Random Blood Glucose: A Robust Risk Factor For Type 2 Diabetes

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Context: Although random blood glucose (RBG) values are common in clinical practice, the role of elevated RBG values as a risk factor for type 2 diabetes is not well described.

Objective: To examine non-diagnostic, RBG values as a risk factor for type 2 diabetes


Participants: 13,792 non-fasting NHANES participants without diagnosed diabetes.

Primary Outcome: Glycemic status (normal glycemia, undiagnosed prediabetes, or undiagnosed diabetes) using hemoglobin HbA1C as the criterion standard.

Analysis: Multinomial logistic regression examined associations between diabetes risk factors and RBG values according to glycemic status. Associations between current US screening strategies and a hypothetical RBG screening strategy with undiagnosed diabetes were examined.

Results: In unadjusted analyses, a single RBG ≥100 mg/dL (5.6 mmol/L) was more strongly associated with undiagnosed diabetes than any single risk factor [Odds Ratio (95% CI) 31.2 (21.3 – 45.5)] and remained strongly associated with undiagnosed diabetes [20.4 (14.0 – 29.6)] after adjustment for traditional diabetes risk factors. Using RBG <100 mg/dL as a reference, the adjusted odds of undiagnosed diabetes increased significantly as RBG increased: RBG 100–119 mg/dL [7.1 (4.4–11.4)], RBG 120–139 mg/dL [30.3 (20.0–46.0)], RBG ≥140 mg/dL [256 (150.0–436.9)]. As a hypothetical screening strategy, an elevated RBG was more strongly associated with undiagnosed diabetes than current USPSTF guidelines (hypertension alone; p < 0.0001) and similar to ADA guidelines (p = 0.12).

Conclusions: A single RBG ≥100 mg/dL is more strongly associated with undiagnosed diabetes than traditional risk factors. Abnormal RBG values are a risk factor for diabetes and should be considered in screening guidelines.

Type 2 diabetes is a significant and costly public health epidemic that is projected to affect 1 in 3 US adults by 2050 (1). This projected increase is driven largely by the 86 million Americans with prediabetes, which if unrecognized and untreated will likely progress to frank diabetes (2, 3). In spite of well-established diabetes screening guidelines (4, 5), over 8 million people with diabetes and 80 million people with prediabetes remain undiagnosed or unaware of their condition (2, 6).

Current US diabetes screening guidelines recommend targeted screening of high risk individuals; however, guidelines define diabetes risk differently. The US Preventative Services Task Force (USPSTF) guideline recommends screening only when an individual has a sustained
elevation in blood pressure (BP) (treated or untreated) >135/80 (5). In contrast, the multifactorial American Diabetes Association (ADA) guideline (4) recommends screening for all individuals age 45 and older and individuals at any age if their BMI is ≥ 25 kg/m² and they have one additional risk factor including: nonwhite race, family history of diabetes, hypertension, dyslipidemia, history of cardiovascular disease, physical inactivity, polycystic ovarian syndrome, history of gestational diabetes, delivery of an infant weighing > 9 pounds, or other clinical conditions associated with insulin resistance. Screening is also recommended for individuals with prediabetes when HbA1C values, fasting glucose values, and 2-hour glucose values obtained via an oral glucose tolerance test (OGTT) are abnormal but fail to reach diagnostic thresholds (4). The International Diabetes Federation guidelines extend these recommendations even further to recommend screening for individuals with random, nondiagnostic glucose values between 100 and 199 mg/dL (5.6 – 11.0 mmol/L), although the evidence supporting this recommendation is limited (7). Random blood glucose values are not included as a risk factor in US screening recommendations.

In order to improve screening strategies and identification of individuals with undiagnosed diabetes and prediabetes, greater understanding of the risk factors for undiagnosed diabetes and prediabetes are needed. This study seeks to: 1) describe the prevalence diabetes risk factors in individuals with undiagnosed diabetes and prediabetes; 2) examine the association between random glucose values and undiagnosed diabetes and prediabetes; 3) explore the associations between ADA screening guidelines, USPSTF screening guidelines, and a hypothetical random glucose screening strategy with undiagnosed disease.

Research Design and Methods

We analyzed merged data from the 2005–2010 National Health and Nutrition Examination Surveys (NHANES). NHANES is a repeated, cross-sectional, stratified survey designed to be representative of the noninstitutionalized US population using a multistage probability sample. Participants complete an in-home interview for basic demographic and health information along with a scheduled visit to a mobile examination center for physical examination and laboratory testing (8). All participants gave written informed consent and the research ethics boards of the National Center for Health Statistics approved all protocols.

Study Population

The study population consisted of nonpregnant adults age 18 and older who completed both the NHANES interview and MEC examination components between 2005 and 2010. We excluded participants with diagnosed diabetes or prediabetes. Participants responding “yes” when asked “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 diabetes and excluded from the analytic sample. Participants responding “yes” to the question: “Have you ever been told by a doctor or other health professional that you have any of the following: prediabetes, impaired fasting glucose, impaired glucose tolerance, borderline diabetes, or that your blood glucose is higher than normal but not high enough to be called diabetes or sugar diabetes?” were also excluded. Participants examined in a nonfasting state who had both hemoglobin HbA1C and random serum blood glucose (RBG) test results were included in analysis.

Measures

Patient characteristics and diabetes risk factors including age, race, family history of diabetes, and family history of cardiovascular disease were obtained from questionnaire data. BMI was calculated from measured height and weight and classified as normal weight (BMI < 25 kg/m²); overweight (BMI 25–30 kg/m²); or obese (BMI ≥ 30 kg/m²). Participants self-reporting hypertension or high cholesterol diagnosed by a physician or other health professional were considered to have hypertension and high cholesterol. Polycystic ovarian syndrome, acanthosis nigricans, and other clinical conditions associated with insulin resistance were not included as a risk factor for diabetes because we were unable to identify these participants within NHANES. Gestational diabetes and delivery of an infant weighing > 9 pounds were not included as risk factors because data were not available in 2005–2006 NHANES. Participants meeting age, BMI, family history, race, hypertension, high cholesterol, or cardiovascular disease criteria were considered to satisfy the ADA screening guideline. We subsequently classified patients using the ADA (4) and USPSTF (5) screening guidelines by whether screening was indicated (yes/no). All questionnaire and examination components utilized in analysis were identical across the 3 survey cycles used.

Serum RBG measurements were determined using the Beckman Oxygen electrode, glucose oxidase method. Between 2007 and 2012, one instrument change occurred [Beckman Synchron LX20 (2007) to the Beckman Unicel CxC800 Synchron (2008–2012)]. All measurements were performed by Collaborative Laboratory Services, LLC (9).

HbA1C assays were conducted using high-performance liquid chromatography (HPLC) methods on instruments certified by the National Glycohemoglobin Standardization Program (9). All HbA1C results were subsequently standardized to the Diabetes Control and Complications Trial reference standard (10). Between 2007 and 2010, all HbA1C assays were performed at a single laboratory site (Minneapolis, MN). The instrument used to analyze HbA1C changed from the Tosoh HbA1C 2.2 Plus (2005–2007) to the Tosoh HbA1C G7 (2007–2010). In spite of this, HbA1C values were analyzed without corrections as recommended by the National Center for Health Statistics (11).

We defined diabetes, prediabetes and dysglycemia using HbA1C as the criterion standard. Diabetes was defined as having an HbA1C ≥ 6.5% (48 mmol/mol) and prediabetes as having an HbA1C 5.7–6.4% (39–46 mmol/mol). Dysglycemia was defined as having an HbA1C ≥ 5.7% (39 mmol/mol). Fasting glucose was not included in our diabetes definition because individuals examined in a fasting state did not have a RBG value available.
Statistical Analysis

We calculated means and percentages of participant characteristics by glycemic status and compared values across groups using Rao-Scott $\chi^2$ tests for categorical variables and $F$ tests for continuous variables. We used multinomial logistic regression to examine associations between risk factors and undiagnosed diabetes and prediabetes. We further aggregated risk factors according to ADA (4) and USPSTF (5) diabetes screening guidelines to examine associations between these screening strategies and undiagnosed diabetes and prediabetes. We also examined unadjusted and covariate adjusted associations between a single RBG $\geq 100$ mg/dL (5.6 mmol/L) with undiagnosed diabetes and prediabetes. Models were adjusted for traditional diabetes risk factors including age, sex, race, BMI, hypertension, hyperlipidemia, cardiovascular disease, and family history of diabetes. The odds ratios of detecting undiagnosed diabetes and prediabetes using ADA, USPSTF, and RBG screening strategies were compared using Wald tests. Analyses were conducted in SAS version 9.3 (SAS Institute Inc., Cary, NC) and Stata/SE version 13.1 (StataCorp LP, College Station, TX) using survey procedures to account for unequal selection probabilities and nonresponse such that estimates are representative of the US noninstitutionalized civilian population (8). P values $< 0.05$ were considered statistically significant. This study was approved by the institutional review board (IRB) at the University of Texas Southwestern Medical Center at Dallas.

Results

A total of 13,792 participants met eligibility criteria. Among all participants aged $\geq 18$ years without diagnosed diabetes, 1.9% had undiagnosed diabetes and 20.2% had undiagnosed prediabetes by HbA1c criteria. Participant characteristics by glycemic status are shown in Table 1. Overall, the prevalence of traditional diabetes risk factors is increased in individuals with undiagnosed prediabetes and diabetes. The prevalence of older age, nonwhite race, positive family history of diabetes, increasing BMI, and a diagnosis of hypertension, hyperlipidemia, and cardiovascular disease increases across the spectrum of dysglycemia from normal to prediabetes, to diabetes, with the highest prevalence of risk factors present in individuals with undiagnosed diabetes (Table 1). Men were more likely than women to have undiagnosed diabetes.

While those with undiagnosed diabetes and prediabetes were more likely to be screened in the past 3 years compared to those with normoglycemia, only slightly more than half of those with undiagnosed diabetes (56.1%) and half (49.6%) of those with undiagnosed prediabetes reported having been screened for diabetes in the past 3 years. However, this does not appear to be for lack of physician visits because only 21.0% and 13.8% of patients with undiagnosed diabetes and prediabetes respectively did not have a doctor’s visit in the past 12 months.

The mean HbA1c increased across the glycemic spectrum: no diabetes HbA1c=5.2% (33 mmol/mol); undiagnosed prediabetes HbA1c=5.9% (41 mmol/mol); and undiagnosed diabetes HbA1c=7.6% (60 mmol/mol) (Table 1). Translating these HbA1c values into estimated average glucose values over the preceding 3 months (12), participants with no diabetes had an estimated average glucose of 103 mg/dL (5.7 mmol/L) compared with 123 mg/dL (6.8 mmol/L) and 171 mg/dL (9.5 mmol/L) in participants with undiagnosed prediabetes and diabetes respectively. The mean value of a single RBG measure across groups

### Table 1. Participant Demographics and Risk Factors by Glycemic Status

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No Diabetes</th>
<th>Undiagnosed Pre-diabetes</th>
<th>Undiagnosed Diabetes</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, years</td>
<td>41.7 (0.3)</td>
<td>55.4 (0.4)</td>
<td>58.6 (0.9)</td>
<td>$&lt; 0.001$</td>
</tr>
<tr>
<td>Female</td>
<td>50.8 (0.5)</td>
<td>51.7 (1.1)</td>
<td>41.3 (3.0)</td>
<td>0.009</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic white</td>
<td>72.9 (1.8)</td>
<td>65.0 (0.9)</td>
<td>57.0 (5.2)</td>
<td>$&lt; 0.001$</td>
</tr>
<tr>
<td>Non-Hispanic black</td>
<td>8.8 (0.6)</td>
<td>15.6 (0.6)</td>
<td>17.0 (2.4)</td>
<td>$&lt; 0.001$</td>
</tr>
<tr>
<td>Mexican American</td>
<td>8.3 (0.9)</td>
<td>8.4 (0.4)</td>
<td>14.0 (2.5)</td>
<td>0.005</td>
</tr>
<tr>
<td>Other Hispanic</td>
<td>4.3 (0.6)</td>
<td>4.5 (0.3)</td>
<td>4.8 (1.0)</td>
<td>0.83</td>
</tr>
<tr>
<td>Other race</td>
<td>5.7 (0.5)</td>
<td>6.5 (0.6)</td>
<td>7.3 (2.7)</td>
<td>0.48</td>
</tr>
<tr>
<td>Education&lt;12 yr</td>
<td>15.3 (0.8)</td>
<td>24.2 (0.9)</td>
<td>29.6 (2.7)</td>
<td>$&lt; 0.001$</td>
</tr>
<tr>
<td>Married</td>
<td>53.7 (1.0)</td>
<td>58.1 (1.1)</td>
<td>56.0 (3.2)</td>
<td>$&lt; 0.001$</td>
</tr>
<tr>
<td>Uninsured</td>
<td>21.4 (0.9)</td>
<td>18.5 (0.8)</td>
<td>22.8 (3.3)</td>
<td>0.012</td>
</tr>
<tr>
<td>Family history diabetes</td>
<td>30.9 (0.6)</td>
<td>40.0 (1.1)</td>
<td>46.1 (2.7)</td>
<td>$&lt; 0.001$</td>
</tr>
<tr>
<td>Mean BMI, kg/m²</td>
<td>27.3 (0.1)</td>
<td>30.2 (0.1)</td>
<td>34.2 (0.5)</td>
<td>$&lt; 0.001$</td>
</tr>
<tr>
<td>Hypertension</td>
<td>20.6 (0.7)</td>
<td>40.5 (1.1)</td>
<td>49.6 (2.8)</td>
<td>$&lt; 0.001$</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>22.1 (0.7)</td>
<td>39.0 (1.1)</td>
<td>37.1 (3.2)</td>
<td>$&lt; 0.001$</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>3.8 (0.3)</td>
<td>9.6 (0.6)</td>
<td>14.8 (1.6)</td>
<td>$&lt; 0.001$</td>
</tr>
<tr>
<td>No doctors visit past 12 months</td>
<td>19.1 (0.5)</td>
<td>13.8 (0.7)</td>
<td>21.0 (2.8)</td>
<td>$&lt; 0.001$</td>
</tr>
<tr>
<td>Screened for diabetes past 3 yr</td>
<td>35.9 (0.5)</td>
<td>49.6 (1.1)</td>
<td>56.1 (2.8)</td>
<td>$&lt; 0.001$</td>
</tr>
<tr>
<td>Mean random blood glucose, mg/dL</td>
<td>89.9 (0.2)</td>
<td>99.1 (0.4)</td>
<td>156.0 (5.3)</td>
<td>$&lt; 0.001$</td>
</tr>
<tr>
<td>Mean HbA1C, %</td>
<td>5.2 (0.01)</td>
<td>5.9 (0.01)</td>
<td>7.6 (0.1)</td>
<td>$&lt; 0.001$</td>
</tr>
<tr>
<td>Mean HbA1C, mmol/mol</td>
<td>33 (0.1)</td>
<td>41 (0.1)</td>
<td>60 (1.1)</td>
<td>$&lt; 0.001$</td>
</tr>
</tbody>
</table>

Data presented as percent (se.) unless otherwise noted. All estimates are weighted to US population estimates. Random glucose (mg/dL) $\times 0.5551 = \text{mmol/liter}$
increased from 89.9 mg/dL (5.0 mmol/L) in patients with no diabetes, to 99.1 mg/dL (5.5 mmol/L) in patients with undiagnosed prediabetes, to 156.0 mg/dL (8.7 mmol/L) in patients with undiagnosed diabetes.

In univariate analyses, the risk factors most strongly associated [Odds Ratio (95% CI)] with undiagnosed diabetes were a single RBG $\geq 100$ mg/dL (5.6 mmol/L) [31.2 (21.3–45.5)], BMI $\geq 25$ kg/m$^2$ [10.9 (6.8–17.5)], and age $\geq 45$ years [7.9 (5.7–10.9)]. Comorbid disease risk factors such as a history of cardiovascular disease, hypertension, or hyperlipidemia were more modestly associated with dysglycemia (Table 2). As a single risk factor, race and family history demonstrated the weakest associations with undiagnosed diabetes.

Age $\geq 45$ years was the risk factor most strongly associated with undiagnosed prediabetes [OR (95% CI); 4.8 (4.2–5.4)] and undiagnosed dysglycemia [4.9 (4.4–5.6)]. A single RBG $\geq 100$ mg/dL (5.6 mmol/L) was more strongly associated with undiagnosed prediabetes [3.3 (3.0–3.8)] and undiagnosed dysglycemia [3.9 (3.5–4.4)] than all other risk factors examined except for age (Table 2).

Table 3 shows a strong ‘dose response’ relationship between increasing RBG values and higher risk-adjusted odds of undiagnosed prediabetes, undiagnosed diabetes, and overall dysglycemia. For individuals with a single RBG 100–119 mg/dL (5.6–6.6 mmol/L), the odds of undiagnosed diabetes were 7.1 (4.4–11.4). For glucose values between 120–139 mg/dL (6.7–7.7 mmol/L) and $\geq 140$ mg/dL (7.8 mmol/L), the odds of undiagnosed diabetes were 30.3 (20.0–46.0) and 256 (150.0–436.9) respectively.

In multivariate models, a single RBG $\geq 100$ mg/dL (5.6 mmol/L) was associated with a twenty-fold increased risk of undiagnosed diabetes [OR (95% CI); 20.4 (14.0–29.6)] and over double the odds of undiagnosed prediabetes [2.4 (2.1–2.7)] even after adjusting for age, sex, race, BMI, hypertension, hyperlipidemia, cardiovascular disease, and family history of diabetes. Overall, a single RBG $\geq 100$ mg/dL (5.6 mmol/L) nearly tripled the risk-adjusted odds of undiagnosed dysglycemia [2.8 (2.5–3.2)] (Table 4).

As shown in Table 4, patients meeting USPSTF and ADA screening guidelines had increased odds of having undiagnosed prediabetes and undiagnosed diabetes. Meeting the single-factor USPSTF guideline criteria (presence of hypertension alone) nearly tripled the odds of prediabetes [OR (95% CI) 2.6 (2.4–2.9)] and dysglycemia [2.7 (2.5–3.0)] and increased the odds of diabetes nearly 4-fold [3.8 (2.9–5.0)]. Individuals meeting the multirisk factor ADA guidelines had approximately a ten-fold increase in the odds of prediabetes [9.8 (8.1–11.8)] and dysglycemia [10.6 (8.8–12.7)]. Meeting ADA guidelines increased the odds of diabetes by over 50-fold [50.6 (17.7–144.5)].

A screening strategy based on a single RBG $\geq 100$ mg/dL (5.6 mmol/L) [OR (95% CI) 20.4 (14.0–29.6)] was much more strongly associated with undiagnosed diabetes than USPSTF guidelines ($P < .0001$) and not statistically different from the ADA screening guideline ($P = .12$). For detecting undiagnosed prediabetes, the single RBG strategy was similar to the USPSTF guideline ($P = .32$) but not as predictive as the ADA screening strategy ($P < .0001$).

### Conclusions

In a nationally representative sample of the US population without diagnosed diabetes, a single RBG $\geq 100$ mg/dL (5.6 mmol/L) is strongly associated with undiagnosed diabetes and demonstrates a robust dose response. In fact, a RBG $\geq 100$ mg/dL (5.6 mmol/L) was the single strongest predictor of undiagnosed diabetes outperforming all other traditional risk factors. As a simple strategy to detect undiagnosed diabetes, the association with undiagnosed disease for a single RBG $\geq 100$ mg/dL (5.6 mmol/L) is stronger than the USPSTF diabetes screening guidelines, which

### Table 2. Univariate Associations Between Risk Factors and Undiagnosed Prediabetes, Diabetes, and Dysglycemia (Prediabetes + Diabetes)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Undiagnosed Prediabetes</th>
<th>Undiagnosed Diabetes</th>
<th>Dysglycemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age $\geq 45$ yr</td>
<td>4.8 (4.2–5.4)</td>
<td>7.9 (5.7–10.9)</td>
<td>4.9 (4.4–5.6)</td>
</tr>
<tr>
<td>BMI $\geq 25$ kg/m$^2$</td>
<td>2.3 (2.0–2.6)</td>
<td>10.9 (6.8–17.5)</td>
<td>2.5 (2.2–2.8)</td>
</tr>
<tr>
<td>Non-white race</td>
<td>1.4 (1.3–1.7)</td>
<td>2.0 (1.4–2.9)</td>
<td>1.5 (1.3–1.7)</td>
</tr>
<tr>
<td>Family history diabetes</td>
<td>1.5 (1.4–1.6)</td>
<td>1.9 (1.5–2.4)</td>
<td>1.5 (1.4–1.7)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>2.6 (2.4–2.9)</td>
<td>3.8 (2.9–5.0)</td>
<td>2.7 (2.5–3.0)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>2.3 (2.0–2.6)</td>
<td>2.1 (1.6–2.8)</td>
<td>2.3 (2.0–2.6)</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>2.7 (2.2–3.3)</td>
<td>4.5 (3.4–5.9)</td>
<td>2.9 (2.4–3.4)</td>
</tr>
<tr>
<td>Random Glucose $\geq 100$ mg/dL</td>
<td>3.3 (3.0–3.8)</td>
<td>31.2 (21.3–45.5)</td>
<td>3.9 (3.5–4.4)</td>
</tr>
</tbody>
</table>

Results presented as odds ratios (95% CI). Weighted standard errors used to compute CIs. Random glucose (mg/dL) $\times 0.5551 = \text{mmol/liter}$
recommend screening based on the presence of hypertension alone (5), and similar to the multirisk factor, more complex ADA screening guidelines (4). Nondiagnostic, random glucose values should be considered in diabetes risk assessments and may improve detection of undiagnosed cases of diabetes and prediabetes.

Among individuals with undiagnosed prediabetes and diabetes, traditional diabetes risk factors are common. In general, the prevalence of individual risk factors increases across the glycemic spectrum from no diabetes, to undiagnosed prediabetes and undiagnosed diabetes. Similar to other studies (13–17), we observed significant associations between age, BMI, hypertension, family history and undiagnosed disease. Although we found race and family history to be significant risk factors, their association with undiagnosed disease was more modest than other risk factors. Similar to a recent study finding that men have a higher prevalence of diagnosed diabetes than women (18), we found that men were also more likely to have undiagnosed diabetes.

Although the vast majority of individuals with undiagnosed diabetes and prediabetes are insured and have visited a healthcare provider in the past 12 months, similar to other studies (19), we found that only half of eligible individuals reported being screened diabetes in the past 3 years. Given the burden of undiagnosed disease and the prevalence of diabetes risk factors, missed opportunities for diabetes screening are common (15). Although the barriers to diabetes screening in clinical practice are poorly understood, the assessment of diabetes risk factors and ordering of diabetes screening is largely at the discretion of individual clinicians and may be an afterthought in time-constrained clinic visits. Automated risk-assessment and clinical decision support can facilitate provider workflow and be effective tools to increase screening rates for cancer (20). However, automation and implementation of multifactorial diabetes screening guidelines in clinical practice is challenging and parsimonious risk assessment models are needed (21).

### Table 3. Dose Response Relationship Between Random Glucose and Undiagnosed Diabetes, Prediabetes, and Dysglycemia (Prediabetes + Diabetes)

<table>
<thead>
<tr>
<th>Glucose Range</th>
<th>Undiagnosed Prediabetes</th>
<th>Undiagnosed Diabetes</th>
<th>Dysglycemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random glucose &lt; 100 mg/dL</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Random glucose 100–119 mg/dL</td>
<td>2.2 (1.9 – 2.5)</td>
<td>7.1 (4.4 – 11.4)</td>
<td>2.3 (2.0 – 2.7)</td>
</tr>
<tr>
<td>Random glucose 120–139 mg/dL</td>
<td>3.3 (2.6 – 4.2)</td>
<td>30.3 (20.0 – 46.0)</td>
<td>3.8 (3.0 – 4.9)</td>
</tr>
<tr>
<td>Random glucose ≥ 140 mg/dL</td>
<td>3.5 (2.2 – 5.5)</td>
<td>256.0 (150.0 – 436.9)</td>
<td>8.4 (5.7 – 12.3)</td>
</tr>
</tbody>
</table>

All values adjusted for age, sex, race, BMI, hypertension, hyperlipidemia, cardiovascular disease, and family history of diabetes. Random glucose (mg/dL) × 0.5551 = mmol/liter

### Table 4. Odds of Having Undiagnosed Diabetes, Prediabetes, or Dysglycemia (Prediabetes + Diabetes) According to Different Screening Strategies

<table>
<thead>
<tr>
<th>Screening Strategy</th>
<th>Undiagnosed Prediabetes</th>
<th>Undiagnosed Diabetes</th>
<th>Dysglycemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>USPSTF Guidelines</td>
<td>2.6 (2.4 – 2.9)</td>
<td>3.8 (2.9 – 5.0)</td>
<td>2.7 (2.5 – 3.0)</td>
</tr>
<tr>
<td>ADA Guidelines</td>
<td>9.8 (8.1 – 11.8)</td>
<td>50.6 (17.7 – 144.5)</td>
<td>10.6 (8.8 – 12.7)</td>
</tr>
<tr>
<td>Random Glucose ≥ 100 mg/dL</td>
<td>2.4 (2.1 – 2.7)</td>
<td>20.4 (14.0 – 29.6)</td>
<td>2.6 (2.3 – 3.2)</td>
</tr>
</tbody>
</table>

All results presented as weighted odds ratios.

USPSTF Guideline: diagnosed hypertension

ADA Guideline: All individuals age ≥ 45 or those with BMI ≥ 25 kg/m² and family history of diabetes, non-white race, hypertension, high cholesterol, cardiovascular disease.

*Adjusted for age, sex, race, BMI, hypertension, hyperlipidemia, cardiovascular disease, and family history of diabetes. Random glucose (mg/dL) × 0.5551 = mmol/liter
A major strength of this study is that the data are nationally representative of the noninstitutionalized, civilian, US population without diagnosed diabetes and prediabetes. However, there are several limitations. First, our analyses are limited to cross-sectional associations between a single RBG value and glycemic status. Because of this, we are unable to examine the development of diabetes over time. Second, individuals with diagnosed diabetes and prediabetes were excluded based on self-report; however, self-reported diabetes is both highly sensitive and specific for diagnosed diabetes (30). Third, because we sought to detect cases of undiagnosed diabetes and prediabetes, we were unable to examine prediabetes as a risk factor for undiagnosed diabetes. However, most individuals with prediabetes remain undiagnosed (2). Additionally, our estimates of the association between the ADA guideline and undiagnosed disease likely underestimate the true association given our inability to include all ADA screening criteria in our definitions. Fourth, our analyses utilize serum glucose values rather than plasma glucose values. However, analytic differences between serum and plasma glucose values are small and unlikely to exceed the day-to-day biologic variation of glucose (31). Thus, our findings reflect real-world practice where serum glucose values are routinely obtained as part of chemistry panels.

Fifth, our analyses focus on community-dwelling NHANES participants and may not directly translate to medical practice if patients are acutely ill. Sixth, our definition of prediabetes and diabetes was based on HbA1C criteria alone because individuals examined in a fasting state did not have random glucose data available. As a result, our findings likely underestimate the burden of undiagnosed prediabetes and diabetes (32).

In conclusion, our findings indicate that a single random glucose value \( \geq 100 \text{ mg/dL} (5.6 \text{ mmol/L}) \) is a robust risk factor for type 2 diabetes and should prompt clinicians to obtain gold standard diabetes screening tests to categorize glycemic status. Considering the large number of individuals in the US with undiagnosed diabetes and prediabetes (2), our findings have important implications for current diabetes screening and the ADA diabetes screening guidelines, which incorporate multiple risk factors, have similar associations with undiagnosed disease. Additionally, the random glucose strategy – even after adjustment for other risk factors – is more strongly associated with undiagnosed diabetes than the USPSTF guidelines, which likewise recommend screening based on a single risk factor.

The usefulness of random glucose values in the diagnosis of diabetes and prediabetes has a strong physiologic basis. Glucose homeostasis is a tightly regulated function of \( \beta \) cell insulin production and insulin sensitivity (26) such that glucose concentrations are maintained in a narrow range (27). Disruptions in glucose homeostasis initially manifest as impaired glucose tolerance and increased glucose variability (26). In clinical practice, this is reflected as nondiagnostic RBG elevations and increased glucose variability. Given that random glucose testing accounts for over 95% of glucose testing in clinical practice, (23) opportunities to recognize random glucose abnormalities and incorporate them into risk assessment exist in routine clinical practice.

Although random glucose is not currently included in US diabetes screening guidelines, our findings demonstrate the potential importance of random glucose values in screening strategies. Existing studies demonstrate that a single RBG \( \geq 125 \text{ mg/dL} (6.9 \text{ mmol/L}) \) is a good predictor of diabetes (28) and performs as well as more complicated models based on age, BMI, and race (29). We demonstrate that RBG values as low as 100 mg/dL (5.6 mmol/L) confer a significant risk for diabetes and are associated with undiagnosed diabetes. Our findings suggest that a hypothetical screening strategy in which individuals with a single RBG \( \geq 100 \text{ mg/dL} (5.6 \text{ mmol/L}) \) undergo gold-standard diabetes screening and the ADA diabetes screening guidelines, which incorporate multiple risk factors, have similar associations with undiagnosed disease. Additionally, the random glucose strategy – even after adjustment for other risk factors – is more strongly associated with undiagnosed diabetes than the USPSTF guidelines, which likewise recommend screening based on a single risk factor.
for screening and case finding strategies. First, our findings highlight the importance of RBG values ≥ 100 mg/dL (5.6 mmol/L) as a risk factor for diabetes and provide evidence to support the inclusion of RBG values ≥ 100 mg/dL as a risk factor in US diabetes screening guidelines. Second, our findings suggest that increased awareness of abnormal random glucose values and targeted diabetes testing may improve diabetes detection among individuals engaged in clinical care. Given the high frequency of glucose testing in clinical practice and the growing repository of computerized laboratory data within electronic medical records, the development of automated, glucose-driven risk assessment strategies may improve the screening and diagnosis of type 2 diabetes in clinical practice.

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