Type 2 diabetes mellitus in sub-Saharan Africa: challenges and opportunities

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Abstract | Type 2 diabetes mellitus (T2DM), which was once thought to be rare in sub-Saharan Africa (SSA), is now well established in this region. The SSA region is undergoing a rapid but variable epidemiological transition fuelled by the pace of urbanization, with disease burden profiles shifting from communicable diseases to non-communicable diseases (NCDs). Information on the epidemiology of T2DM has increased, but wide variations in study methods, diagnostic biomarkers and criteria hamper analytical comparison, and data from high-quality studies are limited. The prevalence of T2DM is still low in some rural populations but moderate or high rates are reported in many countries/regions, with evidence for an increase in some. In addition, the proportion of undiagnosed T2DM is still high. The prevalence of T2DM is highest in African people living in urban areas, and the gradient between African people living in urban areas and people in the African diaspora is rapidly fading. However, data from longitudinal studies are lacking and there is limited information on chronic complications and the genetics of T2DM. The large unmet needs for T2DM care call for greater investment of resources into health systems to manage NCDs in SSA. Proposed health-system paradigms are being developed in some countries/regions. However, national NCD programmes need to be adequately funded and coordinated to stem the tide of T2DM and its complications.

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Several global estimates and projections have confirmed that diabetes mellitus is associated with increased mortality, that it has reached epidemic proportions with a high and increasing prevalence, and that its prevention and control pose a major public health challenge for this century[1–4]. Type 2 diabetes mellitus (T2DM), which was once thought to be rare in sub-Saharan Africa (SSA), has emerged as an important cause of morbidity and mortality in this region. SSA is a region in which, until 10 years ago, the health-care agenda was dominated by infectious diseases (communicable diseases) and health conditions associated with poverty[5–10]. The shift in disease burden profile is attributed to an epidemiological transition (increased longevity, changes in lifestyle and diet, and economic development) induced by urbanization. SSA countries/regions are undergoing some of the fastest rates of urbanization in the world, with countries/regions at different stages of the epidemiological transition[5,6,10]. Therefore, SSA, with the highest proportion of the world's least developed countries, faces the multiple burdens of communicable diseases, resource depletion and now non-communicable diseases (NCDs), such as T2DM, which need to be addressed[7–11].

A major turning point was the United Nations Resolution on the prevention and control of NCDs, and the commitment by African governments to the United Nations Sustainable Development Goals[12,13]. The roadmap is provided by the WHO NCD Global Action Plan, in which the global targets include a 25% decrease in mortality from major NCDs and halting an increase in T2DM[14]. Achievement of these targets requires that health systems are equipped to address changing patterns of disease burden. However, available evidence suggests that countries/regions across SSA do not have appropriate measures in place to aid with reaching these targets[6,10,15,16].

From the most recent estimates and projections of the International Diabetes Federation (IDF), it is projected that, globally, the number of adults with T2DM will increase by 51%, from 463 million in 2019 to 700.2 million in 2045; the greatest increase (143%) is projected for the Africa region, from 19.4 million (2019) to 47.1 million (2045)[3,4]. Information on the burden of T2DM in SSA has increased over the past few decades[5,17]. However, of concern is that high-quality, reliable and population-representative data are still scarce[6].

Key points

- Previously considered rare, type 2 diabetes mellitus (T2DM) is now firmly established in sub-Saharan Africa (SSA).
- Although prevalence is low in some rural populations, moderate or high rates are reported in many countries/regions, with evidence for an increase in prevalence in some areas.
- Information on the burden of T2DM has increased, but there is a need for high-quality epidemiology studies using harmonized approaches for sampling, data collection and diagnostic methods.
- The increase in T2DM in SSA is associated with modifiable risk factors, such as urbanization and obesity, and there is a high proportion of undiagnosed T2DM.
- Data on the genetics of T2DM are emerging and suggests a greater degree of genetic diversity in T2DM susceptibility in African people compared with other populations.
- There are large unmet needs for T2DM care and national programmes need to be adequately funded and coordinated; integrated models of chronic disease health care that leverage resources across health-care systems are being piloted in some countries/regions.

Some of the key messages of the Lancet Diabetes & Endocrinology Commission were that the true burden of T2DM and its chronic complications in SSA are unknown and that health systems in SSA are unable to cope with the current burden of T2DM and its complications[6].

It has been over a decade since there has been a comprehensive review of the multiple facets of T2DM in SSA[5,17]. We aim to provide an updated review of the burden of T2DM and its complications, pathogenesis, standards of care for treatment and preventive strategies in SSA, as well as a discussion of the challenges and opportunities encountered.

Epidemiology

This is a brief overview of the burden of T2DM in non-pregnant adults of African descent (Black African people) in continental SSA from cross-sectional population-based studies over the past decade. To date, there are no longitudinal observational studies on the incidence of T2DM for the region.

Prevalence

T2DM. Since the landmark description of the burden of diabetes mellitus in Africa by McLarty et al. in 1990 (REF.[7]), which reported a very low prevalence, data on the epidemiology of T2DM in Africa has increased considerably, particularly over the past three decades[5,17–19]. Studies have established that T2DM is not rare on the continent, with a variable prevalence depending on the sampling methods and diagnostic criteria[20–22]. Although the prevalence was low (<3%) in some rural populations, moderate prevalence (3–10%) was observed in most studies (rural, semi-rural and urban) and was similar to that reported in the West[5,17,23].

Since the previous reviews were published[5,17], there have been many reports on T2DM prevalence in SSA; however, there are still only a few high-quality studies, which are confined to studies in South Africa, Ghana and Malawi[6,24–27]. The majority of the latest country/region data on T2DM prevalence in SSA are from studies in the World Health Organization (WHO) STEPwise chronic disease risk factor surveillance programme (WHO STEPs), in which the diagnosis is based on fasting blood glucose (FBG) using either venous or, mostly, finger-prick capillary glucose[28].

TABLE 1 shows the studies in which venous blood samples were obtained and for which rigorous methodology was used. Based on current criteria using an oral glucose tolerance test (OGTT), T2DM prevalence is high (>10%) in both studies in urban populations in South Africa[21,24,25,29,30]. Using FPG alone, T2DM prevalence is low in rural Malawi and moderate in urban Malawi and rural Ghana; by contrast, a high prevalence (>10%) is found in resident and migrant urban Ghanaian populations and urban South African populations[25–27]. Measuring levels of HbA_{1c} for detection of T2DM has only been reported from studies in South Africa, with high prevalence in an urban population and moderate overall prevalence in a national study (9.5%; 95% CI 8.0–11.2)[25,31].

From the WHO STEPs country/region reports in which blood glucose samples were analysed, T2DM prevalence ranges from 1.4% to 22.5% (Supplementary Table 1)[28]. However, concerns have been raised regarding the results of some of these studies in relation to the study methods (that is, the sampling strategy, diagnostic biomarkers used and whether true fasting samples were obtained)[32,33]. The very high prevalence reported for some countries/regions is inconsistent with reports from more rigorous studies[24–27]. Nonetheless, the results of these studies do confirm that T2DM is well established in SSA and provide information to inform governments of the need to address T2DM and other NCDs in the region.

Currently, the wide variability in sampling methods, biomarkers and tests (FBG, OGTT and HbA_{1c}) used for the detection of T2DM limits comparative analysis. It is hoped that the results of the multi-country Human Hereditary and Health in Africa (H3Africa) Diabetes study, undertaken in seven SSA countries/regions with a harmonized approach to sampling, data collection and laboratory analysis, will provide a clearer picture[32].

Undiagnosed T2DM. From IDF estimates, in 2019, Africa had the highest proportion (59.7%) of undiagnosed T2DM in adults aged 20–79 years in the world, with a higher proportion in low-income countries/regions than in middle-income countries/regions[3,4]. The effect of inadequate screening on the prevalence of undiagnosed T2DM is further detailed in the 'Risk factors' section later in this article.

Intermediate hyperglycaemia. Prevalence estimates for impaired glucose tolerance (IGT) and impaired fasting glucose (IFG) vary widely, depending on diagnostic criteria, frequency of blood samples (FBG alone or OGTT) and type of blood sample (venous or capillary)[21,29]. The projected increase in T2DM in SSA is thought to be driven not only by economic development and increases in life expectancy but also by the progression of people at high risk of future T2DM, that is, those with intermediate hyperglycaemia (IGT and IFG)[3]. IGT in Africa is projected to increase by 143.3%, from 45.3 million in

Table 1 | **Prevalence of T2DM, IGT and IFG in cross-sectional surveys[a] in SSA 2012–2020[b]**

Country or population	Study population	*n*	Age (years)	Method	Sex	Prevalence[c] (%)		
						T2DM	IGT	IFG
South Africa (Cape Town)[24]	Urban	1,099	25–74	OGTT	All	13.1	11.2	1.2
					Male	11.3	NA	NA
					Female	14.7	NA	NA
South Africa (Durban)[25]	Urban	1,190	≥18	OGTT	All	12.9	3.5	0.8
					Male	8.5	4.0	1.1
					Female	14.0	3.5	1.7
South Africa (Durban)[25]	Urban	1,190	≥18	FPG	All	11.9	NA	NA
					Male	7.3	NA	NA
					Female	13.1	NA	NA
South Africa (Durban)[25]	Urban	1,190	≥18	HbA_{1c}	All	13.1	NA	NA
					Male	8.5	NA	NA
					Female	14.4	NA	NA
People of Ghanaian descent[26]	All	5,679	25–70	FPG	NA	NA	NA	NA
Ghana (Ashanti region)[26]	Rural	1,063	25–70	NA	Male	3.6	NA	13.0
					Female	5.5	NA	10.8
Ghana (Ashanti region)[26]	Urban	1,449	25–70	NA	Male	10.3	NA	14.2
					Female	9.2	NA	11.3
UK (people of Ghanaian descent, London)[26]	Urban	1,080	25–70	NA	Male	10.4	NA	17.0
					Female	8.4	NA	12.8
Netherlands (people of Ghanaian descent, Amsterdam)[26]	Urban	1,540	25–70	NA	Male	12.8	NA	32.4
					Female	9.9	NA	23.9
Germany (people of Ghanaian descent, Berlin)[26]	Urban	547	25–70	NA	Male	15.3	NA	14.4
					Female	10.2	NA	7.9
Malawi[27]	All	28,891	≥18	FPG	All	2.6	NA	NA
Malawi (Karonga)[27]	Rural	13,878	≥18	FPG	All	2.1	NA	0.94
					Male	2.0[d]	NA	1.0[d]
					Female	2.0[d]	NA	1.0[d]
Malawi (Lilongwe)[27]	Urban	15,013	≥18	FPG	All	5.4	NA	0.89[d]
					Male	3.0[d]	NA	1.0[d]
					Female	3.0[d]	NA	1.0[d]

FPG, fasting plasma glucose; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; NA, not available; OGTT, oral glucose tolerance test; T2DM, type 2 diabetes mellitus. [a]Studies measured venous plasma levels of glucose and HbA_{1c} in African-origin populations (Black African people). [b]The data are based on World Health Organization (WHO) criteria. [c]Age-standardized except where noted. [d]Crude prevalence.

2019 to 110.2 million by 2045, which is higher than that for T2DM[3,4]. Data on IGT burden is available only from South African studies, which report moderate[25] or high[24] prevalence; both studies report low IFG prevalence[24,25]. In studies with only FPG measurements, IFG prevalence ranges from low in rural and urban Malawi[27], to high in resident and migrant Ghanaian people[26] (TABLE 1). Country/region reports in the WHO STEPs programme show a widely variable prevalence of IFG, from 0.9% to 19.6%[26] (Supplementary Table 1).

Is T2DM increasing in SSA? Over the past decade, studies from South Africa confirm earlier reports from Tanzania and Cameroon that there has been an increase in T2DM prevalence in these populations[5,24,25]. There was a 1.5-fold increase in Cape Town, from 9.0% in 1993 to 13.1% in 2012 (REFS[24,33]). In Durban, a 2.4-fold increase was seen, from 5.3% in 1984 to 12.6% in 2014 (REFS[25,34]). This finding also confirms an earlier report from West African countries/regions in which time trend analysis suggested an increase in T2DM prevalence over 10 years[35].

Risk factors for T2DM

SSA is at grave risk of an increase of NCDs, especially T2DM, because of many different but inter-related risk factors, both non-modifiable and modifiable[5,17]. This section will focus on the risk factors for which there is information over the past decade from the studies mentioned already[24–27].

Undiagnosed T2DM. The availability of health-care facilities for the detection and treatment of T2DM in a community can be gauged by the proportion of known and undiagnosed (screen-detected) T2DM in surveys[3,5,23]. From previous reviews, in most studies from SSA, more than 50% of participants had undiagnosed T2DM; in some locations, 79–100% of participants were only diagnosed during surveys[5,17].

FIGURE 1 shows the prevalence of known and undiagnosed T2DM in studies from the past few years. There seems to be an improvement, with a lower proportion of undiagnosed T2DM (31.1–47.1%) in rural and urban populations in Malawi and Ghana than previously reported for SSA[5,26,27]. Of concern is the minimal (10.9–14.8%) improvement in the proportion of known T2DM over the past two to three decades in studies in people living in urban areas in South Africa[24,25,33,34]. This finding suggests that screening for T2DM and other NCDs might not be receiving the necessary attention it deserves, possibly owing to primary health-care facilities being overwhelmed by the infectious disease burdens of HIV and tuberculosis.

Urbanization. Rapid urbanization is suggested as a major determinant of the increasing burden of T2DM. SSA is still undergoing one of the fastest rates of urbanization in the world, but with countries at different stages of the epidemiological transition and with the rates being compounded by massive migration from rural areas[3,5,11]. With the pace of urbanization in SSA, T2DM could pose a major challenge over the coming decades.

Studies have shown a clear rural to urban gradient in T2DM prevalence, with rates twofold to fivefold higher in urban residents than in people in rural locations and, where examined, urbanization was a significant risk factor[5]. Further studies confirmed that T2DM prevalence is twofold to threefold higher in people from urban locations than in people from rural locations in Ghana and Malawi[26,27] (TABLE 1). Of concern is that T2DM prevalence in people of Ghanaian descent living in urban areas in Ghana is similar to those in people of Ghanaian descent living in Europe, which suggests that the gradient between African people living in urban areas in SSA and their counterparts living in the diaspora is rapidly fading[26].

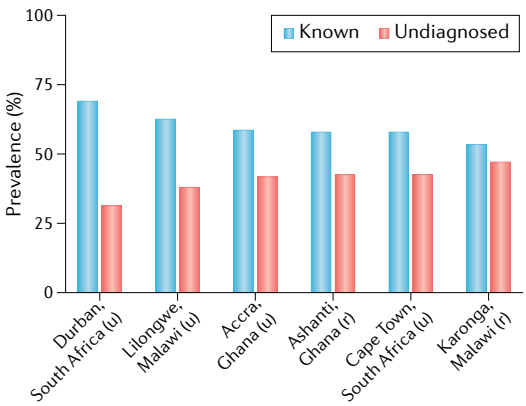

Fig. 1 | **The prevalence of T2DM in studies from some areas of sub-Saharan Africa.** Here, the prevalence (%) of known (blue bars) and undiagnosed (detected in the study, red bars) type 2 diabetes mellitus (T2DM) in cross-sectional epidemiology surveys in urban (u) and rural (r) populations is shown[24–27]. Prevalence is depicted as the proportion of all people in each study who had either known or unknown T2DM.

The effect of migration. The effect of migration was initially indicated by early studies that showed that T2DM prevalence was lower in resident West African people in Nigeria and Cameroon than in communities of West African ancestry living in the diaspora[5]. This finding has now been elegantly confirmed in a Ghanaian study that shows that T2DM prevalence is threefold to fivefold lower in people of Ghanaian descent living in rural areas of Ghana than in people of Ghanaian descent living in Europe[26] (TABLE 1).

Age, sex, family history and ethnicity. As with previous studies[5], T2DM prevalence rises with increasing age, with peak prevalence in the two oldest age groups (55–64 years and ≥65 years), and age is an important risk factor for T2DM[24–27]. A systematic review of 41 studies found a high prevalence (13.7%, 95% CI 11.3–14.3) in people >55 years old and confirmed that T2DM is not rare in older people in SSA[36]. In addition, sex distribution varies widely[24–27]. Where examined, a positive family history of T2DM is more frequent in people with T2DM than in those without T2DM and is an independent risk factor[24,25,37].

Studies in Tanzania and South Africa had previously reported lower T2DM prevalence in indigenous African communities than in migrant people of Asian Indian descent or populations with mixed ancestry[5]. Similar findings were reported from South African studies, both in the national survey and studies in Cape Town and Durban[24,25,31,38,39]. In the national survey, when compared with African people (Black) (8.2%), the prevalence was higher in people of Asian Indian descent (30.7%) and mixed-race (coloured (a recognized racial classification in South Africa)) (13.4%) people[31]. A similar pattern was observed in regional studies[24,25,38,39], in all of which OGTT was performed. In Cape Town, age-standardized T2DM prevalence was twofold higher in the mixed-race (coloured (a recognized racial classification in South Africa)) population than in people of mainly African descent (26.3% versus 13.1%)[24,38]; in Durban, the prevalence was much higher in people of Asian Indian descent (20.1%) than in people of African descent (12.9%)[25,39].

Adiposity. Overweight and obesity are considered central to the increase in the T2DM epidemic[3,10,14]. Consistent with earlier reports, associations (albeit variable) have been found between T2DM prevalence and measures of obesity in SSA. The associations were found with both total body (BMI) and central (waist circumference, waist-to-hip ratio and hip circumference) measurements of obesity. For instance, studies have shown the following: mean BMI, waist circumference and waist-to-hip ratio is higher in people with T2DM than in those without T2DM (normal glucose tolerance, IGT or IFG), as is the prevalence of obesity (both total body and central)[24,25,37]; the probability of T2DM is increased

with increased BMI and waist circumference[26]; and BMI and waist circumference are statistically significant risk factors associated with T2DM[24,25,37].

Physical activity and diet. Information on physical activity from epidemiology studies is lacking. Based on questionnaires, the prevalence of physical inactivity is higher in people with T2DM than in those with normoglycaemia but is not an independent risk factor for T2DM[24,25,37]. Published information on diet and nutritional data is confined to a Ghanaian study, which found that adherence to diets with legumes, rice and/or pasta, meat, fish, cakes, sweets and condiments was inversely associated with T2DM (OR per one SD of 0.80, 95% CI 0.7–0.92) in urban Ghana and Europe but that the role of the traditional diet was unclear[26,40].

Hypertension, dyslipidaemia and T2DM. As with previous studies in urban South African people, the most recent studies have found that mean systolic and diastolic blood pressure and prevalence of hypertension are higher in people with T2DM than in those with normoglycaemia. A similar pattern was observed for dyslipidaemia across glucose tolerance categories[24,25,37].

Effect of HIV

Although there is emerging evidence for an association between HIV infection and treatment and increased cardiometabolic risk[5], information from epidemiology studies in SSA is lacking. Previous clinical studies have shown that, although there was a high prevalence of some components of the metabolic syndrome (for example, dyslipidaemia, adiposity and increased blood pressure), there was a low prevalence of T2DM and increased levels of IFG and total disorders of glycaemia in people being treated for HIV infection[5].

In a study in patients from HIV clinics who either had or had not received anti-retroviral treatment (ART) and participants from an epidemiology who were presumed to be HIV-negative[24], the prevalence of T2DM was similar across the groups (4.9% in the epidemiology study; 3.1% of ART-naive participants; 2.3% in participants receiving first-line ART; and 5.6% in participants receiving second-line ART)[24,41]. In a population study in which HIV status was also examined[25], there was a high overall prevalence of HIV (43.7%), which was higher in people with normal glucose tolerance (47.3%) than in those with IGT (22.0%) or T2DM (25.7%). When stratified by HIV and ART status, T2DM prevalence was higher in the HIV-negative group (4.7%) than in HIV-positive groups (2.1%), both treated (2.8%) and untreated (1.6%). In addition, there was no significant association with T2DM, both in ART-naive people (RR 0.82, 95% CI 0.48–1.22) and in those receiving ART (RR 1.11, 95% CI 0.82–1.97)[25,37]. Clearly, there is a need for further cross-sectional and longitudinal epidemiology studies from SSA to clarify the effect of HIV on T2DM and other NCDs.

Use of HbA_{1c}

The first evidence for the use of HbA_{1c} for the detection and diagnosis of T2DM in Black African people from population-based studies comes from a South African study. T2DM prevalence was similar using OGTT (12.1%), FPG alone (11.9%) or HbA_{1c} (13.1%)[25] (TABLE 1). When OGTT was used as the reference, HbA_{1c} ≥6.5% (48 mmol/mol) detected T2DM with moderate sensitivity (70.3%; 95% CI 52.7–87.8) and high specificity (98.7%; 95% CI 97.7–99.4); the optimal HbA_{1c} cut-off for T2DM detection was 6.0% (42 mmol/mol) (sensitivity 89.2%; 95% CI 78.6–99.8) and specificity 92.0%; 95% CI 90.3–93.7). Similar findings were observed when FPG was used as the reference. The optimal HbA_{1c} cut-off point of 6.0% is consistent with the finding of the NCD-RisC pooled analysis of 96 population-based studies[42]. In a subset of a study conducted in Malawi, HbA_{1c} showed excellent validity for detecting FPG-defined T2DM[43].

The role of HbA_{1c} for the detection and diagnosis of T2DM in Africa has been questioned because of the high burden of conditions such as anaemia, haemoglobinopathy, malaria and HIV infections, which are known to affect red blood cells and haemoglobin and might cause measurements of HbA_{1c} to overestimate or underestimate glycaemia. These issues could limit the ability of HbA_{1c} to accurately reflect glycaemic status and affect its utility for the diagnosis of T2DM on the continent[25,29,30]. A report published in 2021 from the Durban Diabetes Study[44] included a subset without known T2DM (n = 1,067) in which there was a high prevalence of anaemia (28.8%) and HIV infection (45.6%). In this group, there was no significant difference in T2DM prevalence based on OGTT versus HbA_{1c} in individuals with anaemia (2.9% versus 3.3%; P = 0.69) and its sub-groups (normocytic, microcytic and macrocytic), or in those with HIV (2.1% versus 1.4%; P = 0.3) and its sub-groups (untreated HIV (1.6% versus 1.6%; P = 1.0) and ART-treated HIV (2.9% versus 1.2%; P = 0.08)). Additionally, there was only a modest association between HbA_{1c} levels and measures of anaemia or HIV status. These results suggest that anaemia and HIV status are unlikely to materially affect the utility of HbA_{1c} for T2DM detection and diagnosis in this population.

The role of point-of-care HbA_{1c} tests for the detection and diagnosis of T2DM is an attractive option for low-resource settings, such as in SSA, given the advancements and improved accuracy of available devices; however, currently, such tests are advocated only to assess control of T2DM and not for the diagnosis of T2DM[45]. There are no available reports on the use of point-of-care HbA_{1c} tests (versus high-performance liquid chromatography in a laboratory and OGTT) from epidemiology studies in SSA. Moreover, in a population-based study in rural Uganda[46] using point-of-care FPG and HbA_{1c}, the prevalence of T2DM was more than double using HbA_{1c} (11.3%) than with FPG (4.8%) and there were more procedural challenges with HbA_{1c} than with FPG testing. Clearly, there is a need for further population-based studies, particularly prospective studies, to assess the relationship between HbA_{1c} and glucose-based measures and risk of T2DM and its complications in other SSA populations. It is hoped that the H3Africa Diabetes Study will provide clarification[32].

Alternate biomarkers of hyperglycaemia, such as serum levels of glycated albumin and fructosamine,

are not currently recommended for the diagnosis of T2DM[21,29,45]. However, their potential has been explored for the first time in epidemiology studies in Black African people in a study in Cape Town[47]. The study examined the association of serum levels of glycated albumin and fructosamine with glycaemic status based on OGTT. Mean glycated albumin and fructosamine levels were significantly higher with worsening glycaemia and optimal thresholds for dysglycaemia (for instance, IFG, IGT and T2DM) were identified for glycated albumin (15.3%) and fructosamine (227.0 µmol/l). The limitation of that analysis was that HbA_{1c} was not measured. Again, clearly, there is a need for further studies in other African populations, both cross-sectional and, particularly, longitudinal studies, to establish their utility in African people.

Summary

From the available information on T2DM epidemiology, T2DM is now firmly established in SSA and there is evidence of an increased risk in some populations. The major drivers include not only non-modifiable risk factors (such as increasing longevity and an ageing population) but also modifiable risk factors (including increasing urbanization, migration, increased levels of adiposity and continued sub-optimal screening, with a high proportion of undiagnosed T2DM). However, there is a paucity of information on the effect of lifestyle measures (such as diet and physical activity), which are clearly modifiable risk factors that could be addressed to curb the increasing burden of T2DM in the region.

Genetics and other pathogenic factors

There is increasing evidence for genetic susceptibility to T2DM, with more than 400 T2DM-associated loci reported, and environmental factors, principally obesity, thought to precipitate overt hyperglycaemia in genetically predisposed people[48,49]. These pathogenetic factors are further modified by epigenetic and gut microbial influences[50–52].

T2DM heritability in SSA populations is evidenced by reports of an association with a positive family history[25,53–55]. For instance, a positive family history of T2DM was threefold more common in South African individuals with T2DM than in those without T2DM[53]. These findings have been confirmed in a meta-analysis[56].

Candidate gene studies have been reported from several African populations but the validity of such studies is limited by a lack of statistical power. Nonetheless, many have reported an association between the widely replicated *TCF7L2* locus and T2DM in African people[57–59]. There are two reports of genome-wide association studies (GWAS) of T2DM in SSA published in the past few years[60,61]. A meta-analysis of 4,347 people of African descent from South Africa, Nigeria, Ghana and Kenya (2,633 with T2DM and 1,714 control participants), confirmed the association with *TCF7L2* ($P = 5.3 \times 10^{-13}$)[60]. Fine mapping of the *TCF7L2* locus revealed a distinct African-specific variant (rs17746147) in addition to the variant shared with other populations (rs7903146). A novel African-specific variant was also identified (rs73284431), located in an intron of the alkylglycerol monooxygenase (*AGMO*) gene ($P = 5.2 \times 10^{-9}$) and in proximity to other loci associated with T2DM (rs10238625) and dysglycaemia (rs10276674)[62,63].

In addition, a GWAS of 2,342 individuals with T2DM and 2,889 control individuals from Nigeria, Ghana and Kenya replicated the association with *TCF7L2* rs7903146 ($P = 7.288 \times 10^{-13}$)[61]. This study also found a novel association with Zinc Finger RANBP2-Type Containing 3 (*ZRANB3*), single nucleotide polymorphism chr2:136064024 ($P = 2.831 \times 10^{-9}$), as well as a deletion in *HMGA2* (rs138066904, deletion frequency = 0.096; $P = 2.516 \times 10^{-9}$), which differs from the single nucleotide polymorphism rs2258238 that was identified in other populations. Furthermore, evidence for reduced β-cell mass and β-cell dysfunction was shown in *ZRANB3* knockout experiments conducted in zebrafish larvae and cultured murine β-cells[61].

Several studies on the genetic basis of T2DM complications have included African American participants[64], but only a single GWAS has been conducted in participants from SSA with T2DM[65]. This study included 64 participants from West Africa who had proliferative diabetic retinopathy and identified four loci with genome-wide significance (*WDR72*, *HLA-B*, *GAP43/RP11-326J18.1* and *AL713866.1*). One of these loci (*WDR72*) was replicated in 20 African American participants with proliferative retinopathy. Whether this locus can be replicated in other African populations remains to be determined.

The polygenic architecture of T2DM suggests that the genetic variance of disease risk is a composite of small effects of multiple common and rare variants[66]. Thus, additional variants to those discussed already are likely to be discovered in African people in studies with larger sample sizes. The polygenicity of T2DM makes the associated genetic risk of disease amenable to estimation by polygenic risk scores, which capture the cumulative predictive ability of all genetic variation at known risk loci. However, the utility of polygenic risk scores in T2DM risk stratification (as with other complex traits) among African people is limited, largely owing to the Euro-centric nature of current GWAS[67,68].

We also note that emerging evidence suggests a role for epigenetic factors in the pathogenesis of T2DM[52]. Epigenetic changes (such as DNA methylation and histone modification) are heritable phenotypes that influence gene expression without altering gene structure. Unlike genetic changes, epigenetic changes are reversible. The potential role of epigenetic factors in T2DM in African people has been demonstrated in a study of people of Ghanaian descent living in Europe and Ghana[69]. This study, an epigenome-wide association study (EWAS) of 256 individuals with T2DM and 457 control individuals, identified four differentially methylated positions (cg19693031 (*TXNIP*), cg04816311 (*C7orf50*), cg00574958 (*CPT1A*), cg07988171 (*TPM4*)) on the epigenome that were associated with T2DM. One of the loci (cg07988171 (*TPM4*)) was a novel finding, not reported in other populations, which further underscores the possibility that African people have several unique disease-predisposing genetic loci.

Furthermore, specific microRNAs have been shown to be involved in the alteration of β-cells in

T2DM, and there is evidence that adipocyte tissue macrophage-derived microRNAs might influence insulin sensitivity[70,71]. MicroRNAs are small non-coding RNAs that have a role in the regulation of genes through binding to the 3′ untranslated region of messenger RNA. A study of 36 South African mixed ancestry women reported substantial differences in microRNA expression between individuals with T2DM, prediabetes and normal glucose tolerance[72]. Whether microRNA expression is important in the pathogenesis of T2DM in African people remains to be determined.

Taken together, the available evidence suggests a greater degree of genetic diversity in T2DM susceptibility in people of African descent compared with other populations. Whether these genetic factors lead to differences in pathophysiology is unknown; however, differences in insulin sensitivity and adipocyte inflammation reported in women of African descent in South Africa, compared with white women, suggest that different pathogenetic mechanisms might well have a role in the development of T2DM[73]. A study using a euglycaemic hyperinsulinaemic clamp showed greater hepatic insulin sensitivity in women of African descent compared with white women, with no difference in peripheral insulin sensitivity[74], and a separate study showed increased adipocyte inflammatory gene expression in women of African descent compared with white women, independent of adiposity[75].

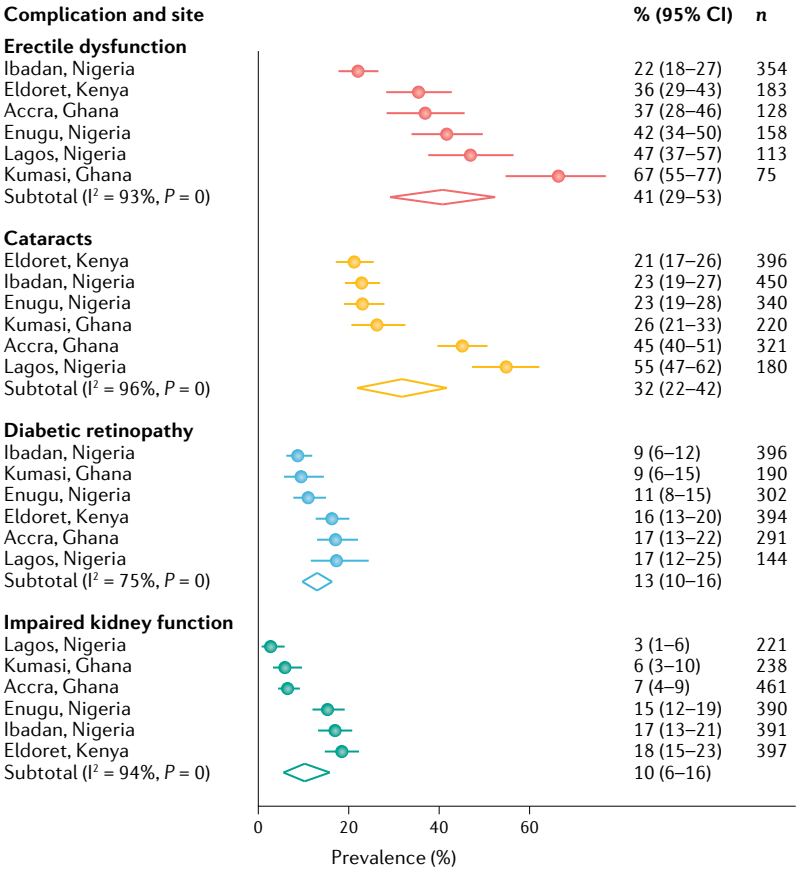

Fig. 2 | **T2DM complications in some middle Africa countries.** Here, the prevalence (percentage of people with type 2 diabetes mellitus (T2DM)) of a range of complications of T2DM, including diabetic retinopathy and impaired kidney function, is shown. Adapted with permission from REF.[77], EClinicalMedicine.

Additionally, early-life malnutrition in African populations might have a role in the future development of hyperglycaemia[76].

Diabetes complications

This section discusses the prevalence and characteristics of microvascular and macrovascular disease associated with T2DM in SSA based on published data over the past two decades[8,77–79]. The prevalence of the most common cardiometabolic comorbidities among patients with T2DM is 60–71% for hypertension, 32–36% for hyperlipidaemia and 25–30% for obesity[77]. The prevalence of diabetic retinopathy varies from 16% to 70% depending on the duration of T2DM, with severe retinopathy in about 15% of patients[77]. About 25% of patients with T2DM have retinopathy at diagnosis[77]. Nephropathy prevalence varies between 32% and 57% after a mean duration of T2DM of 5–10 years, and 5–28% of patients have nephropathy within the first year following the diagnosis of T2DM[77–79]. The prevalence of neuropathy varies widely depending on the methodology used[79]. FIGURE 2 shows T2DM complications in 2,784 participants with T2DM from tertiary health centres and contextualized in 3,209 individuals without T2DM in Ghana, Nigeria and Kenya[77].

Macrovascular complications of T2DM are considered rare in Africa despite a high prevalence of hypertension[78]. Coronary heart disease might affect 5–8% of patients with T2DM and cardiomyopathy affects up to 50% of all patients with T2DM. Almost 15% of patients with stroke have T2DM, and up to 5% of patients with T2DM present with stroke at diagnosis[79]. Peripheral vascular disease prevalence varies from 4% to 28%. This wide variation is due to the different methods used in assessing peripheral arterial disease[77]. Lower extremity amputation varies from 1.5% to 7%, and about 12% of all hospitalized patients with T2DM have foot ulceration[79]. Neuropathy underlies diabetic foot more often than peripheral vascular disease[79]. Cataracts (30–35%) and erectile dysfunction (in men, 35%; range 32–38%) are also frequent findings in this population[79].

In SSA, there is a preponderance of microvascular complications of T2DM compared with other parts of the world[80]. Late diagnosis of T2DM, poor metabolic control and lack of specialized diabetes mellitus care, rather than genetic predisposition, might account for this difference from other populations around the world. This suggestion is supported by a study in which microvascular and macrovascular complication rates were higher in people of Ghanaian descent living in Ghana than in people of Ghanaian descent living in Europe (nephropathy, 32.0% versus 19.8%; peripheral artery disease, 11.2% versus 3.4%; coronary artery disease, 18.4% versus 8.3%; stroke, 14.5% versus 5.6%), except for self-reported retinopathy (11.0% versus 21.6%). The favourable microvascular and macrovascular complications in people who had migrated from Ghana reflects better access to health care[80]. In addition, studies in Malawi found the prevalence of sight-threatening retinopathy in diabetes mellitus clinics to be approximately four times that reported in European studies and the prevalence of proliferative retinopathy was approximately 10 times higher than

in Europe; these complications occurred even in those with low levels of HbA_{1c} in Malawi[81]. These results on T2DM complications highlight the urgent need for the provision of services for nephropathy and retinopathy detection and management to avoid a large burden of chronic kidney diseases and vision loss.

Of great importance in SSA is the growing burden of chronic kidney disease, which is associated with human suffering, high morbidity and mortality rates, low life expectancy, poor quality of life, economic effects and high health-care costs[82,83]. Current projections show that none of the 54 countries/regions in SSA will be able to afford the cost of medical care associated with pre-dialysis (estimated to be US$2,500–$20,000 per patient annually)[82–84].

A growing area of interest in SSA is the increasing prevalence of mental health issues, depression and dental health issues (especially chronic periodontitis) among patients with T2DM[85]. More research is needed in these areas; however, early regular screening of these complications should be conducted by trained health professionals[85,86].

Standards of care for treatment

Low-income and middle-income countries/regions are facing an increasingly disproportionate economic and health burden of NCDs[87,88]. In SSA, NCDs are a leading cause of death among adults[87–89]. The epidemiological and demographic transition occurring in the region will lead to millions being at risk of NCDs, including T2DM[3,90,91]. In 2019, nearly three-quarters of T2DM-related deaths in SSA occurred in economically productive persons (age under 60 years)[3]. Currently, there is a large unmet need for T2DM care in SSA. A study that examined health-care system performance for T2DM management in 28 low-income and middle-income countries/regions using a cascade-of-care approach (testing, diagnosis, treatment and control), showed losses to care from the health-care system at all stages[92]. There were large losses to care at the stage of being tested (63.4%; 95% CI 56.7–69.6) and low rates of T2DM control (22.8%; 95% CI 20.9–24.9). The total unmet need for T2DM care (defined as the sum of undetected, detected but undiagnosed, diagnosed but untreated, and treated but not controlled T2DM) was 77.0% (95% CI 74.9–78.9). Such findings underscore the need for greater investment of health-care resources into health-care systems to manage NCDs using T2DM as a 'tracer' (example) condition and for the capability to achieve universal health coverage[92].

There is growing evidence that the establishment of a comprehensive chronic disease clinic with T2DM as an entry point has a considerable effect on the overall quality of care and reduces mortality and the incidence of comorbidities over time. This effect was highlighted in a report that showed that this shift is possible with a data-driven, team-based integrated care through care reorganization[93]. This approach is based on the evidence that reducing HbA_{1c} by 0.9%, systolic blood pressure by 10 mmHg, low-density lipoprotein cholesterol by 1 mmol/l, or a combination of all three, can independently reduce the risk of cardiovascular disease, all-cause death, or both by 10–20% in patients with T2DM. Reducing multiple risk factors, including by use of statins and renin–angiotensin system inhibitors, can prevent cardiovascular-renal events by 20–40% in individuals with or at risk of having T2DM. Therefore, the use of this approach can reduce cardiovascular disease and all-cause death in patients with T2DM by 20–60%. Sustained weight reduction by 15 kg or more in patients with obesity and T2DM of less than 6 years duration can induce remission of T2DM for up to 2 years. Structured lifestyle intervention and the use of metformin can each prevent or delay T2DM[93].

To promote universal health coverage, the WHO and other global agencies recommend that prevention and care of T2DM and other NCDs must be integrated within the existing health-care systems with a focus on primary care. They also recommend that more than 80% of T2DM and other NCD care be provided at the primary care level and within communities and households by building the capacity of primary care units (health centres and dispensaries) and connecting these with communities. In 2016, the IDF Africa Region developed clinical care guidelines for appropriate T2DM management in SSA, with minimum staffing and equipment requirements recommended for each level of health care[94]. Since then, there has been considerable evolution of care and T2DM is now an integral part of overall NCD care.

In Tanzania, a new health-care system paradigm is being developed in which health care is no longer to be provided from a 'disease' standpoint but from an integrated and broad perspective of 'health'[95]. This strategy is as recommended by the WHO and as embedded within the idealized transition towards universal health coverage, galvanized by the 2030 Sustainable Development Goals[13]. To achieve this vision, a healthy lifestyle will be adopted as the new ideal for society and for the wider target groups to strive for, for example, reducing sugar-sweetened beverage intake, smoking and alcohol consumption, increasing physical activity and promoting healthier diets[95]. From a clinical perspective, devastating complications from uncontrolled or untreated T2DM and other NCDs would be contained and reduced based on different models of integrated primary health care and community-level outreach (FIG. 3).

Although HIV/AIDS is the leading cause of adult death in SSA, there is now clearly a dual HIV–NCD epidemic[95,96]. There has been considerable global investment in the establishment of comprehensive care for HIV, with the provision of ART and a decrease in HIV-related morbidity and mortality; however, an ageing population is now more susceptible to NCDs such as T2DM. HIV management approaches have also changed over time from acute care to chronic care models. However, national NCD programmes have not seen similar international investment or use of care models; these programmes are poorly funded and coordinated[97]. Prevention, care and treatment of T2DM and hypertension remains inaccessible for the majority of people in SSA and chronic care models to manage these diseases have rarely been established or developed[98]. There is a need to manage NCDs in people with HIV and chronic

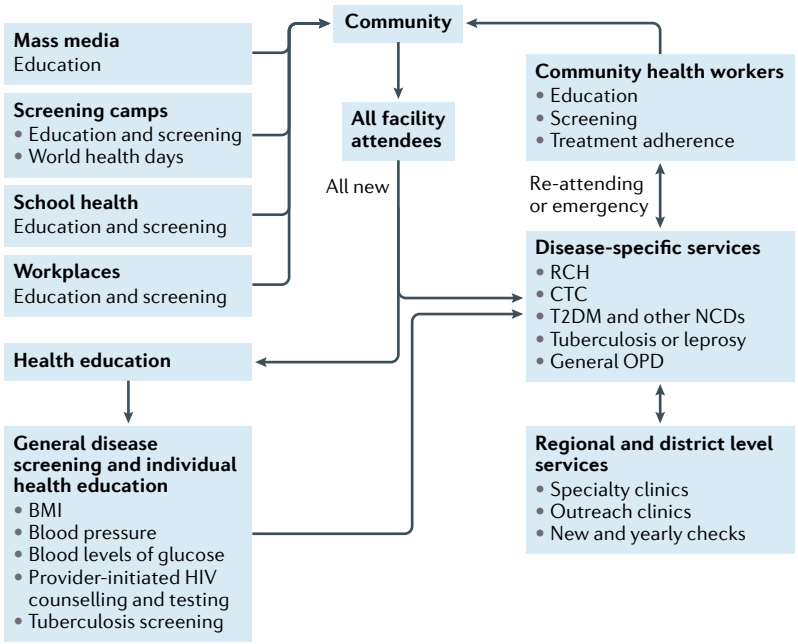

Fig. 3 | **Proposed integrated primary care model of chronic care.** The primary health-care facility becomes the nucleus of integrated chronic care with common triaging ('one stop') and provision of outreach service with community health workers for community, schools and workplace programmes. CTC, care and treatment clinic; NCDs, non-communicable diseases; OPD, out-patients department; RCH, reproductive and child health clinic; T2DM, type 2 diabetes mellitus.

care integration needs to be established to improve cost-effectiveness, quality of services and retention of patients in the programme. Several models of integrated care for HIV and NCDs have been established but uptake of these models is poor in SSA[99,100].

Strategies for prevention

There are currently no reports of studies on interventions for prevention of T2DM or its complications in SSA. A systemic review identified several barriers to lifestyle and dietary change adherence. According to this systematic review, lack of knowledge, poverty (economic constraints), cost of T2DM care and lack of access to health care are the main barriers to adherence to strategies for prevention and management of T2DM in Africa[101]. The strategies to overcome these barriers include health education programmes, advocacy and capacity building. Given the high prevalence of T2DM in SSA, there is a need for mass awareness campaigns through radio, mobile phones and cost-effective mass screening, especially for people with a strong family history of T2DM and other risk factors, including obesity and previous gestational diabetes mellitus.

For prevention strategies to be impactful in SSA, there is a need for a solid coordination and collaboration between health-care professionals, government, non-profit organizations and society to create awareness of the prevention and management of T2DM in Africa. Countries/regions in SSA urgently need demand forecasting tools to help in-country stakeholders understand the potential for paying for T2DM care (that is, what are the sources of revenue and what other financing might be available?). People with T2DM need to receive self-management and adherence support, medications, and health products in line with national guidelines and patient records. T2DM care facilities should have the guidelines available in addition to staff trained in the implementation of such guidelines, with a functional patient records system.

This Review has highlighted the fact that the burden of T2DM, along with its risk factors and complications, is growing substantially in SSA. Growth in the T2DM-related health-care services is required to cater for the numerous unmet needs of people with T2DM. A multisectoral approach is urgently needed, which would involve innovative socioculturally appropriate public health strategies that prioritize the promotion of healthy lifestyles (enabling an environment that fosters physical activity and healthy diets, for instance). In addition, a strengthened health-care system is needed, with accessible and affordable high-quality T2DM care, which includes early detection, free access to insulin and other T2DM medications, other T2DM supplies, and specialized services for tertiary management of T2DM complications.

Opportunities and future directions

More research is needed in SSA to understand the burden and sociocultural aspects of T2DM in Africa. There is a need to introduce more technology for the management of patients, using mobile technology for diabetic retinopathy screening, demand forecasting tools and machine learning. More health professionals, especially those working in rural communities, need to be trained in using web-based and mobile technologies for the management of T2DM, such as digital registries and telemedicine. Development of a T2DM 'care package' with a focus on improving access to affordable, safe, effective and quality-assured medicines and health technology products is also needed.

Conclusions

There is an increasing burden of T2DM in SSA, with a moderate-to-high prevalence reported in many countries/regions, especially in urban populations, and a significant association with preventable and modifiable risk factors. However, more high-quality, population-based studies are needed. Health-care needs for T2DM are largely unmet in SSA. Nevertheless, health-care system-wide integrated models of primary and chronic care have been proposed and are being developed in some countries/regions. Overall, there is a need for better coordination and funding of health-care systems to stem the tide of T2DM and its complications in SSA.

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PubMed was searched using keywords including 'diabetes and sub-Saharan Africa/Africa', 'diabetes prevalence and sub-Saharan Africa/Africa', 'risk of diabetes and sub-Saharan Africa/Africa', 'epidemiology of diabetes and sub-Saharan Africa/Africa', 'urbanization/urban/rural and diabetes and sub-Saharan Africa/Africa', 'physical activity and diabetes and Africa', 'genetics of diabetes and sub-Saharan Africa/Africa', 'GWAS and type 2 diabetes and sub-Saharan Africa', 'mortality and diabetes and Africa', 'HIV and diabetes and Africa', 'standards of care and sub-Saharan Africa', 'diabetes and … [each country in sub-Saharan Africa]'. Published peer-reviewed reviews and book chapters were included. The World Health Organization (WHO), International Diabetes Federation (IDF), United Nations and World Bank publications were used and their websites were also accessed for relevant information.

Supplementary information
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