trends in Age-Adjusted Death Rates From 1996 Through 2005 for the Top Five Organ- and Disease-Specific Causes of Death in the United States**

	Age-Adjusted Death Rates									
	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
<b>Total</b>										
Ischemic heart disease	212.1	203.6	197.1	194.6	186.8	177.8	170.8	162.9	150.2	144.4
Lung cancer	57.9	57.5	57.1	55.5	56.1	55.3	54.9	54.1	53.2	52.6
Stroke	62.5	61.1	59.3	61.6	60.9	57.9	56.2	53.5	50.0	46.6
Accidents	34.5	34.2	34.5	35.3	34.9	35.7	36.9	37.3	37.7	39.1
Chronic lower respiratory diseases	40.6	41.1	41.8	45.5	44.2	43.7	43.5	43.3	41.1	43.2
<b>Men</b>										
Ischemic heart disease	276.8	265.5	256.0	251.2	241.4	228.5	220.4	209.9	194.1	187.4
Lung cancer	82.6	81.2	79.7	76.9	76.7	75.2	73.2	71.7	70.1	69.0
Stroke	65.3	63.9	60.7	63.2	62.4	59.0	56.5	54.1	50.4	46.9
Accidents	49.1	48.6	48.8	49.8	49.3	50.2	51.5	51.8	52.1	54.2
Chronic lower respiratory diseases	54.2	54.6	54.5	58.7	55.8	54.0	53.5	52.3	49.5	51.2
<b>Women</b>										
Ischemic heart disease	165.3	158.4	153.9	152.9	146.5	139.9	133.6	127.2	116.7	111.7
Lung cancer	40.4	40.9	41.0	40.2	41.3	41.0	41.6	41.3	40.9	40.5
Stroke	59.9	58.6	57.6	59.8	59.1	56.4	55.2	52.3	48.9	45.6
Accidents	21.6	21.5	21.8	22.3	22.0	22.5	23.5	24.1	24.5	25.0
Chronic lower respiratory diseases	32.9	33.3	34.4	37.7	37.4	37.6	37.4	37.8	36.0	38.1
<b>Black</b>										
Ischemic heart disease	233.7	226.5	221.1	224.9	218.3	211.6	203.0	195.0	179.8	171.3
Lung cancer	67.9	67.4	66.4	64.8	64.0	62.5	61.9	60.8	59.8	58.4
Stroke	84.4	80.8	79.7	81.8	81.9	78.8	76.3	74.3	69.9	65.2
Accidents	19.1	19.3	18.1	40.1	37.7	37.6	36.9	36.1	36.3	38.7
Chronic lower respiratory diseases	25.4	25.0	25.5	33.5	31.6	30.9	31.2	30.1	28.2	30.6
<b>White</b>										
Ischemic heart disease	211.8	203.1	196.5	193.4	185.6	176.5	169.8	161.7	149.2	143.8
Lung cancer	57.7	57.4	57.0	55.4	56.2	55.6	55.3	54.5	53.6	53.1
Stroke	60.2	59.0	57.2	59.6	58.8	55.8	54.2	51.4	48.0	44.7
Accidents	34.1	33.9	34.3	35.2	35.1	36.0	37.5	38.2	38.8	40.1
Chronic lower respiratory diseases	42.0	42.6	43.3	47.1	46.0	45.6	45.4	45.4	43.2	45.4

438; ICD-10 codes I60 to I69), "accidents" (ICD-9 codes E800 to E869, E880 to E929; ICD-10 codes V01 to X59, Y85 to Y86), and "chronic lower respiratory diseases" (ICD-9 codes 490 to 494, 496; ICD-10 codes J40 to J47).

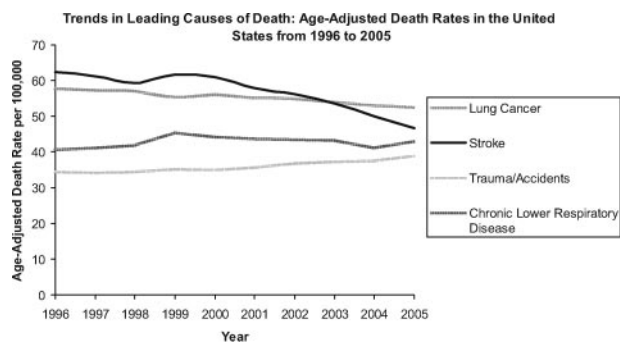
Deaths, death rates, and age-adjusted death rates were assessed in the following groups: (1) total population; (2) women; (3) men; (4) blacks; and (5) whites. Before 2000, the Office of Management and Budget required agencies to report race using 4 single-race categories; however, the newer version, implemented in 2000, increased the categories to 5 and allowed respondents to choose more than one category.<sup>5</sup> To produce death rates by race for 2000 to 2005, the reported population data for multiple-race persons was "bridged" back to single-race categories.<sup>6</sup> Due to inconsistencies in race classification on death certificates, deaths and death rates could only be assessed reliably for the white and black categories.<sup>7</sup>

## Results

The combined organ- and disease-specific age-adjusted death rates for the 5 leading causes of death in the United States from 1996 to 2005 are shown in the first section of the Table and Figure 1. Although age-adjusted ischemic heart disease

death rates declined by 31.9%, ischemic heart disease remained the leading cause of death, nearly 3 times as frequent as the next most common cause. Although stroke was the second leading cause of death in 1996, age-adjusted death rates declined by 25.4% and stroke became the third leading cause of death after ischemic heart disease and lung cancer. Lung cancer age-adjusted death rates decreased only 9.2%. The changes in total number of deaths mirrored changes in age-adjusted death rates (Figure 2).

Sex-specific trends in organ- and disease-specific age-adjusted death rates are shown in the second and third sections of the Table. In both men and women, ischemic heart disease remained the leading cause of death despite substantial declines in age-adjusted death rates (32.3% in men and 32.4% in women). In men, stroke age-adjusted death rates fell by 28.2%, and stroke dropped from being the third to the fifth leading cause of death after ischemic heart disease, lung cancer, accidents, and chronic lower respiratory diseases.



**Figure 1.** Changes in age-adjusted death rates for the second through fifth leading organ- and disease-specific causes of death in the United States from 1996 to 2005. The leading cause of death, ischemic heart disease, is not shown, because display would require increasing the y axis 3-fold and preclude close examination of changes in stroke mortality and shifts in position among causes 2 through 5.

Among women, although the stroke age-adjusted death rates declined by 23.9%, stroke remained the second leading cause of death.

Analysis of race-specific trends revealed that ischemic heart disease declined substantially in both blacks (26.7%) and whites (32.1%) but remained the leading cause of death (Table). Despite a 22.7% decline in age-adjusted stroke death rates, stroke remained the second leading cause of death in blacks. Among whites, on the other hand, the 25.7% decline in stroke age-adjusted death rates resulted in stroke moving from the second to the fourth leading cause of death after ischemic heart disease, lung cancer, and chronic lower respiratory disease. Trends in numbers of deaths mirrored age-adjusted death rates for all sex and race subgroups.

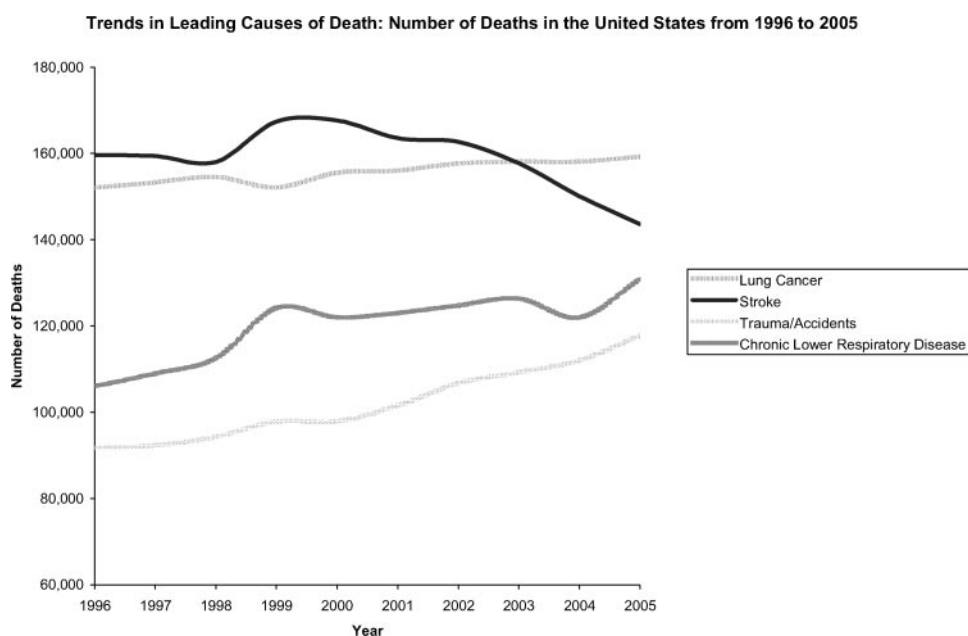
## Discussion

This analysis of US mortality data reveals that after a possible plateau in the 1990s, stroke age-adjusted death rates in the

first years of the 21st century resumed declining, culminating in stroke dropping from the second to the third leading organ- and disease-specific cause of death. This study did not directly address the reasons for the resumption in the fall in stroke death rates and the relative contributions of lower stroke incidence and lower stroke morbidity. One may speculate, however, that these improvements are related to better vascular risk factor control. Supporting this, comparing 1988 to 1994 with 1999 to 2004, blood pressure treatment and control rates improved from 53.1% to 61.4% and 26.1% to 35.1% (both  $P < 0.001$ ).<sup>8</sup> Similarly, between 1988 to 1994 and 1999 to 2004, the use of pharmacological lipid-lowering treatment increased from 11.7% to 40.8% and low-density lipoprotein cholesterol control increased from 4.0% to 25.1% among those with high low-density lipoprotein cholesterol (both  $P < 0.001$ ).<sup>9</sup> In addition, smoking rates declined from 29.3% in 1988 to 1994 to 26.4% in 1999 to 2000.<sup>10</sup>

Factors other than improved vascular risk factor control may have contributed to lower stroke death rates. For example, improved, organized treatment of incident acute stroke with Joint Commission stroke center certification and the use of protocol-driven hospital care to reduce poststroke complications may have resulted in fewer stroke deaths.<sup>11</sup> In addition, if the decline in ischemic heart disease deaths was due to a reduction in the incidence of ischemic heart disease, then, conceivably, the decline in stroke deaths could be partially explained by a reduction in cardioembolic strokes.

Prior studies have used inconsistent methods for classifying causes of death. Some studies report deaths by disease process (such as vascular and cancer), some by organ system (such as diseases of the heart, disease of the lung, and diseases of the nervous system), and some by combined disease process- and organ-specific categories (such as ischemic heart disease and breast cancer). Stroke is an organ-specific (nervous system) manifestation of a general disease



**Figure 2.** Changes in number of deaths for the second through fifth leading organ- and disease-specific causes of death in the United States from 1996 to 2005. The leading cause of death, ischemic heart disease, is not shown, because display would require increasing the y axis 3-fold and preclude close examination of changes in stroke mortality and shifts in position among causes 2 through 5.

process (vascular disease) and thus it is appropriate when comparing death rates to contrast stroke with other combined organ- and disease-specific causes of death. This like-to-like approach was frequently not followed in prior studies, which reported the 3 leading causes of death in the United States as heart disease (an organ-specific category), cancer (a disease process-specific category), and stroke (a combined organ- and disease process-specific category). Our study used a concordant combined organ and disease process categorization for all conditions except trauma/accidents, for which organ-specific information was lacking.

Although stroke age-adjusted death rates decreased substantially throughout the study period in all subgroups, because of differences in starting points and in competing causes of mortality, stroke remains the second leading cause of death among women and blacks even though it dropped to the fifth leading cause of death in men and fourth leading cause of death in whites. This study corroborates prior studies that revealed higher stroke mortality rates in blacks compared with whites<sup>12–14</sup> and women compared with men.<sup>15</sup>

The causes of the sex disparities in stroke death rates are likely multifactorial. First, women are overrepresented in older age groups and stroke mortality is higher with older age. Second, vascular risk factors in women are insufficiently prevented, recognized, diagnosed, and treated.<sup>8,16–18</sup> For example, among individuals with cardiovascular disease, men have their cholesterol measured more often, treated more aggressively, and have lower low-density lipoprotein levels than women<sup>18</sup> and women are significantly less likely to take aspirin than men.<sup>17</sup> Similarly, in those with known hypertension treated with antihypertensive medications, women are less effectively controlled compared with men.<sup>8,19</sup> Third, there are sex differences in stroke care; compared with men, women have greater time delays from emergency department arrival to physician assessment,<sup>20</sup> are less likely to receive diagnostic tests,<sup>21,22</sup> are less likely to be treated with antiplatelet agents<sup>23</sup> or thrombolytic therapy,<sup>24,25</sup> and are less likely to receive outpatient rehabilitation.<sup>26</sup> Finally, compared with men, women are more likely to have a severe stroke<sup>25</sup> and to be disabled after a stroke.<sup>22,25</sup>

Several factors likely contribute to the racial disparities in stroke death rates. First, stroke incidence is higher in blacks compared with whites.<sup>14,27,28</sup> Second, several vascular risk factors such as hypertension, diabetes mellitus, smoking (in men), and overweight/obesity (in women) are more prevalent in blacks.<sup>14,29</sup> Third, blacks are less likely to arrive at the hospital within 3 hours of onset of symptoms.<sup>30</sup> When they arrive, they are less likely to receive diagnostic tests<sup>31</sup> and thrombolytics than whites.<sup>32</sup> Finally, blacks have more severe strokes than whites,<sup>33</sup> have greater physical impairments on admission and at follow-up,<sup>34,35</sup> and have higher in-hospital case-fatality rates than do whites.<sup>36</sup> Of note, one study, with a population sociodemographically similar to the US population, found higher stroke incidence in blacks compared with whites with comparable case-fatality rates, suggesting that the higher stroke mortality rates among blacks were due to higher incidence rates.<sup>27</sup>

Despite improvements in stroke death rates over the past decade, stroke remains a leading cause of death and leading

cause of disability. Further progress in stroke prevention and treatment remains a vital public health priority. Despite improved control of several vascular risk factors, improvements in stroke mortality have likely been tempered by increasing prevalence of obesity, which is linked to both stroke incidence<sup>37,38</sup> and mortality after stroke.<sup>39</sup> In 1988 to 1994, 22.5% of individuals in the United States were obese<sup>40</sup>; currently, approximately 30% are overweight and 32% are obese.<sup>41</sup> Similarly, metabolic syndrome prevalence increased from approximately 50 million in 1990 to approximately 64 million in 2000.<sup>42</sup> In the setting of the obesity epidemic, diabetes mellitus prevalence increased from 7.4% in 1988 to 1994 to 8.1% in 1999 to 2000.<sup>10</sup> Public health initiatives to reduce obesity as well as to further reduce hypertension, dyslipidemia, and smoking are needed to drive further progress in reducing stroke mortality.

This study has limitations. First, the ICD codes changed during the study period; therefore, changes in mortality could be partly due to changes in classification. An analysis of causes of death in 1996, however, revealed no change in rank of the 5 leading causes of death if coded with the use of ICD-9 or ICD-10,<sup>4</sup> suggesting that the changes in classification had little effect on our study. Second, as a result of the guidelines for reporting race after 2000, population data for multiple-race persons were bridged back to single-race categories and the 2000 census counts were modified to be consistent with the previous race categories. As a result, the race-specific death rates were based on special estimation procedures and were not true counts. Because the estimation procedures contain some error, particularly in smaller population groups, results of race-specific deaths should be interpreted with caution. Third, due to inconsistencies in race classification on death certificates, the deaths and death rates could only be assessed reliably for the white and black categories, precluding further assessment of racial/ethnic differences. Although Hispanics are the largest minority group in the United States and have a higher stroke incidence than non-Hispanic whites,<sup>43,44</sup> we were unable to assess temporal trends in Hispanic stroke mortality rates as a result of the changes in race and ethnicity reporting. Finally, with the implementation of primary stroke center designation after December 2003, there may have been changes in death certificate coding.

Nevertheless, this study provides important information regarding recent trends in stroke death rates in the United States using a consistent system for comparison with other organ- and disease-specific causes of death. The overall decline in stroke death rates is encouraging, but the study highlights the need to strengthen stroke prevention and treatment efforts in women and blacks. In addition, the recent decline in stroke mortality will need to be closely monitored in the setting of the obesity epidemic and aging of the US population, factors that may increase stroke death rates in the future.

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## Disclosures

None.

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