

# Trends in the Mortality Burden Associated With Diabetes Mellitus

## *A Population-Based Study in Rochester, Minn, 1970-1994*

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**Background:** The prevalence of diabetes mellitus (DM) has increased markedly in recent decades, but trends in the mortality burden associated with DM are unclear. Therefore, we analyzed population-based longitudinal data to address this issue.

**Methods:** The community-based medical records of all Rochester residents 45 years and older who died between January 1, 1970, and December 31, 1994, were reviewed to identify those who met the standardized criteria for DM before death. Trends over successive quinquenniums were assessed for the proportion of all deaths in the community of persons with prevalent DM, for mortality rates for persons with and without DM, and for the distribution of causes of death among decedents with and without DM.

**Results:** Of 10 152 total deaths in 1970-1994, 1384 (13.6%) met the criteria for prevalent DM. Between 1970-1974 and 1990-1994, the proportion of decedents with

DM increased by 48.2%. Mortality rates for persons with and without DM declined by 13.8% and 21.4%, respectively. This disparity in mortality trends was most apparent for older women and younger men. There were temporal declines in the proportion of all persons dying of cardiovascular disease, but temporal declines in persons dying of cerebrovascular disease were found only in decedents without DM.

**Conclusions:** The mortality burden associated with DM increased significantly between 1970 and 1994, probably due to increases in DM incidence and smaller declines in mortality for persons with DM relative to those without DM. In the absence of improved DM prevention and treatment, the steady declines in mortality observed for the general population since the 1960s will likely begin to slow or even reverse.

*Arch Intern Med.* 2003;163:445-451

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**M**ARKED DECLINES in mortality, primarily from cardiovascular disease (CVD), have been noted in the United States and throughout the world during the past 4 decades.<sup>1,2</sup> This reflects reductions in CVD risk factors (cigarette smoking, high blood pressure, and hypercholesterolemia) and event rates (myocardial infarction and stroke) and improved survival following CVD-related events.<sup>2-6</sup> By contrast, the number of new cases of diabetes mellitus (DM), an important risk factor for CVD-related events and for mortality following CVD-related events, has increased markedly in recent decades.<sup>7-9</sup> In addition, 2 studies<sup>7,10</sup> have shown that persons with DM did not exhibit the same improvements in survival in recent decades as persons without DM. In light of these disparate trends, it is likely that DM is accounting for an increasing proportion of CVD-related morbidity and

mortality within the population. The extent to which this has occurred is unclear, however, because most studies<sup>11-13</sup> of trends in DM-associated morbidity and mortality have relied on death certificate data. The serious limitations of death certificate data for identifying DM are well recognized.<sup>14-16</sup> In particular, only a few patients with DM have the condition listed on the death certificate,<sup>15</sup> and this proportion has changed over time.<sup>7</sup> Thus, reports of trends in the mortality burden associated with DM are lacking.

This report identifies trends in the mortality burden associated with DM by using clinically detailed population-based data sources. The Rochester Epidemiology Project (REP),<sup>17</sup> by virtue of access to complete community medical records for more than 5 decades, affords a unique opportunity to identify and confirm the diagnosis of DM among deceased members of the Rochester population without relying on death certificate

data to document the presence of DM. By using REP resources to overcome and clarify the limitations previously noted, we document an increase in the mortality burden associated with DM during a 25-year period, between January 1, 1970, and December 31, 1994.

## METHODS

### STUDY SETTING

Rochester (2000 census population, 85 806) is located in southeastern Minnesota, approximately 128 km from the nearest major metropolitan area. Population-based epidemiologic research in Rochester is facilitated by its relative isolation and the fact that it is home to one of the world's largest private medical centers, the Mayo Clinic. Nearly all of the medical care delivered to Rochester residents is provided by either the Mayo Clinic and its 2 affiliated hospitals or the Olmsted Medical Center, a second group practice with an affiliated hospital.<sup>17</sup> Since 1907, every Mayo Clinic patient has been assigned a unique identifier and all information from every Mayo Clinic contact (including office, emergency department, and nursing home visits and hospital inpatient or outpatient admissions) is contained within a single dossier for each patient. The detailed information includes a medical history, clinical assessments, consultation reports, dismissal summaries, laboratory and radiology results, and correspondence. The diagnoses assigned at each visit are coded and entered into continuously updated computer files. These files constitute the REP diagnostic index. With funding from the National Institutes of Health, Bethesda, Md (grant AR30582), the diagnostic index was expanded to include the few other providers of medical care to local residents, including the Olmsted Medical Center and the few private practitioners in the area, thereby linking the medical records for community residents.<sup>17</sup> Rochester Epidemiology Project resources also include access to all death certificates and to information on underlying cause of death as coded from the death certificate by the Minnesota Department of Health Vital and Health Statistics System.

### STUDY POPULATION

After receiving approval from the Mayo Clinic and the Olmsted Medical Center Institutional Review Boards, all Rochester residents who were 45 years or older at death were identified between 1970 and 1994. The determination of whether a decedent met the criteria for prevalent DM was ultimately based on manual review of laboratory glucose values. However, because it was not feasible to review all glucose values for all decedents, the determination was made using a 2-stage process: First, the REP diagnostic index was used to identify potential cases, ie, all decedents who were ever assigned any mention of DM or a DM-like condition (hyperglycemia, elevated blood glucose level, impaired glucose tolerance, or diabetic nephropathy) from the date of first contact with any REP health care provider until death. Among all decedents, the median time from the date of first contact until death was 43 years (interquartile range, 24-58 years). Thus, because the range of diagnoses under consideration was broad and the amount of medical history available for review was extensive, 25.7% of all decedents were identified as a potential case. Second, for every potential case, trained nurse abstractors reviewed the entire inpatient and outpatient medical records (including all laboratory glucose values) from the time of first contact with each REP provider until death to confirm the prevalence of DM. The confirmation criteria followed National Diabetes Data Group recommendations, that is, 2 consecutive fasting glucose levels of 140 mg/dL

or more ( $\geq 7.8$  mmol/L) or 1- to 2-hour levels of 200 mg/dL or more ( $\geq 11.1$  mmol/L), obtained using a standard oral glucose tolerance test.<sup>18</sup> Adjustments were made for changes in laboratory methods over time.<sup>19</sup> Based on these criteria, the abstractor determined if and when an individual qualified as a DM case. Individuals who, at their initial contact with a local physician, either were taking an antidiabetic medication or had qualifying glucose values and a history of DM were considered non-incidence prevalence cases. The date these individuals first met the criteria was defined as the date they reported having been first assigned a diagnosis. Details of these criteria have been previously published elsewhere and have been used to track changes in the incidence and prevalence of DM among Rochester residents since 1945.<sup>7,20-23</sup>

### STATISTICAL ANALYSES

Proportionate mortality was defined as the proportion of decedents with DM and was calculated as the number of decedents identified as having ever met the criteria for DM divided by the total number of decedents. For comparison purposes, we also calculated proportionate mortality as the proportion of all decedents with DM coded as the underlying cause of death on the death certificate and as the proportion of all decedents with any mention of DM on the death certificate.

Mortality among persons with DM (number of decedents who ever met the criteria for DM/Rochester DM person-years at risk) and mortality among persons without DM (number of decedents who had not met the criteria for DM/Rochester person-years at risk minus Rochester DM person-years at risk) were calculated. Rochester person-years at risk values were calculated based on decennial census data, with linear interpolation for intercensus years.<sup>24</sup> Rochester DM person-years at risk were based on the number of Rochester residents with prevalent DM (defined by the same criteria used in this study) in 1970, 1980, and 1990,<sup>7</sup> with interpolation for interdecade years. Mortality was calculated for each sex and for 6 age groups (45-54, 55-64, 65-74, 75-84, 85-94, and  $\geq 95$  years) for successive 5-year calendar periods, between 1970 and 1994. Rates were age and sex adjusted by the direct method to the white population of the United States in 1980. Trends over time were assessed using Poisson regression and testing for a significant effect of calendar period. To test if the secular trends differed between persons with and without DM, the data were modeled using stepwise Poisson regression with consideration of all interaction terms and higher-order polynomials (with  $P \geq .05$  as the criterion for exclusion from the model).

The underlying cause of death, as coded from the death certificate by the State of Minnesota Vital and Health Statistics System, was obtained for each decedent. The underlying cause was categorized as diseases of the heart (*International Classification of Diseases, Eighth Revision [ICD-8]* codes 390-398, 402, and 410-429 and *International Classification of Diseases, Ninth Revision [ICD-9]* codes 390-398, 402, 404, and 410-429), cerebrovascular diseases (ICD-8 and -9 codes 430-438), malignant neoplasms (ICD-8 and -9 codes 140-208), respiratory conditions (ICD-8 and -9 codes 460-519), DM (ICD-8 and -9 code 250), and all others. Trends over time in the proportion of deaths due to each cause were assessed for decedents who ever met the criteria for DM and for decedents who had not met the criteria for DM separately using Wilcoxon rank sum tests.

## RESULTS

Altogether, there were 10 152 deaths among Rochester residents 45 years and older between 1970 and 1994 (55.1%

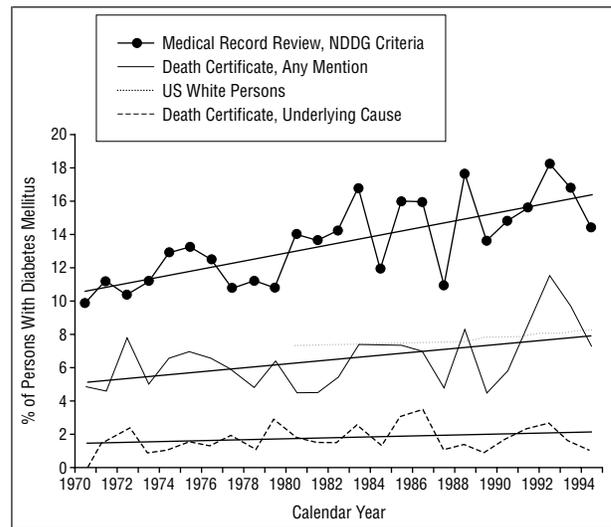
were women; mean±SD age, 77±12 years). A total of 1384 (13.6%) decedents met our criteria for DM before death (55.3% were women; mean±SD age, 76±11 years). This contrasts with the 1.7% of decedents who had DM coded as the underlying cause of death from the death certificate and with the 6.7% who had DM mentioned anywhere on the death certificate.

### TRENDS IN THE PERCENTAGE OF DECEDENTS WITH DM

Temporal trends in the proportion of Rochester decedents who ever met the criteria for DM are illustrated in **Figure 1**, which also provides trends in the proportion of Rochester decedents with DM coded as the underlying cause of death and with any mention of DM on the death certificate. The proportion of Rochester decedents with DM as the underlying cause of death was relatively unchanged during the 25-year period (1970-1994). By contrast, the prevalence of DM, as defined by our criteria, increased 48.2% during this period, from 11.4% (95% confidence interval [CI], 9.0%-13.7%) from January 1, 1970, to December 31, 1974, to 16.9% (95% CI, 14.1%-19.6%) from January 1, 1990, to December 31, 1994. Multivariable Poisson regression analyses confirmed that the proportion of decedents with DM increased significantly over time ( $P<.001$ ) and that the increase was similar across all ages ( $P=.18$  for the interaction between calendar year and age at death). The proportion of decedents with DM did not differ between sexes ( $P=.51$ ), but the model revealed a significant effect of age ( $P<.001$ ). There was a significant effect of age squared ( $P<.001$ ), revealing that the association with age was not linear (ie, for decedents aged 70 years, the model-predicted proportion of decedents who ever met the criteria for DM [13.9%] was greater than the proportions at the age of either 50 years [8.3%] or 90 years [8.2%]).

### TRENDS IN MORTALITY FOR PERSONS WITH AND WITHOUT DM

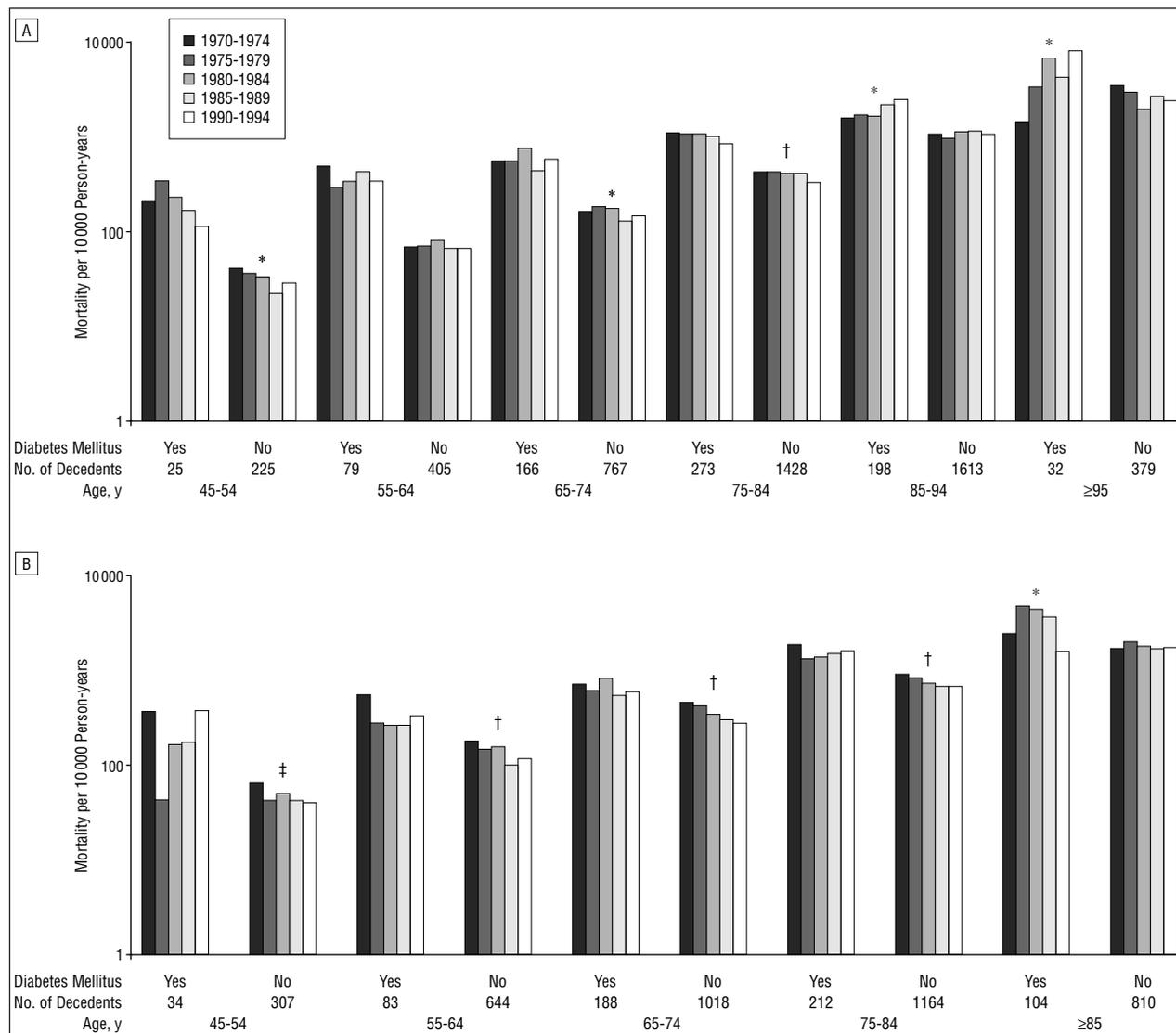
To investigate whether temporal increases in the proportion of decedents with DM reflected temporal differences in mortality for persons with DM relative to those for persons without DM, we estimated trends in mortality for persons with and without DM and compared the 2 groups over time. During the full period, the age- and sex-adjusted mortality rate per 10 000 person-years for persons with DM was 2.5 times the rate for persons without DM. Between 1970-1974 and 1990-1994, persons without DM experienced a 21.4% decline in age- and sex-adjusted mortality per 10 000 person-years, from 227 (95% CI, 215-238) to 178 (95% CI, 170-186), while persons with DM only experienced a 13.8% decline, from 596 (95% CI, 498-693) to 513 (95% CI, 453-573). This difference varied as a function of sex and age, as revealed in **Figure 2**. Figure 2A shows that the higher mortality rates for women with DM compared with women without DM were especially marked at younger ages. Indeed, in every quinquennium except 1990-1994, the mortality rate for women with DM aged 45 to 54 years was



**Figure 1.** The proportion of all Rochester decedents 45 years or older with prevalent diabetes mellitus as defined by various criteria and by year of death, between January 1, 1970, and December 31, 1994, compared with US white persons. (Data for the US white persons are from the National Center for Chronic Disease Prevention and Health Promotion.<sup>12</sup>) NDDG indicates National Diabetes Data Group; the fairly straight lines, the mean for each criterion.

higher than that for women without DM 20 years their senior. Temporal trends in mortality were similar for women with and without DM except at the oldest ages. Women 85 years or older with DM exhibited significant increases over time, while there was no trend over time for older women without DM. Figure 2B reveals that men with DM had higher mortality rates than men without DM, especially at younger ages. Among men in every age group younger than 85 years, there were significant temporal declines in mortality for persons without DM and no significant declines for persons with DM. In those 85 years and older, this disparity was reversed (ie, men with DM exhibited significant declines, while men without DM showed no significant change).

To test for significant differences between persons with and without DM, multivariable Poisson regression models were run separately for women and men (**Table**). Both models confirm that mortality was greater for persons with DM than for those without DM and that the effect of DM was greatest at younger ages (ie, significant age by DM interactions). The model for women reveals that there was an increase in mortality over time for women with DM compared with women without DM, but only at older ages. The model for men reveals an overall decline in mortality with increasing calendar year, but the temporal decline diminished with increasing age (ie, significant interaction between age and calendar year), especially at older ages (ie, significant interaction between age squared and calendar year). The temporal decline was less for men with DM than for men without DM, but only at younger ages (ie, significant interactions between calendar year, DM, and age). To help elucidate these trends, the model-predicted mortality rates for successive quinquenniums are graphed for women and men separately at the ages of 50, 70, and 90 years for persons with and without DM in **Figure 3A** and **B**, respectively.



**Figure 2.** Mortality per 10 000 person-years for successive quinquenniums, between January 1, 1970, and December 31, 1994, among Rochester residents with and without diabetes mellitus, by 10-year age groups for women (A) and men (B). The asterisk indicates  $P < .05$  for the within-group trend; dagger,  $P < .001$  for the within-group trend; and double dagger,  $P < .01$  for the within-group trend.

## TRENDS IN UNDERLYING CAUSE OF DEATH FOR PERSONS WITH AND WITHOUT DM

To further explore these differences in mortality, we compared the percentage distribution of underlying cause of death as coded from the death certificate across successive quinquenniums for decedents with and without DM (**Figure 4A** and **B**). Decedents without DM exhibited temporal declines in the percentage of deaths due to heart disease and cerebrovascular disease that were offset by increases in the proportions of deaths due to malignant neoplasms and respiratory diseases. For persons with DM, there was also a decline in the proportion of deaths due to heart disease and an increase in the deaths due to malignant neoplasms. Persons with DM, however, did not exhibit a temporal decline in the proportion of deaths with cerebrovascular disease listed as the underlying cause of death.

## COMMENT

This study identified prevalent DM among all Rochester residents who died between 1970 and 1994 and who were 45 years or older. Based on a comprehensive review of community-based medical records (including all laboratory glucose values), we found that 13.6% of all decedents had prevalent DM by National Diabetes Data Group criteria.<sup>18</sup> Between 1970-1974 and 1990-1994, however, the proportion of decedents with prevalent DM increased by nearly 50%.

At least 2 factors are thought to explain this increased mortality burden associated with DM in our community. First, the decline in mortality from 1970 to 1994 was less for persons with DM (13.8%) than for persons without DM (21.4%). In fact, the model-predicted rates revealed that diabetic women older than 85 years and diabetic men younger than 50 years exhibited increases in mortality over time. The different trends for persons with

**Factors Associated With Mortality Among Rochester, Minn, Residents Who Died When 45 Years or Older, 1970-1994**

Factor	Women*			Men		
	$\beta$ Coefficient	SE	P Value	$\beta$ Coefficient	SE	P Value
Intercept	-6.465	1.138	<.001	-20.593	5.837	<.001
Age†	.024	.017	.15	.505	.167	.002
Age squared	.0003	.0001	<.001	-.003	.001	.005
Diabetes mellitus	9.850	3.260	.002	-7.112	3.767	.06
Diabetes mellitus by age	-.123	.042	.003	.096	.050	.06
Calendar year	-.028	.013	.03	.116	.070	.10
Calendar year by age	.0003	.0002	.10	-.005	.002	.02
Calendar year by age squared	...	...	...	.000	.000	.01
Calendar year by diabetes mellitus	-.076	.039	.05	.108	.044	.02
Calendar year by diabetes mellitus by age	.001	.001	.03	-.001	.001	.02

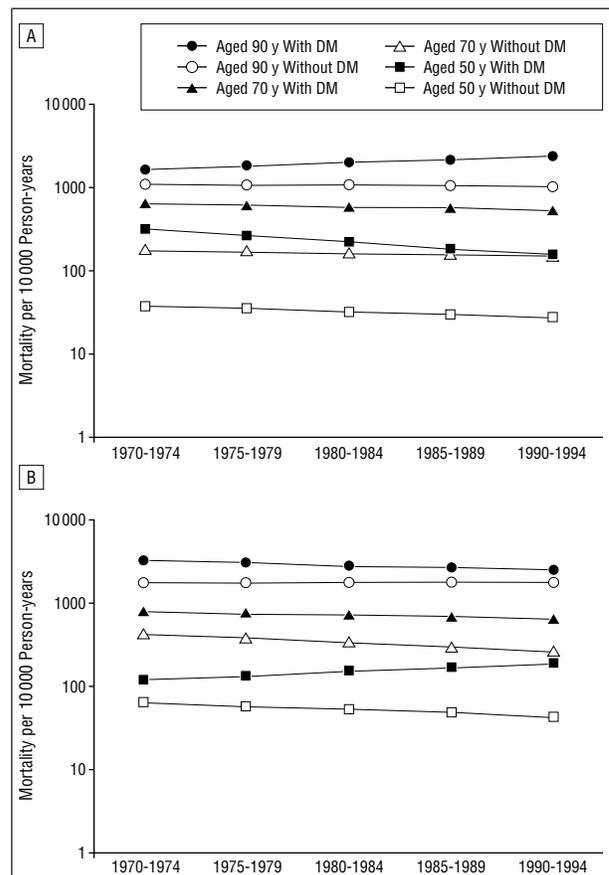
\*Ellipses indicate data not available.

†The midpoint of each age category (45-54, 55-64, 65-74, 75-84, 85-94, and  $\geq 95$  years for women and 45-54, 55-64, 65-74, 75-84, and  $\geq 85$  years for men) was used in the model.

and without DM are consistent with findings from previous studies<sup>7,10</sup> that compared 2 prevalence cohorts of persons with DM from the 1970s and the 1980s for 10-year survival. The studies showed that improvements in survival over time were not as great for persons with DM (especially women) as might have been expected based on improved mortality for the general population<sup>7</sup> or for persons without DM.<sup>10</sup> The differential decline in mortality for persons with and without DM, therefore, seems to explain at least part of the increasing mortality burden associated with DM in our community.

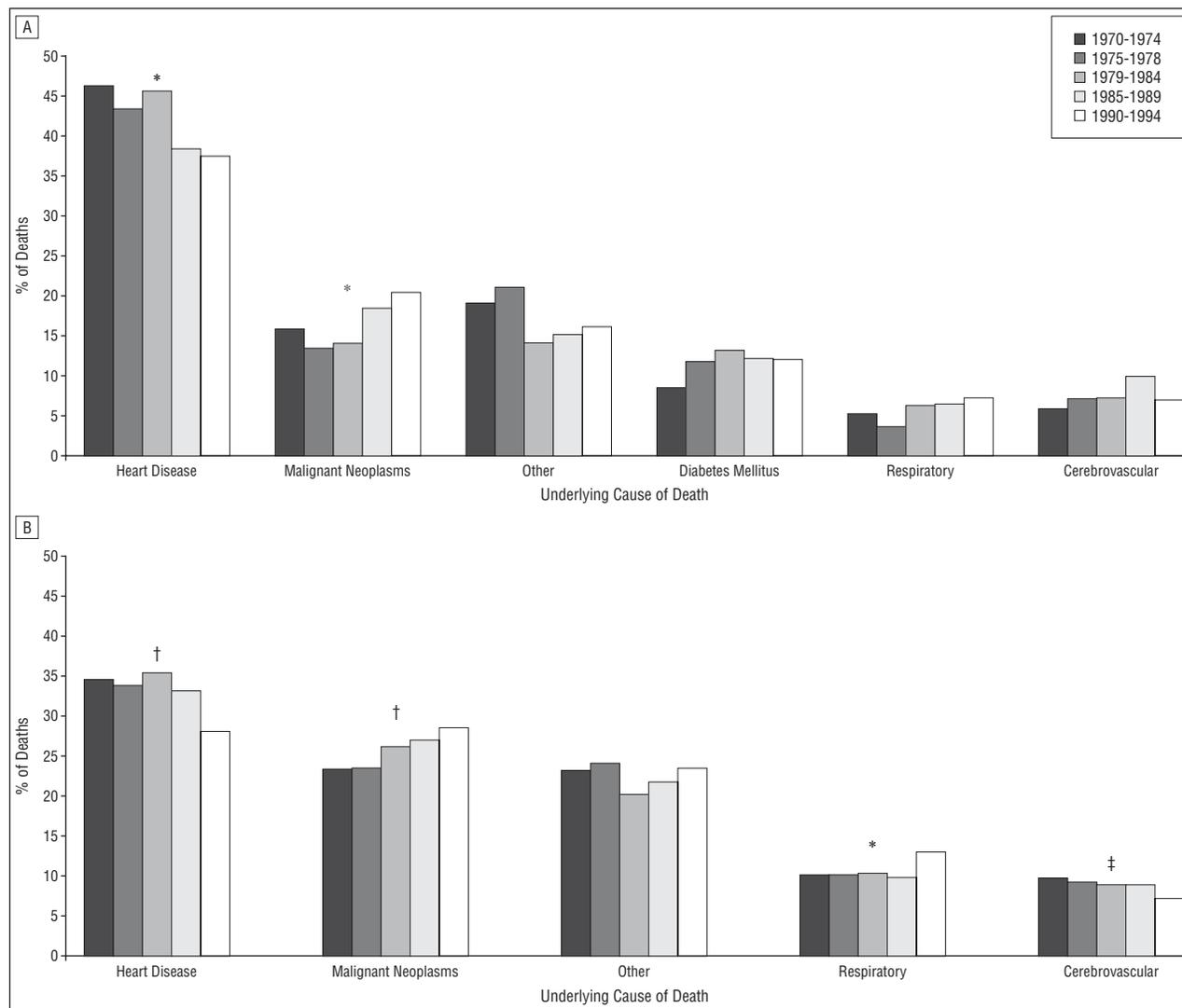
Second, the incidence of DM among adult residents of Rochester increased by 31% between 1970-1974 and 1985-1989.<sup>7</sup> More recently, it was shown that DM incidence rates for 1990-1994 had accelerated compared with 1970-1989.<sup>23</sup> Thus, it is likely that the 54% increase in age- and sex-adjusted incidence of DM (from 243 per 100 000 person-years in 1970-1974 to 373 per 100 000 person-years in 1990-1994 in Rochester)<sup>7,23</sup> was a major factor contributing to the 48.2% increase in the proportionate mortality associated with DM during this period.

Most data on mortality trends associated with DM are based on analysis of death certificates on which DM is recorded as the underlying cause of death or on which there is any mention of DM.<sup>11,12</sup> National data reveal that trends in the rate of deaths for which DM was the underlying cause were relatively constant through the 1980s but increased by 14% from 1988 to 1989, the year in which there was a change in recommendations for filling out death certificates in the United States. Deaths with DM listed as the underlying cause increased an additional 11% between 1989 and 1994. By contrast, deaths for which DM was mentioned anywhere on the death certificate did not display a large increase in 1989 and only increased by 4% between 1980 and 1994.<sup>12</sup> These disparate findings emphasize the well-known limitations of death certificates for identifying DM.<sup>7,14-16</sup> These limitations are reinforced with our finding that the prevalence of DM among Rochester decedents between 1970 and 1994, based on any mention of DM on the death certificate, was only 6.7% compared with 13.6% as determined by review of each decedent's complete medical records. Thus, the mortality burden associated with DM is seriously underestimated in studies that rely on DM as recorded on death certificates.



**Figure 3.** Model-predicted mortality per 10 000 person-years for successive quinquenniums, between January 1, 1970, and December 31, 1994, among Rochester residents with and without diabetes mellitus (DM), at the ages of 50, 70, and 90 years, for women (A) and men (B).

The extent to which the findings from this study can be generalized to the US population is limited by the fact that, during the years of study, the Rochester population was 95% white. Still, our data on the trends in mortality burden as defined by death certificate data (any mention of DM) are consistent with comparable national data for US white persons (Figure 1). Our finding that temporal trends in the proportion of deaths due to cerebrovascular disease differed between persons with and without DM is



**Figure 4.** Distribution of the proportion of deaths by underlying cause as recorded on the death certificate for successive quinquenniums, between January 1, 1970, and December 31, 1994, among Rochester decedents with (A) and without (B) prevalent diabetes mellitus. The asterisk indicates  $P < .05$  for the within-group trend; dagger,  $P < .001$  for the within-group trend; and double dagger,  $P < .01$  for the within-group trend.

limited to the extent that the underlying cause of death was determined from coding of the death certificates by the State of Minnesota Vital and Health Statistics System. For underlying cause of death due to cerebrovascular disease, however, a previous REP study<sup>25</sup> of 30-year trends in mortality due to stroke in the Rochester population demonstrated that the total number of deaths due to stroke based on underlying cause as determined from coding of the death certificates was only 4% greater than the number of deaths due to stroke as determined from review of the complete medical records by a board-certified neurologist, and that the 2 approaches showed similar variations over time. Thus, the limitations of death certificate coding observed for cerebrovascular disease in this population seem to be much less than those observed for DM.

Our study was also limited by the fact that, to minimize misclassification and to ensure a standardized definition throughout the study period, the definition of DM was intentionally strict. As a result, individuals whose glucose values never met National Diabetes Data Group criteria<sup>18</sup> but did meet the more recently introduced Ameri-

can Diabetes Association criteria<sup>26</sup> would have been excluded. Individuals who never had a diagnosis suggestive of DM in the REP diagnostic index, but who would have qualified if prospectively screened, also were not included. Cross-sectional studies<sup>9</sup> that prospectively screen community-dwelling individuals suggest that many of them qualify as diabetic based on oral glucose tolerance or fasting glucose test results even though they report no prior diagnosis of DM. However, because DM is a long-standing progressive disease, many such individuals ultimately come to clinical attention and would have been identified in our system. Indeed, 25.7% of all Rochester decedents had some prior diagnosis suggestive of DM, as delineated in the "Study Population" subsection of the "Methods" section. More important, the percentage was unchanged over time ( $P = .57$ ). In addition, the proportion of Rochester residents 45 years and older who undergo at least 1 blood glucose test each year is high, greater than 35% annually; this proportion was also unchanged during the years of study, reinforcing the relative completeness of DM detection within this population.<sup>23</sup>

The results of the present study have important public health consequences. We found that the mortality burden associated with DM is significant and is increasing. Our data, consistent with previous reports,<sup>7,10</sup> are especially compelling for women. The increase in mortality burden we observed for both sexes is probably due to increases in the incidence of DM in the population and a differential decline in mortality among persons with and without DM. Our findings reinforce the pressing need for primary prevention efforts to help stem the swelling tide of DM in the general population. Successful methods to prevent the development of DM have been reported<sup>27</sup> and have the potential to have a significant population-wide impact if they are effectively applied.<sup>28</sup> In addition, the adverse mortality trends for persons with DM compared with those without DM highlight the need for the application of effective management strategies for persons with DM and associated comorbid conditions (dyslipidemia, hypertension, obesity, renal disease, and CVD).<sup>29-31</sup> Our finding that the proportion of decedents with DM having cerebrovascular disease listed as the underlying cause of death has not decreased over time raises concerns that effective stroke prevention efforts may be lacking in persons with DM. Suboptimal control of hypertension in persons with DM might be one explanation for these findings,<sup>32,33</sup> particularly in view of recent data from Rochester suggesting that hypertension is a risk factor for stroke, but not for coronary heart disease-related mortality, in persons with DM.<sup>34</sup> Suboptimal control of hypertension in persons with DM, therefore, might explain why the percentage of decedents with DM who died of stroke did not change from 1970 to 1994 while the percentage of decedents with DM who died of coronary heart disease declined during that same period.

In the absence of improved DM prevention, treatment, and control, we estimate, based on the trends provided in Figure 1, that nearly 25% of all deaths among persons 45 years and older will meet our strict criteria for prevalent DM by 2020. As a consequence of this increase, the favorable shifts in mortality rates observed in the general population during the past 4 decades are likely to diminish and perhaps even reverse.

Accepted for publication June 14, 2002.

This study was supported by grants AG08729 and AR30582 from the National Institutes of Health, US Public Health Service, Bethesda, Md.

We thank the nurse abstractors on this project, Kris Otto-Higgins, RN, Sue Helling, RN, Kay Traverse, RN, and Susan Stotz, RN, for their excellent contributions; and the computer programmer, Jill Killian, BS.

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