Awareness, Treatment, and Control of LDL Cholesterol Are Lower Among U.S. Adults With Undiagnosed Diabetes Versus Diagnosed Diabetes

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OBJECTIVE—Diabetes is often undiagnosed, resulting in incorrect risk stratification for lipid-lowering therapy. We conducted a cross-sectional analysis of the National Health and Nutrition Examination Survey (NHANES) 2005–2010 to determine the prevalence, awareness, treatment, and control of elevated LDL cholesterol (LDL-C) among U.S. adults with undiagnosed diabetes.

RESEARCH DESIGN AND METHODS—Fasting NHANES participants 20 years of age or older who had 10-year Framingham coronary heart disease (CHD) risk scores <20% and were free of CHD or other CHD risk equivalents (n = 5,528) were categorized as having normal glucose, impaired fasting glucose, undiagnosed diabetes, or diagnosed diabetes. High LDL-C was defined by the 2004 Adult Treatment Panel (ATP) III guidelines.

RESULTS—The prevalence of diagnosed and of undiagnosed diabetes was 8 and 4%, respectively. Mean LDL-C was 102 ± 2 mg/dL among those with diagnosed diabetes and 117 ± 3 mg/dL for those with undiagnosed diabetes ($P < 0.001$). The prevalence of high LDL-C was similar among individuals with undiagnosed (81%) and diagnosed (77%) diabetes. Among individuals with undiagnosed diabetes and high LDL-C, 38% were aware, 27% were treated, and 16% met the ATP III LDL-C goal for diabetes. In contrast, among individuals with diagnosed diabetes and high LDL-C, 70% were aware, 61% were treated, and 36% met the ATP III goal. Subjects with undiagnosed diabetes remained less likely to have controlled LDL-C after multivariable adjustment (prevalence ratio, 0.42; 95% CI, 0.23–0.80).

CONCLUSIONS—Improved screening for diabetes and reducing the prevalence of undiagnosed diabetes may identify individuals requiring more intensive LDL-C reduction.

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According to data from the National Health and Nutrition Examination Survey (NHANES), despite increasing rates of obesity and diabetes, LDL cholesterol (LDL-C) levels among U.S. adults have declined from 1976 through 2010 as a result of improved awareness and more aggressive pharmacologic treatment of high cholesterol (1). However, millions of U.S. adults still have untreated high LDL-C. For example, using data from NHANES 2003–2004, Mann et al. (2) estimated that 33% of U.S. adults had high LDL-C. Importantly, only 36% of those with high LDL-C were using statins and, of those, only 29% had controlled their cholesterol to levels recommended by the Adult Treatment Panel (ATP) III (2,3).

Cholesterol-lowering guidelines use a risk-based approach wherein treatment initiation thresholds and goals are lower for individuals at high risk for coronary heart disease (CHD). The failure to achieve guideline-recommended LDL-C levels may be particularly common in populations of individuals who have undiagnosed conditions that warrant more aggressive lowering of LDL-C, because failure to recognize these conditions results in higher than appropriate LDL-C targets. In 2001, ATP III introduced the concept of CHD risk equivalents (3). Diabetes was classified as a CHD risk equivalent (4). Whether diabetes should be considered a CHD risk equivalent is controversial (5,6); however, because the presence of diabetes affects ATP III risk stratification and decisions about LDL-C treatment, understanding the impact of undiagnosed diabetes is important.

Previous studies have estimated that more than one-third of cases of diabetes are undiagnosed in adults, and the implications of failing to make this diagnosis on the awareness, treatment, and control of LDL-C are not known. The focus of previous studies of high LDL-C awareness, treatment, and control has been on the overall population of U.S. adults with high cholesterol, and there are limited data on the influence of undiagnosed diabetes on uncontrolled LDL-C. Therefore, the objective of our study was to examine the influence that having undiagnosed diabetes has on the awareness, treatment, and control of LDL-C. To examine the direct contribution of undiagnosed diabetes on LDL-C control, we have chosen to limit our analyses to only those individuals who do not have CHD or other CHD risk equivalents because these conditions may affect their ATP III

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LDL-C goals independent of their diabetes status (i.e., individuals with CHD would be treated to a low LDL-C regardless of their diabetes status). To address our objective we analyzed data from the 2005–2010 NHANES.

RESEARCH DESIGN AND METHODS

Study population

NHANES is conducted by the National Center for Health Statistics of the Centers for Disease Control and Prevention. Each 2-year survey includes a sample of the noninstitutionalized U.S. civilian population identified through a stratified multistage probability sampling design. This approach allows nationally representative prevalence estimates to be generated. Detailed methods of the design and conduct of NHANES are available online (7). The protocol for each NHANES was approved by the National Center for Health Statistics of the Centers for Disease Control and Prevention Institutional Review Board. Informed consent was obtained from each participant.

To provide stable estimates, we pooled data from the NHANES 2005–2006, 2007–2008, and 2009–2010. We included adults 20 years of age or older who attended a morning study visit. Because we were interested in identifying individuals whose only indication, per ATP III, for an LDL-C goal <100 mg/dL was the presence of diabetes, we excluded individuals with a 10-year Framingham CHD risk score >20% and those with a self-reported history of CHD or stroke. Data for other CHD risk equivalents such as peripheral arterial disease and aortic aneurysm are not available in NHANES 2005–2010 and therefore are not included in this analysis. Individuals who had not fasted for ≥9 h were missing lipid or glucose values, had triglycerides >400 mg/dL, or who did not answer questions regarding the awareness and treatment of high cholesterol or the awareness of diabetes also were excluded. This resulted in a final sample size of 5,528 (Supplementary Fig. 1).

Data collection

NHANES collects data through standardized procedures that include questionnaires, a medical examination, and phlebotomy. Questionnaires are used to assess age, race/ethnicity, sex, education, annual household income, health insurance status, smoking status, family history of CHD, personal history of CHD or stroke, and a previous diagnosis of, and treatment for, high blood cholesterol and diabetes. Additionally, participants were asked if their cholesterol had ever been checked, where and how recently they have obtained health care, and whether they had been tested for diabetes in the past 3 years. Blood pressure was measured three times and height and weight were measured and used to calculate BMI. Blood collection and processing are detailed in the *NHANES Laboratory/Medical Technicians Procedures Manual* (8). Plasma glucose, hemoglobin A1C, total cholesterol, HDL cholesterol (HDL-C), and triglycerides were directly measured. LDL-C was calculated using the Friedewald equation (9).

Exposures

Participants were categorized based on diabetes status into one of four mutually exclusive categories as follows: *1*) normal fasting glucose; *2*) impaired fasting glucose; *3*) undiagnosed diabetes; and *4*) diagnosed diabetes. Based on guidelines from the American Diabetes Association (10), diabetes was defined as a hemoglobin A1C ≥6.5%, fasting plasma glucose ≥126 mg/dL, or the use of antidiabetes medications in those who reported a history of diabetes. In individuals who reported a history of diabetes, the use of antidiabetes medications was determined by an affirmative response to at least one of the following questions: "Are you now taking diabetic pills to lower your blood sugar (these are sometimes called oral agents or oral hypoglycemic agents)?" or "Are you now taking insulin?" Individuals who met the criteria for diabetes but answered "no" to the question "Other than during pregnancy, have you ever been told by a doctor or health professional that you have diabetes or sugar diabetes?" were considered to have undiagnosed diabetes. Among individuals without diabetes, impaired fasting glucose was defined as a hemoglobin A1C of 5.7–6.4% or fasting plasma glucose of 100–125 mg/dL (10). Normal fasting glucose was defined as a hemoglobin A1C <5.7% and a fasting plasma glucose <100 mg/dL.

Outcomes

All individuals who reported using cholesterol-lowering medications were considered to have high LDL-C. Also, high LDL-C was defined based on the individual's global CHD risk based on the 2004 update of the ATP III guidelines (11) and their LDL-C level as detailed in Supplementary Table 1. We used a goal LDL-C of <100 mg/dL for those with undiagnosed and diagnosed diabetes. Those without diabetes who had two or more other CHD risk factors and a Framingham CHD risk score of 10–20% had an LDL-C goal of <100 mg/dL. Individuals without diabetes who had two or more CHD risk factors and a Framingham CHD risk score of <10% had an LDL-C goal of <130 mg/dL. Those with less than two CHD risk factors had an LDL-C goal of <160 mg/dL. CHD risk factors used to determine global risk included older age (55 years or older for women and 45 years or older for men), current cigarette smoking, hypertension, family history of CHD (history of myocardial infarction or angina before age 50 years among first-degree relatives), low HDL-C (<40 mg/dL), or diabetes status. HDL-C ≥60 mg/dL is considered protective and offsets the presence of one these risk factors.

Awareness of high LDL-C was defined by an affirmative response to the question "Have you ever been told by a doctor or other health professional that your blood cholesterol level was high?" Use of lipid-lowering treatment was defined by affirmative responses to the following two questions: "To lower your cholesterol, have you ever been told by a doctor or other health professional to take prescribed medicine?" and "Are you now following this advice to take prescribed medicine?" LDL-C control was defined based on the individual participant's global cardiovascular risk based on the 2004 update of the ATP III guidelines, as summarized in Supplementary Table 1 (11).

Covariates

We categorized health insurance coverage as private, government, or no insurance. Government insurance included Medicare, Medi-Gap, Medicaid, State Children's Health Insurance Program, military health insurance, Indian Health Service, or a state-sponsored health plan. Hypertension was defined as mean systolic blood pressure ≥140 mmHg, mean diastolic blood pressure ≥90 mmHg, or a self-reported history of high blood pressure in an individual using medications for high blood pressure. Estimated glomerular filtration rate was calculated using the Chronic Kidney Disease Epidemiology Collaboration equation (12). Reduced estimated glomerular filtration

rate was defined as levels <60 mL/min/1.73 m^2. Albuminuria was based on the random spot urine sample and was defined as levels ≥30 mg/g.

Statistical analysis

We calculated descriptive statistics including mean LDL-C levels, the prevalence of high LDL-C, and awareness of high LDL-C by diabetes categories (normal fasting glucose, impaired fasting glucose, undiagnosed diabetes, and diagnosed diabetes). Next, we calculated the percent of each diabetes category who were treated among those with high LDL-C as well as among those aware of their high LDL-C. We then calculated the percent of each diabetes category in which LDL-C was controlled among those with high LDL-C as well as among those who were treated for high LDL-C. We calculated the number of U.S. adults in 2005–2010 with high LDL-C, as well as the number who were aware of their high cholesterol, treated for high cholesterol, and had their LDL-C controlled. Also, we calculated the number of U.S. adults with high LDL-C who were not aware of their diagnosis of high cholesterol, were aware but not treated, were treated but LDL-C was not controlled, and had controlled LDL-C. Next, we used Poisson regression models to calculate the prevalence ratios for having high LDL-C and awareness, treatment, and control of high LDL-C associated with undiagnosed versus diagnosed diabetes. Initial models were unadjusted and age, sex, and race/ethnicity were adjusted. Final regression models included adjustment for age, sex, race/ethnicity, income, education, insurance status, smoking status, BMI, hypertension, reduced estimated glomerular filtration rate, and albuminuria.

Data management was conducted using SAS 9.2 (SAS Institute, Cary, NC) and all analyses were performed using SUDAAN 10.1 (Research Triangle Institute, Research Triangle Park, NC), accounting for the complex sampling design of NHANES. Sampling weights were applied to all calculations to obtain U.S. nationally representative prevalence estimates. These weights adjust for the unequal probabilities of selection of participants, oversampling of certain populations, and participant nonresponse. NHANES sampling weights were recalibrated based on the proportion of participants missing data by 10-year age group, sex, and race/ethnicity. Recalibration of the sampling weights corrects for differences in missing data across age, sex, and race/ethnicity strata, and assumes that data within strata are missing at random.

RESULTS—Among U.S. adults without a history of CHD or other CHD risk equivalents, 8% met criteria for diagnosed diabetes and 4% met criteria for undiagnosed diabetes. The characteristics of NHANES participants by diabetes category are shown in Table 1. In general, those with undiagnosed diabetes were more similar to those with diagnosed diabetes than those with normal or impaired fasting glucose. Although 89% of those with undiagnosed diabetes reported having a regular place for health care and 85% reported having received health care in the past year, only 67% reported being tested for diabetes in the past 3 years. Those with undiagnosed diabetes had higher mean LDL-C than those with diagnosed diabetes overall and among those who were not being treated for high cholesterol (Table 1). Among those treated for high cholesterol, LDL-C levels were similar in subjects with undiagnosed and diagnosed diabetes.

The awareness, treatment, and control of high LDL-C are depicted in Fig. 1. Individuals with undiagnosed diabetes had a similar prevalence of high LDL-C as those with diagnosed diabetes. However, those with undiagnosed diabetes were less likely to be aware of their high cholesterol compared with those with normal and impaired fasting glucose and diagnosed diabetes. They also were less likely to be treated for high cholesterol than those with diagnosed diabetes. Among those with high LDL-C, LDL-C control was worse for those with undiagnosed diabetes than for those with either impaired fasting glucose or diagnosed diabetes. Among those treated for high cholesterol, individuals with undiagnosed diabetes were equally as likely to have their LDL-C controlled as those with diagnosed diabetes but less likely to be at goal when compared with those with normal glucose or impaired fasting glucose. After multivariable adjustment, individuals with undiagnosed diabetes were less likely to be aware of their high LDL-C, be treated for high cholesterol, and among those with high LDL-C, were less likely to be controlled, relative to those with diagnosed diabetes (Table 2).

The number of U.S. adults with high LDL-C and the percent aware of, treated for, and with controlled LDL-C by diabetes status are depicted in Fig. 2. There were ~5 million U.S. adults with undiagnosed diabetes and no history of CHD or other CHD risk equivalents. Of these individuals, 59% were unaware of their high LDL-C, 13% were aware but not treated for high cholesterol, 12% were aware and treated but not at ATP III goals for high LDL-C, and 16% were aware of, treated for, and achieved LDL-C levels. In contrast, among those with diagnosed diabetes and no history of CHD or other CHD risk equivalents, only 28% were unaware of their high LDL-C, 10% were aware and not treated, 22% were aware and treated but it was not controlled, and 40% were aware, treated, and achieved goal LDL-C (Fig. 2).

CONCLUSIONS—In this analysis, we demonstrate that more than half of individuals with undiagnosed diabetes who do not have a history of CHD or CHD risk equivalents have high LDL-C. In addition, these data indicate that undiagnosed diabetes is associated with a lack of awareness of high cholesterol and lower likelihood of treatment and control compared with subjects with diagnosed diabetes. Even after multivariable adjustment, those with undiagnosed diabetes were 36% less likely to be aware of having high LDL-C, 52% less likely to be treated for it, and 58% less likely to have their high LDL-C controlled to guideline-recommended levels when compared with those with diagnosed diabetes. Specifically, of the 5 million U.S. adults with undiagnosed diabetes who did not have CHD or other CHD risk equivalents, only 16% had their LDL-C treated to ATP III goal.

Our findings are supported by at least one previous study that has documented individuals with undiagnosed diabetes and a high prevalence of uncontrolled cardiovascular risk factors. Hunt et al. (13) studied the risk factor profiles of individuals with undiagnosed diabetes in NHANES from 1999 to 2008. In their analyses, individuals with undiagnosed diabetes had a high prevalence of smoking, hypertension, and dyslipidemia. These analyses focused on variations by ethnicity but did not compare those with undiagnosed diabetes to those with diagnosed diabetes. Furthermore, awareness, treatment, and control of LDL-C were not examined. Our data extend these previous findings by demonstrating that individuals with undiagnosed diabetes are less aware of their high cholesterol and therefore are less likely

Table 1—*Characteristics of NHANES participants without CHD or CHD risk equivalents other than diabetes by diabetes category, 2005–2010*

	Diabetes category			
	Normal fasting glucose (n = 2,386)	Impaired fasting glucose (n = 2,439)	Undiagnosed diabetes (n = 245)	Diagnosed diabetes (n = 458)
Age, %				
<50 years	76.9 (1.2)	52.9 (1.8)	31.3 (3.6)	28.2 (3.2)
50–64 years	16.4 (0.9)	30.4 (1.6)	34.3 (4.0)	37.9 (3.0)
≥65 years	6.7 (0.6)	16.7 (0.9)	34.6 (3.8)	33.9 (2.3)
Male, %	39.6 (0.8)	55.3 (1.1)	57.2 (4.2)	44.7 (3.5)
Race/ethnicity, %				
NH white	70.9 (1.8)	68.8 (2.3)	62.2 (4.5)	59.0 (3.8)
NH black	9.9 (1.0)	11.4 (1.1)	16.4 (2.3)	17.3 (2.2)
Hispanic	12.7 (1.1)	13.9 (1.5)	16.7 (2.7)	16.6 (2.5)
Other	6.5 (0.9)	5.9 (0.7)	4.8 (2.6)	7.1 (1.7)
Annual household income <$20,000, %	11.3 (0.7)	13.2 (0.8)	17.8 (2.7)	16.6 (1.7)
High school graduate, %	86.3 (1.0)	81.1 (1.1)	74.2 (3.1)	71.6 (2.5)
Health insurance, %				
Private	67.5 (1.6)	57.4 (1.5)	39.3 (4.2)	48.9 (2.6)
Government	10.8 (0.9)	21.7 (1.2)	39.9 (3.7)	37.0 (2.6)
None	21.7 (1.3)	20.9 (1.2)	20.8 (3.4)	14.1 (2.0)
Smoking status, %				
Current	21.7 (1.1)	20.9 (1.2)	17.1 (2.8)	14.6 (2.0)
Former	20.3 (1.3)	26.4 (1.5)	34.8 (3.7)	30.8 (2.8)
Never	58.0 (1.4)	52.7 (1.6)	48.0 (3.8)	54.6 (2.7)
BMI, %				
<25 kg/m^2	45.1 (1.5)	25.0 (1.2)	16.4 (3.2)	13.2 (2.2)
25–30 kg/m^2	32.3 (1.2)	36.1 (1.0)	24.9 (3.4)	26.5 (2.5)
≥30 kg/m^2	22.6 (1.3)	38.9 (1.1)	58.7 (4.2)	60.4 (3.5)
Hypertension, %	12.1 (0.9)	31.9 (1.3)	53.7 (4.2)	66.2 (3.4)
Fasting glucose, mg/dL	91.2 (0.2)	105.1 (0.2)	146.4 (3.1)	156.4 (4.1)
Hemoglobin A1C, %	5.2 (0.01)	5.5 (0.01)	6.7 (0.1)	7.4 (0.1)
Duration of diabetes, years	—	—	—	6.5 (1.9, 13.0)
Reduced eGFR, %	1.9 (0.3)	5.2 (0.6)	10.4 (1.8)	13.5 (1.8)
Albuminuria, %	5.6 (0.8)	7.3 (0.7)	18.1 (3.3)	27.5 (2.4)
Ever had cholesterol checked, %	66.4 (1.5)	77.2 (1.2)	85.0 (2.6)	93.7 (1.3)
Have a regular place for health care, %	83.5 (0.6)	84.9 (0.9)	89.4 (2.4)	96.0 (0.9)
Type of place where health care is usually sought, %				
Hospital	3.7 (0.5)	2.2 (0.4)	2.6 (1.1)	1.4 (0.7)
Clinic	94.4 (0.6)	96.2 (0.5)	96.2 (1.3)	98.3 (0.7)
Other	1.9 (0.3)	1.6 (0.4)	1.2 (0.8)	0.4 (0.3)
Received health care in the past year, %	81.9 (0.8)	81.8 (0.9)	85.1 (2.8)	95.8 (1.0)
Tested for diabetes in the past 3 years, %	37.2 (1.0)	48.2 (1.3)	66.7 (3.3)	—
LDL-C, mg/dL				
Overall population	114.0 (1.0)	121.8 (0.8)	116.9 (2.8)	101.8 (2.1)***
Treated	115.8 (5.0)*	112.2 (2.6)*	98.7 (5.4)	96.5 (2.2)
Untreated	113.9 (1.0)**	123.5 (0.9)	122.2 (3.2)	106.4 (3.3)***

Numbers are percent (SE) or mean (SE) except for duration of diabetes, which is presented as median (25th percentile, 75th percentile). Reduced eGFR defined as <60 mL/min/1.73 m^2. Albuminuria defined as an albumin-to-creatinine ratio ≥30 mg/g. NH, non-Hispanic; eGFR, estimated glomerular filtration rate. *$P < 0.05$; **$P < 0.01$; ***$P < 0.001$ with undiagnosed diabetes as the referent group.

to be treated for high cholesterol and, as a result, less likely to have their LDL-C controlled than those with diagnosed diabetes, despite similar risk factor profiles.

The finding that individuals with undiagnosed diabetes have adverse risk factor profiles is clinically relevant because undiagnosed diabetes is common among individuals presenting with cardiovascular disease. In the Atherosclerosis Risk in Communities Study, in those with undiagnosed diabetes, higher hemoglobin A1C levels were associated with higher degrees of carotid intima-media thickness (14). In addition, in a study from Germany, 47% of individuals with diabetes presenting for elective coronary angiography were unaware of their diabetes diagnosis (15). In a U.S. study, a total of 28% of individuals admitted to the hospital for acute coronary syndromes had undiagnosed diabetes (16).

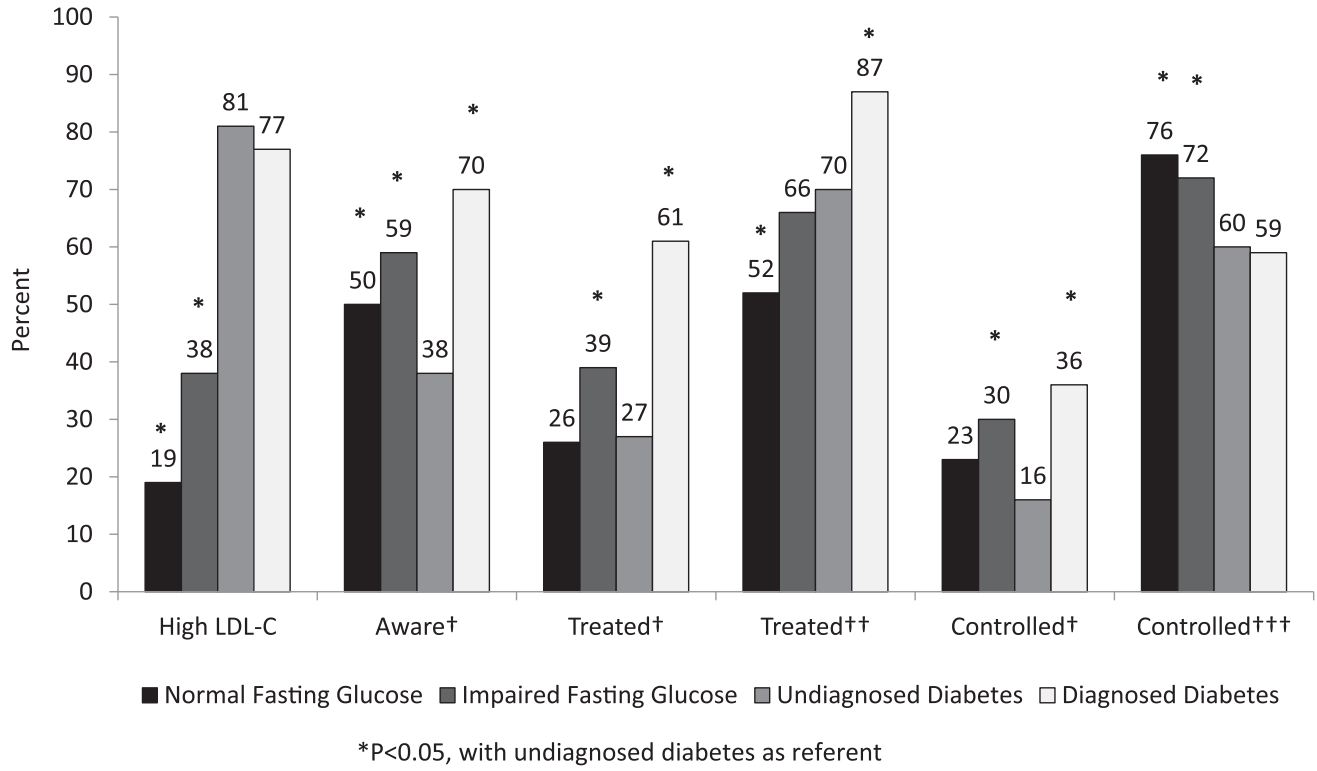


Figure 1—*Prevalence of high LDL-C and the awareness, treatment, and control of high LDL-C among U.S. adults without CHD or CHD risk equivalents other than diabetes by diabetes status, NHANES 2005–2010. *P < 0.05, with undiagnosed diabetes as referent. †Among all individuals with high LDL-C. ††Among individuals aware of their diagnoses of high LDL-C. †††Among those treated for high LDL-C.*

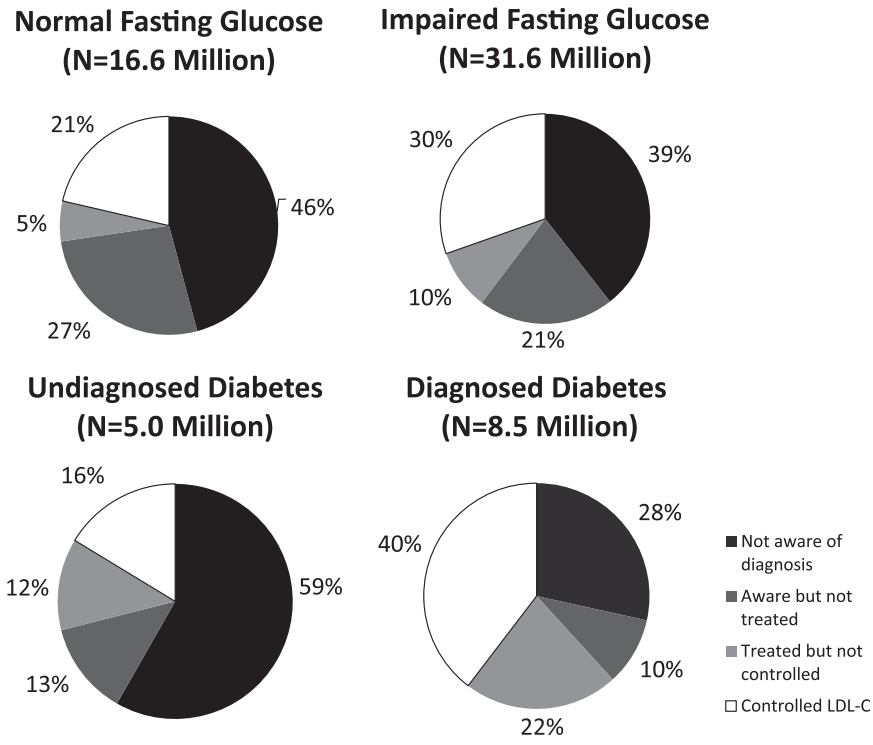
Unfortunately, despite being admitted to the hospital, 65% of these individuals were not recognized as having diabetes and were not treated as such (16). Undiagnosed diabetes also has been associated with increased mortality after cardiac surgery (17). Lauruschkat et al. (17) studied >7,000 patients presenting for coronary artery bypass surgery. Of these patients, >5% had undiagnosed diabetes. Compared with those with diagnosed diabetes or without diabetes, those with undiagnosed diabetes required more resuscitation, had higher rates of reintubation, had more ventilator days, and had higher perioperative mortality (17).

Given the findings from the study by Lauruschkat et al. (17), it would not be surprising if aggressive risk factor modification would reduce cardiovascular events in individuals with undiagnosed diabetes, assuming their diabetes was recognized and appropriate risk factor modification was initiated. One of the clearest implications for making a diagnosis of diabetes is that it would, per the ATP III guidelines, establish the presence of a CHD risk equivalent; in the absence of overt CHD or the presence of other CHD risk equivalents, this would lower the LDL-C treatment goal to <100 mg/dL (3). Our analyses suggest that ~5 million U.S. adults would have their LDL-C goal changed if their diabetes diagnoses were recognized. Recent meta-analyses by Chen et al. (18) and Costa et al. (19) have demonstrated that statins significantly reduce cardiovascular events in individuals with diabetes. These data and the analyses

Table 2—*Awareness, treatment, and control of high LDL-C in U.S. adults with undiagnosed diabetes compared to those with diagnosed diabetes in NHANES participants without CHD or CHD risk equivalents other than diabetes, 2005–2010*

	High LDL-C* (*n* = 550)	Aware† (*n* = 323)	Treated† (*n* = 267)	Treated‡ (*n* = 267)	Controlled† (*n* = 158)	Controlled§ (*n* = 158)
Undiagnosed diabetes, crude	1.06 (0.94–1.19)	0.58 (0.45–0.73)	0.49 (0.33–0.71)	0.81 (0.66–1.01)	0.41 (0.24–0.69)	0.88 (0.59–1.31)
Undiagnosed diabetes¶	1.07 (0.94–1.21)	0.58 (0.46–0.72)	0.48 (0.34–0.69)	0.79 (0.64–0.96)	0.39 (0.23–0.65)	0.83 (0.54–1.26)
Undiagnosed diabetes‖	1.09 (0.89–1.34)	0.64 (0.49–0.84)	0.48 (0.30–0.78)	0.70 (0.55–0.91)	0.42 (0.23–0.80)	0.76 (0.46–1.25)

Data presented as prevalence ratios (95% CIs). *Among all individuals. †Among all individuals with high LDL-C. ‡Among individuals aware of their diagnosis of high LDL-C. §Among individuals treated for high LDL-C. ¶Adjusted for age, sex, and race/ethnicity. ‖Adjusted for age, sex, race/ethnicity, income, education, insurance status, smoking status, BMI, hypertension, reduced estimated glomerular filtration rate, and albuminuria.



	Number of US Adults (in Millions)			
	Normal Fasting Glucose	Impaired Fasting Glucose	Undiagnosed Diabetes	Diagnosed Diabetes
Total with high LDL-C	16.573 (1.266)	31.611 (2.095)	5.001 (0.486)	8.465 (0.669)
Not aware of diagnosis	7.637 (0.690)	12.469 (0.995)	2.943 (0.351)	2.409 (0.330)
Aware but not treated	4.461 (0.591)	6.632 (0.731)	0.631 (0.161)	0.827 (0.202)
Treated but not controlled	0.894 (0.250)	3.011 (0.437)	0.623 (0.158)	1.875 (0.216)
Controlled	3.582 (0.584)	9.499 (0.995)	0.804 (0.203)	3.354 (0.488)

Numbers in table are n in millions (standard error)
LDL-C= low density lipoprotein cholesterol

Figure 2—*Number of U.S. adults with high LDL-C and the number who were aware of, treated for, and whose LDL-C was controlled among U.S. adults without CHD or CHD risk equivalents other than diabetes by diabetes status, NHANES 2005–2010.*

by Matikainen et al. (20) and the Cholesterol Treatment Trialists' Collaborators (21) strongly support aggressive lowering of LDL-C in individuals with diabetes. A previous study has suggested that identifying individuals with undiagnosed diabetes and instituting appropriate risk factor modification, including treatment of high LDL-C, would result in 5–10% absolute risk reduction in CHD events over the course of 10 years (22). Given the millions of U.S. adults with undiagnosed diabetes, this absolute risk reduction means that hundreds of thousands of events could be averted.

A disturbing observation in these data are that although 89% of those with undiagnosed diabetes report having a regular place for health care and 85% report having received health care in the past year, only 67% report being tested for diabetes in the past 3 years. This underscores the need to more aggressively identify individuals who are at risk for having diabetes and to appropriately screen these individuals. The failure to identify the diagnosis of diabetes, especially in this sample of U.S. adults with no history of CHD and no other CHD risk equivalents, represents an important missed opportunity to appropriately risk-stratify these individuals and aggressively lower their LDL-C to guideline-recommended levels. However, among those treated for high cholesterol, individuals with undiagnosed diabetes were as likely as those with diagnosed diabetes to have their LDL-C controlled, suggesting that, if identified, undiagnosed diabetes can be effectively treated.

Our study has a number of limitations. We relied on self-report to define CHD, which may have resulted in the inclusion of some individuals with CHD in our analysis. In addition, laboratory values for glucose and cholesterol were available from only a single point in time, potentially resulting in some misclassification of participants. We chose to exclude individuals with a self-reported history of CHD or other CHD risk equivalents, which limits generalizability of our findings to these populations. However, this allowed us to define how many U.S. adults are not adequately classified according to ATP III recommendations solely on the basis of their undiagnosed diabetes. Despite these limitations, the current study has several strengths. These include its large population-based sample, the complex survey design that permitted the generation of nationally representative estimates, and the availability of fasting glucose and LDL-C measurements.

In summary, undiagnosed diabetes is associated with lack of awareness, treatment, and control of high LDL-C. Approximately 5 million U.S. adults have undiagnosed diabetes and no other CHD risk equivalents. These individuals may not be treated to achieve ATP III–defined LDL-C goals in large part as a result of the failure to make the diagnosis of diabetes. This represents a missed opportunity for the primary prevention of CHD. Strategies to identify individuals at risk for having undiagnosed diabetes and screening these individuals are necessary to appropriately define and achieve ATP III LDL-C treatment targets in these individuals.

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T.M.B. contributed to the design of the analyses and interpretation of the data, wrote the first draft of the manuscript, critically revised the manuscript, and approved the final submitted manuscript. R.M.T., A.P.C., H.Y., R.S.R., M.E.F., J.M.W., E.L.T., S.P.G., M.M.S., and P.M. contributed to the design of the analyses and interpretation of the data, critically

revised the manuscript, and approved the final submitted manuscript. T.M.B. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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