

Mortality Trends in Men and Women with Diabetes, 1971 to 2000

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Background: Whether mortality rates among diabetic adults or excess mortality associated with diabetes in the United States has declined in recent decades is not known.

Objective: To examine whether all-cause and cardiovascular disease mortality rates have declined among the U.S. population with and without self-reported diabetes.

Design: Comparison of 3 consecutive, nationally representative cohorts.

Setting: Population-based health surveys (National Health and Nutrition Examination Surveys I, II, and III) with mortality follow-up assessment.

Patients: Survey participants age 35 to 74 years with and without diabetes.

Measurements: Diabetes was determined by self-report for each survey (1971–1975, 1976–1980, and 1988–1994), and mortality rates were determined through 1986, 1992, and 2000 for the 3 surveys, respectively.

Results: Among diabetic men, the all-cause mortality rate decreased by 18.2 annual deaths per 1000 persons (from 42.6 to

24.4 annual deaths per 1000 persons; $P = 0.03$) between 1971 to 1986 and 1988 to 2000, accompanying decreases in the non-diabetic population. Trends for cardiovascular disease mortality paralleled those of all-cause mortality, with 26.4 annual deaths per 1000 persons in 1971 to 1986 and 12.8 annual deaths per 1000 persons in 1988 to 2000 ($P = 0.06$). Among women with diabetes, however, neither all-cause nor cardiovascular disease mortality declined between 1971 to 1986 and 1988 to 2000, and the all-cause mortality rate difference between diabetic and nondiabetic women more than doubled (from a difference of 8.3 to 18.2 annual deaths per 1000 persons). The difference in all-cause mortality rates by sex among people with diabetes in 1971 to 1986 were essentially eliminated in 1988 to 2000.

Limitations: Diabetes was assessed by self-report, and statistical power to examine the factors explaining mortality trends was limited.

Conclusions: Progress in reducing mortality rates among persons with diabetes has been limited to men. Diabetes continues to greatly increase the risk for death, particularly among women.

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The decrease in cardiovascular disease (CVD) mortality rates and the accompanying increases in overall longevity are major public health successes in the United States over the past 40 years (1). These have been attributed to decreases in CVD risk factors, as well as advances in medical management and revascularization, among persons with diagnosed CVD (2, 3). Aggressive management of CVD risk factors has been shown to be particularly effective among persons with diabetes, and implementation of these findings into practice along with aggressive diabetes care should, in theory, result in increased longevity among persons with diabetes (4–9).

The quality of diabetes care and levels of certain CVD risk factors have improved among the U.S. population with diagnosed diabetes (10, 11). Whether reductions in mortality have occurred among persons with diabetes, however, remains unclear. Although regional studies of persons with diabetes suggest that rates of all-cause mortality and cardiovascular complications have declined in recent decades (12–15), the only nationally representative study to examine trends in mortality rates of adults with diabetes found no improvement between 1971 and 1992 (16). However, no national studies of mortality trends of the U.S. diabetic population have extended through the 1990s, a period of major advances in clinical diabetes management, leaving the question of whether longevity in this population has improved (4, 11, 17).

Thus, we assembled data from 3 consecutive nation-

ally representative cohorts to assess whether all-cause and CVD mortality have declined among the U.S. population with diabetes and whether the disparity in mortality rates between persons with and without diabetes has decreased.

METHODS

Study Design and Population

The National Health and Nutrition Examination Survey (NHANES) is a series of independent, nationally representative health surveys of the U.S. noninstitutionalized population conducted from 1971 to 1975 (NHANES I), 1976 to 1980 (NHANES II), and 1988 to 1994 (NHANES III) (18–20). Each survey used a stratified, multistage probability design that sampled, interviewed, and examined participants to determine their health status.

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Context

Whether the mortality reductions observed over recent decades in the United States have been similar among diabetic and nondiabetic persons is unknown.

Contribution

The 1971–2000 National Health and Nutrition Examination Surveys and vital statistics data reveal higher mortality in the diabetic population than in the nondiabetic population. Over this period, diabetic men experienced mortality reductions that paralleled those of nondiabetic men. However, mortality rates in women have not changed, and the mortality difference between diabetic and nondiabetic women more than doubled.

Implications

Mortality among diabetic women does not reflect improvements in the care of diabetes and other cardiovascular risk factors. Understanding the sex differences in diabetes outcomes should be a research priority.

—The Editors

Sampling approaches, interview, and examination methods were standardized across surveys, and data were linked to death certificate data (21). To minimize bias from differential follow-up, we limited follow-up to 12.2 years, which was the maximum period for the survey with the shortest follow-up (NHANES III). Thus, the follow-up years for the 3 survey cohorts were 1971 to 1986, 1976 to 1992, and 1988 to 2000. Overall, 28 043 persons, 27 801 persons, and 39 695 persons were selected for NHANES I, II, and III, respectively, and 75% (20 749 persons), 73% (20 322 persons), and 78% (30 818 persons) were examined. We restricted our analyses to adults age 35 to 74 years who were examined at baseline. These groups included 8654 (80%), 8213 (76%), and 9399 (90%) persons from each of the 3 cohorts. After excluding persons without information on diabetes (7, 3, and 12 persons) or death (176, 5, and 6 persons), we were left with 8471, 8205, and 9381 persons in the primary analyses. Previous analyses have indicated little bias due to nonresponse (22, 23).

Measurements

Demographic characteristics, self-reported diabetes status, duration of disease, insulin use, and history of CVD (heart attack, heart failure, or stroke) were determined by interview. Weight and height were measured and were used to calculate body mass index (BMI). Underlying causes of death were classified according to the International Classification of Diseases, Ninth Revision, with CVD coded as 390 to 448.

Statistical Analysis

We completed mortality rates as the number of deaths divided by the sum of person-years and standardized by age

and sex to the 2000 U.S. population. We examined changes in absolute standardized mortality rates over time by using *t* tests. We also used proportional hazards models to estimate the hazard rate ratios for the NHANES II and III cohorts compared with the NHANES I cohort among the diabetic and nondiabetic populations, with primary models controlling for age, sex, and race or ethnicity and additional models controlling for duration of diabetes and prevalent CVD. We also examined 2-way interactions of survey among persons with diabetes with each of the covariates mentioned above. We assessed the validity of the proportional hazards assumption by adding time-dependent variables to the model (that is, the interaction of age, sex, or race or ethnicity and the logarithm of follow-up duration). Because this assumption was not met across sex, we fit models separately by sex.

Mortality rate estimation and proportional hazards regression incorporated survey weights such that results are representative of the U.S. noninstitutionalized population and account for the stratified, clustered design and the unequal probabilities of selection from oversampling and nonresponse (24). We combined data across the 3 surveys for regression analyses, using the original survey weights and design variables. We renumbered strata to appropriately represent their respective surveys, and we calculated degrees of freedom as the number of primary sampling units minus the number of strata. Because we used original survey weights (as opposed to constructing new weights for pooled analyses), these analyses make the assumption that each survey sample is drawn from a different population, as opposed to 3 surveys from a single underlying population (25). We conducted all statistical analyses by using SUDAAN, version 9.1 (RTI International, Research Triangle Park, North Carolina), which uses Taylor series linearization to estimate variances.

Role of the Funding Source

The U.S. Department of Health and Human Services is the funding source for NHANES and oversees the conduct and reporting of the NHANES surveys.

RESULTS

Among both men and women with diabetes, the proportion of nonwhite persons roughly doubled across the survey years, the level of education increased substantially, and mean BMI increased (Table 1). In diabetic women—but not diabetic men—the average age at diagnosis decreased statistically significantly (mean decrease, 2.9 years) across the 3 surveys, and the average age of the diabetic population decreased by 2.5 years, from 59.1 to 56.6 years. Almost all of the secular trends in race or ethnicity, education, and BMI observed in persons with diabetes also occurred in those without diabetes.

Between 1971 to 1986 and 1988 to 2000 in the overall nondiabetic population (both men and women), all-cause mortality rates decreased from 14.4 to 9.5 annual

deaths per 1000 persons ($P < 0.001$) and CVD deaths decreased from 7.0 to 3.4 annual deaths per 1000 persons ($P < 0.001$) (Table 2). Among the overall diabetic population, the all-cause mortality rate did not statistically significantly change (30 annual deaths per 1000 persons in 1971 to 1986 vs. 25.2 annual deaths per 1000 persons in 1988 to 2000). For CVD mortality, the absolute difference in mortality among the diabetic population between 1971 to 1986 and 1988 to 2000 (18.2 vs. 11.1 annual deaths per 1000 persons) was greater than that of the nondiabetic population, but this decrease was not significant ($P = 0.09$).

Findings in the overall population, however, obscured important sex-related differences, wherein mortality rates decreased among diabetic men but not among diabetic women (interaction between survey year and sex, $P = 0.005$ for all-cause mortality and $P = 0.59$ for CVD mortality) (Figure 1). All-cause mortality rates among diabetic men decreased by 43% (from 42.6 to 24.4 annual deaths per 1000 persons) between 1971 to 1986 and 1988 to 2000 ($P = 0.03$). In an analysis that controlled for age and race or ethnicity, the all-cause mortality rate ratio for diabetic men in 1988 to 2000 compared with 1971 to 1986 was 0.61 (95% CI, 0.43 to 0.86). Trends for the CVD mortality rate paralleled those of all-cause mortality (26.4 vs. 12.8 annual deaths per 1000 persons; $P = 0.06$ for difference) (Table 2 and Figure 2). In an analysis that controlled for age, sex, and race or ethnicity, the CVD mortality rate ratio for diabetic men in 1988 to 2000 compared with 1971 to 1986 was 0.62 (CI, 0.39 to 1.01)

(Table 2 and Figure 2). Additional adjustment for diabetes duration, BMI, and prevalent CVD had no appreciable effect on the mortality rate ratios (data not shown).

The absolute difference in all-cause mortality rates between men with and without diabetes was 23.6 annual deaths per 1000 persons (42.6 vs. 19.0 deaths) in 1971 to 1986 compared with 12.8 annual deaths per 1000 persons (24.4 vs. 11.6 deaths) in 1988 to 2000 (Figure 1). For CVD mortality, the absolute difference was 16.8 annual deaths per 1000 persons (26.4 vs. 9.6 deaths) in 1971 to 1986 compared with 8.1 annual deaths per 1000 persons (12.8 vs. 4.7 deaths) in 1988 to 2000 (Table 2 and Figure 2). Although absolute changes in mortality rates among diabetic men were at least as great as those among nondiabetic men, an 88% higher all-cause mortality rate and 153% higher CVD mortality rate in diabetic men persisted in 1988 to 2000.

Among diabetic women, however, neither the all-cause nor CVD mortality rate decreased between 1971 to 1986 and 1988 to 2000, and the difference in all-cause mortality rate between women with and without diabetes more than doubled (from 8.3 to 18.2 annual deaths per 1000 persons; $P = 0.04$) (Figure 1). The hazard rate ratios for diabetic women in 1988 to 2000 compared with 1971 to 1986 were 1.31 (CI, 0.86 to 1.98) for all-cause mortality and 0.89 (CI, 0.49 to 1.59) for CVD mortality. Further adjustment for duration of diabetes, BMI, and prevalent CVD attenuated the hazard rate ratios somewhat (1.15 [CI, 0.75 to 1.75] and 0.73 [CI, 0.41 to 1.30], respectively). In 1988 to 2000, the mortality rate ratio associated with diabetes

Table 1. Characteristics of the U.S. Population Age 35 to 74 Years with and without Diagnosed Diabetes*

Characteristic	Diabetes			No Diabetes		
	NHANES I (1971–1975)	NHANES II (1976–1980)	NHANES III (1988–1994)	NHANES I (1971–1975)	NHANES II (1976–1980)	NHANES III (1988–1994)
Men						
Total, <i>n</i>	209	230	416	3397	3629	4021
Mean age, <i>y</i>	58.1	59.3	56.9	51.7	51.8	50.3†
Nonwhite ethnicity, %	11.9	15.5	21.4†	9.6	11.5	20.5†
Poverty income ratio <1.3, %	25.2	20.4	17.2	15.0	13.1	12.9
Less than high school education, %	57.3	43.5	38.3‡	44.4	37.9†	24.5†
Mean age at diagnosis, <i>y</i>	50.0	51.1	48.5	–	–	–
Mean duration of diabetes, <i>y</i>	8.1	8.3	8.3	–	–	–
Mean BMI, <i>kg/m</i> ²	26.6	26.9	29.8†	25.9	26.0	27.1†
History of CVD, %	25.5	23.0	22.6	9.1	8.5	7.4
Women						
Total, <i>n</i>	314	301	589	4551	4045	4355
Mean age, <i>y</i>	59.1	57.6	56.6†	52.2	52.4	50.8†
Nonwhite ethnicity, %	14.7	17.2	33.9†	10.2	11.9	22.0†
Poverty income ratio <1.3, %	27.2	28.1	29.8	18.3	18.9	15.6
Less than high school education, %	59.1	55.5	43.0†	40.8	39.5	22.7†
Mean age at diagnosis, <i>y</i>	51.6	49.9	48.7‡	–	–	–
Mean duration of diabetes, <i>y</i>	7.4	7.7	9.0	–	–	–
Mean BMI, <i>kg/m</i> ²	27.7	28.9	31.5†	25.8	25.9	27.0†
History of CVD, %	16.1	14.0	21.9	5.2	4.9	4.1‡

* BMI = body mass index; CVD = cardiovascular disease; NHANES = National Health and Nutrition Examination Survey.

† Significantly different ($P < 0.01$) compared with NHANES I.

‡ Significantly different ($P < 0.05$) compared with NHANES I.

Table 2. Trends in Mortality Rates in the U.S. Population Age 35 to 74 Years, by Diabetes Status and Sex, 1971–2000*

Cohort	Mortality Rate (95% CI)			Mortality Rate Difference (NHANES I vs. III)	Hazard Rate Ratio (NHANES III vs. I)
	NHANES I (1971–1986)	NHANES II (1976–1992)	NHANES III (1988–2000)		
Both men and women					
All-cause mortality					
No diabetes	14.4 (13.5 to 15.3)	11.0 (10.1 to 11.9)	9.5 (8.4 to 10.6)	–4.9 (–3.4 to –6.3) [†]	0.75 (0.65 to 0.87)
Diabetes	30.0 (22.4 to 37.6)	23.3 (17.9 to 28.7)	25.2 (19.0 to 31.4)	–4.8 (5.0 to –14.6)	0.90 (0.68 to 1.18)
Rate ratio	2.00 (1.63 to 2.46)	1.98 (1.68 to 2.36)	2.31 (1.83 to 2.90)	–	–
CVD mortality					
No diabetes	7.0 (6.4 to 7.7)	4.7 (4.3 to 5.1)	3.4 (2.9 to 3.9)	–3.6 (–2.8 to –4.5) [†]	0.53 (0.44 to 0.65)
Diabetes	18.2 (10.9 to 25.4)	13.0 (9.4 to 16.5)	11.1 (7.6 to 14.6)	–7.1 (1.0 to –15.1)	0.75 (0.51 to 1.10)
Rate ratio	2.28 (1.65 to 3.15)	2.41 (1.95 to 2.98)	2.98 (2.19 to 4.05)	–	–
Men					
All-cause mortality					
No diabetes	19.0 (17.4 to 20.7)	14.6 (13.3 to 15.9)	11.6 (10.2 to 13.1)	– 7.4 (–5.2 to –9.6) [†]	0.68 (0.57 to 0.81)
Diabetes	42.6 (28.5 to 56.7)	32.3 (22.5 to 42.0)	24.4 (16.3 to 32.6)	–18.2 (–1.8 to –34.5) [‡]	0.61 (0.43 to 0.86)
Rate ratio	2.18 (1.66 to 2.85)	1.95 (1.53 to 2.50)	1.88 (1.44 to 2.45)	–	–
CVD mortality					
No diabetes	9.6 (8.5 to 10.7)	6.5 (5.8 to 7.3)	4.7 (3.7 to 5.7)	–4.9 (–3.4 to –6.4) [§]	0.55 (0.42 to 0.72)
Diabetes	26.4 (13.4 to 39.4)	17.1 (10.7 to 23.5)	12.8 (7.1 to 18.6)	–13.6 (0.7 to –27.7)	0.62 (0.39 to 1.01)
Rate ratio	2.40 (1.67 to 3.44)	2.14 (1.57 to 2.91)	2.53 (1.75 to 3.66)	–	–
Women					
All-cause mortality					
No diabetes	10.1 (9.1 to 11.1)	7.9 (6.9 to 8.9)	7.7 (6.4 to 8.9)	–2.4 (–0.8 to –4.1) [§]	0.88 (0.70 to 1.10)
Diabetes	18.4 (12.4 to 24.4)	15.1 (11.1 to 19.1)	25.9 (19.2 to 32.7)	7.5 (16.5 to –1.5)	1.31 (0.86 to 1.98)
Rate ratio	1.83 (1.27 to 2.63)	2.02 (1.61 to 2.53)	2.84 (2.08 to 3.89)	–	–
CVD mortality					
No diabetes	4.7 (4.2 to 5.3)	3.1 (2.6 to 3.6)	2.3 (1.8 to 2.7)	–2.4 (–1.7 to –3.2) [§]	0.51 (0.40 to 0.66)
Diabetes	10.5 (5.8 to 15.2)	9.1 (6.4 to 11.7)	9.4 (5.8 to 13.0)	–1.1 (4.8 to –7.0)	0.89 (0.49 to 1.59)
Rate ratio	2.17 (1.30 to 3.62)	2.85 (2.19 to 3.71)	3.66 (2.48 to 5.42)	–	–

* Mortality rates are calculated as annual deaths per 1000 persons. Rate ratios compare diabetes with no diabetes, unless otherwise indicated. All hazard rate ratios are adjusted for age and race or ethnicity, except for analyses among the total population, which are also adjusted for sex. CVD = cardiovascular disease; NHANES = National Health and Nutrition Examination Survey.

[†] $P < 0.001$ for test of heterogeneity in rates across survey years.

[‡] $P < 0.05$ for test of heterogeneity in rates across survey years.

[§] $P < 0.01$ for test of heterogeneity in rates across survey years.

(compared with women without diabetes) was 2.84 (CI, 2.08 to 3.89) for all-cause mortality and 3.66 (CI, 2.48 to 5.42) for CVD mortality (Table 2). Finally, a comparison of NHANES I and NHANES III (Table 2) revealed that the differences in all-cause mortality rates by sex among people with diabetes in 1971 to 1986 (42.6 vs. 18.4 annual deaths per 1000 persons) were essentially eliminated in 1988 to 2000 (24.4 vs. 25.9 annual deaths per 1000 persons). This occurred to a lesser extent with CVD mortality.

DISCUSSION

Our examination of U.S. adults with self-reported diabetes suggests that the well-documented reductions in mortality rates in the general U.S. adult population in the past 25 years have included men with diabetes, but their female diabetic peers have been left behind. Men with diabetes experienced a 43% relative reduction in the age-adjusted mortality rate, which is similar to that of nondiabetic men. Among women with diabetes, however, mortality rates did not decrease, and the difference in mortality rates between diabetic and nondiabetic women doubled.

Several factors could explain the decrease among diabetic men, ranging from primary prevention of CVD risk factors to use of improved lifesaving technology among persons with CVD or diabetes complications (1–3, 26–28). Rates of smoking, lipid concentrations, and glycemic control have improved, and more patients use aspirin, have an annual lipid profile, and receive influenza vaccination (10, 11, 29). Accompanying dietary trends have favored a less atherogenic profile in the overall U.S. population (1, 26–28). Reductions in hospitalization rates for CVD, ischemic heart disease, and stroke among people with diabetes (particularly men) have also been observed (30).

The lack of improvement among women is concerning. Some studies have documented less improvement in CVD risk factors among women and smaller increases in the use of antihypertensive therapy and aspirin (10, 31, 32). Female sex is also linked to both less aggressive medical management and worse outcomes after revascularization and hospitalization for CVD (33–38). Sex differences in the pathophysiology of coronary heart disease have been proposed, including a greater tendency for women to have microvascular coronary heart disease and left ventricular

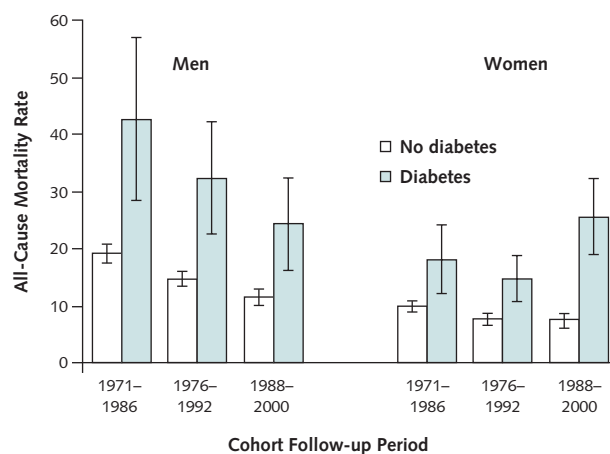
hypertrophy, differences in inflammatory and hormonal responses to risk factors, more complicated patterns of symptoms, and less accurate diagnoses of coronary heart disease (39–42). Whether these factors differentially influence mortality rates among women with diabetes is not clear. A greater decrease in age at diagnosis among women than men may also have influenced mortality rates (29, 43, 44), although adjustment for duration of diabetes in our analyses did not alter the results.

Our findings for men are consistent with reports from regional U.S. populations (14, 15), as well as a recent report from Ontario, Canada (45). The finding among women is consistent with an earlier comparison of the 1970s and 1980s NHANES I cohorts, as well as the finding of an increased ischemic heart disease mortality rate among Native American women (44, 46). Our conclusions differ from those of the Framingham Heart Study, in which incidence and mortality rates for CVD have declined (15); of a study in North Dakota, in which mortality declined among both men and women with diabetes in the 1990s (14); and of the Ontario study over the past 10 years (45). However, those studies examined largely white populations and different periods. The Framingham Heart Study compared mortality rates from cohorts of the 1950s and 1960s, when CVD mortality rates were notably high, with cohorts of the 1980s and 1990s. The North Dakota study was limited to the 1990s.

One limitation of our study is our reliance on self-report to identify diabetes status, because glucose was not measured in NHANES I and was limited to subsamples of the later surveys. Self-reported diabetes has high specificity and positive predictive value but has low sensitivity, because many persons with undetected hyperglycemia are classified as nondiabetic (47). Surveillance data suggest that the proportion of undiagnosed cases of diabetes has declined somewhat over recent decades, albeit not statistically significantly (48, 49). This issue is further complicated by changes in diagnostic criteria during this period. We controlled for demographic factors, BMI, and years since diagnosis to account for these factors, but we cannot rule out the possibility that increasing detection or changing diagnostic criteria led to subtle changes in the severity or type of diabetes cases over the surveys. We consider it unlikely, however, that shifts in the characteristics of diabetes would explain the sex differences in mortality trends that we observed.

Another limitation was the relatively small samples in our sex-specific analyses. Combined with the lack of detailed information on treatments and incident medical events, this limitation precluded a thorough analysis of the factors that might have explained the trends in mortality rates. Finally, the lack of institutionalized persons means that our findings may not fully reflect the experience of people with end-stage cardiovascular and renal disease. In light of these limitations, we interpret our findings as representative of the community-dwelling population with

Figure 1. Age-adjusted all-cause mortality rates among the U.S. population age 35 to 74 years with and without diabetes, by cohort and sex.

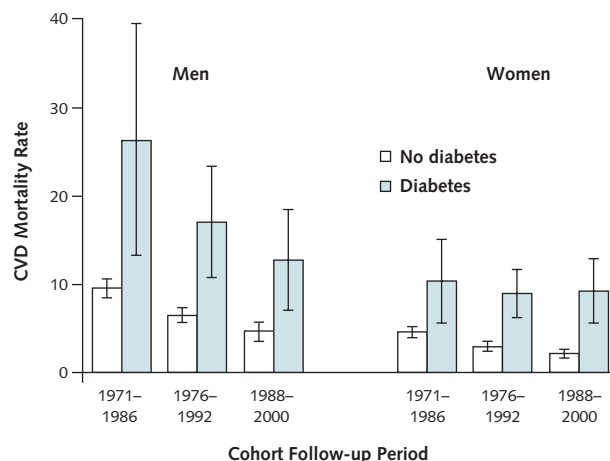


Mortality rates are calculated as annual deaths per 1000 persons. Error bars represent 95% CIs.

self-reported diabetes but suggest that further study is needed to describe mortality trends in the entire diabetic population, especially in women.

In summary, these national data reveal 3 key findings. First, reductions in mortality occurred among diabetic men but not among diabetic women. Second, disparities in mortality rates between women with and without diabetes have worsened. Finally, the female-over-male advantage in mortality rates among the diabetic population has been eliminated. These findings should stimulate more research on why the improvements in diabetes care and important

Figure 2. Age-adjusted cardiovascular disease mortality rates among the U.S. population age 35 to 74 years with and without diabetes, by cohort and sex.



Mortality rates are calculated as annual deaths per 1000 persons. Error bars represent 95% CIs.

risk factors are not reflected in reduced mortality for women with diabetes, as well as continued public health efforts to reduce the excess mortality risk among men and especially among women with diabetes.

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Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the U.S. Department of Health and Human Services and the Centers for Disease Control and Prevention.

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EXPEDITED REVIEW

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