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# Racial differences in performance of HbA1c for the classification of diabetes and prediabetes among US adults of non-Hispanic black and white race

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## Abstract

**Objective:** Higher HbA1c levels in non-Hispanic black compared to white people (black and white) at similar glucose levels could lead to misclassification when using HbA1c to diagnose diabetes, prediabetes and/or dysglycemia. The objective of this study was to characterize black/white differences in optimal HbA1c cutoffs for diabetes and prediabetes.

**Research Design and Methods:** Data were included from the National Health and Nutrition Examination Survey, 2005–2014. Eligible participants were black and white adults (18–70 years) who underwent an oral glucose tolerance test and had fasting plasma glucose (FPG), 2-hour plasma glucose (2hPG), and HbA1c measurements. Diabetes or prediabetes status was defined by FPG and 2hPG, using American Diabetes Association criteria. Classification of diabetes, prediabetes, and dysglycemia by HbA1c was evaluated for a range of HbA1c cutoffs with optimal cutoffs defined as the value that maximized the sum of sensitivity and specificity (Youden's Index; YI).

**Results:** In 5,324 black (32.3%) and white (67.7%) participants, YI (optimal) cutoffs were HbA1c ≥42 mmol/mol (6.0%) and ≥39 mmol/mol (5.7%) for discriminating diabetes vs. non-diabetes, HbA1c ≥ 44 mmol/mol (6.2%) and ≥39 mmol/mol (5.7%) for discriminating diabetes vs. prediabetes (excluding normoglycemia), HbA1c ≥39 mmol/mol (5.7%) and ≥37 mmol/mol (5.5%) for discriminating dysglycemia vs. normoglycemia, and HbA1c ≥39 mmol/mol (5.7%) and ≥37

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mmol/mol (5.5%) for discriminating prediabetes vs. normoglycemia (excluding diabetes), in black and white people, respectively.

**Conclusions:** Consistently higher optimal HbA1c cutoffs in black vs. white people suggest a need for individualizing HbA1c relative to glucose levels if HbA1c is used to diagnose diabetes and prediabetes.

### Keywords

Diagnosis; Race; HbA1c

## INTRODUCTION

Hemoglobin A1c (HbA1c) is widely used to guide diabetes management and diagnosis (1), since blood sampling at any time of day is convenient, levels are reproducible, and assays are standardized (2). However, HbA1c levels tend to be higher in people of non-Hispanic black vs. white race (black, white) (3), and there has been controversy as to whether this reflects differences in underlying glucose levels. When HbA1c was added to the list of measures used to diagnose diabetes in 2009–2010, there was insufficient evidence to determine whether the relationship between HbA1c and glucose differed with black vs. white race. Since then, several studies have suggested that black/white differences in HbA1c may be due to nonglycemic factors (4), prompting further debate (5; 6). However, a recent continuous glucose monitoring study demonstrated that HbA1c levels are generally higher in people of black vs. white race with similar glucose levels (7).

A tendency of black race to be associated with higher HbA1c levels than white race with similar glucose levels – and lower glucose levels than white race with similar HbA1c levels – could contribute to disparities in both diagnosis and management. The use of uniform HbA1c diagnostic cutoffs would be expected to result in a higher rate of overdiagnosis in people of black race, and underdiagnosis in white race, as previously reported (8). In addition, since intensification of treatment may be prompted mainly by HbA1c levels (9), and a given HbA1c level could represent glucose levels 21 mg/dL *lower* with black vs. white race (5), treatment to the same HbA1c targets would be expected to increase the risk of hypoglycemia in people of black race, as was found in both the Action to Control Cardiovascular Risk in Diabetes (ACCORD) and Surveillance, Prevention, and Management of Diabetes Mellitus (SUPREME-DM) studies (9; 10), and in a Medicare population (11).

With this background, our primary objective was to compare HbA1c cutoffs that optimized discrimination of diabetes, prediabetes, and dysglycemia in people of black and white race, using a criterion that would be unaffected by the study population (the maximum sum of sensitivity and specificity), and a criterion that could be affected by the study population (accuracy), in a nationally representative dataset. A secondary objective was to evaluate rates of HbA1c-based misclassification in people of black vs. and white race, using the current American Diabetes Association (ADA) diagnostic criteria.

## RESEARCH DESIGN AND METHODS

### Participants

Data were used from five cycles (2005–2014) of the National Health and Nutrition Examination Survey (NHANES), a representative survey of the US population. NHANES uses a sampling design in which underrepresented groups, including btabllacks, are oversampled to achieve adequate representation (12). The NHANES methodology is described elsewhere (13).

We analyzed data from non-pregnant adults (ages 18 – 70 years) who had complete information for fasting plasma glucose (FPG) and two-hour plasma glucose (2hPG) in an oral glucose tolerance test (OGTT), and HbA1c; OGTTs were not performed in those who reported use of glucose-lowering medication, were pregnant, or did not meet criteria for fasting (≥9 hours). Participants were included irrespective of glycemic status to allow for testing conditions in which disease status was not known; glycemic status based on FPG and 2hPG was taken into account later to partition the sample for the purposes of testing diagnostic classification.

### Measures

HbA1c was determined from venipuncture blood samples using ion exchange High Performance Liquid Chromatography (HPLC). Specimens from the 2005–06 survey were analyzed at the Diabetes Laboratory at the University of Minnesota (Minneapolis, MN) using a Tosoh A1C 2.2 Plus Glycohemoglobin Analyzer (Tosoh Medics, Inc., South San Francisco, CA). Samples from 2007–2012 s were analyzed at the Fairview Medical Center Laboratory at the University of Minnesota, whereas samples from 2013–14 were analyzed at the University of Missouri-Columbia (Columbia, MO). Blood samples from 2007–14 were analyzed using a Tosoh G7 Automated HPLC Analyzer. Because blood specimens were analyzed using different laboratories and instrumentation, there was extensive quality assurance testing and harmonization through the National Glycohemoglobin Standardization Program (NGSP) (2). FPG and 2hPG were determined using the hexokinase method, and values from 2005–06 were adjusted to account for differences in instrumentation between 2005–06 and 2007–2014.

### Design

HbA1c was treated as a ‘screening’ measure and its performance compared to FPG and 2hPG (combined) as ‘reference’ measures of disease status. Based on current ADA criteria (1), diabetes was defined as FPG ≥7.0 mmol/L (126 mg/dL) or 2hPG ≥11.1 mmol/L (200 mg/dL), and among those who did not have diabetes, prediabetes as FPG of 5.6 mmol/L (100 mg/dL) to 6.9 mmol/L (125 mg/dL) or 2hPG of 7.8 mmol/L (140 mg/dL) to 11.0 mmol/L (199 mg/dL). Dysglycemia was defined as diabetes or prediabetes, and normoglycemia as FPG <5.6 mmol/L (100 mg/dL) *and* 2hPG <7.8 mmol/L (140 mg/dL) (1).

We assessed optimal HbA1c cutoffs by race for discrimination of (i) diabetes vs. non-diabetes; (ii) diabetes vs. prediabetes (excluding normoglycemia); (iii) dysglycemia vs. normoglycemia; and (iv) prediabetes vs. normoglycemia (excluding diabetes). To identify

optimal cutoffs, sensitivity, specificity, and Youden's Index (YI) were computed for each HbA1c value in 0.1 increments across a range from ≥26 mmol/mol (4.5%) to ≥53 mmol/mol (7.0%).

We also assessed the performance of current ADA HbA1c diagnostic criteria [HbA1c ≥48 mmol/mol (6.5%) for diabetes; and an HbA1c of 39 mmol/mol (5.7%) – 46 mmol/mol (6.4%) for prediabetes] using 2hPG and FPG as reference measures; accuracy (the proportions correctly classified); misclassification (the proportions incorrectly classified); and false positive and false negative rates.

### Analysis

Analyses were conducted using Stata (version 14, StataCorp, College Station, TX) with appropriate use of survey-weighting procedures to generate representative estimates of means and proportions in the US population (Table 1). Linear regression was used to model the relationship between black and white race and HbA1c, with and without adjustment for FPG, 2hPG, BMI, sex and age.

Survey weights were used to calculate sensitivity, specificity, prevalence, percent misclassified, accuracy, and false positive and false negative rates (Supplemental Tables 2−5).

Sensitivity was defined as the probability of a positive HbA1c screening result among those with positive disease status (based on FPG and 2hPG) – the proportion of true positives correctly identified HbA1c. Specificity was defined as the probability of a negative HbA1c screening result by among those without disease – the proportion of true negatives correctly identified by HbA1c. Accuracy was characterized as the proportion of participants correctly identified by HbA1c screening; misclassification as 1-accuracy; the false positive rate as 1-specificity; and the false negative rate as 1-sensitivity.

YI, the HbA1c value at which [sensitivity + specificity – 1] was maximized, was used as the primary criterion for 'optimal' HbA1c cutoffs; we also identified cutoffs at which accuracy was maximized. Whereas YI is unaffected by differences in disease prevalence, accuracy (sensitivity*prevalence + specificity*[1 – prevalence]) is based in part on prevalence. Although in our dataset, differences in the prevalence of diabetes (whites: 4.8%; blacks: 5.3%) and prediabetes (whites: 44.8%; blacks 50.2%) were relatively small, such differences could differentially influence accuracy; in sensitivity analyses, we explored the impact of perturbations in the prevalence of diabetes and prediabetes.

## RESULTS

Table 1 shows selected sample characteristics. There were 5,324 non-pregnant adults, 67.7% (n=3,603) white and 32.3% (n=1,721) black. Mean HbA1c was slightly higher in those with black than white race [37 mmol/mol (5.53%) vs. 35 mmol/mol (5.34%), respectively, p<0.001]. Mean FPG was slightly lower in those with black than white race [97.9 mg/dL (5.4 mmol/L) vs. 98.9 mg/dL (5.5 mmol/L); p=0.049], but there were no significant differences in 2hPG [6.1 mmol/L (109.5 mg/dL) vs. 6.1 mmol/L (109.9 mg/dL),

respectively, p=0.792]. Based on glucose levels, there was no significant difference in the prevalence of diabetes with black vs. white race (p=0.530), although the prevalence of prediabetes was higher with black race (50.2% vs. 44.8%; p=0.003). With classification by HbA1c levels, there would have been 2.9% and 33.9% diabetes and prediabetes with black race, and 1.3% and 16.3% diabetes and prediabetes with white race, respectively. In a regression model adjusted for FPG, 2hPG, BMI, age and sex, black race was associated with 2.5 mmol/mol (NGSP: 0.22%; 95% CI: 0.20%, 0.25%) higher HbA1c (Supplemental Table 1).

Consistent with higher HbA1c levels despite similar glucose levels in those with black vs. white race, diagnostic misclassification based on HbA1c levels was different with black vs. white race. While overall misclassification was not significantly different between black vs. white race (35.4% vs. 38.2%; p=0.105), false positives were more common with black race (17.6% vs. 6.3%; p<0.001), and false negatives with white race (34.0% vs. 19.8%; p<0.001).

Figure 1 shows the estimated sensitivity and specificity of HbA1c cutoffs from 31 mmol/mol (5.0%) to 48 mmol/mol (6.5%), to discriminate diabetes from non-diabetes and prediabetes. In discriminating diabetes from non-diabetes (Panels A and B), the optimal HbA1c cutoff using YI as the criterion was ≥42 mmol/mol (6.0%) with black (sensitivity: 76.9%; specificity: 86.7%) and ≥39 mmol/mol (5.7%) with white race (sensitivity: 70.7%; specificity: 85.0%). In discriminating diabetes from prediabetes (Panels C and D), the optimal HbA1c cutoff was ≥42 mmol/mol (6.2%) with black (sensitivity: 63.3%; specificity: 88.5%) and ≥39 mmol/mol (5.7%) with white race (sensitivity: 70.9%; specificity: 74.5%). In discriminating diabetes vs. non-diabetes, the HbA1c cutoff with the greatest accuracy was ≥6.9% (52 mmol/mol) with black (accuracy: 96.8%) and ≥6.3% (45 mmol/mol) with white race (accuracy: 96.6%) (Supplemental Table 2). In discriminating diabetes vs. prediabetes, the HbA1c cutoff with the greatest accuracy was ≥52 mmol/mol (6.9%) with black (accuracy: 91.8%) and ≥45 mmol/mol (6.3%) with white race (92.5%) (Supplemental Table 3).

Figure 2 shows the performance of HbA1c in distinguishing dysglycemia and prediabetes from normoglycemia. In discriminating dysglycemia from normoglycemia (Panels A and B), the optimal cutoff was ≥39 mmol/mol (5.7%) with black (sensitivity: 55.5%; specificity: 75.6%) and ≥37 mmol/mol (5.5%) with white race (sensitivity: 50.1%; specificity: 79.0%). In discriminating prediabetes from normoglycemia (Panels C and D), the optimal cutoff was ≥39 mmol/mol (5.7%) with black (sensitivity: 51.3%; specificity: 75.6%) and ≥37 mmol/mol (5.5%) with white race (sensitivity: 46.5%; specificity: 79.0%). The HbA1c cutoff with the greatest accuracy was ≥41 mmol/mol (≥5.9%) with black (accuracy: 69.3%) and ≥37 mmol/mol (5.5%) with white race (accuracy: 65.9%) (Supplemental Table 4). In discriminating prediabetes from normoglycemia, the HbA1c cutoff with the greatest accuracy was ≥41 mmol/mol (≥5.9%) with black (68.8%) and ≥5.6% (38 mmol/mol) in with white race (65.4%) (Supplemental Table 5). In sensitivity analyses, the findings were similar, even if black and white race were both given a diabetes prevalence of 4.8% or 5.3%, or a prediabetes prevalence of 44.8% or 50.2%. Receiver operating characteristic curves of HbA1c as a screening tool is provided in Supplemental Figure 1−2.

Table 2 summarizes the major findings. Compared to white race, YI 'optimal' HbA1c diagnostic values with black race were 3 mmol/mol (0.3%) higher for diabetes, 2 mmol/mol (0.2%) higher for dysglycemia, and 2 mmol/mol (0.2%) higher for prediabetes. Supplemental Tables 2−5 provide sensitivity, specificity, accuracy, and false positive and false negative rates for a wider range of HbA1c cutoffs [31 mmol/mol (5.0%) to 53 mmol/mol (7.0%)] for each of the four discriminant analyses above.

## DISCUSSION

In a representative sample of US adults, using an unbiased criterion, we found that optimal discrimination of ADA glucose-defined diabetes and prediabetes using HbA1c cutoffs requires values that are 2 mmol/mol (0.2%) to 5 mmol/mol (0.5%) higher with black than with white race – 3 mmol/mol (0.3%), 5 mmol/mol (0.5%), 2 mmol/mol (0.2%), and 2 mmol/mol (0.2%) higher for diabetes vs. non-diabetes, diabetes vs. prediabetes (excluding normoglycemia), dysglycemia vs. normoglycemia, and prediabetes vs. normoglycemia, respectively. When the current ADA HbA1c thresholds were used to diagnose diabetes, black race had 6.3 times the rate of false positives as white race, while white race had 1.3 times the rate of false negatives as black race. These differences are consistent with higher HbA1c levels with black vs. white race at similar glucose levels – in our study, 2 mmol/mol (0.22%) higher, after adjustment for age, sex, and BMI. Despite the tendency for higher HbA1c with black vs. white race, significant variation in HbA1c levels vs. glucose levels has been observed with both black and white race (7). Thus, a more personalized approach may be needed, to improve the accuracy of HbA1c levels as a reflection of underlying glucose levels.

It seems likely that our findings result from "mismatches" of HbA1c vs. glucose levels, which tend to be higher with black compared to white race in the US. "Mismatches" can be high or low, with low "mismatches" in patients with sickle cell trait (14) and glucose-6-phosphate dehydrogenase (G6PD) variants (15), and high "mismatches" with black vs. white race with impaired glucose tolerance in the US Diabetes Prevention Program (16). In a separate analysis of both NHANES and the Screening for Impaired Glucose Tolerance studies, we found that HbA1c with black vs. white race was about 1.1 mmol/mol (0.1%) to 2.2 mmol/mol (0.2%), 2.2 mmol/mol (0.2%) to 3.3 mmol/mol (0.3%), and 4.4 mmol/mol (0.4%) to 5.5 mmol/mol (0.5%) higher in individuals with normal glucose tolerance, prediabetes, and diabetes, respectively (4); Lachin also reported that "mismatches" are glycemia-dependent (17). In the Action to Control Cardiovascular Risk in Diabetes (ACCORD) study, in tertiles based on HbA1c relative to FPG, black race comprised 22%, 32%, and 46% of the low, medium, and high "mismatch" tertiles, respectively (9). The tendency of high "mismatches" with black race was also found with continuous glucose monitoring (7).

Our findings of more false positives with black and more false negatives with white race are also consistent with previous reports. Olson et al. (8) observed that blacks had significantly higher false positive rates for diabetes and prediabetes than whites, while false negative diagnoses were more common in whites. Herman and Cohen (18) came to similar conclusions with different datasets.

In addition to the potential diagnostic impact of high “mismatches” in HbA1c vs. glucose with black vs. white race, the tendency may also affect management. To the extent that intensification of therapy is guided by HbA1c more than by glucose levels (9), a “high” mismatch would be expected to increase the risk of hypoglycemia; an increased frequency of severe hypoglycemia with black vs. white race was observed in the ACCORD and SUPREME-DM studies (9; 10), and in Medicare populations (11). In a joint position statement, the ADA and the European Association for the Study of Diabetes (19) also noted the increased risk of hypoglycemia with black vs. white race – a health disparity.

Our findings provide further evidence that an individualized approach may be needed when using HbA1c for diagnosis and management. Despite the tendency of black race to be associated with a *high* “mismatch” of HbA1c relative to glucose, there is also extensive variation in “mismatches” of HbA1c vs. glucose within both black and white groups (9). “Mismatches” may be due to differences in mean red blood cell age (MRBC), since erythrocytic processes may be involved (20), heterogeneity in MRBC appears to be sufficient to account for differences in HbA1c, and measured “mismatches” are consistent with variability in MRBC (21). Because of such variability, providers need to consider for each patient whether HbA1c levels appear to be relatively high or low relative to glucose levels, and glucose measurements should be used to confirm diagnoses rather than relying only on HbA1c, consistent with recent US Veterans Administration and Department of Defense (VA/DoD) guidelines when HbA1c levels are 48 mmol/mol (6.5%) to 52 mmol/mol (6.9%) (22).

The strengths of this study include a large sample representative of the US population, a standardized protocol, and measurement of FPG, OGTT 2hPG, and HbA1c with state-of-the-art procedures. Limitations include the inability to include analyses of participants *taking* diabetes medications because they did not have OGTTs. While we were unable to carry out sensitivity analyses with/without such individuals, we were able to conduct analyses with/without individuals with self-reported diabetes *not taking* diabetes medications (n=41),who had higher average HbA1c (42 mmol/mol; 5.95%) than the analytical sample (35 mmol/mol; 5.38%). Upon their exclusion, the ‘optimal’ YI-based cutoff for diabetes vs. nondiabetes with black race was decreased by 0.2%, without other changes in ‘optimal’ cutoffs, suggesting that excluding those with higher HbA1c values lowers the ‘optimal’ HbA1c cutoff for discriminating diabetes from nondiabetes with black race. Since those with self-reported diabetes *and* use of diabetes medications (n=688) had an average HbA1c that was even higher (7.47%, 58 mmol/mol), these observations suggest that excluding those with self-reported diabetes and use of diabetes medications may have *lowered* the difference in ‘optimal’ HbA1c cutoffs for discriminating diabetes vs. nondiabetes with black vs. white race.

Additionally, we used the FPG and OGTT 2hPG as referent measures of disease status. Although the OGTT has limited reproducibility (23), the reproducibility of FPG is better (24), joint use in combination improves diagnostic classification (25), and variation in both measures would have been included in our findings. Second, cutoffs were calculated without accounting for sampling uncertainty in estimated sensitivity and specificity. Third, the intent of diagnosis is early identification to permit preventive management, but it is not known

whether differences in cutoffs would correspond to differences in development of complications. Current diagnostic thresholds are based largely on the risk of retinopathy (26), but existing studies may not have had sufficient power to distinguish differences according to race/ethnicity (27; 28). Although it has been suggested that HbA1c, via "glycation", may have glucose-independent effects on the risk of micro- and macro- vascular complications (29), the putative effects of a "glycation gap" on complications have been disproved by subsequent analyses (17). Fourth, the majority of those who self-identify as having black race in the US are thought to have African ancestry, but additional studies will be needed to verify the generalizability of our findings to populations outside the US. Finally, while YI is independent of disease prevalence, and widely used for evaluating diagnostic tests (30), it does not take into account whether sensitivity or specificity might be considered to be more important.

In conclusion, we found that the current HbA1c diagnostic cutoffs for diabetes and prediabetes produce differential classification of people with black vs. white race who have similar underlying glucose levels, with more false positives with black and more false negatives with white race; HbA1c-based classification was optimized at cutoffs that were 2 mmol/mol (0.2%) to 5 mmol/mol (0.5%) higher with black vs. white race. These findings appear to be due to differences in the relationship between HbA1c and glucose with black and white race, and point to the need for new approaches to improve the accuracy of HbA1c as a reflection of underlying glucose in both groups. In the interim, consideration could be given to determining how HbA1c relates to glucose in individual patients, to help guide both diagnosis and management.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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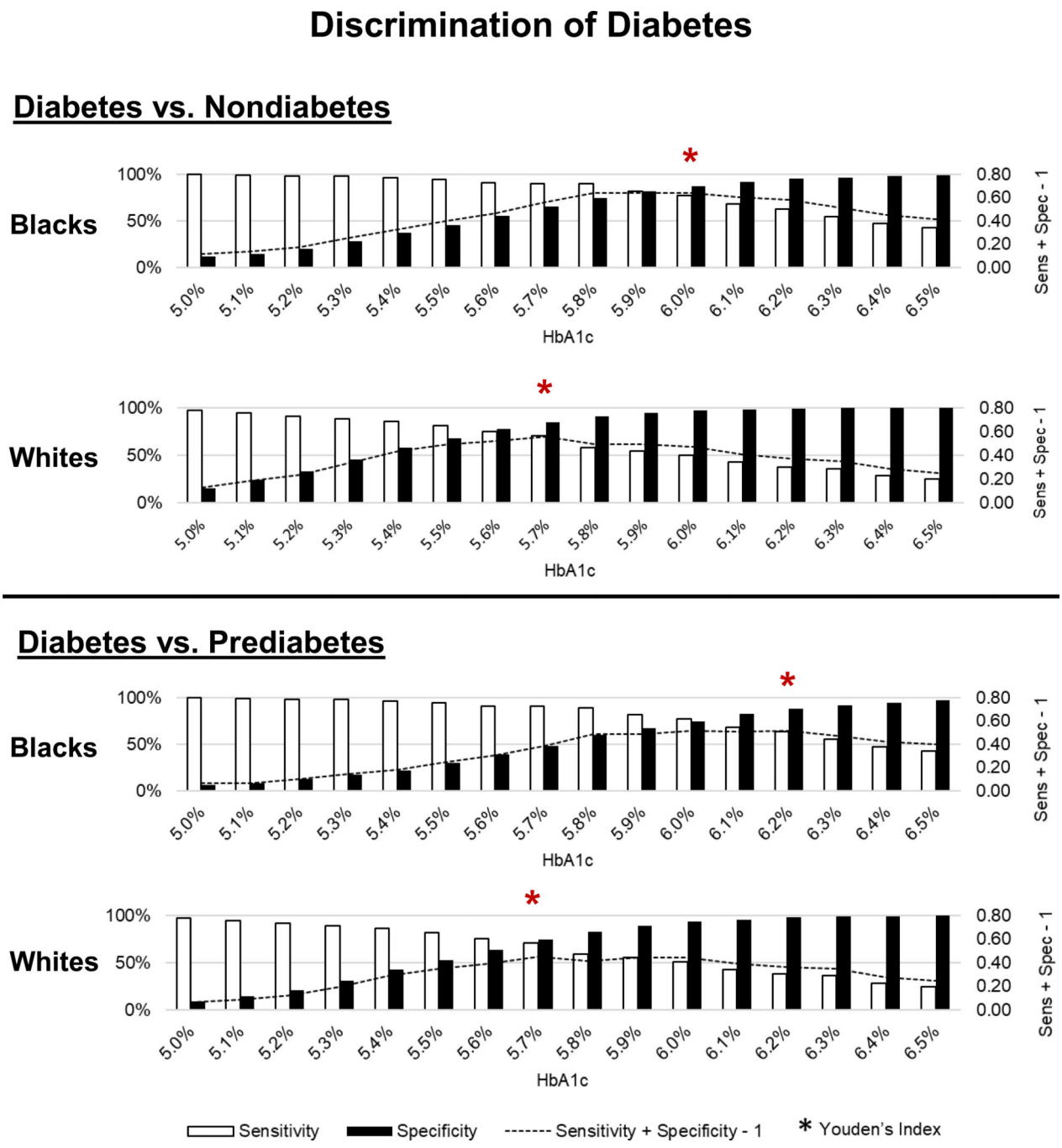


**Figure 1.**

Panel A: Sensitivity, specificity, [sensitivity + specificity – 1], and Youden's Index for HbA1c-based classifica-tion of diabetes in Black respondents regardless of glycemic status. Panel B: Sensitivity, specificity, [sensitivity + speci-ficity – 1], and Youden's Index for HbA1c-based classification of diabetes in White respondents regardless of glycemic status. Panel C: Sensitivity, specificity, [sensitivity + specificity – 1], and Youden's Index for HbA1c-based classification of diabetes in Black respondents, excluding those with normoglycemia as determined by FPG <100 mg/dL *and* 2hPG <140 mg/dL. Panel D:

Sensitivity, specificity, [sensitivity + specificity – 1], and Youden's Index for HbA1c-based classifi-cation of diabetes in White respondents, excluding those with normoglycemia as determined by FPG <100 mg/dL *and* 2hPG <140 mg/dL. Youden's Index corresponds to value at which [sensitivity + specificity – 1] was greatest.

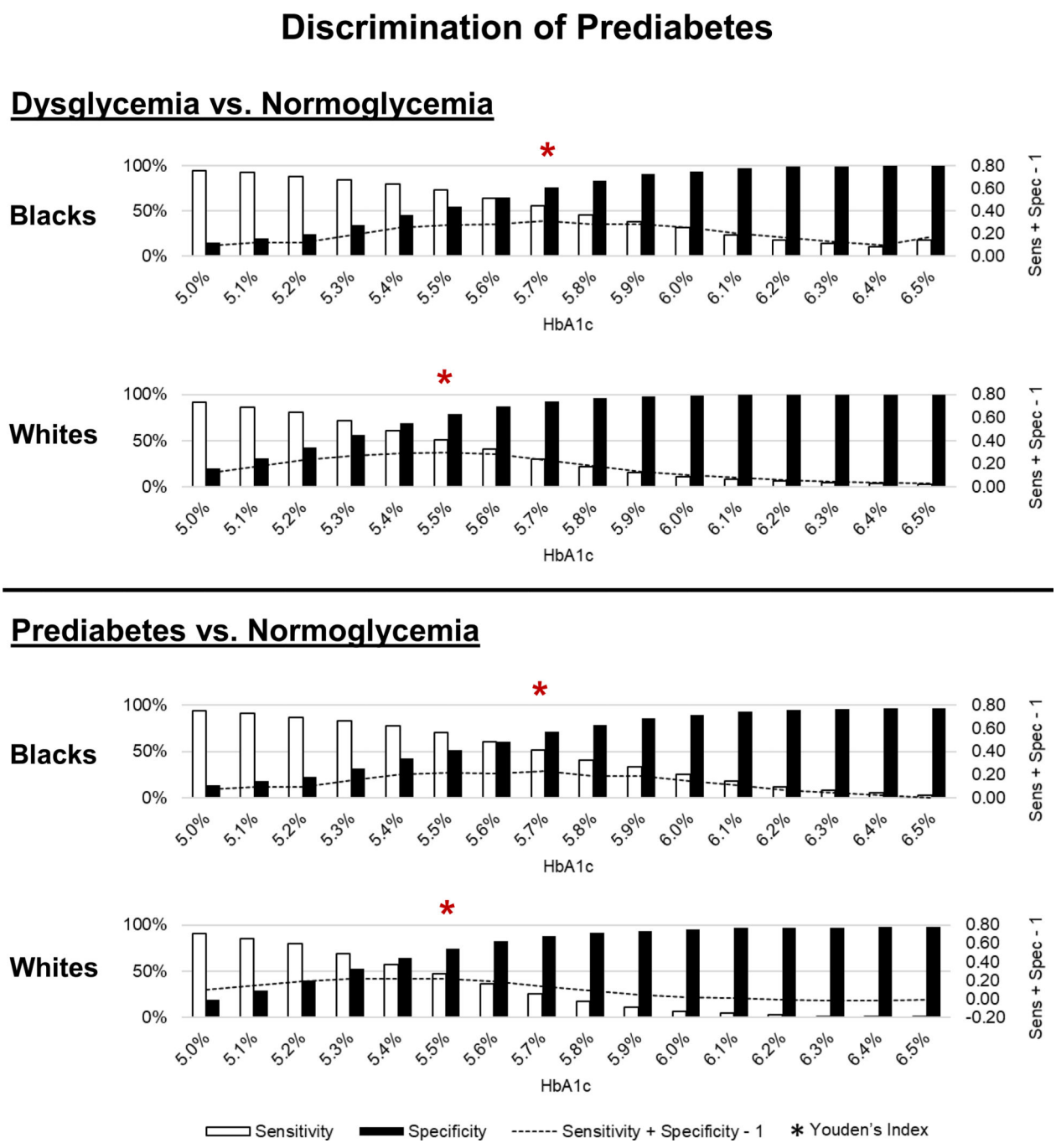


**Figure 2.**

Panel A: Sensitivity, specificity, [sensitivity + specificity – 1], and Youden's Index for HbA1c-based classifica-tion of dysglycemia (defined as ≥126 mg/dL *or* 2hPG ≥140 mg/dL) in Black respondents. Panel B: Sensitivity, specificity, [sensitivity + specificity – 1], and Youden's Index for HbA1c-based classification of dysglycemia (defined as ≥126 mg/dL *or* 2hPG ≥140 mg/dL) in White respondents. Panel C: Sensitivity, specificity, [sensitivity + specificity – 1], and Youden's Index for HbA1c-based classification of prediabetes in Black respondents regardless of glycemic status. Panel D: Sensi-tivity, specificity, [sensitivity +

specificity – 1], and Youden's Index for HbA1c-based classification of prediabetes in White respondents regardless of glycemic status. Youden's Index corresponds to value at which [sensitivity + specificity – 1] was greatest.

**Table 1.**

Sample characteristics [*]

| | Overall | Non-Hispanic black | Non-Hispanic white | *P*-value |
|---|---|---|---|---|
| N | 5,324 | 1,721 (32.3%) | 3,603 (67.7%) | |
| Age, years | 41.8 (0.3) | 39.7 (0.4) | 43.3 (0.4) | < 0.001 |
| BMI, kg/m$^2$ | 28.5 (0.1) | 30.1 (0.2) | 28.3 (0.1) | < 0.001 |
| HbA1c, % | 5.38% (0.01%) | 5.53% (0.01%) | 5.34% (0.01%) | |
| mmol/mol | 35.0 (0.1) | 37 (0.1) | 35 (0.1) | < 0.001 |
| Fasting plasma glucose, mg/dL | 99.2 (0.3) | 97.9 (0.5) | 98.9 (0.3) | |
| mmol/L | 5.5 (0.0) | 5.4 (0.0) | 5.5 (0.0) | 0.049 |
| Two hour plasma glucose, mg/dL | 111.2 (0.7) | 109.5 (1.2) | 109.9 (0.9) | |
| mmol/L | 6.2 (0.0) | 6.1 (0.1) | 6.1 (0.0) | 0.792 |
| Diabetes by glucose levels [†], % | 5.2% (0.3%) | 5.3% (0.6%) | 4.8% (0.4%) | 0.530 |
| Prediabetes by glucose levels [‡], % | 45.8% (0.8%) | 50.2% (1.4%) | 44.8% (1.1%) | 0.003 |
| Diabetes by HbA1c levels [†], % | 1.8% (0.2%) | 2.9% (0.3%) | 1.3% (0.2%) | <0.001 |
| Prediabetes by HbA1c levels [‡], % | 18.9% (0.5%) | 33.9% (1.2%) | 16.3% (0.7%) | <0.001 |
| Misclassified by HbA1c [§], % | 37.9% (0.9%) | 35.4% (1.4%) | 38.2% (1.2%) | 0.105 |
| Combined false positive rate, % | 7.8% (0.3%) | 17.6% (1.1%) | 6.3% (0.4%) | <0.001 |
| False positive rate for diabetes, % | 0.3% (0.1%) | 1.1% (0.2%) | 0.1% (0.1%) | < 0.001 |
| False positive rate for prediabetes, % | 7.6% (0.3%) | 16.5% (1.0%) | 6.2% (0.4%) | < 0.001 |
| Combined false negative rate, % | 32.2% (0.9%) | 19.8% (1.1%) | 34.0% (1.2%) | <0.001 |
| False negative rate for diabetes, % | 3.4% (0.3%) | 2.4% (0.4%) | 3.5% (0.4%) | 0.076 |
| False negative rate for prediabetes, % | 28.8% (0.8%) | 17.4% (0.9%) | 30.5% (1.1%) | < 0.001 |

Abbreviations: BMI, body mass index; HbA1c, hemoglobin A1c; kg, kilograms; m, meters.

[*] Values are given as survey-weighted means and standard errors, shown in parentheses.

[†] Diabetes by glucose levels was defined as FPG ≥7.0 mmol/L (126mg/L), or 2hPG ≥11.1 mmol/L (200 mg/dL).

[‡] Prediabetes by glucose levels was defined as FPG of 5.6 mmol/L (100 mg/dL) to 6.9 mmol/L (125 mg/dL) or 2hPG of 7.8 mmol/L (140 mg/dL) to 11.0 mmol/L (199 mg/dL) and no glucose levels in the diabetes range. Diabetes and prediabetes by HbA1c levels were defined as ≥6.5% (48 mmol/mol) and 5.7–6.4% (39–46 mmol/mol), respectively.

[§] Misclassified was defined as discordance in diabetes or prediabetes diagnosis by HbA1c vs. glucose levels, using ADA guidelines.

**Table 2.**

Summary of HbA1c cutoffs at which Youden's Index (YI [sensitivity + specificity − 1]) was maximized[†]

| | Non-Hispanic blacks (n = 1,721) | | | Non-Hispanic whites (n = 3,603) | | | Difference (blacks - whites) | | |
|---|---|---|---|---|---|---|---|---|---|
| | Cutoff | Sensitivity | Specificity | Cutoff | Sensitivity | Specificity | Cutoff | Sensitivity | Specificity |
| Classification of diabetes in eligible sample[‡] | 42 | 76.9% | 86.7% | 39 | 70.7% | 85.0% | 3 | 6.2% | 1.7% |
| Classification of diabetes, excluding those with normoglycemia[‖] | 44 | 63.3% | 88.5% | 39 | 70.9% | 74.5% | 5 | −7.6% | 14.0% |
| Normoglycemia vs. Prediabetes[§]/Diabetes (dysglycemia)[¶] | 39 | 55.5% | 75.6% | 37 | 50.1% | 79.0% | 2 | 5.4% | −3.4% |
| Classification of prediabetes, excluding those with diabetes | 39 | 51.3% | 75.6% | 37 | 46.5% | 79.0% | 2 | 4.8% | −3.4% |

Abbreviations: HbA1c, hemoglobin A1c; YI, Youden's Index

[†]Values are given as HbA1c%

[‡]Diabetes was defined as having a fasting plasma glucose concentration ≥7.0 mmol/L (126 mg/dL) *or* a 2-hour plasma glucose concentration ≥11.1 mmol/L (200 mg/dL)

[‖]Normoglycemia was defined as having a fasting plasma glucose concentration <5.6 mmol/L (100 mg/dL) *and* a 2-hour OGTT plasma glucose concentration <7.8 mmol/L (140 mg/dL)

[§]Prediabetes was defined as FPG of 5.6 mmol/L (100 mg/dL) to 6.9 mmol/L (125 mg/L) or 2hPG of 7.8 mmol/L (140 mg/dL) to 11.0 mmol/L (199 mg/dL) and no glucose levels in the diabetes range

[¶]Dysglycemia was defined as having a fasting plasma glucose concentration ≥5.6 mmol/L (100 mg/dL) *or* a 2-hour OGTT plasma glucose concentration ≥7.8 mmol/L (140 mg/dL)