Systematic review and meta-analysis

Availability and affordability of essential medicines and diagnostic tests for diabetes mellitus in Africa

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Sustainable Development Goals: Good Health and Wellbeing, Reduced Inequalities

ABSTRACT

Objective: To investigate the current status of the availability and affordability of specific essential medicines and diagnostics for diabetes in Africa.

Methods: Systematic review and meta-analysis. Studies conducted in Africa that reported any information on the availability and affordability of short-acting, intermediate-acting, and premixed insulin, glibenclamide, metformin, blood glucose, glycated haemoglobin or HbA1c, and lipid profile tests were included. Random-effect model meta-analysis and descriptive statistics were performed to determine the pooled availability and affordability, respectively.

Results: A total of 21 studies were included. The pooled availability of each drug was as follows: short-acting insulin 33.5% (95% CI: 17.8% - 49.2%, I^2=95.02%), intermediate-acting insulin 23.1% (95% CI: 6.3% - 39.9%, I^2=91.6%), premixed insulin 49.4% (95% CI: 24.9% - 73.9%, I^2=90.57%), glibenclamide 55.9% (95% CI: 43.8% - 68.0%, I^2=96.7%), and metformin 47.0% (95% CI: 34.6% - 59.4, I^2=97.54%). Regarding diagnostic tests, for glucometers the pooled availability was 49.5% (95% CI: 37.9% - 61.1%, I^2=97.43%), for HbA1c 24.6% (95% CI: 3.1% - 46.1%, I^2=91.64), and for lipid profile tests 35.7% (95% CI: 19.4% - 51.9%, I^2=83.77%). The median (IQR) affordability in days' wages was 7 (4.7-7.5) for short-acting insulin, 4.4 (3.9-4.9) for intermediate-acting insulin, 7.1 (5.8-16.7) for premixed insulin, 0.7 (0.7-0.7) for glibenclamide, and 2.1 (1.8-2.8) for metformin.

Conclusion: The availability of the five essential medicines and three diagnostic tests for diabetes in Africa is suboptimal. The relatively high cost of insulin, HbA1c, and lipid profile tests is a significant barrier to optimal diabetes care. Pragmatic country-specific strategies are urgently needed to address these inequities in access and cost.

Keywords: Availability, Affordability, Essential medicines, Diagnostic tests, Diabetes mellitus, Africa

INTRODUCTION

Currently, Africa is experiencing an exponential increase in the burden of diabetes mellitus (DM). According to recent estimates by the International Diabetes Federation (IDF), 24 million adults (1 in 22 adults) live with DM in Africa and

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the greatest future increase in the prevalence of DM will occur in Africa (1). This high burden of DM and other non-communicable diseases (NCD) coupled with the existing high burden of communicable diseases through HIV and tuberculosis directly poses a significant economic strain on the poorly structured and financed healthcare systems (2).

Despite the well-documented increase in the burden of DM to epidemic proportions, the African continent still faces a persistent challenge of inequitable access to affordable essential medicines and diagnostic tests for DM in most healthcare facilities (2). In the historic September 2011 high-level meeting, the United Nations General Assembly recognised the magnitude of the NCD epidemic globally and its threat to national economic development. One of its resolutions was to improve the access to medicines to treat NCD (DM inclusive) (3).

The optimal availability of affordable essential medicines and diagnostic tests for NCD in healthcare systems is fundamental in addressing the growing morbidity and mortality associated with NCD, DM inclusive. As part of its 2013-2020 Global Action Plan (GAP) for prevention and control of NCD, WHO set a target of ≥80% availability of affordable essential medicines and basic technologies required to treat major NCD (4).

Contemporary evidence on the extent of availability and affordability of essential medicines and diagnostic tests relevant to the management of DM in Africa is needed to guide pragmatic and appropriate strategies to address the perennial challenge of inequitable access to affordable essential medicines and diagnostic tests for DM.

No recent study has comprehensively documented the status of availability and affordability of essential medicines and diagnostic tests for DM in SSA. This systematic review and meta-analysis aimed to document the current status of availability and affordability of specific essential medicines and diagnostic tests for DM in Africa, as recommended by the WHO Package of Essential Non-communicable Disease Interventions for Primary Health Care in Low-Resource Settings (WHO-PEN) (5).

MATERIALS AND METHODS

The review was conducted according to the criteria outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (6). The PRISMA checklist is available as a Supplementary Table 1.

Search strategy

We searched Medline, EMBASE, SCOPUS, Cochrane Library, and Africa Journal Online databases for published studies from January 2000 to December 2021. In consultation with a medical librarian, the following search terms were used and adapted for the various databases: “Access OR availability OR price OR cost OR affordability AND “essential medicines” OR medicines OR drugs OR insulin OR “oral hypoglycaemic agents” OR metformin OR sulfonylureas AND tests OR “laboratory tests” OR “diagnostic tests” OR glucometers OR “glycated haemoglobin” OR “lipid profile”AND “diabetes mellitus" OR diabetes OR “type 2 diabetes” OR “type 1 diabetes” OR “type 2 diabetes mellitus” AND Algeria OR Angola OR Benin OR Botswana OR ‘‘Burkina Faso’’ OR Burundi OR Cameroon OR ‘‘Cape Verde’’ OR ‘‘Central African Republic’’ OR Chad OR Comoros OR ‘‘Democratic Republic of Congo’’ OR Djibouti OR Egypt OR ‘‘Equatorial Guinea’’ OR Eritrea OR Ethiopia OR Gabon OR Gambia OR Ghana OR Guinea OR ‘‘Guinea Bissau’’ OR ‘‘Ivory Coast’’ OR ‘‘Cote d’Ivoire’’ OR Kenya OR Lesotho OR Liberia OR Libya OR Libya OR Madagascar OR Malawi OR Mali OR Mauritania OR Mauritius OR Morocco OR Mozambique OR Namibia OR Niger OR Nigeria OR Rwanda OR ‘‘Sao Tome’’ OR Senegal OR Seychelles OR ‘‘Sierra Leone’’ OR Somalia OR ‘‘South Africa’’ OR “South Sudan” OR Sudan OR Swaziland OR Tanzania OR Togo OR Tunisia OR Uganda OR Zaire OR Zambia OR Zimbabwe OR ‘‘Central Africa’’ OR ‘‘West Africa’’ OR ‘‘Western Africa’’ OR ‘‘East Africa’’ OR ‘‘Eastern Africa’’ OR ‘‘North Africa’’ OR ‘‘Northern Africa’’ OR ‘‘Southern Africa’’ OR ‘‘sub

Saharan Africa'' OR ''sub-Saharan Africa'' OR Africa.

References of the selected eligible articles and published review articles were also hand-searched for any original articles. We restricted the search and selection to articles published in the English language.

Study selection criteria

We included cross-sectional or prospective cohort studies published between January 2000 and December 2021 in the English language and reported any data on the availability and affordability of specific essential diabetes drugs and diagnostic tests. The specific essential diabetes drugs were short-and intermediate-acting insulin, premixed insulin, metformin, and glibenclamide. The essential diabetes diagnostic tests considered were glucometers, glycated haemoglobin (HbA1c), and lipid profile.

We excluded retrospective studies, case series and reports, studies published in languages other than English, and studies whose full texts could not be retrieved.

Data extraction

Articles were retrieved from the various databases, exported to *Endnote version 20,* and duplicates removed. Two independent reviewers (DK and RES) conducted the preliminary screening of titles and abstracts to identify potentially eligible articles. Then, full texts of the potentially eligible studies were reviewed for eligibility. A third reviewer (FB) was used as a tie-breaker for any disagreements.

Eligible articles were collated, and data were extracted by APK, RO, and FB using a spreadsheet. The information of interest included the surname name of the first author, year of publication, country, and region of Africa where the study was performed (Eastern, Western, Central, Southern, and Northern), type of healthcare facility where the study was performed (public/private hospital and pharmacy), number of healthcare facilities surveyed in each study, availability of short-acting, intermediate-acting, and pre-mixed insulin, or any type of insulin, metformin, glibenclamide, glucometers, HbA1c, lipid profile tests, and affordability of these essential medicines and diagnostic tests of interest. The HbA1c test was included in this review despite its exclusion in the WHO-PEN, because of its important role in the diagnosis and monitoring of diabetes in clinical care.

Operational definitions

Availability was defined as the proportion (expressed as a percentage) of healthcare facilities where the surveyed essential medicine(s) and/or diagnostic test(s) of interest were present at the time of primary data collection. Availability of ≥80% was considered optimal as highlighted by the WHO GAP for prevention and control of NCD (4). Affordability was defined as the estimated total number of days' wages the lowest-paid government worker would be required to pay to obtain a full monthly standard dose of the lowest-priced generic (LPG) medicine or to pay for the diagnostic test as recommended by the WHO and Health Action International (HAI) (7). Currently, there is no international consensus definition of optimal affordability.

Assessment of quality of studies

Study quality was assessed by two independent authors (DK and APK) using the modified Newcastle Ottawa scale (Supplementary Table 2) (8). The scale has a total of 10 and studies with a total of >8, 6-8, and <6 were considered of high, moderate, and low quality, respectively.

Data analysis

All statistical analyses were performed using STATA v16.0 software (Stata Corp, USA). The descriptive data of the included studies were summarised using frequencies and 95% confidence intervals (CI) and median and interquartile range (IQR). The pooled availability of the essential medicines and diagnostic tests of interest were determined using a random-effect model meta-analysis and presented in forest plots. The affordability of the essential medicines and diagnostic tests was expressed as median (IQR). A meta-regression was conducted to assess if the differences in healthcare facilities and regions where the studies were conducted could explain the observed heterogeneity.

The heterogeneity of the included studies was assessed using the I^2 value. The I^2 values of <25, 25-50, and >50% were considered low, medium, and high levels of heterogeneity. Publication bias was assessed using the Egger test of bias with $p<0.05$ indicating significant publication bias (Supplementary Table 2) (9). A narrative synthesis was used to present some of the results.

Registration

The study protocol was registered in the PROSPERO International Prospective Register of systematic reviews (CRD-42021289376).

RESULTS

Figure 1 summarises the article selection in a PRISMA flow diagram. After searching the five databases, a total of 875 articles were obtained. From these, 115 duplicates were identified and removed. The titles and abstracts of the remaining 760 articles were screened and 52 articles were identified for full-text review. Of the 52 articles, 31 were excluded and the remaining 21 were included in the systematic review and meta-analysis.

Characteristics of included studies

The characteristics of the included studies are summarised in Table 1. All studies had a cross-sectional design and were conducted in 2,215 health facilities across 15 African countries. Most studies (n=9, 42.9%) were conducted in Eastern African countries (10-18), and the rest in the Southern (n=6, 28.6%) (19-24) and Western (n=4, 19.1%) (25-28) regions. Two studies (10%) were conducted in more than one region of Africa (29, 30). Most of the surveyed healthcare facilities were public (n=1498, 67.6%).

The availability of short-acting, intermediate-acting, and premixed insulin was reported by ten studies (12, 13, 16, 18, 19, 24-26, 28, 30), six studies (12, 16, 18, 19, 25, 28), and four studies (12, 18, 25, 28), respectively. Fourteen studies reported the availability of glibenclamide (10-13, 16, 18, 20, 22, 24-26, 28-30) while 17 studies reported the availability of metformin (10-13, 15-18, 20-22, 24-26, 28-30).

The availability of glucometers, HbA1c, and lipid profile tests were reported by 16 studies (10-12, 14-18, 21-23, 25-27, 29, 30), three studies (16, 18, 25), and five studies (16, 18, 25, 26, 30), respectively.

The affordability of the three diagnostic tests (blood glucose testing, HbA1c, and lipid profile) and the five diabetes medicines (short-acting, intermediate-acting, premixed insulin, metformin, and glibenclamide) was reported by two studies (18, 25) and five studies (18-20, 25, 28), respectively. Generally, high heterogeneity was noted across all the studies with the I^2 value ranging from 83.77% to 98.86%.

Assessment of study quality and publication bias

The assessment of the quality of studies and funnel plots assessing publication bias are summarised in supplementary Table 2 and Supplementary Figures 1, 2, and 3, respectively. Egger's test was also used to assess publication bias across the meta-analyses. Thirteen studies (62%) were of moderate quality while the rest were of low quality. No publication bias was observed across the studies as shown in Supplementary Table 3.

Availability of essential medicines for diabetes mellitus

The individual and pooled availability of the five essential medicines for DM (three types of insulin, glibenclamide, and metformin) are summarised in Tables 1 and 2, and as forest plots in Figures 2, 3, 4, 6, and 7. The pooled availability was highest for pre-mixed insulin (49.4%, 95% CI: 24.9% - 73.9%, I^2=90.57%, p<0.001), followed by short acting insulin (33.5%, 95% CI: 17.8% - 49.2%, I^2=95.02%, p<0.001), and least for intermediate acting insulin (23.1%, 95% CI: 6.3% - 39.9%, I^2=91.6%, p<0.001) (Figures 2, 3, and 4).

Five studies reported information on the availability of any type of insulin (10, 21-23, 29), with availability ranging from 0% in Benin and Eritrea (30) to 89% in Tanzania in a multi-country study including five African countries by Gupta et al (29). The pooled availability of any type of insulin in these studies was 45.9% (95% CI 27.5% - 64.3%, I^2 =98.86%, p<0.001) (Figure 5).

Glibenclamide was the only sulfonylurea whose availability was assessed. The pooled availability of glibenclamide and metformin was 55.9%, 95% CI: 43.8% - 68.0%, I^2=96.7%, p<0.001, and 47.0%, 95% CI: 34.6% - 59.4, I^2=97.54%, p<0.001, respectively (Figures 6 and 7). A wide variation in the availability of the two oral hypoglycaemic agents (glibenclamide and metformin) was noted across the studies, with the availability of glibenclamide and metformin ranging from 9.1% in Malawi (22) to 100% in Uganda (18), and 11% in Ethiopia (10) to 100% in Uganda (18) and Swaziland (current day-Eswatini) (20), respectively.

Availability of essential diagnostic tests for diabetes mellitus

The availability of the three essential diagnostic tests for DM is summarised in Tables 1 and 2, and forest plots in figures 8, 9, and 10. The availability of glucometers ranged from 6% in Mozambique to 100% in Cameroon, with an overall pooled availability of 49.5% (95% CI: 37.9% - 61.1%, I^2=97.43%, p<0.001) (Figure 8). The availability of glucometers was significantly higher in Central (77%) and Northern Africa (75%), and lowest in Western Africa (31.4%, p<0.001).

Availability of the HbA1c test ranged from 9.4% in one study in Uganda (16) to 43.2% in another study in Uganda (18), with an overall pooled availability of 24.6% (95% CI: 3.1% - 46.1%, I^2=91.64, p=0.02) (Figure 9). For lipid profile tests, the availability ranged between 0% in studies from Benin and Eritrea (30) to 65.9% in Uganda (18), with an overall pooled availability of 35.7% (95% CI: 19.4% - 51.9%, I^2=83.77%, p<0.001) across five studies including 263 health facilities (Figure 10).

Affordability of essential medicines and diagnostic tests for diabetes mellitus

The affordability of the essential medicines and diagnostic tests for DM is summarised in Tables 1 and 2. The cost of glibenclamide and metformin was less than 1.3 days' wages in most countries (18-20, 25), except in Uganda and Nigeria, where the cost of metformin was 2.8 and 10.7 days' wages, respectively (18, 28). The LPG glibenclamide cost 3.3 days' wages in private hospital pharmacies in a study conducted in Nigeria (28).

Affordability of insulin was reported by three studies (18, 25, 28). All three classes of insulin cost less than five days' wages in Uganda (18). The cost of short-acting and intermediate-acting insulin was similar in Cameroon (3.85 days' wages) with the cost of premixed insulin almost five times more (18.7 days' wages) (25). The cost of short-acting and premixed insulin was lower in private pharmacies than in private hospital pharmacies (28).

The affordability of the essential diagnostic tests for DM was assessed by only two studies conducted in Uganda (18) and Cameroon (25). Blood glucose testing cost less than 1.4 days' wages in both countries. In comparison, the cost of lipid profile testing in Uganda was twice that in Cameroon (7.5- and 3.6-days' wages, respectively). The cost of HbA1c was higher in Cameroon (12.6 days' wages) than in Uganda (8.6 days' wages).

DISCUSSION

In this systematic review and meta-analysis, we comprehensively assessed the availability and affordability of essential medicines and diagnostic tests for DM as recommended by the WHO-PEN in Africa. Using the WHO GAP goal, availability was suboptimal for all the essential medicines and diagnostic tests studied but particularly worse for the HbA1c test and intermediate-acting insulin. All three types of insulin and diabetes diagnostic tests were reported to be relatively costly in Uganda, Cameroon, and Nigeria.

Similar findings of suboptimal availability and unaffordable essential medicines and diagnostic tests for DM have been widely reported in most Asian, European, and South American low-and middle-income countries, especially in the public sector (30-36). In the Prospective Urban Rural Epidemiology (PURE) study, a large prospective cohort study of 156,625 participants aged 35-70 years from 22 countries across six geographical regions (Asia, Africa, Europe, South and North America, and the Middle East), metformin was available in 88.2%, 86.1%, and 64.7%, of the surveyed pharmacies in upper-middle-income (MI), lower-MI, and lower-income (LI) countries, respectively. Glibenclamide was available in 70.9%, 62.5%, and 57.4% of surveyed pharmacies in the upper-MI, lower-MI, and LI countries, respectively. Availability of insulin was, generally, poor across all LMIC. Insulin was present in only 40.2%, 29.3%, and 10.3% of the surveyed pharmacies in the high-MI, low-MI, and LI countries. Compared to other LI countries, India had higher availability of metformin, glibenclamide, and insulin (100%, 72.7%, and 76.1%, respectively). Most households, especially in the rural LI countries, could not afford most drugs (defined as the cost of medicine >20% of household capacity-to-pay), with insulin being the most unaffordable diabetes medicine (31). Insulin, especially the analog types, and originator brands were also reported to be unaffordable in another study that evaluated 15 surveys on insulin price and availability using the WHO/HAI medicine price and availability measurement methodology in Brazil, China, India, Indonesia, Jordan, Kyrgyzstan, Pakistan, Russia, and five African countries (Ethiopia, Ghana, Kenya, Mali, and Uganda) (34).

In another study that performed a secondary analysis of the availability of specific medicines in 45 national and subnational surveys done using the WHO/HAI methodology, glibenclamide was present in 40.6%, 53.1%, and 69.1% of the surveyed public healthcare facilities in the included Western Pacific, Southeast, and East Mediterranean countries (33).

The poor availability and high cost of essential medicines and diagnostic tests for DM reported in our study and other similar studies conducted in LI countries could be due to several reasons. Due to the high burden of communicable diseases such as HIV, malaria, and tuberculosis in Africa, the healthcare systems are mainly structured to manage these conditions, with less emphasis given to the long-term management of NCD such as DM. In addition, management of these communicable diseases is adequately supported by several global funding initiatives or

programs such as the Global Fund, United Nations Joint Programme on HIV and AIDS (UNAIDS), and President's Emergency Plan for AIDS Relief (PEPFAR) (37), with minimal support towards equitable access to affordable or free essential medicines and diagnostic tests for DM.

Healthcare funding to ensure ready access to free or affordable essential medicines and diagnostic tests for DM remains inadequate, especially in the public sector, in most African countries (2). There is a well-documented reduction in health sector funding across most African countries. This is in contradiction with the 2001 Abuja Declaration that pledged to increase health sector funding in each African country to 15% of the country's national budget (38).

The absence of some essential medicines on the national essential medicine lists (NEML), lack of incentives to maintain optimal medicine stocks at the healthcare facilities, forecast inaccuracy, inefficient purchasing or distribution systems, high taxes, and mark-ups imposed, are other plausible explanations for the poor availability of essential medicines and diagnostic tests for DM in Africa (39-42).

The suboptimal availability and high cost of insulin, a life-saving drug for patients with type 1 diabetes and some patients with type 2 diabetes, is of great concern, especially in LMIC. The high insulin costs may be related to the monopoly of insulin production and marketing by a few international pharmaceutical companies with minimal production of generic or biosimilar insulin. The current clinical recommendation of using the newer insulin analogs as opposed to human insulin, because of their favourable side-effect profile, will further increase the cost of management of DM with insulin therapy in Africa (42).

The Lancet NCD Action Group in their seminal paper on promoting access to essential medicines for NCD, including DM, acknowledged that improving access to affordable medicines requires a comprehensive health system approach, which includes pharmaceutical sector governance, appropriate pharmaceutical workforce training, pharmaceutical management information systems, procurement planning and sustained financing of medicine. The Action group proposed key strategies to improve access to affordable medicines such as legislation to promote generic market entry and submission, appropriate pricing for generic medicines, reduced patient co-payments for generics, rational selection and use of medicines for NCD, good monitoring electronic systems to avert stock-outs, and increased financing for NCD medicines from domestic and international sources (43).

To improve access to medicines for NCD, 21 global biopharmaceutical companies have established access to medicine initiatives mainly in LMIC. One systematic review identified 120 of these initiatives with 52% focused on NCD. A worthwhile example is the Novartis Access program in 7 countries in SSA (Cameroon, Ethiopia, Kenya, Uganda, Rwanda, Malawi, and Tanzania). Its objective is to offer a portfolio of medicines for NCD like metformin to the public sector at a subsidized fee of one US dollar and also build the healthcare system's capacity in preventing, diagnosing, and treating NCD, including DM (44). Novo Nordisk, one of the key multi-national insulin manufacturing companies also adopted an equity pricing initiative to supply insulin at a much-subsidized fee to a selected number of low-income countries in SSA. The company also supports the Changing Diabetes in Children (CDiC) program in 10 countries in SSA in partnership with Roche Pharmaceuticals, the International Society of Paediatric and Adolescent Diabetes, and the World Diabetes Federation by offering free insulin and glucometers to children and adolescents living with type 1 DM (45).

Our review has some strengths and limitations which we acknowledge. This is the first systematic review and meta-analysis evaluating the availability and affordability of essential medicines and diagnostic tests for DM as recommended by the WHO-PEN in SSA. The limitations include heterogeneity in the number and type of the selected

health facilities (private or public) in the selected studies and methods of data collection used by the studies (few studies used the validated WHO-developed Service Availability and Readiness Assessment [SARA] tool). The SARA tool was developed based on nationally representative data and is frequently used globally. However, it does not include price data and hence, cannot be used to obtain information about affordability. None of the studies included in the systematic review and meta-analysis was of high quality on assessment.

Conclusion

This first-of-the-kind systematic review and meta-analysis highlights the glaring challenge of poor availability of essential medicines and diagnostic tests for diabetes in Africa. It also documents the high cost of insulin, a key drug for all patients with type 1 diabetes and some patients with type 2 diabetes, and diagnostic tests especially glycated haemoglobin and lipid profile in studies where affordability was assessed. It provides contemporary evidence about the significant challenge of poor access to affordable essential medicines and diagnostic tests for diabetes in Africa, underscoring the need for country-specific interventions to efficiently address this inequity.

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Table 1. Characteristics and findings of all eligible original studies

2nd name of first author, year of publication, and reference	Country (ies) where the study was performed	Number of healthcare facilities surveyed	Essential medicines and diagnostic tests studied	Study findings
A: Eastern Africa				
1. Bekele A et al, 2017.	Ethiopia.	873 healthcare facilities (445 public and 393 private).	-Insulin (type not specified). -Glibenclamide. -Metformin. -Glucometers.	Availability of essential medicines -Any type of insulin: 9%. -Metformin: 11%. -Glibenclamide: 28%. -Availability of diagnostic tests -Glucometers: 40%.
2. Isabirye VR et al 2021	Uganda	16 public healthcare facilities	-Glibenclamide -Metformin -Glucometers	Availability of essential medicines -Metformin: 58.8%. -Glibenclamide: 58.8%. -Availability of diagnostic tests -Glucometers: 96%.
3. Whyte SR et al, 2021	Uganda.	6 healthcare facilities (5 public and 1 private).	-Short-acting insulin. -Intermediate-acting insulin. -Pre-mixed insulin. -Glibenclamide. -Metformin.	Availability of essential medicines -Glibenclamide: 50%. -Metformin: 16.7%. -Short-acting, intermediate-acting, or pre-mixed insulin: 16.7%. Availability of diagnostic test -Glucometers: 33.3%.
4. Armstrong-Hough M et al, 2018.	Uganda.	196 health facilities (125 public and 71 private).	-Short-acting insulin. -Metformin. -Glibenclamide	Availability of essential medicines for DM - Short-acting insulin: 11.2%. -Metformin: 23.5%. -Glibenclamide: 25.5%.
5. Ishengoma DRS et al 2009	Tanzania	37 healthcare facilities (14 public and 23 private)	-Glucometers	Availability of glucometers: 51%.
6. Peck R et al, 2014	Tanzania.	24 healthcare facilities (18 public and 6 private).	-Metformin. -Glucometers.	Availability of essential medicines -Metformin: 33.3%. Availability of diagnostic test -Glucometers: 33.3%.
7. Rogers HE et al, 2018	Uganda.	53 public health facilities.	-Metformin. -Any sulphonylurea. -Insulin (Ultra short-acting, short-acting, intermediate-acting, and long-acting). -Glucometers. -Lipid profile. -Glycated haemoglobin test	Availability of essential medicines -Short-acting insulin: 52.8% -Intermediate-acting insulin: 47.2%. -Any sulphonylurea: 81.1%. -Metformin: 92.5%. Availability of diagnostic tests -HbA1c: 9.4%. -Lipid profile: 28.3%. - Glucometers: 62.3%.
8. Katende D et al, 2015.	Uganda.	28 healthcare facilities (24 public and 4 private).	-Metformin. -Glucometers	Availability of essential medicines -Metformin: 17.9%. Availability of diagnostic test -Glucometers: 32%.
9. Kibirige D et al, 2017[10]	Uganda.	145 healthcare facilities (22 public hospitals, 23 private hospitals, and 100 private pharmacies).	-Insulin (Short-acting, Intermediate-acting, and Pre-mixed). -Glibenclamide -Glimepiride	Availability of essential medicines - Intermediate-acting insulin-34.7% - Pre-mixed insulin-60.1% - Short-acting insulin-68.8% - Glibenclamide/Glimepiride-100%.

			-Metformin Diagnostic tests -Glucometers -Lipid profile -Glycated haemoglobin test	-Metformin: 100%. Availability of diagnostic tests - Glycated haemoglobin test: 43.2% - Lipid profile-65.9% - Glucometers-97.7% Affordability of essential medicines - Short-acting insulin-4.7 days' wages -Intermediate-acting insulin-4.9 days' wages -Pre-mixed insulin-4.9 days' wages. -Metformin 500 mg-2.8 days' wages. -Glibenclamide 5 mg-0.7 days' wages. Affordability of diagnostic tests - Blood glucose testing-1.1 days' wages. - Lipid profile-7.5 days' wages - HbA1c-8.6 days' wages.
3: Southern Africa				
10. Mendis S et al, 2007	Malawi	36 healthcare facilities (20 public and 16 private)	- Insulin (short-acting insulin, insulin zinc suspension, and insulin isophane) -Metformin -Glibenclamide	Availability of the essential medicines in the public and private sectors respectively: - Short-acting insulin: 25% and 6%. -Insulin zinc suspension: 30% and 25%. -Insulin isophane: 0%. Affordability of the essential medicines. -Glibenclamide and Metformin monotherapy cost < 1 day's wages.
11. Mhlanga B et al, 2014	Swaziland (current day Eswatini)	20 healthcare facilities (10 public and 10 private)	-Glibenclamide. -Metformin.	Availability of the essential medicines -Glibenclamide: 90%. -Metformin: 100%. Affordability of the essential medicines -Metformin and Glibenclamide: 1.2 days' wages.
12. Pfaff C et al 2017	Malawi	30 public healthcare facilities	-Any type of insulin -Metformin -Glucometers	Availability of essential medicines -Any type of insulin: 60% -Metformin: 40% Availability of essential diagnostic tests -Glucometers: 32%
13. Chikowe I et al, 2018.	Malawi.	-55 healthcare facilities (42 public and 13 private)	-Insulin (any type). -Glibenclamide. -Metformin. -Glucometers.	Availability of the essential medicines -Insulin: 1.8%. -Glibenclamide: 9.1%. -Metformin: 14.5%. Availability of the diagnostic tests -Glucometers: 38.2%.
14. Beran D et al, 2005	Mozambique and Zambia	11 public healthcare facilities in Mozambique and 13 public healthcare facilities in Zambia	-Insulin (pre-mixed, short-acting, and intermediate-acting insulin). -Glucometers.	Availability of essential medicine: -Insulin: 0% in 6 surveyed health centres and 20% in 5 surveyed hospitals in Mozambique. -42% in the surveyed referral health centres and 100% in all 13 surveyed hospitals in Zambia. Availability of diagnostic tests:

				-Glucometers: 6% in Mozambique and 25% in Zambia.
15. Kalungia CA et al, 2017.	Zambia	-15 public healthcare facilities.	-Insulin (short-acting and long-acting). -Glibenclamide. -Metformin	Availability of the essential medicines -Short-acting insulin: 22.2%. -Long-acting or intermediate-acting insulin: 37.8%. -Metformin: 51.1%. -Glibenclamide: 67.8%.
C: Western Africa				
16. Jingi A et al, 2014	Cameroon	11 healthcare facilities (2 private and 9 public).	- Insulin (Short-acting, Intermediate-acting, and Pre-mixed). -Glibenclamide -Metformin Diagnostic tests -Glucometers -Glycated haemoglobin -Lipid profile	Availability of medicines: -Intermediate-acting insulin: 10% -Glibenclamide, Metformin, Short-acting insulin, and Pre-mixed insulin: all at 80%. Availability of diagnostic tests -Glycated haemoglobin: 20% -Lipid profile: 40% -Glucometers: 100%. Affordability of essential medicines -Glibenclamide: 0.3 days' wages. -Metformin: 0.7 days' wages. -Short-acting insulin: 3.9 days' wages. -Intermediate-acting insulin: 3.85 days' wages. -Pre-mixed insulin: 18.7 days' wages. Affordability of diagnostic tests -Blood glucose testing: 1.3 days' wages. -Lipid profile: 3.6 days' wages. -Glycated haemoglobin: 12.6 days' wages.
17. Nyarko KM et al, 2016	Ghana.	-24 healthcare facilities (21 public and 3 private).	- Short-acting insulin. -Glibenclamide. -Metformin. -Lipid profile. -Glucometers.	Availability of essential medicines -Short-acting insulin: 20.8%. -Glibenclamide: 20.8%. -Metformin: 25%. Availability of diagnostic tests -Lipid profile: 16.7% -Glucometers: 25%.
18.Okpetu EI et al, 2018	Nigeria.	6 public healthcare facilities.	-Glucometers.	Availability of diagnostic tests -Glucometers: 33.3%.
19. Asuafor NG et al 2021	Nigeria	27 private pharmacies, 13 public pharmacies, and 25 private hospital pharmacies	- Insulin (short-acting, intermediate-acting, and pre-mixed insulin). -Glibenclamide. -Metformin.	Availability of essential medicines in the private pharmacies, public pharmacies, and private hospital pharmacies, respectively -Short-acting insulin: 46.2%, 25.9%, and 24%. -Intermediate-acting insulin: 0%, 7.4%, 4% -Pre-mixed insulin: 69.2%, 37%, 20% -Glibenclamide: 46.2%, 77.8%, 60%. -Metformin: 100%, 92.6%, 68%. Affordability of essential medicines in the private pharmacies, public pharmacies, and private hospital pharmacies, respectively -Short-acting insulin: 7, 7.5, 13.8 days' wages.

				-Pre-mixed insulin: 5.8, 7.1, 16.7 days' wages. -Glibenclamide: 0.7, 0.7, 3.3 days' wages. -Metformin: 2.1, 1.8, 10.7 days' wages.
D: >1 region of Africa				
19. Mendis S et al, 2012	Western (Benin), Eastern (Eritrea), and Northern (Sudan).	30 public healthcare facilities (12 in Benin, 6 in Eritrea, and 12 in Sudan).	-Short-acting insulin. -Metformin. -Glibenclamide. -Glucometers. -Lipid profile.	<u>Availability of essential medicines in Benin, Eritrea, and Sudan, respectively:</u> - Short-acting insulin: 0%, 0% and 28.6%. -Metformin: 25%, 0% and 42.9%. -Glibenclamide: 41.7%, 0% and 71.4%. <u>Availability of diagnostic tests in Benin, Eritrea, and Sudan, respectively:</u> -Glucometers: 67%, 17%, and 75%. -Lipid profile: 25%, 0% and 33%.
20. Gupta N et al 2020	Democratic Republic of Congo/DRC, Ethiopia, Malawi, Senegal, Tanzania	All public healthcare facilities (283 in DRC, 117 in Ethiopia, 43 in Malawi, 37 in Senegal, and 76 in Tanzania)	-Any type of insulin -Glibenclamide -Metformin -Glucometers	<u>Availability of essential medicines</u> -Any type of insulin: 48% in DRC, 79% in Ethiopia, 58% in Malawi, 51% in Senegal, and 89% in Tanzania. -Glibenclamide: 49% in DRC, 86% in Ethiopia, 58% in Malawi, 34% in Senegal, 88% in Tanzania -Metformin: 49% in DRC, 86% in Ethiopia, 58% in Malawi, 34% in Senegal, and 88% in Tanzania. <u>Availability of essential diagnostic tests</u> Glucometers: 77% in DRC, 85% in Ethiopia, 56% in Malawi, 9% in Senegal, 63% in Tanzania

Table 2. Summary of pooled availability and affordability of the five essential medicines and three diagnostic tests for diabetes

Essential medicine/diagnostic test	Number of studies	Pooled availability (%, 95%CI), I^2, p-value
Essential medicines		
Intermediate-acting insulin	5 studies	23.1 (6.3-39.9), I^2=91.60%, p<0.001
Short-acting insulin	10 studies	33.5 (17.8-49.2), I^2 =95.02%, p<0.001
Premixed insulin	4 studies	49.4 (24.9-73.9), I^2 =90.57%, p<0.001
Any type of insulin	5 studies	45.9 (27.5-64.3), I^2 =98.86%, p<0.001
Metformin	17 studies	47.0 (34.6-59.4), I^2 =97.54%, p<0.001
Glibenclamide	14 studies	55.9 (43.8-68.0), I^2 =96.70%, p<0.001
Diagnostic tests		
Glycated haemoglobin	3 studies	24.6 (3.1-46.1), I^2 =91.64%, p<0.001
Lipid profile	5 studies	35.7 (19.4-51.9), I^2 =83.77%, p<0.001
Glucometers	16 studies	49.5 (37.9-61.1), I^2 =97.43%, p<0.001
Essential medicine/diagnostic test	**Number of studies**	**Median (IQR) affordability (days' wages)**
Short-acting insulin	3 studies	7.0 (4.7-7.5)
Intermediate-acting insulin	2 studies	4.4 (3.9-4.9)
Premixed insulin	3 studies	7.1 (5.8-16.7)
Glibenclamide	3 studies	0.7 (0.7-0.7)
Metformin	3 studies	2.1 (1.8-2.8)

Figure 1. PRISMA flow diagram of selection of eligible studies

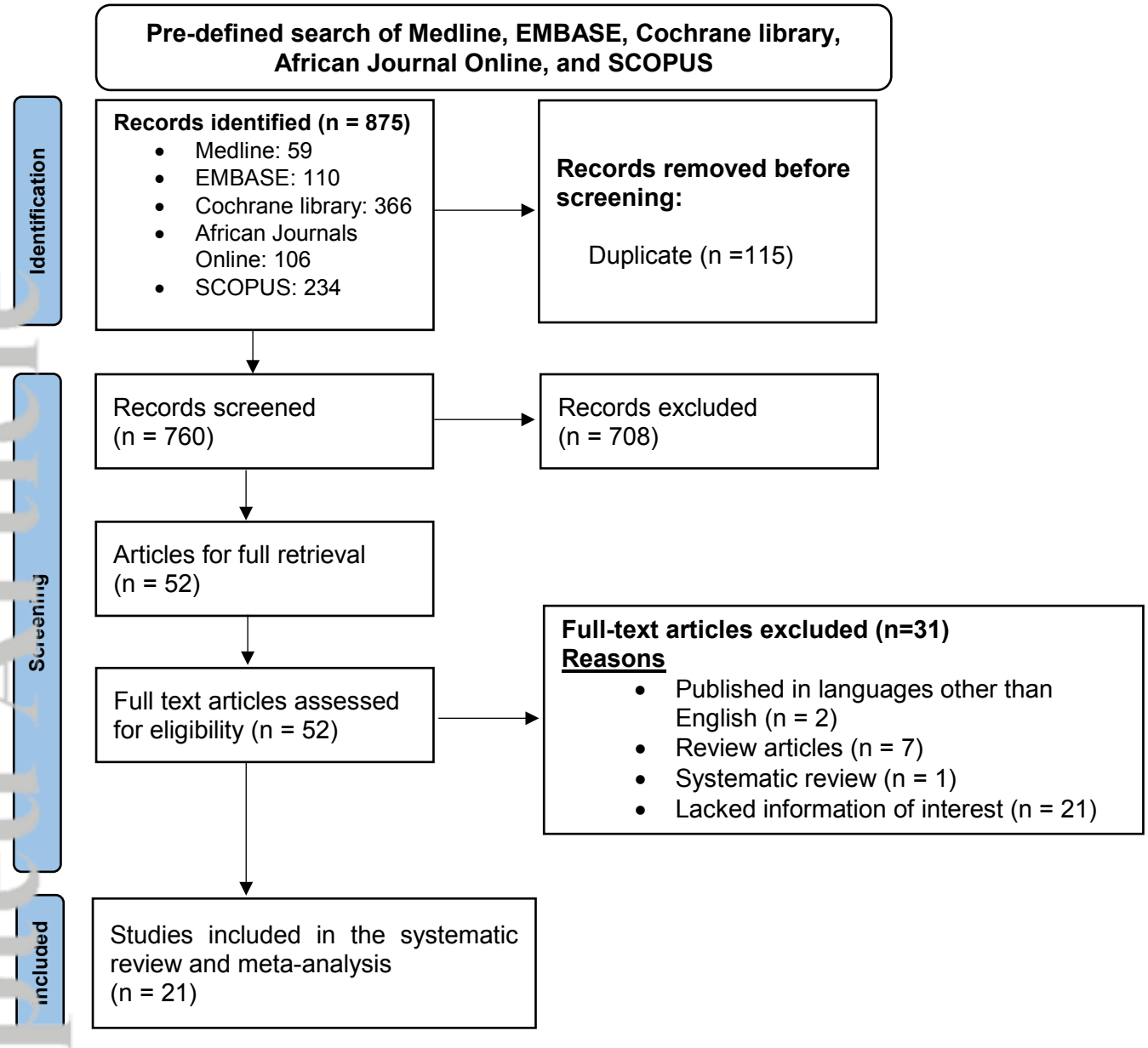

Figure 2. Forest plot showing the availability of short-acting insulin

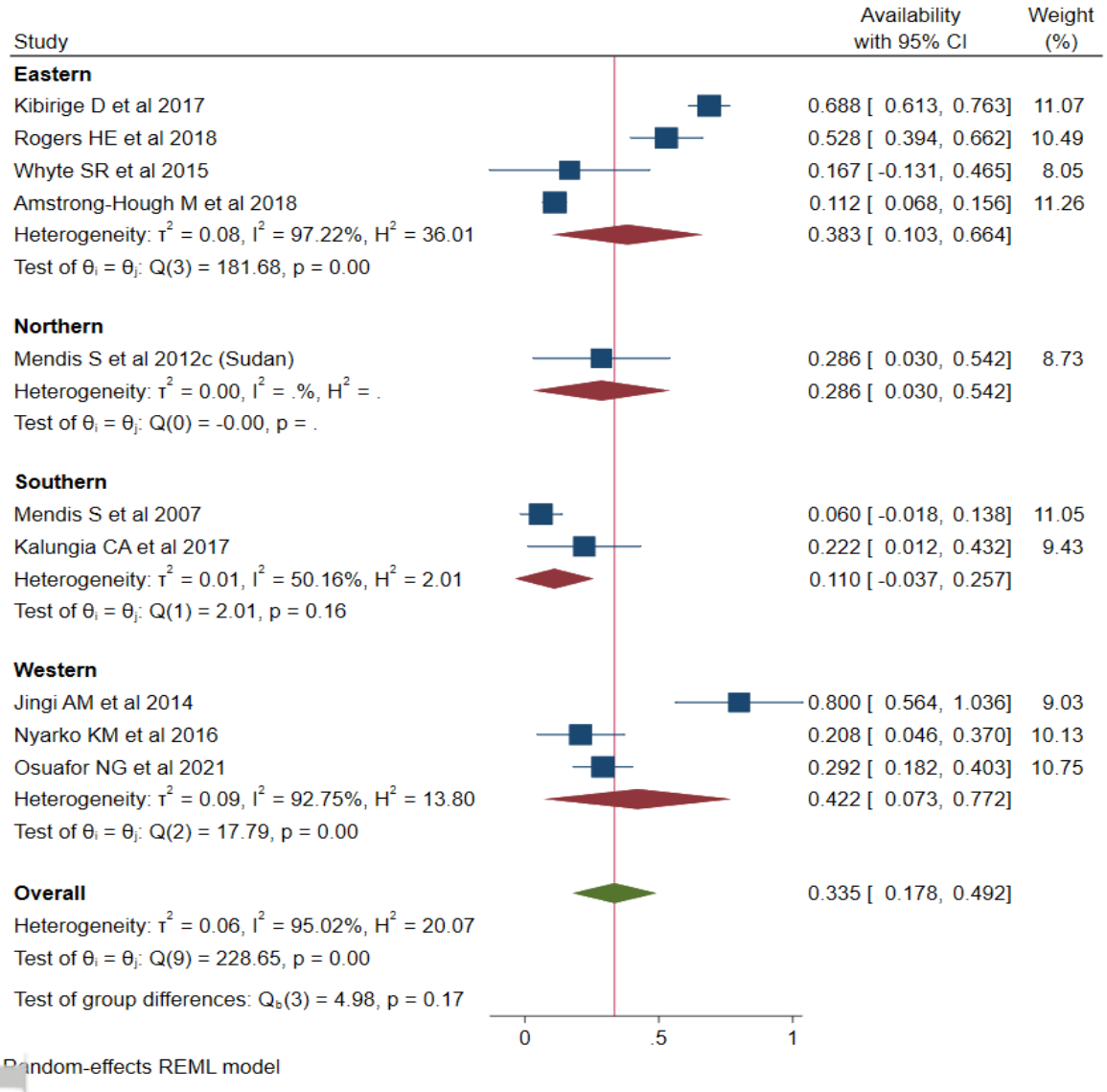

Figure 3. Forest plot showing the availability of intermediate-acting insulin

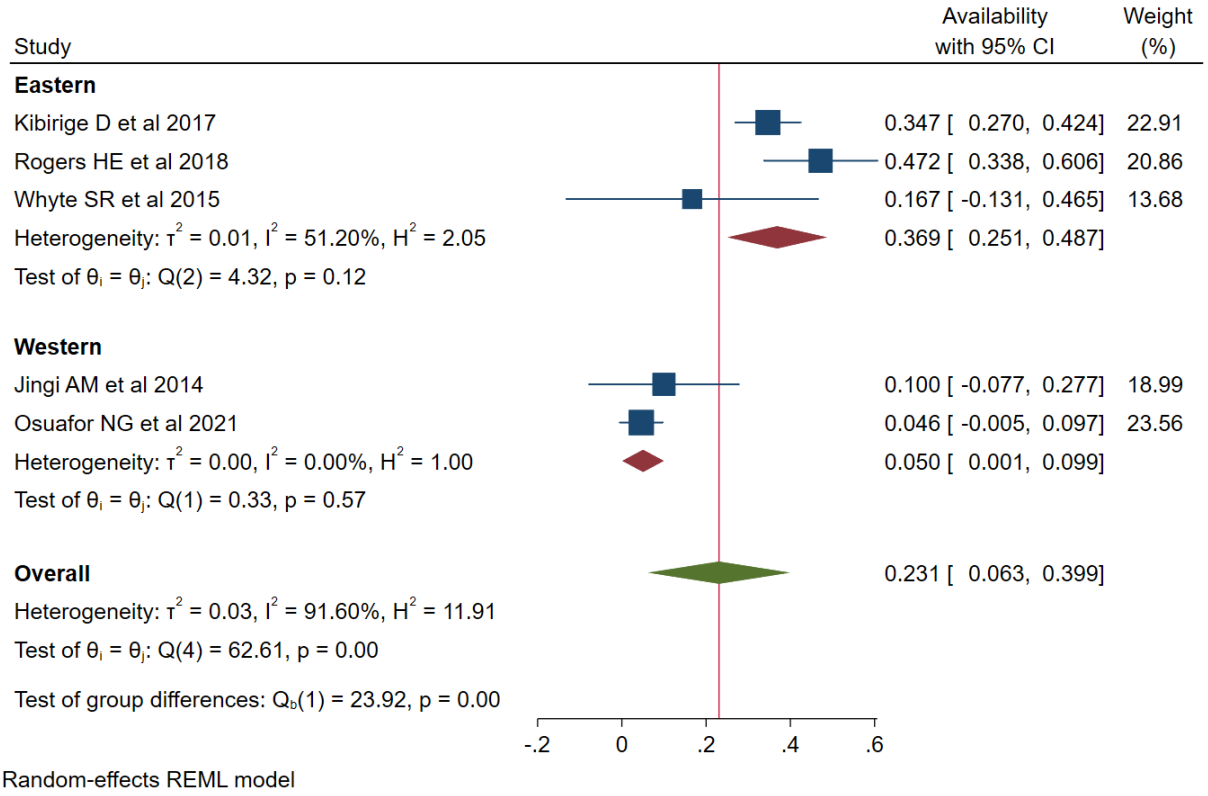

Figure 4. Forest plot showing the availability of pre-mixed insulin

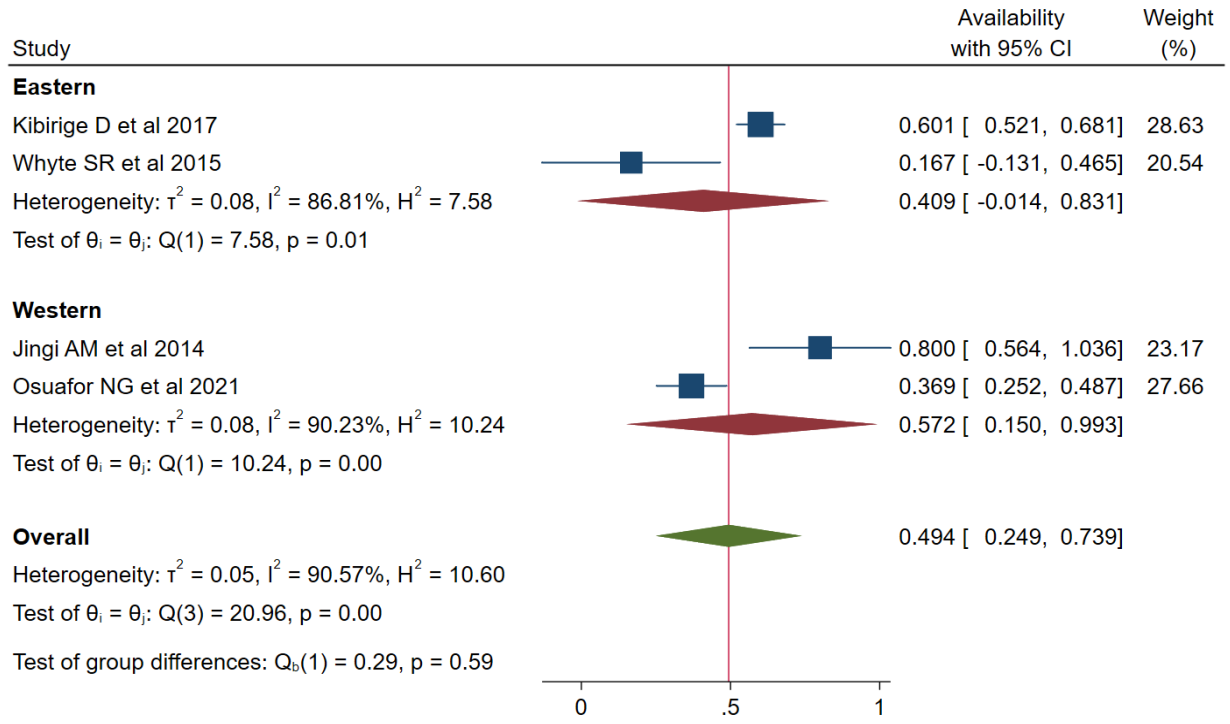

Figure 5. Forest plot showing the availability of any insulin

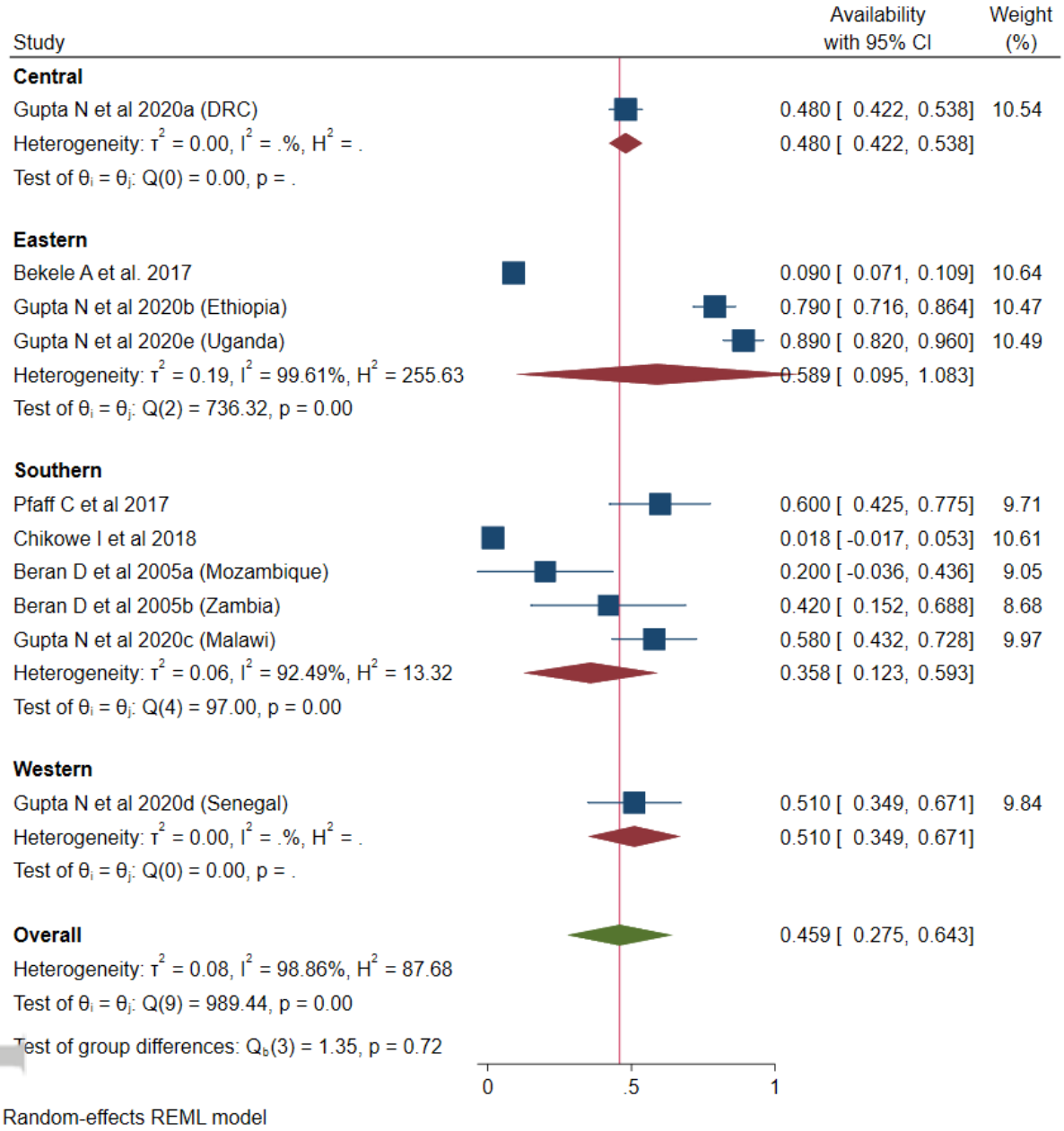

Figure 6. Forest plot showing the availability of glibenclamide

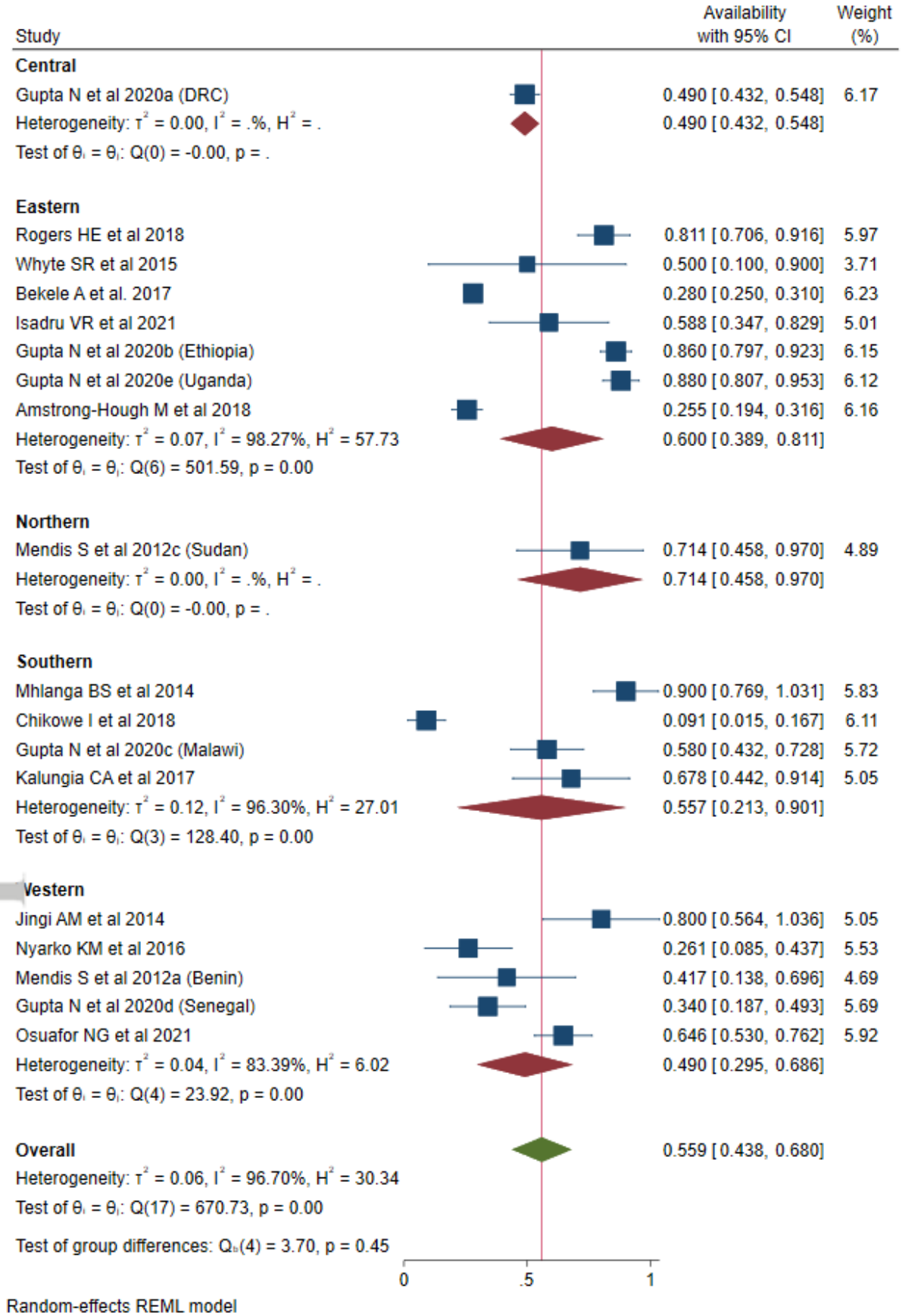

Figure 7. Forest plot showing the availability of metformin

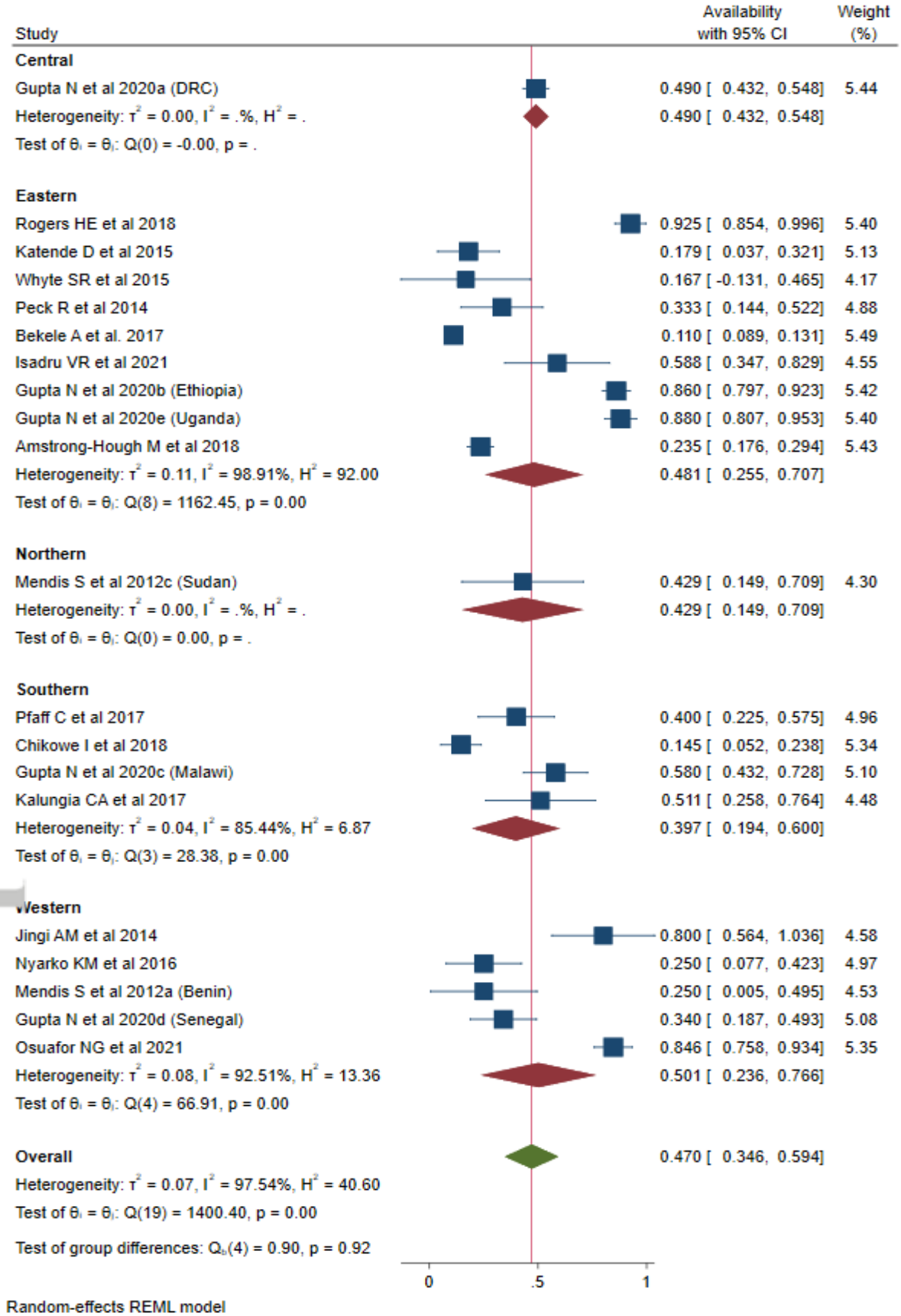

Figure 8. Forest plot showing the availability of glucometers

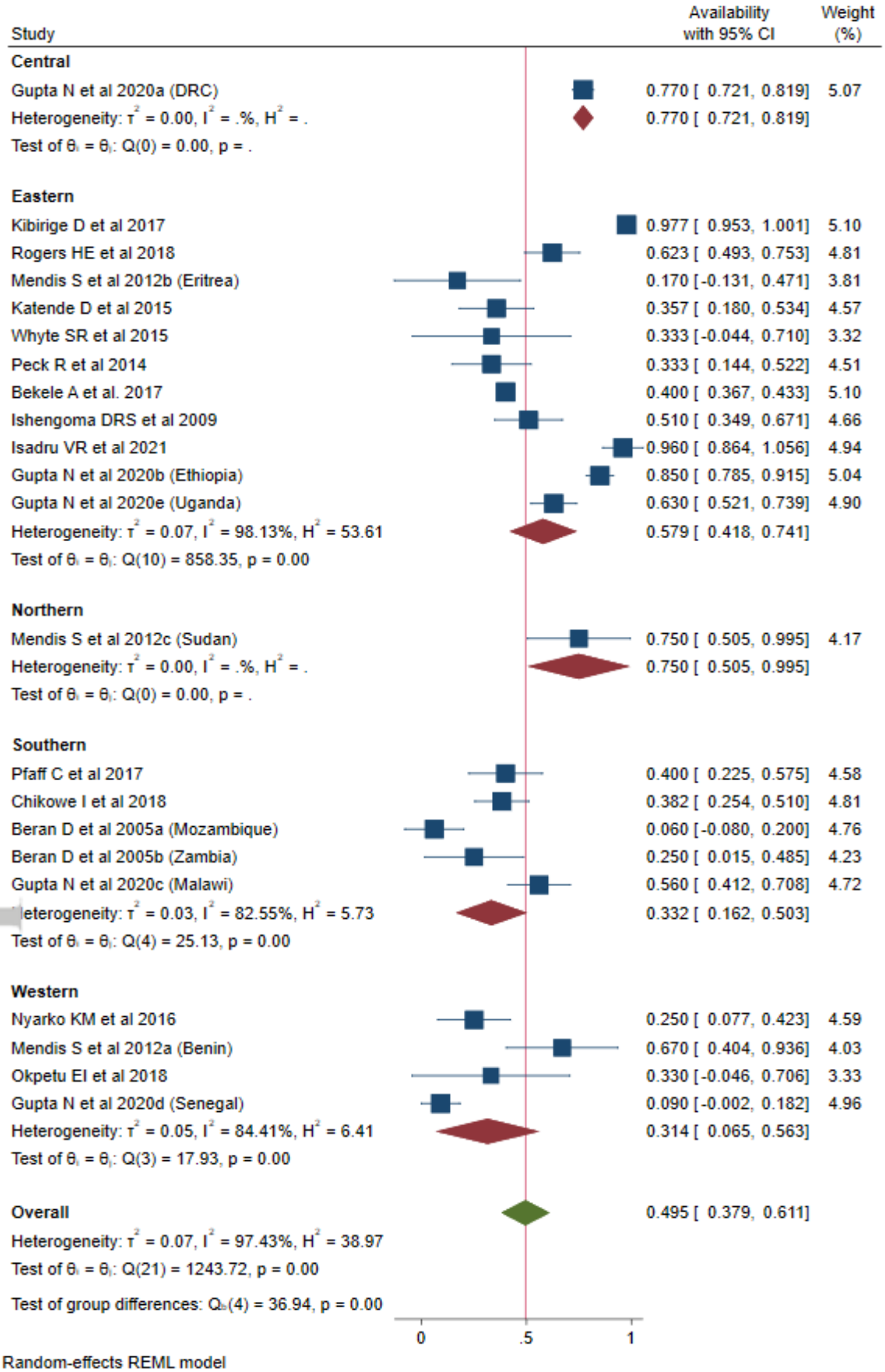

Figure 9. Forest plot showing the availability of glycated haemoglobin

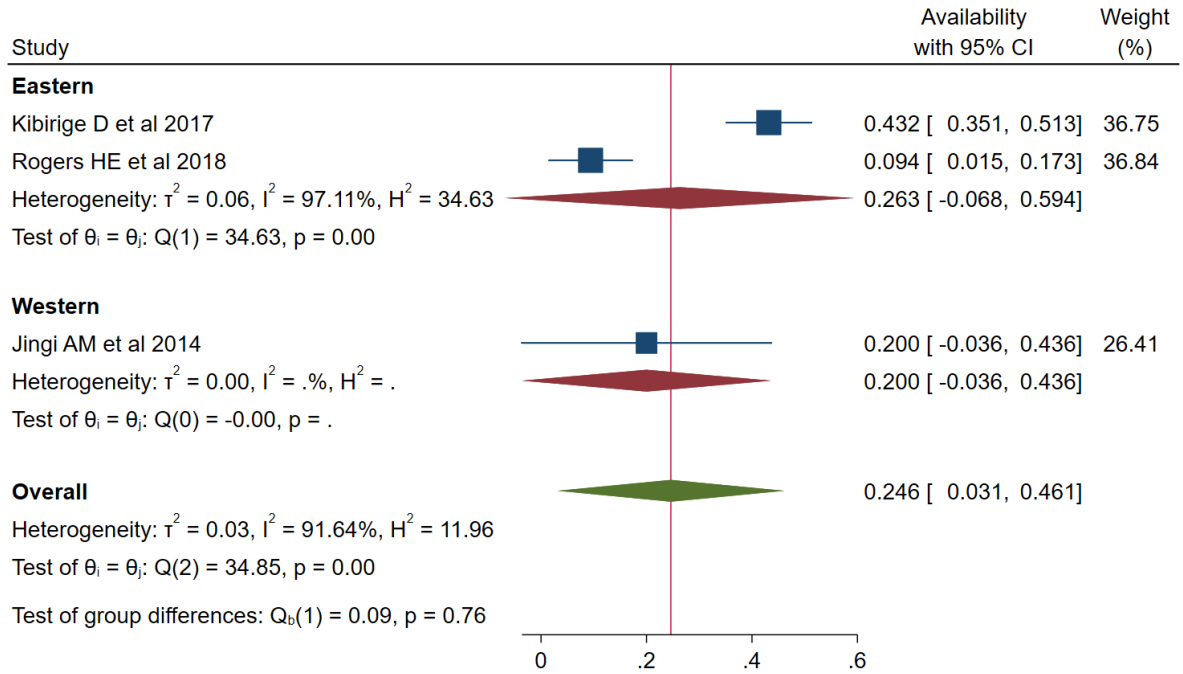

Figure 10. Forest plot showing the availability of lipid profile tests