[8] Fouad Y, Elwakil R, Elsahhar M, Said E, Bazeed S, Gomaa AA, et al. The NAFLD-MAFLD debate: eminence versus evidence. Liver Int 2021 Feb;41(2):255–260. https://doi.org/10.1111/liv.14739. Epub 2020 Dec 2. PMID: 33220154.
[9] Eslam M, Sarin SK, Wong VW-S, Fan J-G, Kawaguchi T, Ahn SH, et al. The Asian Pacific Association for the Study of the Liver clinical practice guidelines for the diagnosis and management of metabolic associated fatty liver disease. Hepatol Int 2020:1–31.
[10] Ratziu V, Rinella M, Beuers U, Loomba R, Anstee QM, Harrison S, et al. The times they are a-changin'(for NAFLD as well). J Hepatol 2020;73:1307–1309.

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The sub-Saharan Africa position statement on the redefinition of fatty liver disease: From NAFLD to MAFLD

To the Editor:

We read with great interest the landmark consensus on the redefinition of fatty liver disease by *Eslam et al.* This includes a shift in nomenclature from non-alcoholic fatty liver disease (NAFLD) to metabolic dysfunction-associated fatty liver disease (MAFLD) as a more apt term, as well as the adoption of a set of simple and pertinent "positive" criteria to diagnose the disease, independent of alcohol intake or other liver diseases.[1,2] These twin proposals provide a major advance in the conceptualisation of fatty liver diseases, but given the variation between different health systems, reaching a broad and global consensus is imperative.

Sub-Saharan Africa (SSA) has more than half of the Earth's arable land, of which <10% is currently cultivated. The region was home to 13% of the global population in 2017 (over 1 billion) and it is forecasted to account for 35% of the global population by 2100. SSA is confronted by a high disease burden accounting for around 24% of the global disease burden. Although, the burden of disease in this region continues to be dominated by infectious diseases, countries in this region are undergoing a demographic transition characterised by industrialization and urbanization leading to an increasing prevalence of non-communicable diseases (NCDs).[3] The burden of NCDs in SSA regions is higher than the global average and it is projected that by 2020, NCDs will account for 27% of mortality in this region.[3] Adults in these regions face twice the risk of NCD mortality than their counterparts living in high-income countries.[4]

Fatty liver disease associated with metabolic dysfunction has emerged as an important NCD in SSA and available data suggest that this region has one of the fastest growing burdens worldwide. The prevalence of NAFLD in Africa was estimated to be about 13%,[5] although this is like to be underestimated because of under-diagnosis and under-reporting. Cirrhosis-related deaths doubled in SSA between 1980 and 2010, and the underlying aetiology of cirrhosis was unknown in 31% of cases.[6] Similarly, 10% of the underlying aetiology for hepatocellular carcinoma in Africa was unknown,[6] suggesting potentially a major contributing role of NAFLD.

The management of NAFLD in SSA comes with unique challenges. Compared to high-income countries, the changes in SSA countries are occurring abruptly and involving massive populations that have rapidly surpassed the capacity of healthcare systems, which are already fragile, fragmented, under-resourced, and limited in terms of infrastructure and ability to cope.[3] Hence, SSA countries do not have the option of simply copying the protocols that have emerged in high-income countries; examining the existing NAFLD guidelines through the contextualisation lens reveals gaps between policy and implementation.

To reach a consensus, the African Middle East Association of Gastroenterology (AMAGE) invited leading members of SSA countries to come to a consensus on this proposal from a local perspective, through a Delphi process. Participating experts have uniformly decided to endorse "MAFLD" as the official term to describe fatty liver disease associated with metabolic dysfunction and be diagnosed by the proposed positive criteria (supported by 100% of participants). We also recommended abandoning the term non-alcoholic steatohepatitis "NASH" and that the single term MAFLD be used, recognising a disease continuum that is dependent on grade of activity and stage of fibrosis.

Why do the SSA experts endorse the novel definition of fatty liver disease?

Besides, the consensus reached through the Delphi method displaying a clear support for the MAFLD proposal, from a national perspective, the panel of experts recognized plenty of

Keywords: MAFLD; NAFLD; Delphi; Africa.
Received 6 January 2021; received in revised form 7 January 2021; accepted 10 January 2021; available online 20 January 2021
https://doi.org/10.1016/j.jhep.2021.01.015

multiscale advantages that are at play in adopting the MAFLD framework, which include:

Value the evidence: To date and in quite a short timeframe, available studies have consistently reached the conclusion that the diagnostic criteria for MAFLD are simple, practical, and superior to the existing NAFLD criteria for identifying high-risk patients with severe liver injury, cardiovascular diseases, and chronic kidney diseases.[7]

Placing proof in pragmatism: SSA countries bear a huge, disproportionate, and growing burden of risk factors for MAFLD, which constitutes a threat to development. Efforts to tackle the global burden of MAFLD may need region-specific fine-tuning measures addressing the challenge of scarce resources. In this regard, the obvious ease of implementing the diagnostic criteria of MAFLD,[7,8] in contrast to the challenging criteria of the old diagnosis of NAFLD, presents a unique opportunity to bridge these gaps and combat MAFLD despite our limited resources.

Turning challenges into moments of opportunity: The redefinition of fatty liver disease associated with metabolic dysfunction presents a unique opportunity to change the perception of MAFLD, engage stakeholders in MAFLD management and rectify the current funding deficit. Increasing awareness and rectifying the funding deficit is partly challenged by a problem of language.[8] This is not the case for more defined areas of health, such as HIV/AIDS or diabetes. One regional lesson from HIV/AIDS that may be useful for MAFLD is to involve local communities actively during national scale-up programmes.[9] An inability to understand the risk of NAFLD and the use of the negative prefix "non" does not give a sense of importance.[8] MAFLD could provide a useful alternative that better reflects risk and may encourage metabolically healthy lifestyle changes. Various studies in other diseases have shown the positive implications of changing disease names on improving the lay perception and beliefs about management and health outcomes.[10]

Enhancing management of multimorbidity in low-income context: Multimorbidity is a growing concern in SSA countries.[11] In contrast to the previous criteria of NAFLD that solely relied on exclusion of other liver diseases, the positive criteria for MAFLD will encourage the recognition of dual burdens of liver disease. A multi-sectoral, integrated approach to healthcare that accounts for all diseases appears to be the way forward, particularly considering the significant burden of HIV in the region. This change would also represent the pillar for establishing HIV-metabolic clinics which are currently needed in many countries in the region. This will also be an opportunity to encourage physicians to evaluate the hepatic manifestation of metabolic disorders.

Strengthening primary healthcare systems: One of the major problems with NAFLD care is that it is primarily hospital-centred and tends to be concentrated in large urban hospitals.[12] This dire situation is aggravated by an extreme shortage of specialists in these centres,[13] causing problems with referrals and counter-referrals, which in turn leads to undiagnosed and untreated diseases. In addition, in 2019, the World Health Organization estimates that out-of-pocket expenditure exceeded 40% of total healthcare expenditure in low-income countries, mainly in SSA. Hence, it is not surprising that studies have shown a high prevalence of undiagnosed NAFLD in real life, even among high-income countries.[14] Therefore, decentralized healthcare is needed to ensure more efficient and effective healthcare delivery at all levels in SSA, especially in rural communities. A simple care system based on simple diagnostic criteria and education has been developed and tested in SSA; this approach has been shown to improve population-level health outcomes, reduce all-cause mortality and is a cost-effective strategy for achieving universal health coverage.[15] Hence, the simplified MAFLD diagnostic criteria would likely lead to similar outcomes.

In conclusion, the SSA experts enthusiastically endorse the MAFLD proposal. In concert with our work, experts from the Asian Pacific Association for the Study of the Liver (APASL), the Latin American Association for the Study of the Liver (ALEH), and the Middle East and North Africa[16–18] previously endorsed the same proposal, indicating that a broad consensus is emerging.

Financial support
No funding was required for this study.

Conflict of interest
The authors declare no competing interests or any conflict of interest.

Please refer to the accompanying ICMJE disclosure forms for further details.

Authors' contributions
All authors contributed to the conceptualisation, drafting of the manuscript and approved the final version.

Supplementary data
Supplementary data to this article can be found online at https://doi.org/10.1016/j.jhep.2021.01.015.

References
[1] Eslam M, Newsome PN, Sarin SK, Anstee QM, Targher G, Romero-Gomez M, et al. A new definition for metabolic dysfunction-associated fatty liver disease: an international expert consensus statement. J Hepatol 2020;73:202–209.
[2] Eslam M, Sanyal AJ, George J. MAFLD: a consensus-driven proposed nomenclature for metabolic associated fatty liver disease. Gastroenterology 2020;158(7). 1999-2014.e1.
[3] Gouda HN, Charlson F, Sorsdahl K, Ahmadzada S, Ferrari AJ, Erskine H, et al. Burden of non-communicable diseases in sub-saharan Africa, 1990–2017: results from the global burden of disease study 2017. Lancet Glob Health 2019;7:e1375–e1387.
[4] Ezzati M, Pearson-Stuttard J, Bennett JE, Mathers CD. Acting on non-communicable diseases in low-and middle-income tropical countries. Nature 2018;559:507–516.
[5] Younossi Z, Anstee QM, Marietti M, Hardy T, Henry L, Eslam M, et al. Global burden of NAFLD and NASH: trends, predictions, risk factors and prevention. Nat Rev Gastroenterol Hepatol 2018;15(1):11–20.
[6] Vento S, Dzudzor B, Cainelli F, Tachi K. Liver cirrhosis in sub-Saharan Africa: neglected, yet important. Lancet Glob Health 2018;6:e1060–e1061.
[7] Fouad Y, Elwakil R, Elsahhar M, Said E, Bazeed S, Ali Gomaa A, et al. The NAFLD-MAFLD debate: eminence vs evidence. Liver Int 2020 Nov 21. https://doi.org/10.1111/liv.14739. Online ahead of print.
[8] Fouad Y, Waked I, Bollipo S, Gomaa A, Ajlouni Y, Attia D. What's in a name? Renaming 'NAFLD' to 'MAFLD'. Liver Int 2020;40(6):1254–1261.
[9] Narayan KV, Ali MK, del Rio C, Koplan JP, Curran J. Global non-communicable diseases—lessons from the HIV–AIDS experience. N Engl J Med 2011;365:876–878.
[10] Shiha G, Korenjak M, Eskridge W, Casanovas T, Velez-Moller P, Högström S, et al. Redefining fatty liver disease: an international patient perspective. Lancet Gastroenterol Hepatol 2021 Jan;6(1):73–79.
[11] Odland ML, Payne C, Witham MD, Siedner MJ, Bärnighausen T, Bountogo M, et al. Epidemiology of multimorbidity in conditions of extreme poverty: a population-based study of older adults in rural Burkina Faso. BMJ Glob Health 2020;5:e002096.
[12] Tesema AG, Ajisegiri WS, Abimbola S, Balane C, Kengne AP, Shiferaw F, et al. How well are non-communicable disease services being integrated

into primary health care in Africa: a review of progress against World Health Organization's African regional targets. PloS one 2020;15:e0240984.
[13] Kinfu Y, Dal Poz MR, Mercer H, Evans DB. The health worker shortage in Africa: are enough physicians and nurses being trained? Bull World Health Organ 2009;87(3):225–230.
[14] Alexander M, Loomis AK, Fairburn-Beech J, van der Lei J, Duarte-Salles T, Prieto-Alhambra D, et al. Real-world data reveal a diagnostic gap in non-alcoholic fatty liver disease. BMC Med 2018;16:1–11.
[15] Pfeiffer J, Montoya P, Baptista AJ, Karagianis M, de Morais Pugas M, Micek M, et al. Integration of HIV/AIDS services into African primary health care: lessons learned for health system strengthening in Mozambique-a case study. J Int AIDS Soc 2010;13:3.
[16] Shiha G, Alswat K, Al Khatry M, Sharara AI, Örmeci N, Waked I, et al. Nomenclature and definition of metabolic-associated fatty liver disease: a consensus from the Middle East and north Africa. Lancet Gastroenterol Hepatol 2021 Jan;6(1):57–64.
[17] Mendez-Sanchez N, Arrese M, Gadano A, Oliveira CP, Fassio E, Arab JP, et al. The Latin American Association for the Study of the Liver (ALEH) position statement on the redefinition of fatty liver disease. Lancet Gastroenterol Hepatol 2021 Jan;6(1):65–72.
[18] Eslam M, Sarin SK, Wong VW, Fan JG, Kawaguchi T, Ahn SH, et al. The Asian Pacific Association for the Study of the Liver clinical practice guidelines for the diagnosis and management of metabolic associated fatty liver disease. Hepatol Int 2020 Oct 1. https://doi.org/10.1007/s12072-020-10094-2.

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Hypertension in NAFLD: An uncontrolled burden

To the Editor:

With great interest we have read the recent consensus statement of Eslam *et al.* suggesting the redefinition of non-alcoholic fatty liver disease (NAFLD) to metabolic (dysfunction)-associated fatty liver disease (MAFLD).[1] One of the proposed metabolic abnormalities within the diagnostic criteria is an office blood pressure (OBP) ≥130/85 mmHg, or antihypertensive drug treatment.[1]

We strongly support the consideration of hypertension as a major (cardio-)metabolic risk abnormality, since NAFLD affects up to 50% of hypertensive patients[2,3] and uncontrolled hypertension has been associated with an increased risk of all-cause and cardiovascular disease (CVD)-related mortality.[4] However, we would like to emphasize the use of out-of-office blood pressure measurement techniques, *e.g.* 24-hour-ambulatory blood pressure monitoring (24-h-ABPM), as the preferred method for diagnosing hypertension as recommended in current guidelines.[5,6]

Although accumulating evidence indicates a bi-directional relationship between hypertension and new-onset or progression of NAFLD,[2,3] patient-centered care programs integrating information on hypertension management and control in patients with NAFLD are lacking. Thus, to improve hypertension management, we initiated a pilot program and included 24-h-ABPM into NAFLD outpatient care.

A total of 107 patients with NAFLD were consecutively recruited during regular follow-up visits in our outpatient liver department. NAFLD was diagnosed according to the current EASL-EASD-EASO clinical practice guidelines.[7] Data collection included a medical history, anthropometric measurements, laboratory examinations, and OBP measurements as well as 24-h-ABPM following a standardized protocol (see supplementary information for details). Hypertension status was defined according to the 2018 European Society of Hypertension/European

Keywords: NAFLD; Hypertension; Ambulatory blood pressure monitoring; Cardiovascular disease; Cardiovascular risk; Masked hypertension.
Received 11 January 2021; accepted 12 January 2021; available online 22 January 2021
https://doi.org/10.1016/j.jhep.2021.01.019