ORIGINAL ARTICLE

Changes in Diabetes-Related Complications in the United States, 1990–2010

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ABSTRACT

BACKGROUND

Preventive care for adults with diabetes has improved substantially in recent decades. We examined trends in the incidence of diabetes-related complications in the United States from 1990 through 2010.

METHODS

We used data from the National Health Interview Survey, the National Hospital Discharge Survey, the U.S. Renal Data System, and the U.S. National Vital Statistics System to compare the incidences of lower-extremity amputation, end-stage renal disease, acute myocardial infarction, stroke, and death from hyperglycemic crisis between 1990 and 2010, with age standardized to the U.S. population in the year 2000.

RESULTS

Rates of all five complications declined between 1990 and 2010, with the largest relative declines in acute myocardial infarction (−67.8%; 95% confidence interval [CI], −76.2 to −59.3) and death from hyperglycemic crisis (−64.4%; 95% CI, −68.0 to −60.9), followed by stroke and amputations, which each declined by approximately half (−52.7% and −51.4%, respectively); the smallest decline was in end-stage renal disease (−28.3%; 95% CI, −34.6 to −21.6). The greatest absolute decline was in the number of cases of acute myocardial infarction (95.6 fewer cases per 10,000 persons; 95% CI, 76.6 to 114.6), and the smallest absolute decline was in the number of deaths from hyperglycemic crisis (−2.7; 95% CI, −2.4 to −3.0). Rate reductions were larger among adults with diabetes than among adults without diabetes, leading to a reduction in the relative risk of complications associated with diabetes. When expressed as rates for the overall population, in which a change in prevalence also affects complication rates, there was a decline in rates of acute myocardial infarction and death from hyperglycemic crisis (2.7 and 0.1 fewer cases per 10,000, respectively) but not in rates of amputation, stroke, or end-stage renal disease.

CONCLUSIONS

Rates of diabetes-related complications have declined substantially in the past two decades, but a large burden of disease persists because of the continued increase in the prevalence of diabetes. (Funded by the Centers for Disease Control and Prevention.)

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Twenty-one years ago, the Diabetes Control and Complications Trial (DCCT) showed that intensive glycemic control could reduce the microvascular complications of type 1 diabetes mellitus.[1] Subsequent studies showed that macrovascular and microvascular complications could be substantially reduced with tight control of glucose levels, blood pressure, and lipid levels in adults with type 2 diabetes.[2-5] Collectively, these studies focused attention on diabetes as a public health problem, with a course that could be altered by a combination of changes in clinical care (e.g., intensive management of risk factors), the health system (e.g., organization of care), health promotion (e.g., support for patients in modifying lifestyle), and society (e.g., tobacco-control policies).[6-8] These studies were followed by steady improvements in diabetes care, self-management behaviors, and risk-factor control and by the dissemination of new, effective pharmacologic approaches and medical procedures, such as statin use and coronary revascularization.[8-10] Given these important trends, we assembled data on four sentinel indicators of diabetes-related morbidity and one indicator of diabetes-related mortality from nationally representative data systems to examine how the spectrum of diabetes complications has changed in the past 20 years.

METHODS

DATA SOURCES

The National Health Interview Survey (NHIS) is a multistage probability survey that samples an average of 57,000 adults per year to estimate the health of the U.S. population, the prevalence and incidence of disease, the extent of disability, and the use of health care services.[11] The National Hospital Discharge Survey (NHDS) is an annual national probability survey of 239 to 474 nonfederal short-stay hospitals in all 50 states; the data collected on discharged patients includes information on seven diagnoses, four surgical procedures, and the age, race, sex, and marital status of the patients. The U.S. Renal Data System (USRDS) is a national registry of data on end-stage renal disease drawn from clinical and claims data reports submitted to the Centers for Medicare and Medicaid Services.[12,13] The National Vital Statistics System (NVSS) is a registry of all U.S. deaths that includes information about decedents' age, race, sex, state of residence, and underlying cause of death.[14] Data from the NHIS and NHDS were weighted to make estimates representative of the demographic characteristics of the U.S. noninstitutionalized population. The USRDS and NVSS are total population registries and thus do not require weighting. Further details of these data sets and definitions of variables have been described previously[15] and are provided, along with further information on methods, in the Supplementary Appendix (available with the full text of this article at NEJM.org). Data for these analyses were collected and processed at the National Center for Health Statistics and the USRDS Coordinating Center. All the authors vouch for the accuracy and completeness of the reported data.

DEFINITIONS

We identified incident cases of five diabetes-related complications: lower-extremity amputation, acute myocardial infarction, stroke, end-stage renal disease, and death from hyperglycemic crisis (namely, diabetic ketoacidosis and hyperosmolar hyperglycemic states). To identify cases in hospital discharge records, we used the *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM). To identify cases in death records, we used the *International Classification of Diseases, Ninth Revision* (ICD-9) for deaths occurring before 1999 and the *Tenth Revision* (ICD-10) for deaths occurring in or after 1999. The specific codes used were as follows: for lower-extremity amputation, ICD-9-CM procedure codes 84.10 to 84.19 (which include amputation of the upper leg, lower leg, ankle, foot, and toe), with hospital discharges for patients with traumatic amputation excluded (ICD-9-CM codes 895 to 897); for acute myocardial infarction as the first listed diagnosis, ICD-9-CM code 410; for stroke as the first listed diagnosis, ICD-9-CM codes 430 to 434 and 436 to 438; and for the underlying cause of death from hyperglycemic crisis, ICD-9 codes 250.1 and 250.2 and ICD-10 codes E10.0, E10.1, E11.0, E11.1, E12.0, E12.1, E13.0, E13.1, E14.0, and E14.1. Each of these outcomes was considered to be related to diabetes if any of the listed diagnoses included diabetes (ICD-9-CM:250). We based the incidence of end-stage renal disease on the number of cases in which dialysis was initiated or kidney transplantation was performed and in which diabetes was listed as the primary cause of renal failure.

DATA ANALYSES

For the primary analyses of the five outcomes (lower-extremity amputation, acute myocardial infarction, stroke, end-stage renal disease, and death from hyperglycemic crisis), we calculated incidence rates in 5-year intervals from 1990 to 2010 with two denominators: the U.S. population 20 years of age or older with diagnosed diabetes, with diagnosis determined on the basis of respondents' answer to the NHIS survey question of whether a health professional had ever told them that they had diabetes, and the overall U.S. population of persons 20 years of age or older as determined by the U.S. Census. Use of the first denominator gives the average incidence rate for an adult with diagnosed diabetes, and use of the second denominator gives the rate of a diabetes-related outcome in the general U.S adult population and thus allows changes in the prevalence of diabetes to influence rates.

To assess the potential effect of a large increase in detection or diagnostic practices, we conducted sensitivity analyses in which persons with newly diagnosed diabetes were excluded from the denominator under the assumption of a hypothetical, linear increase in detection. Specifically, we used NHIS data to estimate the number of people in 1995, 2000, 2005, and 2010 who had diabetes with a duration of less than 3 months, less than 1.0 year, less than 1.5 years, and less than 2.0 years, respectively; used those estimates to reduce the size of the denominator; and then recalculated complication rates for the population of adults with diabetes. This analysis provided an extreme upper bound for the rate of complications in the latter years, compensating for a scenario wherein the denominator is made larger over time by increases in the rate of detection. To examine trends in the relative risk of complications associated with diabetes, we also estimated the incidence of acute myocardial infarction, stroke, end-stage renal disease, and lower-extremity amputation using the population without diabetes as the denominator (estimated with the use of NHIS data) and basing the numerator on the same diagnostic codes, but without codiagnosis of diabetes.

All rates were expressed as the number of events per 10,000 persons per year, with age standardized to U.S. Census data for the year 2000 and with the use of four age groups: 20 to 44 years, 45 to 64 years, 65 to 74 years, and 75 years or more. We used the Proc RATIO procedure in SUDAAN software, version 10.0 (Research Triangle Institute), to obtain point estimates and standard errors that would account for the complex sampling designs of the surveys. We used t-tests to compare rates in 1990 and 2010 and linear tests of trend to examine changes in rates across the 20-year period; a P value of less than 0.05 was considered to indicate statistical significance. To improve precision, we used 3 years of data to calculate estimates for the years 1990 and 2000 (e.g., 1989, 1990, and 1991 data for estimates in 1990) and 2 years of data for the 2010 estimates (2009 and 2010); NHDS data for 2011 were not available at the time of the analysis.

RESULTS

RATES OF DIABETES

Between 1990 and 2010, the number of adults reporting a diagnosis of diabetes more than tripled, from 6.5 million to 20.7 million, whereas the U.S. adult population overall increased by approximately 27%, from about 178 million to 226 million. (Table S1 in the Supplementary Appendix shows the distribution of diagnosed diabetes in the civilian population according to age, sex, and race).

RATES OF DIABETES-RELATED COMPLICATIONS

The rates of all five major complications in the population of adults with diabetes declined significantly between 1990 and 2010 (Table 1 and Fig. 1A). The highest absolute rates and the greatest absolute declines in rates from 1990 to 2010 were observed for acute myocardial infarction (95.6 fewer cases per 10,000 persons per year; 95% confidence interval [CI], 76.6 to 114.6), stroke (58.9 fewer cases per 10,000; 95% CI, 41.6 to 76.2), and lower-extremity amputation (30.0 fewer cases per 10,000; 95% CI, 17.4 to 42.6), followed by end-stage renal disease (7.9 fewer cases per 10,000; 95% CI, 5.5 to 10.2) and death from hyperglycemic crisis (2.7 fewer cases per 10,000; 95% CI, 2.4 to 3.0) (Table 1 and Fig. 1A). A decrease in the rates of these complications was first observed in 1995 and was consistent thereafter. The large decline in the rate of acute myocardial infarction brought this rate to about the same level as the rate of stroke and narrowed the differences in rates for acute myocardial infarction and stroke as compared with the rate differences for amputation, end-stage renal disease, and death

Table 1. Age-Standardized Rates of Diabetes Complications among U.S. Adults with Diagnosed Diabetes.*

Variable	Year					Change, 1990–2010		P Value	
	1990	1995	2000	2005	2010	Absolute Change (95% CI)	Percent Change (95% CI)	Change, 1990–2010	Linear Trend
No. of adults with diagnosed diabetes	6,536,163	7,862,661	11,799,201	16,066,108	20,676,427				
Acute myocardial infarction									
No. of cases	140,122	183,605	191,011	158,616	135,743	−4379			
No./10,000 persons (95% CI)	141.1 (125.3 to 156.8)	145.9 (130.9 to 160.9)	105.7 (96.1 to 115.2)	64.2 (57.4 to 70.9)	45.5 (34.6 to 56.4)	−95.6 (−114.6 to −76.6)	−67.8 (−76.2 to −59.3)	<0.001	0.008
Stroke									
No. of cases	127,016	162,895	178,755	171,429	186,719	59,703			
No./10,000 persons (95% CI)	111.8 (98.9 to 124.7)	116.6 (104.3 to 128.9)	86.2 (78.8 to 93.7)	64.1 (58.1 to 70.1)	52.9 (41.1 to 64.7)	−58.9 (−76.2 to −41.6)	−52.7 (−64.4 to −40.9)	<0.001	0.009
Amputation									
No. of cases	50,364	76,531	80,658	69,074	73,067	22,703			
No./10,000 persons (95% CI)	58.4 (49.3 to 67.4)	70.4 (59.1 to 81.7)	48.7 (41.6 to 55.9)	35.5 (30.9 to 40.1)	28.4 (19.4 to 37.3)	−30.0 (−42.6 to −17.4)	−51.4 (−68.2 to −34.5)	<0.001	0.03
End–stage renal disease									
No. of cases	17,763	29,259	41,477	46,917	50,197	32,434			
No./10,000 (95% CI)	27.9 (25.7 to 30.0)	34.5 (31.9 to 37.1)	28.6 (27.6 to 29.7)	23.6 (22.8 to 24.5)	20.0 (19.1 to 20.9)	−7.9 (−10.2 to −5.5)	−28.3 (−34.6 to −21.6)	<0.001	0.04
Death from hyperglycemic crisis									
No. of cases	2890	2666	2422	2254	2361	−529			
No./10,000 persons (95% CI)	4.2 (3.8 to 4.5)	3.7 (3.3 to 4.0)	2.4 (2.3 to 2.5)	1.9 (1.8 to 2.0)	1.5 (1.4 to 1.6)	−2.7 (−3.0 to −2.4)	−64.4 (−68.0 to −60.9)	<0.001	0.008

* Adults were defined as persons 20 years of age or older. Numerators for rates of acute myocardial infarction, stroke, and lower-extremity amputation are from the National Hospital Discharge Survey, numerators for rates of end-stage renal disease are from the U.S. Renal Data System, and numerators for death from hyperglycemic crisis are from the National Vital Statistics System. Denominators are from the National Health Interview Survey. Rates have been age-standardized to the U.S. population in the year 2000. CI denotes confidence interval.

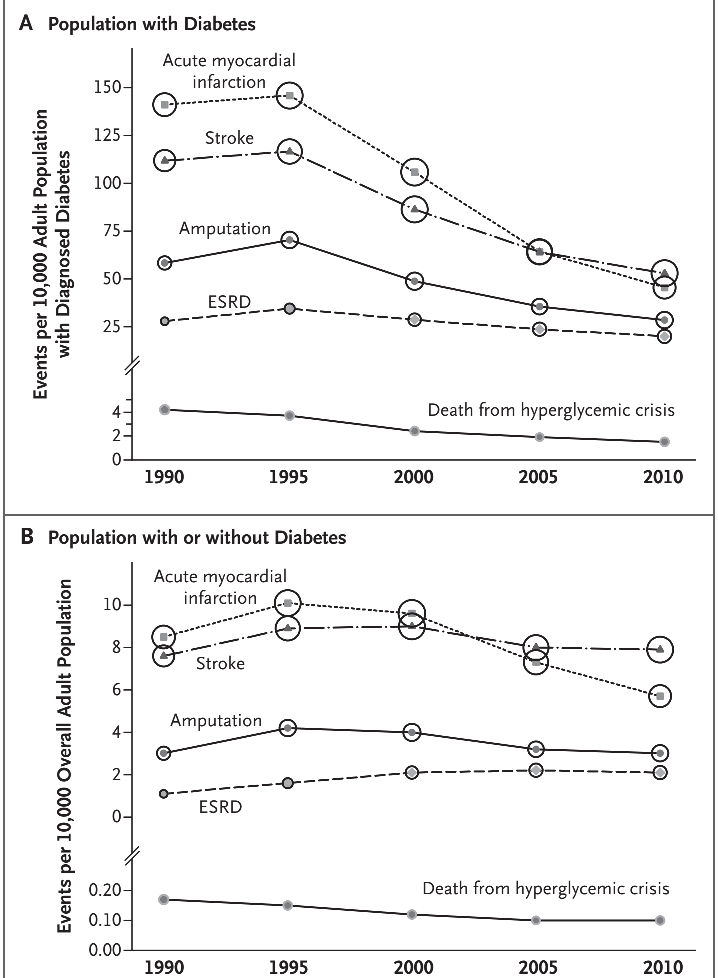

Figure 1. Trends in Age-Standardized Rates of Diabetes-Related Complications among U.S. Adults with and without Diagnosed Diabetes, 1990–2010.

For rates of myocardial infarction, stroke, and leg amputation, numerators are from the National Hospital Discharge Survey; for rates of end-stage renal disease (ESRD), numerators are from the U.S. Renal Data System, and for rates of death from hyperglycemic crisis, numerators are from the National Vital Statistics System. Denominators are from the National Health Interview Survey (Panel A) and the U.S. Census Bureau (Panel B). Circle size is proportional to the absolute number of cases (e.g., the number of cases of acute myocardial infarction ranges from 140,122 in 1990 to 135,743 in 2010, and the number of cases of death from hyperglycemic crisis ranges from 2890 in 1990 to 2361 in 2010). Panel A shows trends for persons with diabetes, and Panel B shows trends for persons with or without diabetes.

from hyperglycemic crisis. When expressed in terms of the absolute number of cases (i.e., irrespective of changes in population size), the annual numbers of cases of stroke, amputation, and end-stage renal disease increased by 59,703 cases, 22,703 cases, and 32,434 cases, respectively, from 1990 to 2010, whereas the number of acute myocardial infarctions declined by 4379 cases and the number of deaths from hyperglycemic crisis declined by 529 deaths (Table 1 and Fig. 1A).

The greatest relative decreases were observed for acute myocardial infarction and death from hyperglycemic crisis, both of which declined by about two thirds (myocardial infarction, −67.8%; 95% CI, −76.2 to −59.3; death from hyperglycemic crisis, −64.4%; 95% CI, −68.0 to −60.9%), followed by stroke and amputation, each of which declined by about half (−52.7%; 95% CI, −64.4 to −40.9; and −51.4%; 95% CI, −68.2 to −34.5, respectively). The smallest decline was observed for end-stage renal disease (−28.3%; 95% CI, −34.6 to −21.6). However, when change was measured from 1995 rather than 1990, the decline in end-stage renal disease was closer to the declines in the other complications. Sensitivity analyses, in which we modified the denominator for later surveys to account for the potential increases in detection in later years, also showed declines in rates of complications (Table S2 in the Supplementary Appendix).

The greatest declines in diabetes-related complications, in both absolute and relative terms, were observed among persons 75 years of age or older, except in the case of end-stage renal disease (Table S3 in the Supplementary Appendix). Thus, by 2010, rates of amputation among older adults were similar to those among younger adults, and rates of death from hyperglycemic crisis were higher among younger adults than among older adults. In addition, differences between younger and older adults narrowed considerably for rates of acute myocardial infarction and stroke. End-stage renal disease was the exception to these age-related trends, with declines in rates among younger persons (20 to 44 years of age and 45 to 64 years of age) but not in rates among older persons. However, when change was measured from 2000 rather than 1990, declines were seen across all age strata. The magnitude of the declines did not differ appreciably according to sex or race (Tables S4, S5, and S6 in the Supplementary Appendix), with the exception of rates of acute myocardial infarction, for which sex-related differences narrowed.

In an analysis in which rates were expressed per 10,000 persons in the overall population (Table 2 and Fig. 1B) and the changing prevalence rate of diabetes was permitted to influence the rates of complications, the greatest relative declines in rates were observed for death from

Table 2. Age-Standardized Rate of Diabetes Complications per 10,000 U.S. Adults, with or without Diagnosed Diabetes.*

Variable	1990	1995	2000	2005	2010	Change, 1990–2010		P Value†	
						Absolute Change (95% CI)	Percent Change (95% CI)	Change, 1990–2010	Linear Trend
No. of adults in overall population	177,705,141	189,632,670	201,595,867	213,680,406	226,144,631				
Acute myocardial infarction									
No. of cases	140,122	183,605	191,011	158,616	135,743	−4,379			
No./10,000 persons (95% CI)	8.5 (7.9 to 9.0)	10.1 (9.5 to 10.6)	9.6 (9.0 to 10.2)	7.3 (6.8 to 7.8)	5.7 (4.9 to 6.5)	−2.7 (−3.7 to −1.8)	−32.3 (−42.7 to −22.0)	<0.001	0.23
Stroke									
No. of cases	127,016	162,895	178,755	171,429	186,719	59,703			
No./10,000 persons (95% CI)	7.6 (7.1 to 8.2)	8.9 (8.3 to 9.4)	9.0 (8.4 to 9.6)	8.0 (7.5 to 8.5)	7.9 (6.7 to 9.1)	0.3 (−1.0 to 1.5)	3.4 (−13.5 to 20.3)	0.35	0.86
Amputation									
No. of cases	50,364	76,531	80,658	69,074	73,067	22,703			
No./10,000 persons (95% CI)	3.0 (2.7 to 3.3)	4.2 (3.8 to 4.6)	4.0 (3.6 to 4.5)	3.2 (2.9 to 3.5)	3.0 (2.5 to 3.6)	−0.01 (−0.6 to 0.6)	−0.5 (−21.3 to 20.4)	0.97	0.90
End–stage renal disease									
No. of cases	17,763	29,259	41,477	46,917	50,197	32,434			
No./10,000 persons (95% CI)	1.1	1.6	2.1	2.2	2.1	1.0	90.9	—	—
Death from hyperglycemic crisis									
No. of cases	2890	2666	2422	2254	2361	−529			
No./10,000 persons (95% CI)	0.17	0.15	0.12	0.10	0.10	−0.07	−42.0	—	—

* Adults were defined as persons 20 years of age or older. Numerators for rates of acute myocardial infarction, stroke, and lower-extremity amputation are from the National Hospital Discharge Survey, numerators for rates of end-stage renal disease are from the U.S. Renal Data System, and numerators for death from hyperglycemic crisis are from the National Vital Statistics System. The denominators are from the U.S. Census.

† P values are not provided for death from hyperglycemic crisis or end-stage renal disease because estimates were based on complete registries of the U.S. population, not on samples. Rates have been age-standardized to the U.S. population in 2000.

hyperglycemic crisis (−42.0%) and acute myocardial infarction (−32.3%). Rates did not change significantly for amputation or stroke, and the rate of end-stage renal disease increased by 90.9% (from 1.1 to 2.1 cases per 10,000 population).

Trends in the population of adults without diabetes were generally not as promising as those in the population with diabetes, with smaller reductions in the rate of acute myocardial infarction, no significant change in rates of stroke and lower-extremity amputation, and an increase in the rate of end-stage renal disease (Table 3). As a result, the relative risk of events associated with diabetes declined substantially for amputation (from 18.8 [95% CI, 15.1 to 22.6] to 10.5 [95% CI, 6.0 to 15.0]), for end-stage renal disease (from 13.7 [95% CI, 12.6 to 14.9] to 6.1 [95% CI, 5.7 to 6.3]), for acute myocardial infarction (from 3.8 [95% CI, 3.3 to 4.2] to 1.8 [95% CI, 1.3 to 2.3]), and for stroke (from 3.1 [95% CI, 2.7 to 3.5] to 1.5 [95% CI, 1.1 to 2.0]).

DISCUSSION

Our analyses of nationally representative hospitalization and registry data showed large reductions in the incidence of a broad spectrum of diabetes-related complications between 1990 and 2010 in the U.S. population of adults with diabetes. The analyses also revealed several trends. The magnitude of reduction was greatest for cardiovascular disease, particularly acute myocardial infarction, which has historically been the most common diabetes-related complication but

Table 3. Age-Standardized Rates of Diabetes Complications and the Relative Risk of Complications, According to the Presence or Absence of Diabetes, 1990, 2000, and 2010.

Complication	1990	2000	2010	Percent Change, 1990–2010
Acute myocardial infarction				
Among adults with diabetes — no. of events/10,000 (95% CI)	141.1 (125.3–156.8)	105.7 (96.1–115.2)	45.5 (34.6–56.4)	−67.8
Among adults without diabetes — no. of events/10,000 (95% CI)	37.5 (35.1–40.0)	37.1 (34.7–39.6)	25.8 (21.6–30.1)	−31.2
Relative risk (95% CI)	3.8 (3.3–4.2)	2.8 (2.5–3.2)	1.8 (1.3–2.3)	
Stroke				
Among adults with diabetes — no. of events/10,000 (95% CI)	111.8 (98.9–124.7)	86.2 (78.8–93.7)	52.9 (41.1–64.7)	−52.7
Among adults without diabetes — no. of events/10,000 (95% CI)	36.3 (33.8–38.9)	35.0 (32.9–37.1)	34.3 (27.5–41.1)	−5.5
Relative risk (95% CI)	3.1 (2.7–3.5)	2.5 (2.2–2.7)	1.5 (1.1–2.0)	
Lower-extremity amputation				
Among adults with diabetes — no. of events/10,000 (95% CI)	58.4 (49.3–67.4)	48.7 (41.6–55.9)	28.4 (19.4–37.3)	−51.4
Among adults without diabetes — no. of events/10,000 (95% CI)	3.1 (2.7–3.5)	2.7 (2.3–3.1)	2.7 (1.9–3.5)	−12.9
Relative risk (95% CI)	18.8 (15.1–22.6)	18.0 (14.3–21.7)	10.5 (6.0–15.0)	
End-stage renal disease				
Among adults with diabetes — no. of events/10,000 (95% CI)	27.9 (25.7–30.0)	28.6 (27.6–29.7)	20.0 (19.1–20.9)	−28.3
Among adults without diabetes — no. of events/10,000 (95% CI)	2.0 (2.0–2.1)	3.0 (3.0–3.1)	3.3 (3.3–3.4)	65.0
Relative risk (95% CI)	13.7 (12.6–14.9)	9.5 (9.2–9.9)	6.1 (5.7–6.3)	

* The relative risk was calculated as the age-adjusted rate among adults with diabetes divided by the age-adjusted rate among adults without diabetes. The relative risk was not calculated for death from hyperglycemic crisis, which by definition occurs only in persons with diabetes.

which is now about as common as stroke. Reductions in rates were smallest for end-stage renal disease, which actually increased among older adults. Finally, decreases in the rates of acute myocardial infarction, stroke, amputation, and end-stage renal disease among the population of adults with diabetes surpassed the rate reductions in the population without diabetes, with large declines in the relative risks of complications attributable to diabetes.

These findings probably reflect a combination of advances in acute clinical care, improvements in the performance of the health care system, and health promotion efforts directed at patients with diabetes.[8-10] An increased emphasis on the integrated management of care for patients with chronic diseases, including enhancements in team-based care, patient education in disease management, and clinical decision-making support, occurred in the years after the DCCT and other major clinical effectiveness trials of the 1990s.[8] These changes, paralleled by enhanced management of risk factors and improvements in blood pressure, lipid levels, and smoking cessation, were likely to have influenced rates of myocardial infarction, stroke, end-stage renal disease, and amputation.[9,16] Similarly, improvements in levels of glycated hemoglobin and in screening for early complications may have contributed to reductions in rates of end-stage renal disease, amputation, and, to a lesser extent. cardiovascular diseases. Advances in more intensive medical procedures, including revascularization approaches and wound treatment, probably played a major role as well.[17,18] Improvements in in-hospital management of diabetic ketoacidosis and hyperosmolar hyperglycemic states, paired with better patient education in disease management, could have driven reductions in the rate of death from hyperglycemic crisis.[19] Finally, social changes may have altered smoking rates, and alterations in eating habits that decreased the consumption of cholesterol and trans fat may have augmented the management of clinical risk factors.[20-22]

The declining rates of diabetes-related complications could also have been partially influenced by changes in the characteristics of the population, given differences in diagnostic criteria or increased detection of disease at earlier stages. However, the degree to which earlier detection is actually occurring is unclear. Reports from national databases have shown a slight reduction in the ratio of undiagnosed to diagnosed cases of diabetes, and recent cohorts of persons with incident diabetes have had higher rates of obesity, have been more ethnically diverse, and may have had fewer physical limitations than earlier cohorts.[23-25] However, we are not aware of clear evidence indicating that the age at the time of diagnosis of incident cases has declined or that there has been greater improvement in the health status of adults at the time of diagnosis than in the health status of adults in the general population.[15] In addition, large decreases in the incidence of disease were observed in sensitivity analyses that excluded a progressively greater number of newly diagnosed cases under the hypothetical assumption of a large increase in rates of detection. Improved quantification would be useful, given the ramifications for clinical and public health practice.

Our finding that rates of stroke are now similar to rates of acute myocardial infarction is probably more attributable to the large decline in cases of acute myocardial infarction rather than to the failure to prevent stroke. This trend could reflect increases in the options for and use of revascularization for coronary artery disease, in contrast to the therapeutic options for cerebrovascular disease.[17] However, the reasons why rates of end-stage renal disease have decreased less than rates of other complications of diabetes are less clear. Rates of end-stage renal disease may be affected by the increase in the proportion of the U.S. population of patients with diabetes who are non-Hispanic blacks, since the rate of end-stage renal disease in this population is twice as high as that among whites. Trends in end-stage renal disease may also be affected by a reduction in competing risks; with declining mortality from cardiovascular disease, older patients with diabetes may have more years of life during which chronic kidney disease can progress to a point where dialysis or transplantation is needed. Since two of our sentinel outcomes — stroke and myocardial infarction — were defined on the basis of discharge and another two — amputation and the initiation of dialysis for end-stage renal disease — were defined on the basis of need for a medical procedure, rates could be affected by changes in medical practices, such as delays in the initiation of dialysis

or amputation. The development of more sensitive cardiac biomarkers, such as troponin levels, may have led to increased diagnosis of acute myocardial infarction, including diagnosis of less severe cases.[26] However, previous validation studies of these hospitalization codes have shown a high positive predictive value (97%).[27]

Although it is difficult to compare rates across countries and studies because definitions of disease may differ, our findings are consistent with trends in cardiovascular disease and all-cause mortality reported from 1997 to 2006 in the United States[28] and with trends in acute myocardial infarction, amputation, and death from hyperglycemic crisis observed in Canada and northern Europe, as well as trends reported by the Department of Veterans Affairs.[29-34] However, we are not aware of other national studies that have compared the rates of a broad spectrum of diabetes-related outcomes or that have documented such a narrowing of differences in rates of acute myocardial infarction, stroke, and end-stage renal disease as we have observed between adults with and those without diabetes.

Although these findings are generally good news for patients with diabetes mellitus, our analyses do not provide a complete picture of trends in risk factors and complications. For example, we lack national data to examine trends in the incidence of diabetic retinopathy, even though diabetes is often cited as the most common cause of adult-onset blindness.[35] Similarly, we lack data on hypoglycemia, which can be a common complication of overtreatment, because emergency department data on hypoglycemia became available only in 2006; in addition, codes for deaths due to hypoglycemia are rarely recorded and their reliability is unclear.[15,36] Neuropathy, chronic kidney disease, peripheral vascular disease, and coronary and cerebrovascular disease are all important targets for efforts to prevent complications of diabetes.[37] However, we lack data to verify whether the frequency of these conditions is declining in parallel with the clinical outcomes captured from data on in-patient stays. Also lacking are data on trends for age-related complications of type 2 diabetes, including cognitive decline, Alzheimer's disease, depression, and physical disability, and for the association of certain cancers with diabetes.[38,39] Finally, we lack data to determine whether these trends in diabetes-related complications differ between persons with type 1 diabetes and those with type 2 diabetes. The wide range of complications for which we lack clear data on trends indicates a need for both enhanced surveillance and improved measurement of quality of life.

The encouraging reductions in the rates of morbidity and hyperglycemia-related mortality in the population of adults with diabetes do not signify imminent reductions in the overall burden of diabetes-related complications. The annual numbers of amputations, cases of end-stage renal disease, and strokes continue to increase because of the large increase in the number of prevalent cases of diabetes; the incidence has doubled in the past 15 years and the prevalence has tripled as mortality has declined.[25,40] These factors, combined with the shifting of the baby-boom generation into an age range characterized by a high incidence of diabetes and related morbidity, suggest that the total burden, or absolute number of cases of complications, will probably continue to increase in the coming decades.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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