



# Diabetes Diagnosis and Control: Missed Opportunities to Improve Health

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## The 2018 Kelly West Award Lecture

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Diabetes is a prevalent condition in the U.S. and worldwide, with expanding impact over time as it affects progressively younger ages as well as older ages as people live longer. Costs of diabetes to those affected and to society as a whole continue to increase. Costs are realized through daily treatment regimens throughout life to control glycemia and other risk factors for complications as diabetes progresses, diabetes complications and disability and their treatments, health care visits and hospitalization, and as indirect costs via lower quality of life and lost productivity. Diagnosing diabetes is key to affording the opportunity to treat diabetes, and diabetes control is key to reducing the risk of complications. Yet the magnitude of undiagnosed diabetes and poor control of diabetes is large. And just as certain subgroups of the population are affected disproportionately by diabetes and diabetes complications, so are they affected disproportionately by undiagnosed diabetes and poor control. This review addresses the epidemiology of undiagnosed diabetes and diabetes control, largely covering their magnitude, demographic variation, trends over time, and predictors. For diabetes control, it focuses on control of A1C, blood pressure, and lipid levels, although there are many other facets of diabetes control and preventive care that also could be examined. The review is based predominantly on data from the National Health and Nutrition Examination Survey (NHANES), a U.S. health survey that includes both an interview and examination component that has been conducted continuously since 1999 and episodically for decades earlier. The interview elicits self-reported health responses pertaining to diabetes and other medical conditions and an examination that measures glycemic indicators, blood pressure, and lipids, which provide much of the material presented herein. Data from other studies are also presented and described.

### UNDIAGNOSED DIABETES

#### Magnitude of Undiagnosed Diabetes

The data from the National Health and Nutrition Examination Survey (NHANES) provide the unique opportunity to examine total prevalence of diabetes in the U.S., assessing both previously diagnosed diabetes based on participant self-report from an interview and undiagnosed diabetes in the remaining individuals from a blood draw obtained during an examination. NHANES currently obtains both A1C and fasting plasma glucose (FPG) measurements to assess diabetes and, in certain years, also a 2-h plasma glucose (2-h PG) from an oral glucose tolerance test (OGTT), with diabetes

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defined by A1C  $\geq 6.5\%$  (48 mmol/mol), FPG  $\geq 126$  mg/dL (6.99 mmol/L), or 2-h PG  $\geq 200$  mg/dL (11.1 mmol/mol) (1). A1C and FPG are most commonly used in clinical practice; however, the more time-consuming and complex OGTT detects additional diabetes from the 2-h PG.

In 2011–2014, the crude prevalence of diagnosed diabetes in adults aged  $\geq 20$  years was 9.6% or 21.6 million in the noninstitutionalized civilian U.S. population. Based on A1C or FPG, an additional 2.9% or 6.6 million had undiagnosed diabetes, amounting to total diabetes of 12.5%, a total of 28.2 million (2). With the addition of the 2-h PG to detect undiagnosed diabetes, 5.0% had undiagnosed diabetes, or 11.4 million, amounting to total diabetes of 14.6% or 33.0 million.

An additional metric to examine the burden of undiagnosed diabetes is the proportion of total diabetes that is undiagnosed. In 2011–2014, using A1C or FPG, 23.3% of total diabetes was undiagnosed; while using A1C or FPG or 2-h PG, 34.5% of total diabetes was undiagnosed.

### Association of Undiagnosed Diabetes With Comorbidity

Beyond elevated blood glucose levels, there is a higher prevalence of other risk factors for complications of diabetes in those with undiagnosed diabetes as compared with those with normal glucose levels. In 2009–2014 using NHANES data, age-standardized prevalence of overweight among adults aged  $\geq 20$  years with undiagnosed diabetes (based on A1C/FPG/2-h PG, 86.4%) was similar to that among adults with diagnosed diabetes (89.0%) but higher than that among those with prediabetes (75.7%) and normal glucose levels (60.7%) (3). Likewise, prevalence of hypertension among those with undiagnosed diabetes was intermediate (51.1%) compared with prevalence among those with diagnosed diabetes (58.8%), prediabetes (34.2%), and normal glucose levels (23.8%). Similar prevalence gradations were found for high waist circumference, hyperlipidemia, low HDL, and high triglycerides. Many of these conditions, however, might have been detected and treated by health care providers regardless of diabetes detection.

Yet it is not uncommon for diabetes complications to present at the time of

diabetes detection. Microvascular complications were intermediate in age-standardized prevalence among adults with undiagnosed diabetes based on the NHANES data, including retinopathy based on A1C/FPG/2-h PG (12.3% vs. 32.7% in diagnosed diabetes, 8.0% in prediabetes, and 5.8% in normal glucose levels; 2005–2008), renal disease based on A1C/FPG/2-h PG (7.4% vs. 13.9% in diagnosed diabetes, 5.5% in prediabetes, and 4.2% in normal glucose levels; 2009–2014), and neuropathy based on A1C/FPG (21.5% vs. 26.2% in diagnosed diabetes, 13.2% in prediabetes, and 10.2% in normal glucose levels; 1999–2004) (3). Increased prevalences among those with undiagnosed diabetes, relative to those with prediabetes and normal glucose levels, were also found for cardiovascular disease, peripheral arterial disease, and liver disease.

Prevalence of diabetic retinopathy at clinical diagnosis of diabetes in 1978–1982 was found to be 20.8% in Wisconsin and 9.9% in Australia and increased linearly with duration of diabetes (4). The authors extrapolated back linearly to indicate the time at which the onset of observable retinopathy was estimated to have occurred. They concluded that onset of retinopathy occurred on average about 4–7 years prior to diagnosis of diabetes. With the lowering of thresholds of diabetes diagnostic criteria and more specific screening guidelines for diabetes, it is likely that the time between onset and detection of diabetes has shortened (5–7).

These data illustrate the considerable prevalence of various complications at clinical detection of diabetes and the need for earlier diabetes detection to prevent or delay complications through treatment of glycemia and concomitant risk factors.

### Variation in Prevalence of Undiagnosed Diabetes by Demographic Factors

Figure 1A shows the prevalence in 2011–2014 of diagnosed and undiagnosed diabetes as well as combined total diabetes, by age, in the total U.S. population based on the NHANES data (2,3). Undiagnosed diabetes was defined based on elevated A1C, FPG, or 2-h PG. Prevalence of diagnosed and undiagnosed diabetes increased similarly up to age 40–49 years; thereafter, prevalence of

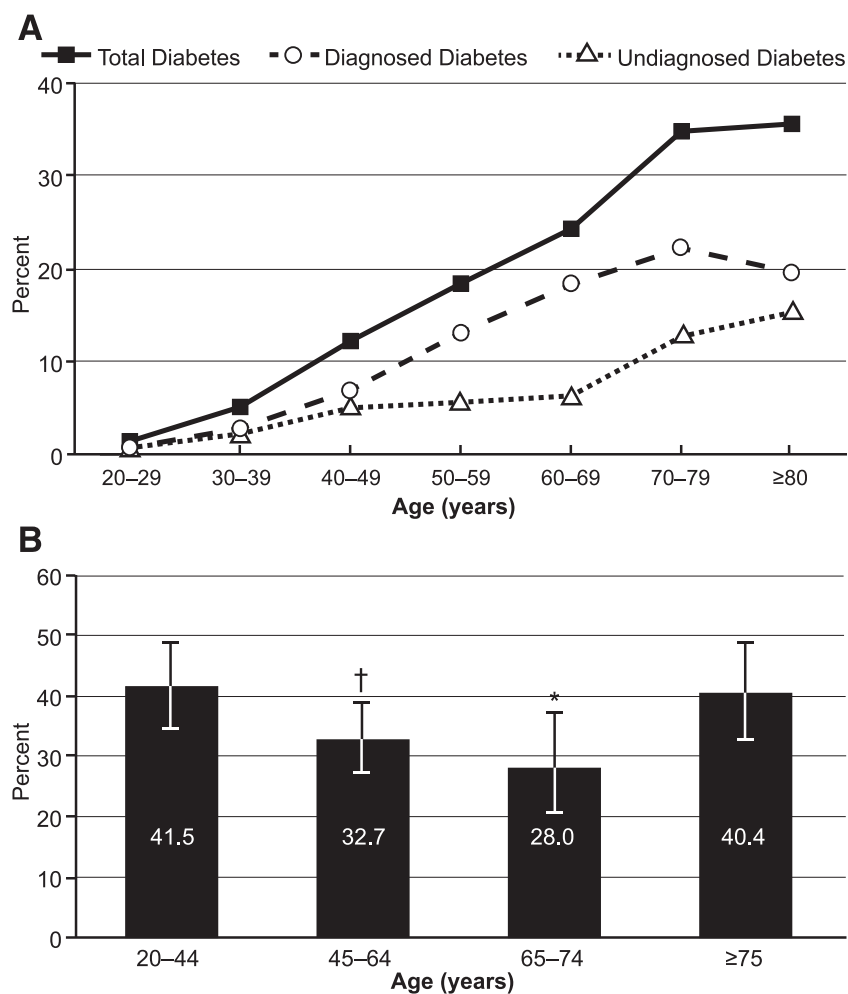
diagnosed diabetes was higher and increased more rapidly until age 70–79 years, when undiagnosed diabetes continued to increase and diagnosed diabetes decreased. Highest prevalence of diagnosed diabetes was at age 70–79 years (22.2%), and highest prevalence of undiagnosed and total diabetes was at age  $\geq 80$  years (15.3% and 35.6%, respectively).

If we examine the prevalence of undiagnosed diabetes based on A1C/FPG/2-h PG as a proportion of total diabetes by age, the proportion undiagnosed was highest in the youngest individuals aged 20–44 years (41.5%), was significantly less among those aged 45–64 (32.7%) and 65–74 years (28.0%), but then rose in those aged  $\geq 75$  years (40.4%) (Fig. 1B) (2). Thus, at young ages, when treatment would be particularly beneficial to delay or prevent diabetes complications, a large proportion of the young with diabetes are undetected.

Prevalence of diagnosed and undiagnosed diabetes in 2011–2014 and resultant total diabetes among the total population were similar by sex (Fig. 2A). By race/ethnicity, however, there was variation. In particular, the highest prevalences of undiagnosed diabetes were found in non-Hispanic Asians (9.3%), Hispanics (8.4%) and specifically Mexican Americans (7.8%), followed by non-Hispanic blacks (6.0%), and the lowest prevalence was found in non-Hispanic whites (4.0%).

The racial/ethnic disparity in undiagnosed diabetes is borne out when we examine the percent of total diabetes that is undiagnosed. As shown in Fig. 2B, 47.9% of total diabetes was undiagnosed among non-Hispanic Asians and 39.0% among Mexican Americans (42.6% among all Hispanics), with intermediate prevalence among non-Hispanic blacks (35.1%) and lowest prevalence among non-Hispanic whites (30.5%).

At least part of the reason for the high proportion of undiagnosed diabetes among non-Hispanic Asians may be due to less screening and diagnostic testing in the less obese and less overweight Asian Americans, despite their greater cardiometabolic risk at lower BMI levels (8). For example, in data from NHANES during 2011–2014, mean BMI among those with undiagnosed diabetes aged  $\geq 20$  years was 34.8 kg/m<sup>2</sup> in non-Hispanic whites, 37.5 kg/m<sup>2</sup> in non-Hispanic



**Figure 1**—Prevalence of undiagnosed diabetes among adults, by age, U.S. 2011–2014. **A:** Age-specific prevalence of diagnosed, undiagnosed, and total diabetes among all adults aged  $\geq 20$  years, U.S. 2011–2014. **B:** Percent of total diabetes that was undiagnosed, by age, U.S. 2011–2014. Data are from NHANES. Total diabetes is the sum of diagnosed and undiagnosed diabetes. Diagnosed diabetes is based on self-report. Undiagnosed diabetes is based on A1C  $\geq 6.5\%$  ( $\geq 48$  mmol/mol), FPG  $\geq 126$  mg/dL ( $\geq 7.0$  mmol/L), or 2-h PG  $\geq 200$  mg/dL (11.1 mmol/L). Error bars are 95% CI. \* $P < 0.05$  vs. age 20–44 years, † $P = 0.05$  vs. age 20–44 years. Adapted from Cowie et al. (2).

blacks, 33.0 kg/m<sup>2</sup> in all Hispanics and 33.7 kg/m<sup>2</sup> in Mexican Americans, but lowest at 27.1 kg/m<sup>2</sup> in non-Hispanic Asians (3). This observation led to the recommendation of the American Diabetes Association (ADA) to consider diabetes testing for all Asian Americans with a BMI  $\geq 23$  kg/m<sup>2</sup> (8).

Differences in the proportion of total diabetes that was undiagnosed were also examined by Hispanic ethnicity from a time period similar to that of NHANES using 2008–2011 data from the Hispanic Community Health Survey/Study of Latinos (HCHS/SOL) (9). Members from several Hispanic heritage groups were randomly sampled from four U.S. communities, aged 18–74 years. The highest

proportions undiagnosed were found among South Americans (46.0%), followed by Cubans (40.8%) and Central Americans (39.3%), about one-third undiagnosed among Mexican Americans (34.4%), and about one-quarter undiagnosed among Dominicans (26.8%) and Puerto Ricans (24.6%).

#### Trends in Undiagnosed Diabetes Over Time

Time trends in undiagnosed diabetes can be examined based on A1C and FPG, which were measured over the entire period of 1988–2012 in NHANES among adults aged  $\geq 20$  years (Fig. 3) (10). Total diabetes prevalence in the U.S. civilian noninstitutionalized population rose from almost 10% in 1988–1994 to about

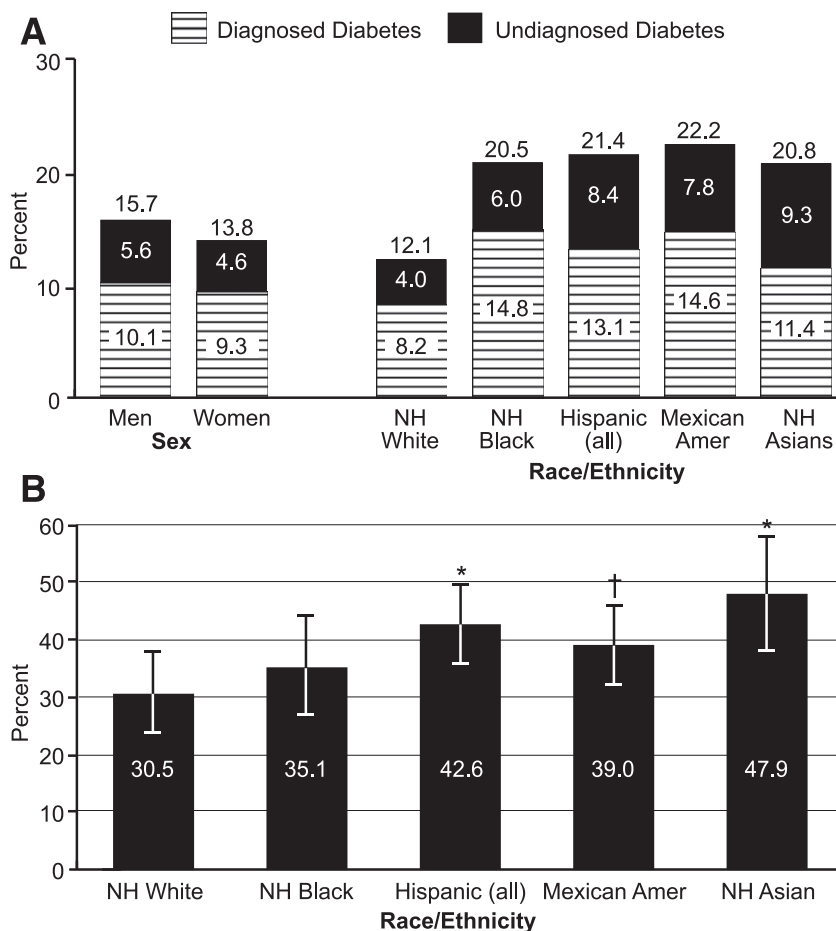
12.5% in 2011–2012, with similar prevalence during 2007–2012. A leveling of diagnosed diabetes prevalence during 2007–2012 based on the National Health Interview Survey (NHIS) among adults aged 20–79 years has been noted by others (11). The overall increase in prevalence in NHANES during 1988–2012 was found in all ages, both sexes, all race/ethnic groups, and all education and income levels (10).

The increase in total diabetes cases was due to rising diagnosed diabetes, while undiagnosed diabetes remained quite constant during this time period (Fig. 3). Consequently, undiagnosed diabetes based on A1C/FPG as a proportion of total diabetes decreased significantly in adults from about 40% to 30% during 1988–2012 (10). A decrease was found in almost all age, sex, and race/ethnic groups, except for the youngest individuals aged 20–44 years and Mexican American participants. While this trend might be considered encouraging, we do not know whether it means there is improved case detection over time. An alternative metric for examining trends over time is the probability of being undiagnosed among persons not reporting they have diabetes, which was relatively constant during 1999–2014 at 3–4% (12). This method may be preferable when there are changes over time in mortality, which has decreased among persons with diabetes (13).

#### Contrasting Detection of Undiagnosed Diabetes by A1C, FPG, and 2-h PG Criteria

Much of the prevalence data described herein are based on the three criteria of A1C, FPG, and 2-h PG from an OGTT, whereas most clinicians in practice now use either the A1C or FPG to screen for and diagnose diabetes because of the burden and cost of using an OGTT. Data have shown, however, that the 2-h PG detects a large proportion of diabetes that is undetected by A1C and FPG.

An analysis examined a Venn diagram of the proportion detected to have undiagnosed diabetes by the three criteria among adults aged  $\geq 20$  years based on NHANES 2005–2006 data (14). The total undiagnosed by any criterion was 5.4%, with 7.8% having diagnosed diabetes and 86.9% not having diabetes. The 2-h PG detected a prevalence of undiagnosed diabetes of 4.9%, which was 90% of all



**Figure 2**—Prevalence of undiagnosed diabetes among adults, by sex and race/ethnicity, U.S. 2011–2014. **A:** Prevalence of diagnosed, undiagnosed, and total diabetes among all adults aged  $\geq 20$  years, by sex and race/ethnicity, U.S. 2011–2014. Percent of total diabetes is at the top of each bar. Standardized to NHANES 2011–2014 total interview population by age or by age and sex. For some groups, total diabetes does not equal the sum of diagnosed and undiagnosed diabetes because of use of different subsamples of survey data. **B:** Percent of total diabetes that was undiagnosed among adults aged  $\geq 20$  years, by race/ethnicity, U.S. 2011–2014. Standardized to the NHANES 2011–2014 total interview population by age and sex. Data are from NHANES. Total diabetes is the sum of diagnosed and undiagnosed diabetes. Diagnosed diabetes is based on self-report. Undiagnosed diabetes is based on A1C  $\geq 6.5\%$  ( $\geq 48$  mmol/mol), FPG  $\geq 126$  mg/dL ( $\geq 7.0$  mmol/L), or 2-h PG  $\geq 200$  mg/dL (11.1 mmol/L). Error bars are 95% CI. \* $P < 0.05$  vs. age 20–44 years, † $P = 0.05$  vs. age 20–44 years. Mexican Amer, Mexican American; NH, non-Hispanic. Adapted from Cowie et al. (2).

undiagnosed diabetes. The 2-h PG alone classified 47% of all individuals with undiagnosed diabetes that were undetected by A1C or FPG.

In addition, there is a disproportionate percentage of persons at older ages who are classified as having diabetes based on the 2-h PG. As noted previously for Fig. 1B, the percentage of total diabetes that was undiagnosed by age using the three markers of A1C/FPG/2-h PG was 41.5% at age 20–44 years, 32.7% at age 45–64 years, 28.0% at age 65–74 years, and 40.4% at age  $\geq 75$  years. By contrast, using the two markers of A1C/FPG, the percentages were 33.4% at age 20–44 years, 23.8% at 45–64 years, 17.0% at

65–74 years, and 19.9% at age  $\geq 75$  years (3). Thus, the 2-h PG detects another 20 percentage points of undiagnosed diabetes in those aged  $\geq 75$  years, and another 11 percentage points in those aged 65–74 years, with fewer in the younger age-groups.

Some caution should be noted in the analyses that have been presented here. Importantly, there is only a single visit in NHANES and therefore only a single measurement of A1C, FPG, and 2-h PG from an OGTT, but ADA clinical guidelines require a repeat measure of A1C or glucose for confirmation. Consequently, the NHANES analyses will overestimate prevalence of undiagnosed diabetes. In

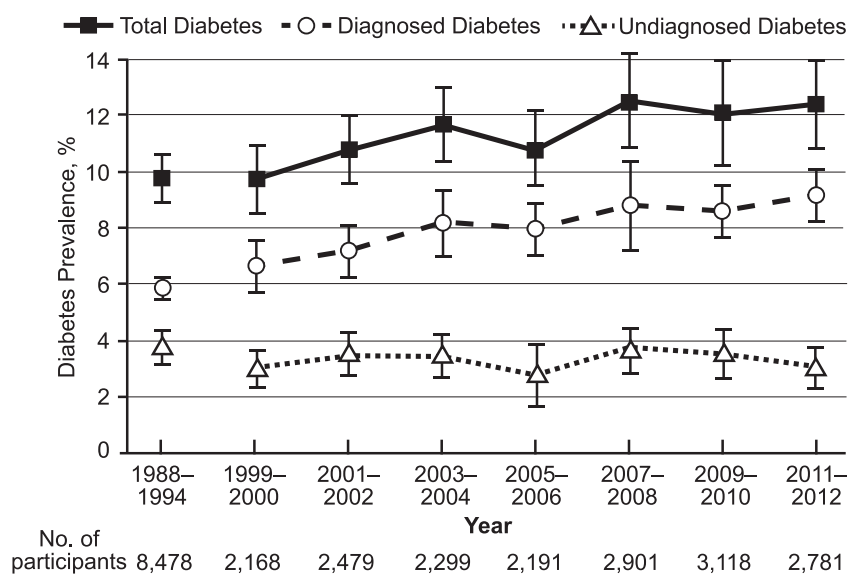
addition, there is less variability in A1C values than in the glucose measures, and of the glucose measures, FPG is less variable than the 2-h PG (15).

**Predictors of Undiagnosed Diabetes**

Several studies have examined factors associated with having undiagnosed diabetes. Data from NHANES 2011–2014 were analyzed in adults aged  $\geq 20$  years to examine factors associated with being undiagnosed relative to those with diagnosed diabetes (16). The multivariable assessment found that family history of diabetes was associated with approximately a 50% reduction in the odds of having undiagnosed diabetes (odds ratio [OR] 0.48, 95% CI 0.33–0.70). Having been hospitalized in the past year was associated with a one-third reduction in undiagnosed diabetes (OR 0.66, 95% CI 0.44–0.99). Having no health care encounter in the past year was associated with an almost sixfold increase in the odds of undiagnosed diabetes (OR 5.85, 95% CI 2.39–14.34). The analysis considered the significance of, and adjusted for, age, race/ethnicity (non-Hispanic white, black, and Asian, and Mexican American), sex and gestational diabetes mellitus, education, income, smoking, BMI, physical activity (work and leisure time), health insurance, routine health care location, hypertension, and hyperlipidemia; none of these factors were significantly associated with undiagnosed diabetes.

A similar analysis was conducted in the HCHS/SOL in which 37% of adults aged 18–74 years had undiagnosed diabetes during 2008–2011 (17). After adjustment, higher odds of being undiagnosed were found among women, individuals with no health insurance, those who received no health care in the past year, those who were overweight (versus normal weight), and those with dyslipidemia. Lower odds of being undiagnosed were found for those with a family history of diabetes and those with hypertension.

An analysis of 2005–2010 data from NHANES and 2006 data from NHIS examined sociodemographic factors associated with self-reported diabetes screening in the past 3 years among adults without diabetes aged  $\geq 20$  years. Three years is the minimum recommended frequency for screening in adults without diabetes, depending on age and risk factors for diabetes (1). The overall



**Figure 3**—Time trends in diabetes prevalence (total, diagnosed, and undiagnosed) among all adults aged  $\geq 20$  years, U.S. 1988–2012. Data are from NHANES. Age-standardized to the NHANES 2011–2012 total interview population. Total diabetes is the sum of diagnosed and undiagnosed diabetes. Diagnosed diabetes is based on self-report. Undiagnosed diabetes is based on A1C  $\geq 6.5\%$  ( $\geq 48$  mmol/mol) or FPG  $\geq 126$  mg/dL ( $\geq 7.0$  mmol/L), which were measured over all of 1988–2012. Error bars are 95% CI. Reproduced with permission from JAMA 2015;314(10):1021–1029. Copyright © 2015, American Medical Association. All rights reserved (10).

proportion who self-reported screening during the years 2005–2010 ranged from 42% to 47% (18); somewhat higher proportions of self-reported screening were reported in individuals with major risk factors for diabetes (19). Prevalence of screening increased with increasing age, was higher in women compared with men, and was higher in non-Hispanic whites and blacks as compared with Hispanics, Mexican Americans, and non-Hispanic Asians. Prevalence of screening was also higher in those with more education, more income, prediabetes as compared with normoglycemia, increasing BMI, health insurance coverage, and other measures of access to care, such as visiting a doctor in the past year and having a greater frequency of doctor visits in the past year (18).

In a multivariable assessment that examined specific ADA screening criteria (i.e., risk factors for diabetes) associated with a self-reported fasting blood test for diabetes in the past 3 years, the odds of screening ranged from 40% to 70% higher in those with a BMI  $\geq 25$  kg/m<sup>2</sup>, being age  $\geq 45$  years, having a relative with diabetes, or having hypertension. There was about a 25% increase in the odds of being screened with having prediabetes or having cardiovascular disease. Meeting multiple screening criteria increased the odds of being tested, with

each additional criterion or risk factor increasing the odds by 51%. The initial logistic regression model also included race/ethnicity and an HDL  $\leq 35$  mg/dL (0.91 mmol/L), both of which were not significantly associated with being screened (18).

#### Summary of Major Points on Undiagnosed Diabetes

- From one-quarter to one-third of all diabetes in the U.S. is undiagnosed, depending on whether elevated A1C or FPG are used to detect diabetes or an elevated 2-h PG is added as a criterion.
- The prevalences of both undiagnosed and diagnosed diabetes as a percentage of the total U.S. population rise with age, and the prevalence of both combined—total diabetes—is more than 20% in Hispanic, non-Hispanic Asian, and non-Hispanic black subgroups.
- The proportion of total diabetes that is undiagnosed is highest in the young—those aged 20–44 years—being more than 40% when defined by A1C, FPG, or 2-h PG. The proportion of total diabetes that is undiagnosed is also highest in non-Hispanic Asians, all Hispanics, and Mexican Americans, when defined by the three criteria.

- Prevalence of diagnosed diabetes is increasing over time, with some leveling in very recent years, while undiagnosed diabetes has remained constant over the past couple of decades.
- The 2-h PG detects substantially more undiagnosed diabetes than do A1C and FPG, particularly in older ages.
- In studies of national data, less access to care is most strongly associated with undiagnosed diabetes and lower screening for diabetes, when based on health insurance coverage, hospitalization, frequency of visits for health care, income, and education.

## DIABETES CONTROL

### Standards of Care for People With Diabetes

A major force in establishing the standards of care for people with diabetes are the findings from the Diabetes Control and Complications Trial (DCCT) (20), which led the ADA to recommend a target of A1C  $< 7\%$  (53 mmol/mol). The DCCT, which began in 1983, randomized 1,441 participants with type 1 diabetes with mean age of 27 years to intensive versus conventional treatment. Intensive treatment consisted of  $\geq 3$  daily insulin injections or use of an external insulin pump, with dosage adjustment based on  $\geq 4$  daily self-monitored blood glucose measurements. The A1C goal was  $< 6.05\%$  (43 mmol/mol), two standard deviations above the nondiabetic mean. Conventional treatment consisted of one or two daily insulin injections and one daily urine or blood glucose test, with the goal of freedom from symptoms of hyperglycemia and hypoglycemia. During the trial, the A1C averaged 7% (53 mmol/mol) in the intensively treated participants and 9% in the conventionally treated participants over an average follow-up of 6.5 years. Intensive treatment resulted in a 50% reduction in the risk of renal disease, a 76% reduction in the risk of retinopathy, and a 60% reduction in neuropathy. Intensive treatment came at a risk, however, of a threefold increase in severe hypoglycemia (20). Observational follow-up of the DCCT cohort in the Epidemiology of Diabetes Interventions and Complications (EDIC) study found further benefits of this initial intensive treatment on microvascular disease (21,22), although A1C levels converged to 8%

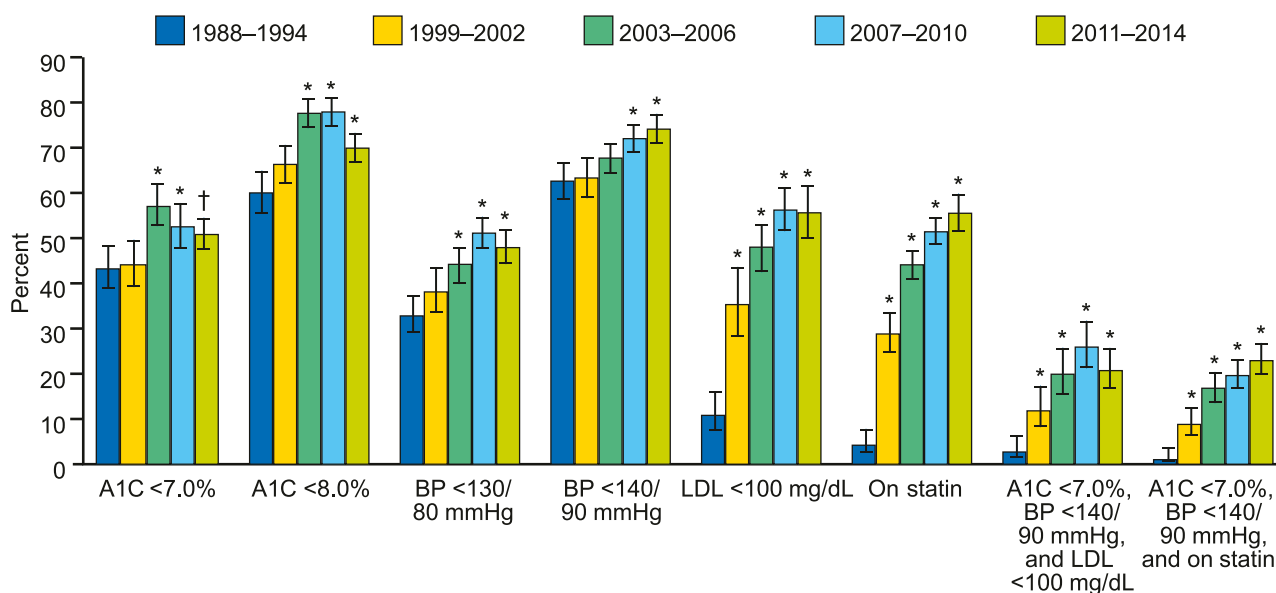
(64 mmol/mol) in both the former intensive and conventional treatment participants approximately 4–5 years into EDIC. This has been termed “metabolic memory.” In EDIC, the favorable effects of intensive treatment on microvascular disease were extended further, with a 57% reduction in the risk of heart disease (23) and a 33% reduction in mortality (24). Since the initial findings of the DCCT, other studies such as the UK Prospective Diabetes Study (UKPDS) have corroborated the beneficial effect of intensive treatment in type 2 diabetes (25–27).

In addition to the major reductions in microvascular and macrovascular disease afforded by A1C control, concomitant control of other risk factors such as blood pressure and lipids is important based on evidence from clinical trials and meta-analyses (28,29). Collectively, management of A1C, blood pressure, and cholesterol or lipids has been termed the ABCs, and there have been target goals associated with them. For all of these goals, however, the targets have steadily evolved over time toward individualized goals (28,29). For A1C, other randomized clinical trials of intensive glycemic control since the DCCT/EDIC and UKPDS did not demonstrate a significant reduction in cardiovascular disease but highlighted potential risks that

might outweigh its benefits, prompting the ADA, the American College of Cardiology Foundation, and the American Heart Association to issue a position statement in 2009 that a less stringent A1C goal than <7% (53 mmol/mol) may be more appropriate for some patients (30). Thus, a goal of A1C <7% (53 mmol/mol) has been considered to be a reasonable target for nonpregnant adults, but an individualized target ranging between <6.5% and <8% (48 and 64 mmol/mol) should be considered by patients and their physicians depending on life expectancy—and by extension, depending on age—duration of diabetes, comorbidity, and risk of hypoglycemia (28). For blood pressure, whereas the older goal was a blood pressure of <130/80 mmHg, beginning around 2013 a less stringent goal was recommended by the ADA for some patients and now ranges from <130/80 mmHg to <140/90 mmHg, depending, for example, on treatment burden, side effects, life expectancy, and cardiovascular disease risk (29). For lipid level goals, whereas previously an LDL <100 mg/dL (2.59 mmol/L) was recommended, beginning in about 2008 statins have been broadly recommended, with their use and dosage dependent on age and atherosclerotic cardiovascular disease risk (29).

**Overall Prevalence of Glycemic, Blood Pressure, and Lipid Control Over Time**

Figure 4 shows an analysis of trends among adults aged ≥20 years with diagnosed diabetes who met various A1C, blood pressure, and cholesterol goals during 1988–2014 (3,31). What is most obvious is the significant improvement over this time period in attaining all of the goals. For A1C <7% (53 mmol/mol), there was dramatic improvement in prevalence from 43.2% to 57.0% during 1988–1994 to 2003–2006, but prevalence then decreased to 50.8% in 2011–2014. Part of the subsequent decrease in attaining A1C <7.0% (53 mmol/mol) may be due to the accumulating evidence and recognition (30) that a less stringent goal may be more appropriate for some. The pattern of trends over time at A1C <8% (64 mmol/mol) was similar to that for A1C <7% (53 mmol/mol), although prevalence was higher; prevalence decreased in 2011–2014 and was about 70%. There were significant increases in the proportion of persons with diagnosed diabetes attaining a blood pressure goal of 130/80 mmHg from 1988–1994 (32.8%) until 2007–2010 (51.1%), but prevalence then decreased slightly (47.9% in 2011–2014), perhaps coinciding with the less stringent blood pressure target recommended by ADA in 2013. At the



**Figure 4**—Time trends in the prevalence of meeting ABC goals among adults aged ≥20 years with diagnosed diabetes, U.S. 1988–2014. Data are from NHANES. Standardized to the NHANES 2007–2010 population with diabetes by age and sex. Diagnosed diabetes is based on self-report. A1C <7.0% (<53 mmol/mol), A1C <8.0% (<64 mmol/mol), LDL <100 mg/dL (2.59 mmol/L). Error bars are 95% CI. \*P < 0.01, †P = 0.05 vs. 1988–1994. BP, blood pressure. Adapted from Stark Casagrande et al. (31). Data updated for 2011–2014 (3).

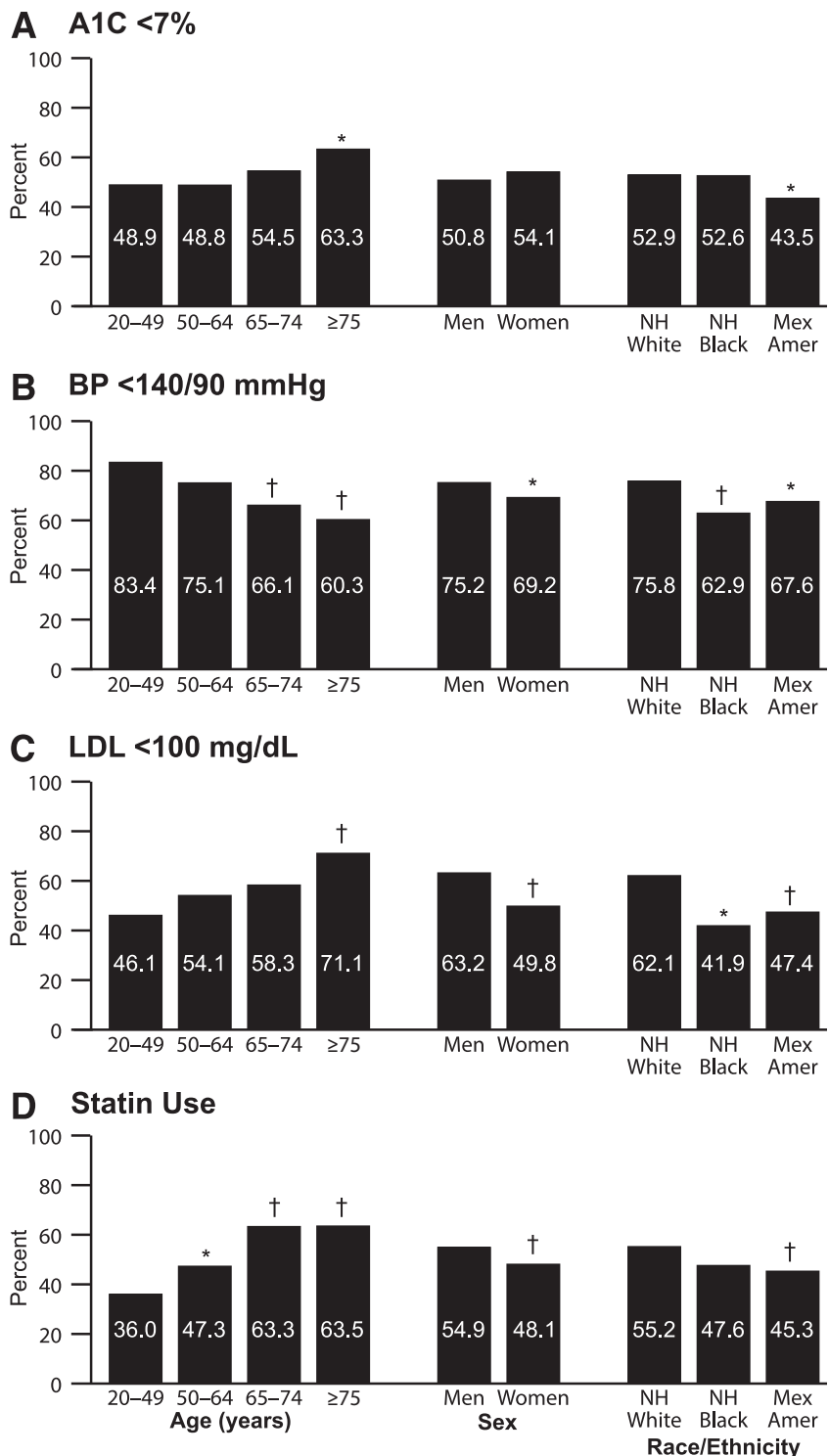
current target of <140/90 mmHg, however, there has been continuous improvement over time with 74.1% at goal in 2011–2014. There were vast improvements in attaining LDL <100 mg/dL (2.59 mmol/L), from 10.8% in 1988–1994 to 55.5% in 2011–2014; prevalence of statin use largely paralleled this increase. The proportion of persons with diagnosed diabetes who achieved all three goals of A1C <7.0% (53 mmol/mol), blood pressure <140/90 mmHg, and LDL <100 mg/dL (2.59 mmol/L) significantly increased over time but was very low: 2.7% during 1988–1994, increasing to a high of 25.9% in 2007–2010, and then decreasing to 20.7% in 2011–2014. Simultaneous achievement of A1C <7.0% (53 mmol/mol), blood pressure <140/90 mmHg, and statin use was achieved only by 22.9% in 2011–2014.

**Variation in Prevalence of Achieving Glycemic, Blood Pressure, and Lipid Control by Demographic Factors**

There is considerable variation in achieving ABC goals by age, sex, and race/ethnicity, as shown in Fig. 5 (31). In Fig. 5A, the prevalence of individuals achieving A1C <7% (53 mmol/mol) was significantly higher among those aged ≥75 years (63.3%) compared with about 50% among those aged 20–64 years (when initiating good control is important given longer life expectancy). Prevalence was similar by sex. Mexican Americans were significantly less likely to achieve A1C <7.0% (53 mmol/mol) compared with non-Hispanic whites and non-Hispanic blacks, whose prevalences were similar at about 53%.

The prevalence of achieving blood pressure <140/90 mmHg reflected the aging effects we would expect, with a higher prevalence (83.4%) in the young aged 20–49 years and significantly lower prevalences in those aged 65–74 years (66.1%) and ≥75 years (60.3%) (Fig. 5B). Women had significantly lower prevalence compared with men (69.2% vs. 75.2%), as did non-Hispanic blacks (62.9%) and Mexican Americans (67.6%) relative to non-Hispanic whites (75.8%).

Prevalence of achieving LDL <100 mg/dL (2.59 mmol/L) (Fig. 5C) was about 70% in elderly individuals aged ≥75 years and significantly higher than that in the



**Figure 5**—Prevalence of achieving ABC goals among adults aged ≥20 years with diagnosed diabetes, by age, sex, and race/ethnicity, U.S. 2007–2010. A: Achieving A1C <7.0% (<53 mmol/mol). \**P* < 0.05 vs. age 20–64 years, vs. NH white. B: Achieving blood pressure (BP) <140/90 mmHg. \**P* < 0.05 vs. men, vs. NH white; †*P* < 0.01 vs. age 20–49 years, vs. NH white. C: Achieving LDL <100 mg/dL. \**P* < 0.05 vs. NH white; †*P* < 0.01 vs. age 20–49 years, vs. men, vs. NH white. D: Statin use. \**P* < 0.05 vs. age 20–49 years; †*P* < 0.01 vs. age 20–49 years, vs. men, vs. NH white. Data are from NHANES. Age-standardized to the 2007–2010 NHANES population with diabetes. Diagnosed diabetes is based on self-report. Mex Amer, Mexican American; NH, non-Hispanic. Adapted from Stark Casagrande et al. (31).

youngest age-group, 20–49 years (46.1%). A significantly lower proportion of women (49.8%) than men (63.2%) achieved these levels, as was the case for non-Hispanic blacks (41.9%) and Mexican Americans (47.4%) relative to non-Hispanic whites (62.1%).

Similar patterns were found for prevalence of statin use as for LDL <100 mg/dL (2.59 mmol/L) (Fig. 5D). Statin use was significantly higher for those aged  $\geq$ 50 years (47.3–63.5%) compared with younger ages 20–49 years (36.0%); even in the absence of atherosclerotic cardiovascular disease, it is recommended that all patients with diabetes use statins beginning at age 40 years (29). Statin use was significantly lower in women (48.1%) compared with men (54.9%). Likewise, it was significantly lower in Mexican Americans (45.3%) relative to non-Hispanic whites (55.2%).

The observation that Mexican Americans from NHANES were significantly less likely to meet ABC goals than non-Hispanic whites prompted exploration in other Hispanic heritage groups (Mexican, Central American, Cuban, Puerto Rican, South American) aged 18–74 years using data from the HCHS/SOL during 2008–2011 (32). Thresholds selected were A1C <7% (53 mmol/mol), blood pressure <130/80 mmHg, ACE inhibitor/angiotensin receptor blocker use, LDL <100 mg/dL (2.59 mmol/L), and statin use. There were no clear patterns by Hispanic ethnicity, but the prevalences of meeting goals were low, on average less than 50–60% for any of the goals, and only 10% achieved A1C, blood pressure, and LDL goals simultaneously.

Another analysis assessed meeting all three ABC goals but used a more individualized definition of the A1C goal in all U.S. adults with diabetes aged  $\geq$ 18 years during 2007–2012. The authors defined the A1C goal in the range of 6.5–8.0% (48–64 mmol/mol) based on age and existing diabetes complications, along with a blood pressure goal of <140/80 mmHg and LDL goal of <100 mg/dL (2.59 mmol/L) (33). To this they added whether the participant was a nonsmoker, with overall nonsmoking prevalence being 78%. A similar age relationship was found where only 9.6% of the young attained goals relative to 28.8% of those aged  $\geq$ 65 years. Significantly fewer women (16.7%) than men

(25.5%) met the goals. Likewise, prevalence was significantly lower in Hispanics (13.6%) and non-Hispanic blacks (13.1%) compared with non-Hispanic whites (24.3%).

The poorer control in the young is particularly disconcerting given their longer life expectancy during which diabetes complications may develop as a result. At the same time, as mentioned previously, achieving an A1C <7% (53 mmol/mol) may not be appropriate for older people who, for example, have diabetes complications or risk hypoglycemia, which has led to the recommended individualized A1C targets. One analysis examined whether a more individualized approach is being followed among adults aged  $\geq$ 40 years with probable type 2 diabetes, using data from NHANES 2009–2014 (34). The authors investigated the prevalence of intensive glycemic control by age, defining intensive control based on both 1) reaching an A1C <7% (53 mmol/mol) and 2) using insulin, a sulfonylurea, or two or more glycemic medications. The analysis adjusted for factors that should affect the decision to target A1C <7% (53 mmol/mol), including duration of diabetes, smoking, comorbidities, disability, multiple medication use, and depression, as well as sociodemographic factors. After adjusting for these factors, prevalence of intensive control was found to be only around 20% at younger ages, but this prevalence significantly increased with age and was about 35% in those aged  $\geq$ 75 years, a 64% increase. Thus, glycemic guidelines for individualized therapy are not being widely followed. Older adults are being treated more aggressively than younger adults to achieve an A1C <7% (53 mmol/mol) despite the presence of comorbidities and other factors such as longer duration of diabetes, disability, and depression.

Similar results were found using a different approach among adults with diabetes aged  $\geq$ 65 years based on NHANES data from 2001–2010 (35). The investigators found no differences in the proportions of individuals with diabetes who attained tight, moderate, or poor glycemic control (A1C <7% [53 mmol/mol], 7–8.9% [53–74 mmol/mol], or  $\geq$ 9% [75 mmol/mol]) across three different health status categories from relatively healthy to poor health. Around 60% of individuals

attained tight control, regardless of their health status.

Variation in the risk of hypoglycemia by age and race was investigated in the cohort aged  $\geq$ 60 years of the Atherosclerosis Risk in Communities (ARIC) Study from baseline in 1996–1998 through 15 years of follow-up (36). Compared with individuals aged 60–69 years, incidence of hypoglycemia was about twofold higher in those aged 70–79 years, with only a slight increase in the next decade of age 80–89 years. Risk of hypoglycemia was about twofold higher in blacks compared with whites regardless of age.

Mean A1C data by age in persons with type 1 diabetes from the T1D Exchange clinic network in 2013–2014 (37) largely corroborate national A1C data by age that is predominantly for type 2 diabetes. Mean A1C was 8.3% (67 mmol/mol) at age 2–4 years and 8.1% (65 mmol/mol) at age 7 years, then peaked at 9.2% (77 mmol/mol) at age 19 years. Mean levels thereafter fell with age to about 7.5–7.8% (58–62 mmol/mol) between ages 30 and 65 years and decreased slightly at older ages to slightly below 7.5% (58 mmol/mol). Only 14% of those aged 18–25 years achieved the ADA goal of A1C <7% (53 mmol/mol). Data from the SEARCH for Diabetes in Youth registry study found that in 2011–2015 among persons with type 1 diabetes (mean age 17.9 years) mean A1C was 9.2% (77 mmol/mol), and among those with type 2 diabetes (mean age 22.1 years) mean A1C was 9.1% (76 mmol/mol) (38). It is clear that these levels are very high at ages when it is important to be establishing good control.

### Predictors of Diabetes Control

Various factors associated with poor control have been examined in national data. An analysis was conducted of NHANES 2007–2010, defining poor control as A1C >9% (75 mmol/mol) in adults aged  $\geq$ 18 years with diagnosed diabetes (39). As reported above, worse control was significantly associated with decreasing age, and in non-Hispanic blacks and Hispanics as compared with non-Hispanic whites. Additionally associated with worse control were being single versus being married or having a partner, having greater duration of diabetes, and using insulin alone or with oral medications—likely reflective of the



severity of diabetes. Not having health insurance versus having insurance was also associated with worse control; whether individuals had Medicare, other public insurance, or private insurance was not differentially associated with poor control. The analysis also considered the effects of other sociodemographic factors such as sex, education, and poverty income ratio, as well as medical care received such as visiting a doctor in the past year and having a usual source of medical care, all of which were not associated once the significant factors were considered. Other investigators have found that lack of health insurance was associated with worse control, as was lack of health care visits in the past year (40).

NHANES includes questions to participants on knowledge of most recent levels and goals for A1C, blood pressure, and lipids. Cross-sectional data from the two time periods of 2005–2008 and 2013–2016 were assessed among individuals with diabetes aged  $\geq 20$  years (3,41). In 2005–2008, only 48% could state their last A1C level, which was not compared with medical records for validation. In 2013–2016, however, there was a significant increase to 72% who could state their most recent A1C. For blood pressure, in 2005–2008 only 63% knew their last blood pressure level and this changed very little (68%) in 2013–2016. A very low proportion could state their last LDL level in 2005–2008 (22%) with no significant difference in 2013–2016 (19%). Participants were also asked whether their health care provider ever specified a personal ABC goal for them to target. For A1C, 81% stated their provider had specified a goal in 2005–2008 but there was no significant change in 2013–2016 (85%). Goals were less often specified by a provider for blood pressure (53% in 2005–2008, 56% in 2013–2016) and LDL cholesterol (59% in 2005–2008, 63% in 2013–2016) with no significant change over time. An additional question was asked as to whether participants' providers ever stated what the ADA goal was for the ABCs. In 2005–2008, 49% of participants reported their providers specified the ADA goal for A1C, but the percentages were only 27% for blood pressure and 6% for LDL cholesterol. In 2013–2016 there was a significant increase for A1C (67%)

but little increase for blood pressure (31%) and LDL (9%).

In addition, among those who stated that their last A1C was  $<7\%$  (53 mmol/mol), actual measured A1C in NHANES was  $<7\%$  (53 mmol/mol) in 83% of participants in 2005–2008 and in a similar percentage (78%) in 2013–2016 (3,41). Knowledge of most recent levels of A1C, blood pressure, and LDL cholesterol was highest in non-Hispanic whites, intermediate in non-Hispanic blacks, and lowest in Mexican Americans and increased with higher income and education (41).

#### Summary of Major Points on Diabetes Control

- There have been significant improvements in control of A1C, blood pressure, and lipid levels over the last three decades.
- However, there are significant gaps in control, with overall prevalence still being low at about 50% for A1C  $<7\%$  (53 mmol/mol), 75% for blood pressure  $<140/90$  mmHg, and 55% for LDL  $<100$  mg/dL (2.59 mmol/L), with about 20% meeting all three goals simultaneously.
- In addition, there are significant gaps in meeting goals among certain subgroups of the population.
  - Younger individuals with diabetes are meeting A1C and LDL goals less frequently than older individuals, both among those with type 1 diabetes and among those with type 2 diabetes.
  - Meeting recommended individualized A1C goals, based on such factors as life expectancy and age, duration of diabetes, comorbidity, and risk of hypoglycemia, is not occurring widely.
  - Women with diabetes are less likely than men to attain blood pressure and LDL goals and to use statins.
  - Hispanic and Mexican American ethnic groups are less likely than non-Hispanic whites to reach A1C, blood pressure, and LDL goals and to use statins; non-Hispanic blacks are less likely than whites to reach recommended blood pressure and LDL levels.
- The most prominent potentially modifiable predictor of better control based on national data analyses is access to care, as measured by health

insurance coverage and health care encounters.

#### CONCLUSIONS AND FUTURE DIRECTIONS

Both undetected diabetes and poor control remain large missed opportunities to improve the health of the U.S. population and those personally affected. Whether detection of undiagnosed diabetes is improving over time is unclear. While there have been improvements in diabetes control over the last several decades, this improvement has slowed or declined in more recent years, most notably for glycemic control, some of which may be due to recognition of the need for more individualized care. As a result, the magnitude of undiagnosed diabetes remains an estimated one-quarter to one-third of all diabetes, and overall control of any of the ABCs is only 50–70%. There are very similar gaps in which groups in particular are undetected or under poor diabetes control: the young, Hispanic heritage groups, and non-Hispanic blacks. In addition, non-Hispanic Asians as a whole are more likely to be undiagnosed and women are more likely to be under poorer control. Most significant potentially modifiable predictors of both undiagnosed diabetes and poor control based on national health data are those related to access to care, such as lack of health insurance and fewer health care encounters.

Continued surveillance of national health survey data on undiagnosed diabetes and diabetes control is needed to monitor trends over time. The surveillance should take advantage of both established and new tools for assessing glycemic status. Although current clinical practice gravitates to A1C and FPG to detect diabetes, surveillance must consider other methods and indicators, such as the 2-h PG, that are also associated with diabetes sequelae and ideally have high validity and predictive value.

Of particular concern are the subgroups of the U.S. population who are disproportionately affected by undiagnosed diabetes and poor diabetes control. Such improvements are needed in the young; the DCCT/EDIC and UKPDS have shown the importance of implementing appropriate treatment as early as possible to reduce the risk of diabetes complications (21,22,25,27). The worse

diabetes control found in women as reported here has been noted by some (42,43) but is not widely reported. The disparities noted for non-Hispanic Asians, Hispanic groups, and non-Hispanic blacks are well known. For all of these subgroups, future investigations must continue to explore the confluence of biological, behavioral, environmental, sociocultural, and health care components that contribute to poor diabetes detection and control (44). Identifying these factors will point to interventions needed to reverse these health disparities.

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