Editorial: The Metabolic (Dysfunction) Associated Fatty Liver Disease (MAFLD)-Non-Alcoholic Fatty Liver Disease (NAFLD) Debate: A Forced Consensus and The Risk of a World Divide

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Abstract   During the past two years, the redefinition of non-alcoholic fatty liver disease (NAFLD) to metabolic dysfunction-associated fatty liver disease (MAFLD) have been endorsed by international societies of hepatology, patient advocacy associations, and stakeholders. More recently, the American Association for the Study of Liver Diseases (AASLD) and the European Association for the Study of the Liver (EASL) have attempted to achieve a consensus. Three main fundamental issues raise concerns regarding the validity of the current consensus process. First, the development of the process and the selection of experts in the consensus panels remain unclear. Second, there is a concern regarding the quantity and quality of the evidence considered by the consensus panels. Third, there has been a lack of input to the consensus panel decisions from the academic and clinical community. This Editorial aims to raise an urgent note of caution regarding the consensus process used by the AASLD and EASL regarding fatty liver disease, to prevent world divide and different global definitions and guidelines from being adopted.

Keywords: Guidelines • Consensus • Metabolic Dysfunction-Associated Fatty Liver Disease • Non-Alcoholic Fatty Liver Disease • Editorial

Worldwide, fatty liver disease associated with metabolic dysfunction remains underdiagnosed and undertreated, despite its increased recognition as a significant threat to health [1,2]. During the past two years, the redefinition of non-alcoholic fatty liver disease (NAFLD) to metabolic dysfunction-associated fatty liver disease (MAFLD) have been endorsed by international societies of hepatology, patient advocacy associations, and stakeholders [1-11]. More recently, the American Association for the Study of Liver Diseases (AASLD) and the European Association for the Study of the Liver (EASL) have activated a process to reach a consensus. We highlight that available insights point to that process as potentially leading to a world divide.

Three fundamental issues raise concerns regarding the validity of the current consensus process. First, the development of the process and the selection of experts in the consensus panels remain unclear. Second, there is a concern regarding the quantity and quality of the evidence considered by the consensus panels. Third, there has been a lack of input to the consensus panel decisions from the academic and clinical community.

How Was the Process Developed and the Experts Selected?

Consensus methods use various strategies to deal with the challenges of controversial topics [12]. These processes are

susceptible to panel selection bias, the idiosyncrasies of a small but vocal group, uncontrolled interactions, variable or inappropriate leadership, and conflicts of interest [12]. These factors may affect the integrity of any process requiring clinical consensus development [12]. The outcome of expert opinion consensus depends on the choice of the participating experts and their views [12]. However, without quality evidence, expert opinions may carry little weight. The approach to overcoming this problem should include inclusive processes in which all regions of the world and social and clinical panelists contribute equally. Currently, the process for consensus has been based in the US and Europe, with less input from other regions of the world.

The Quantity of Evidence Considered

Expert opinion is not equivalent to data from evidence-based studies [12,13]. Science is about the truth not about consensus. Several examples support the importance of evidence rather than opinion or consensus [13]. The Delphi method is a well-established approach to a research question by identifying a consensus view across experts on the subject. However, in 2000, using the Delphi consensus method, Gale and colleagues recommended high-dose chemotherapy and auto-transplantation for some women with high-risk breast cancer [14]. Subsequent randomized controlled trials showed this approach was not clinically effective [15]. Also, in a study of almost 100 consensus statements, the rigor of the development of consensus statements was less than one-third that of evidence-based guidelines [15,16]. The AASLD/EASL consensus process was formulated using a questionnaire of personal views, which was neither validated nor transparent. Therefore, the process should be replaced by one that facilitates the generation of evidence-based recommendations informed by a systematic review of the evidence. This is the only way forward if it is to be hoped that the outcomes will truly represent the current available scientific data and will get accepted.

Discarding the Voice of the Academic and Clinical Community

The third concern is discarding the input from the global academic and scientific clinical community and therefore fails to meet the true definition of 'consensus.' This word is derived from the Latin word, 'consens,' which means, 'to agree.' Several theories have proposed that 'collective intelligence,' or 'the wisdom of the crowd,' may result in more accurate judgments than the views of a few 'experts.' In 1906, the statistician Sir Francis Galton compared the median guess of the weight of an ox to that of several butchers or experts and showed that the median guess of the crowds was more accurate than any

individual guess or of the experts. A recent internet-based repeat of this study demonstrated that responses from over 17,000 random respondents who looked at the photo of a cow guessed a closer median weight compared to a panel of 600 self-declared experts [16].

An alternative to NAFLD was proposed in 2020 as metabolic dysfunction-associated fatty liver disease (MAFLD) [10]. The term MAFLD has generated significant interest in just two years, with more than 700 publications in Pubmed alone. These publications and guidelines are based on reasonable evidence, though much more is required to adopt the terminology of MAFLD fully.

Forced Consensus to Have a Perceived Consensus

There are several implications of developing a perceived consensus view. The reason for reviewing the NAFLD nomenclature is appropriate as there is currently a global division regarding the terminology. It may be argued that a 'forced consensus,' despite its profound limitations, is justified in unifying the field. However, the opinion of the authors of this Editorial is that this process risks dividing rather than unifying opinions. The core principles for unification should be rigor in the evidence and a validated and inclusive approach. Therefore, although statements and recommendations may result from consensus processes, it does not follow that the consensus recommendations will be adopted, particularly if the consensus process is flawed.

Conclusions and a Final Word of Caution

All the above begs a fundamental question on how much should we rely on the AASLD/EASL process? They have adopted the Delhi process for building a consensus. There are several limitations regarding using the Delphi process for achieving clinical consensus. Importantly, the methodology may be flawed, and there is limited evidence of reproducibility and reliability of the data. Unless immediate actions are taken by those running the NAFLD consensus, multiple definitions will get generated and adopted in different regions. This is to be anticipated based on the processes so far. The global validity of recommendations is a distinct issue that national and pan-national professional societies should evaluate. Health authorities will need to analyze the validity of clinical statements based on how they were developed and whether they align with regional views and priorities.

We acknowledge our comments are iconoclastic but we believe them sensible. We conclude with a quote from the Harvard

economist, John Galbraith: "One of my greatest pleasures in my writing has come from the thought that perhaps my work might annoy someone of comfortably pretentious position. Then comes the realization that such people rarely read".

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