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Type 2 diabetes complications and comorbidity in Sub-Saharan Africans

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ABSTRACT

Background: Context-specific evidence of the spectrum of type 2 diabetes (T2D) burden is essential for setting priorities and designing interventions to reduce associated morbidity and mortality. However, there are currently limited data on the burden of T2D complications and comorbidity in sub-Saharan Africa (SSA).

Methods: T2D complications and comorbidities were assessed in 2,784 participants with diabetes enrolled from tertiary health centres and contextualised in 3,209 individuals without diabetes in Nigeria, Ghana and Kenya. T2D complications and comorbidities evaluated included cardiometabolic, ocular, neurological and renal characteristics.

Findings: The most common complications/comorbidities among the T2D participants were hypertension (71%; 95% CI 69–73), hyperlipidaemia (34%; 95% CI 32–36), and obesity (27%; 95% CI 25–29). Additionally, the prevalence of cataracts was 32% (95% CI 30–35), diabetic retinopathy 15% (95% CI 13–17), impaired renal function 13% (95% CI 12–15), and erectile dysfunction (in men) 35% (95% CI 32–38). T2D population-attributable fraction for these comorbidities ranged between 6 and 64%.

Interpretation: The burden of diabetes complications and comorbidity is substantial in SSA highlighting the urgent need for innovative public health strategies that prioritise promotion of healthy lifestyles for prevention and early detection of T2D. Also needed are strategies to strengthen health care system capacities to provide treatment and care for diabetes complications.

1. Research in context

1.1. Evidence before this study

Type 2 diabetes (T2D) is the most common metabolic-endocrine disorder affecting adults. Its multisystemic nature implies that complications and comorbidities can affect many organ systems, especially in the absence of good glycaemic control. Currently,

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there is inadequate data on the burden and risk factors associated with T2D complications and comorbidities in sub-Saharan Africa (SSA). Except for the Diabcare Africa study, most of the published studies have small sample sizes, were conducted in a single hospital and/or did not evaluate associated risk factors. In addition, only a subset of participants included in these studies had data for some complications/comorbidities; for example, 45 percent of patients had fasting lipids in the largest study to date. The data from these studies indicate that hypertension is the most common T2D complication/comorbidity in SSA (up to 65% of patients), ocular complications (cataracts and retinopathy) were present in 14–18% and signs of neuropathy were found in up to 48% of patients.

1.2. Added value of this study

The findings of the present study provide a richer context for the assessment of burden and risk factors for T2D complications/comorbidities in SSA by using a large and well-characterised sample to estimate prevalence of a set of variables that were assessed by clinical examination, laboratory assays and medical history. The study identified risk factors for T2D complications/comorbidities and specifically investigated the effect of study site while adjusting for other covariates to identify heterogeneity between sites which may reflect differential access to care and differences in lifestyle/behavioural characteristics. The prevalence of the metabolic syndrome was particularly high as it was observed in three-quarters of T2D patients. Since many complications/comorbidities (e.g. cataracts) seen in T2D can be due to other disorders, the specific enrolment of controls in the present study facilitated the estimation of risk conferred by T2D on specific comorbidities as well as calculation of population attributable fraction (PAF) of the comorbidity due to T2D. The PAF provides an estimate of the proportion by which the burden of the comorbidity would be reduced in the population if T2D were absent or controlled.

1.3. Implication of all the available evidence

The findings of the present study combined with existing evidence indicate that the burden of T2D complications/comorbidity in SSA is high and specific strategies are needed to limit their deleterious impact on lifestyle, morbidity and mortality. Good glycaemic control and achieving patient weight loss will mitigate the two most critical risk factors for T2D complications/comorbidity. In this regard, increasing the capacity to monitor glycaemic control in SSA is crucial. Regular screening for hyperlipidaemia, renal function, ocular and foot complications in all T2D patients (rather than the current one-half to two-thirds of patients even in major specialist centres) is important and the adoption of a consensus screening checklist may facilitate this goal. Further research is needed to identify the factors responsible for the differences between sites reported by this and previous studies, as there may be the need for region-specific interventions. New research initiatives are needed to generate reliable data on other aspects of T2D complications such as the age of onset, rate of progression and impact on quality of life.

2. Background

The burden of type 2 diabetes (T2D) is substantial and growing across sub-Saharan Africa (SSA), with an estimated diabetes prevalence of 7.1% in 2014 representing a 129% increase since 1980 [1,2]. Additionally, projections by the International Diabetes Federation (IDF) show that, whilst all regions of the world will experience increases in T2D prevalence, the greatest increase between now and 2045 will take place in SSA [3]. A key feature of T2D is the presence of complications and comorbidity which have implications for prognosis, overall disease burden and treatment options [4–9]. Thus, T2D care ought to integrate the prevention and management of comorbidities such as hypertension and dyslipidaemia, as well as complications including stroke, ophthalmological and neurological complications, among others [2,10–12]. This requires a strong evidence base of the key T2D complications and comorbidities in order to determine intervention priorities and assess the effectiveness of such interventions in specific populations. However, with the notable exception of the Diabcare Africa Study [13], most studies of T2D complications and comorbidities from Africa done so far only focus on one or a few specific complications and/or are in limited sample sizes. Indeed, the recent Lancet and Endocrinology Commission report on diabetes in SSA noted the absence of reliable data on the prevalence, age of onset, rate of progression and other aspects of T2D complications in SSA [14]. This study aimed to estimate the burden of T2D complications and comorbidities, identify their risk factors and estimate their population attributable fraction in sub-Saharan Africans enrolled in a large multi-country study.

3. Methods

3.1. Study participants and data collection

Participants included in the present investigation were drawn from a case-control study — the Africa America Diabetes Mellitus (AADM) Study. The AADM study, which enrolled participants between 2000 and 2016, was designed to assess the environmental and genetic determinants of T2Dwere [15,16]. Individuals aged 18 years or older were enrolled from Nigeria (Enugu, Ibadan and Lagos), Ghana (Accra and Kumasi) and Kenya (Eldoret) using a standardized consent and data collection protocol. Individuals with T2D were enrolled from medical centres while individuals without T2D were enrolled from surrounding communities of the respective medical centres. Details of study procedures and enrolment have been described elsewhere [15,16].

Briefly, potential participants were identified by research staff at outpatient clinics and community centres who explained the study objectives and procedures. Informed consent was obtained from willing individuals that met the inclusion/exclusion criteria followed by data collected on demographic, social, lifestyle factors and clinical data including medical history, anthropometry, blood pressure and cardiometabolic parameters as previously described [15,16]. Data were collected by trained research assistants and physicians . Neurological examination including tests of motor reflexes and sensation were conducted by physicians. Eye examination that involved pupillary dilation, applanation tonometry and fundoscopy were conducted by specialist ophthalmologists. The study received ethical approval from the Institutional Review Board at each Africa study site, Howard University and the United States National Institutes of Health.

3.2. Laboratory assays

Fasting samples obtained after an overnight fast of at least 8 h were used to measure clinical biomarkers using an auto-analyser, COBAS Integra 400 plus (Roche Diagnostics, Indianapolis, IN). Fasting plasma glucose was measured using an enzymatic method with hexokinase. HDL-cholesterol, LDL-cholesterol and triglycerides (TG) were determined enzymatically with methods standardized to in-house and other appropriate reference methods (CDC reference methods for HDL-cholesterol and isotope dilution mass spectrometry (ID-MS) for TG from the manufacturer). Creatinine was mea-

sured using a modified Jaffé reaction. eGFR was estimated using the Modification of Diet in Renal Diseases (MDRD) formula.

3.3. Definitions

T2D was defined according to the American Diabetes Association criteria of fasting plasma glucose concentration (FPG) $\geq$ 7.0 mmol/L, or 2-h post load value in the oral glucose tolerance test $\geq$ 11.1 mmol/l on more than one occasion, or pharmacological treatment for T2D confirmed by a review of medical records. Glycaemic control by fasting glucose levels (controlled glucose) among individuals with T2D was defined as fasting plasma glucose <6.1 mmol/L, the American College of Endocrinologists fasting glucose threshold for satisfactory diabetic control [17]. The complications and comorbidity evaluated included: complications by medical history (diabetic coma, visual problems, non-healing ulcers, amputation, stocking/glove numbness, transient ischemic attack/stroke, erectile dysfunction—ED), ocular complications as evaluated by ophthalmologic examination (cataract, retinal detachment, maculopathy, glaucoma, diabetic retinopathy), neurological complication by clinical examination (abnormal ankle reflex, abnormal knee reflex, abnormal touch, abnormal pain, abnormal vibration sense) and cardiometabolic complications including elevated triglycerides ($\geq$2.26 mmol/L), total cholesterol (TC $\geq$ 6.22 mmol/L) and low-density lipoprotein (LDL $\geq$ 4.14 mmol/L), and low high-density lipoprotein (HDL < 1.03/1.3 mmol/L, men/women); [18,19] hypertension defined as systolic blood pressure (SBP) $\geq$ 140 mmHg or diastolic blood pressure (DBP) $\geq$ 90 mmHg, or treatment for hypertension; overweight defined as body mass index (BMI) 25.0–29.9 kg/m^2, obese as BMI $\geq$30 kg/m^2; and metabolic syndrome (MS) was defined according to the International Diabetes Federation harmonized criteria [20]. We used the guidelines of the National Kidney Foundation Kidney Disease Outcome Quality Initiative that defined moderate CKD as eGFR <60 ml/min/1.73 m^2 to denote impaired renal function. We also defined high serum creatinine as serum creatinine >177 μmol/L. Diabetic retinopathy was diagnosed only if a participant had a minimum of one microaneurysm in any field, as well as exhibiting haemorrhages (dot, blot, or flame shaped), and maculopathy (with or without clinically significant oedema) [21].

3.4. Statistical analysis

Continuous variables were summarized using means and standard deviations (SD), or median and interquartile range (IQR) in case of deviation from normal distribution tested by the Shapiro-Wilk test. Categorical variables were summarized using proportions expressed as percentages. Student's *t*-test and Mann-Whitney U test were used to compare continuous variables between two groups; while categorical variables were compared using chi-squared tests. Adjusted prevalence was obtained as marginal predictions from logistic regression models with covariates set to their mean values. Logistic regression models were used to assess the association between each comorbidity/complication and potential correlates among individuals with T2D. We used the I^2-statistic from the random effects meta-analysis model to assess heterogeneity in prevalence across study sites. We computed population-attributable fraction (PAF) due to T2D from multivariable logistic regression models adjusting for age and sex. All statistical tests were two sided and $P < 0.05$ considered significant. Analyses were performed in STATA 15 (StataCorp. 2017. Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC).

4. Results

4.1. Characteristics of T2D cases and controls

We studied 5993 individuals (Table 1) including 2784 T2D cases (39% men) who had a mean age of 56 (SD 11) years and median known duration of T2D of 5 (IQR 2–10) years. Among cases, only 3% were current smokers and 15% were former smokers. Contrastingly, a larger proportion, 77%, were current consumers of alcohol and 20% were former alcohol consumers. Twenty-three percent of the cases had post-secondary education. The median fasting blood glucose level among cases was 9.8 (IQR 5.9–12.5) mmol/L. Glycaemic control as assessed by fasting glucose was low with only 27% of cases achieving controlled levels of blood glucose at enrolment despite nearly all cases being on diabetes treatment. Among the 2784 T2D cases, 112 were diagnosed during the study and were not previously on any T2D treatment. Among the 2672 previously diagnosed cases, 74% were on a combination of lifestyle intervention (diet and physical activity) and oral medication only, 18% used insulin in addition to lifestyle intervention and/or oral medication, 4% were on lifestyle intervention only, and 4% were not on any intervention. Metformin and sulfonylurea were the most common class of drugs, used by 83% of cases taking oral medication (42% metformin + sulfonylurea, 19% metformin only, and 22% sulfonylurea only) (Supplementary Table 1). Participants self-reported to be taking their medications at the time of the study.

Study participants also included 3209 controls (40% men) with a mean age of 45 (SD 16) years. Controls were more likely to have never smoked, less likely to be current consumers of alcohol and had lower prevalence of obesity, hypertension, hyperlipidaemia and low eGFR when compared with cases. In other words, cases had a more adverse lifestyle, metabolic and kidney function risk profile compared with controls (Table 1).

4.2. Prevalence of T2D complications and comorbidities

The prevalence of the evaluated T2D complications and comorbidities is shown in Table 2. Prevalence of cardiometabolic parameters was 71% for hypertension, 27% for obesity, 22% for hypercholesterolemia and 11% for hypertriglyceridemia. Dyslipidaemia for any of the lipid sub-fractions was observed in 34% while three-quarters (78%) had the metabolic syndrome by IDF criteria. Ocular complications of cataracts, glaucoma and diabetic retinopathy were found in 32%, 4% and 15%, respectively. Neurological complications such as abnormal ankle reflex and abnormal vibration sensation were more common (33% and 12%, respectively) in contrast to abnormal pain and abnormal touch sensation (4% and 5%, respectively). On the other hand, stocking/glove numbness by medical history was far more frequent (46%). ED was reported by 35% of the men (Table 2).

4.3. Prevalence of T2D complications and comorbidities by glycaemic control

The median blood glucose in controlled and uncontrolled cases (i.e. glycaemic control measured by fasting blood glucose) was 4.7 (IQR 4.3–5.1) mmol/L and 9.9 (IQR 7.4–14.0) mmol/L, respectively (Table 2). Cases with controlled glucose were older on average, had a shorter known duration of T2D, and comprised a higher proportion of men, when compared with cases with uncontrolled glucose. Therefore, in subsequent analyses we adjusted for age, sex and duration of T2D in comparisons between cases with controlled and uncontrolled blood glucose levels. The adjusted prevalence of many T2D complications and comorbidities did not differ by glycaemic control for most parameters with a few key exceptions as noted for hypertension (76% versus 72%, $P = 0.041$), ED in men (27%

Table 1
Characteristics of participants in the study of T2D complications and comorbidity in sub-Saharan Africa.

Characteristics	Number of participants (Controls/cases)		T2D Cases	Controls	[a]P value
Sex	5993 (3209/2784)	Men	39 (38–41)	40 (39–42)	0.426
Age	5993 (3209/2784)	Mean (SD)	56 (11)	45 (16)	<0.001
Education	5971 (3200/2771)	Post-secondary	23 (21–24)	26 (25–28)	0.001
Smoking	5945 (3181/2764)	Never smoked regularly	82 (80–83)	87 (86–88)	
		Former regular smoker	15 (14–17)	9 (8–10)	
		Current regular smoker	3 (2–4)	4 (4–5)	<0.001
Alcohol	5509 (3092/2417)	Never consumed regularly	3 (2–3)	7 (6–7)	
		Former regular consumer	20 (19–22)	28 (26–30)	
		Current regular consumer	77 (75–79)	65 (64–67)	<0.001
Comorbidity	5954 (3184/2770)	Overweight	36 (35–38)	28 (26–29)	<0.001
	5955 (3184/2770)	Obesity	27 (25–28)	23 (22–25)	0.005
	5904 (3164/2740)	Clinically defined hypertension	70(68–71)	40 (38–42)	<0.001
	5618 (2993/2625)	Raised TG	12 (11–13)	4 (4–5)	<0.001
	5618 (2993/2625)	Raised TC	22 (21–24)	15 (14–16)	<0.001
	5583 (2986/2597)	Raised LDL-cholesterol	24 (23–26)	18 (17–20)	<0.001
	5618(2993/2625)	Hyperlipidaemia (Raised TC, TG or LDL)	28 (27–30)	20 (19–22)	<0.001
	5617 (3209/2784)	Low HDL-cholesterol	60 (58–62)	52 (50–54)	<0.001
	5993(3209/2784)	Metabolic syndrome	77 (75–78)	25 (24–27)	<0.001
	4800 (2204/2596)	eGFR < 60 mL/min/1.73 m^2	13 (12–15)	5 (4–6)	<0.001
	4800 (2596/2204)	Creatinine > 177 µmol/L	2.4 (1.8–3.1)	0.4 (0.2–0.8)	<0.001

Data are percent (95% CI) except where otherwise stated; SD Standard deviation;.
[a] P-values are from Chi-square test; T2D Type two diabetes; TG triglycerides (Raised TG, TG ≥ 2.26 mmol/L); TC total cholesterol (Raised TC, TC ≥ 6.22 mmol/L); LDL Low-density lipoprotein (Raised LDL, LDL ≥ 4.14 mmol/L); HDL High-density lipoprotein (Low HDL, HDL < 1.03 (men); 1.3 (women)); eGFR estimated glomerular filtration rate.

versus 38%, $P = 0.002$), abnormal touch (0%versus4%, $p = 0.004$) and abnormal vibration sense (5% versus 10%, $P = 0.037$) (Table 2).

4.4. Risk factors for T2D complications and comorbidity

Independent associations of individual comorbidity or complication with age, sex, BMI and known duration of T2D, adjusted for study site and glucose control are shown in Tables 3 and 4. The results indicate that hypertension was associated with older age, higher BMI and longer known duration of T2D; while obesity was associated with the female sex and shorter known duration of T2D. Additionally, raised TG was associated with higher BMI; whereas raised TC and raised LDL were associated with the female sex, higher BMI and longer known duration of T2D.

Cataracts was associated with older age, lower BMI and longer known duration of T2D; diabetic retinopathy, and ED were associated with older age and longer known duration of T2D; and glaucoma was associated with older age and male sex (Table 4).

Among complications assessed by medical history (Table 5), visual problems were associated with older age, lower BMI and longer known duration of T2D; diabetic coma with lower BMI and longer known duration of T2D; non-healing ulcers with female sex; amputation with known duration of T2D; stocking or glove numbness with older age, female sex and longer known duration of T2D; and stroke with older age.

4.5. Prevalence of T2D complications and comorbidity by site

We assessed the variation in prevalence across study sites of the most common complications and comorbidities (Figs. 1 and 2). After adjusting for the effect of age, sex and known duration of T2D, there was significant variation in the prevalence of hypertension, obesity, raised TG, raised TC and raised LDL across sites as assessed by the I^2 statistic (I^2 ranging from 74% to 98%) – Fig. 1. A closer examination revealed that this difference was primarily driven by one site (Eldoret, Kenya) for raised TG and raised TC. Other features also showed substantial variation between sites, including the prevalence of visual problems, from 29% in Ibadan (Nigeria) to 74% in Kumasi (Ghana); stocking/glove numbness, from 33% in Lagos (Nigeria) to 70% in Kumasi (Ghana); ED, from 22% in Ibadan (Nigeria) to 67% in Kumasi (Ghana), and cataract from 21% in Eldoret (Kenya) to 55% in Lagos (Nigeria) – Fig. 2. The prevalence of diabetic retinopathy, abnormal knee jerk reflex and abnormal ankle jerk reflex varied less than the preceding complications and comorbidities.

4.6. Sensitivity analysis comparing prevalence of comorbidities between T2D cases and non-diabetes controls

The design of this study which enrolled both cases and controls enabled the conduct of sensitivity analysis comparing T2D cases with controls to evaluate the impact of non-diabetes risk factors on comorbid parameters. To aid the interpretation of comparisons, we assessed potential differences in the socio-demographic and behavioural characteristics of cases and controls; the distribution of sex, education, smoking and alcohol consumption was similar between the groups, whereas cases were older with mean age 56 (SD 11) years compared with 45 (SD 16) years among controls (Table 1). The age- and sex-adjusted prevalence of hypertension, overweight, raised TG and raised TC was higher in cases than controls. Similarly, comorbidities including visual problems, jaundice, stroke, cancer and kidney disease, though less common, were more prevalent in cases compared with controls. More crude- and age-sex adjusted results of the sensitivity analysis are shown in the Supplementary Table 2.

4.7. Population-attributable fraction of comorbidities

As previously noted, most T2D-associated complications and comorbidities can be due to other causes. To estimate the effect of T2D on the prevalence of the measures we studied, we used the population-attributable fraction (PAF). The population attributable fraction (PAF) is a measure that is widely used to assess the public health impact of risk factors or exposures in populations. Conceptually, it is defined as the fraction of all occurrence of a disease or other adverse condition in a population that is attributable to a specific exposure. Therefore, in the present study, PAF provides an estimate of the proportional reduction in the prevalence of the comorbidities that would occur if T2D were reduced to an alternative ideal exposure scenario (e.g. no T2D). Our findings show that the PAF due to T2D varies between 6% and 64% for most comorbidities

Table 2
Complications and comorbidities of T2D in sub-Saharan Africa by glycaemic control.

Controlled	All T2D cases	No. of T2D cases not controlled/No. of T2D cases	T2D cases not controlled	T2D cases controlled	[a]P-value
Participant characteristics					
Age, Mean (SD)	56 (11)	1805/684	55 (11)	58 (11)	<0.001
Sex (Percent men)	39 (37–41)	1805/684	38 (36–40)	43 (39–46)	0.029
Duration of T2D, Median (IQR)	5(2–10)	1805/684	5 (2–10)	3 (1–8)	<0.001
Glucose, Median (IQR)	9.8 (5.9–12.5)	1805/684	9.9 (7.4–14.0)	4.7 (4.3–5.1)	<0.001
Cardiometabolic and renal complications					
Obesity	27 (25–29)	1799/678	25 (23–27)	24 (21–28)	0.863
Clinically defined hypertension	71 (69–73)	1802/684	72(69–74)	76 (72–79)	0.041
Raised TG	11 (10–13)	1789/677	12 (10–13)	10 (8–13)	0.370
Raised TC	22 (20–24)	1789/677	23 (21–25)	19 (16–22)	0.075
Raised LDL-cholesterol	24 (23–26)	1772/669	25 (23–27)	21 (18–25)	0.110
Low HDL-cholesterol	60 (58–62)	1789/677	61 (59–63)	58 (54–61)	0.147
Hyperlipidaemia (Raised TC, TG or LDL)	34 (32–36)	1789/677	34 (32–36)	32 (28–35)	0.246
Metabolic syndrome	78 (77–80)	1805/684	81 (79–83)	80 (76–83)	0.318
eGFR < 60 mL/min/1.73 m^2	13 (12–15)	1522/536	11 (10–13)	12 (10–16)	0.515
Creatinine > 177 µmol/L	2.4 (1.8–3.1)	1522/536	1.5 (1.0–2.2)	2.6 (1.6–4.3)	0.059
Ocular complications					
Cataracts	32 (30–35)	1306/428	29 (27–32)	30 (26–35)	0.680
Retinal detachment	0.2 (0.0–0.6)	1151/385	0.1 (0.0–0.6)	0.1 (0.0–1.4)	0.760
Maculopathy	14 (12–16)	1152/378	13 (11–15)	12 (9–16)	0.538
Glaucoma	4 (4–5)	1805/684	4 (3–5)	4 (3–6)	0.856
Diabetic retinopathy	15 (13–17)	1157/389	14 (12–17)	12 (9–15)	0.165
Neurological complications					
Abnormal ankle reflex	33 (30–37)	554/106	34 (30–38)	29 (21–38)	0.327
Abnormal knee reflex	76 (72–79)	557/106	76 (73–80)	77 (68–84)	0.909
Abnormal touch	5 (4–7)	558/108	4 (3–6)	0 (0–4)	0.004
Abnormal pain	4 (3–6)	559/108	3 (2–5)	2 (1–7)	0.778
Abnormal vibration sense	12 (10–15)	558/107	10 (8–13)	5 (2–10)	0.037
Complications/comorbidity by medical history					
Diabetic coma	8 (7–9)	1758/663	7 (6–8)	8 (6–11)	0.256
Visual problems	47 (45–50)	1724/649	48 (46–50)	46 (42–50)	0.440
Non-healing ulcers	5 (4–6)	1732/655	5 (4–6)	4 (3–6)	0.427
Amputation	1 (1–2)	1765/665	1 (1–1)	1 (1–2)	0.321
Stocking/glove numbness	46 (44–48)	1770/668	46 (43–48)	48 (44–51)	0.434
TIA/Stroke	3 (2–3)	1572/566	3 (2–3)	3 (2–4)	0.965
[b]Erectile dysfunction	35 (32–38)	662/279	38 (34–42)	27 (22–33)	0.002

No. Number; Cases not controlled refers to cases whose glucose in not controlled; Cases controlled refers to cases with controlled glucose; T2D type two diabetes; SD standard deviation; IQR inter quartile range; TG triglycerides (Raised TG, TG ≥ 2.26 mmol/L); TC total cholesterol (Raised TC, TC ≥ 6.22 mmol/L); LDL Low-density lipoprotein (Raised LDL, LDL ≥ 4.14 mmol/L); HDL High-density lipoprotein (Low HDL, HDL <1.03 (men); 1.3 (women)); MS metabolic syndrome.
Data are percentage (95% CI) except for age, duration of T2D and glucose.
[a] Adjusted for age, sex and duration of T2D, except as indicated;.
[b] Men only; eGFR estimated glomerular filtration rate; Proportion of individuals with uncontrolled glucose is 73% (71–74). No. Cases not controlled, and No. Cases controlled do not always add up to 2784 because of missing glucose data.

studied, with it being higher for such conditions as hypertension, hypertriglyceridemia and the metabolic syndrome (Fig. 3).

5. Discussion

T2D is currently one of the most important non-communicable disorders in Africa. While there are increasingly better estimates of T2D prevalence in SSA, reliable data on the burden of T2D complications and comorbidity still lags far behind [14,22]. Estimating the burden and risk factors for T2D complications and comorbidity in SSA is critical because the limited available data shows that only half of people with T2D are diagnosed and only about one in nine patients receive the advice and medication needed to minimize complications [14]. Our findings indicate that the most common T2D comorbidities were hypertension (affecting about three in four persons), visual problems (affecting one in two persons), hyperlipidaemia (raised TC, LDL or TG) and obesity (each affecting about one in three T2D cases). A longer known duration of T2D, higher BMI and older age were important risk factors for most of the complications and comorbidities. These findings have implications for the objective prioritisation of complications for screening among T2D cases for efficient utilisation of scarce health resources in resource limited settings such as SSA.

The large sample size of the present study provided opportunity to present estimates of prevalence of T2D complications and comorbidity with greater precision. Having a control sample of non-T2D adults allowed for the computation of PAFs to facilitate the interpretation of the relative effect of T2D on the prevalence of the complications and comorbidities while the multi-site design enabled us to perform between-site comparisons.

Our findings show important similarities and differences with earlier reports of T2D comorbidity in SSA. Similar to our study, hypertension and raised TC were among the most common T2D comorbidities reported in the Diabcare Africa Study [13]. By contrast the Diabcare Africa study reported a much lower prevalence of raised TG than we report in the current study. Differences in sex distribution, glycaemia control and study design may partly explain the differences between the two studies. Sex differences in

Table 3
Odds ratio associated with risk factors for clinically-assessed T2D cardiometabolic comorbidity and complications.

Complication/comorbidity	Risk factor	uOR[a]	95% CI	P-value	aOR[b]	95% CI	P-value	aOR[c]	95% CI	P-value
Obesity	Age (Years)	0.99	(0.99–1.00)	0.169	1.00	(0.99–1.01)	0.794	1.00	(0.99–1.01)	0.965
	Sex (Ref = males)	3.78	(3.08–4.64)	<0.001	3.86	(3.11–4.80)	<0.001	3.84	(3.08–4.80)	<0.001
	Duration of T2D	0.97	(0.95–0.98)	<0.001	0.97	(0.95–0.98)	<0.001	0.97	(0.95–0.99)	<0.001
	Accra, Ghana	2.48	(2.02–3.04)	<0.001	2.19	(1.60–3.00)	<0.001	2.19	(1.60–3.01)	<0.001
	Kumasi, Ghana	0.36	(0.25–0.51)	<0.001	0.37	(0.24–0.57)	<0.001	0.39	(0.24–0.63)	<0.001
	Enugu, Nigeria	0.47	(0.36–0.63)	<0.001	0.62	(0.43–0.90)	0.012	0.62	(0.43–0.91)	0.013
	Ibadan, Nigeria	1.33	(1.12–1.59)	0.001	1.42	(1.06–1.89)	0.018	1.46	(1.09–1.96)	0.011
	Lagos, Nigeria	0.70	(0.51–0.96)	0.027	1.00	(0.66–1.52)	0.988	0.98	(0.64–1.49)	0.912
Hypertension	Age (Years)	1.07	(1.06–1.07)	0.000	1.06	(1.05–1.07)	<0.001	1.06	(1.05–1.07)	<0.001
	Sex (Ref = males)	1.14	(0.97–1.35)	0.113	0.95	(0.78–1.15)	0.581	0.96	(0.79–1.17)	0.694
	BMI (Kg/m^2)	1.08	(1.07–1.10)	0.000	1.10	(1.08–1.12)	<0.001	1.10	(1.08–1.12)	<0.001
	Duration of T2D	1.03	(1.02–1.05)	0.000	1.02	(1.00–1.03)	0.029	1.02	(1.00–1.03)	0.034
	Accra, Ghana	0.79	(0.64–0.97)	0.022	0.43	(0.31–0.60)	<0.001	0.44	(0.31–0.62)	<0.001
	Kumasi, Ghana	0.65	(0.50–0.83)	0.001	0.55	(0.38–0.79)	0.001	0.61	(0.41–0.91)	0.013
	Enugu, Nigeria	0.86	(0.69–1.08)	0.187	0.61	(0.43–0.85)	0.004	0.62	(0.44–0.87)	0.006
	Ibadan, Nigeria	1.45	(1.22–1.74)	0.000	0.61	(0.45–0.83)	0.002	0.63	(0.46–0.87)	0.004
	Lagos, Nigeria	0.72	(0.55–0.95)	0.019	0.50	(0.34–0.74)	0.001	0.52	(0.35–0.76)	0.001
Raised TG	Age (Years)	1.00	(1.00–1.01)	0.405	1.00	(0.99–1.01)	0.496	0.99	(0.98–1.01)	0.230
	Sex (Ref = males)	0.88	(0.73–1.06)	0.177	0.96	(0.77–1.20)	0.715	0.78	(0.58–1.04)	0.090
	BMI (Kg/m^2)	1.02	(1.01–1.04)	0.008	1.03	(1.02–1.05)	<0.001	1.05	(1.02–1.07)	<0.001
	Duration of T2D	0.98	(0.97–1.00)	0.031	0.98	(0.97–1.00)	0.07	0.98	(0.96–1.00)	0.166
	Accra, Ghana	0.47	(0.36–0.62)	0.000	0.10	(0.07–0.14)	<0.001	0.06	(0.04–0.10)	<0.001
	Kumasi, Ghana	0.57	(0.40–0.81)	0.002	0.12	(0.08–0.18)	<0.001	0.07	(0.03–0.14)	<0.001
	Enugu, Nigeria	0.41	(0.30–0.56)	0.000	0.09	(0.06–0.14)	<0.001	0.06	(0.04–0.11)	<0.001
	Ibadan, Nigeria	0.86	(0.70–1.05)	0.135	0.18	(0.14–0.24)	<0.001	0.13	(0.09–0.11)	<0.001
	Lagos, Nigeria	0.57	(0.39–0.82)	0.002	0.11	(0.07–0.17)	<0.001	0.09	(0.05–0.17)	<0.001
Raised TC	Age (Years)	1.01	(1.00–1.02)	0.013	1.01	(1.00–1.02)	0.267	1.01	(1.00–1.02)	0.272
	Sex (Ref = males)	1.66	(1.36–2.02)	0.000	1.90	(1.53–2.37)	<0.001	1.83	(1.46–2.28)	<0.001
	BMI (Kg/m^2)	1.03	(1.01–1.04)	0.002	1.02	(1.00–1.04)	0.024	1.02	(1.00–1.04)	0.019
	Duration of T2D	1.02	(1.01–1.03)	0.006	1.02	(1.00–1.03)	0.011	1.02	(1.00–1.03)	0.024
	Accra, Ghana	0.77	(0.60–0.98)	0.037	0.29	(0.21–0.40)	<0.001	0.27	(0.19–0.37)	<0.001
	Kumasi, Ghana	0.61	(0.43–0.87)	0.006	0.25	(0.17–0.38)	<0.001	0.23	(0.15–0.37)	<0.001
	Enugu, Nigeria	0.66	(0.50–0.88)	0.004	0.31	(0.22–0.44)	<0.001	0.29	(0.21–0.41)	<0.001
	Ibadan, Nigeria	0.92	(0.76–1.13)	0.437	0.37	(0.28–0.48)	<0.001	0.37	(0.28–0.49)	<0.001
	Lagos, Nigeria	1.01	(0.74–1.39)	0.946	0.41	(0.28–0.61)	<0.001	0.39	(0.27–0.58)	<0.001
Raised LDL-cholesterol	Age (Years)	1.00	(0.99–1.02)	0.368	1.00	(0.99–1.01)	0.873	1.01	(1.00–1.02)	0.136
	Sex (Ref = males)	1.47	(1.13–1.90)	0.003	1.60	(1.21–2.11)	0.001	1.79	(1.45–2.22)	<0.001
	BMI (Kg/m^2)	1.01	(0.99–1.03)	0.249	1.01	(0.99–1.04)	0.262	1.02	(1.01–1.04)	0.008
	Duration of T2D	1.01	(0.99–1.03)	0.304	1.01	(0.99–1.03)	0.329	1.02	(1.00–1.03)	0.017
	Accra, Ghana	0.64	(0.45–0.90)	0.011	0.30	(0.19–0.47)	<0.001	0.57	(0.41–0.79)	0.001
	Kumasi, Ghana	0.74	(0.47–1.15)	0.182	0.39	(0.24–0.66)	<0.001	0.62	(0.42–0.94)	0.022
	Enugu, Nigeria	1.00	(0.71–1.39)	0.977	0.57	(0.38–0.85)	0.006	0.61	(0.44–0.85)	0.004
	Ibadan, Nigeria	0.97	(0.75–1.26)	0.842	0.51	(0.36–0.72)	<0.001	0.59	(0.44–0.78)	<0.001
	Lagos, Nigeria	1.03	(0.68–1.56)	0.897	0.6	(0.37–0.97)	0.038	0.89	(0.61–1.29)	0.529
Low HDL-cholesterol	Age (Years)	1.00	0.99–1.00	0.399	1.00	0.99–1.00	0.281	1.00	0.99–1.00	0.368
	Sex (Ref = males)	1.91	1.62–2.24	<0.001	1.75	1.47–2.10	<0.001	1.73	1.44–2.07	<0.001
	BMI (Kg/m^2)	1.05	1.04–1.07	<0.001	1.04	1.03–1.06	<0.001	1.04	1.03–1.06	<0.001
	Duration of T2D	0.97	0.96–0.99	<0.001	0.98	0.97–0.99	0.002	0.98	0.96–0.99	<0.001
	Accra, Ghana	0.51	0.42–0.62	<0.001	0.77	0.58–1.03	0.078	0.76	0.57–1.01	0.62
	Kumasi, Ghana	1.85	1.38–2.47	<0.001	2.87	2.01–4.10	<0.001	2.50	1.73–3.60	<0.001
	Enugu, Nigeria	1.00	0.80–1.24	0.97	1.68	1.26–2.25	<0.001	1.67	1.25–2.23	0.001
	Ibadan, Nigeria	2.08	1.74–2.48	<0.001	2.71	2.10–3.51	<0.001	2.71	2.10–3.51	<0.001
	Lagos, Nigeria	0.87	0.66–1.13	0.296	1.54	1.10–2.17	0.012	1.51	1.07–2.13	0.018
eGFR < 60 mL/min/1.73 m^2	Age (Years)	1.05	(1.04–1.07)	<0.001	1.05	(1.03–1.06)	<0.001	1.05	(1.03–1.06)	<0.001
	Sex (Ref = males)	1.23	(0.95–1.58)	0.118	1.47	(1.10–1.95)	0.008	1.4	(1.05–1.87)	0.022
	BMI (Kg/m^2)	1.00	(0.97–1.02)	0.801	1.01	(0.98–1.04)	0.407	1.01	(0.98–1.04)	0.412
	Duration of T2D	1.04	(1.58–2.76)	<0.001	1.02	(1.00–1.04)	0.018	1.02	(1.01–1.04)	0.013
	Accra, Ghana	0.42	(0.29–0.60)	<0.001	0.27	(0.17–0.43)	<0.001	0.28	(0.18–0.45)	<0.001
	Kumasi, Ghana	0.39	(0.23–0.67)	0.001	0.30	(0.16–0.53)	<0.001	0.14	(0.06–0.33)	<0.001
	Enugu, Nigeria	1.32	(0.98–1.78)	0.068	0.82	(0.57–1.20)	0.310	0.85	(0.59–1.25)	0.413
	Ibadan, Nigeria	2.09	(1.58–2.76)	<0.001	0.91	(0.64–1.30)	0.610	0.94	(0.66–1.35)	0.746
	Lagos, Nigeria	0.21	(0.10–0.42)	<0.001	0.14	(0.07–0.30)	<0.001	0.15	(0.07–0.31)	<0.001
Creatinine > 177 µmol/L	Age (Years)	1.05	(1.02–1.08)	<0.001	1.03	(1.00–1.06)	0.036	1.03	(1.00–1.06)	0.049
	Sex (Ref = males)	0.36	(0.20–0.63)	<0.001	0.41	(0.22–0.77)	0.005	0.41	(0.22–0.78)	0.007
	BMI (Kg/m^2)	0.96	(0.91–1.02)	0.201	1	(0.94–1.07)	0.940	1	(0.94–1.07)	0.897
	Duration of T2D	1.07	(1.04–1.10)	<0.001	1.05	(1.02–1.08)	0.004	1.06	(1.02–1.09)	0.001
	Accra, Ghana	0.61	(0.29–1.31)	0.205	0.78	(0.27–2.25)	0.645	0.84	(0.29–2.45)	0.746
	Kumasi, Ghana	0.3	(0.07–1.26)	0.1	0.56	(0.12–2.67)	0.466	0.31	(0.04–2.49)	0.269
	Enugu, Nigeria	1.46	(0.78–2.76)	0.24	1.58	(0.65–3.83)	0.316	1.68	(0.68–4.10)	0.259
	Ibadan, Nigeria	2.4	(1.34–4.28)	0.003	1.86	(0.81–4.27)	0.143	1.84	(0.79–4.26)	0.157
	Lagos, Nigeria	0.32	(0.08–1.32)	0.115	0.36	(0.08–1.72)	0.202	0.38	(0.08–1.80)	0.223

[a] uOR, unadjusted odds ratio from logistic regression model.
[b] aOR, adjusted odds ratio from logistic regression model including all variables listed.
[c] aOR, adjusted odds ratio from logistic regression model including all variables listed, plus glucose control (yes/no). The reference site is Eldoret (Kenya). eGFR estimated glomerular filtration rate.

Table 4
Odds ratio associated with risk factors for clinically-assessed ocular complications of T2D in sub-Saharan Africa.

Complication/comorbidity	Risk factor	uOR[a]	95% CI	P-value	aOR[b]	95% CI	P-value	aOR[c]	95% CI	P-value
Cataracts	Age (Years)	1.09	(1.07–1.10)	<0.001	1.09	(1.08–1.10)	<0.001	1.09	(1.08–1.10)	<0.001
	Sex (Ref = males)	0.94	(0.78–1.14)	0.529	1.15	(0.91–1.44)	0.236	1.22	(0.96–1.55)	0.100
	BMI (Kg/m2)	1.06	(1.05–1.08)	<0.001	0.97	(0.95–0.99)	0.005	0.97	(0.95–0.99)	0.014
	Duration of T2D	1.56	(1.22–1.99)	<0.001	1.03	(1.01–1.05)	<0.001	1.03	(1.01–1.05)	0.001
	Accra, Ghana	0.69	(0.51–0.95)	0.024	3.24	(2.27–4.62)	<0.001	3.36	(2.35–4.82)	<0.001
	Kumasi, Ghana	0.7	(0.54–0.90)	0.007	1.28	(0.85–1.94)	0.243	1.18	(0.73–1.91)	0.504
	Enugu, Nigeria	0.95	(0.75–1.19)	0.627	1.08	(0.76–1.55)	0.667	1.18	(0.82–1.70)	0.367
	Ibadan, Nigeria	2.43	(1.79–3.31)	<0.001	1.09	(0.79–1.51)	0.603	0.94	(0.66–1.32)	0.715
	Lagos, Nigeria	0.72	(0.56–0.92)	0.008	4.52	(2.98–6.85)	<0.001	4.81	(3.13–7.38)	<0.001
Glaucoma	Age (Years)	1.03	(1.02–1.05)	<0.001	1.03	(1.01–1.05)	0.001	1.03	(1.01–1.05)	0.004
	Sex (Ref = males)	0.56	(0.39–0.80)	0.002	0.66	(0.44–0.97)	0.036	0.55	(0.36–0.83)	0.004
	BMI (Kg/m^2)	0.96	(0.93–0.99)	0.023	0.98	(0.94–1.02)	0.228	0.98	(0.94–1.02)	0.359
	Duration of T2D	1.03	(1.01–1.06)	0.005	1.02	(0.99–1.05)	0.134	1.02	(0.99–1.05)	0.170
	Accra, Ghana	0.91	(0.56–1.48)	0.697	0.32	(0.18–0.55)	<0.001	0.31	(0.18–0.54)	<0.001
	Kumasi, Ghana	0.67	(0.34–1.34)	0.259	0.2	(0.09–0.44)	<0.001	0.18	(0.07–0.45)	<0.001
	Enugu, Nigeria	0.45	(0.22–0.88)	0.021	0.14	(0.07–0.29)	<0.001	0.12	(0.06–0.26)	<0.001
	Ibadan, Nigeria	0.23	(0.13–0.42)	<0.001	0.08	(0.04–0.15)	<0.001	0.06	(0.03–0.13)	<0.001
	Lagos, Nigeria	1.13	(0.61–2.08)	0.702	0.30	(0.16–0.59)	<0.001	0.30	(0.16–0.59)	<0.001
Diabetic retinopathy	Age (Years)	1.02	(1.01–1.04)	<0.001	1.01	(1.00–1.03)	0.095	1.02	(1.00–1.03)	0.031
	Sex (Ref = males)	0.91	(0.69–1.19)	0.493	1.07	(0.80–1.43)	0.657	1.06	(0.78–1.44)	0.712
	BMI (Kg/m2)	1.07	(1.06–1.09)	<0.001	0.97	(0.94–1.00)	0.063	0.97	(0.94–1.00)	0.058
	Duration of T2D	1.3	(0.92–1.82)	0.135	1.07	(1.05–1.09)	<0.001	1.07	(1.05–1.09)	<0.001
	Accra, Ghana	0.6	(0.36–1.00)	0.048	1.12	(0.74–1.71)	0.586	1.09	(0.71–1.66)	0.689
	Kumasi, Ghana	0.77	(0.53–1.12)	0.168	0.52	(0.30–0.92)	0.024	0.61	(0.32–1.18)	0.141
	Enugu, Nigeria	0.72	(0.51–1.01)	0.059	0.63	(0.40–0.98)	0.041	0.61	(0.39–0.96)	0.032
	Ibadan, Nigeria	1.41	(0.90–2.19)	0.13	0.5	(0.33–0.76)	0.001	0.45	(0.28–0.71)	0.001
	Lagos, Nigeria	1.42	(1.05–1.93)	0.022	1.08	(0.65–1.80)	0.764	1.11	(0.66–1.86)	0.706

[a] uOR, unadjusted odds ratio from logistic regression model.
[b] aOR, adjusted odds ratio from logistic regression model including all variables listed.
[c] aOR, adjusted odds ratio from logistic regression model including all variables listed, plus glucose control (yes/no). The reference site is Eldoret (Kenya).

the relative risk of diabetes complications may be due to sex differences in health seeking behaviour as well as sexual dimorphism in body composition and fat distribution in addition to other cardiometabolic pathways [23]. Additionally, the extent of glycaemic control between the present study and the Diabcare Africa Study cannot be directly compared because of differences in assessment methods. Therefore, it is possible that glycaemic control differed between the studies and explains some of the observed differences in prevalence of complications. Further, information on comorbidities in Diabcare Africa Study was limited to individuals who had at least one specialist visit in the 12 months period preceding the study. Thus, the relevant sub sample from which frequency of comorbidities was estimated was substantially smaller than the overall study sample. In contrast, all the above comorbidities (apart from retinopathy by fundoscopy) were screened for in all participants in the current study.

The co-occurrence of T2D, hypertension, overweight and lipid dysregulation (the constellation of features labelled “the metabolic syndrome” [24]) is well established and is understood to be due to the overlap in the underlying aetiology and disease pathways reflecting shared environmental and genetic risk factors [25]. The conditions often interact and reinforce each other leading to a

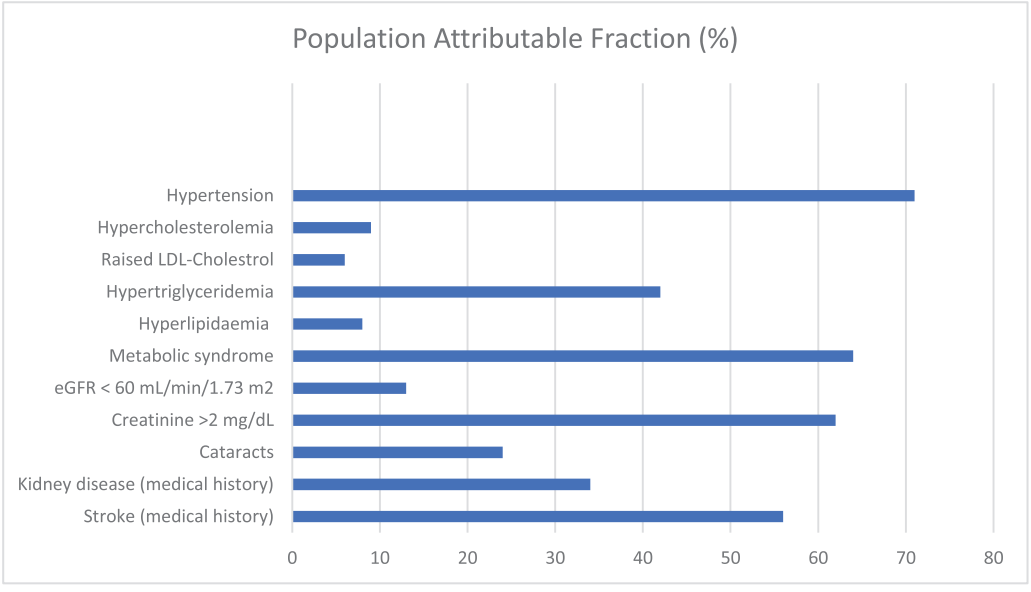


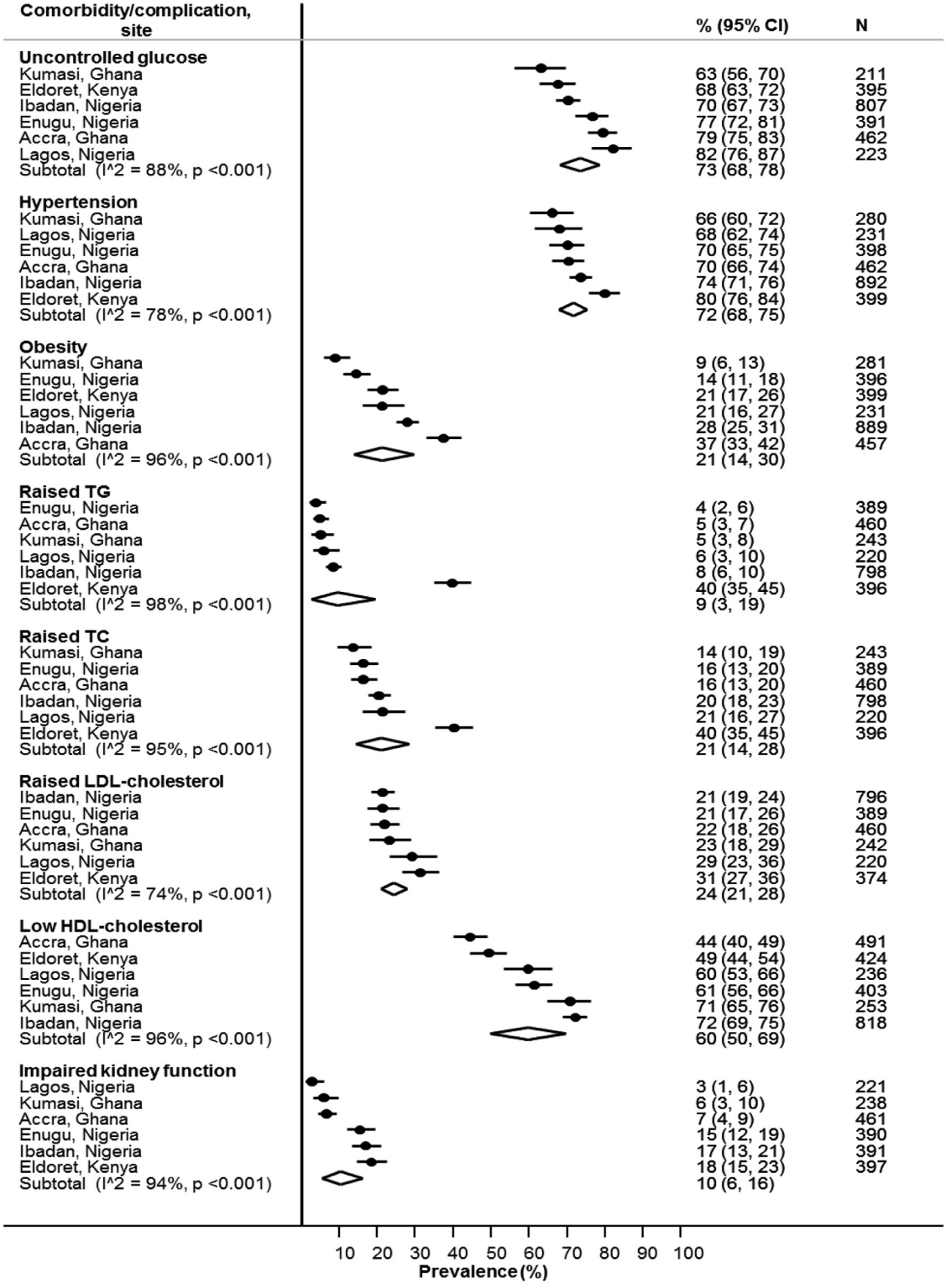
Fig. 3. Population-attributable fraction (PAF) of T2D cardiometabolic complications and comorbidities in sub-Saharan Africa: the AADM Study.

Table 5
Odds ratio associated with risk factors for medical history-ascertained T2D complications and comorbidity in sub-Saharan Africa.

Complication/comorbidity	Risk factor	uOR[a]	95% CI	P-value	aOR[b]	95% CI	P-value	aOR[c]	95% CI	P-value
Diabetic coma	Age (Years)	1.02	(1.01–1.03)	0.004	1.01	(1.00–1.02)	0.161	1.01	(1.00–1.03)	0.100
	Sex (Ref = males)	0.84	(0.63–1.12)	0.246	0.95	(0.70–1.30)	0.756	1.00	(0.72–1.38)	0.983
	BMI (Kg/m^2)	0.96	(0.93–0.99)	0.004	0.96	(0.93–0.99)	0.005	0.96	(0.93–0.99)	0.008
	Duration of T2D	1.05	(1.03–1.07)	<0.001	1.04	(1.02–1.06)	<0.001	1.04	(1.02–1.07)	<0.001
	Accra, Ghana	1.25	(0.88–1.78)	0.218	2.05	(1.17–3.59)	0.012	2.10	(1.19–3.68)	0.010
	Kumasi, Ghana	0.69	(0.41–1.16)	0.160	1.13	(0.57–2.22)	0.731	1.13	(0.54–2.37)	0.748
	Enugu, Nigeria	1.19	(0.81–1.76)	0.375	1.66	(0.93–2.96)	0.086	1.67	(0.93–3.00)	0.084
	Ibadan, Nigeria	1.30	(0.97–1.74)	0.080	1.85	(1.12–3.05)	0.016	1.79	(1.08–2.97)	0.025
	Lagos, Nigeria	0.61	(0.34–1.12)	0.110	0.92	(0.44–1.91)	0.815	0.97	(0.46–2.03)	0.937
Visual problems	Age (Years)	1.00	(1.00–1.01)	0.195	1.01	(1.00–1.02)	0.002	1.02	(1.01–1.03)	<0.001
	Sex (Ref = males)	0.95	(0.81–1.11)	0.537	0.98	(0.82–1.17)	0.82	0.99	(0.82–1.19)	0.889
	BMI (Kg/m^2)	0.95	(0.94–0.97)	<0.001	0.97	(0.95–0.98)	<0.001	0.97	(0.95–0.98)	<0.001
	Duration of T2D	1.03	(1.02–1.04)	<0.001	1.03	(1.02–1.04)	<0.001	1.03	(1.01–1.04)	<0.001
	Accra, Ghana	1.34	(1.10–1.65)	0.004	1.63	(1.23–2.17)	0.001	1.65	(1.24–2.21)	0.001
	Kumasi, Ghana	3.02	(2.30–3.98)	<0.001	3.19	(2.27–4.47)	<0.001	3.64	(2.49–5.31)	<0.001
	Enugu, Nigeria	2.79	(2.20–3.53)	<0.001	2.58	(1.91–3.49)	<0.001	2.62	(1.93–3.56)	<0.001
	Ibadan, Nigeria	0.51	(0.27–0.38)	<0.001	0.51	(0.40–0.66)	<0.001	0.43	(0.33–0.56)	<0.001
	Lagos, Nigeria	0.87	(0.66–1.13)	0.295	0.92	(0.661.28)	0.622	0.91	(0.65–1.29)	0.609
Non-healing ulcers	Age (Years)	1.00	(0.98–1.01)	0.742	1.00	(0.98–1.01)	0.603	1.00	(0.98–1.02)	0.775
	Sex (Ref = males)	0.71	(0.50–1.00)	0.052	0.64	(0.43–0.93)	0.020	0.57	(0.38–0.87)	0.009
	BMI (Kg/m^2)	0.97	(0.94–1.01)	0.102	0.99	(0.96–1.03)	0.730	1.01	(0.97–1.05)	0.763
	Duration of T2D	1.02	(1.00–1.05)	0.044	1.03	(1.00–1.06)	0.027	1.02	(1.00–1.05)	0.098
	Accra, Ghana	1.17	(0.75–1.81)	0.494	2.10	(1.00–4.37)	0.049	2.05	(0.98–4.29)	0.058
	Kumasi, Ghana	2.52	(1.63–3.88)	0.000	4.17	(2.01–8.63)	<0.001	4.70	(2.20–10.06)	<0.001
	Enugu, Nigeria	1.11	(0.68–1.80)	0.688	1.90	(0.90–4.04)	0.100	1.84	(0.86–3.94)	0.117
	Ibadan, Nigeria	0.88	(0.52–1.13)	0.549	1.48	(0.74–2.94)	0.263	1.07	(0.52–2.22)	0.847
	Lagos, Nigeria	0.55	(0.25–1.19)	0.127	0.93	(0.36–2.45)	0.888	0.81	(0.30–2.24)	0.691
Amputation	Age (Years)	1.03	(0.99–1.06)	0.118	1.02	(0.98–1.06)	0.368	1.02	(0.98–1.06)	0.282
	Sex (Ref = males)	0.57	(0.28–1.17)	0.124	0.62	(0.28–1.37)	0.239	0.65	(0.29–1.46)	0.298
	BMI (Kg/m^2)	0.96	(0.89–1.03)	0.230	0.97	(0.89–1.05)	0.391	0.98	(0.90–1.06)	0.548
	Duration of T2D	1.08	(1.04–1.12)	<0.001	1.07	(1.02–1.12)	0.003	1.07	(1.03–1.12)	0.002
	Accra, Ghana	2.07	(0.94–4.55)	0.070	1.31	(0.46–3.76)	0.611	1.37	(0.47–3.97)	0.565
	Kumasi, Ghana	0.93	(0.28–3.09)	0.907	0.73	(0.18–2.96)	0.663	1.01	(0.25–4.16)	0.984
	Enugu, Nigeria	0.94	(0.32–2.70)	0.903	0.65	(0.19–2.25)	0.492	0.70	(0.20–2.45)	0.574
	Ibadan, Nigeria	0.85	(0.25–1.37)	0.729	0.37	(0.12–1.12)	0.077	0.34	(0.11–1.10)	0.072
	Lagos, Nigeria[d]									
Stocking/glove numbness	Age (Years)	1.02	(1.01–1.02)	<0.001	1.02	(1.01–1.02)	<0.001	1.02	(1.01–1.03)	<0.001
	Sex (Ref = males)	1.17	(1.00–1.37)	0.047	1.21	(1.02–1.44)	0.03	1.26	(1.05–1.50)	0.012
	BMI (Kg/m^2)	0.98	(0.96–0.99)	0.001	0.99	(0.97–1.00)	0.126	0.99	(0.97–1.00)	0.100
	Duration of T2D	1.03	(1.02–1.04)	<0.001	1.03	(1.02–1.04)	<0.001	1.02	(1.01–1.04)	<0.001
	Accra, Ghana	0.76	(0.62–0.93)	0.008	0.89	(0.67–1.17)	0.402	0.90	(0.67–1.19)	0.446
	Kumasi, Ghana	2.75	(2.11–3.59)	<0.001	2.80	(2.02–3.89)	<0.001	2.91	(2.03–4.19)	<0.001
	Enugu, Nigeria	1.91	(1.52–2.39)	<0.001	1.91	(1.43–2.56)	<0.001	1.88	(1.40–2.53)	<0.001
	Ibadan, Nigeria	0.96	(0.63–0.87)	0.669	0.86	(0.67–1.09)	0.210	0.77	(0.60–0.98)	0.035
	Lagos, Nigeria	0.50	(0.38–0.67)	<0.001	0.59	(0.42–0.83)	0.003	0.60	(0.43–0.86)	0.005
TIA/Stroke	Age (Years)	1.03	(1.01–1.06)	0.003	1.04	(1.02–1.07)	0.001	1.04	(1.01–1.07)	0.003
	Sex (Ref = males)	1.14	(0.70–1.86)	0.592	1.10	(0.65–1.88)	0.721	1.10	(0.62–1.96)	0.747
	BMI (Kg/m^2)	0.99	(0.95–1.04)	0.711	0.99	(0.94–1.04)	0.742	0.99	(0.93–1.04)	0.627
	Duration of T2D	1.00	(0.97–1.04)	0.961	0.99	(0.95–1.03)	0.512	0.99	(0.95–1.03)	0.709
	Accra, Ghana	1.32	(0.76–2.31)	0.325	5.68	(1.62–19.91)	0.007	5.71	(1.62–20.10)	0.007
	Kumasi, Ghana	1.89	(1.04–3.43)	0.038	7.89	(2.22–28.06)	0.001	6.94	(1.83–26.32)	0.004
	Enugu, Nigeria	1.61	(0.91–2.85)	0.099	6.16	(1.76–21.53)	0.004	6.24	(1.78–21.84)	0.004
	Ibadan, Nigeria	0.79	(0.44–1.41)	0.425	3.23	(0.93–11.26)	0.066	2.37	(0.65–8.72)	0.193
	Lagos, Nigeria	0.67	(0.27–1.69)	0.400	3.15	(0.74–13.34)	0.12	2.53	(0.56–11.48)	0.229
Erectile dysfunction[e]	Age (Years)	1.02	(1.00–1.03)	0.007	1.02	(1.00–1.03)	0.007	1.02	(1.01–1.04)	0.001
	BMI (Kg/m^2)	0.98	(0.95–1.01)	0.186	0.99	(0.96–1.03)	0.647	1.00	(0.97–1.04)	0.804
	Duration of T2D	1.05	(1.03–1.07)	<0.001	1.05	(1.03–1.07)	<0.001	1.04	(1.02–1.07)	<0.001
	Accra, Ghana	0.98	(0.67–1.44)	0.906	1.10	(0.68–1.78)	0.709	1.03	(0.63–1.68)	0.904
	Kumasi, Ghana	3.38	(2.08–5.49)	0.000	3.62	(2.02–6.48)	<0.001	3.52	(1.88–6.57)	<0.001
	Enugu, Nigeria	1.33	(0.94–1.88)	0.106	1.30	(0.83–2.04)	0.243	1.27	(0.81–1.99)	0.306
	Ibadan, Nigeria	0.61	(0.33–0.58)	0.001	0.51	(0.34–0.77)	0.001	0.39	(0.25–0.60)	<0.001
	Lagos, Nigeria	1.59	(1.08–2.35)	0.020	1.62	(0.99–2.64)	0.055	1.54	(0.93–2.55)	0.095

[a] uOR, unadjusted odds ratio from logistic regression model.
[b] aOR, adjusted odds ratio from logistic regression model including all variables listed.
[c] aOR, adjusted odds ratio from logistic regression model including all variables listed, plus glucose control (yes/no).
[d] No amputations reported.
[e] Men only. The reference site is Eldoret (Kenya).

vicious cycle [26,27]. In this regard, the observation that three-quarters of T2D patients in this study meet the IDF definition of the metabolic syndrome is particularly troubling. Therefore, T2D may exacerbate the effects of the above comorbidities and have important implications for cardiovascular disease risk. For example, the high co-occurrence of hypertension and hyperlipidaemia suggests an increased risk of coronary heart disease and stroke among individuals with T2D relative to the general population [28]. We note that, the observed prevalence of obesity and hyperlipidaemia in the current study, though still undesirable, was lower than has

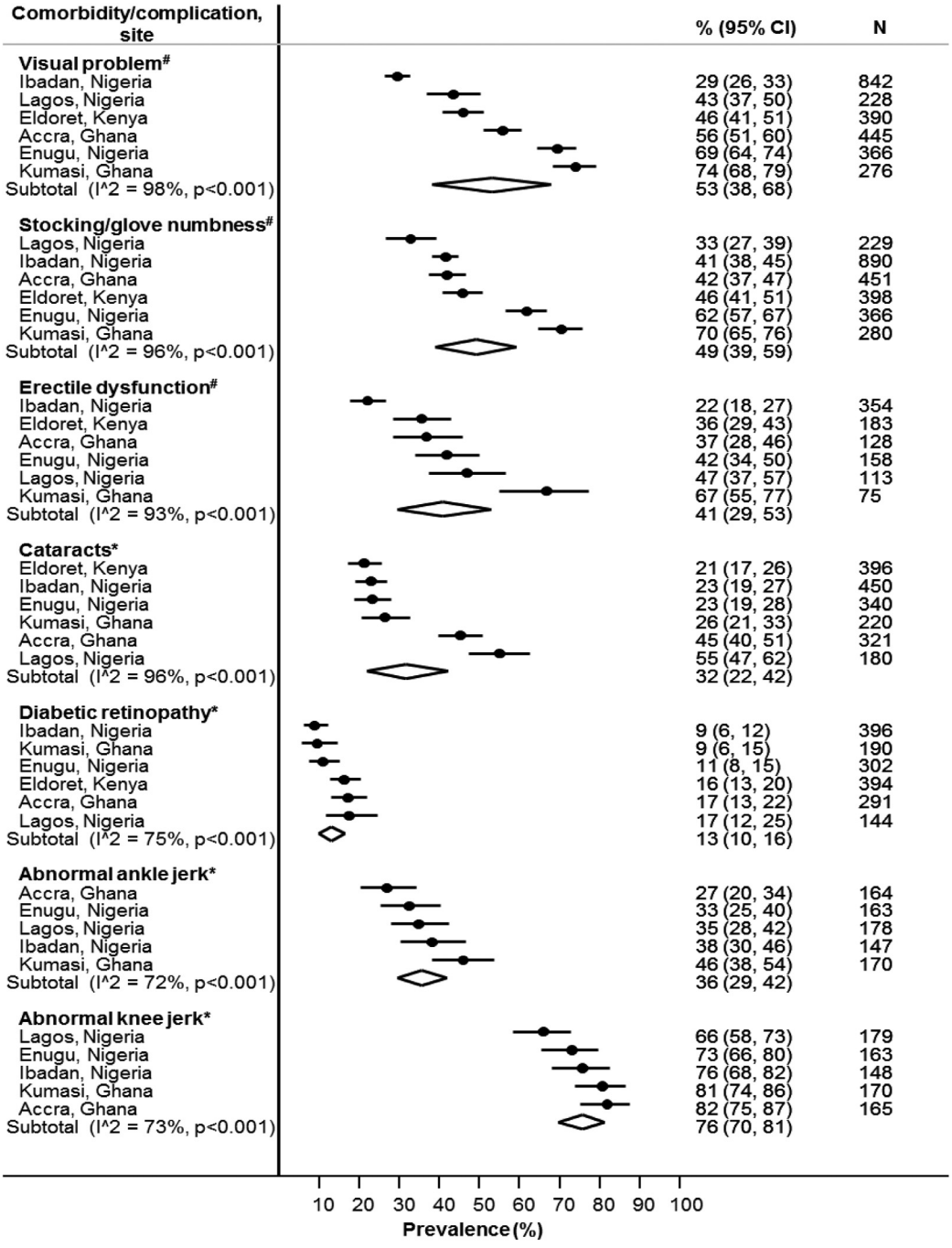


N = Number of participants; % = Prevalence (adjusted for age, sex and duration of T2D across sites); impaired kidney function based on eGFR

Fig. 1. Prevalence of selected comorbidities and complications of type 2 diabetes across sites in sub-Saharan Africa.

been reported in other populations and environmental contexts [29–31]. The reason for this is not clear but perhaps reflects population differences in diet, physical activity, or genetic differences leading to a different pathophysiological mechanism linking these comorbid conditions in this population. Future studies are needed to better define and explain these observations.

An example of a comorbidity that is due to several interacting risk factors is ED. Globally, ED is a well-known T2D complication [32] often with devastating effect on the lifestyle of men



N = Number of participants; % = Prevalence (adjusted for age, sex and duration of T2D across sites); # medical history-ascertained; * clinically-assessed

Fig. 2. Prevalence of selected comorbidities and complications of type 2 diabetes across sites in sub-Saharan Africa.

and is a cause of noncompliance for some ED-implicated antihypertensive medication including some centrally acting agents, beta-blockers and diuretics [33]. In the context of diabetes, ED could result from endothelial dysfunction and microangiopathy due to T2D, from hypertension (which is a frequent comorbidity in T2D) or from antihypertensive treatment [33]. In this regard, it is important to note that in the present study, 68% of T2D men also had hypertension, of whom 34% were on either alpha-methyldopa (a centrally-acting agent), a potassium-sparing diuretic, a thiazide diuretic and/or a beta-blocker. It is therefore not surprising that 35% of men with T2D in this study suffered erectile dysfunction. Risk factors for erectile dysfunction in this study include age, duration of T2D, glycaemic control and study site. Therefore, men with both T2D and hypertension need careful control of both conditions with attention to avoiding (if possible) medications that may increase the risk of this distressing comorbidity.

Ocular complications (including cataract, diabetic retinopathy and maculopathy), neurological complications (including numbness, abnormal knee jerk reflex and abnormal ankle jerk reflex), and erectile dysfunction were the most prevalent T2D complications, with substantial heterogeneity across the three countries, and were associated with longer known duration of T2D, older age

and lower BMI. The association of T2D comorbid conditions and complications with older age and longer duration of disease observed in this study is consistent with accumulation of environmental risks and hyperglycaemic injury to the vascular system. Our results show similarities with those of the Diabcare Africa Study, the only major study to have considered T2D complications across more than one SSA country, as well as those of other single-centre studies that identified retinopathy, cataract, neuropathy and microalbuminuria as the most common complications of T2D, with variation in prevalence across countries [13,34–40]. Our study adds to this evidence by providing more precise estimates of prevalence being, to our knowledge, the largest study of T2D complications and comorbidity in SSA to date. In addition, the identification of risk factors (including study site) help to depict a more complete picture of T2D complications and comorbidity on the continent.

The observed preponderance of microvascular over macrovascular complications despite a high prevalence of hypertension is consistent with observations in other African ancestry populations. In other studies, it is likely to be due to, at least in part, the short average known duration of T2D prior to diagnosis [41,42]. In our study settings, T2D is likely to be diagnosed late and unlikely to be adequately controlled after diagnosis as shown by the low rates of glycaemic control observed in the current study [3]. Therefore, the observed high prevalence of microvascular complications may be due to late initiation of diabetes treatment (because of late diagnoses) and poor glycaemia control, which together mean that the chances of developing complications are much higher than indicated by the reported known duration of T2D alone.

In policy terms, there are three key implications of the present study. Firstly, the prevalence of T2D complications and comorbidities is high in SSA populations. Therefore, regular screening is essential to facilitate early detection and intervention. Regular screening for hyperlipidaemia, renal function, ocular and foot complications in all T2D patients (rather than the current one-half to two-thirds of patients even in major specialist centres) is important and the adoption of a consensus screening checklist may facilitate this goal. In the face of limited access to specialists, training of primary/community health workers on how to screen individuals at increased disease risk, and adapting existing health programmes for other diseases (such as HIV) which are well established in many SSA countries for diabetes management may also be useful [22,43,44]. Secondly, increasing the capacity to monitor glycaemic control in SSA is crucial. Use of HbA1c to monitor glycaemic control is still not routine in much of SSA, including the three countries in which our study was conducted. Thirdly, there is much heterogeneity between and within-countries in the frequency and risk factors for many T2D complications and comorbidities. This may indicate the need for local prioritisation of resources for screening and intervention.

Further research is needed to provide additional insight into the variation observed between the study sites in the three countries with respect to prevalence and risk factors of T2D complications and comorbidities. While a potential explanation may be differences in accuracy of medical examinations and data verification between sites, we sought to minimize these factors by careful standardization of data collection procedures. Other potential explanations include differences in access to clinical care, healthcare resources, diagnostic criteria, and definitions used in routine clinical practice between sites [45]. We did not measure these factors and could not verify their impact on heterogeneity in the present study, empirical data are needed to investigate these issues. Larger studies that includes more SSA geographical regions and adds more potential explanatory variables will be most useful in providing a detailed description of variation in T2D complications and comorbidity across Africa.

The present study has several important strengths, including a large sample size, standardized data collection procedures, inclusion of non-T2D controls and the use of multiple modalities to assess T2D complications and comorbidity. However, there are also a few limitations. T2D cases included in this study were enrolled from medical centres which may limit the generalizability of our findings to the general population, especially in a continent where it is estimated that half of all T2D cases are undiagnosed [14]. The cross-sectional design of the current study means that a temporal relationship between T2D and complications is not established. Finally, use of fasting glucose as an indicator of glycaemic control is sub-optimal compared to HbA1C. However, HbA1c assays are still not routinely available for most of SSA. Population based prospective studies are needed to overcome these limitations.

In summary, our findings point to a high prevalence of complications and comorbidity in patients with T2D in SSA despite reported treatment and a relatively short reported known duration of T2D diagnosis. Age, BMI, known duration of T2D diagnosis, glycaemic control and study site were key risk factors for the evaluated complications and comorbidities. Importantly, these findings suggest the need to strengthen interventions that promote early detection of T2D and ensure optimal glycaemia control to reduce T2D complications and comorbidity in SSA. Such interventions need to prioritize the maintenance of healthy blood pressure, weight and lipid levels, as well as strengthen health system capacities to detect and treat neurological and ophthalmological complications of T2D.

Authors' contributions

Conceptualization and Funding acquisition: CR, AA, GD, and FC; Investigation: CR, AA, OF, GO, BE, KA, JA, WB, AA, JA, TJ, JO, and CA; Methodology, Data curation and Formal analysis: KE, AD, AB, GC, JZ, and DS; Writing - original draft: KE and AA; Writing - review and editing: CR, AA, and KE. All authors reviewed and approved the manuscript.

Declaration of Competing Interest

The authors declare no competing interests.

CRediT authorship contribution statement

Francis Collins: Conceptualization, Funding acquisition. **Georgia Dunston:** Conceptualization, Funding acquisition. **Adebowale Adeyemo:** Conceptualization, Funding acquisition, Investigation. **Charles Rotimi:** Conceptualization, Funding acquisition, Investigation.

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Supplementary materials

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