Determining Stroke’s Rank as a Cause of Death Using Multicause Mortality Data

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Background and Purpose—Stroke has fallen from the second to the fourth leading cause of death in the United States without large declines in stroke incidence or case fatality. We explored whether this decline may be attributable to changes in mortality attribution methodology.

Methods—Multicause mortality files from 2000 to 2008 were used to compare changes in reporting of stroke as underlying cause of death (UCOD) with changes in death certificates reporting any mention (AMCOD) of stroke. In addition, the UCOD/AMCOD ratio was calculated for the 6 leading organ and disease-specific causes of death. If stroke mortality is underestimated by the system of mortality attribution, we hypothesized that we would find: (1) a greater decline in stroke as UCOD than as AMCOD; and (2) a decline in the UCOD/AMCOD ratio compared with other causes of death.

Results—Age-adjusted death rates for stroke as UCOD (61 per 100 000 in 2000 versus 41 in 2008) and AMCOD (102 per 100 000 versus 68) both declined by 33%. The ratio of UCOD to AMCOD for stroke did not change over time (0.595 in 2000 versus 0.598 in 2008). Changes in UCOD/AMCOD ratio for the diagnoses that surpassed stroke as UCOD were too small (no change for lung cancer and a slight increase from 0.49 to 0.52 for chronic lower respiratory diseases) to explain stroke’s decline as UCOD.

Conclusion—Changes in mortality attribution methodology are not likely responsible for stroke’s decline as a leading cause of death. The discordant trends in incidence, case fatality, and mortality require further study. (Stroke. 2012;43: 2207-2211.)

Key Words: epidemiology • mortality • multicause mortality • stroke • underlying cause of death • trends

See related article, p 2033.

Although stroke remains the leading cause of severe adult disabilty in the United States,1,2 the Centers for Disease Control and Prevention (CDC) estimates it has fallen from the second leading organ and disease-specific cause of death to the fourth leading cause of death over the last decade.3,4 Stroke mortality declined by 33% from 1999 to 2008 and was surpassed as a cause of death by 2 conditions with relatively static mortality: lung cancer in 20035 and chronic lower respiratory diseases in 2008.6 The most recent regional epidemiological data do not offer an obvious explanation for the 25% national decline in stroke mortality from 1999 to 2005: incidence fell by only 12%, whereas case fatality increased slightly in the Greater Cincinnati/Northern Kentucky Stroke Study over this interval.7

Determinations of disease-specific mortality rely on assignment of an “underlying cause of death” (UCOD)8 by a complex and annually re-evaluated algorithm to select the UCOD from the up to 20 causes listed on a death certificate. In some clinical contexts such as prostate cancer, substantial changes in the proportion of cases assigned as an UCOD have occurred over time.9 In other contexts such as with chronic lower respiratory diseases, explicit changes to the algorithm have resulted in immediate changes in assigned mortality.10 We explored whether the national decline in stroke mortality may be due to changes in UCOD assignment over time.

Systematic changes in the classification of stroke as the UCOD could occur through one of 2 mechanisms: (1) changes in death certificate completion patterns; or (2) changes in assignment of stroke as UCOD due to changes in the underlying algorithms. Our objective was to investigate evidence for changing prioritization of stroke deaths attributable to the system of mortality assignment over time using national death data. Specifically, we sought to determine whether stroke’s decline as UCOD was accompanied by a similar decline in any mention of stroke on death certificates (AMCOD). If the mortality attribution system deprioritized stroke over time, we would expect greater declines in stroke

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as UCOD than as AMCOD compared with other conditions. We speculated that recent improvements in diagnostic imaging technology,\textsuperscript{11,12} wider vascular risk factor recognition, or broader risk factor definitions\textsuperscript{13} may be relevant to both physician death certificate completion behavior and algorithmic assignment of UCOD.\textsuperscript{14,15} For example, a diabetic who would have been undiagnosed in a prior era whose death certificate listed “stroke” may now be classified as “stroke” due to “diabetes.”\textsuperscript{16} This would lead to an UCOD change from “stroke” to “diabetes.”

Methods

The National Vital Statistics System run by the CDC regulates the reporting and collection of official death records from local municipalities to enable national measurements.\textsuperscript{17} Standardized death certificates are the input to this process and the same death certificate has been used in the United States since 2003.\textsuperscript{18} The overarching goal of this system is to determine the UCOD from the list of diagnoses appearing on the death certificate. The World Health Organization defines UCOD as “the disease or injury which initiated the train of morbid events leading directly to death, or the circumstances of the accident or violence which produced the fatal injury.”\textsuperscript{19} The process of UCOD assignment relies on a complex set of rules enabling classification of death certificates that, for example, list “pneumonia” as the direct cause of death and “stroke” as a secondary diagnosis to be assigned a UCOD of stroke.\textsuperscript{8} If a specific diagnosis appears in any position on a death certificate, that diagnosis is classified as AMCOD for that individual.

In the United States, this process is currently automated by a series of specific computerized algorithms. First, SuperMICAR (Mortality Medical Indexing, Classification, and Retrieval) extracts the information from death certificates and translates the death certificate text into International Classification of Diseases, 10\textsuperscript{th} Revision (ICD-10) codes.\textsuperscript{20} The transition to ICD-10 (cerebrovascular disease codes I60–I69) from ICD-9 codes (cerebrovascular disease codes 430–438) occurred in 1999 and resulted in little net reclassification of stroke to other diagnoses (comparability ratio = 1.059).\textsuperscript{21} Since that time, the ICD-10 system has undergone a series of small regular updates.\textsuperscript{22} These codes are then inputted into a second system, ACME/TRANSAX, that applies a series of prioritization rules to assign the UCOD for each case. Prioritization rules are revised annually by the World Health Organization and distributed as part of the annual ICD revision.

Data Set

Prior reports that stroke has declined as a cause of mortality have relied on UCOD.\textsuperscript{5,6} To assess whether systematic changes in UCOD assignment may have influenced these reports, we relied on CDC multicause mortality files from 2000 to 2008. These files include basic demographics, the assigned UCOD, and all other diagnoses listed on the death certificate translated into ICD-10 codes for every death in the United States in a given year.

Analytic Strategy

We first assessed whether overall patterns of annual cause of death reporting suggested that stroke prioritization has changed by determining whether stroke’s decline as UCOD was accompanied by a parallel decline in stroke as AMCOD. If stroke’s decline as UCOD was not accompanied by comparable declines as AMCOD, it would suggest a systematic deprioritization of stroke in cause of death assignment. We then specifically assessed whether there has been a change in the assignment of stroke as UCOD by analyzing trends in the ratio of deaths where stroke was classified as UCOD to the number with stroke as an AMCOD. These ratios were also calculated for the other 5 most common organ- and disease-specific causes of death in 2008 (ischemic heart disease [ICD-10 codes I20–I25], lung cancer [C33–C34], chronic lower respiratory diseases [J40–J47], accidents [V01–X59, Y85–Y86], and Alzheimer disease [G30]). If stroke were relatively deprioritized through UCOD assignment algorithms, we would expect that the UCOD/AMCOD ratio would decline relative to the other common diseases.

Statistical Analysis

Unadjusted mortality rates were calculated by dividing the total number of UCOD and AMCOD from death certificates for the 6 most common causes of death specified by the CDC in 2008 by age groups (n=11) and dividing by the total US population in each age group in each year. The population in each age group was calculated from summing the number of people in each age group using CDC bridged-race population files.\textsuperscript{23} Age-adjusted mortality rates were then calculated using the standardized population from the Year 2000.\textsuperscript{24} This resulted in age-adjusted mortality rates that differ slightly from those reported by the CDC because estimates of the US population in each age category had not yet been finalized for 2008. We did not apply formal tests of statistical significance to the mortality trend data because the available data included all stroke deaths in the United States and thus there is no sampling variation. To estimate the impact of temporal changes in UCOD/AMCOD ratios on more recent rankings of causes of death, we used the UCOD/AMCOD ratio from 2000 to re-estimate the UCOD rankings in 2008.

Results

Trends in Stroke Mortality

The age-adjusted death rate for stroke as UCOD declined from 61 per 100 000 in 2000 to 41 in 2008, a 33% decline. The age-adjusted death rate for stroke as AMCOD declined by an identical 33% from 102 per 100 000 in 2000 compared with 68 cases in 2008 (Figure 1). The age-adjusted AMCOD and UCOD rates for the 6 leading causes of death in 2008 are displayed in Figures 2 and 3. As of 2008, stroke is ranked fourth (behind lung cancer, chronic lower respiratory diseases, and ischemic heart disease) as UCOD and ranked third as AMCOD (behind ischemic heart disease and chronic lower respiratory diseases). For the 2 diagnoses that surpassed stroke as UCOD from 2000 to 2008, lung cancer mortality declined slightly over this time period (by 11% as an UCOD and 12% as an AMCOD), whereas mortality attributable to chronic lower respiratory diseases was unchanged based on UCOD (0%) but declined substantially based on AMCOD (7%). Chronic lower respiratory diseases had been declining as UCOD before 2007 when a change to the UCOD assign-
ment algorithm led to an increase in number of cases assigned as UCOD.10

Changes in Diagnoses as Both UCOD and AMCOD
The ratio of UCOD to AMCOD for stroke did not change over time (0.595 in 2000 versus 0.598 in 2008). Of the diagnoses that surpassed stroke as UCOD over this time, there was almost no change in the UCOD/AMCOD ratio for lung cancer (0.939 in 2000 versus 0.943 in 2008) and a modest increase in the UCOD/AMCORD ratio for chronic lower respiratory diseases (0.486 in 2000 versus 0.521 in 2008) due to a 7% decline in chronic lower respiratory disease as AMCOD. For the 6 most common organ- and disease-specific UCOD in 2008, the ratio of UCOD to AMCOD for each diagnosis is displayed in the Table. The largest decline in the UCOD/AMCOD ratio was in ischemic heart disease (0.77 in 2000 versus 0.71 in 2008) and the largest increase in the ratio was in Alzheimer disease (0.59 in 2000 versus 0.74 in 2008). The UCOD/AMCOD ratio also increased for accidents (0.73 in 2000 versus 0.79 in 2008).

Impact of Changing UCOD/AMCOD Ratio on Overall UCOD Assignment
To estimate the impact of changing UCOD/AMCOD ratios, we calculated the 2008 age-adjusted UCOD for lung cancer, chronic lower respiratory diseases, and stroke assuming the 2000 UCOD/AMCOD ratio were applied to 2008 death certificates. We estimate that the age-adjusted UCOD in 2008 would be 49.4 per 100 000 population for lung cancer (actual 49.5), 40.6 for stroke (actual 40.8), and 41.0 for chronic lower respiratory diseases (actual 44.0) if the 2000 UCOD/AMCOD ratios were applied.

Discussion
We did not find evidence for substantial underreporting of stroke deaths attributable to the system of mortality assignment over time. If stroke was less commonly reported as an UCOD from 2002 to 2008, we would have expected a smaller decline in stroke’s rate as an AMCOD than as an UCOD and a larger decline in the UCOD/AMCOD ratio for stroke compared with other leading causes of death. Instead, stroke’s 33% decline as UCOD from 2000 to 2008 was exactly paralleled by its 33% decline in AMCOD and the stroke UCOD/AMCOD ratio did not change over time (0.595 in 2000 versus 0.598 in 2008). We conclude that the decline in stroke mortality is not likely to be an artifact of changes to the system of mortality assignment.

We did not find evidence that stroke’s decline as UCOD relative to lung cancer was a reflection of either decreased stroke prioritization or increased lung cancer prioritization.
because UCOD/AMCOD ratios changed very little for both diseases. Conversely, increases in the UCOD/AMCOD ratio for chronic lower respiratory disease indicate that there has been either an accurate increase in attribution of chronic lower respiratory disease mortality and/or a relative overstatement of chronic lower respiratory disease mortality compared with stroke mortality. However, even if these changes were entirely due to overstatement of chronic lower respiratory disease mortality, although the mortality difference between stroke and chronic lower respiratory disease would in fact be more narrow than currently estimated, chronic lower respiratory disease mortality would still be higher than stroke. Given the differing temporal trends in chronic lower respiratory disease (0% change) and stroke (33% decline) as UCOD from 2000 to 2008, the gap in mortality rates between these 2 conditions is likely to widen in the near term.

Although stroke’s decline among leading causes of mortality is not explained by changes in the mortality assignment system, we did find evidence that stroke has been historically and is still given less priority in the algorithm than other causes of death. This trend is reflected in stroke’s lower rank as UCOD (fourth) than as AMCOD (third). Stroke was assigned as the underlying cause of death (UCOD) in only 60% of cases where it appeared on the death certificate in 2008. By comparison, myocardial infarction was assigned as UCOD in 71% of death certificates where it appeared and lung cancer in 94%. Consequently, either stroke has been historically underrecognized as a cause of death by a system of mortality assignment that inadequately prioritizes stroke and incorrectly assigns other conditions as the UCOD in patients with stroke. Similar observations have been made for other disease states such as diabetes, which also has a lower UCOD/AMCOD ratio than most leading causes of death. Determining whether stroke is underrepresented as a cause of death or whether it is less deadly than other diseases requires a method for finding the “right answer” to whether stroke is the UCOD and poses enormous challenges. However, some data suggest that stroke may be underrepresented as a cause of mortality; for example, a detailed medical chart analysis of the causes of death among incident stroke cases that occurred in the Cardiovascular Health Study found that stroke was assigned as the underlying cause of death for 51% of all strokes, which, given that there are an estimated 795 000 incident and recurrent strokes in the United States annually, would result in a much higher rate of stroke as UCOD. However, even with access to such detailed medical records, interobserver agreement for assignment of stroke as the underlying cause of death is poor. The situation is further complicated by the fact that multiple methods have been proposed to assign the UCOD, probably physicians receive little training in how to complete death certificates, and death certificate completion is suboptimal. The combination of substantial declines in national mortality (25%), lesser declines in regional incidence (12%), and a slight increase in regional case fatality in the United States from 1999 to 2005 is challenging to explain. In contrast, in the United Kingdom, the 50% decline in stroke mortality from 1979 to 2004 is mostly explained by a 40% decline in incidence from 1981 to 2004. Our data suggest that changes to the mortality attribution system are not responsible for this disconnect. The question then remains, do measurements of stroke incidence, case fatality, or stroke-related mortality fail to represent the true underlying national trend? Alternatively, is there another explanation such as changes in long-term mortality for this apparent disconnect? This analysis has 2 important limitations. The chief limitation is that, as mentioned previously, there is no gold standard for the assignment of stroke as the underlying cause of death. Additionally, our analysis relied on a series of inferences from patterns of stroke reporting on death certificates that have not been validated relative to detailed clinical data. However, we believe these inferences are reasonable and would be sensitive enough to major changes in assignment of UCOD.

In summary, stroke’s decline as a cause of death in the United States appears to be real. Although stroke’s relative decline may be slightly overstated compared with chronic lower respiratory diseases, it is not likely to be overstated compared with other major causes such as lung cancer. However, major challenges persist; stroke remains the second leading cause of death in women and in blacks and substantial racial and ethnic disparities in stroke incidence persist. Moreover, without persistent diligence, favorable trends in stroke and heart disease mortality may reverse due to the obesity epidemic and the aging population. Given the more rapid decline in stroke mortality than incidence, a shift in focus from stroke-related mortality to other stroke outcomes may be merited. With such a shift, it may be
necessary to develop nationwide systems to measure important stroke-related trends in incidence and stroke-associated disability.

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**Disclosures**
None.

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