Non-alcoholic fatty liver disease in sub-Saharan Africa 2

Health-care provision and policy for non-alcoholic fatty liver disease in sub-Saharan Africa

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Sub-Saharan Africa, which has a population of more than 1 billion people, carries 24% of the global burden of disease and spends the least on health care of any region, relying heavily on international development assistance to deliver health care for HIV, tuberculosis, and malaria. The demographic and epidemiological transitions occurring in sub-Saharan Africa, with rising prevalences of obesity and diabetes, enhance the risk of non-alcoholic fatty liver disease (NAFLD), yet this remains an unrecognised complication of metabolic syndrome. There are no guidance documents on NAFLD from sub-Saharan Africa, and non-communicable disease (NCD) guidance documents do not include the associated burden of fatty liver disease. Combating the health and socioeconomic burden of NAFLD requires an integrated liver health approach, with task-shifting to primary health care. Using clear guidance documents to link education and management of HIV, viral hepatitis, NAFLD, and associated NCDs is also crucial to an integrated approach to infectious diseases and NCDs, which requires targeted funding from both governments and international development agencies.

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This is the second in a Series of two papers on non-alcoholic fatty liver disease in sub-Saharan Africa

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Introduction

Sub-Saharan Africa comprises 47 mostly low-income and middle-income countries (LMICs), with a population of more than 1 billion people. The annual gross domestic product (GDP) is US$1·767 trillion, with an annual GDP growth of 3·2%. With 24% of the global disease burden, sub-Saharan Africa has twice the global burden of disease as measured by disability-adjusted life years (DALYs) per capita and currently has the lowest global life expectancy.[1] It spends the least on health care of any region, despite having the highest global disease burden of both communicable and non-communicable diseases (NCDs). On average, health-care expenditure is 5·085% of annual GDP; per-capita health expenditure is $83·43 per year and out-of-pocket expenditure is $27·80 per year.[2] Furthermore, 20 LMICs in sub-Saharan Africa rely on donor funding for more than a fifth of their health expenditure.[3]

For communicable diseases, the prevalence of tuberculosis and HIV/AIDS in sub-Saharan Africa are the highest globally, with an estimated 970 000 people (95% CI 730 000–1 300 000) infected with HIV and 440 000 (330 000–590 000) dying from HIV-related causes in 2019.[4] For malaria, 94% of all deaths in the world in 2019 were recorded in sub-Saharan Africa.[5] Maternal and child mortality is four times higher than in any other region.[6] To date, governments, national departments of health, non-governmental organisations, and international aid agencies have concentrated on the triple infectious disease burden of malaria, HIV, and tuberculosis. In 2017, sub-Saharan Africa spent $17 976·0 million (95% uncertainty interval 16 297·9–20 523·7) on HIV/AIDS and $702·2 (636·7–801·8) per prevalent case, with development assistance accounting for 63·9% (55·7–70·2) of the total HIV/AIDS spending.[7]

The global COVID-19 pandemic has further affected the ability of international aid agencies to provide developmental assistance and support health-care issues in LMICs.[8] It has been estimated that for sub-Saharan Africa to recover economically, official developmental assistance will need to double, representing an extra $40–50 billion per annum from international donor finance over 2–3 years.[9]

Well known international agencies fund programmes for HIV/AIDS, tuberculosis, and malaria; by contrast, viral hepatitis and its complications of cirrhosis and hepatocellular carcinoma are still under-recognised and receive insufficient funding. In 2019, in the WHO Africa region, there were an estimated 990 000 (95% CI 660 000–1 600 000) new hepatitis B virus (HBV) infections and 80 000 (47 000–110 000) deaths, but only 2% of individuals with HBV infection were diagnosed and only 0·1% treated. For hepatitis C virus (HCV), an estimated 210 000 (150 000–370 000) new infections occurred, with 45 000 (23 000–72 000) attributable deaths.[4]

Evidence is incrementally increasing of the negative impact of non-alcoholic fatty liver disease (NAFLD) and metabolic syndrome on liver disease progression in people with chronic HBV and HCV infections.[10–12] The reported mean prevalence of HCV-associated NAFLD was 55%, with non-alcoholic steatohepatitis (NASH) reported in 4–10% of cases;[12] hence, NAFLD is not only a cause of chronic liver disease in itself but also promotes progression of other liver diseases.

The burden of diabetes is large; there were an estimated 19 million adults with diabetes in Africa in 2019, anticipated to rise to 47 million by 2045. Furthermore, 45 million people are thought to have impaired glucose tolerance, predicted to reach 110 million by 2045.[13] Equally,

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***Panel 1*: Current issues and challenges in the management of NAFLD in sub-Saharan Africa**

- Convergence of infectious and non-communicable diseases in sub-Saharan Africa
- Burden of non-communicable diseases in all four regions of sub-Saharan Africa is higher than the global average
- Increasing prevalence of obesity and type 2 diabetes
- Failure to recognise NAFLD as the hepatic component of metabolic syndrome
- No published national clinical guidelines on NAFLD in sub-Saharan Africa
- Guidance documents on type 2 diabetes, obesity, dyslipidaemia, and hypertension do not include guidance on NAFLD
- COVID-19 pandemic has exacerbated circumstances that drive NAFLD, with quarantine-imposed sedentary lifestyles and associated weight gain and increased alcohol consumption
- Dismantling silos of health-care management
- Limited access to therapeutic trials in sub-Saharan Africa—access is based on liver biopsies and other criteria that make involvement challenging

NAFLD=non-alcoholic fatty liver disease.

obesity in both children and adults in sub-Saharan Africa is increasing.[14] This burden portends substantial NAFLD risk (panel 1).

Health and socioeconomic burden of NAFLD and associated NCDs

Demographic transition, as foreshadowed by globalisation, industrialisation, and urbanisation, has led to an increasing prevalence of NCDs.[15] In sub-Saharan Africa, the age-standardised DALYs due to NCDs approximated the combined DALYs from communicable, maternal, neonatal, and nutritional conditions in 2017, and are projected to exceed deaths due to these conditions by 2030. Of concern, the 2017 Global Burden of Disease study suggested that the burden of NCDs in all four regions of sub-Saharan Africa was higher than the global average, placing additional strain on already pressured and under-resourced health-care systems struggling to cope with the burden of infectious diseases.[15] Compared with their counterparts in high-income countries, adults in sub-Saharan Africa have twice the risk of NCD mortality.[16,17] The morbidity and age-standardised death rates from NCDs are higher in at least four sub-Saharan African countries (DR Congo, Nigeria, Ethiopia, and South Africa) than in high-income countries. Evidence of a convergence of infectious diseases and NCDs is emerging from rural South Africa.[18]

In 2016, the WHO estimates of NCDs accounting for all deaths by country were: 27% in Kenya, 29% in Nigeria, 37% in Côte d'Ivoire, 35% in Cameroon, 42% in Senegal, and 51% in South Africa.[19] To offset the rapid rise of NCDs and associated burden of disease, national departments of health and international aid agencies will need to acknowledge the accelerated epidemiological transition from communicable diseases to NCDs and allocate the necessary resources to manage them. Dismantling silos of health-care management and building upon existing infrastructures, particularly at the primary health-care level, as well as developing multi-disciplinary approaches to NCDs, is needed.

Recognising NAFLD as an NCD in sub-Saharan Africa

NAFLD represents the most under-recognised component of metabolic syndrome. The proposed name change from NAFLD to metabolic dysfunction-associated fatty liver disease (MAFLD) reinforces the role of metabolic diseases in promoting the development of fatty liver disease. The current proposed definition of MAFLD is evidence of hepatic steatosis by histology, imaging, or biomarkers or scores, in addition to one of the following three criteria: overweight or obesity, presence of type 2 diabetes, or evidence of metabolic dysregulation with at least two metabolic risk factors.[20,21] These metabolic risk factors include increased waist circumference, arterial hypertension, hypertriglyceridaemia, low HDL cholesterol, prediabetes, insulin resistance, and subclinical inflammation with elevated C-reactive protein.[20] The diagnosis is thus based on positive diagnostic criteria that are central to metabolic dysfunction, does not exclude alcohol, and can coexist with other liver diseases. This definition avoids the stigmatisation associated with alcohol-associated pathology and acknowledges that, with the rising prevalence of NAFLD, causes of liver disease are often multifactorial. The name change has been supported by patient groups and further endorsed by hepatologists, gastroenterologists, and physicians from sub-Saharan Africa, north Africa, and the Middle East, as well as by the Asian Pacific Association for the Study of the Liver and the Latin American Association for the Study of the Liver.[17,22–25] This new terminology will increase recognition of fatty liver disease and its associated metabolic risk factors, and improve holistic management. It will enable more accurate prevalence estimates because it lessens the stigmatisation associated with NAFLD.

Data about the burden and spectrum of NAFLD in Africa, both from population-based and clinical studies, are scant. Existing data suggest that Africa has a low 13·5% prevalence of NAFLD in the general population, a probable underestimate given the progressively rising prevalence of type 2 diabetes and obesity in the region.[26,27] The lack of accurate NAFLD diagnoses due to limited access to and availability of appropriate diagnostics contributes to this underestimation. Of consideration, cirrhosis-related deaths doubled in sub-Saharan Africa between 1980 and 2010, in which the cause of cirrhosis was unknown in 30% of cases and in 10% of cases of

hepatocellular carcinoma.[28] This finding raises the consideration that NAFLD was a contributing cause of cryptogenic cirrhosis and hepatocellular carcinoma. Apart from the need for better epidemiological studies of NAFLD in sub-Saharan Africa, simultaneous genetic studies to more precisely understand NAFLD and its risks are also required. Generally, African Americans have been shown to have a low risk of NAFLD compared with Hispanic and White Americans, despite having an increased burden of metabolic risk factors.[27] This apparent paradox warrants a better understanding in terms of known genetic factors and gut microbiota associated with NAFLD in sub-Saharan Africa (panel 2).[29,30]

Socioeconomic status and NAFLD

The prevalence of both obesity and type 2 diabetes, important promoters of NAFLD, is higher among adults with lower socioeconomic status. Food insecurity is linked to the affordability and increased consumption of calorie-dense, high-fat, high-sugar, ultra-processed foods. An established link between family socioeconomic inequalities and childhood obesity exists, with obesity in children and adolescents associated with increased liver-related mortality later in life.[31,32]

Health-care systems and NAFLD

The changing health-care landscape in sub-Saharan Africa, with a high burden of communicable diseases and increasing NCDs, requires a transition from a system focused on infectious diseases to an integrated system in which all levels of health care, but particularly primary health care, can address the metabolic factors promoting NCDs. The benefits of a well resourced, functional, and integrated primary health-care system have been shown in HIV/AIDS care delivery. More patients are tested, diagnosed, and placed on anti-retroviral therapy with less loss to follow-up and greater geographical coverage for HIV than with vertical models.[33] The capabilities of well functioning primary health-care-led services need to be leveraged to deliver the requisite care for the promoters of NAFLD, including type 2 diabetes, dyslipidaemia, and hypertension, as well as the education and lifestyle changes required to address obesity.[34]

The epidemiological shift to NCDs will further constrain existing health-care systems in many sub-Saharan African countries. Many challenges are evident and include limited diagnostics and access to essential medicines; limited access to new therapeutics being developed for NAFLD; and no referral pathways to linkage of care for individuals with NCDs who are at risk of advanced liver fibrosis and require more specialised care (see figure). This situation is further exacerbated by little integration of NCDs into primary health-care responses, high out-of-pocket expenditure, and a low density health-care workforce of nurses, primary care doctors, and specialists (panel 1).

***Panel 2*: Research priorities for NAFLD in sub-Saharan Africa**

- Epidemiological studies of NAFLD in sub-Saharan Africa to fully understand the burden of disease
- Genetic factors associated with NAFLD in sub-Saharan Africa
- Gut microbiota associated with NAFLD in sub-Saharan Africa
- Interplay of viral hepatitis, HIV, alcohol, and NAFLD in promoting disease progression
- Improved access to therapeutic NAFLD trials in sub-Saharan Africa

NAFLD=non-alcoholic fatty liver disease.

NCDs in sub-Saharan Africa—existing guidance does not adequately address NAFLD

Although comprehensive national guidelines, protocols, and treatment algorithms exist for the management of NCDs, effective implementation remains inconsistent in all sub-Saharan African countries. Compounding this issue is the fact that almost all guidance documents on type 2 diabetes, obesity, dyslipidaemia, and hypertension do not include the associated burden of fatty liver disease. Type 2 diabetes-mediated risks of cardiovascular disease, chronic kidney disease, and diabetic retinopathy are well recognised and monitored.[35] NAFLD is associated with an approximately two-times higher risk of developing diabetes, independent of obesity and other prevalent metabolic risk factors.[36] The increased risk of incident diabetes parallels the underlying severity of NAFLD.[36] The improvement or resolution of fatty liver disease (on ultrasonography) is associated with a reduction in the risk of type 2 diabetes.[37] Despite this association, the risk of NAFLD is seldom considered or investigated in individuals with type 2 diabetes and obesity.

NAFLD is associated with a 1·43-fold increased risk of incident chronic kidney disease (stage ≥3, estimated glomerular filtration rate <60 mL/min/1·73 m²) over 9·7 years median follow-up. The risk increases with advanced fibrosis and NAFLD also predicts for incident risk of atrial fibrillation.[38,39]

The failure to appreciate NAFLD as the hepatic component of metabolic syndrome is not limited to sub-Saharan Africa. In a 2019 European cross-sectional study of the public health response to NAFLD, none of the 29 participating countries had written strategies or action plans for NAFLD and less than 50% of all national strategies and clinical management guidelines on cardiovascular disease, obesity, or diabetes mentioned NAFLD.[40] The WHO universal health coverage programme's six "best buys" to provide a holistic approach to NCDs do not specifically mention NAFLD.[41] Equally, the UN Sustainable Development Goals do not include NAFLD.[42] In 2020, Malaysia became the first

country in the world to include NAFLD in its clinical practice guidelines for type 2 diabetes.[43]

There are no published national clinical guidelines on NAFLD in sub-Saharan Africa. Specific guidance documents to enhance awareness of the morbidity and mortality of NAFLD are needed by health-care workers, patients, and the general public alike.[44,45]

Risk stratification for advanced fibrosis in NAFLD

The development of NAFLD is influenced by the dynamic interaction of genetic, environmental, and lifestyle factors, and components of metabolic syndrome. Identification of the predominant risk factors is important to optimise treatment in individuals with NAFLD.[21] It is not only important to diagnose NAFLD, but also to distinguish between patients with simple steatosis, who can be managed at primary health-care level, and those with advanced fibrosis (ie, fibrosis stage F2 or higher), who need to be referred to secondary or tertiary levels of care.

The strongest risk factors for NAFLD and NASH are the presence of type 2 diabetes, age older than 50 years, and having a first-degree family member with NASH or NASH-related cirrhosis.[46] Other clinical predictors of NASH with hepatic fibrosis include the presence of three or more features of metabolic syndrome, elevated liver aminotransferases, dyslipidaemia, polycystic ovary syndrome, or obstructive sleep apnoea.[27,47]

Simple point-of-care non-invasive tests should be used to identify individuals with advanced fibrosis. Aspartate aminotransferase (AST)-to-platelet ratio index (APRI), Fibrosis-4 (FIB-4) index, and the NAFLD fibrosis score (NFS), which can all easily be assessed with an online calculator, have good negative predictive values for advanced fibrosis and cirrhosis. FIB-4 is the recommended test in the recent Malaysian type 2 diabetes guidance.[43] Individuals with metabolic syndrome should have these non-invasive tests at first presentation and at their annual follow-up appointments. If the values are indeterminate or high, referral for a more advanced evaluating modality is recommended. These modalities include vibration-controlled transient elastography (FibroScan), acoustic radiation force impulse, two-dimensional shear-wave elastography, or magnetic resonance elastography.

These imaging modalities are, however, costly and not readily accessible in most under-resourced regions. Nevertheless, studies have shown that the FibroScan can be operated by nursing personnel, which, together with its portability, makes it best for use at primary health-care level.[48] It has the added benefit of being able to assess for steatosis with the controlled attenuation parameter score.

A study using electronic health records identified 716 individuals in primary care or endocrine services with probable NAFLD. Probable NAFLD was defined as the presence of type 2 diabetes with one other metabolic component of metabolic syndrome, or having three metabolic components (obesity, hypertension, and hyperlipidaemia), or having type 2 diabetes with elevated aspartate aminotransferase or alanine aminotransferase concentrations (1·5× upper limit of normal) or history of fatty liver by any imaging modality.[49] The APRI, FIB-4 index, and NFS scores were calculated and individuals with two or more non-invasive tests (above the thresholds of APRI >1·0, NFS >1·45, and FIB-4 >1·45) were considered to have high-risk NAFLD (presumed high-risk NASH)—ie, to be at high risk of developing adverse outcomes. These individuals were linked to care at a gastroenterology or hepatology clinic where a FibroScan was done. Linked patients with presumed advanced fibrosis had significantly higher body-mass index (BMI) than those without (36·4 [SD 6·6] *vs* 31·2 [6·4] kg/m², p=0·025) and higher non-invasive test scores (APRI 0·89 [0·52] *vs* 0·33 [0·14]; FIB-4 3·21 [2·06] *vs* 1·88 [0·60]; and NFS 1·58 [1·33] *vs* 0·25 [0·94]). 62 (60%) of 103 patients with high-risk non-invasive test scores had liver stiffness measurements of less than 6 kPa, were at minimal risk of adverse outcomes, and could be down-referred to primary health care to optimise their cardiometabolic risks. In 18 (18%) of the participants with high-risk non-invasive test scores, liver stiffness was 8 kPa or higher, indicating a greater degree of hepatic fibrosis, potential for progressive liver disease, and need for closer monitoring. Of the cohort of patients with high-risk non-invasive test scores, eight patients (8%) had a liver stiffness of 12 kPa or higher, suggesting possible cirrhosis.[49]

Although blood-based non-invasive tests have not been validated against the gold standard of liver biopsy for the detection and grading of fibrosis, they are practical in a real-world LMIC setting, such as sub-Saharan Africa, where access to liver biopsies and expert histopathologists is limited and where there is an increasing prevalence of metabolic risk factors of type 2 diabetes and obesity. Ideally, these tests should be combined with a follow-up FibroScan if non-invasive test scores are indeterminate or high, which might require up-referral to secondary or tertiary level care.

Futhermore, the use of the defining criteria for MAFLD, which identify patients with clinically significant hepatic fibrosis better than the NAFLD criteria (with sensitivity of 93·9% *vs* 73·0%), is more amenable to a real-word setting and is further endorsement for the new nomenclature.[50,51]

In sub-Saharan Africa, where access to many of the future therapeutics specifically targeting NAFLD will probably be limited and unaffordable, primary prevention addressing education and implementation around lifestyle changes will remain the cornerstone of management.[52] It is essential to ensure sustainable access to essential medicines, basic monitoring modalities (home glucose monitoring, HBA_{1c}, lipid profiles, aminotransferase and platelet measurements) with appropriate referral pathways.

Strengthening and adapting health systems to accommodate NAFLD burden

Despite more recent attempts at increasing national budgetary allocations to the health sector in sub-Saharan African countries,[53] major challenges to optimal delivery of health care remain. These challenges include: weakened governance and accountability; inadequate health-care systems (poorly remunerated and skilled health-care workers with under-resourced infrastructures, further compounded by emigration of skilled human resources); adverse social determinants of health; out-of-pocket health expenditure; political crises; and, more recently, the COVID-19 pandemic.[54,55]

A great opportunity exists in sub-Saharan Africa, provided the political will exists and with support, to strengthen health-care systems to pre-emptively deal with the growing NCD burden and its many consequences, including NAFLD. Progress made by many resource-limited sub-Saharan African countries in achieving development goals and promoting community involvement in implementing health policies must be encouraged (figure).

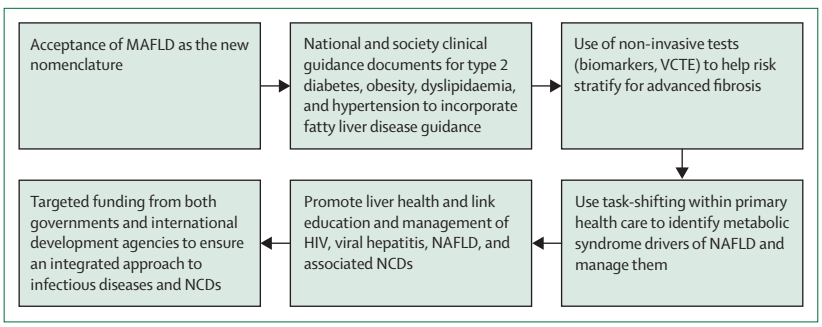

Figure: **A roadmap to NAFLD management in sub-Saharan Africa**
NAFLD=non-alcoholic fatty liver disease. MAFLD=metabolic dysfunction-associated fatty liver disease. VCTE=vibration-controlled transient elastography. NCDs=non-communicable diseases.

Integrating NAFLD into the viral hepatitis, HIV, and sexually transmitted infections package of care

Globally, there is growing pressure for a more integrated approach to health-care service and delivery. Health budgets are limited and universal health coverage is now a globally agreed framework for delivering a package of health care to populations in a manner that improves quality and coverage, does not cause financial hardship, and does not leave people behind.[56]

Within the strategic framework towards elimination as a goal for HIV and viral hepatitis, integrating the delivery of care for HIV, viral hepatitis, and sexually transmitted infections has moved towards policy level. Integrating prevention of mother-to-child infection transmission into maternal and child health-care services will improve overall engagement and uptake of HIV treatment, viral hepatitis treatment, and vaccination among expectant mothers, and so reduce vertical transmission risks. WHO has further endorsed the "triple elimination" initiative—ie, preventing mother-to-child-transmission of HIV, syphilis, and HBV.[4] Such integration is supported by data showing that the integration of HIV and tuberculosis care has synergistic benefits for the control of tuberculosis and can substantially increase treatment success and reduce mortality. There have also been promising results regarding synergistic benefits for HIV, in terms of strengthening health systems and delivery of care.[57,58]

Strategies to integrate HIV and NCD care must also be considered. This approach has further beneficial long-term effects when considering the high burden of HIV in sub-Saharan Africa, the associated increased risk of hepatic steatosis, and the metabolic consequences of long-term antiretroviral therapy.[59] Leveraging existing HIV infrastructures for NCD care, without destabilising HIV programmes, provides a feasible option depending on available programme capacity within countries. The process and clinical outcomes for such integrated models of care are not yet described but are urgently required to further advise policy decisions on HIV and NCD care integration, and will help address the increasing burden of NCDs seen in ageing individuals with HIV.

The burden of NCDs, which have consequent target organ damage if not managed appropriately, must be addressed at all levels of health care. NAFLD cannot be singularly managed within the domain of gastroenterologists or hepatologists, given the nature of the underlying metabolic diseases, which are often treated in primary health care. Managing metabolic factors such as type 2 diabetes, obesity, and hypertension and their potential complications in a fragmented, non-integrated manner will similarly not address these transversal health issues. There is an urgent need for individuals involved with policy to start working together to develop joint policy and guidance on best practice.

The use of implementation science, which is an emerging research area, can help integrated health-care programmes achieve health impact at scale. Resources are scarce but, where available, need to be maximised to deliver optimal care. Integration of care allows for efficient and optimal use of available infrastructure and resources. Sub-Saharan Africa is uniquely positioned to have the benefit of global experience to date regarding the potential burden and consequences of the increasing prevalence of diabetes, hypertension, and obesity, and must attempt to offset this risk in a proactive manner within a population in socioeconomic and nutritional transition. The population in sub-Saharan Africa is young and likely to be receptive to newer technologies promoting more healthy lifestyles. The strong traditions of family and community focus in Africa can also be used positively in this regard.

Effect of COVID-19 on NAFLD

The COVID-19 pandemic has exacerbated circumstances that drive NAFLD, with quarantine-imposed sedentary lifestyles and associated weight gain, increased alcohol

consumption, disruption of school-provided nutritious meals, and loss of household incomes.[60,61] NAFLD, independent of BMI, predicts for an increased risk of severe COVID-19 and intensive care unit admission.[62,63]

As of Sept 6, 2021, Africa has had 5 657 884 confirmed COVID-19 cases with 137 055 attributable deaths, probably an underestimate due to low testing capacity and under-reporting.[64] Already fragile and overstretched health-care systems are being further compromised and individuals with NCDs are affected by the postponement or cancellation of clinic visits, disrupted supply of chronic medicines, and paucity of well established telehealth infrastructures.

In a WHO survey of 41 sub-Saharan African countries, 22% reported that only emergency inpatient care for chronic conditions was available and 37% reported that outpatient care was limited. Hypertension management had been disrupted in 59% of countries and management of diabetic complications in 56%.[65] In South Africa, 61% of patients hospitalised with COVID-19 had hypertension and 52% had diabetes, whereas 45% of people aged 60–69 years who died from COVID-19 had hypertension. In Kenya, approximately 50% of COVID-19 deaths occurred in people with NCDs, and in DR Congo, such patients accounted for 85% of all COVID-19 deaths.[65]

COVID-19 in sub-Saharan Africa has emphasised the need for innovation in health-care delivery—eg, using telehealth networks such as Project ECHO, adapting mechanisms for the delivery of essential medicines and diagnostics, and task-shifting of health care to community-based health-care workers with upscaling of point-of-care diagnostics and implementation of simple management algorithms.[66] Public awareness regarding the heightened health risks associated with obesity, type 2 diabetes, and hypertension has increased. These aspects of the pandemic should be leveraged and are foundational to addressing the burden of NCDs in sub-Saharan Africa.

For **International NASH Day** see https://www.international-nash-day.com

Primary care and community focus on NAFLD

NAFLD, metabolic syndrome, and their long-term health sequelae have reached alarming levels and warrant coordinated interventions.[67,68] Many aspects are poorly understood beyond the liver expert community. Nevertheless, primary health-care providers play a crucial role in education, screening, early diagnosis, and linkage to secondary and tertiary care.[69]

In raising awareness of NAFLD and liver diseases in general, there is the need for NAFLD champions who will highlight the cause. Their designation as NAFLD ambassadors is essential for creating awareness, raising the profile of NAFLD, and more importantly, advocating for action.[70] Social media for advertising or creating awareness is the new normal and efforts at expanding and greater use of these platforms must be embraced. The messaging should highlight the risk factors for NAFLD and engage community-based organisations for the purpose of disseminating information.[71,72]

A liver health approach to NAFLD

Targeting a public liver health approach further enables integration, linking education and management of HIV, viral hepatitis, NAFLD, and associated NCDs.[4,73–75] The metabolic syndrome diseases are transversal and there is a need to form collaborations with NCD patient groups for hypertension, diabetes, obesity, and cancer for the purpose of directing a common message for NCD prevention and therapy.[70,76] A liver health approach stresses the fact that dietary choices, smoking, obesity, and harmful alcohol consumption act synergistically to promote liver injury, and also stresses the need to know one's HIV, HBV, and HCV status.[77–80] The entire focus is thus about lifestyle choices and the necessary interventions for optimal liver health.

Education about risk factors and lifestyle choices

Poor nutritional knowledge in the general population, together with aggressive marketing towards young people, has led to the increased consumption of sugar-sweetened beverages and ultra-processed foods.[81] Ultra-processed foods are energy-dense; high in saturated fats, refined starches, free sugars, and salt; and poor sources of protein, dietary fibre, and micronutrients.[82]

Data from high-income and low-income high school students in peri-urban South Africa showed an inverse relationship between level of parental education and employment status (particularly that of mothers) and fast-food consumption in adolescents.[83] Similarly, physical exercise has been linked to income status, with active participation in physical exercise being lower in adolescents from families of lower socioeconomic status.[84] These findings emphasise the need to include education and policy around the benefits of healthy diets and formal exercise in school curriculums.

International NASH Day

The Global Liver Institute has convened an International NASH Day every June since 2018, with the objective of increasing awareness of the increasing global burden of NAFLD. The campaign highlights the need for screening, early detection, and prevention, and includes education on lifestyle modification and management of the disease. Various themes are chosen for each year with clearly defined objectives as determined by the prevailing global health status. The 2021 theme was "NASH around the world".[85] These global commemorative events offer an opportunity to focus attention on NAFLD.

Health policy and NAFLD

Similar to viral hepatitis, NAFLD is a mostly silent disease with substantial liver-related morbidity and mortality consequent to cirrhosis, liver failure, and hepatocellular carcinoma. However, NAFLD has the additional issue that most of the mortality burden is attributable to cardiovascular disease, along with an added increased risk of extrahepatic malignancies, mainly colorectal

cancers.[75] NAFLD—together with its associated NCDs and consequent burden of disease—is a public health problem that requires integrated and implementable prevention and treatment policies.

NAFLD and policy development

Tackling NAFLD and the associated metabolic syndrome will require a public health approach with implementable policies. A modelling study done in Europe by the Organisation for Economic Co-operation and Development, based on alcohol consumption, blood pressure, BMI, physical activity, type 2 diabetes, and sedentary behaviours, assessed the effect of policies on population health. The study showed that implementation of a comprehensive package of interventions and food reformulation—involving a 20% calorie reduction for foods high in sugar, saturated fats, salt, and calories—followed by setting of alcohol price policies through minimum unit pricing and taxation, were the most effective measures in improving population health.[86]

From a global perspective, situational analyses showing the considerable health and economic burden of NAFLD are an important first step in raising the profile of the disease. Concerted advocacy efforts, particularly by political and community leaders, and a strong communication strategy are required to increase public and political awareness of the public health importance of NAFLD, to generate resources, and to mobilise action. The policy-making process will require evidence-based discussions to identify priorities and solutions and develop policies for the public health control of NAFLD and its risk factors. Existing global policies for tobacco use, unhealthy diet, physical inactivity, and harmful use of alcohol, which are also major risk factors for the development of NCDs, can be leveraged to frame and shape the policy agenda for NAFLD.

Key stakeholders include funders, academic institutions, hepatology organisations, civil society organisations, global health initiatives, UN agencies, the African Union Development Agency-New Partnership for Africa's Development (AUDA-NEPAD), and WHO. Alongside clinical services, intersectoral and cross-sectoral collaboration with other sectors, including environment, food, and agricultural organisations, is desirable to address determinants of health to achieve greater sustainability of results through determining and confronting risk factors.[87] Increasing involvement of primary health care in identifying patients at risk of NAFLD has cost implications with regard to additional blood tests and imaging and this will require resourcing.[88]

Existing policies around NCDs

In 2016, NCDs were included in the Sustainable Development Goal target 3.4: "By 2030, reduce by one third premature mortality from non-communicable diseases through prevention and treatment and promote mental health and well-being".[89] The WHO Global Action Plan for the Prevention and Control of NCDs (2013–20) recommended that countries strengthen their health systems and address NCDs through people-centred primary health care and universal health coverage. In 2020, more than half of countries in the WHO Africa region had not achieved the interim NCD targets.[90]

Recognising the increasing burden of disease attributable to NCDs in Africa, the 67th Session of the WHO Regional Committee for Africa adopted a framework for integrating essential NCD services at the primary health-care level and set four targets to be achieved by 2030: adapt and use the WHO Package of Essential Noncommunicable Disease Interventions; more than 80% of the primary health-care workforce should receive formal training in NCD management; have the essential medicines and basic technologies needed for NCD management available at primary health-care facilities; and have systems for collecting mortality data routinely.[91]

In 2020, WHO reported on the progress of the 47 countries in the WHO African region and found that no country had met all of the recommended indicators to integrate NCD services into primary health care. Seven countries had met none of the indicators.[92] Only 14 (30%) had nationally approved guidelines for NCD management and very few reported on the availabilities of all essential NCD medicines (six [13%]) and technologies (five [11%]) in primary health-care facilities. There was no overall correlation between a country's GDP per capita and the aggregate of targets being met (r=0·23; p=0·12). There was a modestly negative correlation between out-of-pocket expenditure and overall country progress (r=–0·58; p<0·001).[92] Enhanced government commitment and careful resource allocation with development assistance is needed to prioritise NCDs. Particular areas of focus that were identified included increasing the uptake of simplified treatment algorithms, capacity building of health-care workers, and ensured access to essential medicines and diagnostics.[92]

Policies about the marketing of sugar-sweetened beverages and ultra-processed foods

Although NAFLD is not specifically mentioned, the WHO-recommended "best buys" are cost-effective interventions for guiding evidence-based policies for tackling the drivers of NCDs.[93] Included in the interventions are mandatory front-of-pack labelling; reformulation of food products to reduce salt, sugar, and fat content; and raising taxes on sugar-sweetened beverages.[93] These beverages are one of the leading causes of childhood and adult obesity and associated NAFLD.[94,95] Advertising via formal channels and social media platforms invariably targets children and young people and drives consumption of low nutritional value and calorie-dense foods and beverages. Population-based policies need to address the environmental and socioeconomic drivers of obesity and food insecurity.[96,97] A WHO meta-analysis of 11 systematic reviews on the

Search strategy and selection criteria

References for this paper were identified through searches of PubMed with the search terms "metabolic dysfunction-associated fatty liver disease" "MAFLD", "non-communicable diseases", "healthcare policy", "social determinants", and "sub-Saharan Africa" from Jan 1, 2011, to June 17, 2021. Articles were also identified through searches of the authors' own files. Only papers published in English were reviewed. The final reference list was generated on the basis of originality and relevance to the broad scope of this paper.

effectiveness of fiscal policies to reduce bodyweight, improve diet, and prevent chronic diseases including NCDs concluded that the strongest evidence to date was for levies on sugar-sweetened beverages, which reduced their consumption by 20–50%.[98]

Role of AUDA-NEPAD in NAFLD

AUDA-NEPAD plays a key role in strengthening capacity of African Union member states and regional bodies to advance knowledge-based advisory support, including realisation of Agenda 2063.[99] Agenda 2063 is an affirmation declared by the African heads of state and governments in May, 2013, and serves as a blueprint and strategic framework for transforming Africa into a global powerhouse of the future, through inclusive and sustainable development. Two of the Agenda 2063 goals focus on attaining a high standard of living, quality of life, and wellbeing for all citizens, as well as having a healthy and well nourished citizenry. To ensure that all African citizens attain a high standard of living, quality of life, and wellbeing, AUDA-NEPAD will work with existing evidence to ensure inclusion of NAFLD in NCD guidance documents with integration of strategies to detect, prevent, and treat NAFLD.

Conclusions

NAFLD is a focal point for the confluence of the metabolic diseases that form the basis of most NCDs. The term MAFLD is more acceptable to patients, highlights the driving metabolic risk factors, and identifies those at risk for advanced fibrosis. The liver as a target organ in metabolic syndrome has not been appreciated until now, and sub-Saharan Africa, given its social and economic transition, is at risk of this additional disease burden. Sub-Saharan Africa is uniquely poised to proactively address these issues so as to offset this further health burden.

Contributors

CWS conceived of the manuscript. CWS and MWS developed the preliminary outline. All authors contributed to the writing of the manuscript, reviewed the full draft of the manuscript and subsequent revisions, and approved the final version for submission. MWS provided additional technical expertise.

Declaration of interests

We declare no competing interests.

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