The Evolving Diabetes Burden in the United States

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A diabetes epidemic emerged during the 20th century and continues unchecked into the 21st century. It has already taken an extraordinary toll on the U.S. population through its acute and chronic complications, disability, and premature death. Trend data suggest that the burden will continue to increase. Efforts to prevent or delay the complications of diabetes or, better yet, to prevent or delay the development of diabetes itself are urgently needed.

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Diabetes was first described in ancient times with the cardinal symptoms of polyuria, polydipsia, and polyphagia (1). The use of uniform diagnostic criteria provided a means to reliably track the disease and unveiled a worldwide epidemic that emerged during the second half of the 20th century and is now extending into the 21st century (2–4). This report examines the evolution of the diabetes epidemic in the United States and the burden imposed by its complications.

Classification of Diabetes Mellitus

There are 3 major types of diabetes (5). Type 1 diabetes usually involves children and was previously called *insulin-dependent diabetes mellitus* or *juvenile-onset diabetes*. It develops when the body's immune system destroys pancreatic β cells, which make insulin. Type 1 diabetes accounts for 5% to 10% of all diagnosed cases of diabetes in the United States. Type 2 diabetes, previously called *non–insulin-dependent diabetes mellitus* or *adult-onset diabetes*, usually begins as insulin resistance, in which target tissues do not use insulin properly. It accounts for approximately 90% to 95% of all diagnosed cases of diabetes. Gestational diabetes is glucose intolerance diagnosed during pregnancy with return to a normal metabolic state after delivery. Other, lesser types of diabetes result from specific genetic conditions (such as maturity-onset diabetes of youth), surgery, drugs, malnutrition, infections, and other illnesses; these account for 1% to 5% of all diagnosed cases of diabetes (5).

Diagnosis of Diabetes

Uniform diagnostic criteria for diabetes were first recommended by the American Diabetes Association and the World Health Organization in 1979 and 1980 and were updated in the late 1990s (5, 6). Currently, when typical symptoms of diabetes are present (for example, polyuria, polydipsia, or unexplained weight loss), a casual (that is, at any time without regard to the last meal) plasma glucose level of 11.1 mmol/L (200 mg/dL) or greater confirms the diagnosis. In addition, the diagnosis can be made with a fasting plasma glucose level of 7.0 mmol/L (126 mg/dL) or greater or an oral glucose tolerance test with a 2-hour value of 11.0 mmol/L (200 mg/dL) or greater. A positive diagnostic test result should be followed by a repeated test on a different day to confirm the clinical diagnosis. In contrast, for epidemiologic studies, a single fasting plasma glucose or 2-hour oral glucose tolerance test measurement is used to estimate the prevalence of diabetes in a population.

Tracking the Diabetes Epidemic

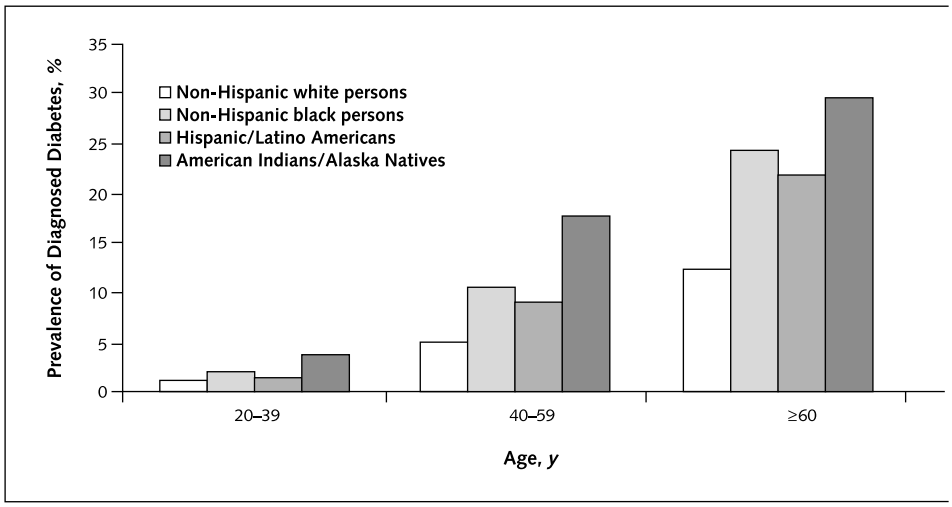
Currently, 3 periodic national surveys track diabetes prevalence in the United States. The National Health Interview Survey and National Health and Nutrition Examination Survey (NHANES) use national population-based samples and query persons in face-to-face interviews about whether they have been told by their health care provider that they have diabetes. A third survey, the Behavioral Risk Factors Surveillance System, asks a similar question of state-based population samples during telephone interviews of residents. Unlike the other 2 surveys, NHANES includes a laboratory-based examination that measures glucose levels and identifies persons with undiagnosed diabetes. All 3 surveys provide national estimates of the prevalence of diagnosed diabetes. Only the Behavioral Risk Factors Surveillance System provides state-based estimates, and only NHANES provides estimates of undiagnosed diabetes.

Prevalence

In 2002, an estimated 6.3% of the U.S. population (about 18.2 million persons) had diabetes (7). Diabetes affects various sociodemographic groups unequally. According to data from the National Health Interview Survey, persons 65 years of age or older make up almost 40% of all persons with diagnosed diabetes, and the prevalence in this age group is more than 10 times that in persons younger than 45 years of age (8). Minority race and ethnic groups, including black persons, Hispanic persons, and Native Americans, are disproportionately affected; the prevalence of diagnosed diabetes is generally 2 to 4 times higher in these groups than in the majority population (**Figure 1**) (7, 8).

The longest running of the surveys, the National Health Interview Survey, found a 4- to 8-fold increase over the last half-century in the number of persons who received

Figure 1. **Prevalence of diagnosed diabetes in people 20 years of age and older by age and race or ethnicity, United States, 2002.**

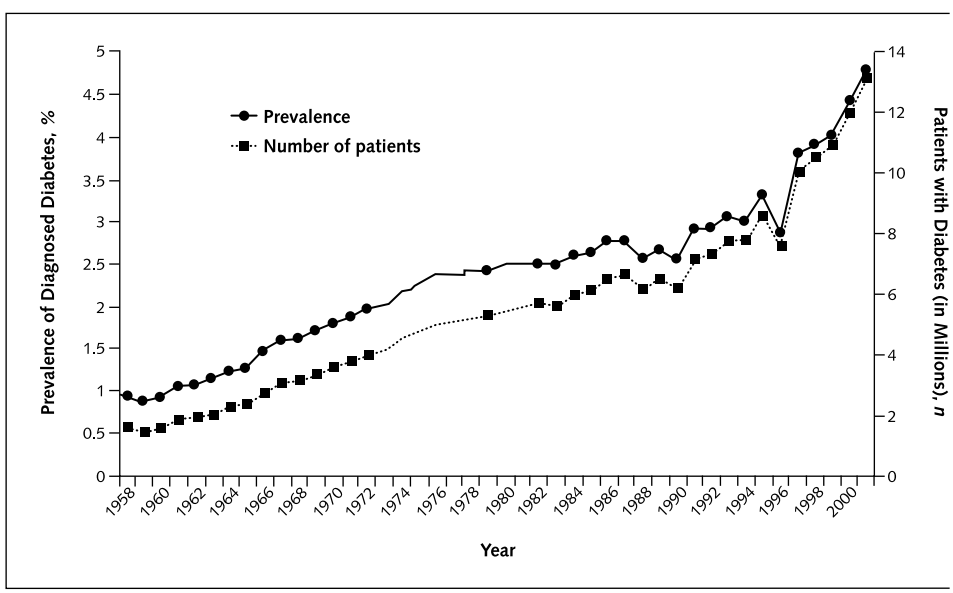


Data obtained from the 1999 to 2001 National Health Interview Survey estimates projected to 2002 and the 2002 outpatient database of the Indian Health Service.

a diagnosis of diabetes (1.6 million in 1958 and 12.1 million in 2000) and the prevalence of diagnosed diabetes in the United States (0.9% in 1958 and 4.4% in 2000) (**Figure 2**) (8, 9). Increases occurred across all demographic categories, including sex, race or ethnicity, and age (8). Between 1990 and 2001, data from the Behavioral Risk Factors Surveillance System indicate that the largest relative increases in diagnosed diabetes occurred in persons 30 to 39 and 40 to 49 years of age (95% and 83%, respectively); increases in other age groups were 40% in persons 18 to 29 years of age, 49% in persons 50 to 59 years of age, 42% in persons 60 to 69 years of age, and 33% in persons 70 years of age or older (10, 11). Although the magnitude of the increase varied, the prevalence of diagnosed diabetes among adults increased in every state in the United States (**Figure 3**). Trends are also disturbing in children and adolescents, in whom type 2 diabetes is increasingly being recognized, but as yet less commonly than type 1 diabetes (12). Studies of estimates of the incidence of type 1 diabetes in the United States, which are limited by sparse data, do not find a consistent pattern—some show an increase, some show a decrease, and some remain unchanged (13).

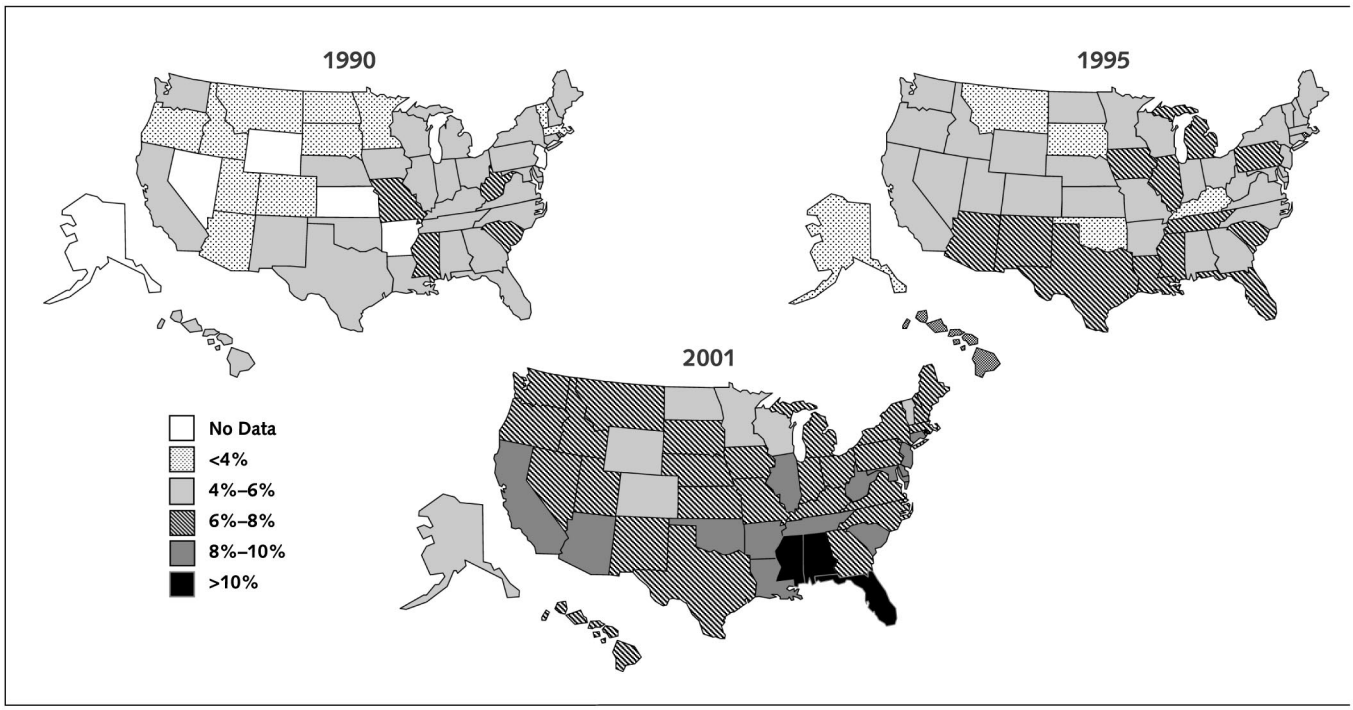
The NHANES found that diabetes is undiagnosed in approximately one third of all persons with diabetes and that this fraction has changed little over time (14). Many factors may have affected these uptrends in the prevalence

Figure 2. **Prevalence of diagnosed diabetes and the number of people with diagnosed diabetes in the United States, 1958 to 2000.**



Data obtained from the National Health Interview Survey.

Figure 3. **Prevalence of diagnosed diabetes (including gestational diabetes) by state in the United States, 1990 to 2001.**



Data obtained from the Behavioral Risk Factors Surveillance System survey.

of diabetes, including changes in diagnostic criteria, improved or enhanced detection, decreasing mortality, changes in demographic characteristics of the population (for example, aging), and growth in minority populations in whom the prevalence and incidence of diabetes are increasing.

DIABETES COMPLICATIONS

Morbidity

Cardiovascular Disease

Data on cardiovascular disease among the diabetic population are scant. However, in 2000, 37.2% of diabetic persons age 35 years and older reported receiving a diagnosis of a cardiovascular disease (8). Prevalence of ischemic heart disease among persons with diabetes was about 14 times the rate among those without diabetes in persons 18 to 44 years of age (2.7% vs. 0.2 %), 3 times as high in persons 45 to 64 years of age (14.3% vs. 4.7%), and almost twice as high in those 65 years of age or older (20% vs. 12%) (15). Other studies have shown that the absolute rates of cardiovascular disease in persons with diabetes are higher in men than in women (as in the general population), but the relative risk (comparing those with and without diabetes) is higher in women than in men (relative risk, 2 to 4 for women and 1.5 to 2.5 for men) (16, 17).

Eye, Kidney, and Lower-Extremity Disease

Visual impairment and blindness are major disabling complications of diabetes. Diabetic retinopathy, the leading cause of blindness (visual acuity $\leq$ 20/200) in persons age 20 to 64 years, accounts for 12% of all new cases of blindness and leads to 12 000 to 24 000 new cases each year in the United States (18). Considerable visual impairment (best corrected [for example, with glasses] visual acuity in either eye $<$ 20/40) among persons with diabetes is much more common than blindness and is associated with reduced functional status. A national population-based survey based on self-reports found that 25% of all persons with diabetes had considerable visual impairment, approximately double the proportion among persons without diabetes (19). Impairment among persons with diabetes can have several causes. Some are specific to diabetes, such as macular edema and diabetic retinopathy, and others are not specific to diabetes but occur more commonly in diabetic than in nondiabetic persons. Examples of conditions not specific to diabetes are cataracts (32% vs. 20% in persons 65 to 74 years of age) and glaucoma (6.0% vs. 2.3% in persons 65 to 74 years of age) (20–23).

In the United States in 2000, diabetic nephropathy accounted for more than 40% of new cases of end-stage renal disease (that is, kidney failure that requires dialysis or transplantation) (8). Persons with diabetes are the fastest-growing group of recipients of dialysis and transplantation (8). Several factors may account for the increase in incidence, including greater recognition of the etiologic role of diabetes, more use of treatments for end-stage renal disease,

a true increase in the incidence of diabetes-related end-stage renal disease, or a combination of these factors.

Lower-extremity disease, which includes peripheral neuropathy and peripheral arterial disease or both, results in elevated rates of lower-extremity amputations among persons with diabetes. An estimated 15% of persons with diabetes will have a diabetic foot ulcer during their lifetime (24); of these, 6% to 43% will ultimately undergo a lower-extremity amputation (25). Among persons with diabetes who have had an amputation, as many as 85% may have had a preceding foot ulcer (25). Currently, more than half of all nontraumatic lower-extremity amputations in the United States occur among people with diagnosed diabetes (8).

An analysis of the 1999 to 2000 NHANES found that an estimated 8.1% of the diabetic population age 40 years or older have peripheral arterial disease (defined as an ankle to brachial artery blood pressure ratio < 0.90) versus 4.0% in those without diabetes (26). People with diabetes also had 2 to 3 times the prevalence of peripheral neuropathy symptoms (29.9% vs. 10.2%), insensate feet (on the basis of monofilament testing, 26.4% vs. 14.0%), or either peripheral neuropathy or insensate feet (45.3% vs. 20.7%). In summary, 47.4% of people with diabetes had at least one lower-extremity condition (peripheral arterial disease, peripheral neuropathy, insensate feet, ulcer, or lower-extremity amputation) (26).

Acute Metabolic Complications

Diabetic ketoacidosis is an acute metabolic complication that may require hospitalization and even result in death. The number of hospitalizations in the United States for which diabetic ketoacidosis was listed as the first diagnosis increased from 61 800 in 1980 and 99 913 hospitalizations in 2001 (8). Deaths due to diabetic ketoacidosis are rare and have declined between 1980 and 2000 by 28% (32 to 23 per 100 000 diabetic population) (8). Population-based data on the occurrence of hypoglycemia are scant, but 2 major clinical trials that carefully assessed its significance found that intensive glycemic control increases the risk for hypoglycemia. The United Kingdom Prospective Diabetes Study examined intensive glycemic control among persons with type 2 diabetes and found that the rate of major hypoglycemia (that is, at a minimum requiring attention from persons other than the patient) was significantly more common in those treated intensively with insulin than in those receiving conventional care (1.8% versus 0.7%; $P < 0.001$). The Diabetes Control and Complications Trial studied intensive glycemic control among persons with type 1 diabetes and found that the rate of severe hypoglycemia (coma, seizure, or needing help from other persons) in the intensive treatment group was 3 times that of persons in the conventional group (62 vs. 19 episodes per 100 patient-years; $P < 0.001$) (27, 28).

Disability

Persons with diabetes suffer disproportionately from physical and cognitive disability. The National Health Interview Survey indicates that persons with diabetes have about twice the prevalence of physical disability as persons without diabetes (66% vs. 29%; $P < 0.001$) (29). In a prospective study, newly developed functional disability was also nearly twice as common in persons with diabetes than in their counterparts without diabetes (yearly incidence, 9.8% vs. 4.8%), and, after adjustment for potential confounders, diabetes remained associated with a 42% risk for any incident disability (30). Among elderly persons, diabetes-related cognitive impairment or dementia has been documented. Several prospective studies that used repeated neuropsychological tests and diagnostic protocols found an approximate doubling of the overall risk for dementia in persons with diabetes compared with those without diabetes (31).

Mortality

National data estimate that among Americans age 25 years and older who die, approximately 17% have diabetes (32). Age-adjusted mortality among adults with diabetes is about twice that of people who do not have diabetes (32). A large meta-analysis that included 10 prospective studies found a relative risk of 1.9 for men and 2.6 for women when their counterparts without diabetes were the referent (33). Among middle-aged people with diabetes, life expectancy is reduced by 5 to 10 years (32), and, for the entire population with diabetes, an estimated 13 years is lost by both men and women (34). The increased risk for death associated with diabetes is greater for younger people (ratio of 3.6:1 for people age 25 to 44 years and 1.5:1 for those age 65 to 74 years) (34).

In 2000, under the new 10th version of the International Classification of Diseases, diabetes was the sixth leading cause of death in the United States (35). This ranking is based on the 69 301 death certificates on which it was listed as the underlying cause (7). Diabetes was listed as a contributing cause of death on an additional 143 761 death certificates. However, only about 35% to 40% of decedents with diabetes have it listed anywhere on the death certificate, and only about 10% to 15% have it listed as the underlying cause of death (36). Thus, data from death certificates substantially underestimate the impact of diabetes.

Cardiovascular disease is the reported cause of up to 65% of all deaths in persons with diabetes in the United States (32). In addition, a recent U.S. study involving cohorts from 1971 to 1984 and 1982 to 1993 found that the population with diabetes did not experience the reductions in heart disease mortality experienced by those without the disease (37). Comparing rates for the 2 periods, the authors found that both men and women without diabetes had statistically significant declines in age-adjusted heart disease mortality (36% and 27%, respectively), whereas men and women with diabetes did not have statistically significant changes (13% decline and 23% increase, respectively). In a

more recent population-based study in Rochester, Minnesota, the mortality rate for persons with diabetes declined between 1970 and 1994 by 13.8%, which is smaller than the corresponding decline among those without diabetes (21.4%) (38).

Major Risk Factors for Developing Diabetic-Related Complications

Among persons with diabetes, the major risk factors for microvascular complications (eye disease, kidney disease, and peripheral neuropathy) are long-term poor glycemic control, as measured by hemoglobin A_{1c} levels, and hypertension (39).

Risk factors for cardiovascular disease among persons with diabetes are similar to those in persons without diabetes; however, the magnitude may be greater. The Multiple Risk Factor Intervention Trial (MRFIT) followed a large cohort (approximately 350 000 persons that included 5000 persons with diabetes) for 12 years and found that systolic hypertension, elevated cholesterol level, and cigarette smoking independently predicted cardiovascular mortality and that the presence of any one risk factor affected important clinical outcomes more in persons with diabetes than in those without diabetes (40).

The risk for cardiovascular disease associated with hyperglycemia or other underlying factors is less clear, but it may be related to insulin resistance or the metabolic syndrome. Among persons with diabetes, large prospective studies have found high blood glucose concentrations to be associated with a greater incidence of cardiovascular disease (41). In a Finnish cohort of 1373 persons without diabetes and 1059 with the disease who were followed for 7 years, the incidence of either fatal or nonfatal acute myocardial infarction largely depended on diabetes status. Among persons with diabetes, the incidence was 45% in those with a history of heart disease and 20.2% in those with no such history; for those without diabetes, the incidence was only 18.8% for persons with a history of heart disease and 3.5% for those with no such history (42). However, in another study of a United Kingdom cohort of 3477 persons with diabetes and no history of myocardial infarction and 7414 without diabetes but a history of myocardial infarction, the risk for cardiovascular events (either fatal or nonfatal) was higher in the group without diabetes (adjusted risk ratio, approximately 3) (43). A third study, which combined 22 prospective studies with follow-up for up to 11 years, found J-shaped cardiovascular disease mortality rates for the fasting glucose concentration, with mortality highest at low and high fasting glucose values (44). By contrast, the 2-hour glucose concentrations had a graded and increasing hazard ratio across the entire range of values (44).

The Future

Projections of diabetes into the 21st century are of concern. One in 3 people born in the United States in 2000 are projected to develop diabetes at some point in their lifetime (45). On the basis of age-, sex-, and race-specific rates for diagnosed diabetes from the 1984 to 2000 National Health Interview Survey and census projections, a 225% increase is projected between 2000 and 2050, a rise from 12 to 39 million diagnosed persons of all ages and an increase in prevalence from 4.4% to 9.7% (120% increase) (46). Persons 75 years of age or older are expected to have the largest increase in terms of numbers of persons affected (460%), followed by increases of 241% among those 65 to 74 years of age, 159% among those 45 to 64 years of age, 125% among those 20 to 44 years of age, and 97% among those 0 to 19 years of age. Among racial and ethnic groups, the prevalence is expected to increase by 149% among Hispanic persons, 118% among black persons, and 104% among white persons. These increases are due to expected demographic changes in the population (26%), population growth (20%), and, mostly, changes in prevalence (54%). However, increasing prevalence among younger age groups and the emergence of type 2 diabetes in children may worsen these projections.

Conclusion

The diabetes epidemic has already taken an extraordinary toll on the U.S. population, but the price it exacts in the future will be far greater if the current trends continue. Urgent efforts are needed to stem this tide. Because the possibility of delaying or preventing the complications of diabetes and diabetes itself is a reality (27, 28, 47), efforts must be directed at realizing these possibilities.

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