HbA₁c Performance in African Descent Populations in the United States With Normal Glucose Tolerance, Prediabetes, or Diabetes: A Scoping Review

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Abstract

Introduction
African descent populations in the United States have high rates of type 2 diabetes and are incorrectly represented as a single group. Current glycated hemoglobin A₁c (HbA₁c) cutoffs (5.7% to <6.5% for prediabetes; ≥6.5% for type 2 diabetes) may perform suboptimally in evaluating glycemic status among African descent groups. We conducted a scoping review of US-based evidence documenting HbA₁c performance to assess glycemic status among African American, Afro-Caribbean, and African people.

Methods
A PubMed, Scopus, and Cumulative Index to Nursing and Allied Health Literature (CINAHL) search (January 2020) yielded 3,238 articles published from January 2000 through January 2020. After review of titles, abstracts, and full texts, 12 met our criteria. HbA₁c results were compared with other ethnic groups or validated against the oral glucose tolerance test (OGTT), fasting plasma glucose (FPG), or previous diagnosis. We classified study results by the risk of false positives and risk of false negatives in assessing glycemic status.

Results
In 5 studies of African American people, the HbA₁c test increased risk of false positives compared with White populations, regardless of glycemic status. Three studies of African Americans found that HbA₁c of 5.7% to less than 6.5% or HbA₁c of 6.5% or higher generally increased risk of overdiagnosis compared with OGTT or previous diagnosis. In one study of Afro-Caribbean people, HbA₁c of 6.5% or higher detected fewer type 2 diabetes cases because of a greater risk of false negatives. Compared with OGTT, HbA₁c tests in 4 studies of Africans found that HbA₁c of 5.7% to less than 6.5% or HbA₁c of 6.5% or higher leads to underdiagnosis.

Conclusion
HbA₁c criteria inadequately characterizes glycemic status among heterogeneous African descent populations. Research is needed to determine optimal HbA₁c cutoffs or other test strategies that account for risk profiles unique to African American, Afro-Caribbean, and African people living in the United States.

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Introduction

People of African descent in the United States have a disproportionate burden of type 2 diabetes; prevalence is higher in African descent populations, 14%, compared with White populations of European descent (White populations), 9% (1). Additionally, African descent populations are represented as a single group, despite being comprised of African American (91%), Afro-Caribbean (4.7%), and African (3.7%) people (2,3). Limited evidence examines how intraethnic differences in cardiometabolic risk criteria, social determinants of health, and genetic admixture affect diabetes risk in these 3 populations (4,5). Current glycated hemoglobin A1c (HbA1c) cutoffs (HbA1c 5.7% to less than 6.5% for prediabetes; HbA1c of 6.5% or higher for type 2 diabetes), determined from predominantly White population cohorts (4–8), may perform suboptimally in evaluating glycemic status in this diverse population of African American, Afro-Caribbean, and African populations (9–12). African American people may have higher HbA1c values across the glycemic spectrum (9,13), and African immigrants may have lower HbA1c values compared with White people (14). To ensure accurate detection of type 2 diabetes, there is a need to understand the ability of HbA1c to correctly classify type 2 diabetes status and to evaluate intraethnic variation among African American, Afro-Caribbean, and African people (15–17).

Compared with random glucose, fasting plasma glucose (FPG), and the 2-hour oral glucose tolerance test (OGTT), HbA1c has multiple benefits. It does not require fasting, tracks plasma glucose over the preceding 2 to 3 months, and better predicts complications such as cardiovascular disease (4,18). The HbA1c test is stable, unaffected by external variables (eg, exercise, recent meals, and environmental stressors), and easily added to blood tests (19,20). However, interpretation of HbA1c results is affected by the reduced lifespan of red blood cells in patients with type 2 diabetes, anemia, and hemoglobinopathies, conditions which disproportionately affect African descent populations (21–25).

The goal of our study was to conduct a scoping review of US-based peer-reviewed evidence documenting HbA1c performance in African American, Afro-Caribbean, and African populations in the United States with the objectives of 1) summarizing evidence on HbA1c performance in each subethnic group; 2) demonstrating variations in HbA1c performance by each subethnic group; and 3) identifying potential future areas of research.

Methods

Data sources

In early January 2020, we searched PubMed, Scopus, and Cumulative Index to Nursing and Allied Health Literature (CINAHL) for peer-reviewed studies published between January 1, 2000, and January 1, 2020, by using complex search strings that were tested and developed in partnership with our institution’s health sciences librarian (L.A.F.). The search string included medical subject headings (MeSH) terms and key words such as “African continental ancestry group,” “African Americans,” “Caribbean,” and “West Indian” to describe population groups and “Glycated Hemoglobin A,” “hemoglobin A1c,” and “hba1c” to describe the testing indicator of interest for type 2 diabetes (Appendix).

Study selection

Throughout the review process, we screened articles for studies meeting the following inclusion criteria:

1. Articles were original studies published between January 2000 and January 2020, that evaluated HbA1c performance in African descent groups.
2. Study populations included African Americans, Afro-Caribbeans, or Africans.
3. Study participants were living in the United States.
4. Study was a database analysis, epidemiologic study, or clinical study.
5. HbA1c performance was reported specifically in one or more of the African descent groups.
6. HbA1c performance was assessed in healthy populations or for screening or diagnosis of prediabetes or type 2 diabetes.
7. HbA1c performance was assessed by statistical methods (eg, sensitivity, specificity, and positive predictive value), compared with other tests in the same population, or compared African descent populations to other racial groups.

During the study selection process, we included studies that compared various diabetes screening tests against HbA1c, including the OGTT, FPG, and glycated protein tests, to avoid excluding major findings. Although the OGTT is considered optimal for comparison, it is far more costly, resource intensive, and time consuming than the FPG and glycated protein tests (6–8); additionally, research supports the use of other tests along with OGTT or in place of OGTT to enhance detection of diabetes (7,18–22). Because African descent populations are less likely to be adequately represented in clinical research and simultaneously experience health care inequities (4,19), we wanted to be inclusive of all the data, in comparison to HbA1c, that were available for the populations.

On the basis of the title and abstract review, we excluded articles that did not match the set inclusion criteria above (Figure). Two authors (L.K. and S.B.) conducted independent title and abstract reviews. In the full-text review, we excluded articles with insufficient data (eg, case studies), narrative reviews, and articles that fell under a previously set exclusion criterion not detected during the title and abstract review. Full-text articles for potential studies...
were reviewed by 2 authors (L.K. and S.B.) independently. When multiple exclusion criteria were met, we categorized the article by the exclusion criterion that appeared first in title, abstract, or full text review. A third author (M.H.R.) verified that the exclusion criteria were relevant throughout the article.

Data extraction

We created a data extraction sheet to record the study author and name, populations (sample size, male/female breakdown, race/ethnicity distribution, age, and study location), HbA1c laboratory methods, study design, HbA1c evaluation methods, findings, and HbA1c performance. We successfully retrieved any missing information by 1) searching through cited articles from which the studies retrieved data; 2) identifying parent studies and protocol descriptions given in prior publications; and 3) emailing corresponding authors. HbA1c performance was classified using 2 labels: 1) greater risk of false positive (GRFP) label indicated that the HbA1c test may result in overdetection of glycemic status (eg, type 2 diabetes) that the study is measuring or 2) greater risk of false negatives (GRFN) label indicated that the HbA1c test may result in underdetection of glycemic status. This classification system (GRFP or GRFN) was based on text analysis of the language used by the authors of each study in the way they interpreted their results (eg, lower sensitivity, lower specificity, more misdiagnoses). This allowed for standardization of labeling findings from different study designs. GRFP was assigned if studies reported 1) higher HbA1c values in African descent participants compared with other ethnic groups (eg, White participants) at the same glycemic level; 2) lower sensitivity because of less true positives; or 3) lower specificity because of more false positives. GRFN was assigned if studies reported 1) lower HbA1c values in participants compared with other ethnic groups at same glycemic level; 2) lower sensitivity because of more false negatives; or 3) lower specificity because of less true negatives. Discrepancies in the review process and data extraction were resolved with input from a third author (M.H.R.).

Included studies were grouped based on study population (African American, Afro-Caribbean, and African) and then organized in alphabetical order by the first author’s last name. Studies were labeled numerically as 1 through 12 based on this ordering.

Results

Of the 12 articles that met the inclusion criteria, studies numbered 1 through 7 analyzed HbA1c performance among African American people (26-32), study number 8 analyzed HbA1c performance among Afro-Caribbean people (33), and studies numbered 9 through 12 analyzed HbA1c performance among African people
In the Afro-Caribbean population, HbA1c testing at the 6.5% or higher cutoff has a GRFN (33). Using FPG as a standard for diagnosis of type 2 diabetes, study 8 showed that more participants were correctly diagnosed as having type 2 diabetes if the cutoff was lowered to 6.26% or higher, suggesting that HbA1c values are generally lower in Afro-Caribbean people (Table 2).

The Africans in America studies 9 through 12 all showed that HbA1c has a GRFN in African people at the HbA1c cutoff of 5.7% to less than 6.5% for prediabetes and HbA1c cutoff of 6.5% or higher for type 2 diabetes (34–37). Using OGTT as a diagnostic standard for glycemic status, studies 9 through 12 demonstrated that using an HbA1c cutoff of 5.7% to less than 6.5% will lead to underdiagnosis of prediabetes in Africans. Additionally, study 9 showed that using an HbA1c cutoff of 6.5% or higher will lead to an underdiagnosis of type 2 diabetes in Africans (34) (Table 2).

Discussion

We assessed 12 studies that evaluated the ability of HbA1c to correctly identify African American, Afro-Caribbean, and African people with prediabetes or type 2 diabetes. Studies among African American people found that HbA1c of 5.7% to less than 6.5% or HbA1c of 6.5% or higher led to underdiagnosis. In one study of Afro-Caribbean people, HbA1c of 6.5% or higher had a greater risk of false negatives (GRFN). Among African people, HbA1c of 5.7% to less than 6.5% or HbA1c of 6.5% or higher led to greater risk of underdiagnosis.

Overdiagnosis of diabetes was likely among African American people in 3 ways. African American people had consistently higher HbA1c levels than White people regardless of glycemic status (26,27,29,30,32). Furthermore, half of normoglycemic African American people had HbA1c values greater than 5.7% (28); and lastly, African American people were more likely to be diagnosed with type 2 diabetes by HbA1c of 6.5% or higher alone but not by OGTT (29,31). Although study 6 did suggest a GRFN at HbA1c less than 5.7%, by misdiagnosing some participants as having normal glycemic status if their HbA1c was less than 5.7% (31), the finding is limited by the smaller sample size of 83 participants when compared with the other studies. This finding must be investigated further.

In Afro-Caribbean people, the HbA1c cutoff of 6.5% is likely to result in underdiagnosis of type 2 diabetes because study 8 showed that more participants were correctly diagnosed as having type 2 diabetes if the cutoff was lowered to 6.26% (33). However, this finding may not be generalizable to other Afro-Caribbean populations because of the smaller sample size and limitation of the study population to Haitian American people. Additionally, because only 1 study provided this conclusion, generalizability is further limited. For African people, underdiagnosis of prediabetes and...
type 2 diabetes is also likely at the standard HbA$_{1c}$ cutoffs because diagnosis was missed by HbA$_{1c}$ despite being detected by OGTT (34–37). The findings among African people hold true regardless of hemoglobin variant or obesity status (35,36).

Genetics are often thought to be responsible for the differences of HbA$_{1c}$ performance in African descent populations (24,40–43). In fact, genetic analysis in study 5 shows that the HbA$_{1c}$ difference was primarily because of the genomic principal component analysis (PCA) factor in African American people when compared with White people (30). The study demonstrated that the PCA factor was associated with increased HbA$_{1c}$ values in African American people. However, genetics do not fully explain HbA$_{1c}$ differences among African American people (44), because increases in HbA$_{1c}$ may be mediated by social determinants of health (eg, chronic financial strain as seen in study 3) or chronic inflammation (sIL-6R) (28,45). Additionally, G6PD variant or deficiency is often correlated with lower HbA$_{1c}$ values in various populations (40), especially in African American people and African people because of its higher prevalence in these groups (14,46,47). Similarly, the sickle cell trait is associated with lower HbA$_{1c}$ values in African descent populations (21,25). However, study 1 showed that the sickle cell trait may not actually correlate to changes in HbA$_{1c}$ values for African American people (26). Findings regarding associations of genetics with HbA$_{1c}$ are still being researched in this population. Research accounting for genetically linked HbA$_{1c}$ differences in Afro-Caribbean people is also lacking. Genetic polymorphisms between African American people and Haitian people have been researched and show that differences in the PPARGC1A gene will correlate to risk of type 2 diabetes in African American people as opposed to protective associations with type 2 diabetes in Haitian people, suggesting that other genetic associations may explain differences in diabetes for Haitian people (48). Although little research explains the role of genetics in HbA$_{1c}$ differences for Haitian people, one likely contributor to lower HbA$_{1c}$ values may be the G6PD variant because of its higher prevalence in populations of African descent (47). Nevertheless, opposing findings regarding the role of genetics in influencing HbA$_{1c}$ values (eg, PCA factor is associated with higher HbA$_{1c}$ whereas the sickle cell trait is associated with lower HbA$_{1c}$) make it difficult to ascertain the overall impact genetics has in causing the differences in HbA$_{1c}$ that were found for the African descent populations and therefore require further evaluation.

Socioeconomic factors and health behaviors such as diet, smoking, and exercise may explain some differences in glycemic control and HbA$_{1c}$ values among the 3 groups. Higher income and educational attainment appear to decrease the odds of diabetes among African immigrants, whereas only higher education lowers the odds for African American people (5). Neither education nor income appear to affect diabetes risk among Afro-Caribbean people (5,49). Additionally, study 3 found that financial stress and chronic inflammation were associated with higher HbA$_{1c}$. Chronic inflammation resulting from social and environmental stressors, including experiences of racism, correlate to higher HbA$_{1c}$ in non-diabetic adults (50). In terms of health behaviors, compared with African American people, African and Afro-Caribbean people are less likely to smoke. As African and Afro-Caribbean immigrants settle in the United States, they are affected by dietary acculturation often characterized by increased caloric intake and diets higher in refined carbohydrates, animal protein, fat, and sodium (5). Although diet may affect glycemic control, it is unlikely that diet explains the differences in HbA$_{1c}$ performance illustrated in this study. These socioeconomic factors highlight the diversity of experience within African descent groups, which is often overshadowed by perceived homogeneity of the “Black” experience in the United States. Since immigration to the United States presents unique socioeconomic circumstances that can affect factors like HbA$_{1c}$ (4), impacts of these circumstances are important to analyze distinctly from global concerns.

With these factors affecting HbA$_{1c}$ performance, results must be interpreted with caution. Some alternative diagnostic tests are suggested to aid or replace HbA$_{1c}$ for classification of glycemic status. For example, FPG in combination with HbA$_{1c}$ increases the sensitivity for type 2 diabetes diagnosis in African people (study 10) (35). A stronger relationship between HbA$_{1c}$ and FPG at higher FPG levels in most ethnic groups has been suggested as well (51). Study 8 suggests that FPG may be a better measure of glycemic status than HbA$_{1c}$ in Afro-Caribbean people (33). At the same time, studies 3, 6, and 9 through 12 suggest that OGTT more accurately measures glycemic status than HbA$_{1c}$ in both African American and African people (28,31,34–37). Comparisons between HbA$_{1c}$ and OGTT in Afro-Caribbean people are lacking and should be studied further.

Convenient nonfasting alternatives for type 2 diabetes testing are other glycated proteins (eg, glycated albumin, fructosamine, and other advanced glycation end products) either in combination with or in place of HbA$_{1c}$ (36,37,52–55). Although this approach is supported in multiethnic studies, these glycated proteins should be evaluated specifically in African descent groups.

Several limitations exist for the findings of our review. Despite constructing a comprehensive search, articles published in peer-reviewed journals that were not indexed in PubMed, Scopus, and CINAHL may have been missed. The search contained nouns and adjectives as identification for African descent countries and regions of origin and HbA$_{1c}$ testing. However, study participant groups may be based on self or researcher categorization rather than actual region, country, or ethnic group of the participant.
Findings must be interpreted with caution because of this subjective labeling within studies. Additionally, we did not use a specific protocol to evaluate the quality of the included studies, as this is not a part of scoping review methodologies and can increase risk of bias (56,57). Another limitation that must be considered is that time may pass between HbA1c testing and alternate testing in some studies and glycemic status of individuals can change in that time; this limitation will usually exist in this nature of clinical research methodology and therefore must be recognized when evaluating the conclusions from those studies.

According to our review process, there is only 1 study protocol in the United States that examines performance of diabetes screening tests among African immigrants to the United States (34–37). However, studies 9 through 12 demonstrate distinct comparisons within this cohort that illustrate significant conclusions about HbA1c performance. This is because the protocol is ongoing, and the number of participants increased over time. In turn, this also lends strength to the findings, because the similarity in protocol is balanced by the increasing diversity of the sample for each study design.

Finally, the lack of existing studies for Afro-Caribbean people in the United States presents a substantial limitation; our findings for this group must be interpreted cautiously. Further research is needed to understand the performance of HbA1c and evaluate alternate tests in place of the HbA1c in specific African descent populations, especially Afro-Caribbean people. Unique settings like New York City, where 32% of the African descent population is Afro-Caribbean and 4% is African (58), may serve as key locations for public health researchers to investigate type 2 diabetes screening and diagnostics.

Our review also has several strengths. In partnership with our institution’s research librarian, we tested several search constructions and selected the searches that provided the broadest selection within the scope of our topic. Additionally, we searched 3 databases without limiting article type or study designs on title and abstract review and had 2 reviewers independently screen the articles. This improved the selection of articles available for review and reduced selection bias. Finally, we were able to provide clear findings by constructing a label categorization scheme (GRFP/GRFN) that allowed for grouping of studies that used different comparative analytic and statistical methods to analyze HbA1c.

In African descent populations in the United States, the utility of HbA1c is limited in screening for glycemic status, determining care methods, assessing risk of type 2 diabetes complications, or analyzing health disparities. Current HbA1c cutoffs for prediabetes and type 2 diabetes may overestimate glycemic status in African American people and underestimate glycemic status in Afro-Caribbean and African people. Reasons for variations in HbA1c have been attributed to genetic, biochemical, and socioeconomic factors. Alternate testing such as OGTT, FPG, and other glycated blood proteins in place of or in combination with HbA1c may better assess glycemic status in African descent populations. Intraethnic HbA1c heterogeneity within the African descent groups must be recognized, and identification of more reliable type 2 diabetes screening and diagnostic tests is urgent.

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### Table 1. Study Characteristics for Articles Reporting on Glycated Hemoglobin A1c (HbA1c) Performance Among African Descent Populations Living in the United States, 2010–2019

| Study | First Author (Year); Study | N; Sex | Race/Ethnicity\(^a\) (%) | Age, y | Location | Study Design | HbA1c Laboratory Analysis Method |
|-------|-----------------------------|--------|---------------------------|--------|----------|-------------|----------------------------------|
| African American | | | | | | | |
| 1 | Bleyer (2010) (26) | N = 885; 43.2% male and 56.8% female | 43.5% African American; 56.5% White | ≥18 | Winston-Salem, North Carolina | Clinical; retrospective study | Cation-exchange column chromatography on an automated HPLC instrument (Variant II Turbo, Bio-Rad Laboratories). |
| 2 | Carson (2016); CARDIA study (27) | N = 2,692; 45.5% male and 54.5% female | 44% African American; 56% White | Mean (SD): 45.3 (3.6) | Minneapolis, Minnesota; Chicago, Illinois; Birmingham, Alabama; Oakland, California | Database analysis | Whole blood aliquot by ion-exchange HPLC using a Tosoh G7 (Tosoh Bioscience). |
| 3 | Cutrona (2015); FACHS (28) | N = 312; 100% female | 100% African American | 26–92; Mean (SD): 47 (7) | Ames, Iowa; Athens, Georgia | Database analysis | Whole blood aliquot by turbidimetric immunoinhibition (University of Iowa Clinical Pathology Laboratories). |
| 4 | Getaneh (2011); NHANES III and DIAMOND Study (29) | N = 16,056; 48.1% male and 51.9% female | 4.3% Dominican; 28.9% Hispanic; 26.9% African American; 39.9% White | Range of mean ages: 38.2–63.3 | NHANES III: United States. DIAMOND: New York, New York | Database analysis | Diamat HPLC from Bio-Rad Laboratories.\(^c\) |
| 5 | Hivert (2019); DPP (30) | N = 2,658; 33% male and 67% female | 55.5% White; 20.2% African American; 17.0% Hispanic; 4.4% Asian; 2.9% American Indian | ≥25; Mean (SD): 50.7 (10.7) | 27 US clinical centers\(^d\) | Clinical | Ion-exchange HPLC instrument (Variant; Bio-Rad Laboratories). |
| 6 | Homko (2012) (31) | N = 83; 7.2% male and 92.8% female | 100% African American | Mean (SD): 53 (10.4) | Philadelphia, Pennsylvania | Clinical | CDC-approved automated point-of-care analyzer (DCA 2000, Bayer Corporation): monoclonal antibody recognizes glycated N terminus of β chain of hemoglobin. |
| 7 | Meigs (2014); BACH Prediabetes Study (32) | N = 1,387; 37.4% male and 62.6% female | 27.3% African American; 29.6% Hispanic; 43.0% White | 34–87 | Boston, Massachusetts | Clinical | Tina-Quant HbA1c generation 2 assay with analytic measurement range of 3.4%–18% (Quest Diagnostics). |
| Afro-Caribbean | | | | | | | |
| 8 | Exebio (2012) (33) | N = 128\(^e\) | 100% Haitian American | ≥35 | Miami, Florida | Clinical | Whole blood with close tube sampling, in duplicate |

Abbreviations: AIA, Africans in America; BACH, Boston Area Community Health; CARDIA, Coronary Artery Risk Development in Young Adults; CDC, Centers for Disease Control and Prevention; DIAMOND, Diabetes Among Dominicans and Other Minorities in Northern Manhattan; DPP, Diabetes Prevention Program; FACHS, Family and Community Health Study; HPLC, high performance liquid chromatography; NHANES III, the third National Health and Nutrition Examination Survey; NIH, National Institutes of Health; NGSP, National Glycohemoglobin Standardization Program.

\(^a\) For all studies, White refers to Caucasian, Non-Hispanic White, and/or European White.

\(^b\) Participant data extracted from Table 1, “Sociodemographic Characteristics of Dominicans and the Third National Health and Nutrition Examination Survey Populations, Stratified by Hemoglobin A1c-Based Diabetes Diagnosis” (29).

\(^c\) Laboratory analysis data extracted from “Plan and Operation of the Third National Health and Nutrition Examination Survey, 1988–94. Series 1: Programs and Collection Procedures” (38).

\(^d\) Location data extracted from “The Diabetes Prevention Program. Design and methods for a clinical trial in the prevention of type 2 diabetes” (39).

\(^e\) Breakdown for sex/gender not available.

(continued on next page)
Table 1. Study Characteristics for Articles Reporting on Glycated Hemoglobin A<sub>1c</sub> (HbA<sub>1c</sub>) Performance Among African Descent Populations Living in the United States, 2010–2019

| Study | First Author (Year); Study | N; Sex | Race/Ethnicity<sup>a</sup> (%) | Age, y | Location | Study Design | HbA<sub>1c</sub> Laboratory Analysis Method |
|-------|---------------------------|-------|-------------------------------|--------|----------|-------------|---------------------------------|
| African |                          |       |                               |        |          |             | (coefficient of variation <1.7%), with Roche Tina Quant Second Generation A1c immunoassay method of Laboratory Corporation of America. |
| 9     | Brier (2019); The AIA Study (34) | N = 430; 65% male and 35% female | 100% African immigrants in the United States | Mean (SD): 38 (10) | Bethesda, Maryland | Clinical | NGSP-certified instruments: BioRad Laboratories Classic Variant (n = 32), Bio-Rad Laboratories Variant II (n = 158), and BioRad Laboratories D10 (n = 240) used sequentially by the NIH Clinical Center for HPLC. |
| 10    | Sumner 1 (2015); The AIA Study (35) | N = 216; 68% male and 32% female | 100% African immigrants in the United States | 20–64; mean (SD): 37 (10) | Bethesda, Maryland | Clinical | NGSP-certified instruments: Classic Variant, Variant II, and D10 for HPLC (Bio-Rad Laboratories); Whole blood samples in 90 participants analyzed by boronate affinity chromatography method on NGSP-certified Premier Hb9210 analyzer (Trinity Biotech). |
| 11    | Sumner 2 (2016); The AIA Study (36) | N = 236; 69% male and 31% female | 100% African immigrants in the United States | 20–64; Mean (SD): 39 (10) | Bethesda, Maryland | Clinical | NGSP-certified instruments: Variant II and D10 for HPLC (Bio-Rad Laboratories). |
| 12    | Sumner 3 (2016); The AIA Study (37) | N = 217; 69% male and 31% female | 100% African immigrants in the United States | 20–64; Mean (SD): 39 (10) | Bethesda, Maryland | Clinical | NGSP-certified instruments: Variant II and D10 for HPLC (Bio-Rad Laboratories). |

Abbreviations: AIA, Africans in America; BACH, Boston Area Community Health; CARDIA, Coronary Artery Risk Development in Young Adults; CDC, Centers for Disease Control and Prevention; DIAMOND, Diabetes Among Dominicans and Other Minorities in Northern Manhattan; DPP, Diabetes Prevention Program; FACHS, Family and Community Health Study; HPLC, high performance liquid chromatography; NHANES III, the third National Health and Nutrition Examination Survey; NIH, National Institutes of Health; NGSP, National Glycohemoglobin Standardization Program.

For all studies, White refers to Caucasian, Non-Hispanic White, and/or European White.

Participant data extracted from Table 1, “Sociodemographic Characteristics of Dominicans and the Third National Health and Nutrition Examination Survey Populations, Stratified by Hemoglobin A<sub>1c</sub>-Based Diabetes Diagnosis” (29).

Laboratory analysis data extracted from “Plan and Operation of the Third National Health and Nutrition Examination Survey, 1988–94. Series 1: Programs and Collection Procedures” (38).

Location data extracted from “The Diabetes Prevention Program. Design and methods for a clinical trial in the prevention of type 2 diabetes” (39).

Breakdown for sex/gender not available.
Table 2. Evaluation of Glycated Hemoglobin A1c (HbA1c) Performance: Greater Risk of False Positives Versus Greater Risk of False Negatives Among African Descent Populations Living in the United States, 2010–2019

| Study | HbA1c Evaluation Method | Findings | Performance |
|-------|-------------------------|----------|-------------|
| 1     | Compared with other ethnic groups (ie, White people) | Main finding: Higher HbA1c values for African American than for White people at all fasting glucose levels (26). Additional findings: • Relationship between HbA1c and simultaneous serum glucose did not differ between African American people with and without the SCT. • SCT does not impact relationship between HbA1c and serum glucose concentration, and does not account for differences between African American and White people. | Greater risk of false positives |
| 2     | Compared with other ethnic groups (ie, White people) | Main finding: African American people without previous diagnosis of type 2 diabetes by OGTT had higher mean values of HbA1c than White people ($\beta = 0.19$ points; 95% CI = 0.14–0.24) (27). Additional finding: HbA1c values were compared for participants free of type 2 diabetes based on the OGTT. | Greater risk of false positives |
| 3     | Compared with other measures (ie, previous diagnosis)<sup>a</sup> | Main finding: Chronic financial strain increased sIL-6R, an inflammatory marker, and HbA1c (28). Additional finding: Although African American women had no previous prediabetes or type 2 diabetes diagnosis, 54% had HbA1c $>$5.7%. | Greater risk of false positives |
| 4     | Compared with other ethnic groups (ie, White people); Compared with other measures (ie, FPG and OGTT) | Main findings: • For African American people (N = 408) classified as having normal glucose tolerance by either FPG or OGTT, HbA1c misclassified 3.5% of them as having type 2 diabetes (29). • HbA1c diagnosed type 2 diabetes in 67% of African American people and 37.9% of White people. | Greater risk of false positives |
| 5     | Compared with other ethnic groups (ie, White people) | Main finding: HbA1c was higher in African American (mean [SD], 6.2% [0.6]) than in White people (mean [SD], 5.8% [0.4]) (30). Additional findings: • Genomic analysis showed that 3 genetic factors contributed to the differences in HbA1c: PCA factor, SCT, and GRS. • 60% of HbA1c differences between African American and White people are explained by first genomic PCA factor (degree of African ancestry). • SCT explained 16% of the difference and GRS explained 14% of difference in HbA1c between African American and White people. | Greater risk of false positives |
| 6     | Compared with other measures (ie, OGTT) | Main findings: • For patients with type 2 diabetes diagnosis by HbA1c, OGTT classified 48.3% with type 2 diabetes, 38.7% with IGT, and 12.9% with normal glucose tolerance. | Greater risk of false positives at HbA1c $\geq$6.5% and greater risk of false negatives at HbA1c $\leq$5.6% |

Abbreviations: OGTT, 2-hour oral glucose tolerance test; FPG, fasting plasma glucose; IGT, impaired glucose tolerance; PCA, principal component analysis; GRS, genetic risk score; SCT, sickle cell trait; ROC, receiver operating characteristic.

<sup>a</sup> Exact temporality between the previous diagnosis and HbA1c testing was not provided within the study, with an estimate of less than 12 months extrapolated from the study design. Findings from this study may represent new onset diabetes. This provides a limitation in the conclusive findings for HbA1c performance in this study.
Table 2. Evaluation of Glycated Hemoglobin A \(_{1c}\) (HbA\(_{1c}\)) Performance: Greater Risk of False Positives Versus Greater Risk of False Negatives Among African Descent Populations Living in the United States, 2010–2019

| Study | HbA\(_{1c}\) Evaluation Method | Findings | Performance |
|-------|---------------------------------|----------|-------------|
|       |                                 | • HbA\(_{1c}\) ≤5.6% does not exclude type 2 diabetes or IGT. Among 33.7% of patients with HbA\(_{1c}\) ≤5.6%, 64.3% had IGT or type 2 diabetes (31). | Greater risk of false positives |<|
Table 2. Evaluation of Glycated Hemoglobin A\textsubscript{1c} (HbA\textsubscript{1c}) Performance: Greater Risk of False Positives Versus Greater Risk of False Negatives Among African Descent Populations Living in the United States, 2010–2019

| Study | HbA\textsubscript{1c} Evaluation Method | Findings | Performance |
|-------|----------------------------------------|----------|-------------|
|       | and glycated albumin)                  | Among subjects with prediabetes by OGTT, HbA\textsubscript{1c} of 5.7% to less than 6.5% had 37% sensitivity in nonobese African immigrants and 64% sensitivity in obese African immigrants (36). Additional finding: For HbA\textsubscript{1c} of 5.7% to less than 6.5% combined with glycated albumin $\geq$13.77%, sensitivity increased to 72% for nonobese African immigrants. | Greater risk of false negatives |
| 12    | Compared with other measures (ie, OGTT and glycated albumin) | Main findings: • When type 2 diabetes was detected by glycated plasma proteins (albumin or fructosamine; $n = 24$), average HbA\textsubscript{1c} was mean (SD) 5.2% (0.4). • OGTT detected prediabetes in 74 individuals (13 of 74 had low HbA\textsubscript{1c}) (37). Additional findings: • HbA\textsubscript{1c} detected $\leq$50% of African immigrants with prediabetes. • HbA\textsubscript{1c} combined with the glycated albumin test increases sensitivity to 80% for diagnosing prediabetes. | Greater risk of false negatives |

Abbreviations: OGTT, 2-hour oral glucose tolerance test; FPG, fasting plasma glucose; IGT, impaired glucose tolerance; PCA, principal component analysis; GRS, genetic risk score; SCT, sickle cell trait; ROC, receiver operating characteristic.

\textsuperscript{a} Exact temporality between the previous diagnosis and HbA\textsubscript{1c} testing was not provided within the study, with an estimate of less than 12 months extrapolated from the study design. Findings from this study may represent new onset diabetes. This provides a limitation in the conclusive findings for HbA\textsubscript{1c} performance in this study.
Appendix. Search Strings Used in a Scoping Review of HbA1c Performance in African Descent Populations in the United States With Normal Glucose Tolerance, Prediabetes, and Diabetes

| Database                      | Search String                                                                                                                                                                                                 |
|-------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| PubMed                        | (africa[tiab] OR african[tiab] OR americans[tiab] OR afro[tiab] OR block[tiab] OR "african ancestry group"[MeSH Terms] OR "african americans"[MeSH Terms] OR Angola[tiab] OR Angolan[tiab] OR Benin[tiab] OR Beninese[tiab] OR Botswana[tiab] OR Botswana[tiab] OR Burundi[tiab] OR Burundi[tiab] OR Cape Verde[tiab] OR "Central African Republic"[tiab] OR "Central African"[tiab] OR Chad[tiab] OR Chadanian[tiab] OR Comoros[tiab] OR Comorian[tiab] OR Congo[tiab] OR Congolese[tiab] OR "Equatorial Guinean"[tiab] OR Equainguinean[tiab] OR Eritrea[tiab] OR Eritrean[tiab] OR Ethiopia[tiab] OR Ethiopian[tiab] OR Gabon[tiab] OR Gabonese[tiab] OR Gambian[tiab] OR Gambian[tiab] OR Ghana[tiab] OR Ghanaian[tiab] OR Guinea[tiab] OR Guinean[tiab] OR "Guinea-Bissau"[tiab] OR "Bissau-Guinean"[tiab] OR "Ivory Coast"[tiab] OR Ivorian[tiab] OR Kenya[tiab] OR Kenyan[tiab] OR Lesotho[tiab] OR Mosotho[tiab] OR Basotho[tiab] OR "South Africa"[tiab] OR "South African"[tiab] OR "South Sudan"[tiab] OR "South Sudanese"[tiab] OR Sudan[tiab] OR Sudanese[tiab] OR Swaziland[tiab] OR Swazi[tiab] OR Tanzania[tiab] OR Tanzanian[tiab] OR US Virgin Islands[tiab] OR "Virgin Islands"[tiab] OR "West Indies"[tiab] OR "West Indian"[tiab] OR AND ("Glycated Hemoglobin A"[mesh] OR "hemoglobin A1c"[tiab] OR "hba1c"[tiab] OR "A1c"[tiab]) AND (+"0000/01/01[PDAT]: "2020/01/01[PDAT]) |
| Database                         | Search String |
|---------------------------------|---------------|
| Malawi OR Malawian OR Mali OR Malian OR Mauritanian OR Mauritius OR Mauritian OR Mozambique OR Mozambican OR Namibia OR Namibian OR Niger OR Nigerian OR Nigeria OR Nigerian OR Rwanda OR Rwandan OR “Sao Tome and Principe” OR Senegal OR Senegalese OR Seychelles OR Seychellois OR “Sierra Leone” OR “Sierra Leonian” OR Somalia OR Somalian OR “South Africa” OR “South African” OR “South Sudan” OR “South Sudanese” OR Sudan OR Sudanese OR Swaziland OR Swazi OR Tanzania OR Tanzanian OR Togo OR Uganda OR Ugandan OR Zambia OR Zambian OR Zimbabwe OR Zimbabwean OR anguilla OR anguillian OR “Antigua and Barbuda” OR antiguan OR barbudan OR aruba OR aruban OR bahamas OR bahamian OR barbados OR barbadian OR belize OR belizean OR bermuda OR bermudian OR “British Virgin Islands” OR caribbean OR “Cayman Islands” OR “Costa Rica” OR “Costa Rican” OR cuba OR cuban OR curacao OR curacaos OR dominica OR “Dominican Republic” OR dominican OR grenada OR grenadine OR guadeloupe OR guadeloupian OR guyana OR guyanese OR haiti OR haitian OR honduras OR honduran OR jamaica OR jamaican OR martinique OR martiniquais OR montserrat ORMontserrat OR nevis OR nicaragua OR nicaraguan OR panama OR panamanian OR “Puerto Rico” OR “Puerto Rican” OR “St. Barts” OR “St. Christopher” OR “St. Croix” OR “St. Johns” OR “St. Kitts and Nevis” OR “St. Lucia” OR “St. Martin” OR “St. Thomas” OR “St. Vincent” OR vincentian OR suriname OR surinamese OR “Trinidad and Tobago” OR trinidadian OR trini OR tobagonian OR “US Virgin Islands” OR venezuela OR venezuelan OR “Virgin Islands” OR “West Indies” OR “West Indian”)