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### Letters to the editor

#### MAFLD or MASLD: Let the evidence decide again



To the Editor:

We thank Ramírez-Mejíaa et al. [1] and Kamal et al. [2] for their interest and comments on our work [3]. A discussion about the redefinition of the most common liver disease, fatty liver disease due to metabolic dysfunction is still actively ongoing. Ramírez-Mejíaa et al. emphasize that time will ultimately determine the outcome of this discussion and any new version of diagnostic criteria must present significant conceptual advances over previous ones to be accepted.

Kamal *et al.* expressed concerns about the recently proposed definition of metabolic dysfunction-associated steatotic liver disease (MASLD) and the process that led to this outcome. They underscore the importance of distinguishing between consensus and evidence, the controversy surrounding the term and concept of MetALD [4,5], and question how changing "F" to "S" from metabolic dysfunction-associated fatty liver disease (MAFLD) to MASLD addressed previous concerns about the MAFLD definition. They also advocate for editorial flexibility when dealing with various disease nomenclatures.

Debates are inevitable in research, but they can only be resolved by relying on robust evidence rather than an eminencebased approach [6]. Within a short period, a significant amount of evidence has quickly accumulated, confirming that the definition of MAFLD identifies a more uniform group of patients with fatty liver caused by metabolic dysfunction. This surpasses not only the previous non-alcoholic fatty liver disease (NAFLD) definition but also the recently suggested MASLD definition. Therefore, MAFLD is currently the best available definition for this disease to date [7-12]. MAFLD presents a meaningful conceptual framework and practical definition and for approaching the disease and developing a patient-centred holistic approach to management considering multiple driving modes, with the ultimate aim of enhancing health outcomes. The emerging research signifies the beginning of a new era in reshaping the ongoing discussion by obtaining the essential evidence that will resolve the debate and open up new paths for further research. The only way to move forward is through additional studies and evidence.

In conclusion, the insights shared by Ramírez-Mejíaa *et al.* [1] and Kamal *et al.* [2] emphasize the importance of distinguishing between "evidence" and "opinion" in the field of medicine. It is crucial to engage in discussions and prioritize gathering evidence to resolve debates. Once robust evidence is available, it should guide our directions.

## **Declaration of interests**

None.

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#### References

- [1] Ramírez-Mejíaa. NAFLD-MASLD-MAFLD continuum: a swinging pendulum? Ann Hepatol 2024.
- [2] Kamal E. MAFLD vs. MASLD: consensus is unlike evidence!. Ann Hepatol 2024.
- [3] Pan Z, Derbala M, AlNaamani K, Ghazinian H, Fan JG, Eslam M. MAFLD criteria are better than MASLD criteria at predicting the risk of chronic kidney disease. Ann Hepatol 2024:101512. https://doi.org/10.1016/j.aohep.2024.101512.
- [4] Fouad Y, Sanai F, Alboraie M, Zheng MH. What the new definition of MASLD left behind: dual etiology with viral hepatitis. Clin Gastroenterol Hepatol 2023. https://doi.org/10.1016/j.cgh.2023.11.026.
- [5] Méndez-Sánchez N RMM. MetALD: The outcome of living under the shadow of alcohol for 4 decades. CGH 2024. https://doi.org/10.1016/j.cgh.2024.05.009.
- [6] Fouad Y, Elwakil R, Elsahhar M, Said E, Bazeed S, Ali Gomaa A, et al. The NAFLD-MAFLD debate: eminence vs evidence. Liver Int 2021;41(2):255–60. https://doi.org/10.1111/liv.14739.
- [7] Alharthi J, Gastaldelli A, Cua IH, Ghazinian H, Eslam M. Metabolic dysfunctionassociated fatty liver disease: a year in review. Curr Opin Gastroenterol 2022;38 (3):251–60. https://doi.org/10.1097/MOG.000000000000823.
- [8] Pan Z, Al-Busafi SA, Abdulla M, Fouad Y, Sebastiani G, Eslam M. MAFLD identifies patients with significant hepatic fibrosis better than MASLD. Hepatol Int 2024:1– 9. https://doi.org/10.1007/s12072-024-10673-7.
- [9] Pan Z, Eslam M, Choudhury A, Sahoo B, Lesmana CR, Sanai FM. The MASLD criteria overlook a number of adolescent patients with severe steatosis. J Hepatol 2024. https://doi.org/10.1016/j.jhep.2024.03.042.
- [10] Pan Z, Shiha G, Esmat G, Méndez-Sánchez N, Eslam M. MAFLD predicts cardiovascular disease risk better than MASLD. Liver Int 2024. https://doi.org/10.1111/ liv.15931.
- [11] Ramírez-Mejía MM, Jiménez-Gutiérrez C, Eslam M, George J, Méndez-Sánchez N. Breaking new ground: MASLD vs. MAFLD—which holds the key for risk stratification? Hepatol Int 2024;18(1):168–78. https://doi.org/10.1007/s12072-023-10620-y.
- [12] Zhou XD, Lonardo A, Pan CQ, Shapiro MD, Zheng MH, WMU MAFLD Clinical Research Working Group. Clinical features and long-term outcomes of patients diagnosed with MASLD, MAFLD, or both. J Hepatol 2024. https://doi.org/10.1016/ j.jhep.2024.03.039.

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#### MAFLD vs. MASLD: Consensus is unlike evidence!



To the Editor:

We read with interest the study by Pan et al., demonstrating that metabolic dysfunction associated fatty liver disease (MAFLD) is

superior to metabolic dysfunction associated steatotic liver disease (MASLD) in identifying individuals at risk of chronic kidney disease [1]. The study extends recent similar findings showed that MAFLD is better than MASLD identifying metabolic dysfunction, hepatic and extra-hepatic outcomes [2-4].

These findings beg an interesting question, why the MASLD definition, which came second after MAFLD, failed to provide a conceptual advance. Although the actual causes may be not clear, a key obvious cause is consensus is unlike evidence. The MASLD proposal is grounded on a questionnaire of personal views that might be heavily compounded by various types of conflict of interests and could be influenced by the view of few but vocal participants in this consensus process. Additionally, it is crucial to realise scientific truth is about evidence not consensus alone and in many circumstances the expert opinions turned to be not the same as evidence-based data [5]. A recent analysis of over a hundred consensus demonstrates that the rigor of statement development in consensus statements is less than one-third of that of evidence-based guidelines [6].

Notably, when the metabolic dysfunction associated fatty liver disease (MAFLD) revolutionary proposal was introduced [7,8], the opponents raised multiple concerns. One of the key concerns that was raised by Moreno et al., on behalf of the EASL Consortium for the Study of Alcohol-related LiVer disease in Europe (SALVE) that in a patient satisfying criteria for MAFLD but with another risk factor including alcohol intake, the term "dual-aetiology fatty liver disease" [9]. They went very heavily to suggest that this would lead to separating individuals exposed to alcohol consumption into two categories (ALD for individuals with normal weight and dual etiology fatty liver disease for overweight or obese individuals) and that patients satisfying metabolic risk criteria would no longer be recorded as having ALD. This could lead to overlooking the importance of the amount of alcohol consumption on fibrosis and the importance of reductions in alcohol consumption to outcomes and could impact the funding of alcohol research [9].

However, the MAFLD proposal dealt carefully with these aspects by suggesting "dual-etiology" as a "concept" and not a "term". This concept encompasses patients with MAFLD and ALD as well as those of MAFLD with other aetiologies as chronic hepatitis B or C. [10] However, the fundamental and logic question where these concerns went with the proposal of "metALD" that introduced an actual term not just a concept? This term separates patients with ALD, with the vast majority of ALD patients would now be labelled as MetALD.

Similarly, we recently raised concerns on how the change of F to S from fatty to steatotic addressed all concerns that were raised in the popular editorial that was published raising doubts on the potential negative impact of the premature change from NAFLD to MAFLD on various aspects including epidemiology, noninvasive score performance and clinical trials [11]. It is not clear why suddenly the premature became mature [12].

Another striking example, I bet every researcher in the field who submitted a manuscript over the last few years using the MAFLD term has encountered comment that "you cannot use MAFLD to describe data generated under the NAFLD term". Therefore, again how it became not only OK but encouraged and sometimes forced to use data generated under the NAFLD term using the MASLD term.

In total, "You can hide memories, but you can't erase history that produced them". Let the evidence not opinion guide our path, as unbiased evidence is a self-fulfilling guarantee that the evidence will not be affected by conflicts of interest. More studies as the current study [1] are required to generate evidence-based recommendations.

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YF and EK were involved in the conceptualization, and writing the original draft while All authors revised the original draft, added comments, and approved the final draft.

#### **Declaration of interest**

None.

#### References

- [1] Pan Z. MAFLD criteria are better than MASLD criteria at predicting the risk of chronic kidney disease. Ann Hepatol 2024.
- [2] Pan Z, Eslam M, Choudhury A, Sahoo B, Lesmana CR, Sanai FM. The MASLD criteria overlook a number of adolescent patients with severe steatosis. J Hepatol 2024.
- [3] Pan Z, Shiha G, Esmat G, Méndez-Sánchez N, Eslam M. MAFLD predicts cardiovascular disease risk better than MASLD. Liver Int 2024.
- [4] Ramírez-Mejía MM, Jiménez-Gutiérrez C, Eslam M, George J, Méndez-Sánchez N. Breaking new ground: MASLD vs. MAFLD—which holds the key for risk stratification? Hepatol Int 2024;18(1):168–78.
- [5] Fouad Y, Elwakil R, Elsahhar M, Said E, Bazeed S, Ali Gomaa A, et al. The NAFLD-MAFLD debate: eminence vs evidence. Liver Int 2021;41(2):255–60.
- [6] Jacobs C, Graham ID, Makarski J, Chasse M, Fergusson D, Hutton B, et al. Clinical practice guidelines and consensus statements in oncology—an assessment of their methodological quality. PLoS One 2014;9(10):e110469.
- [7] Eslam M, Alkhouri N, Vajro P, Baumann U, Weiss R, Socha P, et al. Defining paediatric metabolic (dysfunction)-associated fatty liver disease: an international expert consensus statement. Lancet Gastroenterol Hepatol 2021;6(10):864–73.
- [8] 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(1):202–9.
- [9] Moreno C, Sheron N, Tiniakos D, Lackner C, Mathurin P. "Dual aetiology fatty liver disease": a recently proposed term associated with potential pitfalls. J Hepatol 2021;74(4):979–82.
- [10] Fouad Y, Sanai F, Alboraie M, Zheng M-H. What the new definition of MASLD left behind: dual etiology with viral hepatitis. Clin Gastroenterol Hepatol 2023.
- [11] Younossi ZM, Rinella ME, Sanyal AJ, Harrison SA, Brunt EM, Goodman Z, et al. From NAFLD to MAFLD: implications of a premature change in terminology. Hepatology 2021;73(3):1194–8.
- [12] Fouad Y, Alboraie M, El-Shabrawi M, Zheng M-H. How F to S turned the premature to be mature? Hepatology 2023;10:1097.

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# NAFLD-MASLD-MAFLD continuum: A swinging pendulum?



To the editor:

We read with interest the study by Pan and colleagues showing that criteria for metabolic dysfunction associated fatty liver disease (MAFLD) are superior to metabolic dysfunction associated steatotic liver disease (MASLD) in identifying individuals at risk of chronic kidney disease [1]. This study is consistent with what we and others have recently demonstrated that MAFLD outperforms MASLD in identifying metabolic dysfunction, fibrosis, cardiovascular disease and mortality [2-5]

The concept of MASLD is derived from MAFLD. It is not a secret that the proponents of MASLD have been vocal in their resistance accepting the MAFLD definition and opposing the mainstream in the field, opting to accept anything rather than MAFLD including even retaining the clinical status quo despite its limitations. This leads to an intriguing question: is the NAFLD-MASLD-MAFLD continuum merely the pendulum clock swinging back and forth? NAFLD and