Diabetes in sub-Saharan Africa
Lancet Diabetes and Endocrinology Commission Report

Atun R*^, Gale E*, Davies J, Bärnighausen T, Beran D, Binagwaho A, Levitt N, Mangutu F, Nyirenda M, Manguyu F, Nyirenda M, Nyonator F, Ogle GD, Ramaiya K, Sewankambo N, Sobngwi E Tesfaye S, Yudkin JS, Basu S, Manne-Goehler J, Postolovska I, Salomon J, Vollmer S, Abbas ZG, Abdullah M, Adeyi O, Besançon S, Bukhman G, Burgess P, Burton M, Dodson P, Joel D, Jong S, Mbaye MN, Mwagomba B, Reja A, Rotimi C, Siraj ES, Stefan C, van Acker K, for the Lancet D&E Diabetes in sub-Saharan Africa Collaborators and Researchers

*Joint first authors
^Corresponding author

Introduction

Sub-Saharan Africa (SSA) is experiencing a rapid rise in in the prevalence of non-communicable diseases (NCDs). Rapid demographic (growing and ageing population), socio-cultural (with lifestyle changes and eating habits) and economic transitions (with higher income and urbanization) are driving sharp rises in the risks and prevalence of diabetes, a risk factor for cardiovascular disease, with severe health and economic consequences.

The impact of these transitions is evident. In 1990 the leading causes of death in SSA were HIV/AIDS, lower respiratory infections, diarrheal diseases, malaria and vaccine preventable diseases in children, but by 2012 stroke was in the top five, displacing vaccine preventable diseases.[1]

In SSA, the fastest growing risk factor for morbidity and mortality is high body mass index, which has increased more than 200 percent between 1990 and 2010 and the second largest risk factor growth was in fasting plasma glucose, which jumped 80%. Between 1990 and 2010 the number of DALYs attributed to diabetes rose by 88%.[2] Over 90 percent of diabetes cases in SSA are Type 2, suggesting that modifiable risk factors are the major contributor to the burden of disease.[3]

In SSA, tuberculosis ands antiretroviral medications required for the suppression of HIV also contribute to rising burden of type two diabetes.[4] The confluence of these epidemics presents unique clinical and health systems challenges. In 2015 Africa was the only continent in the world where morbidity and mortality from infectious diseases still outnumbered those from NCDs.[5] Yet, this balance will soon change as SSA, where health systems are not ready to manage this transition, experiences the full blown impact of rapid rise in diabetes and NCDs.

The aim of the Lancet Diabetes and Endocrinology Commission on Diabetes in SSA is to provide a comprehensive analysis of the nature and magnitude of change in diabetes burden, preparedness of health systems to diabetes, and its health and economic consequences, to inform the development of an effective response.

The Commission report is organized in nine sections. Introduction is followed by new estimates of current and future burden of diabetes by country. Section three explores characteristics of diabetes in SSA. Section four presents new analysis on health system readiness for managing diabetes. Section five is a new multi-country analysis of unmet need for diabetes. Section six presents projections of the economic consequences of diabetes. Estimates of costs and health benefits of scaling up interventions for treating diabetes follows. Section eight is a review of new service delivery models and

technologies for managing diabetes. Section nine identifies opportunities for an effective response to fight diabetes in SSA.

Context and the burden of diabetes in sub-Saharan Africa

The World Health Organization (WHO) estimates that in 2014 of the 422 million people with diabetes mellitus 25 million lived in the WHO Africa region, which corresponds to SSA. In 1980 globally there were 108 million people with diabetes, of which 4 million lived in SSA.[6]

While the worldwide prevalence of diabetes increased by 80.9% from 4.7% in 1980 to 8.5% in 2014, the prevalence in SSA had risen by 129.0%, from 3.1% in 1980 to 7.1% in 2014. This rapid rise was only second to that observed in Eastern Mediterranean Region where the prevalence had risen by 132.2%, to reach 13.7% in 2014 from 5.9% in 1980, but higher than that observed in other regions of the world (Table 1)

Table 1

The International Diabetes Federation (IDF) estimates that in 2015 the prevalence of diabetes in SSA among adults aged 20-79 was 3.2% (uncertainty interval [UI] 2.1-7.6%), with 14.2 million people (UI 9.5-29.4 million) affected by diabetes. Seychelles had the highest estimated prevalence at 17.4%. The IDF further estimates that by 2040, the prevalence of diabetes would rise to 4.2% (UI 2.6-7.3%) to reach 34 million people (UI 23.7-67.7 million). The projected increase in the adult population (aged 20-79 years) from 441 million in 2015 to 926 million in 2040 will drive much of increase in the numbers of people with diabetes. Around 46,400 children aged 0-14 years, were estimated to have Type 1 diabetes. The IDF estimated that in 2015, around 321,000 deaths were attributed to diabetes, with 79% of these deaths occurring in persons aged 60 years or less – a proportion higher than any other region in the world.[7]

Other studies of prevalence of diabetes in SSA also confirm this rising trend, with rapidly increasing prevalence in rural populations.[8] This rise is also true of older population groups. For example, a systematic review and of all published studies in the period 2000-2015 on diabetes prevalence in north Africa and SSA in persons aged 55 years or more suggests an average prevalence of 13.8%, with a 95% confidence interval of 13.2-14.3%.[9]

The context: rapid transitions driving a rise in diabetes prevalence

Three major drivers account for the rising diabetes prevalence: (i) change in prevalence itself (ii) change in population size and age structure and (iii) change due to interaction between change in prevalence and change in population size and age structure.[10]

The first driver, change in prevalence itself, is influenced by economic, socio-cultural and nutritional transitions, which are leading to urbanisation, changing food availability, new eating habits, and evolving lifestyle and work practices to produce higher levels of obesity – the greatest contributor to the diabetes epidemic – which is influenced by genetic factors, and rising fasting plasma glucose levels. Rapid economic transition is evident: the International Monetary Fund expects sustained strong growth in economies of these countries with a projected increase in the Gross Domestic Product (GDP) per capita of 2.5% each year through to 2020.[11]

Economic transition is driving urbanisation in SSA, with urban population projected to rise from 360 million in 2015 (37.4% of total) to 732 million (46.6% of total).[12] Although few studies have compared the prevalence of diabetes in rural and urban populations in the same country, published studies estimate prevalence of 0.1% in in rural areas of Ghana[13], 2.8% in rural Angola[14], 3.9% in South Africa[15], 6.1% in rural areas and 13.4% in urban areas of Guinea[16], and 5.3 % in urban slum Nairobi[17], 10.1 for men and 11.2% for women urban dwellers in Cameroon[18], and 17.9% in Dakar Senegal[19].

Urbanisation has affected the global nutritional transition and obesity levels which have reached 5.3% in Uganda to 30% in Nigeria and 45.7% in South Africa.[20] The availability of cheap energy sources, such as vegetable oil, has greatly increased calorie intake and resulted in profound changes in body composition in populations globally as well as SSA.

The dynamics of the obesity epidemic are well illustrated by the demographic and health surveys undertaken in seven African countries at intervals of 10-13 years over the period 1992-2005. The surveys indicate that in city-dwellers 31.4% of women were overweight or obese, (38% in Kenya to 28-29% in Burkina Faso and Senegal), with an increase of one third in the prevalence of urban overweight/obese in just over a decade. Obesity was correlated with household income, education, and working status of women; the most rapid increase (50% overall) was in the poorest urban dwellers, especially women, but in women with secondary education or higher obesity levels declined by 10%.[21]

While access to food is still a major daily challenge in most countries of SSA, a larger body size is perceived as a sign of affluence and good living. In many communities it is a deeply rooted status symbol conferring respect, influence, health and attractiveness.[22,23,24] Being overweight also has positive connotations in societies in which a strong stigma is attached to weight loss and wasting associated with HIV/AIDS[25]; which paradoxically may mean that obesity may be perceived as an indication of health.

The second driver, population growth: the population of SSA is projected to rise from 962 million in 2015 to 1.24 billion in 2025 and 1.57 billion in 2035.[26]

The third driver, population structure, is also projected to change rapidly, producing an ageing population – with the number of persons aged 50 years or more projected to

increase from 95 million in 2015 to 186 million in 2035.[27] Average life expectancy is projected to rise from 57.2 years in 2010-2015 to 65.9 years in 2035-2040.[28]

Prevalence of obesity and diabetes in sub-Saharan Africa: empirical analysis of national surveys

While many studies have estimated the prevalence of diabetes and obesity in SSA, few empirical analyses at country level exist. We estimated the prevalence of diabetes in 10 countries using individual level patient data from 10 nationally representative surveys to obtain an up do date estimate. The surveys included the WHO Stepwise Approach to Surveillance Surveys (STEPS) undertaken in 2005-2013 in Benin (2008), Comoros (2011), Guinea (2007-08), Liberia (2011), Mozambique (2005), Tanzania (2012), Togo (2010) and Seychelles 2013), a Demographic and Health Survey undertaken in Namibia in 2013, and the South African National Health and Nutrition Examination Survey undertaken in 2012.

The data sources and methodology are discussed in detail elsewhere and a summary included in supplementary appendix.[29] We approached WHO to obtain data from the STEPS surveys, which have been made available to other researchers, but were refused access.[30] We therefore, approached separately each country where STEPS surveys were undertaken and obtained responses and data from 12 of them. We excluded two surveys from DR Congo due to data incompleteness. The complete pooled dataset included 39,062 individuals across 10 countries over the period from 2004-2014.

The analysis reveals a strong relationship between increasing age and the prevalence of diabetes and obesity, with higher prevalence for women across all age groups. Cross-country prevalence of diabetes ranged from 1.3% in Benin to 21.6% in Seychelles based on biomarker measurement and self-reported use of diabetic medications. Age stratified prevalence level of diabetes revealed rising prevalence levels with age, with levels reaching 35-30% in men and women in South Africa and Seychelles (Figure 1).

Figure 1

Obesity levels (body mass index >25) also varied across countries, with age-stratified levels ranging from less than 10% in men aged 25-39 years old in Benin and Togo to more than 70% in South Africa and almost 80% in women aged 55-65 years (Figure 2).

Figure 2

The prevalence of diabetes and obesity also varied in populations in employment and in those not employed, with higher levels observed in the employed populations across all countries (Appendix).

Rising diabetes and double burden of disease in SSA countries, has major implications for health systems, which are not ready to manage this rapid transition.[31] We explore in the next section the characteristics of diabetes in SSA, which needs to be well understood if an effective response is to be developed.

Characteristics of Diabetes in Africa

Diabetes was a rare disease until about a century ago, but now affects up to a third of the population in some parts of the world[32], indicating that its causes are predominantly environmental. The relative risk of developing diabetes within a population is however modulated by genetic susceptibility as well as environmental exposures.

Diabetes in Africa is different

Sub- Saharan Africa, the cradle of mankind, is a region with greater genetic variation than the rest of the world put together, together with an exceptionally wide range of environmental variation. The genetic and phenotypic features of diabetes vary from one population and culture to another, due to environmental differences and variations in genes which affect body composition and metabolic function. Because of this variation, Western models of diabetes care are not necessarily appropriate for unmodified use in other parts of the world.

Although there is probably no place on earth where the environmental and genetic determinants of diabetes exhibit greater variation than in SSA, the African population has been studied in less detail than many other populations around the world. African studies of excellent quality do exist, but their generalizability to other parts of the continent is not well established. This environmental and genetic diversity is matched with political diversity and many differences in health systems in SSA.

The spectrum of diabetes in Africa

Diabetes is classified into primary varieties, for which no extrinsic cause has been identified, and secondary varieties for which there is a known extrinsic cause.
Primary diabetes is classed as type 1 and type 2. Both forms have risen in prevalence over the past half-century. The hallmark of type 1 diabetes is severe insulin deficiency which, if untreated leads to the hyperglycaemic emergency of diabetic ketoacidosis (DKA). It is due to immune-mediated loss of pancreatic beta cells and can occur at any age, although it typically affects younger non-obese people and has its greatest impact in childhood and adolescence. Its incidence began to rise in Western populations around the middle of the last century, and it is still increasing in many parts of the world. Early onset is associated with higher degrees of genetic susceptibility, and there is a secular trend towards earlier onset suggesting increased penetrance of the disease; a similar shift has been reported in Africa.

The cause of type 1 diabetes is unknown, but susceptibility is strongly associated with certain HLA types, whereas other types are strongly protective. The rapid secular increase in the condition points to environmental causation superimposed upon genetic susceptibility. Estimates of its prevalence have risen sharply in some parts of Africa, most probably as a consequence of improvements in case detection (Appendix: Rwanda case study), but mortality levels are very high due to failures in diagnosis and management including lack of access to insulin.[33]

African-Americans were once considered "immune to diabetes"[34] and the condition was considered very uncommon in Africa itself until the 1960s, when studies first showed an increasing prevalence of obesity, hypertension and diabetes in city-dwellers in Southern Africa[35]. The prevalence of type 2 diabetes subsequently rose rapidly in Africa, in parallel with the rise of obesity, and early-onset forms of type 2 diabetes associated with severe obesity have emerged in many susceptible populations including those of African descent. These may sometimes overlap with type 1 diabetes, a condition that has been called "double diabetes".

Type 2 diabetes is best viewed as a syndrome exhibiting genetic, metabolic, and clinical heterogeneity, and its impact upon metabolic pathways ranges from decreased insulin secretion to increased glucose production and insulin insensitivity. The relative contribution of such imbalances may differ between populations.[36]

While international guidelines are heavily influenced by western practice, the African population has been studied in less detail, and shows important differences from other parts of the world. For example, in Africa, most people affected by type 2 diabetes are 30-59 years old, whereas most people in Europe with diabetes are aged over 60 years.[37] Type 2 diabetes is strongly associated with obesity in all parts of the world, but Africans may be twice as likely to develop diabetes for a given level of body mass, as compared with people of European origin. These observations suggest that although the "epidemiological transition", driven by high rates of urbanization and associated behavioural risk factors influencing diet and physical activity has had a world-wide impact, the African population may be inherently susceptible to the diabetogenic effects of "westernization".

The biological mechanisms underlying heightened susceptibility to diabetes are unknown, and may include evolutionary adaptation to ancestral famine (the "thrifty genotype" hypothesis). In addition, there is increasing recognition that developmental influences can affect long-term risk of disease. Fetal exposure to maternal malnutrition generates a phenotype that promotes survival in a nutrient poor environment but substantially increases the risk of diabetes and cardiovascular disease in the presence of abundant nutrition.[38] Rapid weight gain following a period of childhood stunting is a well-recognised risk factor, as is gestational diabetes with its risk of intergenerational transfer of diabetes to the offspring.

The speed of epidemiological transition in Africa has been such that high rates of infectious disease, notably tuberculosis and HIV, coexist with a rising prevalence of NCDs such as diabetes. Tuberculosis and diabetes interact, each predisposing to the other[39], and HIV – itself associated with an increased risk of vascular disease – is treated with anti-retroviral (ARV) drugs which may provoke or exacerbate diabetes[40].

Type 2 diabetes is often preventable – or even reversible – by low cost measures such as lifestyle intervention[41]. Its high mortality is largely due to accelerated cardiovascular disease, and the condition typically – but by no means always – occurs in association with obesity, hypertension, lipid abnormalities and other vascular disease factors. It is also associated with obesity-related forms of cancer.

Most complications of type 2 diabetes can be prevented with existing forms of therapy when properly applied. Although many people with type 2 diabetes can be brought into safe glucose control with lifestyle change and oral medication in the early stages of their disease, their ability to secrete insulin diminishes with time, and insulin replacement therapy often becomes necessary. Ongoing monitoring and escalation of glucose-lowering therapy is thus an essential element of diabetes management.

Clinical types of diabetes in Africa
Variant forms of diabetes have been described in people of African descent since the 1950s, and have been associated with metabolic decompensation resulting in ketosis.

Reports from African-American populations indicate that the condition is seen in new-onset patients, typically middle-aged, overweight, and with a family history of type 2 diabetes in 80% of cases. Despite presentation with ketosis, such individuals can usually be managed without insulin over the longer term.[42] The extent to which it represents a true variant form of diabetes remains uncertain, but it does show the need for more detailed investigation of the pathophysiology of diabetes in people of African descent.

Secondary diabetes falls into three main categories. The first category is associated with a defined, typically monogenic, genetic syndrome. The second occurs when insulin secretion is compromised by pancreatic damage, such as acute or chronic pancreatitis or pancreatic cancer. The third arises when the onset of diabetes is associated with extra-pancreatic factors affecting insulin resistance, for example hyper-secretion of hormones that antagonize the secretion of insulin, or some types of drug-induced diabetes[43]. Secondary diabetes is relatively uncommon, affecting fewer than 5% of patients, but it is important to diagnose it correctly, since this can has a major impact upon its treatment and prognosis.

Malnutrition related diabetes has been reported from tropical areas in Africa, South America and South Asia, but its classification as a distinct subtype has been controversial.[44] Also known as fibrocalculous pancreatic diabetes, it is usually seen in underweight, malnourished patients and is characterized by severe hyperglycaemia without ketosis, high insulin requirements, and lack of autoimmunity, making it distinct

from classical type 1 diabetes. Patients, predominantly male, have a later age of onset, very low BMI, low socioeconomic status and a history of malnutrition. The contribution of exocrine pancreatic disease to diabetes in western populations has probably been underestimated, and its contribution to diabetes in Africa is still largely unknown.

The sub-Saharan African environment for diabetes

The rapid rise in diabetes prevalence is driven by many factors including increasing obesity – influenced by economic, socio-cultural and nutritional transitions – and increasing age[45]. The prevalence of obesity is highly dependent upon the environment, and the proportion of overweight people in a population reflects living conditions, cultural beliefs and food availability. Within that population, individual risk of obesity will depend upon a combination of genetic, cultural and socioeconomic determinants. This is reflected in the wide variation in the prevalence of obesity in sub-Saharan Africa.[46]

Urbanization has played a key role in the global nutritional transition, and the availability of cheap energy sources has greatly increased calorie intake and resulted in profound changes in body composition in populations around the world[47]. The health burden of these changes varies between ethnic groups, due to differences in patterns of fat deposition and their cardiac and metabolic consequences, which become manifest in African and Asian populations at lower levels of BMI than in those of European descent.[48,49]

Further to these disparities between countries, there are also major gradients between the prevalence of obesity in urban and rural populations; differences between countries may thus reflect the proportion of city-dwellers within a country or variations in sampling technique. The dynamics of the obesity epidemic were well illustrated by demographic and health surveys undertaken in 7 African countries at intervals of 10-13 years over the period 1992-2005. At the time of the latest survey in city-dwellers, 31.4% of women were overweight or obese, with a range from 38% in Kenya to 28-29% in Burkina and Senegal. The prevalence of urban overweight/obesity had increased by one third in a little over a decade, with a year-on-year increase of 5%. Obesity was inversely associated with household income and education, and the most rapid increase (50% overall) was seen in the poorest urban dwellers, notably women. In contrast, a fall of 10% was seen in women with secondary education or higher.[50]

These trends are consistent with increased food availability, especially refined energy-dense foods which have been adopted at the expense of more varied traditional diets which provide more essential nutrients.

The genetic contribution to diabetes in sub-Saharan Africa

Although genes predisposing to diabetes influence the relative risk of diabetes within a given population, environmental factors determine the absolute risk of diabetes within the population as a whole. Age and obesity are the two major environmental influences upon type 2 diabetes, and major obesity increases the risk of future diabetes by 80-100 fold, an order of magnitude greater than the best available genetic markers of risk. It is nevertheless important to define the genetic contribution to the diabetes epidemic in Africa, in order to define future susceptibility and (potentially) to permit future development of more targeted therapies.

Mankind originated in Africa, and the exodus of daughter populations from Africa passed through genetic bottlenecks created by small founder populations with rapid subsequent expansion. African populations are in consequence characterized by greater genetic diversity in both the nuclear and mitochondrial genomes together with lower levels of linkage disequilibrium (an indication of more ancient ancestry) than non-African populations. At least 13 genetically distinct ancestral African populations have been described, and African people are also characterized by genetic adaptations, which have evolved in response to infectious and nutritional challenges in the past environment.[51,52] This complex and diverse genetic structure has been relatively understudied, and it seems likely that considerable genetic variation and disease-associated genes remain to be uncovered within the African population.

Some gaps have been filled by the study of African-American populations, and comparison between groups of differing ethnicity in "melting pot" societies such as the USA. This is a potentially useful way of disentangling environmental from ethnic differences in the presentation of diabetes, but such comparisons must be interpreted with caution. African-Americans mostly originated from West or Central Africa and are therefore not representative of SSA as a whole, or indeed of their own parent populations.[53] Admixture with other ethnic groups and socio-economic differences are also potential confounders of such comparisons between migrant populations.

Since much of our evidence about the genetic characteristics of diabetes in Africans comes from the study of African-Americans, African-based studies are badly needed. It is nonetheless clear that African-American populations have a two-fold risk of type 2 diabetes compared with those of European extraction[54], and also have a much higher current prevalence of type 2 diabetes than most African populations. This may indicate future patterns of diabetes development in Africa itself.

Genetics of type 1 diabetes in Africa

Although GWAS studies have identified more than 40 genetic loci in association with type 1 diabetes in all populations, by far the greatest contribution comes from the HLA region, with odds ratios ranging from 0.02 to >11 for specific DR-DQ haplotypes; only 2 other loci achieve an odds ratio in excess of 1.5.[55] Notably, genes associated with type 1 diabetes influence immune mechanisms rather than beta cell function.

The dominant role of the HLA system in conferring susceptibility to diabetes is seen in all populations worldwide, but the relative importance of specific alleles varies with the genetic architecture of the population concerned. Large-scale analyses have yet to be performed in SSA, but studies in African Americans show some unique associations. In particular the DR4/DR9 genotype, which contains an African-derived "DR9" haplotype, confers an odds ratio of 30.88, comparable to the highest risk genotypes found in European origin populations.[56]

Genetics of type 2 diabetes in Africa

To date, nearly 80 genetic loci have been implicated in susceptibility to type 2 diabetes in global populations[57], but none have an effect comparable to that of the HLA region in type 1 diabetes. Populations vary in terms of the relative contributions of insulin resistance and beta cell deficiency to the onset of diabetes, but most of the genes known to be associated with type 2 diabetes influence beta cell function rather than insulin resistance.[58] Furthermore, progression of established diabetes is predominantly related to declining insulin secretion rather than increasing insensitivity to its action.[59]

As with type 1 diabetes, the same genes tend to emerge in diverse populations. GWAS analysis of type 2 diabetes in African Americans identified three known loci at genome-wide significance (*TCF7L2*, *HMGA2* and *KCNQ1*) together with two novel loci (*HLA-B* and *INS-IGF2*), indicating the existence of Africa-specific susceptibility genes.[58] Africa itself has been incompletely studied, but a genome-wide association study is being conducted on type 2 diabetes among continental African populations in the H-3 Africa project [http://h3africa.org]. Epigenetic changes are know to have differential effects on diabetes incidence dependent on population studied[60], however, little is known about the effects of the epigenome on African populations.

Sub-Saharan Africans appear to have undergone natural selection for a range of genomic regions associated with obesity and type 2 diabetes. This may explain why a study that mapped the genetic risk of type 2 diabetes by measuring the allelic frequency of 16 associated variants in 51 populations suggested that Africans face the highest known genetic risk for type 2 diabetes (http://geneworld.stanford.edu/hgdp.html). This selection has implications for the future prevalence of type 2 diabetes in SSA.

Type 2 diabetes is a syndrome, and analysis of the genetic contribution to hyperglycaemia does not capture the full prognostic implication of a diagnosis of diabetes. For example, in the Third National Health and Nutrition Examination Study (NHANES III), individuals over the age of 50 who had diabetes but no features of the 'metabolic syndrome' did not have an increased risk of coronary heart disease, as compared with non-diabetic individuals (7.5% diabetes: 8.7% non-diabetes), whereas individuals with both diabetes and metabolic syndrome features had a 19.2% age-adjusted prevalence.[61] Equally, it has long been known that vascular disease, hypertension and diabetes aggregate in African-American pedigrees.[62] Given the high prevalence of adverse risk constellation in African Americans, further study of its genetic basis in continental Africa is needed.[63]

The challenge of diabetes in in sub-Saharan Africa

Type 1 Diabetes

The recorded incidence of type 1 diabetes in SSA appears relatively low compared with many other parts of the world, with six of the seven published studies showing incidence of <3 cases per 100,000 <15 years per year, and Sudan at 10.1 cases.[64] These figures are almost certainly an underestimate as awareness of the presenting features of childhood onset diabetes is low in the general population and among medical personnel.

Little is known about the genetic and phenotypic characteristics of juvenile diabetes in SSA. Autoantibodies are less common than in studies in Western populations but it is not clear whether this is due to differing methodologies or aetiologies. There is some variation in HLA alleles affecting predisposition to type 1 diabetes.[65]

The peak age of onset of type 1 is around 12 years in western countries, but appears to have been deferred into the late teenage years in SSA.[66] This is possibly due to a combination of two factors, since younger children are less likely to be diagnosed and treated, and environmental factors that may have accelerated onset of the condition in western countries may still be lacking in SSA.

Countries in north-east SSA (Somalia, Eritrea, northern Ethiopia, Djibouti) appear to have considerably higher incidence rates compared with African countries south of this region, as well as populations in the Middle-East and north Africa.[67]

The apparent prevalence is also low, probably as a result of high attrition of diagnosed cases. Medical care is especially compromised by limited health professional experience; lack of access to insulin, blood glucose monitoring equipment, diabetes education; distance to treatment centres; and political instability[68] (Figure 3). Various studies have demonstrated the very high relative cost for families of diabetes care for a child or young person with diabetes – for instance in Benin, Burkina Faso, Central African Republic, Ivory Coast, Malawi and Mauritania the annual cost of consumables for minimal reasonable care for a child with type 1 ranged from 74-377% (median 126%) of per capita Gross National Income.[69]

Figure 3

The cost includes not only supplies (insulin, syringes and blood glucose meters and strips) but also laboratory tests such as HbA1c, and sometimes hospitalisation costs. There are also indirect costs such as travel costs (travel distances of over 200km are common), missed parental work time and others. Costs are particularly high when the cost of blood glucose strips per day is factored in – with the median cost of a blood glucose strip in seven African nations being $0.50 (range $0.20-$1.20). Even at two tests per day, this supply is usually more expensive than a supply of insulin. The financial and emotional impact on young people and their families is often severe, and undoubtedly many die due to lack of access to and affordability of care.[71]

Even safe insulin storage is a problem – many families do not have access to refrigeration and so clay pots are used for evaporative cooling. Encouragingly, preliminary evidence indicates that these methods are effective in reducing storage temperatures down towards room temperature (Ogle – personal correspondence).

Earlier reports from SSA document an appallingly high mortality for type 1 diabetes. Beran and colleagues have estimated life expectancy for children aged less than 15 years in Mozambique and Zambia on the assumption of equal incidence in rural and urban areas.[70] In Mozambique, the estimated life expectancy was 3.5 years, and a child developing diabetes in a rural area was unlikely to survive for more than a year.[72] Data from some other countries is a little more encouraging: in Soweto in South Africa from 1982-92, the mortality rate was 16% over 10 years (with half the deaths from renal failure, with others from ketoacidosis, hypoglycaemia and sepsis); a follow-up study showed 43% mortality at 20 years' duration.[71] Recent data from Rwanda showed a five-year survival of 93.8%, but the status of a number of patients was unknown and mortality could have been up to almost triple the crude mortality rate of 13.9 per 1,000 patient years. The same study found high rates of microalbuminuria, retinopathy, neuropathy and hypertension.[67] These figures should be set against in more affluent parts of the world, where life expectancy for young people diagnosed with type 1 is now only a few years less than that of the general population.[72]

Experience has shown that that the number of cases with type 1 diabetes rises sharply as interventions become available, diagnosis improves and mortality from acute complications (diabetic ketoacidosis and severe hypoglycaemia) falls. In Tanzania, known numbers of young people with type 1 rose from 50 in 2005 to 1,200 in 2015.[73] In Mali, known numbers of young people with insulin-requiring diabetes <25 years of age have risen from 14 in 2007 to over 350 in 2016, and in Rwanda from 35 to over 900 (See Appendix Rwanda Country Profile). According to international convention, estimates have to date focused on children under the age of 15 years. The only published prevalence figure that covers the young adult age group is from Rwanda – 16.4/100,000 population <26 years.[67] As noted, type 1 diabetes presents later in SSA, and children with diabetes also grow up (if they survive). The actual number of people with type 1 in Africa will thus be an unknown multiple of those under 15 years – in Rwanda there are 3.5 times as many cases aged <26 years as <15 years. [67]

In the absence of adequate care for people with type 1 diabetes within health systems, in the last 12-years, multiple initiatives have developed to improve care of children and adolescents with diabetes in Africa. The International Diabetes Federation Life for a Child Program (LFAC) commenced support in Africa in 2004 and now assists 9,873 young people aged <26 years in 20 countries. The Changing Diabetes in Children Program (CDiC) commenced in Africa in 2009 and assists over 7,700 young people in seven countries. Both programs work by strengthening the main existing diabetes centres in each country, providing insulin, blood glucose meters and strips, HbA1c testing, educational materials and health professional training, capacity building, and

other support including technical support in developing registers. Documentation of impact is now appearing[67], with sharply falling HbA1c levels in some countries.

'Ageing-out' of programmes – i.e. cessation of support at a given age – is an increasing problem. LFAC, for example, provides support until 26 years of age. After this age, there are some initiatives for example, tied to vocational training in Rwanda, microfinance in Tanzania, and support from Insulin for Life and Marjorie's Fund in some countries, but there is a large gap still at this age group.

Type 1 is a complex disorder, and diabetes education of the young person, their family, and health professionals, tailored to culture, language and education/knowledge levels, are critical in achieving good outcomes. LFAC, CDiC, and institutions in DR Congo, Sudan, South Africa have developed resources for diabetes education for children, their families and health professionals [http://www.idf.org/lifeforachild/diabetes-education-resources]. LFAC and the International Society for Pediatric and Adolescent Diabetes have also published Pocketbook Guidelines for use in under-resourced countries.

There are also nascent efforts to train specialists in countries in SSA. For example, in 2008, Gertrude Children's Hospital and other institutions in Nairobi, in partnership with the European Society of Pediatric Endocrinology, established the Pediatric Endocrinology Training College in Africa.. A second college opened in Lagos, Nairobi in 2013. The course runs for 18-months, with two six-month placements in the College and two three-month periods at the fellow's home institution. As at 2015, 54 paediatric endocrinologists from 12 African countries have been trained in Nairobi alone.[74]

Type 2 diabetes in sub-Saharan Africa

Few large scale studies have been performed on the prevalence of type 2 diabetes in Africa[75] and most countries do not routinely collect population level data on diabetes burden. A systematic review of reports of diabetes in people age >55 years in Africa reported an overall prevalence of 13.7%, higher in urban than in rural environments (19.7% vs. 7.9%). The prevalence was higher as measured by oral glucose tolerance test than by measurement of fasting glucose (23.9% vs. 10.9%), and in non-STEPS than in STEPS studies. (17.1% vs. 9.6%).[9] The study highlights the challenges in reaching an accurate estimate of the prevalence of diabetes, which is often asymptomatic or unrecognised in older people. Unfortunately, the two main diagnostic measures, fasting plasma glucose and the oral glucose tolerance test identify different groups of people, and the 2-hour value on the oral glucose tolerance test identifies a higher proportion of people in ageing populations compared with fasting plasma glucose measurement.[76]

From a clinical perspective, presentation with diabetes is often delayed in SSA and the great majority of people with overt diabetes will have unequivocal increases in random glucose and will therefore be diagnosed correctly whatever the test employed.[76] Choice of a cut-off point for borderline cases or choice of test (fasting plasma glucose, oral glucose tolerance test or HbA1c) are thus of less immediate relevance in the context of routine

clinical diagnosis and care, but this issue is nonetheless of great practical importance for the future as earlier detection of the condition becomes feasible.[76] Screening for diabetes is not recommended, even in affluent environments,[77] but opportunistic testing of at-risk patient groups (for example, those with TB) will become more widespread as health services improve, and guidance is needed on the most cost-effective means of doing so. The immediate priority, however, is to identify and treat those at greatest need.

Gestational diabetes in sub-Saharan Africa

In 2013, the global prevalence of hyperglycaemia in pregnancy in women 20-49 years is estimated to be 16.9%, affecting 21.4 million live births. More than 90% of these cases are estimated to occur in low and middle-income countries. Worldwide there is significant variability in prevalence due to difference in the diagnostic criteria used, but Africa ranks second after south east Asia.[78]

As the epidemic of type 2 diabetes spreads to younger people, the prevalence of GDM is likely to rise sharply in Africa. Systematic reviews of studies conducted in some African countries, notably Nigeria, found a prevalence ranging from 0 to 13.9%. Higher prevalence was noted in studies done after the year 2000 and those which used more current diagnostic criteria. A study of around 1000 pregnant women in Nigeria, for example, found prevalences of 3.8%, 8.1%, 7.5% and 8.6% respectively when modified IADPSG and original IADPSG criteria were used.[79]

Gestational diabetes has well-recognised associations with adverse maternal and perinatal outcomes and long-term sequelae including pregnancy-induced hypertension, preeclampsia, ante-partum haemorrhage, caesarean section, preterm birth, birth trauma, congenital anomalies and perinatal mortality.[80] Women with GDM are at high risk for developing type 2 diabetes, with up to seven-fold increased risk. Furthermore, their offspring have higher susceptibility to glucose intolerance and obesity later in life.

There have been several studies of diabetes in pregnancy in Africa, although mostly from urban areas and with relatively few participants in the majority. A study from Kenya in 1982 revealed a perinatal mortality rate of 254 in 1000; five times higher than in the non-diabetic population (based on 14 perinatal deaths in 55 pregnant women with diabetes, over a 6-year study period).[81] In Sudan, the influence of obstetric factors and indices of maternal metabolic control on perinatal morbidity and mortality were studied in 88 pregnant diabetic and 50 pregnant non-diabetic control women. The incidence of neonatal complications was 54.4% of in diabetic mothers vs. 20% in other mothers ($p<0.001$), and maternal hyperglycaemia was identified as the contributing factor.[82].

The benefits of treating diabetes in pregnancy have been widely shown – in South Africa, a reduced overall perinatal mortality was seen in treated compared to untreated women with diabetes in pregnancy.[83] An earlier study found a perinatal mortality of 10 in 1000 in the treated group with diabetes in pregnancy compared with the rate of 145 in 1000 in untreated group.[84] However, the form of treatment to use is debated. In South Africa, the form of therapy during pregnancy for 379 women with type 2 diabetes impacted on

perinatal mortality; with a higher rate (125 per 1000 births) in women managed on metformin and glibenclamide alone compared to women converted to insulin from oral agents (28/1000) and in the group treated with insulin alone/converted from diet to insulin (33/1000). However, there was no relationship between early exposure to metformin and glibenclamide and risk of foetal anomalies.[85] Perinatal mortality rate was similar, at 28/1000 live births in a study of 214 mothers with type 2 diabetes, who delivered at Baragwaneth Hospital in Soweto South Africa, all but five of whom were managed with insulin.[84] All of these studies were observational, however, and randomised controlled trials comparing agents in Africa need to be done.

Although the prevalence of GDM is rising, risk factors and optimal treatments unique to SSA are not clear. Reported risk factors for GDM, in SSA as elsewhere, are overweight and/or obesity, family history of type 2 diabetes, GDM in a previous pregnancy, previous still birth, previous macrosomic child and age >30 years. At present time, selective GDM screening programmes offer the most cost-effective option in SSA, but will require the development of simple criteria for identifying women at risk, which may differ in countries across SSA.[86,87,88] As yet no studies have assessed whether the ADA or IADSPG criteria are most applicable to women in SSA.

Given that SSA is undergoing rapid demographic and epidemiological transition with the associated changes in diet and lifestyle, and the burden of diabetes in pregnancy is already increasing rapidly, and there is a high risk that many women with diabetes in pregnancy will either go undiagnosed or will be inappropriately managed.

Better understanding of the prevalence and the risk for GDM in SSA will help guide studies of management approaches and also more targeted interventions. In resource-rich countries, insulin still remains the benchmark for managing hyperglycaemia in pregnancy, but oral agents are less expensive and are usually better tolerated and accepted. The two oral agents commonly used are metformin and glibenclamide. Of these, metformin is more effective, more readily available and more commonly used in SSA. However, trials are sorely needed to ensure that these agents are as effective and safe as insulin in pregnant women in SSA. High quality patient-centred care is also required to enable informed and shared decision making with patients.

Diabetic nephropathy in sub-Saharan Africa

Globally, prevalence of chronic kidney disease (CKD) has risen. In 2010, globally hypertension was the leading cause of deaths from kidney disease.[89] In 2013 the number of cases attributable to hypertension fell, but that attributable to diabetes rose.[90]

Although data from SSA are lacking estimates suggest that CKD prevalence in adults is around 13.9% (95% CI 12.2–15.7)[91], and between 4-24% in those with diabetes[92]. A meta-analysis of 64 307 people with CKD in SSA showed a mean age of 41·4 years (SD 9·9). Of these 46 494 (72%) had diabetes, 2765 (4%) were obese, 37 169 (58%) were HIV positive, and 7845 (12%) had hypertension.[93]

Although reliable information on the causes of CKD in SSA is lacking, it is known that African Americans are at greater risk of CKD. The Human Heredity and Health in Africa (H3Africa) project is currently collecting data to enable better elucidation of these factors in SSA and understand genetic contributions to CKD and their interactions with other environmental factors.[93] There is a genetic component to this increased risk, especially in people of West African descent where selection for the *APol1* gene has been driven by protection from Trypanosomiasis.[94]

In addition to a likely genetic predisposition and increased risk from poorly managed diabetes and hypertension, HIV also causes CKD. HIV and diabetes may act in synergy to worsen CKD and accelerate progression to cardiovascular disease.**[93]** These factors combined with other underlying causes mean that the average age of onset of end stage renal disease in SSA is 20 years younger than in those in Western countries. For those who reach end stage renal disease and require renal replacement therapy the situation is troubling as services are unable to meet demand in most countries in SSA.**[94]**

Worldwide, 1.8 million people received renal replacement therapy in 2004, and 5% of these were SSA.**[93]** If 5-10% of people with CKD reached end stage renal disease, health systems in SSA countries would be overwhelmed**[94]** could not afford to provide care.[95] In 2010, an estimated 50% of patients in SSA who needed renal replacement therapy due to underlying diabetes did not receive it – a number expected to double by 2030.**[92]**

In SSA renal replacement therapy is often paid for out of pocket (at a cost of US $ 10-20, 000 per year) – hence for most people, it is either unaffordable or leads to catastrophic expenditures for families. In university hospitals sampled in Nigeria and Kenya, less than 50% of those who needed dialysis were unable to pay.**[94]** This percentage figure does not reflect those who never make it to a university hospital. For those who can afford to pay for end stage renal disease, mortality is likely to be high. Outcomes are poor, but gradually improving in patients receiving end stage renal disease globally[96], but in SSA are worse than levels achieved in high-income countries.[97]

Diabetic retinopathy in sub-Saharan Africa

Diabetes causes visual impairment through early onset cataract formation and diabetic retinopathy. Globally, cataract and diabetic retinopathy are the second and sixth leading causes of visual impairment, respectively.[98] The sight-threatening manifestations of diabetic retinopathy, proliferative retinopathy and maculopathy, are preventable and treatable before vision is lost.

There are few community-based cross-sectional or cohort studies of diabetic retinopathy from SSA.[99] A population based survey (n = 4,414) in Nakuru, Kenya, which reported a prevalence of diabetes of 6.5% in adults over 50 years, showed a prevalence of 'any diabetic retinopathy' and 'severe non-proliferative diabetic retinopathy or proliferative diabetic retinopathy' of 35.9% (95% CI: 29.7, 42.6) and 13.9% (95% CI: 10.0, 18.8),

respectively.[100] A population-based study from Cape Town, South Africa, of visual loss using WHO methods identified DR as the cause of 8% of blindness and 11% of severe visual loss in people ≥50 years.[101]

Currently few populations in SSA have access to systematic diabetic retinopathy screening and treatment. Nascent case detection and treatment programmes, which serve as prototypes for how services might be structured, include regional-level outreach screening, services integrated into hospital diabetes clinics or eye departments.[102] The Kilimanjaro Diabetic Programme is an integrated, clinic-based, mobile photographic retinal screening service in northern Tanzania.[103] Diabetes clinics at 18 hospitals in the region are visited monthly. By 2015, 5729 individuals were registered and 3463 (60·4%) had been screened.[104] Only 40% of patients with referable eye disease attended their appointment at a tertiary referral centre providing laser, intravitreal injections and vitreoretinal surgery. This shortfall was attributed to limited understanding of diabetic retinopathy, logistics of attending referral appointments and the costs incurred.

Another diabetic retinopathy screening programme is that organised by the Ophthalmologic Society of South Africa which emphasises its importance as a biomarker for systemic risk.[105] And has recruited optometrists and general practitioners to increase access to screening opportunities close to the point of primary care. A systemic risk calculator serves as a counselling tool for patients and to determine follow-up.[106]

Poorly resourced health services and poverty hinder diabetic retinopathy care in SSA, as do a lack of patient knowledge of diabetes and limited access to healthcare. Referral pathways between diabetic clinics and ophthalmic services are underdeveloped and poorly organized. Indirect costs of attending hospital are high, and leading to delays when eye disease is not apparent prior to visual loss. There are few ophthalmologists or opticians to perform opportunistic screening.[107] Non-physician cadres such as ophthalmic clinical officers receive relatively little training in retinal disease, and eye services are overwhelmed by cataract, glaucoma, ocular trauma, infectious disease and paediatric ophthalmology. Limited access to imaging and treatment infrastructure results in the under-development of skills in diabetic retinopathy management.

Screening and care delivery programmes from industrialised countries are unlikely to be cost-effective in resource poor settings. Digital photography with telemedicine links has the potential to deliver cost-effective, accessible screening to rural and remote populations. Fundus cameras remain prohibitively expensive. Validation studies are in progress for a number of portable fundus cameras.[108,109] Automated grading of fundus photographs is used within established services including the Scottish National Diabetic Retinopathy Screening Programme and has been studied in Nakuru, Kenya.[110]

Diabetic foot disease in sub-Saharan Africa

Around 40-60% of all lower extremity non-traumatic amputations are performed in patients with diabetes.[111] Amputations are not only devastating on their impact on people

with diabetes and their families, leading to loss of independence and livelihood; they are also very expensive. In SSA diabetic foot problems are associated with high morbidity and mortality.[112,113]

Risk factors for diabetic foot ulceration (DFU) and amputations in SSA include: poor understanding of diabetes and its complications among healthcare professionals and patients, bare-foot walking, delays in seeking medical attention, poor diabetes control, and in some cases a preference by patients for alternative traditional therapies (faith or herbal healers) in the first instance. "Time is tissue" in the diabetic foot, and early recognition and treatment of DFU can prevent lower limb amputation and even death.[114] Unfortunately there is often a delay in accessing emergency foot care leading to poor foot outcomes in SSA management of a complex diabetic foot ulcer can cost more than 2 years of average income for the patient and lead to catastrophic expenditures .[112] The loss of productivity caused by unemployment or sick leave during foot ulcer management is an added cost to the family, relatives, friends and communities.[115]

Although well designed, community based studies are not available, published data from SSA suggest that diabetic peripheral neuropathy (DPN) is the most common complication of diabetes, occurring in in up to 75% of patients with diabetes[116,117] as a result of poor glycaemic control. In contrast to in high-income countries where peripheral vascular disease is closely associated with development of the diabetic foot, in SSA DPN remains the most common initiating factor for DFU. Yet, in most countries of SSA there is no foot/DPN screening for diabetic patients for risk stratification for DFU in order to provide preventive care. Hence, it is not surprising that DFUs have become the most frequent cause of prolonged hospital admission in diabetic patients. [112]

Peripheral arterial disease is important in determining whether a DFU will heal. In SSA foot complications are generally neuropathic and/or infective in origin, but the pattern is changing as the prevalence of peripheral arterial disease is rapidly rising in the diabetic population. As compared with prevalence rates of less than 10% in the 1990s, recent studies show much higher rates of PAD between 20-54%.[118,119,120]

A study of clinical outcome of patients with DFUs in Tanzania showed that 15% of diabetic admissions are due to DFU, 80% of which have occurred for the first time.[112] Amputations are frequent outcomes in DFUs and one-third of these are associated with neuro-ischemia and/or progressive infection. The hospital mortality rate can be as high as 54% in those with severe DFUs (Wagner score >4) managed without surgery or amputation.[112] Similar findings have been recorded in other parts of SSA. Sadly, some patients with severe DFUs discharge themselves from hospital against medical advice, putting themselves at increased risk of severe sepsis and death at home.[121]

Unhygienic conditions and poverty may be associated with DFUs in SSA. Other risk factors for DFUs in SSA include walking barefoot or delay in seeking medical attention. Barefoot walking, a common practice in rural Africa is often related to low income but may be cultural as well. For patients living at or below poverty line, the purchase of

appropriate footwear might not be affordable, feasible or of high priority. Barefoot walking substantially increases the risk of DFU in those with DPN. Moreover, those with DPN who habitually sleep on the floor or outdoors may suffer painless rodent bites on the toes. DPN masks such injuries until the patient finally becomes symptomatic and presents with a DFU that has progressed to fulminating foot sepsis. Patients who do not have access to ongoing foot care, advice, or education are most at risk.

In SSA patients often present to hospital only after the onset of gangrene or during stages of sepsis that may not respond to conventional supportive treatment with antimicrobials, intravenous fluids and insulin, resulting in progression to systemic infection and death.[112] Initial antimicrobial therapeutic regimens are usually selected empirically and then modified as appropriate once the results of culture and antimicrobial susceptibility testing become available. Cultures of superficial swab specimens are not very useful since they tend to yield polymicrobial growth. Deep tissue biopsy would yield more useful data, but many microbiology services in SSA do not have the resources to provide or maintain such routine culture services

Infection, ulceration, and limb amputation are preventable through organised foot care programmes. A multidisciplinary approach with an emphasis on a comprehensive, preventive strategy, including patient and staff education, and multi-factorial treatment of DFUs such as the *Step by Step Foot Project* piloted and carried out in Tanzania and India showed that infection, ulceration, and limb amputation are potentially preventable through organized foot care programs including patient and staff education, joint medical and surgical management of foot ulcers, appropriate use of microbiology resources, and regular follow-up to reduce amputations by more than 50%.[122]
It is not surprising, that foot infections are especially common where such services are especially scarce in SSA. Chiropody services, pivotal for foot care are non-existent in SSA. Consequently, lesions are either ignored or detected relatively late in the course of the infection after unsuccessful home therapy, such as soaking in hot water or application of unproven home remedies. Foot infections of this nature culminate in the onset of gangrene or infection with ensuing limb amputation or death from overwhelming sepsis.

Epidemiological data on the prevalence of painful DPN in Africa is sparse and shows variations in prevalence rates.[123] This is primarily because of using differing criteria of defining painful DPN and the assessment small and often unrepresentative samples of diabetic patients. The clinical features of painful DPN appear similar to that encountered outside Africa and results in poor quality of life, insomnia and depression. The four first-line drugs include amitriptyline, gabapentin, duloxetine and pregabalin. However, the availability and cost of a drug may be the determining factor for its use, which in most cases is amitriptyline.

The most important intervention for the prevention of DFU is education of the patient about appropriate foot care. It is now well recognised that the establishment of foot clinics has resulted in the reduction of amputations. In low-income countries, the

inadequacy of foot services results in increase in the number of needless amputations. Preventative strategies for DFUs are virtually non-existent in many countries in SSA. Education is the most powerful preventive tool in low-income countries, and should be an integral part of prevention programs, and be simple and repetitive.[124]

DFUs and amputations rates in patients with diabetes can be reduced by >50% by better education of patients and implementation of strategies, which are feasible in SSA countries: (i) regular inspection of foot and footwear at patient's regular clinic visits (ii) preventive footwear prescribed for patients with high-risk feet (iii) implementation of a multidisciplinary approach to the management of foot ulcers in diabetes clinics (iv) early diagnosis of peripheral neuropathy and PAD (v) continuous follow-up of patients with previous foot ulcers and registration of amputation and foot ulcers for affected patients.

HIV, tuberculosis and diabetes interaction in in sub-Saharan Africa

HIV and TB are closely associated with diabetes. The association between diabetes and tuberculosis was known long before the discovery of insulin but the precise mechanisms underlying the alterations in macrophage function, cytokine production and T-cell subtypes in diabetes are not fully understood.[125] Although research is ongoing to better elucidate the relationship.[126]

Increasing prevalence of diabetes is hindering progress towards global targets for TB by 2035.[127] Pan and colleagues have found that with current rates of increase in prevalence of diabetes, in 13 countries studied by 2035, the cumulative reduction in tuberculosis incidence would be 8·8% and mortality would be 34·0%.[128] They estimate that halting the increase in diabetes would avoid 6·0 million incident cases and 1·1 million tuberculosis deaths over 20 years. However, most of the evidence for relationships between TB and diabetes come from Asia, and African studies have reported an inconsistent association. No association between diabetes and tuberculosis was reported in Guinea Bissau despite an almost three-fold increased prevalence of diabetes relative to the general population in Nigeria.[129,130,131] Hyperglycaemia may be transient at onset of TB, complicating evaluation of the true extent of the association with diabetes. Since HBA1c gives an assessment of glycaemia over a 2-3 month period it might be inferred that this, rather than shorter-term glucose measures, would perform better as a screening test. Although this was not shown in a study from Tanzania, where the strong association between TB and diabetes disappeared after - months of anti-TB therapy, regardless of the test used to diagnose diabetes.[132]

Evidence that-pre-existing diabetes is associated with more severe symptoms and clinical presentation of TB is conflicting. People with both diabetes and TB do tend to be older and to have a higher BMI compared to TB cases without diabetes. Radiologically, people with diabetes tend to have a higher occurrence of lower lobe involvement, a non-segmental distribution, and multiple cavities within a tuberculous lesion. Of greater concern, diabetes and TB combined are associated with worse outcomes such as

increased risk of recurrence, delayed sputum clearance, and higher mortality. The same holds for drug sensitive and multi drug resistant TB.[133]

Glycaemic control is frequently more difficult to achieve in patients with TB and diabetes than in diabetes alone, and TB may cause anorexia, weight loss and reduce physical activity as well as increasing insulin resistance and glucose levels, especially soon after TB is diagnosed. There may be drug-drug interactions. Rifampicin, for example, one of the cornerstones of TB regimens, reduces the efficacy of many sulfonylureas because it induces CYP2CP in the liver and lowers the area under the curve of these drugs by 22-70%. INH may cause peripheral neuropathy, which may be confused with that due to diabetes.[134]

The pathophysiological basis for the association between diabetes and HIV and this interaction leading to cardiovascular disease is not clear. It is thought that the chronic inflammatory state induced by HIV contributes to insulin resistance, which may persist despite exposure to ART. In addition to this, some of the older protease inhibitors and nucleoside reverse transcriptase inhibitors induce dysregulation of mitochondrial function leading to insulin resistance and diabetes.[134]

The reported incidence and prevalence of diabetes in people living with HIV is highly variable, most likely due to factors such as diabetes prevalence in the general population, diagnostic method used, sample sizes, duration of follow up, year of the study and the use of specific antiretrovirals.[135] Agents such as stavudine and zidovudine are known to be associated with diabetes, and efavirenz, the preferred non-nucleoside reverse transcriptase inhibitor (NNRTI) for first line ART in low and middle income countries, has since been associated with a modest increased risk of developing diabetes (Hazard ratio 1.27 (95% CI 1.10 to 1.46) compared to nevirapine, after controlling for multiple confounders in a large South African cohort study with 113,297 patient-years of follow-up on first line ART.[136] Although stavudine has been withdrawn from most first line regimens long term therapy with efavarinz and zidovudine may require regular screening for diabetes. Ideally, this could be in the form of a two-step process involving administration of a validated diabetes risk score followed by a blood test in those with a high score. Unfortunately, there is no validated risk score for diabetes in Africa per se, let alone in people who are HIV infected.[137]

There is sparse information on the prevalence of diabetes in people with comorbid HIV and, or TB in Africa. Current evidence suggests that diabetes prevalence is lower in individuals with both TB and HIV compared to those with either disease alone, although that may change given the rising numbers of people with diabetes in SSA, the earlier introduction of ART and the ageing of the patients with HIV receiving ART.[138,139]

Many unresolved issues remain, however. These include understanding attributable risk of diabetes and HIV for tuberculosis in a high-risk HIV setting. We still need to identify the most reliable and cost effective screening method for diabetes in HIV and/or TB infected persons and *visa verse*, and when the screening should take place. Beyond this,

there is the need to achieve optimal glycaemic control in those identified as suffering from co-morbidity, and to establish whether management of hyperglycaemia, and to what level, even in the short term, alters outcome. In Africa, sulfonylureas and metformin are the backbone of therapy for type 2 diabetes. Given that access to self-blood glucose monitoring and insulin is frequently problematic even for children with type 1 diabetes in most SSA countries, the use of intensive insulin therapy in comorbid diabetes and TB is likely to be limited to tertiary or specialised centres.

Cardiovascular disease, hypertension and diabetes in sub-Saharan Africa

The relationship between diabetes, hypertension, hyperlipidaemia, and the subsequent increased risk on cardiovascular disease has been reported extensively elsewhere.[140] Most of this literature, however, pertains to high-income countries, and very little is known about either the prevalence of co-morbid risk factors and related CVD, or how these conditions interact in an African setting.[141,142] Although diabetes and obesity contribute to cardiovascular morbidity and mortality, hypertension (often found in association with diabetes) is the largest contributor to cardiovascular deaths globally.[143] In low-income and middle-income countries, the epidemiological transition is characterized by a gradient in blood pressure from rural to semi-urban and communities,[144] and prevention is the key cost-effective intervention.[145] Obesity and hypertension are the most common cardiovascular risk factors in SSA where access to healthcare, cardiovascular screening and treatment are a constant challenge.[146]

The prevalence of high blood pressure has increased rapidly over the past two to three decades. It is estimated that 150 million Africans will be treated for hypertension by 2025 compared to 80 million in 2010, an increase attributed to increased tobacco use, excessive alcohol consumption, reduced physical activity and adoption of "Western" diets and other features of the economic transition. According to the WHO STEPS surveys conducted in the region, the prevalence of high blood pressure ranges from 19.3% in Eritrea to 39.6% in Seychelles.[147]

Low public awareness and inadequate control and treatment of hypertension are major public health concerns in Africa. Recent systematic review of data from 33 surveys involving over 110, 000 participants in SSA found a pooled prevalence of hypertension of 30%, but only 27% of people with hypertension were aware of their status before the surveys, only 18% were on treatment and only 7% had acceptably controlled blood pressure.[148] Another major problem is access to and affordability of drugs, since out of pocket expenses are the main source of medications and treatment. There are thus many barriers to effective control of blood pressures despite the availability of cost effective medications. These include: poor implementation of screening programs, lack of access to affordable medicines and commodities, and poor knowledge amongst patients and health care providers of the need for adherence, monitoring and early identification of complications.

We discuss next how health systems in SSA have responded to the growing burden of diabetes and examine in selected countries the readiness of health systems and key functions in managing diabetes.[149]

Health system responses to diabetes in sub-Saharan Africa

The majority of research on diabetes in SSA has generally focused on epidemiology and clinical presentation, with few studies that explored health systems, but these studies were limited in scale and scope.[150]

We used published studies and analysis of surveys to explore health system responses to the rising burden of diabetes in SSA. We used a health systems framework to guide our analysis and systematically examined repose to diabetes in key health systems functions of organization and governance, financing, resource management, and service delivery[151].

Organization and governance of diabetes in health systems of sub-Saharan Africa

The state capacity, organizational and governance structures and institutional strength of health systems vary across SSA. By 2010, 42 of the 45 countries of SSA had reported having a unit or department within their ministries of health with responsibility for NCDs.[152] However, just seven countries had a national operational policy, strategy, or plan for diabetes, lower than other NCDs (Figure 4)

Figure 4

A majority of countries in each World Bank income group had plans for two or fewer of the NCDs and NCD risk factors (Figure 5).

Figure 5

The availability and the stage of implementation of guidelines, protocols, or standards for diabetes management varied across countries. Just four countries across SSA had guidelines, protocols or standards that were fully implemented (Figure 6).

Figure 6

Financing of diabetes in sub-Saharan Africa

In 2001, African nations adopted the Abuja Declaration, pledging to allocate at least 15% of their national annual budgets to health spending.[153] Yet, by 2013 only seven countries in SSA – the Central African Republic, Ethiopia, Malawi, Rwanda, Swaziland, Togo and Uganda – had reached that target.

In 2010, average health expenditure per capita was $135.[154] In 2012, total health expenditure in SSA as a proportion of GDP average 6.3%, ranging from 6.6% in the 23 low income countries, 6.1% in the three low middle-income countries and 5.5 in the five upper middle-income and one high income country. [155] In the same year, average public spending on health accounted for 49 percent of total health spending.[156]

In 2012, the average level of out of pocket expenditures as a proportion of total expenditures on health was 36 percent, ranging from 76 percent in Sierra Leone to two percent in the Seychelles.[157] In 12 countries, out-of-pocket expenditure comprised more than 50% of total health expenditure – vastly exceeding public health spending. [158] External funding ranged between 46 percent in the Gambia to one percent in Equatorial Guinea, with an average of 25 percent.[159]

To increase health financing for NCDs, several countries such as Cameroon, Botswana and Seychelles, have introduced earmarked taxation to influence health behaviours, with revenues channelled to health promotion activities. Others have launched reforms to increase public funding for health systems and to achieve universal health coverage, but large informal sectors hinder effective tax collection to invest in health systems.[160]

Low levels of public funding, low income levels and high out-of-pocket expenditures have adversely affected the uptake and provision of care for diabetes patients, increasing the likelihood of long-term complications.[161,162] In Malawi, for example, families spent 22 percent of their monthly per capita budget on out-of-pocket expenditures related to NCDs.[163] For patients with Type 1-diabetes high out of expenditures have and unaffordability of care has grave consequences, with high mortality levels among patients, as regular insulin injections are not always affordable.[164]

There is major variation in health system spending on diabetes in SSA. According to the International Diabetes Federation (which estimates costs based on the cost to the patient, as well as the cost to the health system), in US$ purchasing power parity, using 2013 World Bank country income groups, the average cost was $67.4 in low-income countries, $201.1 in low middle-income countries, $683.2 in upper middle-income countries and $2,036 in the one high-income country.[165,166]

Resource management in health systems for tackling diabetes in sub-Saharan Africa

Sub-Saharan Africa has an acute shortage of healthcare professionals: the WHO African Region accounts for 25 percent of the current global health workforce shortage, expected to rise to 34 percent by 2035 as a result of population growth in Africa.[167] The shortage of health workers, exacerbated by emigration[168], has constrained achievement of Millennium Development Goals.[169,170]

There is shortage of medical graduates (more than half of the countries in SSA have only one medical school, and 11 countries have no medical school)[171] and nurses, whose level of training and skills vary greatly across countries[172]. More than half of SSA countries have a category of non-physician clinician (providers who complete an average of about three-years of post-secondary clinical training)[173] and many countries such as Ethiopia and Malawi have successfully used community health workers (CHW) to scale up HIV, tuberculosis, malaria and other essential services.[174,175]

Service delivery for diabetes in in sub-Saharan Africa

To inform the 2010 *Global Status Report on Noncommunicable Diseases*[176], WHO led several country-level surveys to assess national capacity of countries in prevention and control of NCDs. The WHO Service Availability and Readiness Assessment (SARA) survey, which measured the availability of diagnostic tools, essential medications and trained staff at the facility level for series of tracer conditions, including diabetes and cardiovascular disease, was applied in eight SSA countries.[177] The SARA questionnaire, reference manual, implementation guide and completed reports, but not the study data, are available on the WHO website for countries wishing to conduct a survey.[178]

The findings from the country-level SARA reports indicate that there are major gaps in front-line service delivery. In the eight study countries, less than one half of facilities offered diabetes management.[179] Of the facilities that did offer diabetes services, only 40 to 60 percent were ready to provide diabetes services (Table 2).

Table 2

With the exception of Uganda, only about one-third of facilities offering diabetes services had guidelines for treatment, and one-third or fewer had at least one trained staff.[179] The discrepancy between trained staff and availability of diagnostic supplies and medication is concerning as it is not clear how supplies and medications are being used in the absence of staff with formal training in diabetes care.[179] The availability of blood glucose testing ranged from 14 percent in Burkina Faso to 80 percent in Uganda – although only 31 percent of Uganda sites reported the availability of trained staff.

Availability and access to medicines for diabetes in sub-Saharan Africa

The availability of oral hypoglycaemic medicines, such as metformin and glibenclamide, was as low as six percent in Burkina Faso, and as high as 70 percent in Zambia, although once again, Zambia reported trained staff at only 20 percent of facilities. Insulin was available in fewer than half of facilities in all countries.[179] A separate study of access to treatment and medicines in Mozambique, Mali, and Zambia corroborated the findings of SARA surveys in difficulty accessing drugs for control of diabetes.[179]

According to WHO, essential medicines for diabetes are not available in all SSA countries: oral medicines for as metformin and glibenclamide are available in 29 and 35

countries respectively, insulin in 32 countries and aspirin (acetyl salicylic acid – ASA 100) tablets used for primary prevention of cardiovascular disease in patients with diabetes is available in 41 of the 45 countries[180] (Figure 7).

Figure 7

An integral part of the WHO Global Action Plan (GAP) for the Prevention and Control of Noncommunicable Diseases 2013-2020 (NCD GAP) is the target of 80% availability of the affordable basic technologies and essential medicines, including generic drugs, required to treat major NCDs in both public and private facilities.[181] This target is essential to enable countries to meet the 25% relative reduction in premature mortality from NCDs by 2025, as defined by the WHO in the NCD GAP. However, studies reveal access challenges due to a lack of availability and affordability of insulin with median availability of insulin in the public sector of 75% in the public sector (5 countries) and 46% in the private sector (6 countries).[182] Availability and affordability of diabetes medicines in also a challenge in SSA.[183,184,185,186,187]

A recent study which used from the World Trade Organization found that only 16.7% of SSA countries bought insulin every year during the period 2004-2013, but 29.2% of countries did not buy insulin over this period and 38% of countries were reliant on less than one supplier for their insulin.[188]

WHO SARA survey reports provide countrywide assessment on the availability of insulin, metformin and glibenclamide for 9 countries in SSA. For insulin median overall availability was found to be 13% of facilities surveyed (Range: 3%-39%). For insulin median availability decreased at lower levels of the health system, was actually more available in rural versus urban areas (median of 12% versus 7%) and had higher in the private contrasted with the public sector (median of 11% versus 3%). Metformin had a higher overall median availability in comparison to insulin of 22% (Range: 2% to 57%). Similar trends as with insulin were found: decreasing availability at lower levels of the health system; higher availability in rural areas; and higher availability in the private sector. Glibenclamide shows similar trends except that for this medicine the availability is higher in urban versus rural areas.[189,190,191,192,193,194,195,196,197] These data are presented in Table 3.

Table 3

These data clearly show that the countries studied are far from achieving the 80% target included in the GAP. However, availability varied with regards to level of the health system, urban versus rural, and public versus private – suggesting disparities.

Analysis of the prices of diabetes medicines in SSA can be undertaken using data from Management Sciences for Health (MSH), which provides the international reference prices for many medicines.[198] The prices quoted by MSH are from tenders from ministries of health, and represent the price of the medicine without any add-on costs at

the point of entry to a given country. Analysis of data from 1996 to 2013 The median price for insulin (10ml 100IU/ml vial) in SSA (8 countries) is US$ 7.15 (Range: US$ 1.52 to US$ 17.58) at constant 2015 prices.[199] For metformin (500mg; 10 countries), gliclazide (80mg; 4 countries) and glibenclamide (5mg; 13 countries) the median prices are respectively US$ 0.018 (Range: US$ 0.002 to US$ 3.304), US$ 0.023 (Range: US$ 0.012 to US$ 0.060) and US$ 0.004 (Range: US$ 0.0004 to US$ US$ 0.032). Using Defined Daily Dosage (DDD)[200] the yearly treatment costs are presented in Table 4.

Table 4

Table 4 shows that treatment with insulin presents a significantly higher cost for individuals versus the use of oral medicines for diabetes. The prices presented in Table 4 do not take into account of mark-ups, such as value added sales tax, local taxes, international purchasing verification tax, insurance, defence levy, overheads mark-up, bank fees, fee for import declaration form, port clearance, importer margin, handling cost, wholesale mark-up, retail mark-up, health facility mark-up, dispensing charge or other mark-ups within the system. Although data are lacking for these mark-ups, specifically for insulin, for other medicines the additional cost of these have been found to range from 18.4% to 94.4% of the price of the medicine.[201]

These add-on costs as well as subsidies within health systems mean that there are many factors influencing the affordability of insulin, the price of for which can vary substantially.[180] For example data from 4 studies in 3 African countries suggest that in 2003 in Mozambique and 2004 in Mali between the central government and facilities there was an increase in price to recuperate some of the storage and transportation costs.[180] This increase in price was not observed in Zambia and in Mozambique in 2009.[180,202] In two studies from Mozambique and in Zambia the price between the facility and the patient was subsidised, whereas in Mali there was an additional mark-up meaning that between the government purchase price and patient purchase price there was a 47% price increase. In order to present different prices of insulin different data sources were combined to show the median price at different levels of the health system at 2015 prices[180, 199,202,203] (Figure 8).

Figure 8

In comparing the MSH prices to those obtained by different ministries of health Figure 8 shows that many countries are purchasing insulin at the best price possible, but there are still some outliers. For patients in the public sector in some countries insulin is provided for free or subsidised, whereas in others the price can be quite high. That said these prices are relatively low in comparison to prices in the private sector, highlighting the importance of ensuring proper availability in the public sector. Clearly some of the prices presented in Figure 8 are not affordable to individuals in these countries, for example US$ 10.88 in the public sector in Mali or US$ 50.57 in the private sector in Ethiopia.[199]

Data from WHO/HAI found that in terms of days wages people in some countries in SSA had to pay between 0.9 to 6.7 days of wages to be able to pay for their treatment (Figure 9).[186] Based on that affordability for the WHO/HAI approach is that the lowest paid government worker should only pay one-day's wage for treatment. The data presented in Figure 9 suggests only glibenclamide in Ethiopia is affordable.

Figure 9

However, in SSA many individuals do not work in the formal sector, and therefore measuring affordability in terms of the wage of the lowest paid government worker does not take into account that most people do not make a monthly wage and live on less than US$ 1.90 and US$ 3.10 per day.[204] Comparing annual cost of diabetes medicines (Table 4) and daily costs of the different diabetes treatments with different thresholds of poverty using daily income show that daily drug costs represent from 0.5% to 15.1% of income for someone living on US$ 1.90 per day (Table 4). These costs correspond to the prices paid when a ministry of health has purchased medicines, and not the prices individuals might pay when purchasing these drugs in the public or private sector.

Affordability is not only important for the individual, but also for the health system. For some countries in SSA it has been found that depending on the price of insulin the cost to the health system can vary from 0.2% of total GDP in South Africa to 13.4% in Malawi for their total insulin needs.[205]

The costs of medicines are significant, but are only one part of the overall cost which include the cost of delivering medicines which require a well-functioning health system to ensure proper diabetes care including: trained health professionals, organised centres for care, diagnostic tools, data collection, national policies, an active diabetes association, patient education, measures to improve adherence and prevention measures.[206]

Health service delivery for diabetes in sub-Saharan Africa: analysis of Service Delivery Indicator Surveys

To better understand service delivery gaps in diabetes care we were able to receive the Service Delivery Indicator (SDI) surveys conducted in six SSA countries by the World Bank in cooperation with the African Economic Research Consortium, and the African Development Bank in SSA.[207]

The SDI surveys include primary health facility level data on expenditures, provider effort (absence rate, caseload per provider), provider knowledge and ability (diagnostic accuracy, adherence to clinical guidelines, and management of maternal and neonatal complications), and inputs (availability of supplies, equipment, and drugs). Diagnostic accuracy is measured through patient case simulations (vignettes) for the following seven tracers: (i) malaria with anaemia; (ii) diarrhoea with severe dehydration; (iii)

pneumonia; (iv) diabetes; (v) pulmonary tuberculosis; (vi) postpartum haemorrhage; and (vii) neonatal asphyxia.

The SDI surveys are complementary to the surveys that focus on the availability of resources and provide valuable data beyond those provided by WHO SARA surveys, which are designed to capture availability of resources in facilities for management of NCDs, including diabetes, to ascertain health system readiness for service provision.[208] (Panel 1) Hence, our analysis of SDI surveys builds on the analysis of SARA surveys to broaden and deepen our understanding of service delivery as well as the quality of these the care provided management of diabetes by providing insights into the knowledge ability and effort of providers (technical quality) as well as measures on the availability of key inputs, such as drugs, equipment and infrastructure (structural quality).[209]

The first rounds of SDI surveys in Senegal and Tanzania (2011) did not include a diabetes vignette and were excluded from our analysis. The total sample consists of Kenya (2012), Mozambique (2014), Nigeria (2013), Tanzania (2014), Togo (2013) and Uganda (2013).

Panel 1: World Bank Service Delivery Indicators survey: methodology

The surveys use a multi-stage, cluster sampling strategy, which allows for disaggregation by geographic location (rural and urban), by provider type (public and private non-profit) and facility type (e.g. dispensaries/health posts, health centres, and first level hospitals).

The tracer conditions for the patient simulation vignettes were chosen based on the disease burden among children and adults, and whether the condition could be effectively presented during the simulation in order to assess provider's ability to give the correct diagnosis. During the vignette, one of the fieldworkers acts as a case study patient and presents the symptoms to the clinician. The symptoms are carefully scripted to allow comparability across providers and countries. The clinician is aware of the case simulation but is asked to proceed as if the fieldworker is a real patient. The other enumerator acts as the observer. For the physical examination and laboratory components of the visit, the provider is told to ask questions rather than performing the actual task. The patient responds verbally with the appropriate measures. Up to ten health workers who typically conduct outpatient consultations are randomly selected to assess the patient simulation. If there are fewer than ten health workers providing outpatient care at the facility, all providers are interviewed.

The vignettes offer several advantages. Since all clinicians are presented with the same case study patients, we are able to standardize the case mix and severity of the conditions to allow for comparability across providers. The ethical approval process is relatively simple given than no patients are observed, and the choice of tracer conditions is not dependent on the patient's ability to mimic certain symptoms. As discussed in the introduction, however, performance on vignettes is likely to represent the upper bound of true clinical ability and is likely to be higher than the average level of care available to real patients[210,211]

Provider's Ability
Provider's ability is measured using two indicators: diagnostic accuracy and process quality. First, we examine whether the provider was able to diagnose diabetes correctly during the patient case simulation. We create a binary variable equal to 1 if the provider was able to diagnose diabetes correctly and 0 otherwise. Secondly, we assess process quality for diabetes care by investigating the degree to which the provider adhered to clinical guidelines during the patient case simulation. The clinical guideline score is calculated as a share of relevant tasks performed in four domains: symptoms, patient history, physical exam, and laboratory diagnostics. All components are given equal weight. Due to the standardization of the vignettes, we are able to compare diagnostic accuracy and process quality across and within countries.

Covariates
In our analysis we control for both provider and facility level characteristics that could independently predict quality of care. At the provider-level, these include covariates for gender and cadre of provider.

Facility-level characteristics include facility type (dispensary/health clinic, health centre, or district hospital), location (rural, semi-urban, or urban), and ownership (private or public). In addition, we also construct an equipment index, calculated as the unweighted average of available and functioning essential equipment (sphygmomanometer, adult weighing scale, thermometer, and stethoscope). In Tanzania and Uganda, the surveys also collected data on whether facilities had a glucometer available. We control for the presence of a glucometer separately for these two countries. Data on whether providers received any diabetes or NCD-related training are not available.

Statistical analysis
We calculated descriptive statistics of the sample of health workers for all variables of interest, presenting the proportions for binary variables and mean and standard deviation (SD) for continuous covariates. We separately examined the associations between diagnostic accuracy and the clinical guideline score with observed provider and facility-level characteristics. For diagnostic accuracy, we used a logistic regression since the variable was binary (equal to 1 if provider correctly diagnosed diabetes, 0 otherwise).

We used ordinary least squares (OLS) regression to examine the association between the clinical guideline score and covariates of interest. To normalize the distribution, we log transformed the clinical guideline score. All analyses were conducted in Stata 14.0 (StataCorp, College Station, Texas).

We provide a summary of the provider characteristics in Table 5. The total sample consisted of 7,414 providers, with the largest number of providers in the sample coming from Nigeria. The sampled providers are on average five years younger in Kenya and Uganda compared to the other countries. With the exception of Tanzania, nurses, midwives, and community health workers represented more than half of the sampled

providers. In Tanzania, 74% of the sample consisted of physicians, medical or clinical officers. In Nigeria, physicians represented only 9% of the sample, while nurses, midwives, and community health workers represented 81% (largely community health workers). In Kenya, Nigeria and Uganda, the majority of sampled providers were female.

Table 5

Descriptive statistics in Table 5 shows that higher shares of providers in all countries were employed at lower level facilities (dispensaries/health clinics or health centres) and were primarily located in rural areas. On average, providers worked at facilities with a high equipment index, suggesting that they had access to a thermometer, adult weighing scale, sphygmomanometer, and stethoscope. In Nigeria and Uganda, however, more than a third of providers did not have access to all four pieces of equipment.

Less than 50% of the sampled providers in all countries were able to accurately diagnose diabetes, with the exception of Kenya where 82% of providers gave the correct diagnosis. As shown in **Error! Reference source not found.**4, compared to other tracer conditions simulated in the vignettes, diabetes was the second least diagnosed condition (after diarrhoea with severe dehydration). Conversely, more than 80% of providers were able to diagnose tuberculosis and neonatal asphyxia, with the share as high as 97% and 91% in Kenya and Tanzania, respectively. Only 6% of the sample was able to diagnose all seven conditions (six in the case of Togo). The share was highest in Kenya, where almost 27% of the surveyed providers correctly diagnosed all conditions presented during the patient simulation. On the contrary, only 1% of the surveyed providers in Mozambique were able to diagnose all cases.

Figure 10

While the average clinical guideline score was less than 30 percent, we observed a wide range of performance scores with some providers performing all the necessary tasks (**Error! Reference source not found.**11).

Figure 11

Providers scored consistently higher in the laboratory domain (Figure 12), indicating that they would order the appropriate laboratory diagnostics to diagnose the patient. Conversely, with the exception of Tanzania, providers scored lowest in the patient history domain – asking less than 20 percent of the appropriate questions.

Figure 12

The majority of providers who correctly diagnosed diabetes could not prescribe the appropriate treatment and indicated that they would refer the patient for a follow up visit at a specialist diabetic clinic or higher level facility (Figure 13). In Tanzania, however, 80 percent of providers indicated that they would prescribe oral

hypoglycaemic, with 49 percent of providers referring patients to more specialized facilities.

Figure 13

Table 6 presents the logistic regression results of the factors associated with a provider's ability to diagnose diabetes. Female providers had significantly lower odds of correctly diagnosing diabetes in Kenya (0.81 OR; 0.37 - 0.99 95% CI) and Nigeria (0.8 OR; 0.68 - 0.94 95% CI). Relative to the highest cadre category (physicians, medical or clinical officers), lower cadres had significantly lower odds of diagnosing diabetes in all countries except for Mozambique, where we did not find statistically significant differences.

Table 6

Table 6 shows that providers employed at district hospitals in Mozambique (2.11 OR; 1.25 - 3.56 95% CI), Nigeria (2.25 OR; 1.53 - 3.32 95% CI), and Tanzania (2.26 OR; 1.21 - 4.20 95% CI), were significantly more likely to diagnose diabetes. Location was only a significant predictor in Nigeria and Togo, with providers in urban areas having higher odds of diagnosing diabetes than those in rural areas. We did not find a statistically significant relationship between the ability of providers to diagnose diabetes and whether the facility was public (Table 6). Interestingly, in Kenya, Nigeria, and Uganda, a higher equipment index was found to significantly increase the odds of correctly diagnosing diabetes. As mentioned earlier, the variation in the equipment index was quite low with the majority of providers having access to the basic equipment (particularly in Kenya), thus the significant odds ratios suggest that ensuring universal availability of basic equipment could substantially improve diagnostic accuracy.

Table 7 presents the OLS regression results of the factors associated with higher clinical guideline scores. The dependent variable is the log transformed clinical guideline score. The results are consistent with the findings related to diagnostic accuracy. Lower cadre providers are less likely to have higher clinical guideline scores. Nurses, midwives, and community health workers are found to have 5-7% lower clinical guideline score than physicians, medical and clinical officers. In Mozambique, Nigeria, and Tanzania, providers at district hospitals are found to have a 6-9 % higher clinical guideline score than providers at the lowest level facilities. The equipment index is also positively associated with the clinical guideline score in Kenya, Nigeria, and Uganda.

Table 7

Health system responsiveness to diabetes: implications for sustainable health systems in sub-Saharan Africa

The examination of reports from WHO SARA surveys undertaken in nine countries, and analysis of World Bank Service Delivery Indicator surveys in six countries reveals that health systems of the countries examined are not yet ready for delivering effective health

services for diabetes patients. However, a comprehensive understanding of health systems readiness for managing diabetes in SSA is constrained by a lack of data, especially how resource and service gaps affect demand, and how the interaction of supply-side gaps and demand-side dynamics translate to unmet need. We provide in the next section new analysis that uses surveys in 10 countries of SSA to examine the nature and extent of unmet need at each critical stage of the care process.

Analysis of Cascade of Care and Unmet Need for diabetes in sub-Saharan Africa

The examination of reports of SARA surveys and analysis of Service Delivery Indicator surveys in Section 3 of the commission report lay bare the consequences of underfunded and weak health systems and years of suboptimal investments in human resources[212], which have led to large resource gaps for diabetes care in SSA.

Limited availability of diabetes services means that persons affected by diabetes in SSA consume less care than those in Europe, China and North America. However, when patients with diabetes are able to access healthcare services, they consume more healthcare services at all levels of care than their peers who do not have diabetes – as a study in Cameroon, Mali, South Africa and Tanzania indicates, where patients with diabetes had 6.27 times more inpatient admissions, 12.95 times more inpatient days, and 7.54 times more outpatient visits per person per year than a matched comparison group of non-diabetics.[213] However, extant research does not provide detailed insights or quantify the extent of unmet need for diabetes services in SSA.

Understanding how health systems resources are allocated to diabetes care, how these resources are used and how providers provide care provides valuable insights into the response to the diabetes burden. It is important, however to understand better the consequences of the health system response, in order to ascertain if and how the demand for diabetes care is being met, and where gaps exist.

Analysis of cascade of care for diabetes in sub-Saharan African health systems

One innovative analytic approach to assessing health system performance for single diseases is the construction of a cascade of care. The cascade of care has been used to monitor progress toward coverage goals for populations affected by HIV/AIDS.[214,215] This method typically involves a quantitative depiction of the step-wise care system for the population affected by a disease of interest, including screening, diagnosis, linkage to treatment programmes, adherence to treatment and finally achievement and maintenance of control.

The strengths of the cascade of care analysis include the opportunity to identify where in the continuum of care the areas where there is unmet need and where the greatest losses

occur. The cascade approach depicts the product of the interaction and dynamics between health system responses and demand at each step of the care continuum – in effect, showing the process by which inputs translate to outputs and outcomes, and where attrition in care occurs. This in turn can help to facilitate effective, evidence-based targeting of programmes and policies to address the demonstrated gaps. In addition, cascades can be used to monitor responses to new interventions, programmes or policies, assess progress toward achieving public health goals and to share best practices (and challenges) among policy makers and providers.

The cascade of care approach is being applied in understanding better management of chronic non-communicable diseases such as diabetes, by using administrative or survey data. For example, in one study in the United States, data from the National Health and Nutrition Examination Survey (NHANES) from 2007 to 2012 was used to construct a diabetes cascade of care for the US to show that nearly one third of patients with diabetes were unaware of their diagnosis and that those who remained undiagnosed were less likely to achieve health targets for multiple chronic diseases.[216]

We used the cascade of care approach, drawing on population-based surveys in selected SSA countries that included diabetes to assess the care for diabetes and the extent of disease control. The cascades were constructed based on individual-level data from 10 surveys in 10 countries in SSA countries that were conducted between 2005 and 2013. The World Health Organization's STEPS Survey was available for 8 countries. The STEPS Survey is a standardised approach to collecting data about NCDs among adults aged 25-64 years in WHO member countries (Appendix). In brief, the STEPS Surveys include collection of demographic data (STEP 1), physical measurements such as blood pressure and BMI (STEP 2) as well as biochemical measurements, including fasting plasma glucose (STEP 3).[217,218] Further details about the STEPS instrument are provided elsewhere.[4] Given that a standardised approach is used across all countries, data from the STEPS Surveys can be used to compare epidemiology and health system performance across countries. STEPS Survey data were available for the following countries: Benin, Comoros, Guinea, Liberia, Mozambique, Seychelles, Tanzania and Togo.

We supplemented the data from the eight STEPS with information from the Demographic and Health Survey for Namibia (2013), which as with STEPS surveys includes both fasting plasma glucose measurement and self-reported data on access to diagnosis and treatment for diabetes.[219] For South Africa, we utilized the South Africa Nutrition and Health Examination Survey (SANHANES), a nationally representative cross-sectional health and nutrition study that was led by the South African Human Sciences Research Council.[220] Together, the STEPS, DHS and SANHANES surveys represented 39,062 individuals across 10 countries over the period from 2004-2014.

Definitions and constructing the diabetes care cascade

Diabetes was defined based on the current WHO and American Diabetes Association diagnostic criteria as any one of the following: a fasting plasma glucose greater than or

equal to 7.0 mmol/l (126mg/dl); a 2–hour plasma glucose ≥ 11.1mmol/l (200mg/dl) or; a HbA1c measurement ≥ 6.5%.[221] This definition represents the current gold-standard clinical practice guidelines that are being used internationally. Those reporting use of medication for diabetes were also classified as diabetic irrespective of the biomarker values. Respondents who self-reported a diagnosis of diabetes but were not on medication and lacked the criteria indicated above were not classified as diabetic. In addition, we quantified met need for four different metrics of diabetes care in the diabetic population: ever receiving a blood glucose measurement as a measure of diagnosis; ever having been told about the diagnosis of diabetes as a measure of awareness of diagnosis; receipt of any advice from a healthcare provider to lose weight or exercise (hereafter "any advice') and use of either oral medications or insulin, for treating diabetes (hereafter "any medication").

Using these metrics, we constructed a diabetes care cascade for each of the 10 countries. This cascade, created using individual data, shows the percent of the total diabetic population that self-reported reaching each subsequent step in the care process, conditional on having reached the previous step. The first stage in our cascade is ever having had a blood glucose measurement (prior to the STEPS or other Survey on which the diagnosis was made) as an indicator of having had an appropriate diagnostic test for diabetes. Second, among those who had received this test, we then quantified the percentage of all diabetic patients who had been informed about their diabetes diagnosis by any healthcare provider as a measure of awareness of diagnosis. Third, among those who had received a diagnostic test and were aware of their diagnosis, we calculated the percentage of the total diabetic population who then received any advice regarding lifestyle modification and finally, among that group, the percentage that had received oral medications or insulin for diabetes control.

The diabetes care cascade by country is displayed in Figure 14. The first step in the cascade is receipt of a diagnostic test, specifically a blood glucose measurement. This initial diagnostic test was associated with the largest loss to care across all countries, with an average of 40% and ranging from 23% to 81%. (Figure 14)

Figure 14

Second, among the group who self-reported having received glucose measurement, the cascade shows that on average 18% of the total diabetic population was then lost to follow-up at the stage of being told about their diagnosis by a healthcare provider, with a range of 0% to 26% (Figure 14).

Third, among those who reported completing the first two steps in the cascade, figure 14 shows that an additional 16% of the total diabetic population was lost to care and follow up at the stage of receiving advice on lifestyle modification, with a range of 5% to 15%.

Fourth, a further 2% was lost to care between the stages of receiving advice and receiving any medication treatment (range 3% to 10%), including oral medication or insulin, for

diabetes control. Overall the analysis of the data from the 10 surveys shows that the percentage of the diabetic population who completed the care cascade in different countries averaged 24% with a range of from 9% to 58%. (Figure 14)

The pattern of care cascade by country varied. In Benin, there was a very rapid drop in the first step with 60% of patients with diabetes not having their glucose measured. Thereafter, there was a steady decline with a 14-percentage point decline from patients who were aware of diagnosis to receiving advice. Overall, just 22% of the patients with diabetes received medicines (Figure 15a).

Figure 15a

In Comoros, which had the second best profile of care cascade, there was steady decline at each step with 33% of patients received advice and medication overall. (Figure 15b)

Figure 15b

In Guinea, which has a weak health system and has been affected by the Ebola virus outbreak, there was a sharp drop at the first step as with Benin, with 40% of patients with diabetes having glucose measured. A steady decline after each step therafter meant that overall just 20% of patients received advice and 17% received medication. (Figure 15c)

Figure 15c

The pattern of cascade in Liberia, which also has a weak health system and has been affected by the Ebola virus outbreak, mirrored that in Guinea, but decline at the first step was wach greater. Only 19% of patients with diabetes had their glucose measured and overall the proportion of patients receiving advice and medication was 8%. (Figure 15d)

Figure 15d

In Mozambique, the patttern was similar to that observed in Benin and Guinea, with a sharp drop at the first step in the care cascade by 69% so that only 31% of diabetic patients had their blood glucose measured and a steady attirition in the care cascade meant that 19% of patients received medication. (Figure 15e)

Figure 15e

Namibia had the best profile of diabetes care cascade among the 10 countries studied, with a less sharper decline of 39% at the first step, with 61% of patients with diabetes having their glucose measured. The declines at each step thereafter were less marked such that 39% of patients with diabetes received advice and 36% received medication. (Figure 15f)

Figure 15f

The cascade pattern in Seychelles was different to the rest of the study countries. Seychelles, which has one of the highest prevalence rates of diabetes in SSA (see Section 1 of the report), had by far the biggest proportion of diabetic patients (92%) whose blood glucose levels were measured. However, there was a sharp decline at step two with a fall of 52 percentage points, so that just 40% of patients were aware of their diagnosis and 24% were receiving medication. The findings suggest a well functioning screening programme but a weak health system where there is considerable loss to follow up of patients diagnosed with diabetes. (Figure 15g)

Figure 15g

In South Africa, the pattern of cascade of care mirrored that of Namibia, but the lost to follow-up at each step was greater than that observed in Namibia, so that 29% of patients were able to receive advice and 26% receive medication. (Figure 15h)

Figure 15h

Tanzania had the third best profile after Namibia and Comoros. Following a decline of 50% in the patients at the first step, one half of patients had their glucose measured, and almost all of those receiving a glucose test were aware of their diagnosis (49%). Steady attrition at steps 3 and 4 meant that 34% of patients with diabetes received advice and 29% received medication. (Figure 15i)

Figure 15i

Togo had the least favourable profile, along with Guinea and Liberia, with a sharp drop at the first step, with 29% of patients receiving a test to measure their glucose levels. There was a decline at each step so that just 9% of patients received advice and only 7% received medicines. (Figure 15j)

Figure 15j

The analysis of diabetes care cascade in 10 countries clearly shows the health system challenges faced by countries of SSA in managing diabetes, with unmet need at every step of the care process that leaves the largest proportion of patients with diabetes going undiagnosed. For those diagnosed with diabetes the health systems are not able to provide the service needed, with the majority of the patients with diabetes not receiving advice and the medication they need. Unmet need and suboptimal care means that patients will likely have delayed presentation to the health system and receive advice and medication late in the care process, with adverse effect on health outcomes. Not only do unfavourable health outcomes produce difficulties for patients and their families due to ill health, they also have adverse economic consequences for patients, their families and the economy at large.

We present in the next section our estimates on the economic consequences of diabetes in SSA.

Economic consequences of diabetes in sub-Saharan Africa

Beyond ill health and lowering quality of life substantially, diabetes mellitus imposes a non-negligible financial burden on affected individuals, families and societies. While patients with diabetes face increased direct costs of illness through medical treatment of the disease, its comorbidities and sequelae, they also simultaneously experience income losses through reduced productivity and disability, which in severe cases leads to inability to work.

Economic burden of diabetes to individual patients

Earlier studies in SSA have found that in the early 2000's treatment costs of diabetes for oral medication and insulin for one course (30 days) amounted to wages earned between 1.1 and 8.4 days.[222] These costs did not take into account complications and sequelae or additional medical needed.[223] Other studies have estimated direct cost of diabetes per person per year at $138 in Tanzania in 1989/1990[223], and $489 in Cameroon in 2001[224]. International Diabetes Federation estimates put per person per year expenditures in 2015 in SSA for diabetes at $243-$419.[225]

Given the paucity of data on cost of diabetes in SSA, we undertook a cost of illness study, published elsewhere, to ascertain direct costs of diabetes. We estimated that in 2015, in SSA, overall health expenditure including average direct costs of diabetes and its complications was $264 per person with diabetes, including both those diagnosed and undiagnosed.[226] These estimates relied on a set of assumptions using data from developed countries and are likely to underestimate the costs of diabetic comorbidities and sequelae, given the larger proportion of undiagnosed and untreated cases in low income countries[227] who are more likely to experience potentially costly complications.[228,229] Hence, notwithstanding these limitations we argue that the overall number provides a lower bound of direct treatment costs in developing countries. A summary of the methodology and assumptions is provided in supplementary appendix and a more detailed discussion of the methods and the results is available in Bommer et al.[227]

In SSA out-of-pocket expenditures are estimated to be 50% of overall health expenditures.[230] This proportion is likely to be substantially higher for diabetes, and will often be prohibitive, producing financial barriers to access and leading to many diabetic individuals not seeking care (and thus avoiding short-term treatment costs but potentially accumulating larger health deficits which lead to even higher long-term direct costs through more severe sequelae and in addition to shorter life spans). Co-morbidities

and target organ damage for diabetes will result in many instances in 'catastrophic' or 'impoverishing' healthcare expenditures, shifting many patients and their families beneath the poverty line.[231] Simultaneously, these adverse effects are likely to be perpetuated in absence of adequate social security systems, where families may attempt to offset such catastrophic expenditures by shifting children into workforce, thus effectively bereaving them of any future prospects of financial wellbeing.

Indirect costs of illness on individual level result from productivity losses of diabetic workers during their productive years (as costs of early mortality are not borne by diseased individuals themselves we do not consider this position in this section). These losses can result from absenteeism (sick workers failing to appear for work), presenteeism (unfit workers coming into work where they are unable to perform to full capacity), and employment effects (the decision to drop out of labour force temporarily or permanently).[227]

Panel 2: Labour-market effects of diabetes

A meta-analysis of labour-market effects of diabetes estimates that the drop in labour force participation of diabetic individuals can range between 10.5 to 17.8% for women and 8.9 to 17.8% for men.[227] Male diabetics who are in labour force are found to be absent from work for 1.7 to 14.2 additional days due to diabetes, whereas absenteeism due to diabetes for women is estimated at 1.5 to 2.9 days. Finally, diabetic workers' productivity losses while at work (presenteeism) are found to vary between 4.5 to 5.5% for men and 2.0 to 3.0% for women relative to non-diabetics. The underlying empirical evidence largely draws on data from high-income and upper-middle income countries. Effects on labour market participation are based on studies from the USA[232,233,234,235,236,237], Australia[238,239], Canada[240], Taiwan[241] and Mexico[242], and absenteeism studies from USA[236,243,244], and Slovenia[245], and presenteeism estimates are based on studies from the US[235,237] and Canada[246].

It is hence not known whether these labour market effects accurately capture the situation in SSA. For instance, the lack of job security and the importance of informal work on SSA labor markets may translate in a lower propensity of individuals to be absent from work, thus leading to increased presenteeism. Moreover, the combination of limited capabilities for blood sugar levels management and a shortage of preventive treatment is likely to lead to higher rates of severe complications in the long-run, hence increasing the rate of labour force drop-out.

Furthermore, while in high-income-country productivity losses may be partially or fully offset by social security systems (e.g. continued pay during sick leave, insurance payments in case of permanent disability), in SSA they are likely to fully accrue at the level of sick individuals through foregone wages from formal or informal work as well as reduced agricultural yield in the case of subsistence farmers.

Economic burden of diabetes to countries

In addition to adverse effects to individual wellbeing and socioeconomic conditions, the increasing prevalence of diabetes is creating a considerable economic burden to health systems worldwide. The economic burden of diabetes in SSA is also thought to be large, though no recent estimates are available.

A recent study by Bommer et al., analysed direct health expenditure and indirect costs of diabetes caused by premature mortality and disability, to estimate the global economic burden in 2015 to be 1.7% of world GDP. [227]

Based on the same approach and using prevalence, mortality and direct health expenditure estimates from the 7th edition of the IDF Diabetes Atlas[247] for 45 SSA economies, as well as national account data from the World Development Indicators database[248], we estimated the overall costs of diabetes in 2015 for SSA to be $16.49 billion or 0.80% of cumulative GDP of the whole of SSA.

Around $11.04 billion of the $16.49 billion (66.97%) was in Southern Africa, mainly driven by the relatively wealthy South Africa, which contributes the largest share to the overall economic burden is SSA, and $2.57 billion (15.58%) in Eastern Africa (Figure 16). Around 76% of this burden ($11.54 billion) arose from indirect costs (Figure 16).

Figure 16

Direct costs were estimated based on countries' per capita health expenditure assuming a fixed ratio between the age- and sex-specific treatment costs treatment costs for diabetic and non-diabetic individuals.[246,249] Indirect costs were defined as productivity losses due to mortality or disability, as measured by forgone labour earnings. As the wage data from SSA countries are scarce, labour earnings were proxied by the labour income share in GDP per working age person as measured in 2015 US$. A more detailed discussion of the methodology, including necessary data imputations, is provided in Bommer et al. [227]

Productivity losses consisted of four components: (i) premature mortality (which amounted for 74.68% of total indirect costs), as dead individuals are permanently unavailable to the labour market (ii) diabetes-related complications and malaise, which make diabetic patients less likely to participate in the work force ("drop out" accounting for 16.60% of total indirect costs (iii) more likely to take sick leave ("absenteeism", accounting for 2.77%) and (iv) decrease their productivity while working ("presenteeism", which amounted to 6.13%) (Figure 17).

Figure 17

An important question for health systems and governments in SSA is how the economic costs of diabetes are going to evolve in the short- and medium-term.

To investigate this important question, we used five-yearly United Nations Population Prospects data for the years 2015 – 2030 (using the medium variant provided by the UN Population Division as well as projected urbanization rates projected by the UN[250,251] when estimating our projections of economic cost. Our projected economic costs also take into consideration real GDP and GDP per capita growth, the projected change in the demographic composition, future population size as well as urbanization (as an urban sedentary lifestyle is considered an important risk factor for diabetes).[252] The main scenario we present further assumes that age- and sex-specific mortality and diabetes prevalence would grow at a rate of 5% per year, as increases in wealth may further amplify the adoption of Western consumption patterns.

Our estimates suggest that the economic costs are projected to increase from $16.49 billion in 2015 to $52.35 billion (in 2015 prices) (Figure 18). Using an alternative scenario, which is more optimistic and assumes that future changes in lifestyle are already accounted for by urbanization, suggests that the economic costs will increase from $16.49 billion in 2015 to $25.44 billion in 2030 (using the medium variant provided by the UN) (Figure 18). The presented 95% confidence intervals (blue and green dashed lines) reflect uncertainties in prevalence and mortality estimates as well as labour market effects.

Based on the main scenario projections, the economic burden in 2030 is forecasted to reach 4.60% of GDP in Southern Africa, 1.34% in Eastern Africa, 0.87% in Middle Africa and 0.25% in Western Africa (Figure 19).

Figure 19

The high economic burden SSA is predicated to face and the high indirect costs create a strong incentive for policy makers to increase efforts to reduce diabetes-related complications and premature mortality. But, as the analysis of this report shows health systems in sub-Saharan countries are not prepared to effectively manage diabetes, the current health systems response is weak, the care provided suboptimal and the unmet need very large.

If diabetes is effectively managed, the health and economic burden it brings could be substantially reduced. We explore in the next section the benefits that might be realised if diabetes in SSA were to be managed according to international guidelines and evidence.

Benefits of scaling up diabetes interventions in sub-Saharan Africa

Effective treatment of diabetes in rapidly developing countries is likely to require complex considerations on expansion of services for early diagnosis and for those diagnosed how to dispense the best available treatments to the maximum number of patients who could benefit from therapy, all within tight cost constraints.

Among people with diabetes, high blood pressure, disordered lipid profiles and poor glycaemic control constitute the three principal co-existing risk factors for morbidity and mortality, and the aim of diabetes treatment is to prevent their long-term complications.

Comparing Benefit-Based Treatment with Treat to Target Strategies in an African context

In SSA patients with diabetes experience unmet need at every step of the care process, with the result that the majority of patients are undiagnosed, and a large proportion of those diagnosed receive sub optimal treatment and care. In addition to the adverse health consequences, diabetes leads to economic burden for individuals, families and the economy. Prevention, early diagnosis and effective treatment of diabetes could help to alleviate the burden on health and the economy.

In treating diabetes, while all three risk factors impact on both large- and small-vessel complications, there are substantial differences in their relative impact, in the complexity of their treatment and monitoring regimens, in their therapeutic window, and in the costs of therapy. There are important interactions between the risk factors for both the large vessel (coronary heart disease, stroke) and small vessel (retinal, renal, neuropathic) complications of diabetes,[253,254,255] with treatment guidelines emphasizing the importance of addressing all three[256].

For both blood pressure and lipid therapies, there has been a move towards targeting treatment to individuals at higher levels of risk, rather than according to levels of blood pressure or lipids[257,258,259], under the understanding that different individuals may experience different benefits and risks from therapy depending on their co-morbid conditions. For example, people with previous myocardial infarction or stroke may benefit from being initiated on treatment at lower levels of blood pressure or LDL-cholesterol than others. T in both high income and middle income settings, the risk-based approach to treating blood pressure, termed benefit-based, tailored treatment (BTT), has been shown to be more effective and less costly, than treating blood pressure to target levels (a treat-to-target (TTT) strategy).[257,260,261]

The question remains whether a BTT approach or a TTT approach would overall be beneficial to people with diabetes in SSA for overall diabetes risk factor management.

We constructed a microsimulation model to compare the approaches to reducing the risk of major macrovascular (myocardial infarction, stroke) and microvascular (neuropathy, retinopathy, and end-stage renal disease) complications of diabetes among two populations aged 30-70 years old in SSA, from Malawi (*N*=35,730), "participating in the Karonga Prevention Study[262] and from Ghanaian plus South African datasets (N=3,938 and 2,352 respectively),[263] representing the spectrum for SSA.

Two alternative management approaches were compared. The first was a "treat to target" (TTT) strategy involving titration of blood pressure treatment agents, statins and glucose lowering drugs to predefined targets. The second was a "benefit-based tailored" (BTT) treatment strategy, which comprised treating individuals at high macro-vascular risk with blood pressure treatment agents and statins, and those at high micro-vascular risk with glucose lowering agents, until they achieved low risk levels. Thus treat to target involved treating individuals with blood pressure treatment agents until they achieved a blood pressure <130/80 mmHg[256]; with a statin to a low-density lipoprotein <2.59 mmol/L (100 mg/dL)[264]; and with metformin, sulfonylureas and, if needed, substituting the sulfonylurea with insulin, until they achieve a hemoglobin A1c <7%[265].

The benefit tailored treatment strategy involved treating individuals with a 10-year combined risk of myocardial infarction (MI) and stroke >10% with antihypertensive agents and a statin until their risk lowered below the 10% threshold (provided blood pressure remained >110/55 mmHg for safety), and for those with a *lifetime* risk of the three major micro-vascular outcomes (blindness, end-stage renal disease, and amputation secondary to neuropathic ulcer) of >4%, treating elevated glucose with metformin, sulfonylureas and, if needed, substituting the sulfonylurea with insulin until lifetime micro-vascular risk was below 4% (provided fasting blood glucose remained >3.33 mmol/L [60 mg/dL], for safety).

We employed WHO guidelines for blood pressure medication and statin medication choice,[256] and the Yale Diabetes Center Guidelines for dose escalation algorithms for metformin, sulfonylurea and insulin.[266] Cases averted, disability-adjusted life-years saved (based on disability weight values estimated by the Global Burden of Disease Project),[267] and drug costs for therapy (based on per-unit global buyer cost estimates from the International Drug Price Indicator Guide)[268] were integrated over the simulated life-course of all persons with diabetes who were alive, or born, during the next 10 years, per standard cost-effectiveness guidelines[269]. DALYs and costs were discounted at a 3% annual rate, and costs were expressed in 2016 U.S. Dollars.

We found that a BTT strategy was more effective, and cost-effective, than a TTT strategy from a population perspective (Table 8). Although a similar fraction of people with diabetes were typically recommended treatment of any kind (a mean of 86% under TTT

versus 88% under BTT in Malawi; see Table 8), those typically treated with the BTT strategy were treated more intensively (4.5 versus 3.5 medications per person, respectively).

As shown in Table 8, the BTT strategy would recommend more adults with diabetes to receive blood pressure lowering agents to a significant extent, and increase to a non-significant extent the number treated with statins and glucose lowering agents, as compared to TTT. Correspondingly, the BTT strategy was estimated to avert two to four times as many macro-vascular events (MIs and strokes), but did not significantly differ from the TTT strategy in the number of micro-vascular events prevented.

Using the TTT strategy the estimated total drug costs in 2016 would be $1,346.6 million (CI: 471.1- 2,206.7 million). With the BTT strategy, the total drug costs would be higher at $1,407.9 million (CI: 464.7 - 2,332.5 million). In terms of total DALYs averted, the benefits of BTT were higher, however (Table 8) with BTT leading to saving of 1.9 million DALYs (CI: 0.9 – 3.4 million) and TTT 1.2 million DALYs (CI: 1,161.3 (0.6 - 2.1 million).

With BTT, the average costs were between $137.5 and $2,600.2 per DALY averted (Mean $743.4) versus $227.6 to $4,047.5 per DALY averted (Mean $1,159.5) for the TTT strategy (Table 8).

The results show substantial benefits of effective scale up of diabetes services to address unmet need. The question remains on the ability of countries to strengthen health systems to respond to the needs. There are encouraging examples of successful models of diabetes care emerging in low-income countries and in SSA. In the next section we explore these models and provide country case examples of innovative approaches introduced in the SSA context for effectively managing diabetes to illustrate what might be possible in the future.

New and established service delivery models for managing diabetes mellitus in sub-Saharan Africa

The environmental and genetic determinants of diabetes and its care exhibit great variation in SSA. Yet, diabetes has been studied in much less detail in SSA countries than other parts of the world. Most studies on diabetes originate from Western countries where international guidelines for management of diabetes typically originate. Few studies exist on innovative and country responses that have helped to manage diabetes mellitus, and the barriers to its effective management.

We undertook a systematic review to examine current approaches to diabetes care in SSA (See supplementary appendix for methods and study design). In addition, we reviewed briefly current practices in eight countries (Botswana, Ethiopia, Kenya, Malawi, Mali, Rwanda, Senegal and South Africa) and undertook detailed country studies in Ghana and Tanzania, using a proprietary tool (SYSRA)[270], which has been used previously for tuberculosis[271], HIV[272,273], malaria[274], mental illness[275] programmes in a number of settings, including several African countries[276], and was adapted for diabetes to enable rapid and simultaneous assessment of the health system and the diabetes program. We also assessed new technologies that are currently in use for health and could be used to improve diabetes care. We describe below our findings: first the results of the review, second the brief case studies, third the detailed cases on Ghana and Tanzania, and fourth technological innovations.

The review identified 467 studies, of which 32 from 11 different countries (Cameroon, Eritrea, Ethiopia, Ghana, Kenya, Malawi, Mozambique, South Africa, Sudan, Tanzania and Uganda) met inclusion criteria (Supplementary appendix).

In many countries of SSA diabetes care is still largely available only in hospital setting, requiring patients to travel great distances to access services and follow-up care which is important for effective diabetes management. As a result several countries in SSA have introduced new care delivery models for managing diabetes care at primary health care, community or home setting.

Cameroon and Tanzania, have attempted to introduce community-based management of diabetes.[277] In Ethiopia, physicians and diabetes-trained nurses have travelled from hospitals to peripheral medical centers for training and care provision with early encouraging results in improving access to services.[278,279] In Cameroon, facility-based interventions for high blood pressure and diabetes with task shifting and nurse-led care in rural health districts significantly improved retention levels for management of patients.[280] Similarly, in Kenya, it was possible to devolve management of high blood pressure ad diabetes to rural primary health care clinics with good retention rates and control.[281]

In South Africa, a chronic disease outreach programme in the public sector, which used primary health care nurses to provide educational and follow up advice to patients with diabetes, improved early detection and referral of high risk, poorly controlled patients to specialist centres.[282] Decentralisation of diabetes management to community level was also successful in the private sector in South Africa with a community-based capitation and risk-sharing model for diabetes management, where the care of diabetes was transferred to primary care physicians working in community-based facilities affiliated with a diabetes and endocrinology centre. The scheme led to major reductions in hospital admission rates for both acute metabolic emergencies and all causes, reduced costs, delayed progression of micro-vascular complications, and improved outcomes.[283] Nurse-led diabetes care, with nurse-led protocol and education-based system, was also shown to be successful in rural Kwazulu Natal in South Africa with improved control of HbA1c levels, and higher satisfaction for patients, their families and health workers[284], but the improvements in glycaemic control achieved at 18 months following the introduction of the scheme were not sustained at 48 months, although the HbA1c levels at 48 months were lower than baseline figures[285]. As with South Africa, introduction of protocol-driven nurse-led management of diabetes in primary care setting in rural and urban Cameroon also led to improvements in glycaemic control and blood pressure.[286]

Community health worker (CHW) model of outpatient care was introduced in one study in South Africa for diabetes and hypertension that involved monthly home visits, counseling services, and access to monthly supplies of medication. While the CHW model improved hypertension control, the same was not true for diabetes care however, with 26% of the patients at the clinic showing improved diabetic care in comparison to 9% of the CHW-targeted home visit patients.[287] In Cameroon, integration of care for high blood pressure and type 2 diabetes was effectively achieved in eight rural health districts by task shifting to non-physician clinician facilities, with improved control in patients attending services.[288] In Cameroon, a pilot study which trained traditional healers in health promotion for diabetes and referral for glucose testing showed effective collaboration of traditional healers with the diabetes programme to improve referral rates.[289]

Home glucose monitoring has also been introduced in SSA. For example, in South Africa home glucose monitoring using urine testing has been introduced even to illiterate patients with good compliance and lower random glucose levels compared to non-compliers.[290] In Kenya, a home glucose-monitoring programme that used mobile phones to enable CHWs to regularly communicate to patients to modify the dose of insulin injections helped to improve HbA1c levels.[291]

Patient education has also been used in several settings to improve services across the care continuum and to decentralise care away from hospitals to patient level. For example, in Cameroon, motivational counseling and education was integrated into a screening program to improve rates of follow-up for newly diagnosed individuals.[292] In South Africa group education was used at community health centers to improve patient's

knowledge and management of diabetes, but there was no improvement in diabetes self-care activities, weight loss, HbA1c levels and quality of life, or improvements in self-efficacy, locus of control, mean blood pressure, mean weight loss, mean waist circumference, and mean total cholesterol levels.[293] Another study from South Africa showed that group education programme for patients with Type 2 Diabetes could be implemented in rural areas with a dietician or health promoter to provide a supportive environment for patients for learning and coping with significant improvement in adherence to a diabetic diet, physical activity, foot care and the perceived ability to teach others, but no significant change in smoking or adherence to medication.[294] In Tanzania, a hospital-based education programme for children with Type 1 Diabetes on symptom management, correct insulin storage and insulin administration led to reduction in severe hypoglycaemia, but no improvement in HbA1c levels.[295] In Mozambique, twinning programmes have been used to successfully establish patient education programmes and to improve their effectiveness.[296]

In addition to patient education, health-provider education at hospital, primary health care and community-level has been used to improve early recognition of diabetes and diabetic sequelae, and to enhance disease management in SSA. In Tanzania, where 70% of leg amputations occur in diabetic patients, training of healthcare personnel at different levels and centres in diabetic foot management has led to improved case finding, earlier referrals, establishment of well-functioning foot clinics, and strengthened management of diabetic foot ulcers with better health outcomes.[297] In Eritrea, a co-operative diabetes project, which emphasised multidisciplinary training of physicians, laboratory scientists, diabetes nurse practitioners, patient educators, and dieticians and improved quality of laboratory services, led to improved management of diabetes with better HbA1c levels.[298] Multidisciplinary training for diabetes, involving physicians, dietitians and nurse educators and pharmacists has also been introduced in Ghana to strengthen diabetes services[299], while raining of patient educators has been introduced in Sudan[300].

Development of new models of diabetes care and attempts to transition in some countries of SSA to primary care, community- and home-based management of diabetes has been facilitated by the availability of electronic medical records (sometimes building on existing systems for HIV)[301], and the use of treatment protocols and guidelines, which have helped to improve the consistency and quality of diabetes care[302].

Some countries such as Malawi have successfully used existing service delivery platforms and expertise for management of tuberculosis, which is associated with diabetes and has well-established care models, based on directly observed therapy, as well as structured monitoring and reporting mechanisms.[303] Others, such as South Africa, have successfully used mobile units for HIV counselling and testing as an entry point for screening for NCDs (high blood pressure and diabetes) with high yield of new case, but linkage to care and follow up was noted to be a challenge.[304] Similarly, in Uganda, community-based HIV testing campaigns were used to offer offering diagnostic, preventive, treatment and referral services for HIV, malaria, TB, hypertension and diabetes, with the identification

of high burden of HIV, high blood pressure and diabetes with effective linkage to care.[305] In Kenya, HIV counsellors were trained to screen for diabetes and high blood pressure in home-based screening and local district hospital based staff conducting community-based screening, with effective uptake and results for both approaches, but in both groups there was low levels of follow-up with only around one fifth of patients returning after a random glucose test. [306]

African experience of diabetes management suggests a particular distinctiveness with strong reliance on non-physician health workforce including nurses, community health workers, and health extension workers, as well as traditional healers in some settings. Several countries, such as Botswana, Ghana, Ethiopia, Kenya, Malawi, Mali, Rwanda, Tanzania and South Africa included in the study, have introduced innovative approaches to address resource constraints when managing diabetes (Panels 3- 10).

Panel 2: Botswana country case study

Botswana, a country of 2.2 million people, which has introduced a highly successful response to the HIV epidemic in SSA, provides diabetes care largely through the public sector (see supplementary appendix – Botswana case). In 2015, the prevalence of diabetes was estimated to be 4.0% in adults aged 20-79 years.[307] Specialist human resources for diabetes are few in the country, with one adult endocrinologist (in the private sector), two paediatric endocrinologists (in the public sector), and two nurses with full training in diabetes education and care (one each in private and public sectors).

In Botswana, patients with diabetes have access to general nursing, psychology, and social work services both in the private and public sector. In addition, among the community health care workers six diabetes youth leaders, who are fully trained in diabetes peer education, provide diabetes education and public health screening campaigns, and are involved in running diabetes youth camps.

Insulin treatment and oral hypoglycaemic drugs metformin and glibenclamide are available to all citizens free of charge. Patients can receive diabetes care in local clinic or a healthcare facility that are typically available within 5 km of households, and can have blood and urine tests for diabetes (free of charge), which are analysed in a local laboratory in the tertiary centres (with capacity to test for HbA_{1c}, urea and electrolytes, blood glucose, full blood count, blood gas, thyroid function, insulin concentration, and C-peptide. Tests such as urine microalbumin, coeliac screen, insulin autoantibodies, intracytoplasmic autoantibody, and glutamic acid decarboxylase antibody are outsourced to South Africa). In addition, clinics and health facilities provide blood glucose test strips to all patients with diabetes free of charge.

Diabetic patients with complex co-morbidities and children with diabetes are managed by specialists in the tertiary facilities located in major urban centres—for example, the Paediatric Endocrinology Clinic in Princess Marina Referral Hospital in Gaborone. Similarly, yearly ophthalmology examinations with specialised cameras are available in

tertiary centres. The Diabetes Association of Botswana has 100 members and is involved in diabetes education, care and support.[308]

Panel 3: Ghana country case study

Ghana has a population of approximately 26.3 million people.[309] The prevalence of diabetes in 2015 was estimated to be 1.9% in the adult population aged 20-79 years[310], but an estimated 70% of diabetics in Ghana are currently unaware of their condition.[311] The National Health Insurance Scheme (NHIS) covers 38% of the population and covers maternal and child-health services as well as curative services, but not preventative services or medical equipment, including for NCDs or diabetes such as prosthetic limbs.[312]

The national NCD Control Programme, which was established in 1992, coordinates inter-sectoral response in partnership with other agencies in the health sector for NCDs and diabetes to promote lifestyle changes and early disease detection.[313] Curative facilities for diabetes treatment are available in urban areas, but despite the planned expansion of diabetes services in the 2014 Non-Communicable Disease Strategic Plan, the majority of the urban population and the rural populations remain without access to diabetes diagnostic or follow-up care.

The lack of clinic access, screening equipment, and health workers who understand how to diagnose and treat diabetes remain particularly apparent in rural areas where infrastructure is weak.[314] While selected medical treatments, including two-monthly insulin refills, are paid for by the NHIS for those covered by the scheme, patients still face difficulties in following treatment guidelines and accessing pharmacies, but face financial barriers as in hospitals ad health centres they are of ten charged for tests and examination, as well as for prosthetic limbs. Patients without NHIS coverage face encounter further financial barriers to treatment.[315]

Panel 4: Ethiopia country case study

Ethiopia, the second most populous country in SSA with a population of around 97.0 million people, has experienced strong economic growth in 2005-2014 of average 10% rise in GDP each year, with rapid urbanisation and nutritional transition to energy rich foods and beverages.[316]

Ethiopia has effectively used this economic growth and overseas development assistance for health to increase per person health expenditure from $16.1 in 2007/08 to $25.0 in 2013. The Five Year Health Sector Transformation Plan 2015-2020 has set the goal of expanding community-based health insurance from 1% in 2015 to 50% in 2020.[317] The prevalence of diabetes in Ethiopia was estimated by International Diabetes Federation to be 2.9% in the adults aged 20-79 years, with an estimated 1.33 million deaths.[318]

Diabetes services are delivered mainly at primary health care centres. Specialised clinics located in the major university teaching hospitals also provide diabetes care either by endocrinologists or by general internists who have received short-term training in

diabetes management. One teaching hospital in Addis Ababa employs the only five endocrinologists in the country. Nurses, health officers and general practitioners provide most of the diabetes care in health centres and general hospitals. There are plans to extend the role of urban health extension workers to provide prevention and education services for diabetes. In 2014 with an estimated six out of 10 health facilities, excluding health posts.[319] However, the majority of patients with diabetes are undiagnosed. A cross-sectional population-based survey in northwest Ethiopia, which estimated the prevalence of diabetes mellitus among adults aged 35 years and older to be 5·1% for urban dwellers and 2·1% for rural dwellers, showed that 69% of the cases diagnosed with diabetes during the survey had not been previously diagnosed.[320] The Ethiopian Diabetes Association which has more than 20 000 members undertakes advocacy activities, andeducation for healthcare professionals and for people with diabetes.

Panel 5: Kenya country case study

In Kenya, the prevalence of diabetes was estimated to be 3.6% in the adult population aged 20-79 years, with almost 60% of cases undiagnosed.[321] Diabetes services at community and primary care levels are hampered by inconsistent availability of drugs, equipment and testing for HbA_{1c}. Consequently, patients are often referred to hospitals.[322] High costs and out-of pocket expenditures impede access to drugs for diabetes.[323]

Following the launch of the national diabetes strategy in 2010 Kenya began to expand health system capacity for managing diabetes, with training of healthcare professionals and community health workers, developing national guidelines, and expanding diabetes screening.[324] In particular there is an emphasis in increasing the number of community health workers and training them in the management of diabetes to enhance access to diabetes services.[325]

Panel 6: Malawi country case study

Malawi, which has a population of 16 million, is one of the poorest countries in SSA, and around a 65% of the Malawian population lives below the poverty threshold of less than US$1 a day. The prevalence of diabetes in Malawi was estimated by the International Diabetes Federation to be 2.7% in the adult population aged 20-79 years in 2015.[326] However, an earlier study, which used the STEPS survey data from 2009, estimated the prevalence of diabetes (prevalence of raised fasting blood glucose or currently on medication for diabetes) to be 5.6%.[327] One study of clinic attenders in the country's teaching hospital showed that 75% of the patients had poorly HbA1c levels >7.5%, 50% had systolic blood pressure >140mmHg, 34.7% had nephropathy, 34.7% had retinopathy, and 46.4% had neuropathy.[328] Other studies have shown care to sub-optimal due to resource constraints.[329]

Malawi has low levels of health human resources with two doctors and 38 nurses per 100 000 population. There is one endocrinologist in the country. However, in spite of the resource constraints, Malawi has introduced successful programmes for HIV,

tuberculosis and malaria to reach the MDG 4 target of halving child mortality. It has also incorporated management of high blood pressure and diabetes in its essential health package with evidence-based national guidelines and standards of care that is being introduced in primary health care centres with services provided predominantly by nurses.

Malawi is piloting the WHO package of essential noncommunicable disease interventions for primary health care in low-resource settings and has started a programme to train 1000 health workers by 2016. However, low numbers of health workforce and other resource shortages mean that patients with diabetes are under diagnosed and when diagnosed not well controlled with high levels of complications.[330] To overcome resource constraints and to improve consistency of diabetes care provided Malawi has introduced new service delivery models by using DOTS approach used in tuberculosis care to manage diabetes[331], as well as home-based care and peer-support successfully used in the management of HIV in Malawi[332].

Panel 7: Mali country case study

Mali is the biggest country in western Africa with a population of 17.3 million, where around 45·6% of the population lives below the poverty threshold of US$1·25 per day. The prevalence of diabetes in 2015 was estimated to be 1.8% in the adult population aged 20-79 years.[333]

In Mali, effective management of diabetes has been hampered by resource constraints: there are only two diabetes specialists located in the national hospitals in the capital, Bamako; there is a shortage of human resources, medicines and equipment (such as blood glucose meters and test strips), leading to delayed diagnosis, suboptimal treatment and limited monitoring. To overcome these challenges Mali has introduced a national strategy to manage NCDs, with a training programme for diabetes to train 500 health-care professionals in 2015, establish 30 diabetes consultation sites, improve procurement and strengthen supply chain management to increase availability of insulin, other anti-diabetic medicines, and equipment, and to prevent stock outs.[334]

Panel 8: Rwanda country case study

Rwanda has a population of 10.5 million people[335]. It has a per capita income of $718.0, and 39.1% of population live below the national poverty line[336]. Rwanda has substantially improved social and economic conditions and the health system since the genocide against the Tutsi population in 1994, with rapid declines in maternal and child mortality.

In 2004, Government of Rwanda introduced a public health insurance program, “Mutuelle de Sante.” Patients covered by insurance pay 10% for healthcare services. The ovrnment and development partners meet the cost of the insurance premia and the 10% of co-pay for the poorest 25% of the population. More than 90% of the population is covered by public or private health insurance.[337] The health system is underpinned by strong community and primary health care that includes 45,000 community health

workers working at village level, 400 health posts and 491 health centres staffed by nurses, providing population access to health centres under one hour.[338]

Estimates from the Rwanda STEPS survey in 2012-13 suggest that around 16.1% of the adult population was overweight and 2.7% was obese.[339] NCDs are a priority in Rwanda's national development plans, including in Vision 2020, 2013-2018 Economic Development Poverty Reduction Strategy, Health Sector Strategy III, Non-Communicable Disease National Policy, and NCD Strategic Plan.[340] Rwanda is introducing clinical NCD services and care package across all health facilities, which are equipped with, glucose meters, ophthalmoscopes, sphygmomanometers and urine strips, and 'NCD clinic model' in district hospitals and health centers, but faces a shortage of health professionals[341]. To effectively use existing health staff, Rwanda has introduced pre-service and in-service training for management of NCDs, including for diabetes and associated risk factors. In order to expand health workforce, Rwanda has created a new cadre of health professionals – Home Based Care Practitioners – who are working at community level to provide home-based services for diabetes and other NCDs. The NCD package has made possible to implement screening and early diagnosis at health clinics, annual prevention campaigns and a widespread check-up at the community level.

Rwanda has strengthened its health system to improve diagnosis, care and treatment of diabetes and has explicit plans to develop a national, multisectoral diabetes program to improve response to diabetes. For example in order to expand access to drugs for treating diabetes, oral hypoglycaemic drugs (glibenclamide, metformin) and insulin (Insulin regular, Insulin NPH/lente, Insulin mix 70/30) have been added to Rwanda's List of Essential Medicines, which are covered through health insurances and systematically available through the NCD clinics located at district hospitals.[342]

Improved access to diagnostic and treatment services in Rwanda has meant that the number of people living with diabetes and requiring close follow-up has increased[343,344] with a commensurate rise in demand for health services. To effectively manage the increasing demand and Rwanda has started a programme of task shifting to transition chronic disease management to home setting. The task shifting involves careful transitioning of services provided by a degree-holding professional at health facility level to a vocationally-trained professional in the community, and has the additional benefit of lowering access barriers by reducing the need for travel and long waits at health facilities

Rwanda's progress in improving diagnosis, treatment and care of diabetes has been made possible through joint efforts of public institutions and civil society. In collaboration with the ministry of health, the Rwanda Diabetes Association contributes to partners' integrated efforts to assist the public sector with advocacy for diabetes inclusion in policy development, strategic planning, and treatment, while also offering financial and psychosocial patient assistance.[345] As diabetes has been integrated into the public health system, local organizations have helped to track the number of patients with diabetes in the community. The number of young people aged 25-years or less with

diabetes supported by Rwanda Diabetes Association rose 30-fold in the last 10 years, to reach from 33 in 2005 to more than 900 in 20105.[346]

Panel 9: Tanzania country case study

Tanzania has a population of 33.9 million, with a growth rate of 3.2% each year, with children under 15 constituting 44.1%. Around 46.6% of Tanzania's population still lives in poverty with limited access to water, sanitation and electricity.[347]

Tanzania has a decentralized health system with three functional levels. District level provides primary health care services through dispensaries, health centres and district hospitals. Regional Hospitals, with more specialized services, serve as a referral point for District Hospitals. Highly specialized care is provided at Referral/Specialized Hospitals. There is a mix of public, faith based, private for-profit and private not-for-profit providers.

Health expenditure accounts for 7.3% of GDP, and amounts to $49 per person per year. Around 33.2% of health expenditures are externally funded through the Health Basket Fund, 36.3% from public sources and the rest from private out-of-pocket pay.[348]
Tanzania has a National Action Plan for the Prevention and Control of Non-Communicable Diseases 2013- 2020 as a response to the findings of the 2012 STEPS survey, which showed increased prevalence of NCDs, especially diabetes and high blood pressure. The Ministry of Health and Social Welfare has established an NCD Unit to implement the Action Plan by strengthening leadership and policies for NCDs, building capacity, integrating services, and improving monitoring and evaluation.

The National Diabetes Program in Tanzania was established in 2011 as collaboration between the Ministry of Health and Social Welfare and the Tanzania Diabetes Association – the implementing agency for the Program – in partnership with the Association of Private Health Facilities in Tanzania to expand access. The Program in has three major goals: (i) o strengthen existing diabetes clinics and establish new ones especially at district and regional levels (ii) to train healthcare personnel at all levels of care and management of people with diabetes and strengthen referral systems, and (iii) carry out community outreach to create awareness on diabetes and encourage lifestyle changes.

Tanzania Diabetes Association, which received funding from international NGOs and private sector firms, has used existing government facilities and staff (who are salaried government employees) to establish 148 diabetes clinics in zonal, regional and district hospitals, and provides funding for equipment (e.g. glucometers, sphygmomanometers, scales) and training of personnel. No additional staffing or salary bonuses were required to establish the clinics. The Program has funded training of more than 2000 healthcare staff, including nutritionists, nurses, medical officers, assistant medical officers and clinical officers. The network of clinics provides care for around 800,000 people with diabetes in Tanzania. Consultations in facilities, laboratory investigations, and diabetes

drugs are free of charge to patients at the government pharmacies, but availability of medications is tenuous.

In addition to the National Diabetes Program, Tanzania has initiated a National Primary Prevention Program as part of the National School Health Program. The project which runs from 2014 -2017 seeks to promote healthy eating habits and exercise in schools through involvement of students, teachers, parents and food vendors. International private firms and the International Diabetes Federation have provided donations to support treatment and care of children and adolescents, but beginning in 2017 Tanzanian government is expected to finance these medications.

All patient visits are provided free of charge to patients and as the government mandates that diabetes drugs should be given for free to patients, there are no patient fees collected at the district and regional diabetes clinics. All the diabetes medications (with exception of the donated insulin and supplies for type I diabetics) are financed and procured by the government. While the district and regional hospitals can charge patients up to 75% of the cost for most medications, they do not get this revenue for dispensing diabetes drugs, and therefore the financial burden of the diabetes medications is partly shouldered at the district and regional level.

Panel 10: South Africa Case Study

In 2014, South Africa had a population of 54 million – compared to 17.4 million in 1960 – with a total fertility rate of 2.6 and GDP per capita level of $6086.45. Around 65.8% of the population lives in urban areas, 64.8% is aged between 15 and 64 years and 28.5% aged less than 15-years. Average life expectancy at birth has risen from 57-years in 2009 to 62.5 years in 2015, following improved treatment of AIDS.

Diabetes is the seventh most common cause of adult mortality.[349], The estimated national prevalence of type 2 diabetes in people aged 30-years or more is 9%, which leads to an estimated 8,000 new cases of blindness and 2,000 new amputations each year, and accounting for 78,900 years lived with disability.[350] In Cape Town, the prevalence in people aged 55-65 years was 22.7% (CI 16.2- 30.2), and 38.2% (CI 21.1-42) in the 65-74 year age group.[351] There are no reliable data on the prevalence or incidence of type 1 diabetes.

The public sector provides care to about 84% of the population and accounts for 4.2% of GDP with a yearly per capita expenditure of $140, while the private sector consumes 4.3% of national GDP for 16.4% of the population with a yearly per capita expenditure of $1,400. There are 86.5 specialists per 100,000 beneficiaries in the private sector compared to 11.4 in the public sector and a similar shortage exists for general practitioners. The majority of the registered 75 endocrinologists are in the private sector.

A network of National Health laboratories provides services to over 80% of the population for all standard diabetes related investigations. Not all primary care clinics have access to the standard diagnostic equipment, which includes glucometers and

strips, urine protein and glucose strips, sphygmomanometers with different cuff sizes, scale and tape measure for height and weight, monofilaments to screen for peripheral neuropathy, Snellen charts and ophthalmoscopes, and HbA1c test due to budgetary constraints.[352] Retinopathy screening using retinal cameras is limited to tertiary level and at primary level in Cape Town. The essential medicines list includes metformin, sulphonylureas (glibenclamide or glimepramide) and human insulins – regular, 30/70 premix and NPH at all levels of care. Analogue insulins are available at tertiary and quaternary hospitals.[353]

There are two professional diabetes associations: the Society for Endocrinology, Metabolism and Diabetes of South Africa[354], a scientific society, and the Diabetes Educators Society of South Africa, an association of diabetes educators. Diabetes South Africa, an NGO, has provided support to and acted as an advocate for all people with diabetes in South Africa since 1969. It has a national office and 8 branches around the country, which in turn have linkages to over 100 smaller local branches and support.

Harnessing new technologies to improve diabetes care in sub-Saharan Africa

New technologies for global health have helped to accelerate the fight against infectious diseases and maternal and child health. However, technologies currently available for diabetes care were developed for use in resource-rich health systems and not for those in SSA, which have different and distinctive needs. Consequently, in SSA for diabetes care: (i) necessary technologies do not exist – with consequent unmet needs in health systems that require the development of novel healthcare technologies (ii) technology exists but is not accessible – due to cost and health system factors and (iii) accessible technology is not adopted – as a result of factors that hinder the adoption of health technologies that are available and accessible.[355]

The resource-poor health systems in SSA several context-specific challenges: first, there is a substantial shortage of health workforce and expertise, leading to inadequate staffing for diabetes and healthcare services in general, and impeding the establishment of multi-disciplinary teams, which play an important role in successful care models for managing diabetes in resource-rich health systems. Second, most of the health technologies that are necessary to diagnose, monitor and treat diabetes and its complications are not affordable to patients and health systems. Third, access to health services is a major constraint in SSA, as patients often need to travel large distances to reach health centres and when they do access services they cannot afford to pay for healthcare services, medicines and diagnostics – as a result experiencing impoverishing expenditures.[356,357,358,359,360,361]

The development of novel low-cost point of care diagnostics offers the potential to mitigate some of the constraints in delivering effective diabetes care in these issues that has proven particularly promising (Panel 11).

Panel 11: Point of care technologies for diabetes care

New low-cost point-of-care diagnostics services will be critical in diagnosis, treatment and monitoring of diabetes in SSA, in particular the distributive model of care being developed in several countries that rely on PHC and community-based services provided by community health workers, and health extension workers.

Effective early detection of diabetic retinopathy, which may reduce the risk of blindness by 95%, currently requires the availability of both clinical staff with ophthalmological training and costly equipment to carry out eye exams. Both requirements are a major obstacle to care as illustrated by the case of Malawi, a country with around 16.4 million inhabitants who are served by just six ophthalmologists. New technologies are required to manage diabetes complications in such resource-poor settings.

New devices such as the "The Portable Eye Examination Kit (PEEK)" app (http://www.peekvision.org) which uses a smartphone and the hand-held "epiCam" device (http://www.epipole.com/epicam/) which can capture images digitally for store-and forward using a lap-top computer, offer the possibility of screening for diabetic retinopathy by health workers in PHC, community-based services and in remote rural areas. While these devices still rely on expert analysis and interpretation of fundus images, which can be done remotely, distributed screening is possible. In future diagnostic algorithms could be used to remotely analyse and provide automated grading of such images at considerably low cost.

Peripheral neuropathy, another important complication of diabetes, is where there is an urgent need for new diagnostics tools for early detection. The prognosis for diabetic peripheral neuropathy is poor if these are not diagnosed early. However, accurate diagnosis such diabetic neuropathy represents a major challenge, even in the context of resource-rich health systems.[362] The development and adoption of new non-invasive diagnostic devices that enable point-of-care testing and not require specialised training to use, for example SUDOSCAN (http://www.sudoscan.com) and NC-stat DPNCheck (http://www.dpncheck.com), could improve screening and early detection of diabetic peripheral neuropathy in resource poor settings.

In addition to easy to use diagnostic devices for retinopathy and neuropathy, low cost diagnostic devices that enable point-of-care testing of blood glucose, HbA1c, glycosuria and proteinuria and could be for screening, diagnosis, treatment initiation, and monitoring. If applied with mobile telephones or smart phones these diagnostic devices would help to transform prevention, treatment and care of diabetes, which could be used for targeted messaging for prevention[363], communicating test results[364], for self-monitoring of diabetes[365] (that would help improve adherence and reduce the need for follow-up appointments) or to attend clinics when needed[366]. Mobile phones and telephone consultations have been used successfully in resource-

poor settings for effective management of HIV to improve health outcomes[367] and could be readily applied for management of diabetes.

Improving access to existing technologies for better diabetes care in sub-Saharan Africa

In addition to developing new low-cost technologies for diagnosis and management of diabetes, another key challenge is to ensure timely and affordable access to existing cost-effective technologies. These technologies include appropriate forms of insulin commensurate within available budgets[368], and medicines, discussed in detail this report, as well as miniaturised blood glucose sensors, and strips for testing of urinary glucose of protein.

Making the best use of limited resources for expanding access to existing medicines and technologies for diabetes care in SSA will require efforts to improve technology assessment, procurement and supply chain management to achieve greater value for money, better procurement prices and timely delivery of available medicines to avoid interruptions to service delivery and treatment.[369]

Development of ICT infrastructures for health

The Lancet Commission on Technologies for Global Health[355], suggested that strategies for strengthening the role of technology in addressing pressing health needs in resource-poor settings should focus not only on 'health technologies' (such as new therapeutics, diagnostics, and medical devices), but also on 'technologies for health' (that include technologies such as communication and transport used in the broader context of health systems but impact on health).

Information and communication technology (ICT) has a particularly important role to play in improving the management of chronic diseases such as diabetes. While there have been efforts to improve uptake of ICT in health systems in SSA, in particular for HIV and tuberculosis[370], overall, ICT remains underutilised. The current underutilisation of ICT may present an opportunity, as the absence of legacy systems would enable introduction and adoption of up-to-date ICT platforms and solutions that can utilise mobile telephony to enhance access.[371,372,373] Integration of electronic health records and mobile device data presents an important challenge, however.

While electronic health records were typically not designed to facilitate data sharing, mobile data are. New solutions, using 'cloud technologies' offer an important opportunity for readily capturing and integrating real-time data across multiple mobile phones, point of care devices, diagnostics laboratory tests, and electronic health records (Panel 12). Such cloud-based systems, which are being tested in SSA for management of tuberculosis (Panel 12), would provide a step change in creating a disease monitoring system for diabetes, and for the development of more targeted prevention, screening, monitoring and treatment approaches.

Panel 12: Cloud-based health information systems

Cloud-based health information systems offer the possibility of capturing data from multiple sources and devices in real-time and the integration of these data, for monitoring, analysis, and decision support to improve management of diabetes.

One example of the use of cloud-based health information solutions is the expansion in Mozambique of almost 18,000 modules of the Xpert MTB/RIF system through the TBXpert Project, managed by the WHO Global Tuberculosis Programme and the Stop TB Partnership Secretariat.[374]

The Xpert system is an automated, cartridge-based nucleic amplification assay for the detection of tuberculosis and rifampicin resistance from sputum in less than two-hours. The scale-up of this system has been accompanied by the development of a range of cloud-based services that integrate data collected through these devices into online 'data clouds'.[x] Data in the data clouds have been used to produce real-time disease monitoring information at the level of individual patients, populations, geographical regions, as well as at the level of the laboratories and staff responsible for operating these devices. Such data have improved decision support for stakeholders, ranging from individual patients, clinical practitioners and public health officials, involved in the management of tuberculosis.

As a complex disease that is associated with tuberculosis, HIV, high blood pressure, ischaemic heart disease and cancer, diabetes provides an excellent entry point to introduce the use of cloud-based health information systems in SSA to improve the management of NCDs. Such cloud-based systems could help mitigate several barriers to effective diabetes care in SSA. First, data cloud solutions are lower costs and scalable as compared with traditional data storage systems that rely on hard drives or other hardware that require constant electricity supply. Second, there is no need to buy expensive hardware or to service them. Third, by integrating data from multiple devices and sources, cloud-solutions can help manage the complex data needed across multiple facilities, levels and over long periods of time for management of diabetes. Fourth, diabetes in SSA is characterised by its heterogeneity. Pooling patient data in cloud-based health information systems across various settings and levels will enable better understanding of the epidemiology, geographic and population coverage, and the responses to interventions (e.g. based on geography, treatment regimen, as well as genotype and phenotype characteristics), and offer the possibility of developing better targeted policies and intervention approaches for diabetes.

Improving the adoption and diffusion of new health technologies for diabetes care in sub-Saharan Africa

The third challenge that needs to be addressed in relation to technology relates to addressing factors that hinder adoption and diffusion of new technologies. These factors include inadequate definition of the problem being addressed, complexity and scalability of the technology or intervention, resistance from the adoption system (health professionals and service users for example), characteristics of the health system that create rigidity or provide inadequate incentives, and poor appreciation or recognition of the challenge of diabetes in the broader context (among the population and the politicians) so that it is not seen as an urgent and major societal challenge. [375,376,]

Existing and new technologies that can address distinctive needs of populations and health systems in SSA could have substantial and positive impact on health outcomes in these countries. Yet, the availability of new technologies for diabetes care in SSA and the use of existing technologies have been patchy.

Improving management of diabetes and health outcomes will only be possible by investing in R&D and innovation to develop necessary technologies that do not exist, ensuring technologies that exist are accessible, and enabling rapid adoption and diffusion of accessible technologies. However, SSA should not replicate Western models, but develop health systems with innovative delivery models for diabetes that reflect the African context.

As with HIV[377], new models of care delivery are emerging for management of diabetes in SSA, with distinctive features that uses a public health approach with simplification and decentralisation, strong reliance on non-physician health workforce including nurses, community health workers and health extension workers, community involvement, peer support and, self-management strategies, underpinned by efforts aimed at strengthening health systems.

Elements of a successful response to diabetes in *in sub-Saharan Africa*

The Commission findings reveal rapidly rising prevalence of overweight and obesity, type 2 diabetes, and gestational diabetes in SSA. Little is known about the prevalence of type 1 diabetes. In SSA the interaction of diabetes with infectious diseases, further increase the burden of illness on resource constrained weak health systems.

Our analysis has shown that health systems in SSA are unprepared for managing the current burden of diabetes and the impending epidemic. As a result, many people go undiagnosed, those that are diagnosed are not screened for comorbidities, do not receive treatment, or are not adequately controlled. The resultant morbidity and mortality is therefore high, with very large human, economic and societal consequences.

Whilst some countries in SSA achieved good progress towards health-related-MDGs (often enabled by donor funded vertical programs) health expenditures from domestic sources remain low. Apart from notable exceptions (for example Tanzania and Ethiopia), few countries have actionable plans to manage the complexities of caring for diabetes and NCDs. In-country data systems are too weak to allow reliable estimates of prevalence of diabetes and related comorbidities, creating further challenges for health system planning.

Disease-specific initiatives are generally launched on the presumption that the condition in question is a clearly defined entity with well-established therapeutic rules for its management. Diabetes, a life-long condition associated with multiple vascular risk factors and sequelae, requires a more nuanced approach, for its prevalence reflects not just a disease but a changing phenotype. A complex and heterogeneous disorder such as this cannot be managed effectively without the understanding and co-operation of the person involved, and effective prevention requires increased awareness and education within the community as a whole. Hence, specific therapeutic measures are not enough; successful management of diabetes requires creation of a medical, social and political context within which lifelong care can be delivered. In this respect, there are lessons to be learned from the HIV response in Africa, which brought together governments, civil society, healthcare providers, community, donors and private sector.

The sheer burden of diabetes in SSA and its impact on individuals, populations, health systems and economies, means that governments must act to bring together wide ranging stakeholders to spur action at country and global level.

Government responsibilities

Ultimately, governments should respond to the wishes of their populations. In addition to enabling individuals to access health services, governments must introduce public

health measures to impact NCDs. Government interventions to ban smoking in public places, restrict advertising, increase taxes on cigarettes and sugar sweetened beverages, and limit portion size of sugar sweetened beverages have reduced demand and consumption.[378]

A health-literate population is critical for generating demand, improving access to health system and ensuring uptake of preventative measures. Much of the increase in health literacy in SSA has come from successful media campaigns via radio, poster adverts, and education via interaction with CHWs. These campaigns have generally focussed on prevention of HIV (e.g. condom use) and malaria (e.g. use of insecticide treated bed nets). Investment is needed to increase population's awareness of diabetes and to generate demand. Therefore, we recommend that countries in SSA consider developing media campaigns to educate the public about the symptoms of type 1 and type 2 diabetes and encourage those with symptoms to seek care. In particular, media campaigns should be deployed to educate citizens about preventative lifestyle measures, combined with government regulations that limit advertisements for unhealthy foods.

In addition to population level public health measures to improve health literacy, given the strong causal link between NCDs (including type 2 diabetes), sugar sweetened beverages, salt, and tobacco, we strongly advise countries to consider raising revenues by taxing these products to pay for health care provision. Although all-too- often considered as a disease of the rich, in LMIC the burden of type 2 diabetes and its comorbidities is increasingly being born by the poor[379]. Encouraging healthy choices and taxing unhealthy choices should help promote health of the poorer sectors of society, whilst raising revenue for treasuries to finance health systems and expand access to health services, medicines and diagnostics.

Many governments in SSA have limited fiscal space against competing demands for funding. There should be concerted efforts to expand fiscal space in order to increase investment in health. Hence, taxes on tobacco, unhealthy foods and sugar sweetened beverages to expand fiscal space, should be combined with national plans for diabetes that can drive system-wide changes to improve efficiency and reduce waste, while improving health outcomes. In order to develop sustainable plans to manage diabetes, governments should undertake a health system assessment to ascertain what needs to be done to establish an effective response for dealing with the burden of diabetes. Such an assessment should detail the burden of diabetes and its co-morbidities, their management at all levels of the health system, and how the services and platforms developed for communicable diseases can best be leveraged to also provide services for diabetes. A detailed exploration of the capability of human resources, availability of drugs and equipment and their costs (both to the health system and individuals), and functioning of supply chain management should be part of this assessment.

Governments should prioritise data collection for the improvement of their population health. There is an urgent need for countrywide integrated digital health information systems to collect data on diabetes (including a diabetes registry), its comorbidities, and

their management in the health system. Governments face multiple pressures to provide data on global targets. Countries should prioritise data collection systems, which could be used for health system planning at local and national level, and also inform global targets.

Governments should allocate sustainable funding to tackle the diabetes epidemic. We have calculated that in 2015 the economic burden of diabetes in SSA was $27.24 billion or 1.33% of cumulative GDP of the whole of SSA. Unchecked, the estimated economic burden is projected increase to $120.35 billion by 2030, equal to 5.64% of GDP in Southern Africa, 3.48% in Eastern Africa, 3.11% in Middle Africa and 1.39% in Western Africa.

Diabetes and its sequelae can be treated cost-effectively. Most of the medicines required for treating diabetes that are on the WHO 2015 essential medicines list are off-patent and are relatively low cost. In addition to anti-diabetic medicines, off-patent drugs such as ACE inhibitors should be made available to protect against diabetic nephropathy (including enalapril, which is currently listed as an antihypertensive on WHO list of essential medicines) and diabetic retinopathy[380]. Insulin is a special case, as generic forms are not widely available. However, countries can purchase vials of human insulin at prices comparable cost per person per year to that paid for one-year supply of fixed-combination ARV treatment. Given the absolute need for insulin treatment for type 1 diabetes and increasing need for type 2 diabetes, human insulin should be widely available for all those who need it. We consider that in the context of low-income countries of SSA, more expensive analogue insulins do not provide enough extra benefit to justify the current prices, as argued by Beran et al.[381]

Considering treatment, we urge countries to make all necessary medicines on the WHO essential medicine list for diabetes, hypertension, and cardiovascular disease available at no cost to all patients who need them. Newer treatments for type 2 diabetes may have some benefit over standard oral anti-hyperglycaemic agents and insulin. However, we would only consider these a worthwhile investment for the public sector after the countries in SSA have been able to provide essential services and medicines for diabetes.

There is a clear need to educate all groups of health professionals – ranging from community health workers to specialist physicians at all levels of the health system – on the management of diabetes along the care continuum to enable increased detection improved treatment. This need is especially great in settings dealing with children, so that a diagnosis of type 1 diabetes is not, fatally, missed. It is also essential in perinatal care and infectious disease clinics, to ensure diagnosis and treatment of gestational diabetes and to effectively manage interactions between diabetes and communicable diseases. Once recognised, diabetes – especially type 2 – can be effectively managed. Hence, we would advise countries to consider leveraging the existing human resources by training them to diagnose and treat diabetes before investing in training specialist diabetologists.

The sequelae of diabetes are insidious and present late in the disease course. Their effective management requires yearly monitoring at well-equipped health centres for glycaemic control and other cardiovascular risk factors in order to improve micro-vascular outcomes such as retinopathy, nephropathy, and diabetic foot.

Civil Society

Civil society plays a critical role in demanding change to improve access to health care and holding governments to account. Advocacy from civil society was instrumental in the global movement for HIV, which prompted the convening of a special session of the UN General Assembly in 2001 and led to the first UN declaration focusing on a disease.[382] Civil society can frame diabetes as integral part of the global commitments to address NCDs and to achieve UHC, given its links to so many risk factors and conditions, and use this narrative for awareness building and mobilising support among a broad of stakeholders.

Effective deployment of civil society requires strengthening and expanding networks in SSA, an increase in the health literacy of the population and improved modes of communication. In many of the countries in SSA, foundations are playing a key role in educating the public, health care providers, and governments about diabetes. Diabetes foundations should catalyse the continuing improvement in management of diabetes by tracking progress towards objectives set out in national NCD or diabetes plans and holding governments account for their implementation. However, funding is needed to ensure that their work can continue and expand. We urge donors and diabetes foundations in other countries to consider funding and, or partnering with foundations in SSA to enable mutual learning, strengthen the agenda for change and ensure sustainability.

Of particular urgency is the matter of T1DM, where it is suspected, although not definitively known, due to lack of data, that the majority of sufferers may die without a diagnosis or access to treatment. Civil society should play a key role in raising awareness of T1DM and they should ensure that governments are held to account regarding guaranteeing a supply of insulin to all sufferers, not just children

To date, most international health NGOs have focused their efforts on maternal, neonatal, and child health, communicable diseases, and on providing health care in conflict settings. While some NGOs, such as Life for a Child (http://www.idf.org/lifeforachild) and Sante Diabete (http://www.santediabete.org/en/), have focussed on diabetes, these are far and few. It is encouraging to note that MSF is increasing its involvement in NCDs.

Whilst recognising the importance of focusing on their core business, we encourage NGOs working in SSA to recognise the importance of diabetes and obesity in their patient populations and, where possible, work in concert with country health systems to find solutions to incorporate improving diabetes care. This is particularly important for

NGOs who deal with communicable diseases and improving maternal and neonatal health, where diabetes impact on outcomes.

Donors

While NCDs have been identified as a priority at the 2011 UN High Level Commission, with renewed commitment in health SDG, they still do not feature prominently on the agendas of most global health funders, whose assistance to countries has plateaued. To date, donor agencies have channelled their funding to meeting MDGs while the growing epidemic of T2 Diabetes, and its precursors (overweight and obesity), have received limited support – especially T1DM, which has 100% mortality rate without treatment, but can be effectively managed.

Overweight, obesity, and diabetes are often perceived as 'lifestyle' problems and lack the prominence of maternal, neonatal, and child health, communicable diseases. Yet, evidence strongly suggests overweight, obesity, and diabetes are influenced more by environment than individual factors. NCDs, which include diabetes, are now the major cause of morbidity and mortality in LMICs, and there is an imperative to invest in their management if the health gains due to improvements in maternal, neonatal, and child health, communicable diseases are to be sustained. Hence, donors should transition channelling funds to vertical disease programmes but invest in health systems improving health of individuals, who all so often have multiple ailments.

Global agencies

Global agencies have been slow to transition to a new world where NCDs predominate. In 2011, the United Nations High Level Meeting on NCDs[383] produced the UN General Assembly Resolution on the prevention and control of NCDs[384], committing the UN member states to prevention and control of NCDs[385]. In 2013, at the 65th World Health Assembly member states agreed to reduce premature mortality from NCDs by 25% by the year 2025 relative to their 2010 levels.[386] However, in spite of these resolutions and targets apathy prevails.[387] Although a global coordination mechanism, a monitoring framework, an action plan, and an UN interagency task force have been established, it is not clear what has been achieved to positively impact on the lives of those living with NCDs. As with many countries globally, health systems in SSA are not ready for the rapid demographic, epidemiological, social and economic transition that has brought rising levels of diabetes along with multimorbidity and disability.[388,389]

As with the Ebola crisis, the response of WHO to NCDs, the world's predominant global health agency has been lacklustre. Yet, there is an opportunity. WHO is well respected in SSA countries and is well placed to play a leadership role to address diabetes – and not just in SSA but globally. However, this opportunity can only be realised if WHO reflects on the criticisms[390] (for example lack of leadership, sluggish responses, and introspection) and learns lessons from the Ebola crisis to emerge as a leader in the battle against diabetes and NCDs.

Learning from the lessons of the Ebola crisis, WHO has the opportunity and the legitimacy to work with member states, international agencies and civil society organisations to mount an urgent and coordinated response to the burgeoning diabetes epidemic. The coordination among partner institutions should be replicated internally among WHO departments. As a start, we urge WHO to make available global diabetes data available to researchers wishing to do analyses to help improve the health systems of people in countries in SSA and globally.[391]

While WHO has the potential to lead coordinated action, an urgent response to diabetes in SSA can only be achieved with decisive contribution of international institutions such as the World Bank, with its financing and development capability and expertise in health systems, the Global Fund, which can catalyse an integrated response to bring together communicable diseases, MNCH and NCDs, GAVI, with its capability in innovative financing and cold chain development, UNITAID, in creating market dynamics and expanding access to new technologies and medicines, USAID, which has successfully helped countries to scale up MNCH and reproductive health response and is now championing integration and quality improvement, and among others, UNICEF to build on the effective platforms established for managing children's problems.

We urge all multi and bilateral global health and development agencies to recognise the importance of preventing and treating diabetes in order for SSA to achieve the SDG goals and to avert an economic burden that will arrest development.

Research, development and innovation

A global response to diabetes would be incomplete without an ambitious research and development (R&D), and innovation agenda to address the scale and urgency of diabetes. There is an urgent need to scale up research and learning to improve functioning of health systems.[392] There is also a need to invest in R&D and innovation in development of new low cost technologies and medicines, which are affordable in SSA, as well as innovations in financing and service delivery[393] to address resource shortages and accelerate adoption and diffusion of existing and new technologies in health systems[394]. An enabling environment is critical for ensure effective adoption of complex innovations – such as novel primary health care services[395,396] – which are critical for establishing a comprehensive health system response.

Current global shortage of health professionals is a major barrier to expanding services in SSA. While additional human resources are needed, resource constraints mean that in the near term rapid expansion in numbers is not realistic. Addressing human resource shortages will require a combination of strategies. The first of these strategies is task shifting, which has been effectively implemented in several countries of SSA to use a broader group of health professionals in diabetes care (se Section 7). The second strategy is to use novel technologies to improve the knowledge and competences of existing health workforce, by leveraging advances in communications, including distance

learning and e-learning through use of online courses[397]. The third, among others, is to use mobile technologies and SMS text messaging to better manage communications and processes in health systems, for example in communicating results[398], attending appointments in clinics[399], rapidly scaling up public health interventions and prevention to population[400], and to improve self-management of long-term illness by patients themselves[401].

There are also opportunities for increasing financing diabetes. In spite of the global economic crisis, countries in SSA have achieved sustained economic growth, and are projected to do so in the next decade.[402] In addition, innovative financing (such as Airline Solidarity Levy and Debt2Health), which has been used successfully for AIDS, tuberculosis, malaria and children's immunisation programmes, offers possibilities for mobilising, pooling, channelling and funding health systems and diabetes.[403,404] as well as late stage research[405].

Targets

Countries are overwhelmed with goals, targets and indicators. There are 17 Sustainable Development Goals (SDGs) with The third SDG (Ensure healthy lives and promote well-being for all at all ages) alone has 13 targets. Of these, six targets are most readily applicable to diabetes as targets for SSA. These include:

(i) By 2030, reduce by one third premature mortality from non-communicable diseases through prevention and treatment
(ii) Achieve universal health coverage, including financial risk protection, access to quality essential health-care services and access to safe, effective, quality and affordable essential medicines and vaccines for all
(iii) Strengthen the implementation of the World Health Organization Framework Convention on Tobacco Control in all countries, as appropriate
(iv) Support the research and development of vaccines and medicines for the communicable and noncommunicable diseases that primarily affect developing countries, provide access to affordable essential medicines and vaccines
(v) Substantially increase health financing and the recruitment, development, training and retention of the health workforce in developing countries, especially in least developed countries
(vi) Strengthen the capacity of all countries, in particular developing countries, for early warning, risk reduction and management of national and global health risks

In addition, at the 65th World Health Assembly member states approved the WHO Global Action Plan for the Prevention and Control of NCDs 2013-2020 nine voluntary targets to reduce premature mortality due to NCDs by 25%, reduce physical inactivity by 10%, reduce tobacco consumption by 30%, achieve a 25% reduction in high blood pressure, achieve 80% coverage of essential medicines and technologies for NCDs and achieve 0% increase in the prevalence of obesity and diabetes by the year 2025.[406] The Global Action Plan is underpinned by the Global Monitoring Framework with 25 indicators that are monitored by member states – of which 12 are relevant to diabetes.[407]

Achieving the targets set in the SDGs, and the Global Action Plan will transform the management of diabetes in SSA and help avert needless suffering, illness and death, and reduce the economic burden of diabetes on individuals, households and societies. The critical ingredient to an effective response to diabetes in SSA is solidarity and collective action at local, national, African and Global level – collective action, which lies at the heart of sustainable diabetes response and sustainable development in SSA.

References

[1] WHO. Health Statistics and Information Systems Cause-specific mortality Estimates for 2000-2012. Geneva: World Health Organization, 2012. http://www.who.int/healthinfo/global_burden_disease/estimates/en/index1.html (Accessed March 12, 2015)

[2] Institute for Health Metrics and Evaluation. The Global Burden of Disease: Generating Evidence, Guiding Policy — Sub-Saharan Africa Regional Edition. Seattle, WA: IHME, 2013.

[3] Levitt NS. Diabetes in Africa: epidemiology, management and healthcare challenges. *Heart* 2008, 94(11):1376-82.

[4] Levitt NS, Steyn K, Dave J, Bradshaw D. Chronic Noncommunicable Diseases and HIV-AIDS on a collision course: Relevance for health care delivery, particularly in low-resource settings – insights from South Africa. Am J Clin Nutr 2011;94 (suppl):1690S–96S.

[5] Institute for Health Metrics and Evaluation. GBD Database: By cause Sub-Saharan Africa Both sexes All ages Deaths. Seattle, WA: IHME, University of Washington, 2014. Available from http://www.healthdata.org/search-gbd-data?s=Tension-type%20headache (Accessed March 5, 2015.)

[6] WHO. Global report on diabetes. WHO; Geneva, 2016. http://apps.who.int/iris/bitstream/10665/204871/1/9789241565257_eng.pdf (Accessed April 11, 2015.)

[7] International Diabetes Federation. IDF Diabetes Atlas. 7th Edition. http://www.idf.org/diabetesatlas (accessed June 16, 2015).

[8] Hwang CK, Han PV, Zabetian A, Ali MK, Narayan KM. Rural diabetes prevalence quintuples over twenty-five years in low- and middle-income countries: a systematic review and meta-analysis. *Diabetes Res Clin Pract* 2012; **96:** 271–85.

[9] Werfalli M, Engel ME, Musekiwa A, Kengne AP, Levitt NS. The prevalence of type 2 diabetes among older people in Africa: a systematic review. Lancet Diabetes-Endocrinol 2015. Published Online November 5, 2015. http://dx.doi.org/10.1016/S2213-8587(15)00363-0

[10] *NCD Risk Factor Collaboration (NCD-RisC)*. Worldwide trends in diabetes since 1980: a pooled analysis of 751 population-based studies with 4·4 million participants. *Lancet* 2016; 387: 1513–30

[11] International Monetary Fund. World Economic Outlook (WEO) Database. https://www.imf.org/external/pubs/ft/weo/2015/02/weodata/index.aspx (accessed 16 Jan 2016)

[12] United Nations, Department of Economic and Social Affairs, Population Division (2014). World Urbanization Prospects: The 2014 Revision, custom data acquired via website. http://esa.un.org/unpd/wup/DataQuery/ (Accessed April 12, 2015)

[13] Cook-Huynh M, Ansong D, Steckelberg RC, Boakye I, Seligman K, Appiah L, Kumar N, Amuasi JH. Prevalence of hypertension and diabetes mellitus in adults from a rural community in Ghana. Ethn Dis. 2012 Summer;22(3):347-52.

[14] Evaristo-Neto AD, Foss-Freitas MC, Foss MC. Prevalence of diabetes mellitus and impaired glucose tolerance in a rural community of Angola. Diabetol Metab Syndr. 2010 Nov 1;2:63. doi: 10.1186/1758-5996-2-63.

[15] Motala AA, Esterhuizen T, Gouws E, Pirie FJ, Omar MA.Diabetes and other disorders of glycemia in a rural South African community: prevalence and associated risk factors. Omar, Diabetes Care, 2008 Diabetes Care. 2008 Sep;31(9):1783-8. doi: 10.2337/dc08-0212. Epub 2008 Jun 3.

[16] Baldé NM, Diallo I, Baldé MD, Barry IS, Kaba L, Diallo MM, Kaké A, Camara A, Bah D, Barry MM, Sangaré-Bah M, Maugendre D. Diabetes and impaired fasting glucose in rural and urban populations in Futa Jallon (Guinea): prevalence and associated risk factors. Diabetes Metab. 2007 Apr;33(2):114-20. Epub 2007 Mar 23.

[17]Ayah R, Joshi MD, Wanjiru R, Njau EK, Otieno CF, Njeru EK, Mutai KK. A population-based survey of prevalence of diabetes and correlates in an urban slum community in Nairobi, Kenya. BMC Public Health. 2013 Apr 20;13:371. doi: 10.1186/1471-2458-13-371.

[18] Echouffo-Tcheugui JB, Dzudie A, Epacka ME, Choukem SP, Doualla MS, Luma H, Kengne AP. Prevalence and determinants of undiagnosed diabetes in an urban sub-Saharan African population. Prim Care Diabetes. 2012 Oct;6(3):229-34. doi: 10.1016/j.pcd.2012.05.002. Epub 2012 Jun 7.

[19] Duboz P, Chapuis-Lucciani N, Boëtsch G, Gueye L. Prevalence of diabetes and associated risk factors in a Senegalese urban (Dakar) population. Diabetes Metab. 2012 Oct;38(4):332-6. doi: 10.1016/j.diabet.2012.02.011. Epub 2012 Apr 19.

[20] Kengne AP, June-Rose McHiza Z, Amoah AG, Mbanya JC. Cardiovascular

diseases and diabetes as economic and developmental challenges in Africa. Prog Cardiovasc Dis. 2013 Nov-Dec;56(3):302-13. doi: 10.1016/j.pcad.2013.10.011. Epub 2013 Oct 23. Review.

[21] Ziraba AK, Fotso JC, Ochako R. Overweight and obesity in urban Africa: A problem of the rich or the poor? BMC Public Health. 2009 Dec 15;9:465. doi: 10.1186/1471-2458-9-465.

[22] Mbanya JC, Motala AA, Sobngwi E, Assah FK, Enoru ST. Diabetes in sub-Saharan Africa. Lancet. 2010 Jun 26;375(9733):2254-66. doi: 10.1016/S0140-6736(10)60550-8. Review,

[23] Gill GV, Mbanya JC, Ramaiya KL, Tesfaye S. A sub-Saharan African perspective of diabetes. Diabetologia. 2009 Jan;52(1):8-16. doi: 10.1007/s00125-008-1167-9. Epub 2008 Oct 10. Review.

[24] Prentice A, Webb F. Obesity amidst poverty. Int J Epidemiol. 2006 Feb;35(1):24-30. No abstract available.

[25] Levitt NS. Diabetes in Africa: epidemiology, management and healthcare challenges.Heart. 2008 Nov;94(11):1376-82. doi: 10.1136/hrt.2008.147306. Epub 2008 Jun 2. Review.

[26] United Nations, Department of Economic and Social Affairs, Population Division (2015). World Population Prospects: The 2015 Revision, custom data acquired via website. Total population by sex (thousands) http://esa.un.org/unpd/wpp/DataQuery/ (Accessed April 12, 2015)

[27] United Nations, Department of Economic and Social Affairs, Population Division (2015). World Population Prospects: The 2015 Revision, custom data acquired via website.

Population by age and sex (thousands) http://esa.un.org/unpd/wpp/DataQuery/ (Accessed April 12, 2015)

[28] United Nations, Department of Economic and Social Affairs, Population Division (2015). World Population Prospects: The 2015 Revision, custom data acquired via website. Data query Life expectancy, e(x), at exact age x (years). http://esa.un.org/unpd/wpp/DataQuery/ (Accessed April 12, 2015)

[29] Manne-Goehler J, Atun R, Stokes A, et al. Unmet need for diabetes care in sub-Saharan Africa: a cross-country analysis. Lancet Diabetes and Endocrinology 2016; (In press)

[30] Davies J, Yudkin J, Atun R. Liberating data: the crucial weapon in the fight against NCDs. Lancet Diabetes Endocrinology 2016. Published Online January 27, 2016. http://dx.doi.org/10.1016/S2213-8587(16)00037-1

[31] Atun R, Jaffar S, Nishtar S, et al. Improving responsiveness of health systems to non-communicable diseases. *Lancet* 2013; 381:690-97.

[32] NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in diabetes since 1980: a pooled analysis of 751 population-based studies with 4·4 million participants. Lancet 2016; 387: 1513–30

[33] Beran D, Ewen M, Laing R. Constraints and challenge in access to insulin: a global perspective. Lancet Diabetes Endocrinol 2016;4:275-85

[34] Joslin EP. The Treatment of Diabetes Mellitus. Sixth Edition, Lea and Febiger, Philadelphia, 1937

[35] West KM. Epidemiology of Diabetes and its Vascular Lesions. Elsevier, New York, 1978

[36] Ohn JH, Kwak SH, Cho YM,et al. 10-year trajectory of β-cell function and insulin sensitivity in the development of type 2 diabetes: a community-based prospective cohort study. Lancet Diabetes Endocrinol 2016; 4: 27–34

[37] IDF, International Diabetes Federation. Diabetes Atlas, 7th Edition, Brussels, Belgium,2015

[38] Gillman MW. Prenatal famine and developmental origins of type 2 diabetes. The Lancet Diabetes & Endocrinology, Vol. 3, No. 10, p751–752

[39] Lönnroth K, Roglic G, Harries AD. Improving tuberculosis prevention and care through addressing the global diabetes epidemic: from evidence to policy and practice. The Lancet Diabetes & Endocrinology, Vol. 2, No. 9, p730–739

[40] Nou E, Lo J, Hadigan C, Grinspoon SK. Pathophysiology and management of cardiovascular disease in patients with HIV. The Lancet Diabetes & Endocrinology, Vol. 4, No. 7, p598–610

[41] Li G, Zhang P, Wang J, and others. The long-term effect of lifestyle interventions to prevent diabetes in the China Da Qing Diabetes Prevention Study: a 20-year follow-up study. The Lancet, Vol. 371, No. 9626, p1783–1789

[42] Umpierrez GE, Smiley D, Kitabchi AE. Narrative review: Ketosis-prone Type 2 diabetes. Ann Int Med 2006;144:350-357

[43] Chen N, Unnikrishnan R, Mohan AR, Mohan V, Pitchumoni CS. The Complex Exocrine-Endocrine Relationship and Secondary Diabetes in Exocrine Pancreatic Disorders. JOURNAL OF CLINICAL GASTROENTEROLOGY. Volume: 45 Issue: 10 Pages: 850-861

[44] Gill, GV, Mbanya J-C, Ramaiya KL, Tesfaye S. A sub-Saharan African perspective of diabetes. Diabetologia 2009; 52(1): 8-16.

[45] Werfalli M, Engel ME, Musekiwa A, Kengne AP, Levitt NS. The prevalence of type 2 diabetes among older people in Africa: a systematic review. The Lancet Diabetes & Endocrinology, Vol. 4, No. 1, p72–84.

[46] NCD Risk Factor Collaboration (NCD-RisC). Trends in adult body-mass index in 200 countries from 1975 to 2014: a pooled analysis of 1698 population-based measurement studies with 19·2 million participants. The Lancet, Vol. 387, No. 10026, p1377–1396

[47] Popkin BM, Hawkes C. Sweetening of the global diet, particularly beverages: patterns, trends, and policy responses. The Lancet Diabetes & Endocrinology, Vol. 4, No. 2, p174–186.

[48] Mbanya JC, Notala AA, Sobngwi E, Assah FK, Enoru ST. Diabetes in Sub-Saharan Africa. Lancet 2010;375: 2254-2266.

[49] Kengne AP, Echouffo-Tcheugui J-B, Sobngwi E, Mbanya J-C. New insights of diabetes mellitus and obesity in Africa – Part 1: prevalence, pathogenesis and comorbidities. Heart 2013;99:979-983.

[50] Ziraba AK, Fotso JC, Ochako R. Overweight and obesity in urban Africa: A problem of the rich or the poor? BMC Public Health 2009 Dec 15;9:465.

[51] Campbell MC, Tishkoff SA. African genetic diversity: Implications for human demographic history, modern human origins, and complex disease mapping. Annu Rev Hum Genet 2008;9:403-433.

[52] Rotimi CN, Jorde LB. Ancestry and disease in the age of genomic medicine. New Engl J Med 2010;363:1551-8

[53] Tull ES, Roseman JM. Diabetes in African Americans. Diabetes in America, 2nd Edition, NIH Publication no 95-1468, pages 613-630, 1995; Bethesdaa, Maryland, USA.

[54] Centers for Disease Control and Prevention. National diabetes fact sheet: national estimates and general information on diabetes and prediabetes in the United States. Atlanta GA: US Department of Health and Human Services, Centers for Disease Control and Prevention, 2011, Atlanta, Georgia, USA.

[55] Understanding type 1 diabetes through genetics: advances and prospects Polychronakos C, Li Q. NATURE REVIEWS GENETICS. Volume: 12 Issue: 11 Pages: 781-792.

[56] Noble JA, Johnson J, Lane JA, Valdes AM. HLA Class II genotyping of African American Type 1 diabetic patients reveals associations unique to African haplotypes. Diabetes 2013;62:3292-3299.

[57] Ng MC, Shriner D, Chen BH, Li J, Chen W-M et al. Meta-analysis of genome-wide association studies in African-Americans provides insights into the genetic architecture of type 2 diabetes. PLOS Genetics 2014;10(8): e1004517.

[58] McCarthy MI. Genomics, Type 2 diabetes and obesity. New Engl J Med 2010;363:2339-5.

[59] Ohn JH, Kway SH, Cho JM, Lim S, Jang HC et al. 10-year trajectory of β-cell function and insulin sensitivity in the development of type 2 diabetes: a community-based prospective cohort study. Lancet Diabetes Endocrinol 2015;3:624-637.

[60] Chambers JC, Loh M, Lehne B, Drong A, Kriebel J, Motta V, and others. Epigenome-wide association of DNA methylation markers in peripheral blood from Indian Asians and Europeans with incident type 2 diabetes: a nested case-control study. The Lancet Diabetes & Endocrinology 2015; 3 (7): 526–534.

[61] Alexander CM, Landsman PB, Teutsch SM, Haffner SM. NCEP-defined metabolic syndrome, diabetes, and prevalence of coronary heart disease among NHANES IIIparticipants age 50 years and older. Diabetes 2003;52:1210-1214.

[62] Rotimi C, Cooper R, Cao G, Sundarum C, McGee D. Familial aggregation of cardiovascular diseases in African-American pedigrees. Genetic Epidemiology 1994;11:397-407.

[63] Tekola-Ayele F, DoumateyAP, Shriner D, BentleyAR, Chen G et al. Genome-wide association study identified African-ancestry specific variants for metabolic syndrome. Mol Genet Metab 2015;116:305-313.

[64] International Diabetes Federation. IDF Diabetes Atlas. 7th Edition. http://www.idf.org/diabetesatlas (accessed June 16, 2015).

[65] Noble JA, Johnson J, Lane JA, Valdes AM. HLA Class II genotyping of African American Type 1 diabetic patients reveals associations unique to African haplotypes. Diabetes 2013;62:3292-3299.

[66] Marshall SL, EdidinD, Sharma V, Ogle G, Arena VC, Orchard T. Current clinical status, glucose control, and complication rates of children and youth with type 1 diabetes in Rwanda. Pediatr Diabetes 2015.

[67] International Diabetes Federation. IDF Diabetes Atlas. 7th Edition. http://www.idf.org/diabetesatlas (accessed June 16, 2015).

[68] Mark A Atkinson, Graham D Ogle. Improving diabetes care in resource-poor countries: challenges and opportunities. The Lancet Diabetes & Endocrinology, Vol. 1, No. 4, p268–270.

[69] Ogle GD, Kim H, Middlehurst AC, Silink M, Jenkins AJ, Financial costs for families of children with Type 1 diabetes in lower-income countries. Diabetic Med 2016;33:820-6

[70] Beran D, Yudkin JS, de Courten M. Access to care for patients with insulin-requiring diabetes in developing countries: Case studies of Mozambique and Zambia Diabetes Care 2005;28:2136-2140.

[71] Gill GV, Huddle KR, Monkoe G. Long-term (20 years) outcome and mortality of Type 1 diabetes in Soweto, South Africa. Diabet Med 2005;22:1642-1646

[72] Livingstone SJ, Levin D, Looker HC, et al Estimated Life Expectancy in a Scottish Cohort With Type 1 Diabetes, 2008-2010. JAMA. Volume: 313 Issue: 1 Pages: 37-44

[73] Majaliwa ES, Elusiyan BE, Adesiyun OO, Laigong P, Adeniran AK et al. Type 1 diabetes in the African population: epidemiology and management challenges. Acta Biomed 2008;79:255-259.

[74] Odundo GO, Ngwiri T, Otuoma O, Chanzu NM. Developing equity in capacity of paediatric endocrinology subspecialists worldwide. Lancet Diabet Endocrinol 2016;4:204-5

[75] NCD Risk Factor Collaboration (NCD-RisC). Effects of diabetes definition on global surveillance of diabetes prevalence and diagnosis: a pooled analysis of 96 population-based studies with 331,288 participants. Lancet Diabet Endocrinol 2015;3:624-637.

[76] Elizabeth G O'Hara, Bernardo Nuche-Berenguer, Nicholas K Kirui, Stephanie Y Cheng, Patrick M Chege, Victor Buckwalter, and others. Diabetes in rural Africa: what can Kenya show us? The Lancet Diabetes & Endocrinology

[77] Simmons RK, Echouffo-Tcheugi JB, Sharp SJ, Sargeant LA, Williams KM et al. Screening for type 2 diabetes and population mortality over 10 years: a cluster-randomized clinical trial. Lancet 2012;380:1741-1748

[78] Guariguata L, Linnenkamp U, Beagley J, Whiting DR, Cho NH. Global estimates of the prevalence of hyperglycaemia in pregnancy. DIABETES RESEARCH AND CLINICAL PRACTICE. Volume: 103 Issue: 2 Pages: 176-185

[79] Olagbuji BN, Atiba AS, Olofinbiyi BA, Akintayo AA, Awoleke JO et al. Prevalence and risk factors for gestational diabetes using 1999, 2013 WHO and IADPSG criteria upon implementation of a universal one-step screening and diagnostic strategy in a sub-Saharan population. Eur J Obstet & Gynecol Reprod Biol 2015;189:27-32

[80] Poston, Lucilla – complications of obesity in pregnancy. The Lancet Diabetes & Endocrinology 2016. (In press)

[81] Fraser RB. The fate of the pregnant diabetic in a developing country: Kenya. Diabetologia 1982; 22: 21-24.

[82] Zeck W, McIntyre HD. Gestational Diabetes in Rural East Africa: A Call to Action. J Women's Health 2008;17:403-411.

[83] Huddle, K.R., 2005. Audit of the outcome of pregnancy in diabetic women in Soweto, South Africa, 1992–2002. Journal of Endocrinology, Metabolism and Diabetes of South Africa, 10(3), pp.102-107.

[84] Coetzee EJ, Jackson WP. The management of non-insulin dependent diabetes during pregnancy. Diabetes Res Clin Pract 1985-6; 1:281-7.

[85] Ekpebegh CO, Coetzee EJ, Van Der Merwe L, Levitt NS. A 10-year retrospective analysis of pregnancy outcome in pregestational Type 2 diabetes: comparison of insulin and oral glucose-lowering agents. Diabetic Medicine 2007; 24(3): 253-258.

[86] Hall V, Thomsen RW, Henriksen O, Lohse N. Diabetes in Sub Saharan Africa 1999-2011: epidemiology and public health implications. A systematic review. BMC Public Health. 2011; 11:564

[87] Macaulay S, Dunger DB, Norris SA. Gestational Diabetes Mellitus in Africa: A Systematic Review. PLoS One. 2014; 9 (6).

[88] Mwanri AW, Kinabo J, Ramaiya K, Feskens EJ. Gestational diabetes mellitus in sub-Saharan Africa: systematic review and metaregression on prevalence and risk factors. Trop Med Int Health 2015;20:983-1002

[89] The Global Burden of Metabolic Risk Factors for Chronic Diseases Collaboration. Cardiovascular disease, chronic kidney disease, and diabetes mortality burden of cardiometabolic risk factors from 1980 to 2010: a comparative risk assessment. *The Lancet Diabetes & Endocrinology*, Vol. 2, No. 8, p634–647

[90] Global Burden of Disease Study 2013 Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *The Lancet*, Vol. 386, No. 9995, p743–800

[91] The Lancet Diabetes & Endocrinology. Diabetic kidney disease: what does the next era hold? *The Lancet Diabetes & Endocrinology*, Vol. 3, No. 9, p665

[92] Stanifer JW, Jing B, Tolan S, and others. The epidemiology of chronic kidney disease in sub-Saharan Africa: a systematic review and meta-analysis. *The Lancet Global Health*, Vol. 2, No. 3, e174–e181

[93] Kidney Disease Research Network. The H3Africa Kidney Disease Research Network. Genomic approaches to the burden of kidney disease in Sub-Saharan Africa: the Human Heredity and Health in Africa (H3Africa). *Kidney International* (2016) 90, 2–5.

[94] Genovese, G, Friedman, DJ, Ross, MD et al. Association of trypanolytic ApoL1 variants with kidney disease in African Americans. *Science*. 2010; 329: 841–884

[95] Naicker, S. Burden of end-stage renal disease in sub-Saharan Africa. *Clin Nephrol*. 2010; 74: S13–S16

[96] Bruce M Robinson, Tadao Akizawa, Kitty J Jager, Peter G Kerr, Rajiv Saran, Ronald L Pisoni. *The Lancet*. Published online: May 22, 2016

[97] Wasiu A Olowu, Abdou Niang, Charlotte Osafo, Gloria Ashuntantang, Fatiu A Arogundade, John Porter, and others. Outcomes of acute kidney injury in children and adults in sub-Saharan Africa: a systematic review. *The Lancet Global Health*, Vol. 4, No. 4, e242–e250

[98] Pascolini D, Mariotti SP: Global estimates of visual impairment: 2010. BJO 2012, 96:614–618.

[99] Burgess PI, Maccormick IJ, Harding SP, Bastawrous A, Beare NA, Garner P: Epidemiology of diabetic retinopathy and maculopathy in Africa: a systematic review. Diabet Med 2013, 30:399–412.

[100] Mathenge W, Bastawrous A, Peto T, Leung I, Yorston D, Foster A, Kuper H. Prevalence and correlates of diabetic retinopathy in a population-based survey of older people in Nakuru, Kenya. Ophthalmic Epidemiol. 2014; 21(3): 169-77

[101] Cockburn N, Steven D, Lecuona K, Joubert F, Rogers G, Cook C, Polack S: Prevalence, causes and socio-economic determinants of vision loss in Cape Town, South Africa. PLoS One 2012, 7:e30718.

[102] Poore S, Foster A, Zondervan M, Blanchet K. Planning and developing services for diabetic retinopathy in Sub-Saharan Africa. Int J Health Policy Manag. 2014 Dec 16;4(1):19-28.

[103] Cleland CR, Burton MJ, Hall C, Hall A, Courtright P, Makupa WU, Philippin H. Diabetic retinopathy screening: experiences from northern Tanzania. Lancet Diabetes Endocrinol. 2016 Jan;4(1):10-2.

[104] Cleland CR, Burton MJ, Hall C, Hall A, Courtright P, Makupa WU, Philippin H. Diabetic Retinopathy in Tanzania: prevalence and risk factors at entry into a regional screening programme. Trop Med Int Health. 2015 Dec 8. doi:10.1111/tmi.12652.

[105] Cook S. Diabetic retinopathy - the Ophthalmology Society of Southern Africa screening programme. S Afr Med J. 2013 Jun 10; 103(7):449-51. doi: 10.7196/samj.7136.

[106] Poore S, Foster A, Zondervan M, Blanchet K. Planning and developing services for diabetic retinopathy in Sub-Saharan Africa. Int J Health Policy Manag. 2014 Dec 16; 4(1):19-28.

[107] Burgess PI, Msukwa G, Beare NAV. Diabetic retinopathy in Sub-Saharan Africa: meeting the challenges of an emerging epidemic. BMC Medicine. 2013; 11: 157

[108] Matimba A, Woodward R, Tambo E, Ramsay M, Gwanzura L, Guramatunhu S. Tele-ophthalmology: Opportunities for improving diabetes eye care in resource- and specialist-limited Sub-Saharan African countries. J Telemed Telecare. 2015 Sep 24. pii: 1357633X15604083

[109] Bastawrous A, Rono HK, Livingstone IA, Weiss HA, Jordan S, Kuper H, Burton MJ. Development and Validation of a Smartphone-Based Visual Acuity Test (Peek Acuity) for Clinical Practice and Community-Based Fieldwork. JAMA Ophthalmol. 2015 Aug;133(8):930-7.

[110] Hansen MB, Abràmoff MD, Folk JC, Mathenge W, Bastawrous A, Peto T. Results of Automated Retinal Image Analysis for Detection of Diabetic Retinopathy from the Nakuru Study, Kenya. PLoS One. 2015 Oct 1;10(10):e0139148.

[111] Abbas ZG, Archibald LK. Challenges for management of the diabetic foot in Africa: doing more with less. Int Wound J 2007; 4:305–13.

[112] International Working group on the Diabetic Foot (IWGDF). The development of global consensus guidelines on the management and prevention of the Diabetic Foot 2015, www.iwgdf.org.

[113] Abbas ZG, Lutale JK, Morbach S, Archibald LK. Clinical outcome of diabetic patients hospitalized with foot ulcers, Dar es Salaam, Tanzania. Diabet Medicine 2002;19:575–9.

[114] Benjamin A Lipsky, Jan Apelqvist, Karel Bakker, Jaap J van Netten, Nicolaas C Schaper. Diabetic foot disease: moving from roadmap to journey. The Lancet Diabetes & Endocrinology, Vol. 3, No. 9, p674–675.

[115] Cavanagh P, Attinger C, Abbas ZG, Bal A, Rojas N, Xu ZR. Cost of treating diabetic foot ulcers in five different countries. Diabetes Metab. Res. Rev. 2012; 28(Suppl.-1):107-111

[116] Jarso G, Ahmed A, Feleke Y. The prevalence, clinical features and management of peripheral neuropathy among diabetic patients in Tikur Anbessa and St. Paul's Specialized University Hospitals, Addis Ababa, Ethiopia. Ethiop Med J. 2011; 49(4):299-311.

[117] Ugoya SO, Echejoh GO, Ugoya TA, Agaba EI, Puepet FH, Ogunniyi A. Clinically diagnosed diabetic neuropathy: frequency, types and severity. J Natl Med Assoc. 2006; 98(11):1763-6.

[118] Levitt NS, Bradshaw D, Zwarenstein MF, Bawa AA, Maphumolo S. Audit of public sector primary diabetes care in Cape Town, South Africa: high prevalence of complications, uncontrolled hyperglycaemia, and hypertension. Diabet Medicine 1997; 14(12):1073-7.

[119] Okello S, Millard A, Owori R, Asiimwe SB, Siedner MJ, Rwebembera J, Wilson LA, Moore CC, Annex BH. Prevalence of lower extremity peripheral artery disease among

adult diabetes patients in southwestern Uganda. BMC Cardiovasc Disord. 2014 Jun 10;14:75. doi: 10.1186/1471-2261-14-75.

[120] Kumar A, Mash B, Rupesinghe G. Peripheral arterial disease - high prevalence in rural black South Africans. S Afr Med J. 2007; 97(4):285-8.

[121] Abbas ZG, Archibald LK. The diabetic foot in Sub-Saharan Africa: a new management paradigm. Diab Foot J 2007; 10:128–36.

[122] Pendsey S, Abbas ZG. The Step-by-Step program for reducing diabetic foot problems: a model for the developing world. Curr Diab Rep. 2007; 6:425-8

[123] Kuate-Tegueu C, Temfack E, Ngankou S, Doumbe J, Djientcheu VP, Kengne AP. Prevalence and determinants of diabetic polyneuropathy in a sub-Saharan African referral hospital. J Neurol Sci. 2015; 355:108-12.

[124] Abbas Z, Morbach S. Diabetes foot damage in developing countries: the urgent need for education. Diabetes Voice 2005; 50:15-17.

[125] Ronacher, K, Joosten, SA, Crevel R, Dockrell, HM, Walzl G, & Ottenhoff TH. Acquired immunodeficiencies and tuberculosis: focus on HIV/AIDS and diabetes mellitus. Immunological reviews, 2015; 264(1), 121-137

[126] Reinout van Crevel, Hazel M Dockrell, for the TANDEM Consortium. TANDEM: understanding diabetes and tuberculosis. The Lancet Diabetes & Endocrinology, Vol. 2, No. 4, p270–272.

[127] Anna Odone, Rein M G J Houben, Richard G White, Knut Lönnroth. The effect of diabetes and undernutrition trends on reaching 2035 global tuberculosis targets. The Lancet Diabetes & Endocrinology, Vol. 2, No. 9, p754–764.

[128] Sung-Ching Pan, Chu-Chang Ku, Diana Kao, Majid Ezzati, Chi-Tai Fang, Hsien-Ho Lin. Effect of diabetes on tuberculosis control in 13 countries with high tuberculosis: a modelling study. The Lancet Diabetes & Endocrinology, Vol. 3, No. 5, p323–330.

[129] Haraldsdottir TL, Rudolf F, Bjerregaard-Andersen M, Joaquim LC, Stochholm K et al. Diabetes mellitus prevalence in tuberculosis patients and the background population in Guinea-Bissau, a disease burden study from the capital, Bissau. Trans Roy Soc Trop Med Hyg 2015;109:400-407

[130] Kibirige D, Ssekitoleko R, Mutebi E, Worodria W. Overt diabetes mellitus among newly diagnosed Ugandan tuberculosis patients: a cross-sectional study. BMC Infect Dis 2013 Mar5;13:122

[131] Workneh MH, Bjune GA, Yimer SA. Prevalence and Associated Factors of Diabetes Mellitus among Tuberculosis Patients in South-Eastern Amhara Region, Ethiopia: A Cross Sectional Study. PloS one, 2016;11:1

[132] Boillat-Blanco N, Ramaiya KL, Mganga M, Minja LT, Bovet P, et al. Transient Hyperglycemia in Patients With Tuberculosis in Tanzania: Implications for Diabetes Screening Algorithms. J Infect Dis 2016;213:1163-72.

[133] Riza AL, Pearson F, Cesar Ugarte-Gil C, and others. Clinical management of concurrent diabetes and tuberculosis and the implications for patient services. The Lancet Diabetes & Endocrinology, Vol. 2, No. 9, p740–753.

[134] Samaras K. Prevalence and pathogenesis of diabetes mellitus in HIV-1 infection treated with combined antiretroviral therapy. JAIDS Journal of Acquired Immune Deficiency Syndromes 2009; 50:499-505.

[135] Nigatu Haregu T, Oldenburg B, Setswe G, Elliott J. Magnitude of diabetes comorbidity among people living with HIV: a systematic review. Int J Diabetes Res 2012;1:81-86

[136] Karamchand S, Leisegang R, Schomaker M, et al. Risk Factors for Incident Diabetes in a Cohort Taking First-Line Nonnucleoside Reverse Transcriptase Inhibitor-Based Antiretroviral Therapy. Lapadula. G, ed. Medicine. 2016;95(9):e2844. doi:10.1097/MD.0000000000002844.

[137] The Lancet Diabetes & Endocrinology. HIV and NCDs: the need to build stronger health systems. The Lancet Diabetes & Endocrinology, Vol. 4, No. 7, p549–550

[138] Anwara, O., Manafa, P., Chucks, E., Okeke, K., Alo, M., & Oka, G. (2015). The prevalence of diabetes mellitus in human immunodeficiency virus seropositive subject's co-infected with mycobacterium tuberculosis. Journal of AIDS and HIV Research, 7(8), 109-116.

[139] Faurholt-Jepsen D, Range N, PrayGod G et al. Diabetes is a risk factor for pulmonary tuberculosis: a case–control study from Mwanza, Tanzania. PLoS ONE 2011;6, e24215.

[140] Anoop Dinesh Shah, Claudia Langenberg, Eleni Rapsomaniki, Spiros Denaxas, Mar Pujades-Rodriguez, Chris P Gale, and others. Type 2 diabetes and incidence of cardiovascular diseases: a cohort study in 1·9 million people. The Lancet Diabetes & Endocrinology, Vol. 3, No. 2, p105–113

[141] Kaveh Hajifathalian, Peter Ueda, Yuan Lu, Mark Woodward, Alireza Ahmadvand, Carlos A Aguilar-Salinas, and others. A novel risk score to predict cardiovascular disease risk in national populations (Globorisk): a pooled analysis of prospective cohorts and health examination surveys. The Lancet Diabetes & Endocrinology, Vol. 3, No. 5, p339–355

[142] Atun R, Gale EAM. The challenge of diabetes in sub-Saharan Africa. The Lancet Diabetes & Endocrinology, Vol. 3, No. 9, p675–677.

[143] The Global Burden of Metabolic Risk Factors for Chronic Diseases Collaboration. Cardiovascular disease, chronic kidney disease, and diabetes mortality burden of cardiometabolic risk factors from 1980 to 2010: a comparative risk assessment. The Lancet Diabetes & Endocrinology, Vol. 2, No. 8, p634–647

[144] Gersh BJ, Sliwa K, Mayosi BM, Yusuf S. Novel therapeutic concepts: the epidemic of cardiovascular disease in the developing world – global implications. Eur Heart J. 2010;31:642– 648.

[145] Abegunde DO, Mathers CD, Adam T, Ortegon M, Strong K. The burden and costs of chronic diseases in low-income and middle-income countries. Lancet. 2007;370: 1929–1938.

[146] Gaziano TA. Cardiovascular disease in thedeveloping world and its cost-effective management. Circulation. 2005;112:3547–3553

[147] Addo J, Smeeth L, Leon DA. Hypertension in sub-Saharan Africa: a systematic review. Hypertension. 2007;50:1012–1018.

[148] Feven Ataklte, Sebhat Erqou, Stephen Kaptoge, Betiglu Taye,Justin B. Echouffo-Tcheugui, Andre P. Kengne. Burden of Undiagnosed Hypertension in Sub-Saharan Africa. A Systematic Review and Meta-Analysis; Hypertension.2015;65:291-298

[149] Hendriks M, Brewster L, Wit F, Bolarinwa O, et al. Cardiovascular disease prevention in rural Nigeria in the context of a community based health insurance scheme: QUality Improvement Cardiovascular care Kwara-I (QUICK-I). BMC Public Health. 2011;11(1):186.

[150] Dalal S, Beunza JJ, Volmink J. et al. Non-communicable diseases in sub-Saharan Africa: what we know. *Int J Epidemiol* 2011; **40:** 885-901.

[151] Atun R, et al. Universal health coverage in Turkey: Enhancement of equity. *Lancet* 2013; **382**: 65-99.

[152] WHO. Global Health Observatory Data Repository. Polices, strategies, and action plans: data by country. http://apps.who.int/gho/data/node.main.A907?lang=en (Accessed January 8, 2015).

[153] African Union Heads of State. Abuja declaration on HIV/AIDS, tuberculosis and other infectious diseases and plan of action. Available from: http://www.rollbackmalaria.org/microsites/wmd2011/abuja_declaration_final.html (Accessed April 12, 2016).

[154] WHO. Report State of Health Financing in the Africa Region. Geneva: World Health Organization, 2013.

[155] World Bank. Health Nutrition and Population Statistics http://data.worldbank.org/topic/health (Accessed February 9, 2015).

[156] World Bank. Health Nutrition and Population Statistics http://data.worldbank.org/topic/health (Accessed February 9, 2015).

[157] World Bank. Health Nutrition and Population Statistics http://data.worldbank.org/topic/health (Accessed February 9, 2015).

[158] World Health Organization. Global Health Observatory data repository. Health expenditure ratios, all countries, selected years: estimates by country. 2015. Available from: http://apps.who.int/gho/data/node.main.75.

[159] World Bank. Health Nutrition and Population Statistics http://data.worldbank.org/topic/health (Accessed February 9, 2015).

[160] Lagomarsino G, Garabrant A, Adyas A, Muga R, Otoo N. Universal Health Coverage 3: Moving towards universal health coverage: health insurance reforms in nine developing countries in Africa and Asia. Lancet 2012; 380:933–43.

[161] Mbanya JCN, Motala AA, Sobngwi E, Assah FK, Enoru ST. Diabetes in sub-Saharan Africa. Lancet 2010; 375:2254–66.

[162] Levitt NS. Diabetes in Africa: epidemiology, management and healthcare challenges. Heart 2008; 94:1376–82.

[163] Wang Q, Fu AZ, Brenner S, Kalmus O, Banda HT, De Allegri M (2015) Out-of-Pocket Expenditure on Chronic Non-Communicable Diseases in Sub-Saharan Africa: The Case of Rural Malawi. PLoS ONE **10**(1): e0116897. doi: 10.1371/ journal.pone.0116897

[164] Hall V, Thomsen RW, Henriksen O, Lohse N. Diabetes in Sub Saharan Africa 1999-2011: Epidemiology and public health implications. A systematic review. BMC Public Health 2011; 11:564.

[165] International Diabetes Federation. IDF Diabetes Atlas 6th Edition, 2014 Update. http://www.idf.org/atlasmap/atlasmap (Accessed March 5, 2015).

[166] World Bank. Country and Lending Groups. http://data.worldbank.org/about/country-and-lending-groups (Accessed March 5, 2015).

[167] Global Health Workforce Alliance, World Health Organization. A Universal Truth: No health without a workforce. Geneva: World Health Organization, 2013.

[168] Mullan F. et al. Medical schools in sub-Saharan Africa. *Lancet* 2011; 377: 1113-1121.

[169] Scheffler et al Estimates of healthcare professional shortages in SSA by 2015. *Health Affairs* 2009; **28**(5); w849-w862.

[170] Mullan F. et al. Medical schools in sub-Saharan Africa. *Lancet* 2011; 377: 1113-1121.

[171] Global Health Workforce Alliance, World Health Organization. A Universal Truth: No health without a workforce. Geneva: World Health Organization, 2013.

[172] Global Health Workforce Alliance, World Health Organization. A Universal Truth: No health without a workforce. Geneva: World Health Organization, 2013.

[173] Mullan F, Frehywot S. Non-physician clinicians in 47 sub-Saharan African countries. *Lancet,* 2007; **370**: 2158-2163.

[174] Celletti F. et al. Can the deployment of community health workers for the delivery of HIV services represent an effective and sustainable response to health workforce shortages? Results of a multicountry study. *AIDS* 2010**; suppl 1**, S45-S57.

[175] Mwai GW, Mburu G, Torpey K et al. Role and outcomes of community health workers in HIV care in sub-Saharan Africa: a systematic review. *J Int AIDS Society* 2013; **16**: 18586.

[176] WHO. Global Status Report on Noncommunicable Diseases 2010. Geneva: World Health Organization, 2011.

[177] WHO. Health Statistics and Information Systems: Service Area Readiness Assessment, 2014. http://www.who.int/healthinfo/systems/sara_reports/en/ (Accessed April 12, 2015).

[178] WHO. Health Statistics and Information Systems: Service Area Readiness Assessment, 2014. http://www.who.int/entity/healthinfo/systems/sara_introduction/en/index.html (Accessed April 12, 2015).

[179] Beran D, Yudkin JS. Looking beyond the issue of access to insulin: What is needed for proper diabetes care in resource poor settings. *Diabetes Research and Clin Prac* 2010; *88: 217-221.*

[180] WHO. Global Health Observatory Data Repository. Polices, strategies, and action plans: data by country. http://apps.who.int/gho/data/node.main.A911?lang=en (Accessed January 8, 2015).

[181] WHO. Global action plan for the prevention and control of noncommunicable diseases 2013-2020. Geneva: World Health Organization, 2013.

[182] Beran D, Ewen M, Laing R. Constraints and challenges in access to insulin: a global perspective. *The Lancet Diabetes & Endocrinology*.

[183] Peck R, Mghamba J, Vanobberghen F, et al. Preparedness of Tanzanian health facilities for outpatient primary care of hypertension and diabetes: a cross-sectional survey. *The Lancet Global health* 2014; **2**(5): e285-e92.

[184] Beran D, Yudkin JS. Looking beyond the issue of access to insulin: what is needed for proper diabetes care in resource poor settings. *Diabetes Res Clin Pract* 2010; **88**(3): 217-21.

[185] Cameron A, Ewen M, Ross-Degnan D, Ball D, Laing R. Medicine prices, availability, and affordability in 36 developing and middle-income countries: a secondary analysis. *Lancet* 2009; **373**(9659): 240-9.

[186] Mendis S, Fukino K, Cameron A, et al. The availability and affordability of selected essential medicines for chronic diseases in six low- and middle-income countries. *Bulletin of the World Health Organization* 2007; **85**(4): 279-88.

[187] Beran D, Yudkin J, de Courten M. Access to care for patients with insulin-requiring diabetes in developing countries: case studies of Mozambique and Zambia. *Diabetes Care* 2005; **28**(9): 2136-40.

[188] Kaplan W, Sharma A. Global trade in insulin and its public health consequences: Technical Report July 2015. Amsterdam: Health Action International, 2015.

[189] Direction de la Programmation et de la Prospective du Ministère de la Santé du Bénin. Rapport d'enquête sur les services de sante: Disponibilité et capacité opérationnelle des

services de santé au Bénin. Cotonou: Ministère de la Santé du Bénin and World Health Organization, 2013.

[190] Ministère de la Santé Burkina Faso. Enquête nationale sur les prestations des services de sante et la qualité des données sanitaires Ouadadougou: Ministère de la Santé Burkina Faso, 2014.

[191] Government of Sierra Leone Ministry of Health & Sanitation. Sierra Leone Service Availability and Readiness Assessment. Freetown: Government of Sierra Leone Ministry of Health & Sanitation, 2012.

[192] République Islamique de Mauritanie. Indice de disponibilité et de capacité opérationnelle des services (SARA). Nouakchott: République Islamique de Mauritanie, 2013.

[193] Ministry of Health and Social Welfare Tanzania. Tanzania Service Availability And Readiness Assessment (SARA) Dar es Salaam: Ministry of Health and Social Welfare Tanzania, 2013.

[194] Ministry of Health Uganda. Uganda Services Availability and Readiness Assessment 2013: Summary Report. Kampala: Ministry of Health Uganda, 2013.

[195] Ministry of Health Republic of Zambia. Zambia Services Availability and Readiness Assessment 2010: Summary Report. Lusaka: Ministry of Health Republic of Zambia, 2010.

[196] Ministry of Health. Kenya Service Availability and Readiness Assessment Mapping. Nairobi: Ministry of Health, 2013.

[197] Ministère de la Santé Publique République Démocratique du Congo. Indice de disponibilité et de capacité opérationnelle des services (SARA), 2014. Kinshasa: Ministère de la Santé Publique, République Démocratique du Congo, 2014.

[198] MSH. International Drug Price Indicator Guide. 2015. http://erc.msh.org/mainpage.cfm?file=1.0.htm&module=dmp&language=english (accessed 22 August 2015).

[199] Beran D, Ewen M, Laing R, Frye J. Price analysis of Management Sciences for Health International Drug Price Indicator Guide. Amsterdam: Addressing the Challenge and Constraints of Insulin Sources and Supply Study (in press).

[200] WHO Collaborating Centre for Drug Statistics Methodology. Drugs used in diabetes. 2013. http://www.whocc.no/atc_ddd_index/?code=A10A (accessed 6 February 2015).

[201] HAI. Database of medicine prices, availability, affordability and price components. 2012. http://www.haiweb.org/MedPriceDatabase/ (accessed 9 July 2015)

[202] Beran D, Silva Matos C, Yudkin JS. The Diabetes UK Mozambique Twinning Programme. Results of improvements in diabetes care in Mozambique: a reassessment 6 years later using the Rapid Assessment Protocol for Insulin Access. *Diabet Med* 2010; **27**(8): 855-61.

[203] ACCISS Study. Price survey of insulin. Amsterdam: Addressing the Challenge and Constraints of Insulin Sources and Supply Study, in publication.

[204] World Bank. Global Poverty Line Update. 2015. http://www.worldbank.org/en/topic/poverty/brief/global-poverty-line-faq (accessed 12 January 2016).

[205] Beran D, Ewen M, Laing R. Price analysis of Management Sciences for Health International Drug Price Indicator Guide. Amsterdam: Health Action International, 2015.

[206] Beran D, Yudkin JS. Diabetes care in sub-Saharan Africa. *Lancet* 2006; **368**(9548): 1689-95.

[207] World Bank. Service Delivery Indicators Survey. http://datatopics.worldbank.org/sdi/ (Accessed April 13, 2016)

[208] World Bank. Service Delivery Indicators Survey. Methodology. http://siteresources.worldbank.org/AFRICAEXT/Resources/SDI_methodology_revision.pdf (Accessed April 13, 2016)

[209] World Bank. Service Delivery Indicators Survey. Survey Instruments. http://siteresources.worldbank.org/AFRICAEXT/Resources/SDI_instruments_Kenya.pdf (Accessed April 13, 2016)

[210] Kenneth L. Leonard and Melkiory C. Masatu. Variations In The Quality Of Care Accessible To Rural Communities In Tanzania *Health Affairs* published online March 27, 2007

[211] Das, Jishnu, Jeffrey Hammer and Kenneth Leonard. 2008. "The Quality of Medical Advice in Low-Income Countries." *Journal of Economic Perspectives*, 22(2): 93-114.

[212] Bowser D, Sparkes SP, Mitchell A, Bossert TJ, Bärnighausen T, Gedik G, Atun R. Global Fund investments in human resources for health: innovations and missed opportunities for health systems strengthening. *Health Policy and Planning* 2014; **29**: 986-997.

[213] Brown JB, Ramaiya K, Besancon S et al. Use of Medical Services and Medicines Attributable to Diabetes in Sub-Saharan Africa. *PLoS ONE* 2014; **9**(9): e106716. doi:10.1371/journal.pone.0106716

[214] Tudor Car L, Brusamento S, Elmoniry H, van Velthoven M, Pape UJ, Welch V, Tugwell P, Majeed A, Car J, Atun R. The uptake of integrated perinatal prevention of mother-to-child transmission programs in low- and middle-income countries: a systematic review. PLoS One 2013; 8(3):e56550

[215] Haber N, Pillay D, Porter K, Barnighausen T. Constructing the cascade of HIV care: methods for measurement. *Curr Opin HIV AIDS* 2016; **11**(1): 102-8.

[216] Ali MK, Bullard KM, Gregg EW, Del Rio C. A cascade of care for diabetes in the United States: visualizing the gaps. *Ann Intern Med* 2014; **161**(10): 681-9.

[217] World Health Organization. The STEPS Instrument and Support Materials. 2015. http://www.who.int/chp/steps/instrument/en/ (accessed December 11 2015).

[218] Riley L, Guthold R, Cowan M, et al. The World Health Organization STEPwise Approach to Noncommunicable Disease Risk-Factor Surveillance: Methods, Challenges, and Opportunities. *American journal of public health* 2016; **106**(1): 74-8.

[219] Namibia Ministry of Health and Social Services. Namibia Demographic and Health Survey 2013. Windhoek, Namibia, 2013.

[220] Labadarios D, Shisana O, Rehle T, Simbayi L. SANHANES: a unique survey series in the health landscape. *S Afr Med J* 2014; **104**(10): 675-6.

[221] American Diabetes Association. Standards of medical care in diabetes--2014. *Diabetes Care* 2014; **37 Suppl 1**: S14-80.

[222] Cameron A, Ewen M, Ross-Degnan D, Ball D, Laing R. Medicine prices, availability, and affordability in 36 developing and middle-income countries: a secondary analysis. Lancet 2009; 373(9659): 240-9.

[223] Chale SS, Swai ABM, Mujinja PGM, McLarty DG. Must Diabetes Be a Fatal Disease in Africa? Study of Costs of Treatment. British Medical Journal. 1992;304:1215–18.

[224] Nkegoum AV. 2002. "Coût direct et indirect du diabéte en l'absence de complications chroniques a Yaoundé, Cameroun." MD thesis, University of Yaoundé I, Cameroon. Cited in Mbanya JC and Ramiaya K. Chapter 19. Diabetes Mellitus. In Disease and Mortality in Sub-Saharan Africa. 2nd edition. Jamison DT, Feachem RG, Makgoba MW, et al., editors. Washington (DC): World Bank; 2006. http://www.ncbi.nlm.nih.gov/books/NBK2291/ (Accessed 14 April, 2016)

[225] International Diabetes Federation. IDF Atlas 2015. Brussels, Belgium: International Diabetes Federation, 2015. http://www.diabetesatlas.org (Accessed 14 April, 2016)

[226] Bommer C, Heesemann E, Sagalova V, Manne-Goehler J, Atun R, Bärnighausen T, Vollmer S. The Global Economic Burden of Diabetes: A Cost-of-Illness Study. Mimeo, 2016.

[227] Hall V, Thomsen RW, Henriksen O, Lohse N. Diabetes in Sub Saharan Africa 1999-2011: epidemiology and public health implications. A systematic review. *BMC public health* 2011; *11*(1): 1.

[228] Khuwaja AK, Khowaja LA, Cosgrove P. The economic costs of diabetes in developing countries: some concerns and recommendations. Diabetologia 2010; 53(2): 389-390.

[229] Mutlu F, Bener A, Eliyan A. Delghan H, Nofal E, Shalabi L, Wadi N. Projection of diabetes burden through 2025 and contributing risk factors of changing disease prevalence: an emerging public health problem. Journal of Diabetes & Metabolism, 2014.

[230] World Health Organization. Global Health Observatory data repository. Health expenditure ratios, all countries, selected years: estimates by country. 2015. Available from: http://apps.who.int/gho/data/node.main.75. (Accessed 14 April, 2016)

[231] Atun R, Gale EA. The challenge of diabetes in sub-Saharan Africa. The Lancet Diabetes & Endocrinology 2015; 3(9): 675-677.

[232] Bastida E, Pagán JA. The impact of diabetes on adult employment and earnings of Mexican Americans: Findings from a community based study. Health Econ 2002; 11:403–13.

[233] Brown HS, Pérez A, Yarnell LM, Pagán JA, Hanis CL, Fisher-Hoch SP, McCormick JB. Diabetes and Employment Productivity: Does Diabetes Management Matter? Am J Manag Care 2011; 17:569–76.

[234] Fletcher M, Richards MR. Diabetes's 'Health Shock' To Schooling And Earnings: Increased Dropout Rates And Lower Wages And Employment In Young Adults. Health Affairs 2012; 31:27–34.

[235] Kahn ME, Health and Labor Market Performance: The Case of Diabetes. Journal of Labor Economics 1998; 16:878–99.

[236] Minor T. The effect of diabetes on female labor force decisions: new evidence from the National Health Interview Survey. Health Econ 2011; 20:1468–86.

[237] Minor T. An investigation into the effect of type I and type II diabetes duration on employment and wages. Economics and Human Biology 2013; 11:534–44.

[238] Harris A. Diabetes, Cardiovascular Disease and Labour Force Participation in Australia: An Endogenous Multivariate Probit Analysis of Clinical Prevalence Data. The Economic Record 2009; 85:472–84.

[239] Zhang X, Zhao X, Harris A. Chronic diseases and labour force participation in Australia. Journal of Health Economics 2009; 28:91–108.

[240] Latif E. The impact of diabetes on employment in Canada. Health Econ 2009; 18:577–89.

[241] Lin SJ. Estimating the impact of diabetes on employment in Taiwan. Economic Bulletin 2011; 31: 3089–102.

[242] Seuring T, Goryakin Y, Suhrcke M. The impact of diabetes on employment in Mexico. Economics and Human Biology 2015b; 18:85–100.

[243] Tunceli K, Bradley CJ, Nerenz D, Williams LK, Pladevall M, Lafata JE. The Impact of Diabetes on Employment and Work Productivity. Diabetes Care 2005; 28:2662–7.

[244]

[245] Škerjanc A. Sickness absence in diabetic employees. Occup Environ Med 2001; 58:432–6.

[246] Kraut A, Walld R, Tate R, Mustard C. Impact of Diabetes on Employment and Income in Manitoba, Canada. Diabetes Care 2001; 24:64–8.

[247] International Diabetes Federation. IDF Diabetes, 7th ed. Brussels, Belgium: International Diabetes Federation, 2015. http://www.diabetesatlas.org (Accessed 14 April, 2016)

[248] The World Bank. World Development Indicators. The World Bank Group, 2016. http://data.worldbank.org/data-catalog/world-development-indicators (Accessed 14 April, 2016)

[249] International Diabetes Federation. IDF Diabetes, 3rd ed. Brussels, Belgium: International Diabetes Federation, 2006.: http://www.diabetesatlas.org (Accessed 14 April, 2016)

[250] United Nations, Department of Economic and Social Affairs, Population Division (2015). World Population Prospects: The 2015 Revision, CD-ROM Edition.

[251] United Nations, Department of Economic and Social Affairs, Population Division (2014). World Urbanization Prospects: The 2014 Revision, CD-ROM Edition.

[252] Assah FK, Ekelund U, Brage S, Mbanya JC, Wareham NJ. Urbanization, physical activity, and metabolic health in sub-Saharan Africa. Diabetes Care 2011; 34:491–6.

[253] Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. UK Prospective Diabetes Study Group. *BMJ*. 1998;317(7160):703-713.

[254] Zoungas S, Chalmers J, Neal B, et al. Follow-up of Blood-Pressure Lowering and Glucose Control in Type 2 Diabetes. *New England Journal of Medicine*. 2014;371(15):1392-1406. doi:10.1056/NEJMoa1407963.

[255] Glucose Control and Vascular Complications in Veterans with Type 2 Diabetes — NEJM. http://www.nejm.org/doi/full/10.1056/nejmoa0808431. Accessed January 27, 2016

[256] World Health Organization. *Package of Essential Noncommunicable (PEN) Disease Interventions for Primary Health Care in Low-Resource Settings*. Geneva: WHO; 2013.

[257] Sussman J, Vijan S, Hayward R. Using benefit-based tailored treatment to improve the use of antihypertensive medications. *Circulation*. 2013;128(21):2309-2317. doi:10.1161/CIRCULATIONAHA.113.002290.

[258] Hayward RA, Krumholz HM, Zulman DM, Timbie JW, Vijan S. Optimizing statin treatment for primary prevention of coronary artery disease. Annals of Internal Medicine. 2010;152:69-77.

[259] Mancia G, Fagard R, Narkiewicz K, Redon J, Zanchetti A, Böhm M, Christiaens T, Cifkova R, De Backer G, Dominiczak A, others. 2013 ESH/ESC Guidelines for the management of arterial hypertension The Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). Eur Heart J. 2013;34:2159–2219.

[260] Sundström J, Arima H, Woodward M, et al. Blood pressure-lowering treatment based on cardiovascular risk: a meta-analysis of individual patient data. *Lancet (London, England)*. 2014;384(9943):591-598. doi:10.1016/S0140-6736(14)61212-5.

[261] Basu S, Yudkin JS, Sussman J, Millett C, Hayward R. Alternative Strategies to Achieve Cardiovascular Mortality Goals in China and India. Circulation (2016) **133:** 840-848.

[262] Crampin AC, Dube A, Mboma S, et al. Profile: The Karonga health and demographic surveillance system. Int. J. Epidemiology 2010; 41 (3): 676-685.

[263] WHO Study on global AGEing and adult health (SAGE). http://www.who.int/healthinfo/sage/en/ (Accessed April 14,2016)

[264] American Diabetes Association. Dyslipidemia Management in Adults With Diabetes Diabetes Care 2004; 27 (suppl 1): s68-s71. doi:10.2337/diacare.27.2007.S68 http://care.diabetesjournals.org/content/27/suppl_1/s68.full

[265] American Diabetes Association. Standards of Medical Care in Diabetes. Diabetes Care 2014; 37: S14-S80.

[266] Inzucchi, S. The Yale Diabetes Center's Diabetes Facts and Guidelines, 11th edition. New Haven: Yale Diabetes Center. 2011.

[267] Salomon JA, Vos T, Hogan DR, et al. Common values in assessing health outcomes from disease and injury: disability weights measurement study for the Global Burden of Disease Study 2010. Lancet 2012; 380: 2129–43.

[268] Management Sciences for Health. *International Drug Price Indicator Guide*. Cambridge, MA: Management Sciences for Health; 2015. http://www.msh.org/sites/msh.org/files/international-drug-price-indicator-guide.pdf. Accessed January 28, 2015.

[269] World Health Organization. *Choosing Interventions That Are Cost Effective (WHO-CHOICE)*. Geneva: WHO; 2010. http://www.who.int/choice/publications/p_2003_generalised_cea.pdf (Accessed April 15,2016)

[270] Atun RA, Lennox-Chhugani N, Drobniewski F, Samyshkin YA, Coker RJ. A framework and toolkit for capturing the communicable disease programmes within health systems: tuberculosis control as an illustrative example. *European journal of public health* 2004; 14(3): 267-73.

[271] Atun RA, Samyshkin YA, Drobniewski F, et al. Barriers to sustainable tuberculosis control in the Russian Federation health system. Bulletin of the World Health Organization 2005; 83 (3); 217-23.

[272] Shigayeva A, Atun R, McKee M, Coker R. Health systems, communicable diseases and integration. *Health policy and planning* 2010; 25 Suppl 1: i4-20.

[273] Atun RA, McKee M, Drobniewski F, Coker R. Analysis of how health system context shapes responses to the control of human immunodeficiency virus: case studies from the Russian Federation. Bulletin of the World Health Organisation 2005; 83(10): 730-8.

[274] Atun R, Lazarus JV, Van Damme W, Coker R. Interactions between critical health system functions and HIV/AIDS, tuberculosis and malaria programmes. *Health Policy and Planning* 2010; 25 (Suppl 1): i1-i3.

[275] Jenkins R, Lancashire S, McDaid D, et al. Mental health reform in the Russian Federation–an integrated approach to achieve social inclusion and recovery. *Bulletin of the World Health Organization* 2007; 85:858-66.

[276] Atun R, Pothapregada SK, Kwansah J, Degbotse D, Lazarus JV. Critical Interactions Between the Global Fund–Supported HIV Programs and the Health System in Ghana. J Acquir Immune Defic Syndr. 2011: 57 (Supplement 2); S72-S76.

[277] Unwin N, Mugusi F, Aspray T, Whiting D, Edwards R, Mbanya J et al. Tackling the emerging pandemic of non-communicable diseases in sub-Saharan Africa. Public Health. 1999;113(3):141-146.

[278] Watkins P. Delivering care for diabetes in Ethiopia. Transactions of the Royal Society of Tropical Medicine and Hygiene. 1999;93(4):355-356.

[279] Mamo Y, Seid E, Adams S, Gardiner A, Parry E. A primary healthcare approach to the management of chronic disease in Ethiopia: an example for other countries. Clinical Medicine. 2007;7(3):228-231

[280] Labhardt N, Balo J, Ndam M, Manga E, Stoll B. Improved retention rates with low-cost interventions in hypertension and diabetes management in a rural African environment of nurse-led care: a cluster-randomised trial. Tropical Medicine & International Health. 2011;16(10):1276-1284.

[281] Sobry A, Kizito W, Van den Bergh R, Tayler-Smith K, Isaakidis P, Cheti E et al. Caseload, management and treatment outcomes of patients with hypertension and/or diabetes mellitus in a primary health care programme in an informal setting. Trop Med Int Health. 2013;19(1):47-57

[282] Katz I, Schneider H, Shezi Z, Mdleleni G, Gerntholtz T, Butler O et al. Managing type 2 diabetes in Soweto—The South African Chronic Disease Outreach Program experience. Primary Care Diabetes. 2009;3(3):157-164.

[283] Distiller L, Brown M, Joffe B, Kramer B. Striving for the impossible dream: a community-based multi-practice collaborative model of diabetes management. Diabetic Medicine. 2010;27(2):197-202.

[284] Gill G, Price C, Shandu D, Dedicoat M, Wilkinson D. An effective system of nurse-led diabetes care in rural Africa. Diabetic Medicine 2008 ;25(5):606-611.

[285] Price C, Shandu D, Dedicoat M, Wilkinson D, Gill G. Long-term glycaemic outcome of structured nurse-led diabetes care in rural Africa. QJM 2011;104(7):571-574.

[286] Kengne A, Fezeu L, Sobngwi E, Awah P, Aspray T, Unwin N et al. Type 2 diabetes management in nurse-led primary healthcare settings in urban and rural Cameroon. Primary Care Diabetes. 2009;3(3):181-188.

[287] Ndou T, van Zyl G, Hlahane S, Goudge J. A rapid assessment of a community health worker pilot programme to improve the management of hypertension and diabetes in Emfuleni sub-district of Gauteng Province, South Africa. Global Health Action. 2013;6(0).

[288] Labhardt N, Balo J, Ndam M, Grimm J, Manga E. Task shifting to non-physician clinicians for integrated management of hypertension and diabetes in rural Cameroon: a programme assessment at two years. BMC Health Services Research 2010;10(1):339.

[289] Mbeh G, Edwards R, Ngufor G, Assah F, Fezeu L, Mbanya J. Traditional healers and diabetes: results from a pilot project to train traditional healers to provide health education and appropriate health care practices for diabetes patients in Cameroon. Global Health Promotion 2010;17(2 Suppl):17-26.

[290] Joubert P, Sebata P, Bam W, Skene D. Home urinary glucose testing. Its impact on a Third World diabetic population. South African Medical Journal 1984; 65(18): 731-3.

[291] Pastakia S, Karwa R, Kahn C, Nyabundi J. The Evolution of Diabetes Care in the Rural, Resource-Constrained Setting of Western Kenya. Annals of Pharmacotherapy 2011;45(6):721-726.

[292] Gessler N, Labhard N, Stolt P, et al. The lesson of Monsieur Nouma: Effects of a culturally sensitive communication tool to improve health-seeking behavior in rural Cameroon. Patient Education and Counseling. 2012;87(3):343-350.

[293] Mash RJ, Rhode H, Zwaranstein M, et al. Effectiveness of a group diabetes education programme in under-served communities in South Africa: a pragmatic cluster randomized controlled trial. Diabetic Medicine 2014; 31: 987-993.

[294] Van der Does A, Mash R. Evaluation of the "Take Five School": An education programme for people with Type 2 Diabetes in the Western Cape, South Africa. Primary Care Diabetes 2013;7(4):289-295.

[295] Mukama L, Moran A, Nyindo M, Philemon R, Msuya L. Improved glycemic control and acute complications among children with type 1 diabetes mellitus in Moshi, Tanzania. Pediatric Diabetes. 2012

[296] Beran D, Silva Matos C, Yudkin J. The Diabetes UK Mozambique Twinning Programme. Results of improvements in diabetes care in Mozambique: a reassessment 6 years later using the Rapid Assessment Protocol for Insulin Access. Diabetic Medicine 2010;27(8):855-861.

[297] Abbas Z, Lutale J, Bakker K, Baker N, Archibald L. The 'Step by Step' Diabetic Foot Project in Tanzania: a model for improving patient outcomes in less-developed countries. International Wound Journal 2011 ;8(2):169-175.

[298] Windus D, Ladenson J, Merrins C, Seyoum M, Windus D, Morin S et al. Impact of a Multidisciplinary Intervention for Diabetes in Eritrea. Clinical Chemistry 2007; 53(11):1954-1959.

[299] Amoah A, Owusu S, Acheampong J, Agyenim-Boateng K, Asare H, Owusu A et al. A national diabetes care and education programme: the Ghana model. Diabetes Research and Clinical Practice 2000;49(2-3):149-157.

[300] MakkiAwouda F, Elmukashfi T, Hag Al-Tom S. Designing an Educational and Training Program for Diabetes Health Educators at Diabetic Health Centers, Khartoum State, Sudan; 2007-2010. Global Journal of Health Science. 2013;5(5).

[301] Kouematchoua Tchuitcheu G, Rienhoff O. Options for Diabetes Management in Sub-Saharan Africa with an Electronic Medical Record System. Methods of Information in Medicine 2009;50(1):11-22.

[302] Steyn K, Lombard C, Gwebushe N, Fourie J, Everett-Murphy K, Zwarenstein M et al. Implementation of national guidelines, incorporated within structured diabetes and hypertension records at primary level care in Cape Town, South Africa: a randomised controlled trial. Global Health Action 2013;6(0).

[303] Allain T, van Oosterhout J, Douglas G, Joukes S, Gadabu O, Darts C et al. Applying lessons learnt from the 'DOTS' Tuberculosis Model to monitoring and evaluating persons with diabetes mellitus in Blantyre, Malawi. Tropical Medicine & International Health 2011;16(9):1077-1084.

[304] Govindasamy D, Kranzer K, van Schaik N, Noubary F, Wood R, Walensky R et al. Linkage to HIV, TB and Non-Communicable Disease Care from a Mobile Testing Unit in Cape Town, South Africa. PLoS ONE 2013;8(11):e80017.

[305] Chamie G, Kwarisiima D, Clark T, Kabami J, Jain V, Geng E et al. Leveraging Rapid Community-Based HIV Testing Campaigns for Non-Communicable Diseases in Rural Uganda. PLoS ONE 2012;7(8):e43400.

[306] Pastakia S, Ali S, Kamano J, Akwanalo C, Ndege S, Buckwalter V et al. Screening for diabetes and hypertension in a rural low income setting in western Kenya utilizing home-based and community-based strategies. Globalization and Health 2013;9(1):21.

[307] International Diabetes Federation. IDF Diabetes Atlas-7th Edition; Brussels, 2015. http://www.idf.org/membership/afr/botswana accessed April 25, 2016.

[308] Lancet D&E Botswana case study

309. The World Factbook. Ghana. Central Intelligence Agency. Accessed March 10, 2016. https://www.cia.gov/library/publications/the-world-factbook/geos/print_gh.html

[310] International Diabetes Federation. IDF Diabetes Atlas-7th Edition; Brussels, 2015. http://www.idf.org/membership/afr/ghana Accessed April 25, 2016.

[311] Ministry of Health Ghana. 2012. Strategy for the Management, Prevention, and Control of Chronic Non-Communicable Diseases in Ghana 2013-2017. Ministry of Health.

[312] NHIS 2013 annual report. Http://www.nhis.gov.gh/files/2013%20annual%20report-final%20ver%2029.09.14.pdf. Assessed 4/6/2016

[313]Ministry of Health Ghana. (2013). Strategy for the management, prevention and control of chronic non- communicable diseases in ghana 2014-2017. Ministry of health

[314] Saleh, Karima. 2013. The Health Sector in Ghana: A Comprehensive Assessment. Washington, DC: World Bank. doi: 10.1596/978-0-8213-9599-8.

[315] Lancet D&E Ghana case study

[316] Lancet D&E Ethiopia case study

317 Ministry of Health, Federal Democratic Republic of Ethiopia, Health Sector Transformation Plan, 2015-2020, August 2015.

[318] International Diabetes Federation. IDF Diabetes Atlas-7th Edition; Brussels, 2015. http://www.idf.org/membership/afr/ethiopia accessed April 25, 2016.

[319] Ethiopia Service Provision Assessment Plus Survey 2014. Ethiopian Public Health Institute, Addis Ababa, Ethiopia, Federal Ministry of Health, Addis Ababa, Ethiopia, and ICF International, Maryland, USA; 2014. http://www.ephi.gov.et/images/pictures/FINAL%20Key%20finding%20SPA+%20%20-%20Aug%2017%20-%202015.pdf Accessed April 25, 2016.

[320] Abebe SM, Berhane Y, Worku A et al. Diabetes mellitus in North West Ethiopia: a community based study. BMC Public Health. 2014; 14: 97. Published online Jan 30, 2014. doi: 10.1186/1471-2458-14-97

[321] International Diabetes Federation. IDF Diabetes Atlas-7th Edition; Brussels, 2015. http://www.idf.org/membership/afr/kenya Accessed April 25, 2016.
[322] Institute for Health Metrics and Evaluation (IHME). Health Service Provision in Kenya: Assessing Facility Capacity, Costs of Care, and Patient Perspectives. Seattle, WA: IHME, 2014.

[323] Lancet D&E Kenya case study

[324] Kenya National Diabetes Programme WDF09-436. http://www.worlddiabetesfoundation.org/projects/kenya-wdf09-436 Retrieved April 25, 2016.
[325] Pastakia SD, Karwa R, Kahn CB, Nyabundi JS. The evolution of diabetes care in the rural, resource-constrained setting of western Kenya. The Annals of Pharmacotherapy. 2011;45(6):721-6.

[326] International Diabetes Federation. IDF Diabetes Atlas-7th Edition; Brussels, 2015. http://www.idf.org/membership/afr/malawi Accessed April 25, 2016.

[327] Msyamboza KP, Mvula CJ, Kathyola D. Prevalence and correlates of diabetes mellitus in Malawi: population-based national NCD STEPS survey BMC Endocrine Disorders 2014, 14:41.

[328] Cohen DB, Allain TJ, Glover S, Chimbayo D, Dzamalala H, Hofland HW, Banda NPK, Zijlstra EE: A survey of the management, control, and complications of diabetes mellitus in patients attending a diabetes clinic in Blantyre, Malawi, an area of high HIV prevalence. Am J Trop Med Hyg. 2010, 83 (3): 575-10.4269/ajtmh.2010.10-0104.

[329] Assayed AA, Muula AS, Nyirenda MJ. The quality of care of diabetic patients in rural Malawi: A case of Mangochi district. Malawi Medical Journal 2014; 26 (4): 109-114.

[330] Lancet D&E Malawi case study

[331] Alain TJ, van Ooosterhout JJ, Douglas GP, et al. Applying lessons learnt from the 'DOTS' Tuberculosis Model to monitoring and evaluating persons with diabetes mellitus in Blantyre, Malawi. Tropical Medicine and International Health 2011; 16 (9): 1077–1084.

[332] Bui TD, Kadzakumanja O, Munthali C. Mobilizing for the Lilongwe Diabetes Peer Support Programme in Malawi. Malawi Med J. 2014; 26(4): 124–125.

[333] International Diabetes Federation. IDF Diabetes Atlas-7th Edition; Brussels, 2015. http://www.idf.org/membership/afr/mali Accessed April 25, 2016.

[334] Plan stratégique national de lutte contre les Maladies Non Transmissibles (MNT) 2015 – 2019. République du Mali. Octobre 2014.

[335] Republic of Rwanda, Ministry of Health. (2012). Fourth Population and Housing Consensus. Retrieved from: http://statistics.gov.rw/survey-period/fourth-population-and-housing-census-2012.

[336] National Institute of Statistics of Rwanda. (2015). *Rwanda Statistical year book 2015*. Retrieved from: http://statistics.gov.rw/publication/statistical-yearbook-2015

[337] Makaka A, Breen S, Binagwaho A. Universal health coverage in Rwanda: A report of innovations to increase enrolment in community-based health insurance. *The Lancet 2015; 380:* (S7).

[338] National Institute of Statistics of Rwanda (2015). *Rwanda Statistical year book 2015*. Retrieved from: http://statistics.gov.rw/publication/statistical-yearbook-2015

[339] Rwanda STEPS Noncommunicable Disease Risk Factor Survey, 2012-2013 Report. Republic of Rwanda. Ministry of Health, Kigali, 2015. http://www.who.int/chp/steps/Rwanda_2012_STEPS_Report.pdf?ua=1

[340] Republic of Rwanda, Ministry of Health. (2015). *The Health Sector Policy*. Kigali, Rwanda. http://www.moh.gov.rw/fileadmin/templates/policies/Health_Sector_Policy___19th_January_2015.pdf (accessed July 18, 2016)

[341] Binagwaho A, Kyamanywa P, Farmer PE, et al. The human resources for health program in Rwanda—a new partnership. *New England Journal of Medicine;2013: 369*(21): 2054-2059.

[342] Republic of Rwanda, Ministry of Health. (2016). *Diabetes Prevention and Control in Rwanda*. Unpublished document. Kigali, Rwanda.

[343] Marshall SL, Edidin DV, Arena VC, et al. Glucose control in Rwandan youth with type 1 diabetes following establishment of systematic HbA1c based, care and education. *Diabetes Res Clin Pract. 2015; 107*:113-122.

[344] Marshall SL, Edidin D, Arena VC, et al. Prevalence and incidence of clinically recognized cases of Type 1 diabetes in children and adolescents in Rwanda, Africa. Diabet Med. 2015; 32(9):1186-92. DOI: 10.1111/dme.12701.

[345] International Diabetes Federation. (2013). *IDF Diabetes Atlas*. 6th Edition. Brussels.

[346] Rwanda Diabetes Association. (2016). *Children and Youth <25 in Rwanda with Diabetes, Raw Data*. Unpublished raw data. Kigali, Rwanda.

[347] World Bank. World Development Indicators 2014. World Bank. Wasdhington D.C. 2014.

[348] The United Republic of Tanzania. Ministry of Health and Social Welfare. HMIS Report 2011.

[349] Msemburi W, Pillay-van Wyk V, Dorrington RE et al.. Second national burden of disease study for South Africa: Cause-of-death profile for South Africa, 1997–2010. Cape Town: South African Medical Research Council, 2014.

[350] Bertram MY, Jaswal AV, Van Wyk VP, Levitt NS, Hofman KJ. The non-fatal disease burden caused by type 2 diabetes in South Africa, 2009. *Glob Health Action* 2013; *6*(Suppl 1): 206-212).

[351] Peer N, Steyn K, Lombard C, Lambert EV, Vythilingum B, Levitt NS. Rising Diabetes Prevalence among Urban-Dwelling Black South Africans. PLoS One. **2012**;7(9):e43336. Epub **2012** Sep 4.

[352] Amod A, Ascott-Evans BH, Berg GI et al. Guideline Committee. The 2012 SEMDSA Guideline for the Management of Type 2 Diabetes (Revised). JEMDSA 2012; 17(2)(Supplement 1): S1-S95. http://www.semdsa.org.za/images/2012_SEMDSA_Guideline_July_FINAL.pdf (accessed July 18, 2016)

[353] Republic of South Africa. Essential Drugs Programme. Primary Healthcare Standard Treatment Guidelines and Essential Medicines List. 5th ed. Republic of South Africa: National Department of Health; 2014. http://www.kznhealth.gov.za/pharmacy/edlphc2014a.pdf (accessed July 18, 2016)

[354] Society for Endocrinology, Metabolism and Diabetes of South Africa. http://www.semdsa.org.za/ (accessed July 18, 2016

[355] Howitt P, Darzi A, Guang-Zhong Y, Ashrafian H, Atun R et al. Technologies for Global Health. Lancet 2012; 380(9840):507-35.

[356] Wang Q, Brenner S, Leppert G, Banda HT, Kalmus O, et al. (2014) Health Seeking Behavior and the Related Household Out-of-Pocket Expenditure for Chronic Non-communicable Diseases in Rural Malawi. Health Policy Plan. doi: 10.1093/heapol/czu004

[357] Goudge J, Gilson L, Russell S, et al. Affordability, availability and acceptability barriers to health care for the chronically ill: longitudinal case studies from South Africa. BMC Health Services Research 2009;9:75-92.

[358] Haque M, Emerson SH, Dennison CR, et al. Barriers to initiating insulin therapy in patients with type 2 diabetes mellitus in public-sector primary health care centres in Cape Town. South African Medical Journal 2005;95:798-802.

[359] Hjelm K, Atwine F. Health-care seeking behaviour among persons with diabetes in Uganda: an interview study. BMC International Health and Human Rights 2011;11:11-8.

[360] Kolling M, Winkley K, von Deden M. 'For someone who's rich, it's not a problem'. Insights from Tanzania on diabetes health-seeking and medical pluralism among Dar es Salaam's urban poor. Globalization and Health 2010;6:8-16.

[361] Wang Q, Fu AZ, Brenner S, Kalmus O, Banda HT, De Allegri M. Out-of-Pocket Expenditure on Chronic Non-Communicable Diseases in Sub-Saharan Africa: The Case of Rural Malawi. Catapano A, ed. *PLoS ONE*. 2015;10(1):e0116897. doi:10.1371/journal.pone.0116897.

[362] Dyck PJ, Overland CJ, Low PA. et al. Signs and Symptoms vs Nerve Conduction Studies to Diagnose Diabetic Sensorimotor Polyneuropathy, Cl vs NPhys Trial Investigators, Muscle Nerve 2010;42(2):157-64. doi: 10.1002/mus.21661.

[363] Vodopivec-Jamsek V, de Jongh T, Gurol-Urganci I, Atun R, Car J. Mobile phone messaging for preventive health care. Cochrane Database of Systematic Reviews 2012 Dec 12;12:CD007457. doi: 10.1002/14651858.CD007457.pub2..

[364] Gurol-Urganci I, de Jongh T, Vodopivec-Jamsek V, Car J, Atun R. Mobile phone messaging for communicating results of medical investigations. Cochrane Database of Systematic Reviews 2012 Jun 13;6:CD007456.

[365] De Jongh T, Gurol-Urganci I, Vlasta Vodopivec-Jamsek V, Car J, Atun R. Mobile phone messaging telemedicine for facilitating self management of long-term illnesses. Cochrane Database of Systematic Reviews 2012 Dec 12; 12:CD007459. doi: 10.1002/14651858.CD007459.pub2.

[366] Car J, Gurol-Urganci I, de Jongh T, Vodopivec-Jamsek V, Atun R. Mobile phone messaging reminders for attendance at healthcare appointments. Cochrane Database of Systematic Reviews 2012 Jul 11; 7: CD007458. DOI: 10.1002/14651858.CD007458.pub2.

[367] Van Velthoven MHMMT, Tudor Car L, Car J, Atun R. Telephone consultation for improving health of people living with, or those at risk of HIV: a systematic review PLoS ONE. 2012 7(5): e36105. doi:10.1371/journal.pone.0036105.

[368] Gill GV, Yudkin JS, Keen H, Beran D. The insulin dilemma in resource-limited countries. A way forward? Diabetologia 2011; 54(1):19-24.

[369] Atun R, Jaffar S, Nishtar S, et al. Improving responsiveness of health systems to non-communicable diseases. *Lancet* 2013; 381:690-97.

[370] Fraser HS, Allen C, Bailey C, Douglas G, Shin S, Blaya J. Information systems for patient follow-up and chronic management of HIV and tuberculosis: a life-saving technology in resource-poor areas. J Med Internet Res 2007; 9(4): e29. doi:10.2196/jmir.9.4.e29.

[371] Shiferaw F, Zolfo M. The role of information communication technology (ICT) towards universal health coverage: the first steps of a telemedicine project in Ethiopia. Global Health Action 2012; 5: 15638 - DOI: 10.3402/gha.v5i0.15638 .

[372] Kah JG, Joshua SY, Kahn JS. Mobile Health Needs And Opportunities In Developing Countries. *Health Aff* February 2010; 29: 252–8. doi:10.1377/hlthaff.2009.0965.

[373] Chandrasekhar CP, Ghosh J. Information and communication Technologies and health in low income countries: the potential and the constraints. Bull World Health Org 2001; 79: 850–5.

[374] Cowan J, Michel C, Manhiça I, et al. Remote monitoring of Xpert® MTB/RIF testing in Mozambique: results of programmatic implementation of GxAlert. Int J Tuberc Lung Dis. 2016; 3: 335-341(7).

[375] Atun, R, De Jongh, T, Secci, F, Ohiri, K, and Adeyi, O. Integration of targeted health interventions into health systems: a conceptual framework for analysis. *Health Policy Plan*. 2010; 25: 104–111.

[376] Atun R. Health Systems, Systems Thinking and Innovation. Health Policy and Planning 2012; 27:iv4–iv8.

[377] Van Olmen J, Schellevis F, van Damme W, Kegels G, Rasschaert F. Management of Chronic Diseases in Sub-Saharan Africa: Cross-Fertilisation between HIV/AIDS and Diabetes Care. Journal of Tropical Medicine 2012; 2012:349312. doi: 10.1155/2012/349312. Epub 2012 Oct 31.

[378] Popkin BM, Hawkes C. Sweetening of the global diet, particularly beverages: patterns, trends, and policy responses. *Lancet Diabetes Endocrinol 2016; 4; 174-186*.

[379] Tian Y, Jiang C, Wang M, Cai R, Zhang Y, He Z, and others. BMI, leisure-time physical activity, and physical fitness in adults in China: results from a series of national surveys, 2000–14. The Lancet Diabetes & Endocrinology, 2016; 4: 487–497.

[380] Mauer M, Zinman B, Gardiner R. Renal and retinal effects of enalapril and losartan in type 1 diabetes. NEJM 2009;361(1):40-51.

[381] Beran D, Ewen M, Laing R. Constraints and challenges in access to insulin: a global perspective. The Lancet Diabetes & Endocrinology 2016; 4: 275–285.

[382] United Nations. Declaration of Commitment on HIV/AIDS. Global Crisis — Global Action. http://www.un.org/ga/aids/coverage/FinalDeclarationHIVAIDS.html (accessed July 5, 2015)

[383] United Nations. High-level Meeting on Non-communicable Diseases. http://www.un.org/en/ga/president/65/issues/ncdiseases.shtml (Accessed July 5, 2015)

[384] United Nations. Resolution Adopted By The General Assembly On 13 May 2010. 64/265. Prevention And Control Of Non-Communicable Diseases. http://www.un.org/en/ga/search/view_doc.asp?symbol=A/RES/64/265&Lang=E (Accessed July 5, 2015)

[385] United Nations. Political declaration of the high-level meeting of the General Assembly on the prevention and control of non-communicable diseases, A/66/L.1. Sept 16, 2011. http://www.un.org/ga/search/view_doc.asp?symbol=A/66/L.1 (Accessed June 25, 2016)

[386] WHO. Sixty-fifth World health Assembly. A/65/54. Second report of the Committee A. http://apps.who.int/gb/ebwha/pdf_files/WHA65/A65_54-en.pdf

[387] Atun R. Decisive action to end apathy and achieve 25×25 NCD targets. Lancet 2014; 384: 384-5.

[388] Atun R. Transitioning health systems for multimorbidity. Lancet. 2015 Jun 5. pii: S0140-6736(14)62254-6.

[389] Atun R, Jaffar S, Nishtar S, et al. Improving responsiveness of health systems to non-communicable diseases. *Lancet* 2013; 381:690-97.

[390] Moon S, Sridhar D, Pate MA, et al. Will Ebola change the game? Ten essential reforms before the next pandemic. The report of the Harvard-LSHTM Independent Panel on the Global Response to Ebola. Lancet 2015; 386: 2204–2221

[391] Davies J, Yudkin J, Atun R. Liberating data: the crucial weapon in the fight against NCDs. *Lancet Diabetes Endocrinol* 2016. Published Online January 27, 2016.

[392] Evans T, Nishtar S, Atun R, Etienne C. Scaling up research and learning for health systems: time to act. Lancet 2008; 372; 1529-31.

[393] Adeyi O, Atun R. Universal access to malaria medicines: innovation in financing and delivery. Lancet 2010; 376: 1869-71.

[394] Atun R. Health Systems, Systems Thinking and Innovation. Health Policy and Planning 2012; 27:iv4–iv8.

[395] Atun RA, Kyratsis I, Gurol I, Rados-Malicbegovic D, Jelic G. Diffusion of complex health innovations-implementation of primary care reforms in Bosnia and Herzegovina. Health Policy and Planning 2007; 22(1): 28-39.

[396] Atun RA, Menabde N, Saluvere K, Jesse M, Habicht J. Implementing Complex Health Innovation—Primary Health Care Reforms in Estonia: multimethods evaluation. Health Policy 2006; 79(1): 79-91.

[397] Al-Shorbaji N, Atun R, Car J, Majeed A, Wheeler E. eLearning for undergraduate health professional education: a systematic review informing a radical transformation of health workforce development http://www.who.int/hrh/documents/14126-eLearningReport.pdf (accessed July 5, 2015)

[398] Gurol-Urganci I, de Jongh T, Vodopivec-Jamsek V, Car J, Atun R. Mobile phone messaging for communicating results of medical investigations. Cochrane Database of Systematic Reviews 2012 Jun 13;6:CD007456.

[399] Car J, Gurol-Urganci I, de Jongh T, Vodopivec-Jamsek V, Atun R. Mobile phone messaging reminders for attendance at healthcare appointments. Cochrane Database of Systematic Reviews 2012 Jul 11; 7: CD007458. DOI: 10.1002/14651858.CD007458.pub2.

[400] Vodopivec-Jamsek V, de Jongh T, Gurol-Urganci I, Atun R, Car J. Mobile phone messaging for preventive health care. Cochrane Database of Systematic Reviews 2012 Dec 12;12:CD007457.

[401] De Jongh T, Gurol-Urganci I, Vlasta Vodopivec-Jamsek V, Car J, Atun R. Mobile phone messaging telemedicine for facilitating self management of long-term illnesses. Cochrane Database of Systematic Reviews 2012 Dec 12; 12:CD007459.

[402] The World Bank. *Global Economic Prospects 2015*. http://www.worldbank.org/en/publication/global-economic-prospects

[403] Atun R, Knaul FM, Akachi Y, Frenk J. Innovative financing for health: what is truly innovative?. Lancet 2012;380:2044-9.

[404] Atun R, Silva S, Ncube M, Vassall A. Innovative financing for HIV response in sub-Saharan Africa. *J Glob Health. 2016* Jun;6(1):010407.

[405] Fitchett JR, Fan Li J, Atun R. Innovative financing for late-stage global health research and development: the Global Health Investment Fund. Int Health. 2015 Nov 26. pii: ihv067.

[406] WHO. Global Action Plan for the Prevention and Control of NCDs 2013-2020 http://www.who.int/nmh/events/ncd_action_plan/en/ (Accessed July 5, 2015)

[407] WHO. NCD Global Monitoring Framework. http://www.who.int/nmh/global_monitoring_framework/en/ (Accessed July 5, 2015)