

The diagnostic accuracy of HbA_{1c}, compared to the oral glucose tolerance test, for screening for type 2 diabetes mellitus in Africa—a systematic review and meta-analysis

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Abstract

Objective

To assess the diagnostic accuracy of HbA_{1c}, compared to fasting plasma glucose (FPG) and the oral glucose tolerance test (OGTT), in screening for type 2 diabetes (T2D) in Africa.

Methods

We systematically searched databases for studies that compared the HbA_{1c} to either the OGTT, or the FPG for T2D diagnosis were included. The QUADAS 2 tool was used for assessing the quality of included studies. We used the split component synthesis (SCS) method for the meta-analysis of diagnostic accuracy studies to pool the studies for meta-analysis of sensitivity and specificity, primarily at the HbA_{1c}≥48mmol/mol (6.5%) cut-off and at other cut-offs. We assessed heterogeneity using the I² statistic and publication bias using Doi plots.

Results

Eleven studies, from seven African countries, with 12925 participants, were included. Against the OGTT, HbA_{1c}≥48mmol/mol (6.5%) had a pooled sensitivity of 57.7% (95%CI 43.4-70.9) and specificity of 92.3% (95%CI 83.9 – 96.5). Against the FPG, HbA_{1c}≥48mmol/mol (6.5%) had a pooled sensitivity of 64.5% (95%CI 50.5 – 76.4) and specificity of 94.3% (95%CI 87.9 – 97.5). The highest sensitivity for HbA_{1c}, against the OGTT, was at the 42mmol/mol (6.0%) cut off.

Conclusion

In Africa, the HbA_{1c}≥48mmol/mol (6.5%) cut-off may miss almost half of the individuals with T2D based on blood glucose measures.

PROSPERO Registration: CRD42017073078

Key Words

Type 2 diabetes mellitus, glycated haemoglobin A_{1c}, diagnostic accuracy, sensitivity, specificity, Africa

Background

Type 2 diabetes mellitus (T2D) prevalence has doubled in Africa from 4% in 1980 to 9% in 2014 (1) and the number of people with diabetes is expected to increase more in Africa, compared to other regions by 2040 (2). An estimated two-thirds of individuals have undiagnosed diabetes in Africa, partly attributable to the lack of adequate

screening for diabetes in people who are at high risk (3). For many African countries, the true estimates of diabetes prevalence are not known and are extrapolated from their neighboring countries, due to a lack of data from epidemiological studies (4). This is the same with estimates of impaired glucose tolerance states such as gestational diabetes and prediabetes (4). This lack of reliable estimates of prevalence of diabetes and other altered glucose metabolism states is likely to hinder planning and allocation of resources as well as determination of diabetes prevention programs.

The oral glucose tolerance test (OGTT), fasting plasma glucose alone (FPG) and haemoglobin A_{1c} (HbA_{1c}) are the three tests which are recommended by major guideline bodies (5-7) for screening and diagnosis of T2D. However, research suggests that these three methods may identify individuals with different types of glucose intolerance and result in different estimates of diabetes prevalence with the full OGTT (FPG or 2-hour OGTT) giving the highest prevalence and HbA_{1c} the lowest prevalence of diabetes (8). The OGTT is time and resource demanding, and often viewed by participants as unpleasant (9). Consequently, it has been suggested that FPG only or HbA_{1c} be used in screening for T2D(9). However, FPG alone may miss a significant proportion of individuals with T2D (10), especially those with isolated insulin insensitivity which is thought to be represented by postprandial glucose intolerance (11). Compared to both the FPG and the OGTT, HbA_{1c} offers an attractive alternative as the blood sample can be drawn anywhere and anytime and does not require prior fasting. Furthermore, HbA_{1c} samples are more stable than those for glucose-based measures and are less likely to be affected by storage, sample transport conditions or day to day variations in plasma glucose and HbA_{1c} tends to reflect the average plasma glucose over the past 12 weeks (12, 13).

Initially, HbA_{1c} assays were not as reliable as the glucose-based measurements, but, improvements in instrumentation and standardization mean laboratory based HbA_{1c} assays are now as accurate as glucose based measures (14, 15) (16, 17). However, HbA_{1c} still has limitations as it cannot be used in diagnosing T2D in children, adolescents, people with haemoglobinopathies, pregnant women or women in the immediate postnatal period, acutely ill persons, and persons with renal failure (17). Meta-analyses (18-22) from other populations have shown that the HbA_{1c} cut-off of

48mmol/mol (6.5%), compared to the OGTT, has reasonably high specificity but low sensitivity, and that its use could result in missing up to 50% of cases that would have been identified by the OGTT. The disparity in prevalence estimates may be worse in Africa, where more than half of people with diabetes are undiagnosed (4). Indeed, several studies have shown evidence that the OGTT, the FPG and the HbA_{1c} may, in many cases, identify different individuals with diabetes (14, 15, 23, 24). In Africa, the few existing studies (10, 23-26) suggest that the use of HbA_{1c} may result in different prevalence estimates compared to either the OGTT or FPG in research settings, although HbA_{1c} has been used to estimate diabetes prevalence in a national survey in South Africa (27). Widely ranging sensitivities of HbA_{1c} against the OGTT have been reported in a previous systematic review, which did not include African studies, suggesting that HbA_{1c} performance may differ between populations (28). This raises another problem, the possibility of different diagnostic accuracy and performance of HbA_{1c} in different populations and ethnic groups (28, 29). In Africa, despite a high prevalence of haemoglobinopathies (30), no systematic review has been conducted to investigate the diagnostic accuracy of the HbA_{1c} in screening for T2D. The aim of this study was to assess the diagnostic accuracy of HbA_{1c} in the screening of T2D in Africa, first compared to the OGTT and then against the FPG. We assessed the sensitivity and specificity of the HbA_{1c} cut-off at 48mmol/mol (6.5%) primarily, and then investigated the optimal cut-off points for HbA_{1c} compared to the OGTT and FPG in screening for T2D in Africa.

Methods

We carried out a systematic review and meta-analysis of diagnostic studies in all African populations resident in Africa, comparing the diagnostic accuracy of the HbA_{1c} to either FPG or the OGTT. This report followed the Preferred Reporting systematic reviews and meta-analyses of diagnostic test accuracy studies (PRISMA-DTA) guidelines (31). The protocol for this study is registered on the prospective register of systematic reviews (PROSPERO CRD42017073078).

Search methods for identification of studies

We searched the following electronic databases; PubMed, Cochrane Central, CINAHL and Scopus. The first search was carried out on the 2nd of November 2017. A second search was carried out on the 6th of December 2020. We further searched the reference lists of all publications including original studies, letters, guidelines such as World Health Organization guideline for the diagnosis of diabetes (6), and reviews and also contacted prominent authors for published and unpublished studies. Full details of the search strategy are in Supplementary Document S1.

Types of studies

We included all cross-sectional studies which compared the diagnostic accuracy of HbA_{1c} to either FPG or the OGTT in Africa, without language restrictions. In all the studies, the index test was the HbA_{1c} while the reference test was either FPG or OGTT. We excluded modeling studies, case-control studies and experimental studies, studies where participants were not fasting, reviews and commentaries, studies of African populations residing out of Africa, studies which included participants with diagnosed diabetes and studies which included pregnant women. We excluded studies with participants with established diabetes as they would most likely have been on blood glucose lowering treatments and therefore their HbA_{1c} values would be lower than expected. This could potentially have resulted result in a lower accuracy for HbA_{1c} as HbA_{1c} would have classified some of the participants as people without diabetes.

Data collection and analysis

After searching, articles were retrieved and transferred to End Note to remove duplicates. After duplicates removal, two independent reviewers screened the articles by title, abstract and full text for inclusion and disagreement was settled by a third independent reviewer.

Data extraction and management

Two authors independently extracted data from the included studies into a structured record form in Microsoft Office Excel 2016. The data extracted included study design, age of participants, number of participants, country where study was conducted, T2D

diagnosis criteria, data on HbA_{1c} analyser used, methods used for the measurement of HbA_{1c} and blood glucose, sample size, which reference standard (FPG or OGTT) the study used, reported sensitivity and specificity for each cut-off of HbA_{1c} and, for each HbA_{1c} cut-off, the numbers of true and false positives (TP and FP), and true and false negatives (TN and FN). RevMan 5.4.1 (32) was used to calculate the numbers of true and false positives, and true and false negatives when missing from study reports. When insufficient data were available, we contacted authors for additional data.

Assessment of methodological quality

Assessment of risk of bias, internal and external validity in included studies, was done by two independent reviewers using the QUADAS 2 appraisal tool (33). The QUADAS 2 tool evaluates the risk of bias and applicability of diagnostic accuracy studies. The tool is structured into four key domains of patient selection, index test, reference standard and flow and timing.

Statistical analysis and data synthesis

Data that could not be pooled into a meta-analysis, such as study characteristics, were presented in tables and described narratively. The accuracy of the HbA_{1c} at cut-off points between 42mmol/mol (6.0%) and 53mmol/mol (7.0%) was compared against the FPG and the OGTT as standards. For each cut-off point, where there were less than four studies, we presented the individual sensitivity and specificity in a table and described narratively. For the HbA_{1c} 48mmol/mol (6.5%) cut-off, we presented study level estimates of sensitivity and specificity from included studies using paired forest plots, which were created in RevMan 5.4.1 (32). We used the split component synthesis (SCS) method for the meta-analysis of diagnostic accuracy studies (34) to pool data at cut-offs where at least four studies had data available, and reported summary estimates of sensitivity, specificity, and likelihood ratios and their 95% confidence intervals (95%CI). The SCS uses the assumption-free inverse variance heterogeneity model (35) to pool diagnostic odds ratios (DOR) from different studies and then partitions the pooled DOR into its component sensitivity and specificity. The partitioning of the pooled DOR into the summary sensitivity and specificity is done using least square regression of study logit sensitivity and logit specificity on the centered $\ln(\text{DOR})$, where the regression intercepts show the summary logit sensitivity and logit specificity. The SCS method has a smaller

bias, mean standard error and performs better than the traditional bivariate models especially in the case where a few studies are available and when there is high between study heterogeneity (34). For the HbA_{1c} ≥48mmol/mol (6.5%) cut-off, we presented a summary receiver operating characteristics curve (sROC) for each analysis against the FPG and OGTT. We carried out the analyses using the *diagma* (36) module in Stata. We carried out sensitivity analysis using bivariate and hierarchical summary receiver operating characteristic (HSROC) models using *metandi* in Stata, for the main outcome (diagnostic accuracy of HbA_{1c} 48mmol/mol (6.5%) against OGTT and FPG). The bivariate and HSROC methods are random effects hierarchical methods which account for the correlation between specificity and sensitivity in included studies, in addition to accounting for the between study variation in test performance (37). Although the two methods use different parameters, they are mathematically equivalent in the absence of other covariates (37). Both methods first model the frequencies of the 2X2 tables for each study and then model the between study heterogeneity. The bivariate model jointly models pairs of logit transformed sensitivity and specificity and the correlation between them using a linear mixed random effect model, assuming a bivariate normal distribution of the logit sensitivity and logit specificity (38), whereas the HSROC is a multilevel non-linear generalized mixed model which uses scale and accuracy parameters of functions of specificity and sensitivity to describe an assumed underlying ROC curve.

A limitation of the bivariate and HSROC approaches is that these models may either fail to converge or give result in unreliable meta-analytic estimates when there are few studies or when data are sparse (37). This limitation of the bivariate and HSROC methods is why we used the SCS method in this meta-analysis, as we had a few studies overall and sparse data for many of the cut-off points of interest. Further, we carried out sensitivity analysis, for the comparison with the OGTT, where we removed one study with poor applicability (39) and another study where details of HbA_{1c} assay were not available.

We quantified heterogeneity using the I^2 statistic and Cochran's Q statistic. Although there was high heterogeneity between studies at each cut-off, we did not carry out

subgroup analysis to explore heterogeneity because there were only a few studies included.

We assessed the presence of publication bias by examining Doi plots, and the Luis Furuya-Kanamori (LFK) index, as there were too few studies (less than 10) for each of the cut-off points assessed, therefore making funnel plots unsuitable (40). LFK index values above 1 or below -1 are indicative of asymmetry or publication bias.

Ethical considerations

This review did not require ethical approval as we used secondary data from published studies.

Results

Fig. 1. Study Flow Chart

Search results

A total of 2677 studies were identified from the search, from which 21 studies were screened using full text. Ten studies were excluded after screening the full text, three studies had participants with established diabetes, three studies where either the full text or diagnostic accuracy data were not available, and four for other reasons (Fig. 1 and Supplementary Table 1).

Characteristics of included studies

All the 11 studies (10, 23-26, 39, 41-45) which met the inclusion criteria were published between the years 2010 to 2020 (Table 1) and were from only seven countries. Four were from South Africa (10, 23, 39, 45), two from Uganda (26, 44), and one study each from Nigeria (41), Kenya (25), Malawi (24), Tanzania (43) and Mauritius (Fig. 2).

Additional summary data on TP, FP, TN and FN were supplied by authors for five studies (10, 24, 25, 39, 42), where some data were missing from published reports. Six

studies used the OGTT (10, 23, 39, 42, 43, 45) as standard while the remainder used only FPG.

Sample sizes ranged from 31 participants in Nigeria (41) to 3645 in Malawi (24). Five of the studies were from urban populations (10, 23, 39, 41, 45), four from both rural and urban (24, 25, 42, 44), one from a rural setting (26) and one study did not specify the setting (43). The ethnic backgrounds of participants were predominantly Black African, from eight studies (23-26, 41-44), Mixed Ancestry from one study (45), South Africans of Indian descent (10) and one study had a mix of Black African and Mixed Ancestry (39). Seven (10, 23-26, 42, 45) of the studies were in general populations while one study (39) was in women who had hyperglycaemia first detected in pregnancy 5 years previously, two studies (43, 44) compared the diagnostic accuracy of HbA1C between individuals with and without HIV and one study (41) included participants with hypertension only.

The World Health Organization 2006 diabetes diagnosis guideline was used by nine of the 11 studies, (23-26, 39, 41, 43-45), with one using the World Health Organization 1998 (42) the other the American Diabetes Association 2015 guideline (10). The majority of studies used HbA_{1c} cut offs that ranged between 42mmol/mol (6.0%) and 64mmol/mol (8.0%), with one study (44) investigating HbA1C cut off points that started at 37mmol/mol (5.5%)

Fig. 2. Map showing the country of origin of the included studies

Table 1. Characteristics of included studies

**Raw data supplied by the authors*

Methodological quality of included studies

The assessments of bias and applicability of included studies are shown in Supplementary Table 2. Most of the included studies had low risk of bias for selection bias and concerns about suitability of participants for the review question, except one study which included only participants with a known history of systemic hypertension and on lifestyle modification (41) and another which included only women with a history of hyperglycaemia first detected in pregnancy (39). The remaining studies were community-based surveys where participants were selected through probability sampling. Most of the studies (n=8) had low risk of bias concerning the conduct of the index test (HbA_{1c}), but two studies used point of care devices (26, 44), and the details of the HbA_{1c} assay were not reported in one study (10) .

Diagnostic accuracy of HbA_{1c} against the OGTT as standard

Six studies (10, 23, 39, 42, 43, 45), with a total of 6183 participants, assessed the diagnostic accuracy of HbA_{1c}≥6.5% against the OGTT, with a mean T2D prevalence of 13%. At the HbA_{1c}≥48mmol/mol (6.5%) cut-point, the reported sensitivity ranged from 46% in one study from South Africa (45) to 75% in a study from Kenya (43) and the specificity ranged from 74% in Nigeria (41) to 99% in Kenya (43) and South Africa (23) (Fig. 3). Against the OGTT, HbA_{1c}≥48mmol/mol (6.5%) had a pooled sensitivity of 57.7 % (95% CI 43.4 - 70.9), and a specificity of 92.3% (95% CI 83.9 – 96.5), with high between-study heterogeneity ($I^2 = 91.8\%$, $p<0.01$) (Table 2 & Fig. 4A) and evidence of possible publication bias (Supplementary Fig. 1). The pooled sensitivity and specificity were slightly higher, 60.2% (95%CI 51.6 - 68.1) and 95.8% (95% CI 89.7 - 98.4), respectively, when the bivariate model was used (Supplementary Table 3, Supplementary Fig. 2). The highest sensitivity for HbA_{1c} was at the 42mmol/mol (6.0%) cut off (sensitivity 74.9%, specificity 71.8%) and the highest specificity at the HbA_{1c} ≥53mmol/mol (7.0%) cut-off (sensitivity 49.7%, specificity 97.1%) (Table 2).

Fig 3. Paired forest plot of studies evaluating diagnostic accuracy of HbA_{1c}≥48mmol/mol (6.5%) against the OGTT

Table 2. Pooled diagnostic accuracy of HbA_{1c} at different cut-offs against the OGTT as standard

All pooled estimates are from the SCS model. Findings were not pooled for cut-offs that had less than 3 studies.

Fig. 4 – Summary receiver operating characteristic curve for HbA_{1c} ≥6.5% against OGTT (A) and FPG (B) – based on the SCS model

Each circle represents a study estimate, with the size being proportional to the sample size. The black solid square represents the summary sensitivity and specificity intersection point. The shaded rectangle represents the confidence interval of the summary sensitivity and specificity intersection point. The confidence limit of the summary sensitivity are represented by the upper and lower boundaries of the shaded rectangle and the confidence limits of the summary specificity are represented by the left and right boundaries of the shaded rectangle. The solid curved line represents the summary receiver operating characteristics curve and the dotted curves, the confidence limits

Diagnostic accuracy of HbA_{1c} against FPG as standard

Eight studies (23-26, 39, 41, 44, 45), with a total of 7 042 participants, assessed the sensitivity of HbA_{1c}≥48mmol/mol (6.5%) against the FPG, with a mean T2D prevalence of 4.5%, reported sensitivity ranged from 46% in Uganda (44) to a high of 88% in Kenya (25) and specificity ranged from 68% in Nigeria (41) to 99% in Kenya (25) (Fig. 5). Against the FPG, HbA_{1c}≥48mmol/mol (6.5%) had a pooled sensitivity of 64.5% (95% CI 50.5 – 76.4), specificity of 94.3 (95% CI 87.9 – 97.5), with high heterogeneity ($I^2 = 86.6$, $p < 0.01$) (Table 3 & Fig. 4B) and low evidence of publication bias (Supplementary Fig. 3). The pooled sensitivity and specificity were almost similar, 65.1% (95% CI 52.9 - 75.6) and 94.8% (95%CI 88.7-97.7), respectively, when the bivariate model was used (Supplementary Table 3, Supplementary Fig. 4). The highest pooled sensitivity was at HbA_{1c}≥43mmol/mol (6.1%) cut off (sensitivity 81.1%, sensitivity 84.1%) and the highest specificity at the HbA_{1c}≥53mmol/mol (7.0%) (sensitivity 65.3%, specificity 96.8%) (Table 3).

Fig. 5 – Paired Forest plot of studies evaluating diagnostic accuracy of HbA_{1c}≥48mmol/mol (6.5%) against the FPG

Table 3. Pooled diagnostic accuracy of HbA_{1c} at different cut-offs against the FPG as standard

All pooled estimates are from the SCS model. Findings were not pooled for cut-offs that had less than 3 studies.

Discussion

In this systematic review and meta-analysis of 11 studies from seven African countries, with a total of 12 925 participants, the pooled sensitivity for HbA_{1c} at the recommended 48mmol/mol (6.5%) cut-off was low against both the OGTT and FPG, of 57.7% (95% CI 43.4 - 70.9) and 64.5% (95% CI 50.5 – 76.4), respectively, although the specificity was high, 92.3% (95% CI 83.9 – 96.5) and 94.3% (95% CI 87.9 – 97.5), respectively. HbA_{1c} had the highest pooled sensitivity against the OGTT at the 42mmol/mol (6.0%) cut-off and 43mmol/mol (6.1%) against FPG.

Our findings suggest that, in Africa, the use of the HbA_{1c}≥48mmol/mol (6.5%) cut-off may underestimate the population prevalence of diabetes as it will miss up to 42% and 35% of individuals with diabetes who are identified by the OGTT and FPG, respectively. These estimates were not very different when we used the bivariate model. These findings are consistent with other meta-analyses, both global and from other regions. A global meta-analysis (19) of 37 studies from all regions, with only three studies from Africa, reported a pooled sensitivity of 50% specificity of 97.3% for HbA_{1c} at the 48mmol/mol (6.5%) level against the OGTT, and a sensitivity of 59.4% and specificity 98.8%) against the FPG. Another global meta-analysis (8), this time with of 96 studies found an even lower sensitivity of HbA_{1c}≥48mmol/mol (6.5%) of 30.5% against the OGTT and 52.7% against FPG, although they included only one African study (45). In Chinese individuals (21), findings of a meta-analysis showed a pooled sensitivity of 51.8% and a pooled specificity of 95.6% of HbA_{1c}≥48mmol/mol (6.5%) against the OGTT. Another meta-analysis (18), which included 17 studies, 14 of which were European and three in Arabic populations only, reported an even lower pooled

sensitivity of 42% and a specificity of 97%, although this was against either OGTT or FPG. Together, our findings and the findings of the existing meta-analyses, suggest that the use of either HbA_{1c} or the glucose measures alone in screening may underestimate the prevalence of diabetes and fail to detect significant proportions of people who are at high risk of diabetes complications in Africa. The latter is perhaps a more concerning problem for African populations where up to two-thirds of people with diabetes are undiagnosed (4). To ensure that the diabetes prevalence measured by HbA_{1c} in epidemiological surveys is similar to that when blood glucose-based measures are used, one suggestion is for researchers to measure FPG in a sub-sample of the study and assess the agreement between the two tests (8). Nevertheless, there is a need for longitudinal studies in African populations to investigate optimum cut-off points, not only for HbA_{1c}, but for the glucose-based measures, to increase their diagnostic accuracy in detecting diabetes and its complications.

An important consideration is that glucose-based measures are not the gold standard for screening for diabetes, and that there is no current gold standard that diagnoses the different diabetes phenotypes and the micro and macrovascular complications that arise from the diabetes. This is different to clinical settings, where physicians have more information and may use multiple biomarkers, in combination with symptom assessments for an accurate diabetes diagnosis. Although it is not the gold standard, the OGTT (FPG and 2-hour OGTT) has long been accepted as the most reliable test for diabetes screening (9, 46) but this test is costly, time consuming, requires more human resources and is not easily accepted by many participants. The HbA_{1c}≥48mmol/mol (6.5%) cut-off was recommended by an International Expert Association, from the ADA, International Diabetes Federation, and the European Association for the Study of Diabetes in 2009, based on the findings of the DETECT-2 study which showed HbA_{1c}≥48mmol/mol (6.5%) had high sensitivity and specificity to identify individuals at risk of diabetic retinopathy (13). Based on data from this multinational cohort (13), HbA_{1c}≥48mmol/mol (6.5%) had almost similar sensitivity and specificity to FPG≥7.0mmol/L and 2-hour OGTT≥11.1mmol/L. However, the risk of future complications from altered glucose metabolism is on a continuous scale with either HbA_{1c} or the blood glucose-based biomarkers, and that finding an empirical cut-off

across different populations is a challenge. Although many meta-analyses have reported a low sensitivity of $\text{HbA}_{1c} \geq 48 \text{ mmol/mol}$ (6.5%) when compared to the glucose-based measures, the inverse is also true as there is mounting evidence that, in some cases, these biomarkers may identify individuals with different phenotypes of diabetes (8). HbA_{1c} has several advantages when compared to the glucose-based measures, in terms of ease of administration of the test, stability of assays and being able to assess long term dysglycemia, and therefore would be a good alternative to the OGTT. However, the problem of different prevalence estimates and missed diabetes diagnoses when the different biomarkers are used, remains, and requires further research to establish cut-off points where T2D prevalence estimates will be equivalent.

Our findings suggest that, compared to the OGTT and FPG, HbA_{1c} has the highest sensitivity at cut-offs of 42 mmol/mol (6.0%) and 43 mmol/mol (6.1%) respectively. These cut-offs are similar to those that have been suggested by primary studies in African populations (23, 45) and previous meta-analyses in other populations (19, 22). A major drawback of the lowered HbA_{1c} cut-off is that the specificity of HbA_{1c} is decreased. This may result in more false positives, overestimate diabetes prevalence and place an unnecessary burden of treatment to healthcare systems when used in screening. Some studies (47, 48) have suggested combining a lower HbA_{1c} cut-off and FPG, although this may be costly, especially for African studies, and optimum cut-offs in such a scenario need to be determined. More research is needed to establish a clearly ascertainable, measurable and cheaper gold standard for T2D diagnosis.

Our study has several limitations. We only included 11 studies from seven African countries, of which four (39, 41, 43, 44) had external validity concerns, and therefore more good quality data from other African countries are required. We did not investigate the sources of heterogeneity and causes of the possible publication bias as there were few studies included at each cut-off point. The heterogeneity and publication bias could have been due to methodological differences and variations in the settings of studies and populations. Lastly, some of our included studies were of low quality.. One study (41) had only 31 participants, two studies (26, 44) used HbA_{1c} point of care devices which have been shown to be unreliable (49) and in one study (10) the HbA_{1c} assay

methods were not described. Strengths of this review were a rigorous study design and conduct following the PRISMA-DTA guidelines. Further, this is the only meta-analysis that has assessed the utility of HbA_{1c} in screening for diabetes in African populations.

Conclusion

In African populations, using the recommended HbA_{1c} ≥ 48 mmol/mol (6.5%) cut-off may miss almost half of the individuals with diabetes based on the blood glucose measures. While this may not mean that the glucose-based measures are more accurate in classifying T2D, this lack of agreement in classification of T2D between these tests may result in different estimates of the prevalence of T2D when HbA_{1c} is used compared to when glucose measures are used.

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CRedit author statement

TC – conception, methodology, software, validation, formal analysis, investigation, resources, data curation, writing – drafting original draft, writing – reviewing and editing, visualization, project administration.

JH - methodology, validation, investigation, formal analysis, writing – reviewing and editing, supervision

JTM - investigation, data curation, writing – reviewing and editing, visualization

MC – conception, methodology, writing – reviewing and editing

AF - conception, methodology, formal analysis, investigation, validation, writing – reviewing and editing, supervision

SN – conception, methodology, resources, writing – reviewing and editing, supervision

NL - conception, methodology, resources, writing – reviewing and editing, supervision

Competing interests

The authors declare no competing interests.

Abbreviations

T2D – type 2 diabetes

IDF - International Diabetes Federation

WHO – World Health Organization

OGTT – oral glucose tolerance test

FPG – fasting plasma glucose

ROC – Receiver operating curve

IGT – impaired glucose tolerance

HbA_{1c} – Glycated haemoglobin A_{1c}

HSROC - hierarchical summary ROC; ROC = receiver operating characteristic

SCS – split component synthesis

DOR – diagnostic odds ratios

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