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.

# **Funding**

There has been no kind of support for this manuscript by any source.

### **Author contribution**

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

MAFLD are like 12 and 6 on a clock, representing 180-degree different concepts. MASLD, on the other hand, represents a movement of the clock and falls somewhere between 3 and 4 on the clock, closer to MAFLD. In support of this hypothesis, the discussion has shifted currently from do we need the change or not to what this change should be. Thus, perhaps MASLD represents another phase of transient resistance to MAFLD, while the pendulum continues to move. This could at least partially explain the accumulating recent data suggest that the MAFLD definition performs better than the MASLD definition [2,4,5]. This outcome is curious, as new definitions should provide substantial conceptual advances over previous ones; alternatively what is the point of the change. As the key purpose of the MASLD proposal was likely just to resist the widespread of the endorsement of MAFLD rather than devoting the effort and getting benefit of the opportunity of coming second to provide an actual conceptual advance capitalising on the MAFLD definition.

Interestingly, it took more than a decade for Helicobacter pylori to be universally accepted, which became known as the "gastric ulcer war" [6]. Only time will tell if the same will happen for the NAFLD-MASLD-MAFLD continuum, and if so, how long will it take.

# **Declaration of competing interest**

None

### **Funding**

None

### References

- 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.
- [2] 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.
- [3] Pan Z, Shiha G, Esmat G, Méndez-Sánchez N, Eslam M. MAFLD predicts cardiovascular disease risk better than MASLD. Liver International 2024.
- [4] 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.

- [5] Zhou X-D, Lonardo A, Pan CQ, Shapiro MD, Zheng M-H, Zheng KI, et al. Clinical features and long-term outcomes of patients diagnosed with MASLD, MAFLD, or Both. I. Hepatol. 2024.
- [6] Guide S, Embargo P, Home A, Mobile A. The Great Ulcer. War: how It All Happened; 2014.

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