Diabetes and Decline in Heart Disease Mortality in US Adults

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Mortality from heart disease has declined substantially in the United States during the past 30 years.\textsuperscript{1-4} Because heart disease is the major cause of death associated with diabetes,\textsuperscript{5,6} it would be expected that the mortality decline in the United States as a whole also would have been experienced by those with diabetes. However, no study has examined whether people with diabetes in the United States have benefited from this general phenomenon and, if so, whether the extent of their mortality rate decline is similar to that of people without diabetes.

To examine these issues, we analyzed mortality in 2 representative national cohorts derived from subjects in the First National Health and Nutrition Examination Survey (NHANES I) of 1971 through 1975 and the NHANES I Epidemiologic Follow-up Survey (NHEFS) of 1982 through 1984. Both cohorts were followed up prospectively for mortality for an average of 8 to 9 years.

METHODS
NHANES I included a national probability sample of 14,376 persons aged 25 to 74 years who were interviewed for sociodemographic information and history of diabetes. The NHANES I subjects were followed up in 1982-1984, 1986, 1987, and 1992-1993 in the NHEFS. In each follow-up, the subjects (or their proxies) were interviewed again to determine vital status (alive or dead), whether diabetes had been diagnosed, and other information. Follow-up was completed for 96\% of subjects.\textsuperscript{2} Two nationally representative cross-sectional samples of adults aged 35 to 74 years were created from these data. Cohort 1 was derived from 10,649 people in NHANES I who were aged 35 to 74 years at the time of their 1971-1975 interview. Cohort 2 was derived from 9,233 subjects in NHEFS who were aged 35 to 74 years on the date of the self or proxy interview in 1982-1984.

Cohort 1
Of the 10,649 subjects aged 35 to 74 years in NHANES I, 670 subjects (285 men and 385 women) reported a physician diagnosis of diabetes and were defined as having diabetes. It has previously been demonstrated that a self-report of physician-diagnosed diabetes is accurate and valid.\textsuperscript{7,8} Of the 9,979 subjects without a history of diabetes, 1,110 individuals were excluded from analysis, including 1,070 subjects for whom any follow-up interview data indicated that they had been diagnosed as having diabetes and 40 subjects who had diabetes listed on their death cer-
tificate. The remaining 8869 subjects (3826 men and 5043 women) were defined as not having diabetes. The follow-up period for cohort 1 was from the date of the 1971-1975 interview to the date of the self or proxy interview in 1982-1984. The mean follow-up was 9.1 years, during which time there were 264 deaths among subjects with diabetes and 1625 deaths among subjects without diabetes.

Cohort 2
Of the 9233 subjects in NHEFS who were aged 35 to 74 years on the date of the self or proxy interview in 1982-1984, there were 637 subjects (233 men and 404 women) with diabetes. This included 271 who had diabetes in the 1971-1975 survey and 366 who did not have diabetes in 1971-1975 but stated in the 1982-1984 interview that they had been diagnosed as having diabetes. Of the remaining 8596 subjects, 770 were excluded from analysis, including 435 subjects who had a diagnosis of diabetes made after the 1982-1984 interview, 10 subjects without diabetes in 1982-1984 who died and had diabetes listed as a cause of death on their death certificate, and 325 subjects with unknown diabetes status. The remaining 7826 subjects (2841 men and 4985 women) were defined as not having diabetes. The follow-up period for cohort 2 was from the date of the 1982-1984 interview to the date of death or the date of the last follow-up interview. The mean follow-up was 8.7 years, during which time there were 184 deaths among subjects with diabetes and 747 deaths among those without diabetes.

Although all cohort 1 and cohort 2 members were part of the NHANES I survey, there was only a 3% to 8% overlap in the 10-year age and diabetes groups used in analysis. The lack of overlap occurred because the beginnings of the cohort observation periods were an average of 9.7 years apart and, thus, most subjects aged 65 to 74 years in cohort 1 were not in cohort 2, most subjects aged 35 to 44 years in cohort 2 were not in cohort 1, and most subjects aged 35 to 64 years in cohort 1 were in an older 10-year age group in cohort 2. In addition, 366 subjects had diabetes in cohort 2 but not in cohort 1.

The type of diabetes in this study could not be determined, but the adult...
age of the cohorts and the high proportion of type 2 diabetes in the US population with diabetes indicate that the cohorts contained type 2 diabetes almost exclusively. Death due to any heart disease or ischemic heart disease was based on the underlying cause of death on the death certificates, which were coded using the International Classification of Diseases, Ninth Revision. Codes used for heart disease were 390-398, 402, 404, 410-417, and 420-429, and for ischemic heart disease, 410-414. Death certificates were obtained for 97.3% of decedents who had had diabetes and 96.5% of decedents who had not had diabetes.

**Statistical Analyses**

Age-specific mortality rates per 1000 person-years were calculated using the number of deaths as the numerator and total person-years as the denominator for 3 age groups (35-54, 55-64, and 65-74 years) stratified by cohort, diabetes status, and sex. The variance of the person-year rate was estimated by the Chiang method. Age-adjusted mortality rates for each cohort stratified by diabetes status and sex were calculated by the direct method, using four 10-year age groups (35-44, 45-54, 55-64, and 65-74 years) and the 1980 US population as the standard. The variance of the age-adjusted rate was calculated by summing the variance of each age-specific rate multiplied by the square of its US population proportion. The percentage difference between cohort 1 and cohort 2 was calculated as the mortality rate in cohort 2 minus the rate in cohort 1, divided by the rate in cohort 1, and multiplied by 100. The variance of the percentage difference was estimated by a Taylor series approximation for estimation of the variance of a ratio from a sample. Variance of the relative risk was computed by the same method.

**RESULTS**

Figure 1 shows mortality from all causes, heart disease, and ischemic heart disease for men and women with and without diabetes in cohort 1 and cohort 2, according to age at baseline. Details about sample sizes; person-years of follow-up; number of deaths by age, sex, and diabetes status; and statistical...
significance are provided in Table 1 and Table 2. For all groups, mortality rates increased with age, were higher in men than women, and were higher in subjects with diabetes than their counterparts without diabetes. Among men and women without diabetes, mortality rates were higher in cohort 1 than cohort 2 for almost all age groups and causes of death. The differences between cohort 1 and cohort 2 were statistically significant for men without

| Table 2. Mortality Rates for Heart Disease and Ischemic Heart Disease as the Underlying Cause of Death for Adults in Cohorts 1 and 2, by Diabetes Status, Sex, and Age* |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|                                  |                  |                  |                  |                  |                  |
|                                  | Male            | Female           | Male            | Female           |
|                                  | With diabetes   | Without diabetes | With diabetes   | Without diabetes |
| Age at Baseline, y               | Rate per 1000 Person-Years (95% CI) | Rate per 1000 Person-Years (95% CI) | Change from Cohort 1 to Cohort 2, % | P Value |
| No. of Deaths                   |                  |                  |                  |                  |
| Heart Disease                   |                  |                  |                  |                  |
| Men With diabetes               |                  |                  |                  |                  |
| 35-54                           | 6               | 5.1 (0.9-9.4)    | 5               | 5.1 (0.9-9.4)    | 30.9             | .58              |
| 55-64                           | 8               | 11.8 (4.1-19.5)  | 10              | 12.0 (5.0-19.0)  | 1.7              | .97              |
| 65-74                           | 38              | 22.7 (16.3-29.2) | 23              | 31.6 (20.6-42.6) | 39.0             | .17              |
| 35-74 (Age standardized)        | 51              | 9.8 (6.6-13.0)   | 44              | 12.0 (8.7-15.3)  | 22.9             | .34              |
| Women With diabetes             |                  |                  |                  |                  |
| 35-54                           | 5               | 5.1 (0.9-9.4)    | 11              | 6.7 (3.0-10.4)   | 30.9             | .58              |
| 55-64                           | 8               | 11.8 (4.1-19.5)  | 10              | 12.0 (5.0-19.0)  | 1.7              | .97              |
| 65-74                           | 38              | 22.7 (16.3-29.2) | 23              | 31.6 (20.6-42.6) | 39.0             | .17              |
| 35-74 (Age standardized)        | 51              | 9.8 (6.6-13.0)   | 44              | 12.0 (8.7-15.3)  | 22.9             | .34              |
| Without diabetes                |                  |                  |                  |                  |
| 35-54                           | 24              | 0.9 (0.5-1.3)    | 15              | 0.5 (0.3-0.7)    | −44.6            | .07              |
| 55-64                           | 24              | 3.4 (2.0-4.7)    | 23              | 2.7 (1.6-3.8)    | −20.0            | .44              |
| 65-74                           | 170             | 12.2 (10.5-14.0) | 51              | 9.2 (6.8-11.7)   | −24.5            | .05              |
| 35-74 (Age standardized)        | 218             | 3.6 (3.1-4.1)    | 89              | 2.6 (2.1-3.2)    | −27.1            | .009             |
| Ischemic Heart Disease          |                  |                  |                  |                  |
| Men With diabetes               |                  |                  |                  |                  |
| 35-54                           | 5               | 8.2 (1.6-14.8)   | 2               | 3.7 (−1.2-8.5)   | −55.3            | .28              |
| 55-64                           | 9               | 24.7 (10.4-38.9) | 12              | 19.5 (9.5-29.5)  | −20.9            | .56              |
| 65-74                           | 44              | 37.4 (28.3-46.6) | 20              | 37.7 (24.0-51.3) | 0.6              | .98              |
| 35-74 (Age standardized)        | 58              | 17.0 (11.5-22.6) | 34              | 14.2 (9.1-19.4)  | −16.6            | .46              |
| Without diabetes                |                  |                  |                  |                  |
| 35-54                           | 53              | 3.4 (2.5-4.3)    | 22              | 1.6 (0.9-2.2)    | −53.8            | <.001            |
| 55-64                           | 48              | 8.1 (5.9-10.3)   | 21              | 3.4 (1.9-4.8)    | −58.4            | <.001            |
| 65-74                           | 226             | 19.5 (17.2-21.8) | 52              | 13.4 (10.0-16.8) | −31.4            | .003             |
| 35-74 (Age standardized)        | 327             | 7.4 (6.6-8.2)    | 95              | 4.2 (3.4-5.0)    | −43.8            | <.001            |
| Women With diabetes             |                  |                  |                  |                  |
| 35-54                           | 4               | 4.1 (0.2-7.9)    | 6               | 3.6 (0.8-6.5)    | −10.8            | .85              |
| 55-64                           | 3               | 4.4 (0.5-9.3)    | 6               | 7.2 (1.6-12.8)   | 62.8             | .46              |
| 65-74                           | 33              | 19.7 (13.6-25.8) | 17              | 23.3 (13.5-33.2) | 18.3             | .54              |
| 35-74 (Age standardized)        | 40              | 6.8 (4.2-9.5)    | 29              | 7.6 (5.0-10.1)   | 10.7             | .76              |
| Without diabetes                |                  |                  |                  |                  |
| 35-54                           | 12              | 0.4 (0.2-0.7)    | 6               | 0.2 (0.0-0.4)    | −55.7            | .10              |
| 55-64                           | 14              | 2.0 (0.9-3.0)    | 19              | 2.2 (1.2-3.2)    | 13.3             | .72              |
| 65-74                           | 127             | 9.1 (7.6-10.7)   | 38              | 6.9 (4.8-9.0)    | −24.7            | .03              |
| 35-74 (Age standardized)        | 153             | 2.4 (2.0-2.8)    | 63              | 1.9 (1.4-2.4)    | −20.4            | .12              |

*Data for numbers of subjects and person-years of follow-up are virtually identical to all-cause mortality data, except for the exclusion of 59 subjects (6 with diabetes, 53 without) in cohort 1 and 23 subjects (6 with diabetes, 17 without) in cohort 2 for whom the cause of death could not be ascertained because a death certificate was not obtained. CI indicates confidence interval.
diabetes in all age groups for all 3 causes of death (P < .01). For women without diabetes, differences were statistically significant only at ages 65 to 74 years for all-cause and heart disease mortality (P < .05). Among men with diabetes, mortality rates in cohort 1 were generally higher than in cohort 2 at ages 35 to 54 and 55 to 64 years and were slightly lower at ages 65 to 74 years. Among women with diabetes, mortality rates in specific age groups tended to be lower in cohort 1 than in cohort 2. However, 95% confidence limits around the rates of diabetes for both men and women were large, and no differences between cohort 1 and cohort 2 were statistically significant for any cause of death (Table 1 and Table 2).

**FIGURE 2.** Age-Adjusted Mortality Rates for Death Due to All Causes, Heart Disease, and Ischemic Heart Disease for Men and Women With and Without Diabetes in Cohorts 1 and 2, According to Age at Baseline

Mortality rates are shown per 1000 person-years with 95% confidence intervals. Cohort 1 was defined in 1971-1975 and was followed up for mortality through 1982-1984. Cohort 2 was defined in 1982-1984 and was followed up for mortality through 1992-1993. Details about sample sizes, number of deaths, point estimates, and statistical significance are shown in Tables 1 and 2.

**FIGURE 3.** Percentage Change from Cohort 1 to Cohort 2 in Mortality From All Causes, Heart Disease, and Ischemic Heart Disease for Men and Women With and Without Diabetes

Data are shown as percentage change in the age-adjusted mortality rates, with 95% confidence intervals. Percentage change was calculated as the mortality rate in cohort 2 minus the rate in cohort 1, divided by the rate in cohort 1, and multiplied by 100. Details about sample sizes, number of deaths, point estimates, and statistical significance are shown in Tables 1 and 2.

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from cohort 1 to cohort 2. For men without diabetes, there were substantial decreases in the mortality rates for each cause of death, ranging from a 19.7% decline in the all-cause rate to a 43.8% decline in the rate for ischemic heart disease. For men with diabetes, the decreases were smaller and ranged from a 1.1% decline for all causes of death to a 16.6% decline for ischemic heart disease. Women without diabetes also experienced declines in age-adjusted mortality, including a 12.9% decrease in the all-cause rate, a 27.1% decrease in the heart disease rate, and a 20.4% decrease in the ischemic heart disease rate. In contrast, women with diabetes had increases in their mortality rates that ranged from a 10.7% increase for ischemic heart disease to a 22.9% increase for heart disease. The percentage changes for subjects without diabetes were statistically significant. However, because the 95% confidence intervals for diabetic subjects were wide, the mortality changes for men and women with diabetes did not achieve statistical significance.

The mortality data were recomputed using any listing of heart disease or ischemic heart disease on the death certificate. As expected, these multiple-cause mortality rates were higher than those based on heart disease or ischemic heart disease coded only as the underlying cause of death. However, the direction and magnitude of the percentage change from cohort 1 to cohort 2 were similar to those found using the underlying cause alone. The data were also analyzed by retaining, in the components of cohort 1 and cohort 2 without diabetes, those individuals who developed diabetes after the beginning of the mortality observation periods. There was only an approximately 3% increase in the age-adjusted mortality rates for subjects without diabetes. This change thus had virtually no effect on the results.

**Figure 4** shows the age-adjusted relative risk for mortality (subjects with diabetes compared with subjects without diabetes) in cohort 1 and cohort 2. The relative risk was lower in cohort 1 than in cohort 2 for each of the causes of death in both men and women. The smaller declines in mortality for men with diabetes compared with men without it and the increases in mortality for women with diabetes compared with women without it resulted in increased relative risks for mortality associated with diabetes in cohort 2.

**COMMENT**

These data, based on nationally representative samples of adults with and without diabetes, indicate that mortality from all causes, heart disease, and ischemic heart disease appears to have decreased slightly for men with diabetes during the period 1971-1993 and may have increased for women with diabetes. The data also indicate that adults with diabetes experienced less decline in their mortality rates compared with the declines experienced by adults without diabetes during this period. The lower declines for subjects with diabetes occurred for all causes of death, heart disease, and ischemic heart disease. However, confidence limits around the mortality rate changes for subjects with diabetes were large and the magnitude of the changes could not be determined precisely. In contrast, there were large and statistically significant declines in mortality for adults without diabetes, which mirror the changes in the general US population found in other studies.1-4

The decline in coronary heart disease mortality in the US population has been attributed to improvement in risk factors for heart disease and improvement in medical treatment of patients with heart disease.15-17 These changes have resulted in decreased incidence of heart disease and increased survival of patients. Based on these studies, there are several possible reasons that smaller mortality declines among adults with diabetes compared with adults without diabetes may have occurred. First, risk factors for mortality, particularly heart disease risk factors, may have decreased less over time in those with diabetes. Second, the incidence of coronary heart disease, including the incidence of recurrent myocardial infarction, may have decreased less in...

In our study, there may have been differences between the 1971-1975 cohort and the 1982-1984 cohort that we could not measure that may have accounted for the lower declines in mortality for subjects with diabetes compared with subjects without diabetes. In addition, the completeness and accuracy of listing of heart disease and ischemic heart disease on the death certificate may have changed during the 2 cohort periods. However, the fact that the percentage changes from cohort 1 to cohort 2 were similar when multiple causes of death were analyzed indicates that this may not be a major reason for the lower declines in mortality for those with diabetes. Coding of the underlying cause of death was not a factor because the same procedure to select the underlying cause of death was used for all deaths in the study.

Our study could not precisely differentiate the types of diabetes, but the adult age of the NHANES I cohort and the high proportion of type 2 diabetes in the US population with diabetes indicate that the results reflect mortality in type 2 patients. Our data also do not permit identification of people with undiagnosed diabetes because neither fasting nor postchallenge glucose samples were obtained. Other studies have shown that mortality rates for individuals with undiagnosed diabetes are approximately equal to the rates for patients with diagnosed diabetes.20,21

In summary, this study indicates that mortality rates for all causes, heart disease, and ischemic heart disease in men and women with diabetes have not decreased to the extent that they have for adults without diabetes. Many changes have caused the declines in death rates in the general US population. These changes appear to have been less favorable or less effective for people with diabetes, particularly for women. With the increasing prevalence of diabetes in the United States22 and the smaller decline in mortality for these individuals, we anticipate that diabetes may become an increasingly important factor for heart disease mortality in the United States.

REFERENCEs

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