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EDITORIAL

# NASH vs MASH- a Paradigm Shift from Exclusion to Pathophysiology

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For decades, non-alcoholic steatohepatitis (NASH) has been used to describe the inflammatory and progressive form of fatty liver disease occurring in individuals without significant alcohol consumption. Embedded within the broader construct of non-alcoholic fatty liver disease (NAFLD), the term NASH reflected the clinical thinking of its time. However, as understanding of fatty liver disease has evolved, it has become increasingly clear that defining a condition by what it is *not*—rather than by what it *is*—is conceptually flawed. The recent transition from NASH to metabolic-associated steatohepatitis (MASH), within the umbrella of metabolic-associated steatotic liver disease (MASLD), represents a major paradigm shift from exclusion-based diagnosis to one rooted in pathophysiology.

The NAFLD–NASH framework was primarily anchored in the exclusion of excess alcohol intake and secondary causes of steatosis. While pragmatic, this approach placed disproportionate emphasis on alcohol, despite mounting evidence that metabolic dysfunction—particularly obesity, insulin resistance, type 2 diabetes mellitus, and dyslipidaemia—is the principal driver of disease development and progression. Epidemiological studies consistently demonstrate that cardiovascular disease, rather than liver failure, is the leading cause of mortality in patients with fatty liver disease, highlighting its systemic metabolic nature rather than an isolated hepatic disorder.[1]

Moreover, the exclusionary definition of NASH has struggled to accommodate the biological and clinical heterogeneity of the disease. Patients with identical histological features often exhibit markedly different metabolic risk profiles, rates of fibrosis progression, and extrahepatic outcomes. The rigid separation between “alcoholic” and “non-alcoholic” liver disease has also proved increasingly artificial, as many patients encountered in routine practice have mixed aetiologies, combining metabolic risk factors with modest alcohol intake. Under the NAFLD–NASH paradigm, such patients were frequently excluded from research studies and clinical trials, limiting the generalisability of emerging evidence.

In response to these limitations, an international consensus group proposed a new nomenclature centred on metabolic dysfunction. Initially introduced as metabolic dysfunction–associated fatty liver disease (MAFLD), the terminology was further refined in 2023 through a multi-society Delphi process, resulting in the adoption of MASLD and MASH.[2] Under this framework, hepatic steatosis is diagnosed in the presence of at least one cardiometabolic risk factor, while MASH designates the inflammatory and fibrotic phenotype previously labelled as NASH. Crucially, the diagnosis is based on positive metabolic criteria rather than the mere exclusion of alcohol.

Importantly, MASH does not represent a new disease entity. From a histopathological standpoint, MASH is indistinguishable from NASH, characterised by hepatic steatosis, lobular inflammation, hepatocellular ballooning, and varying degrees of fibrosis. What has changed is the conceptual lens through which the disease is understood. By explicitly anchoring steatohepatitis to metabolic dysfunction, the MASH framework aligns nomenclature with contemporary insights into disease biology and systemic metabolic regulation.[3]

The clinical implications of this shift are substantial. Reframing NASH as MASH encourages clinicians to adopt a more integrated approach to patient care, recognising fatty liver disease as a hepatic manifestation of multisystem metabolic dysfunction. This perspective reinforces the importance of aggressive management of cardiometabolic risk factors, including obesity, diabetes, hypertension, and dyslipidaemia, alongside liver-specific assessment. It also facilitates clearer communication with patients, avoiding the stigmatising and often misleading implication that alcohol is central to disease causation.

For clinical research and drug development, the transition to MASH offers a more inclusive and biologically coherent framework. Many pivotal trials in NASH have struggled with patient selection, high screen-failure rates, and limited external validity. A definition grounded in metabolic dysfunction allows for the inclusion of patient populations more reflective of real-world practice, including those with low-level alcohol consumption but clear metabolic risk. This shift may enhance the interpretability of trial outcomes and accelerate the translation of therapeutic advances into clinical care.[4]

The public health implications are equally compelling. The global burden of fatty liver disease continues to rise in parallel with obesity and type 2 diabetes, particularly in low-income and middle-income countries undergoing rapid nutritional and lifestyle transitions. By explicitly linking steatohepatitis to metabolic disease, the MASH construct strengthens the case for upstream preventive strategies targeting diet, physical activity, and social determinants of health. It also aligns fatty liver disease policy with broader non-communicable disease frameworks, facilitating coordinated public health responses.[5]

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Despite its advantages, the transition from NASH to MASH is not without challenges. NASH remains deeply embedded in clinical guidelines, regulatory pathways, and the lexicon of ongoing therapeutic trials. A period of dual terminology is inevitable, and careful cross-referencing will be required to preserve continuity in clinical care and research. Education of clinicians, researchers, patients, and policymakers will be essential to ensure consistent adoption and avoid confusion during this transitional phase.

Nevertheless, the shift from NASH to MASH represents a decisive step towards precision and pathophysiological relevance in liver disease nomenclature. As hepatology increasingly intersects with endocrinology, cardiology, and public health, terminology that reflects shared mechanisms rather than artificial exclusions is both timely and necessary. The success of this paradigm shift will ultimately depend not on language alone, but on whether it catalyses more integrated care, more inclusive research, and more effective prevention strategies.

In conclusion, replacing NASH with MASH marks more than a semantic revision. It reflects a fundamental reorientation of fatty liver disease from an exclusion-based diagnosis to one grounded in metabolic pathophysiology. By aligning terminology with biology, reducing stigma, and enhancing clinical relevance, MASH offers a more coherent framework for addressing one of the most pressing liver disease challenges of the 21st century.

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