Declining Death Rates From Hyperglycemic Crisis Among Adults With Diabetes, U.S., 1985–2002

JING WANG, MPH
DESMOND E. WILLIAMS, MD, PHD
K.M. VENKAT NARAYAN, MD
LINDA S. GEISS, MA

OBJECTIVE — To examine trends in death rates for hyperglycemic crisis (diabetic ketoacidosis or hyperglycemic hyperosmolar state) among adults with diabetes in the U.S. from 1985 to 2002.

RESEARCH DESIGN AND METHODS — Deaths with hyperglycemic crisis as the underlying cause were identified from national mortality data. Death rates were calculated using estimates of adults with diabetes from the National Health Interview Survey as the denominator and age adjusted to the 2000 U.S. population. The trends from 1985 to 2002 were tested using joinpoint regression analysis.

RESULTS — Deaths due to hyperglycemic crisis dropped from 2,989 in 1985 to 2,459 in 2002. During the time period, age-adjusted death rates decreased from 42.4 to 23.8 per 100,000 adults with diabetes (4.4% decrease per year, *P* for trend <0.01). Death rates declined in all age-groups, with the greatest decrease occurring among individuals aged ≥65 years. Age-adjusted death rates fell for all race-sex subgroups, with black men experiencing the smallest decline. About one-fifth of deaths occurred at home or on arrival at the hospital, and the death rates for hyperglycemic crisis occurring at these places declined only modestly over time (2.1% decrease per year, *P* for trend = 0.049).

CONCLUSIONS — Overall death rates due to hyperglycemic crisis among adults with diabetes have declined in the U.S. However, scope for further improvement remains, especially to further reduce death rates among black men and to prevent deaths occurring at home.

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Diabetic ketoacidosis (DKA) and hyperglycemic hyperosmolar state (HHS), referred to as hyperglycemic crisis in the current article, are two serious acute metabolic complications of diabetes that can be life threatening. These conditions, however, are largely preventable if patient education and access to care are adequate (1). Indeed, when these conditions do occur, death is generally avoidable with early diagnosis and proper treatment (2). With advances in monitoring and treatment of glycemia in the past decades (3,4) as well as promotion of the National Diabetes Education Program in recent years (5), one could reasonably expect that death rates from hyperglycemic crisis among people with diabetes are falling. In this study, we examined trends between 1985 and 2002 in death rates for hyperglycemic crisis among U.S. adults (≥18 years old) with diabetes.

RESEARCH DESIGN AND METHODS

Numerator

Deaths with DKA or HHS as the underlying cause were identified from national mortality data compiled by the National Center for Health Statistics (6). Before 1999, causes of death were classified and coded according to the ICD-9 (7), but in 1999, the ICD-10 (8) was adopted. Deaths due to DKA without mention of coma were identified using ICD-9 250.1 and ICD-10 E10.1, E11.1, E12.1, E13.1, or E14.1; deaths due to DKA or HHS with coma were identified using ICD-9 250.2 and ICD-10 E10.0, E11.0, E12.0, E13.0, or E14.0. Beginning in 1992, data on place of death became available. To examine place of death, we classified deaths as occurring at health care sites (i.e., inpatient or outpatient or admitted to the emergency room of a hospital, clinic, or medical center; at a nursing home) or "at home" (i.e., at residence or on arrival at the hospital).

Denominator

Estimates of the people with diabetes were obtained from the National Health Interview Survey, an annual nationally representative household survey of the noninstitutionalized civilian population of the U.S. (9). Before 1997, the question on diabetes was, "During the past 12 months, did anyone in the family have diabetes?" In 1997, the question was changed to, "Have you ever been told by a doctor or health professional that you have diabetes or sugar diabetes?" People who answered "yes" to these questions were considered to have diabetes. Women with diabetes only during pregnancy were not included.

Statistical analyses

For each year from 1985 to 2002, we calculated death rates per 100,000 adults with diabetes by age-group (18–44, 45–64, and ≥65 years), race (white and black), and sex (male and female). We excluded younger individuals because reliable diabetes prevalence estimates were not available. In addition, from 1992 to 2002, we calculated death rates by place of death (at health care sites versus at home). Rates were age adjusted to the 2000 U.S. standard population using the direct method (10). Because mortality data are complete counts of deaths, we

From the Division of Diabetes Translation, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Atlanta, Georgia.

Address correspondence and reprint requests to Jing Wang, MPh, Northrop Grumman Contractor, Division of Diabetes Translation, Centers for Disease Control and Prevention, 4770 Buford Hwy., N.E. Mailstop K-10, Atlanta, GA 30341. E-mail: zrr4@cdc.gov.

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Abbreviations: DKA, diabetic ketoacidosis; HHS, hyperglycemic hyperosmolar state.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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Table 1—*Death rates from hyperglycemic crises per 100,000 people with diabetes, 1985–2002*

	Death rate		Trend 1			Trend 2		
	1985	2002	Period	Annual % change	95% CI	Period	Annual % change	95% CI
Overall age-adjusted rates	42.4	23.8	1985–2002	−4.4	−5.3 to −3.5*			
Age-specific rates								
18–44 years	42.2	31.4	1985–2002	−3.0	−4.2 to −1.7*			
45–64 years	26.3	12.7	1985–2002	−5.0	−5.9 to −4.1*			
≥65 years	71.4	19.7	1985–1989	0.2	−8.4 to 9.6	1989–2002	−9.2	−10.1 to −8.2*
Age-adjusted rates								
Race and sex								
White men	43.0	30.7	1985–2002	−3.6	−5.2 to −1.9*			
White women	32.0	16.5	1985–2002	−4.6	−5.3 to −3.8*			
Black men	65.2	57.6	1985–2002	−2.5	−4.6 to −0.4†			
Black women	89.7	21.4	1985–2002	−6.1	−7.2 to −5.0*			
	1992	2002*						
Place of death								
Home	9.0	8.0	1992–2002	−2.1	−4.2 to −0.0†			
Health care site	26.0	13.7	1992–2002	−6.9	−8.3 to −5.5*			

The annual percentage change differs significantly from zero (*$P < 0.01$, †$P < 0.05$). *Data on place of death available from 1992 to 2002.

assumed no variance in the numerator. Estimates of the denominator (with SEs) were obtained using SUDAAN software (Research Triangle Institute, Research Triangle Park, NC) (11) to account for the complex sample design of the National Health Interview Survey. SEs for death rates were obtained using Taylor linearization methods (12) in SAS (13). We used Joinpoint software (14) to assess trends over time. Details for joinpoint regression analysis have been previously published (15). In brief, this method uses permutation tests to identify the points (the "joinpoints") where linear trends change significantly in either direction or magnitude (e.g., 0 joinpoints indicates a simple straight line on log-scale). The rate of change for each trend is tested to determine whether it is significantly different from zero. Each trend in the final model is described by an annual percentage change. In the figures, the observed mortality rates are represented by symbols and the predicted trends from the joinpoint regression model are represented by solid lines. Statistical significance for this analysis was fixed to $P < 0.05$.

RESULTS — From 1985 to 2002, a total of 49,063 adults died because of hyperglycemic crisis, almost two-thirds (31,057) from DKA without coma and one-third (18,006) from DKA or HHS with coma. Annual deaths due to hyperglycemic crisis dropped from 2,989 in 1985 to 2,459 in 2002. In 1992–2002, 82% of deaths occurred within health care sites; 18% occurred "at home" (as noted in RESEARCH DESIGN AND METHODS, including case subjects dead on arrival at the hospital). Among decedents aged 18–44 and 45–64 years, even higher proportions of deaths occurred "at home" (38 and 26%, respectively).

From 1985 to 2002, age-adjusted death rates for hyperglycemic crisis decreased from 42.4 to 23.8 per 100,000 people with diabetes, a 4.4% decrease per year (P for trend <0.01) (Table 1). During the period, age-specific death rates due to hyperglycemic crisis decreased 3.0 and 5.0% per year for individuals aged 18–44 years ($P < 0.01$) and 45–64 years ($P < 0.01$), respectively (Table 1). Unlike the continuous linear trends in all other groups, joinpoint regression analysis indicated that death rates for people aged ≥65 years did not start to decline until 1989 (Fig. 1). Yet, thereafter, their death rates declined at 9.2% per year ($P <$

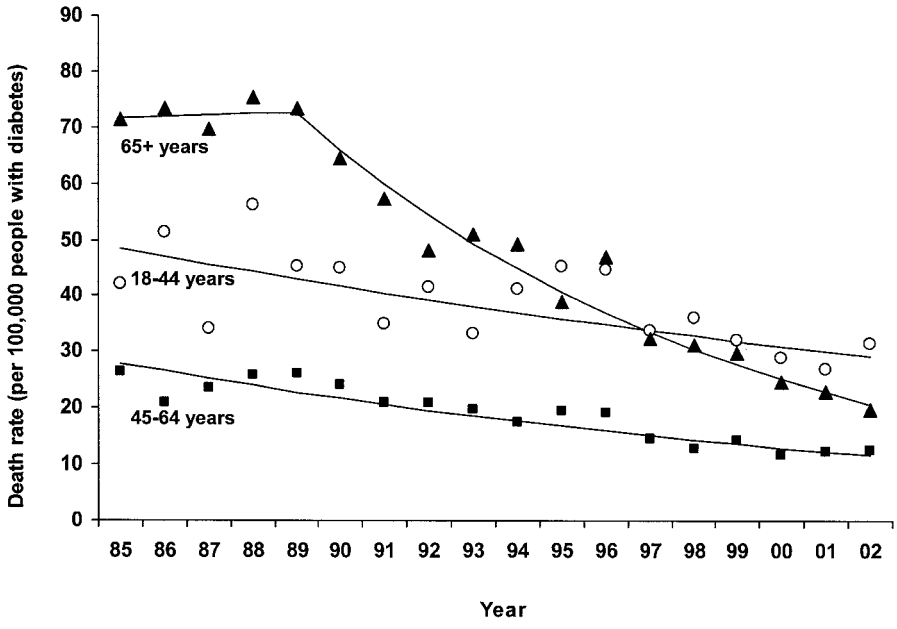

Figure 1—*Age-specific death rates for hyperglycemic crisis, U.S., 1985–2002.*

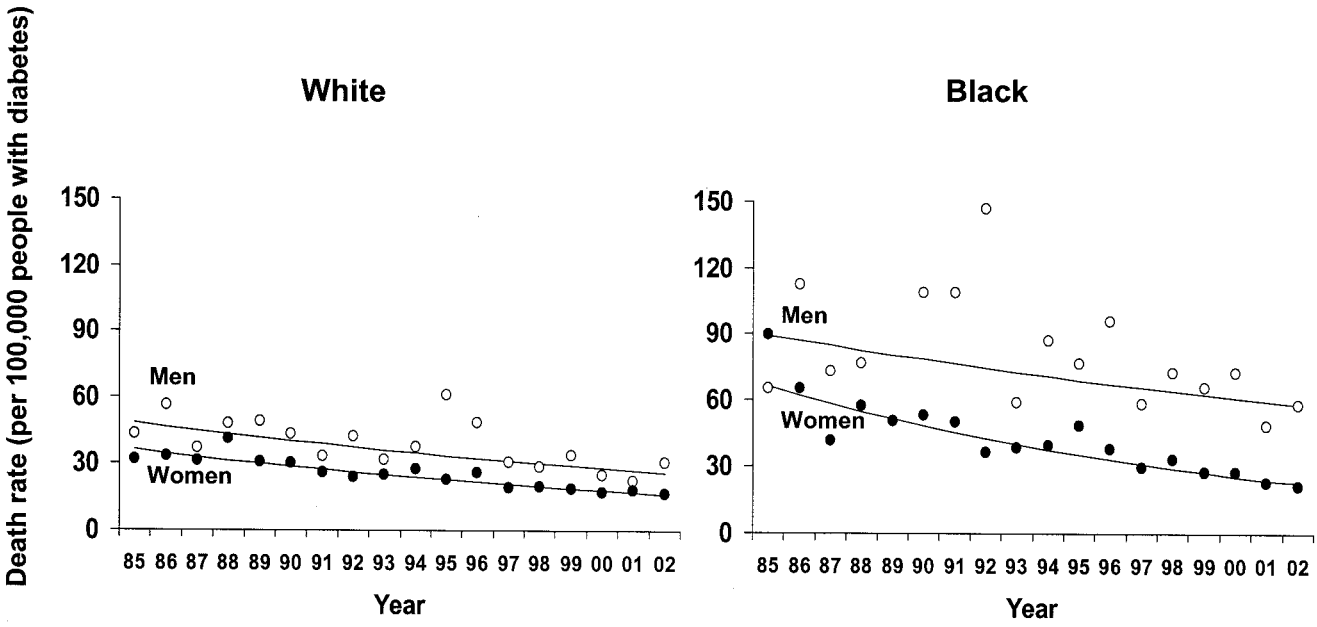

Figure 2—*Age-adjusted death rates for hyperglycemic crisis, by race and sex, U.S., 1985–2002.*

0.01), and this age-group had the greatest absolute decrease for 1989–2002 (Table 1). Although hyperglycemic crisis death rates were the highest for the oldest age-group at the beginning of the study period, eventually, by the end of the time period, death rates for this age-group dropped below those for individuals aged 18–44 years (Fig. 1).

Age-adjusted death rates decreased in all race-sex subgroups, with the greatest decrease (in both absolute decrease and annual percentage change) seen for black women (Table 1, Fig. 2). White women and then white men followed, with black men having the smallest annual decline. Black men also had the highest age-adjusted death rates. In 2002, the age-adjusted death rate for black men was 1.9, 3.5, and 2.7 times the rate for white men, white women, and black women, respectively (Table 1).

From 1992 to 2002, death rates for hyperglycemic crisis occurring at health care sites decreased from 26.0 to 13.7 per 100,000 people with diabetes, with an annual percentage change of −6.9% ($P <$ 0.01) (Table 1). In contrast, rates for death occurring "at home" only decreased from 9.0 to 8.0 per 100,000 people, an annual percentage change of −2.1% ($P =$ 0.049).

CONCLUSIONS — Among Americans with diabetes, death rates for hyperglycemic crisis declined substantially between 1985 and 2002, and the downward trend was seen in all age-groups and sex-race groups examined.

The decreases seen in hyperglycemic crisis death rates may be a consequence of lower incidence of hyperglycemic crisis, improved survival after actual episodes, or both. Hospitalization data from both the U.S. and Ontario suggest that decreases in incidence may indeed be occurring. Between 1985 and 2002, hospitalization rates for DKA among people with diabetes in the U.S. fell 36% (16). Similarly, in Ontario, hospitalization rates for hyperglycemic emergencies among people with diabetes declined 33% between 1994 and 1999 (17). In addition, rates of daily self-monitoring of blood glucose have increased (18), which may have played a role in reducing the incidence. On the other hand, survival from the condition may have improved with advances in monitoring and treatment of hyperglycemic crisis in the past decades. The availability and evolution of point-of-care or near-patient testing, especially measurement of β-hydroxybutyrate for blood ketone monitoring, has sped diagnosis and accelerated response to episodes of DKA (19,20); low-dose intravenous insulin regimens have become an established procedure for treating DKA (21); and more uniform agreement has been reached on the key principles on fluid and electrolyte replacement (22). Unfortunately, with mortality data, we cannot determine the extent to which lower incidence or better survival accounts for the decrease in hyperglycemic crisis death rates.

Because the treatment of hyperglycemic crisis in the elderly is generally complicated by underlying medical conditions (23,24), it is particularly encouraging that individuals aged ≥65 years had the greatest decrease in mortality. Because ICD codes do not allow separation of HHS from DKA, we cannot determine whether these encouraging trends are due to decreases in DKA, HHS, or both. However, we examined trends by coma status and found that death rates for DKA/HHS with coma decreased 80% (from 37.6 to 7.6 per 100,000 people with diabetes) and death rates for DKA without coma decreased 64% (from 33.8 to 12.1 per 100,000 people with diabetes) for people with diabetes aged ≥65 years from 1985 to 2002. Nevertheless, with available data, we cannot determine the relative impact of reduced incidence and improved treatment on these trends. A recent study of Medicare beneficiaries with diabetes suggests reductions in the incidence of hyperglycemic crisis in the elderly (25). This study found that from 1992 to 2002, self-monitoring of blood glucose increased, emergency department admission for metabolic crisis decreased, and hospitalization for DKA decreased in the aged Medicare population with diabetes.

In 2002, the hyperglycemic crisis death rate among black men was disproportionably high (e.g., 3.5 times the rate for white women), and black men experi-

enced the smallest decline during the time period. Some factors may be at play. Among urban blacks, omission of insulin therapy has been identified as a major precipitating factor for DKA, with financial reasons the most common cause of discontinuance (26,27). In addition, an intermediate type between type 1 and type 2 (type 1.5 diabetes) has been reported among blacks (28,29), and DKA is often a presenting symptom in new-onset case subjects. Therefore, socioeconomic and pathophysiological characteristics for blacks need to be considered to identify effective strategies in preventing a hyperglycemic crisis for this population.

Because hyperglycemic crisis is treatable if recognized and treated early, it is concerning that almost one-fifth of deaths overall or one-third among those younger than 65 years occurred "at home." In addition, it is disconcerting that "at home" death rate declined only modestly over time. A better understanding of why hyperglycemic crisis deaths occurred "at home" is essential to develop effective preventive interventions.

Possible limitations of our study pertain to the unreliability of data on death certificates, design changes in the survey used to obtain estimates of individuals with diabetes, and changes in the classification system for coding cause of death. It has been documented that the cause of death listed on death certificates may be inaccurate (30,31). To what extent this problem may apply to hyperglycemic crisis, particularly for individuals who died "at home," however, is unknown. Theoretically, our estimates could be biased, but the direction of the trends should not have been affected, assuming miscoding did not change differentially over time. Additionally, we repeated the analysis for hyperglycemic crisis coded as any cause for death (rather than the underlying cause) and found similar trends. Furthermore, disease characteristics such as duration and type of diabetes are not available from death certificate data. Therefore, we cannot examine how trends differ by these characteristics.

Redesign of the National Health Interview Survey in 1997 (32) could have affected our estimates of people with diabetes by changing whether people gave a positive answer to the question about diabetes, in turn affecting the death rates. In addition, it is unknown what impact the 1997 changes (including the lowering of fasting plasma glucose ≥140 mg/dl to ≥126 mg/dl) in diagnostic criteria for diabetes (33) had on subsequent changes in the prevalence of diabetes. Regardless of the growth in diabetes prevalence, however, the absolute number of deaths due to hyperglycemic crisis fell over the time period examined. In addition, for most of the groups we analyzed, the death rates declined gradually over the entire time and there was no deviation in trend or change in slope of rates in 1997 or in subsequent years. Similarly, we saw no deviation in trends in 1999 when ICD-9 was replaced by ICD-10 to classify causes of death, indicating the change in the ICD system was unlikely to have affected our trends.

Public health implication

The declining death rates from hyperglycemic crisis nationally reported here are consistent with other encouraging trends in the U.S. population with diabetes: the levels of several preventive care practices have increased (34,35), the prevalence of risk factors for cardiovascular disease have declined (36), and the incidence of end-stage renal disease and lower-extremity amputation have decreased (34,37,38). However, scope for further improvement in death from hyperglycemic crisis remains. Strategies to ensure timely access to health care and prescription medication and to increase the self-management skills of individuals with diabetes are needed to continue and extend the current promising trend in death rates from hyperglycemic crisis.

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