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Perspective

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NAFLD to MAFLD: collaboration, not confusion - rethinking the naming of fatty liver disease

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Abstract

The recent shift from "non-alcoholic fatty liver disease" (NAFLD) and "metabolic associated fatty liver disease" (MAFLD) to "metabolic dysfunction-associated steatotic liver disease" (MASLD) has raised questions about its scientific basis and impact on patient understanding. This renaming may create confusion rather than clarity. A collaborative approach involving healthcare professionals, researchers, and patients to establish terminology that balances scientific accuracy with accessibility is needed. Effective disease naming should be accurate, unique, consistent, objective, and accessible - qualities essential for clear communication in healthcare. Disease name is more than scientific correctness because naming conventions for public use, especially anything related to health, must be a matter of convenience, ethics, and cultural and social acceptance. Education and straightforward communication should take precedence over renaming, helping patients and healthcare providers fully understand the complexities and implications of liver disease for treatment. After all, from a scientific and public health perspective, MAFLD has clear advantages over MASLD.

Keywords: MAFLD, MASLD, NAFLD, disease nomenclature convention, disease definition, public health, political correctness, education, metabolic syndrome

INTRODUCTION

The recent suggestion for shifting disease nomenclature from NAFLD (non-alcoholic fatty liver disease) [Figure 1] to metabolic dysfunction-associated steatotic liver disease (MASLD) raises several concerns[1]. The justification for a change seems unclear from a scientific standpoint. The process itself, fraught with limitations, has the potential to create more confusion than clarity. Rather than renaming, it would seem that a focus on education is more important. Moving forward, collaboration between healthcare professionals, researchers, and patients is crucial. Together, we can establish clear and understandable disease terminology that strikes the necessary balance between scientific accuracy and the needs of the public.

WHAT'S IN A NAME?

Are we seeing more name changes these days? From countries and places to monuments and to diseases? Are we connecting names with our socio-political identities more than before? Name changes were always a part of science. Whether it is Carolus Linnaeus's "binomial nomenclature" for the naming of organisms, the International Union of Pure and Applied Chemistry (IUPAC) nomenclature for chemical compounds, or the International Union of Pure and Applied Physics (IUPAP) for physics, terminologies have one goal - to formulate scientific, practical, consistent, and uniform nomenclature. Unlike these systems, in medical sciences, the terminology has another important element - the requirement for social engagement, acceptability, and public education. This involves meticulous consideration of linguistic, cultural, and ethical dimensions, along with meaningful collaboration with patients and stakeholders.

WHY DO WE HAVE DICTIONARIES AND DEFINITIONS?

Frequently, we turn to dictionaries not just to acquire new words but to understand their definition and usage. Dictionaries can generally be classified into prescriptive and descriptive types: prescriptive dictionaries aim to establish language rules, while descriptive ones record actual language usage. In the realm of a living language, both types hold significance. However, in scientific naming and nomenclature, priority should be given to descriptive methods that mirror current practices in the field. Standards should only be enforced when no established norms exist. However, these standards must be flexible and responsive to evolving practices and advances in the field. Disruptive nomenclature should not be

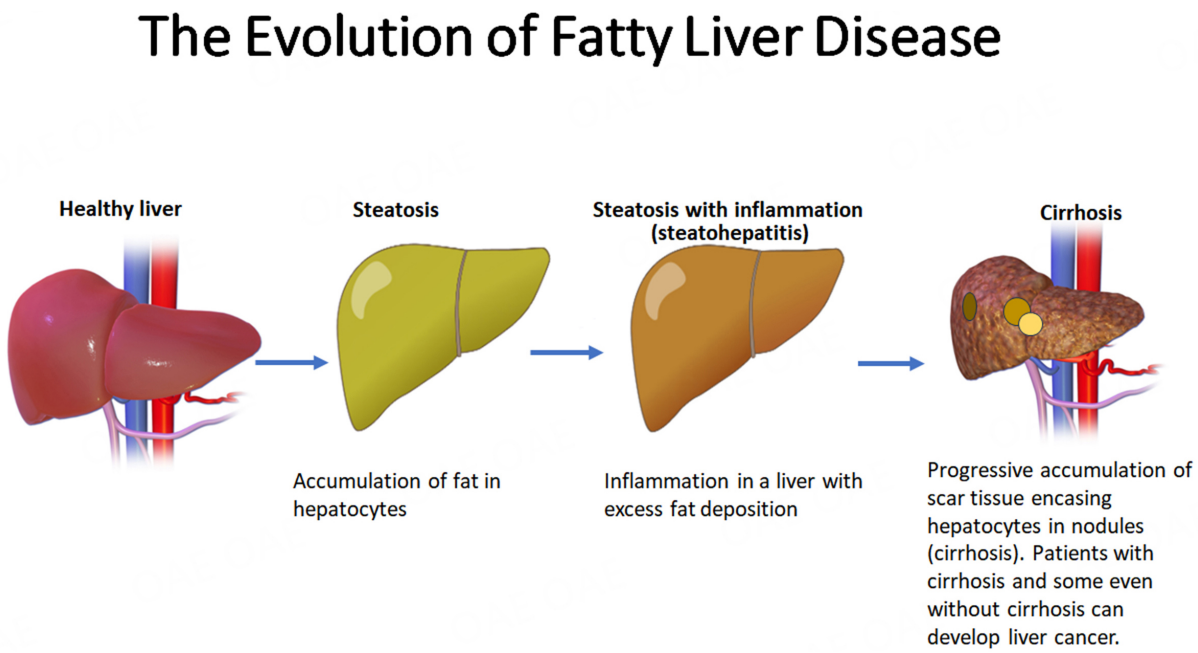

Figure 1. The evolution of fatty liver disease. Image source: https://commons.wikimedia.org/wiki/File:Liver_Cirrhosis.png; https://commons.wikimedia.org/wiki/File:NAFLD_liver_progression.svg.

introduced unless there is a compelling reason to do so.

DISEASE NOMENCLATURE IS MORE THAN SCIENTIFIC CORRECTNESS

The method of science is logic, experiments, proofs, and facts. Science is not what you establish by an opinion poll. We do not conduct opinion polls to accept or reject "human evolution". However, it is important to note that the naming conventions for public use, especially anything related to health, must be a matter of convenience, ethics, and cultural and social acceptance. Therefore, due deliberation is required. However, when we analyze the suggested change in nomenclature to MASLD, one cannot find a robust scientific or socio-political rationale to justify this change. The change does not have a cogent scientific basis and the authors do not see a logical sequence for this name change. In addition, does MASLD provide a better ethical perspective?

WHAT ARE THE KEY REQUIREMENTS OF A DISEASE NOMENCLATURE?

A good disease nomenclature should meet several key requirements to be effective for healthcare professionals, researchers, public health officials, and more importantly, the public. Here are some of the important ones:

Accuracy: Terms should accurately reflect the current scientific understanding of a disease, including its causes, symptoms, and progression.

Uniqueness: Each disease should have a unique identifier to avoid confusion and ensure clear communication.

Consistency: Terminology should be consistent across different contexts, like medical records, research papers, and public health communications.

Objectivity: Terms should be objective and avoid subjective interpretations or value judgments about the disease.

Granularity: The name should allow for different levels of detail depending on the specific needs. For example, a general classification might be sufficient for some purposes, while a more detailed sub-classification will be needed for others.

Comprehensiveness: The nomenclature should encompass a wide range of diseases and conditions.

Adaptability: As human understanding progresses, the system must remain flexible to incorporate new knowledge, discoveries, and evolving perspectives on diseases. Equally crucial is its ability to adjust to changes in an ever-changing socio-political landscape.

Accessibility: The terminology should be clear and understandable for both healthcare professionals and the public, whenever possible.

International applicability: Ideally, the nomenclature should be usable across different continents, countries and languages, facilitating global health communication.

IS SCIENCE A DEMOCRATIC PROCESS?

In science, can we decide what is right by voting? Are experts always right? How can a consensus be manipulated? Does making a democratic decision make it more appropriate? Can participants in a survey be influenced by a caucus of people with vested interests as it happens in national or international politics? Perhaps we all know the answers.

Fortunately, the scientific process does not care for human consensus. We cannot decide whether the earth is flat or not through a democratic consensus, but only through scientific observations and their validation. Instead, "democracy in science" refers to the idea that scientific processes should be transparent and open to scrutiny. While scientific principles are based on evidence, peer review, and replication, the process itself is not inherently democratic. Scientific research involves a mix of individual expertise, rigorous testing, and peer-reviewed replication rather than democratic voting.

The beauty of scientific exploration lies in the freedom to use terminology that best reflects current understanding. Enforcing a single term for everyone is not exactly democratic, is it? As recently pointed out, "When the evidence is not sufficient to support a unanimous vision, consensus becomes nothing more than the convergence of opinions of many researchers on a particular topic"[2]. However, the question remains: Was there a real need for this? Was it driven by the stigma surrounding alcoholism and obesity? As further commented, "Whether unanimous or not, the scientific consensus is the pillar of the relationship between science and society as it avoids confusion and misinformation"[2]. Has the renaming initiative resolved confusion or exacerbated it? If the former were true, we would not have witnessed a plethora of responses including the above comments. Alternatively, could the name change represent another facet of the crisis outlined: "In the last years, the integrity, quality, and reliability of scientific research have been the subject of criticism both from within and outside the scientific community." The term metabolic associated fatty liver disease (MAFLD) was proposed principally because of the need for an affirmative diagnosis unrelated to the presence or absence of other concomitant liver diseases, while also reflecting its underlying pathogenesis. On these grounds, there has not been any argument. Removing the word "Non-Alcoholic" has also not been contested and is of particular value in parts of the world where alcohol consumption is frowned upon due to

religious or cultural norms. Hence, what was the need to come up with another term?

FINDING A BETTER TERM?

The term "NAFLD" is imprecisely defined; there is uncertainty regarding its pathogenesis and there is a perceived need for a new nomenclature. However, renaming was not attempted because of certain fundamental concerns regarding the identity of the entity[3]. Limiting people's choices in a survey to select a suitable term restricts their options to the provided list. In the recent survey, which leads to the suggestion of "MASLD"[1], only a constrained set of terms was presented simply based on an *a priori* decision that NAFLD needs to be renamed rather than for conceptually advancing the field. The proposed set of terms potentially influenced participants' responses, prompting and steering them toward predetermined outcomes. If there were more options, there is a good chance that the outcomes of the survey would have been different. Metabolic dysfunction-associated fatty liver disease is a good term. A patient might ask, "What is metabolic dysfunction?" There are clear and simple criteria for this, which can be easily understood by patients. This simplicity and clarity can be invaluable in fostering patient understanding, empowerment, and education.

IS IT WISE TO COMPARTMENTALIZE ALCOHOL RELATED FATTY LIVER DISEASE AND NAFLD?

It is difficult to isolate practically or mechanistically alcohol-associated liver disease and NAFLD because many people (and perhaps a majority in many countries) consume alcohol. Some studies suggest that hepatic steatosis is more highly correlated with obesity than heavy drinking[4]. This implies that overweight individuals may be at a greater risk for developing this condition compared to those who primarily consume large amounts of alcohol. However, the amount of alcohol consumed and its cut-offs are arbitrary and "less meaningful", considering the complexity and heterogeneity of alcohol metabolism, the genetics of the body's anti-oxidant systems, immunity and inflammation, as well as endogenous gut microbial alcohol production[5]. Furthermore, many common signaling pathways and genes result in similar responses that decide the prognosis in both conditions. This makes it very difficult to separate the two entities. Again, MAFLD defines, in affirmative terms, the criteria which patients must meet to be diagnosed with the condition, and which will adversely impact their liver health. The amount of alcohol they drink, or for that matter, whether they have viral hepatitis, has no bearing on whether the patient has metabolic dysfunction-associated fatty liver disease or not. Thus, MAFLD deftly disentangles itself from the mix of positive and negative criteria (arbitrarily defined levels of reported alcohol consumption) required for a MASLD diagnosis.

FATTY LIVER AS A DISEASE

Polar bears, codfish, and sharks, to name a few, have livers full of fat. It is their natural depot for fat storage after adipose tissue[6]. Even in humans, some amount of liver fat storage is physiological and varies across the lifespan, but not when it is in excess for a person's stage in their lifespan. A few studies suggest that fatty liver is present in up to 80% of octogenarians at postmortem[7]. Interestingly, murine studies suggest that liver fat in older age is associated with longevity[8]. In humans, however, excess liver fat typically signals an underlying metabolic disease. It also serves as an excellent, cost-effective surrogate maker for predicting liver, cardiovascular, and pancreatic morbidities, as well as cancer[3,6].

IS MASLD ABOUT BEING POLITICALLY CORRECT?

The SI unit of force is Newton, named after Sir Isaac Newton. Sir Newton invested heavily in a company called The South Sea Company[9]. The major business of this company was shipping of enslaved Africans

across the Atlantic. Should we advocate for renaming the unit of force due to this historical association? There is a heightened sensitivity these days around race, gender, appearance, and so on, which is sometimes engineered and exploited by people with vested interests. The effects include removing historic structures and statues[10], altering eponyms (e.g., Wegener's granulomatosis)[11,12], medical terms (consumption for tuberculosis)[13], *etc*.

The renaming of fatty liver disease, the transition from NAFLD to MAFLD, is grounded in objective criteria, focusing on underlying metabolic dysfunction and fat accumulation in the liver. However, a change to MASLD appears subjective and imperative.

Some argue it aims to reduce stigma without clear supporting evidence. The term "NON-ALCOHOLIC fatty liver disease" explicitly indicates the absence of alcohol consumption, and as alluded to earlier, the amount of drinking and its cut-offs are arbitrary and cannot be arbitrated upon, but rather require evidence. MASLD may be attributed to a genre of political correctness, characterized by heightened sensitivity to prejudice, sometimes surpassing logical reasoning. Claims of body shaming due to the term "fatty" in NAFLD or MAFLD are considered symptomatic of this sensitivity. It is even more true since the term "fatty liver" does not refer to one's external appearance but to the presence of fat in an internal organ. Contrary to assumptions, India has the highest number of fatty liver patients globally, attributed to its status as the diabetes capital. In India, obesity is not stigmatized, and moderate obesity is often perceived as healthy and appealing. Unfortunately, in the survey[1], patient and geographical representation especially from the most populated continents (and those harboring the greatest burden of liver disease) - Asia and Africa was poor and this fact generated a predictable reaction[14-20].

Irrespective of regional differences, clarity in communication remains crucial. Communication between doctors and patients should not leave any kind of ambiguity. When discussing medical conditions such as fatty liver disease with patients, it is critical that healthcare professionals use language that is clear, concise and easy to understand. This includes avoiding jargon or technical terms that may be unfamiliar to patients. In the West and other parts of the world, when communicating with patients, it is common practice to tell patients they have a fatty liver, as most would not understand the term "steatotic".

FATTY LIVER DISEASE: MERELY A PRACTICAL DIAGNOSIS

Diagnosing fatty liver disease is a nuanced and practical challenge from both scientific and clinical perspectives. It is particularly difficult to disentangle and evaluate the relative and independent contributions of various aetiologies that lead to the accumulation of fat in the liver. The main contributing factors include metabolic syndrome (specifically insulin resistance), alcohol consumption, and viral infections[3,6,21-26].

Determining the extent to which each factor - alcohol intake, insulin resistance, or infection -contributes to the presence of fat and inflammation in the liver is especially challenging when a patient presents with multiple potential causes. This complexity arises because these factors can interact in ways that are not yet fully understood, making it hard to pinpoint their individual impacts.

One positive development is the effective treatment of viral aetiologies, which has led to a decrease in liver fat due to viral infections. However, this progress does not extend to alcohol-related liver disease, as excess alcohol consumption remains a significant and persistent problem. Additionally, it is important to recognize that a substantial amount of alcohol is produced endogenously within our bodies[5], and the role of this internal alcohol production in contributing to fatty liver disease is currently not well understood.

NEED FOR A CRITERIA WHICH IS OF PUBLIC HEALTH UTILITY

"Steatosis" like "hepatitis" - is considered as a histological diagnosis. While MAFLD can be a clinical diagnosis, MASLD cannot because steatosis needs to be established by histopathology. This would be important from a public health perspective, especially for mass diagnosis and for various epidemiological association studies where a liver biopsy is not possible either because of resource constraints, associated risks, or ethical concerns. Additionally, the non-invasive markers of non-alcoholic steatohepatitis (NASH) and liver cirrhosis are slowly improving, which makes liver biopsy less justifiable.

Even if one could argue that newer ultrasound equipment can detect steatosis with reasonable efficiency, the gold standard remains histological. The use of the term "steatotic" could also cause further confusion from this perspective. The severity of steatosis can be graded based on the percentage of hepatocytes containing fat. The grading of steatosis is mild (Grade 1) when less than 33% of hepatocytes are affected, moderate (Grade 2) when 34% to 66% of hepatocytes are affected, and severe (Grade 3) when more than 66% of hepatocytes are affected can be decided only by histology[27].

APPRAISING THE EVIDENCE: MAFLD HAS THE EDGE

From the perspective of a screening tool, MAFLD captures the mortality and morbidity in a population better than MASLD, especially because it gives due importance to metabolic and adiposity risk factors[28]. MAFLD is also proven to be highly effective in identifying individuals at elevated risk for metabolic complications and a range of liver and non-liver diseases[29]. In addition, MAFLD criteria are better than MASLD at predicting the risk of chronic kidney disease[30] and identifying individuals who have both fatty liver and significant fibrosis when assessed using non-invasive tests[31]. Finally, the MASLD definition, when used in children, is flawed, underscoring the advantages of the consensus criteria for pediatric MAFLD[29,32]. To summarize, based on published evidence, the MASLD criteria fall short in comparison to the MAFLD criteria [Table 1].

BALANCING ACCURACY AND ACCESSIBILITY

Finding a balance between scientific accuracy and accessibility in disease naming is crucial for effective communication in the medical field. While using common language can enhance understanding among the wider public, certain medical terminology is indispensable for precise communication by healthcare professionals and researchers, such as the terms fatty liver or fatty streaks or fatty pancreas.

One of the primary considerations in disease naming is ensuring that the terminology is accessible to the public. Using language that is easily understood by patients and the broader community fosters clear communication between healthcare providers and individuals seeking medical information. For example, replacing complex scientific terms with simpler, more familiar language can help patients grasp the nature of their condition and the recommended treatment options. This approach promotes patient education and empowers individuals to make informed decisions about their health.

However, it is also important to recognize the necessity for scientific accuracy in disease naming. Certain medical terms, rooted in Latin or Greek origins, convey specific meanings that are essential for precise diagnosis and treatment. While common language may provide accessibility, it may not always capture the nuanced characteristics of a disease. For instance, replacing the term "NAFLD" with a simplified version may sacrifice the specificity needed for accurate medical diagnosis and management.

Table 1. NAFLD *vs.* MASLD

Feature	NAFLD	MAFLD	MASLD
Definition	Fatty liver, not due to alcohol	Fatty liver with metabolic dysfunction	Fatty liver with metabolic dysfunction
Diagnostic criteria	Fat in liver, low alcohol intake	Fat in liver, with metabolic abnormality	Fat in liver, low alcohol intake, metabolic abnormality and no other cause for liver disease (e.g., viral hepatitis or autoimmune disease)
Focus	Presence of fat but not due to alcohol	Metabolic link	Metabolic link with exclusion of other diseases
Current status	Well-established term	Replacement	Latest proposed controversial replacement
Advantage	Simple, well-established, classic; Self-explanatory-easy to understand by the public	Focus on fatty liver associated with metabolic syndrome	Inventors claim the term is more politically correct
Disadvantages	An umbrella term (less focus on the cause/association with metabolic syndrome)	Metabolic dysfunction-associated fatty liver disease- does not specify which metabolic dysfunction; Dysfunction is clarified in the detailed classification	Does not define a disease based solely on positive criteria; Diagnostic criteria require positive attributes (fat and metabolic dysfunction) and negative attributes (particular levels of alcohol consumption, exclusion of other diseases, *etc.*); Creates an extra term (metALD precisely because it does not define the disease in positive terms); Changes in nomenclature cause confusion among the scientific community and the public; Frequent changes in nomenclature cause confusion among the scientific community and the public; The new nomenclature has no additional scientific merit to earlier terms; Technically, steatosis is a histopathological diagnosis that requires a biopsy; The term was proposed through a less transparent process and did not involve proportionate representation of different geographic locations across the world
Metabolic criteria	Diagnosis is made without the need for a standardized assessment of metabolic dysfunction	Patients are placed in homogenous groups represented by those with: (1) Obesity: BMI greater than or equal to 25 kg/m^2 (or greater than or equal to 23 kg/m^2 in Asian populations); (2) Type 2 diabetes: A formal diagnosis of diabetes; (3) Normal weight by ethnic-specific criteria with two or more of 7 defined metabolic risk factors	MASLD necessitates that a patient has at least one of five prescribed metabolic risk factors
Alcohol consumption	Consumption of alcohol above a certain arbitrary level is an exclusion criterion	MAFLD diagnosis is made only on the basis of metabolic dysfunction	A MASLD diagnosis allows for a certain arbitrary level of alcohol consumption

NAFLD: Non-alcoholic fatty liver disease; MAFLD: metabolic associated fatty liver disease; MASLD: metabolic dysfunction-associated steatotic liver disease; BMI: body mass index.

Moreover, renaming diseases solely to make them more accessible can inadvertently perpetuate stigma and misconceptions. For example, renaming "pancreatic cancer" to "pancreatic karkinos" (to counter stigma and fear associated with cancer) or telling patients they have a "hematoma" (instead of bruise), "epistaxis" (instead of nose bleed), "dyspnoea" (instead of breathlessness), or "urticaria" (instead of hives), may not only confuse patients but also inadvertently reinforce negative associations and fears surrounding the disease. Instead, efforts should be directed toward education and awareness campaigns to destigmatize diseases and promote early detection and treatment.

In navigating the balance between accuracy and accessibility in disease naming, collaboration among healthcare professionals, researchers, patients, and advocacy groups is crucial. By engaging in open dialogue and considering diverse perspectives, stakeholders can develop terminology that is both accurate and

understandable to the public. Additionally, leveraging advancements in health communication and technology can facilitate the dissemination of accurate information in a clear and accessible manner.

In conclusion, finding the balance between scientific accuracy and accessibility in disease naming is essential for effective communication with patients, for clinical practice and for research. By collaborating and considering diverse perspectives, stakeholders can develop terminology that promotes clear communication, empowers patients, and reduces the stigma associated with the disease.

DECLARATION

Authors' contributions

Drafted the manuscript: Sanal MG, George J

Involved in manuscript revision and approval of final draft: Gish RG, Méndez-Sánchez N, Yu ML, Chan WK, Wei L, Zheng M, Grønbæk H

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Conflicts of interest

Gish RG has a speaker's contract to do promotional talks for: AbbVie, AstraZeneca, BMS, Diasorin, Eisai, Genentech, Gilead Sciences Inc., Intercept, Ipsen Biopharmaceuticals, Madrigal, Mallinckrodt, and VBI Vaccines. Minor stock shareholder (liver space noted only): RiboSciences, and CoCrystal. Stock Options: Abacus, Eiger, Genlantis, HepQuant, AngioCrine, HepaTx, JBS Science, and Virion (details provided separately). Gish RG has served as Consultant and/or Advisor to (in the last two years): Abacus, Abbott, AbbVie, Albireo, Aligos, Altimunne, Antios, Arrowhead, AstraZeneca, Audentes Therapeutics, Corcept, Dynavax, Effectus, Eiger, Eisai, Enyo, Genentech, Genlantis, Gerson Lehrman Group, Gilead Sciences, GlaxoSmithKline, Helios, HepaTX, HepQuant, Intercept, Ipsen, Janssen, JBS Science, Kinnate Bio, Merck, Precision BioSciences, Pfizer, Seres Therapeutics, Topography Health, Tune Therapeutics, Venatorx, and Virion. (details provided separately). Wei L: Consultant of Abbott, Abbvie, BMS, Gilead, Roche, and Roche diagnostics; Speaker of Abbvie, BMS, Eisai, Gilead, Roche, and Roche diagnostics. Grønbæk H, Consulting Fees: Ipsen, NOVO, Pfizer. Lecturer: AstraZeneca, EISAI; Data Monitoring Committee: CAMURUS AB. Chan WK: Chan WK has served as a consultant or advisory board member for Abbott, Roche, Abbvie, Boehringer Ingelheim, and Novo Nordisk; and a speaker for Abbott, Novo Nordisk, Echosens, Viatris, and Hisky Medical. Zheng M has received honoraria for lectures from AstraZeneca, Hisky Medical Technologies, and Novo Nordisk, consulting fees from Boehringer Ingelheim, serves as a consultant for Eieling Technology. George J serves on Advisory Boards and receives honoraria for talks from Novo

Nordisk, Astra Zeneca, Roche, BMS, Pfizer, Cincera, Pharmaxis, Gilead, AbbVie, and Boehringer Ingelheim. Wei L consults for BI, Gilead, Hisky Medical, Kaiyin, MSD, Novo Nordisk, Pfizer, Roche, and VirsiRNA, Speaker for Novo Nordisk and Sanofi, and receives research grants from Amoytop, AZ, Gilead, Kaiyin, Pfizer, and Sanofi. The other authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

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Consent for publication

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