Online ISSN 3007-3197 Print ISSN 3007-3189

http://amresearchreview.com/index.php/Journal/about

Annual Methodological Archive Research Review
http://amresearchreview.com/index.php/Journal/about
Volume 3, Issue 7 (2025)

Non-Alcoholic Fatty Liver Diseases To Metabolic Dysfunction-Associated Fatty Liver Diseases: a Paradigm Shift

[1]Dr. Sharoz Mukhtar Shah, [2]Dr. Esha Azhar, [3]Dr. Talha Tanveer , [4]Dr. Mariam Farooq

Article Details

Keywords: NAFLD, MAFLD, Metabolic Dysfunction, Fatty Liver Disease, Clinical Diagnosis, Public Health Policy, Liver Disease Classification.

Dr. Sharoz Mukhtar Shah
Medical Officer, Department of Internal Medicine, Allied Hospital II (DHQ), Faisalabad, Pakistan.
Sharozmukhtarshah@gmail.com
Dr. Esha Azhar
House officer, Sir Ganga Ram Hospital, Lahore, Pakistan. iameshaazahar@gmail.com
Dr. Talha Tanveer
Medical Officer, Department of Internal Medicine, District Headquarter Hospital, Khushab, Pakistan.
talhatanveer855@gmail.com
Dr. Mariam Farooq
Medical Officer, Department of Internal Medicine, Faisal Hospital, Faisalabad, Pakistan.
mariamfarooq.mf@gmail.com

ABSTRACT

NAFLD has historically been diagnosed by excluding other liver diseases and alcohol use, but given its global prevalence (~30%), recent evidence has prompted its reconceptualization as metabolic dysfunction-associated fatty liver disease (MAFLD) to reflect a metabolism-centered pathogenesis. This review explores the conceptual, clinical, and policy implications of the renaming of NAFLD to MAFLD, examining etiological and diagnostic differences, clinical outcomes, controversies, and future research and policy directions. A critical review of peer-reviewed studies, consensus statements, and policy reports was conducted to evaluate the implications of this nomenclature transition. MAFLD offers a positive diagnostic framework requiring metabolic dysfunction, including patients previously excluded (e.g., those with coexisting liver etiologies) and identifying a higher-risk cohort with more metabolic comorbidities and worse outcomes, such as increased cardiovascular and renal complications. The MAFLD shift influences research design and enhances clinical recognition, but introduces challenges for global consensus, regulatory coding alignment, and comparability with historical NAFLD data. In conclusion, MAFLD provides a more inclusive, clinically relevant model focusing on metabolic drivers and personalized, multidisciplinary care. However, unresolved controversies (including some expert opposition), coding inconsistencies, and global policy inertia hinder its full adoption, indicating a need for harmonized terminology, updated clinical guidelines, and improved public health strategies..

Received on 23 June 2025
Accepted on 02 July 2025
Published on 27 July 2025

DOI: Availability

INTRODUCTION

The modern lifestyle, characterised by unhealthy diets and sedentary habits coupled with social inequalities, induced stress, is leading to a silent epidemic called metabolic dysfunction-associated fatty liver disease (MAFLD). MAFLD, previously known as non-alcoholic fatty liver disease (NAFLD), has become the leading cause of liver-related mortality, with the global prevalence rate reaching 30.1% (from 1990-2019). The situation is alarming considering the growing trajectory, which shows that the prevalence rate has increased from 25.3% (1990-2006) to 38.2% (2016-2019)[i]. Thus, MAFLD is a major health crisis that not only puts a major health and economic burden around the globe but also has no approved pharmacotherapy[ii].

The term Non-alcoholic fatty liver disease, first coined by Schaffner, was primarily developed to distinguish patients with steatotic change in the liver caused by unknown agents from patients with alcohol induced steatohepatitis. Thus, the term NAFLD was loosely associated with any fatty liver inflammation that was not induced by alcohol. However, the recent body of evidence and advanced understanding of the disease etiology and pathogenesis have led to a more inclusive term, MAFLD.

This review article aims to critically investigate the current and future implications of this paradigm shift from NAFLD to MAFLD, highlighting the etiological differences between the two terms, evaluating the clinical implications, and analysing the potential challenges and opportunities the transition can bring from the viewpoint of researchers, clinicians, and policymakers.

CONCEPTUAL EVOLUTION

Non-alcoholic fatty liver disease (NAFLD) was recognized in the early 1980s and coined by Schaffner and Thaler in 1986 to describe fatty liver in patients without significant alcohol intake[iii]. NAFLD was defined by the presence of hepatic steatosis and the exclusion of other causes of liver fat (e.g., heavy alcohol use, viral hepatitis, or drugs)[iv]. On the one hand, the prevalence of NAFLD has been rising for decades, reaching the levels of a significant worldwide problem nowadays, with about a quarter of adult individuals comprising its global burden in parallel with the rising rates of obesity and type 2 diabetes (T2D) [3].

The way non-alcoholic fatty liver disease (NAFLD) has been conceptualized has been brought under serious examination. NAFLD diagnosis is arrived at as a diagnosis of exclusion; therefore, it becomes difficult when there is the existence of multiple risk factors or the co-occurrence of other co-morbid liver diseases [4]. A typical example is a moderately addicted,

obese, diabetic patient who additionally has viral hepatitis; he or she may not be able to be diagnosed with NAFLD even though there is obvious metabolic fatty liver on board[4].

In 2020, specialists suggested changing the name of NAFLD to metabolic dysfunction-associated fatty liver disease (MAFLD) since it has an underlying metabolic pathogenesis [4]. Defined as a meta-positive disease, MAFLD is characterized by the presence of hepatic steatosis and metabolic risks (e.g., obesity or T2D), without the need to exclude other liver diseases. Therefore, in contrast to NAFLD, metabolic dysfunction in a case of a viral infection of the liver (viral hepatitis) or alcohol consumption, will lead to diagnosing a patient with MAFLD[v]. This paradigm shift toward inclusive criteria directly identifies the appearance of fatty liver disease, which is driven by metabolism, and the pathophysiology of this condition is better captured [4]. Some experts have urged the use of fatty Liver as a metabolic disease, similar to other organs in the body. This change of nomenclature is rationalized by the fact that this would potentially enable providers to finally conduct correct clinical diagnosis and reduce stigmatization connected to the term of liver disease without alcohol as non-alcoholic [3].

The term MAFLD,shortenedto metabolic-related fatty liver disease, has become a widespread term in the scientific world quite quickly. The revised classification has been supported by many experts, and the Asia Pacific Association of the Study of the Liver was among the very first organizations to include the revised classification in official guidelines[vi]. Nevertheless, there is still a heated discussion, whereas more and more specialists use the terminological change to MAFLD. In the recent discussions, it has been proposed that the re-classification of NAFLD with all other metabolic disorders better reflects the pathogenesis as compared to an exclusionary model and, hence, better reflects the underlying mechanism of the condition [4].

ETIOLOGICAL AND PATHOPHYSIOLOGICAL DIFFERENCES

ETIOLOGY: NAFLD VS. MAFLD

NAFLD is defined by hepatic steatosis (>5% of hepatocytes) when other reasons, like heavy drinking or viral hepatitis, are not present[vii], making it essentially adiagnosis of exclusion[viii]. MAFLDis instead recognized by positive criteria: fatty liver must coexist with metabolic dysfunction, including conditions like obesity and T2D or other metabolic syndrome features. MAFLD,as a result, explicitly links fatty liver to underlying metabolic derangements as the causal driver. Notably, a global group of specialists agreed in 2020 to propose adopting the term "MAFLD" to better reflect this metabolic etiology[6].

PATHOGENESIS AND METABOLIC DYSFUNCTION

Both NAFLD and MAFLD share a pathogenesis rooted in metabolic derangements. Insulin resistance (IR) is a central mechanism connecting metabolic syndrome factors (obesity, dyslipidemia, hyperglycemia) to fat buildup in the liver. Under insulin-resistant conditions, hepatic lipogenesis (fat synthesis) persists despite impaired insulin signaling[ix]. Chronic metabolic stress also triggers inflammation and other injury pathways. The earlier "two-hit" hypothesis for progression from simple steatosis to steatohepatitis (NASH) has been superseded by a multiple-hit model, in which parallel insults such as oxidative stress, inflammatory cytokines, endoplasmic reticulum stress, and mitochondrial dysfunction act in concert to drive hepatocellular injury, inflammation, and fibrogenesis[x].

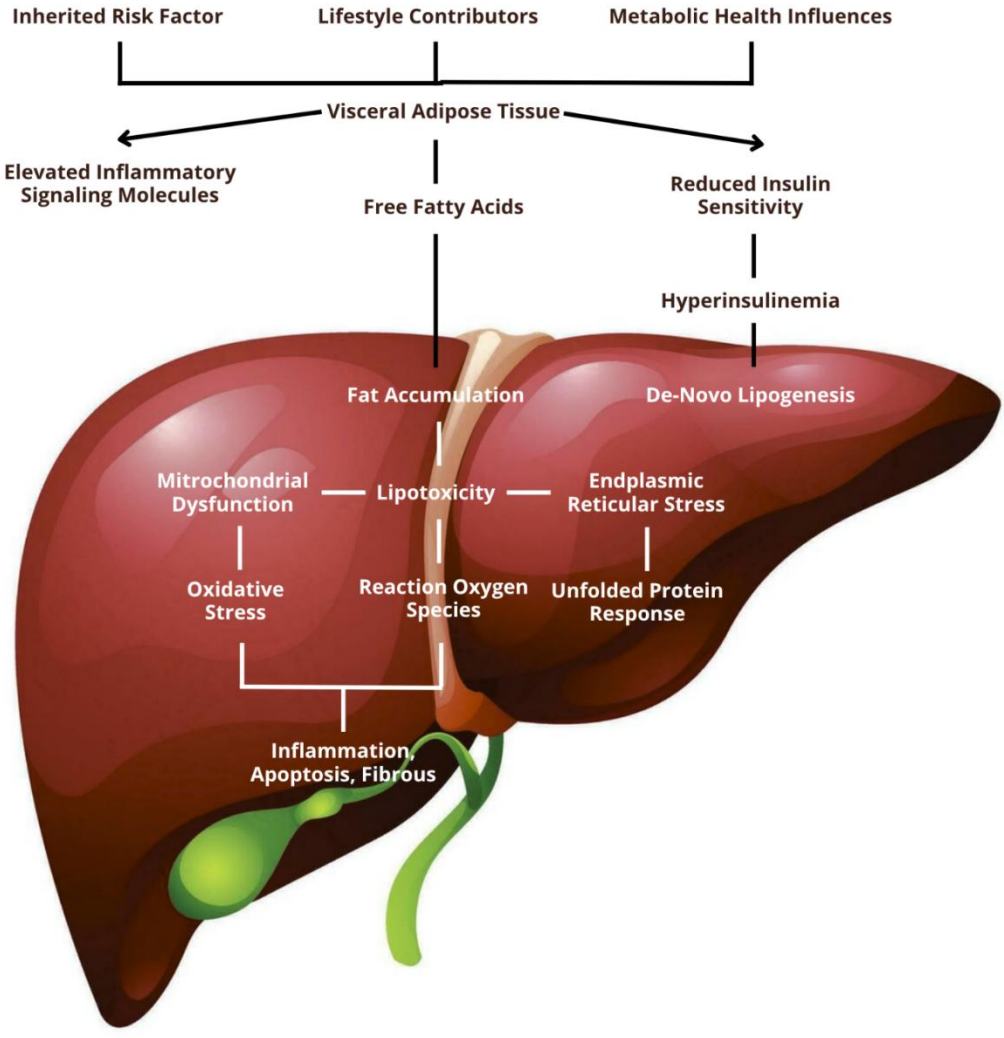

FIGURE 1. PATHOGENESIS OF MAFLD: A MULTI-HIT MODEL

These processes underlie both NAFLD and MAFLD, but the MAFLD definition specifically requires metabolic dysfunction, underscoring the central role of metabolic dysfunction [9].

HISTOLOGICAL OVERLAPS AND DIFFERENCES

Histologically, NAFLD and MAFLD cover the same spectrum of liver damage, from simple steatosis to NASH and up to advanced fibrosis/cirrhosis[xi]. As a result, their histopathological features largely overlap. However, patients meeting MAFLD criteria (who, by definition, have metabolic dysfunction) often have more severe steatosis and disease activity. For example, MAFLD patients tend to show higher steatosis grades and NAFLD activity scores than metabolically healthier NAFLD patients[xii]. By contrast, the prevalence of advanced fibrosis or severe inflammation is similar between MAFLD and NAFLD when metabolic risk factors are comparable [12]. One study found that the MAFLD definition captured ~38.9% more patients with fatty liver and preferentially identified those with more advanced disease for early intervention[xiii].

COEXISTING CONDITIONS AND DUAL ETIOLOGY

A key advantage of the MAFLD framework is its allowance for dual etiologies**.** NAFLD's exclusionary definition forbids diagnosing fatty liver if other liver diseases, e.g., viral hepatitis or alcohol-related disease, are present, even though metabolic fatty liver often coexists with such conditions. MAFLD, however, allows a dual diagnosis of metabolic dysfunction; fatty liver can be identified alongside other liver diseases in a patient [8]. This approach is considered more practical clinically, as it reflects the real-world overlap of causes in liver disease[xiv]. For instance, obesity and metabolic syndrome often coincide with alcohol-related or viral liver disease, compounding liver injury; under the MAFLD criteria, such metabolic steatosis is still recognized and managed as part of the diagnosis, acknowledging that metabolic dysfunction worsens outcomes even in other liver disorders [11].

DIAGNOSTIC CRITERIA: OLD VS. NEW

DIAGNOSTIC CRITERIA: NAFLD VS MAFLD

The 2020 redefinition of fatty liver disease marked a significant shift in how clinicians approach diagnosis[xv]. Instead of relying on exclusion, the new criteria emphasize metabolic dysfunction as the core of the disease process[xvi]. To understand this paradigm shift, the following table compares the major features of the older NAFLD definition with the newer MAFLD framework:

TABLE 1: NAFLD VS MAFLD CRITERIA

Aspect	NAFLD (Old Criteria)	MAFLD (New Criteria)
Diagnostic definition	Steatosis with no other chronic liver disease or significant alcohol use[xvii].	Steatosis with metabolic dysfunction[xviii].
Other liver conditions	Excludes patients with any alternative liver disease (viral, alcoholic, etc.).	Allows dual diagnoses (e.g., "MAFLD with hepatitis B" or "MAFLD with alcohol-related liver disease") if metabolic criteria are met [18].
Patient inclusion	Many fatty liver patients were excluded under the NAFLD definition due to coexisting causes [17].	More inclusive – captures previously excluded patients and identifies high-risk cases for targeted management[xix].

The following schematic highlights how diagnostic boundaries shift when applying MAFLD criteria, enabling a more inclusive and clinically relevant classification:

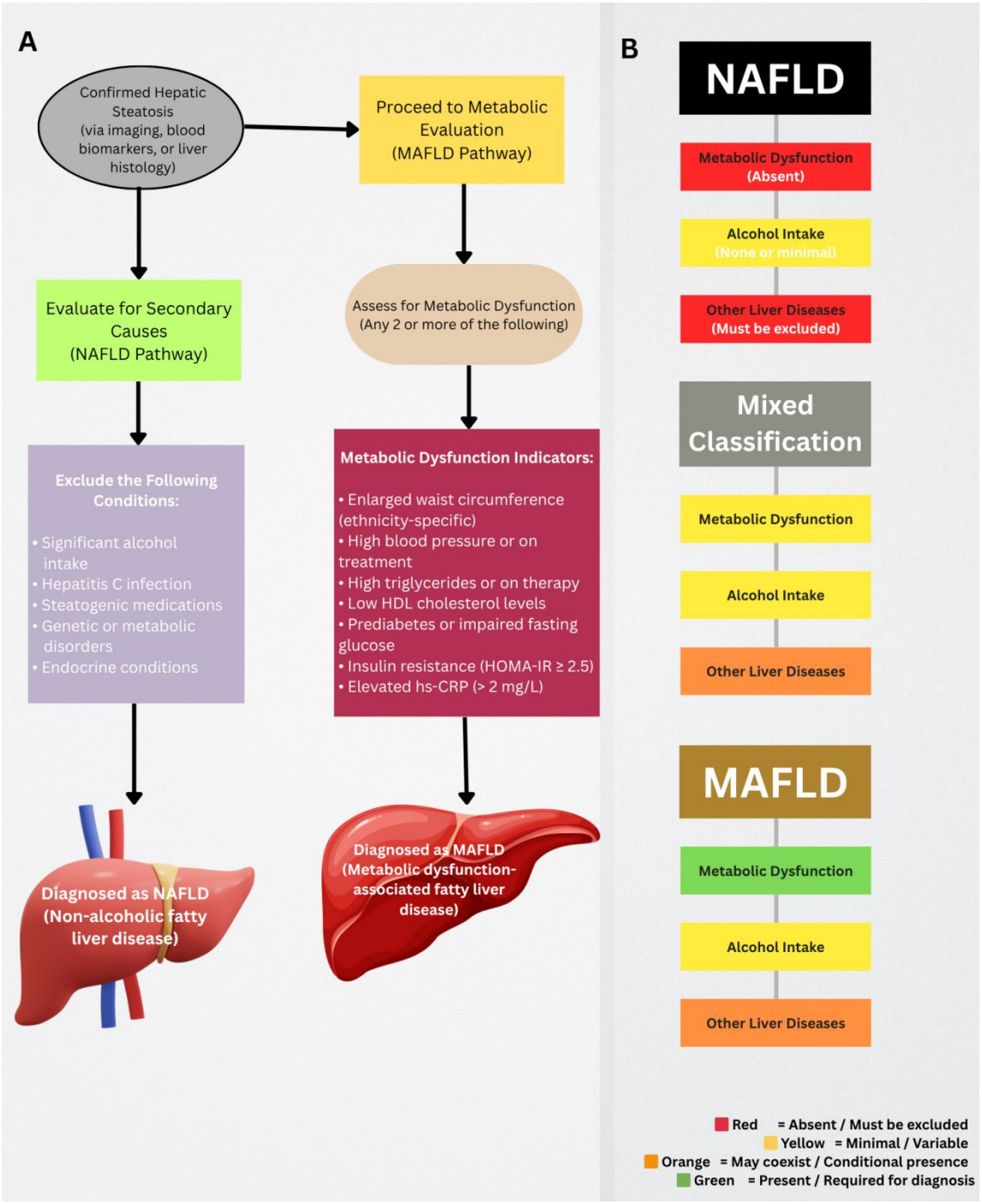

FIGURE 2. COMPARATIVE CLASSIFICATION AND DIAGNOSTIC OVERLAP OF MAFLD VS NAFLD. THE SCHEMATIC HIGHLIGHTS HOW THE INCLUSION OF METABOLIC CRITERIA IN MAFLD ALLOWS DIAGNOSIS EVEN IN THE PRESENCE OF COEXISTING LIVER DISEASES, UNLIKE THE EXCLUSION-BASED NAFLD DEFINITION

Notably, retrospective studies report that only ~5% of fatty liver patients are "NAFLD-only" (steatosis without metabolic dysfunction), meaning the majority with fatty liver would be identified under MAFLD, leaving only a small "lean NAFLD" group outside the new definition [19].

EVOLVING BIOMARKER-BASED PREDICTION MODELS

The shift in terminology has paralleled efforts to improve non-invasive prediction models for fatty liver disease. For example, a new blood-based multi-marker panel for metabolic steatohepatitis (MASH) achieved high diagnostic accuracy, reducing the need for liver biopsy[xx]. Similarly, a machine-learning model using clinical data showed strong performance (area-under-curve ~0.82) in predicting 5-year mortality in MAFLD patients [17]. Non-invasive indices like FibroScan-AST (FAST) and NIS4 are also being validated to detect high-risk NASH in the MAFLD population [20].

CLINICAL IMPLICATIONS AND PROGNOSIS

TREATMENT APPROACHES

Renaming NAFLD to MAFLD carries important treatment implications. By defining fatty liver disease in positive metabolic terms rather than by exclusion, MAFLD encourages clinicians to address metabolic risk factors and coexisting liver conditions in parallel. This approach promotes holistic, multi-faceted care and earlier intervention. Indeed, the simpler MAFLD criteria have improved recognition of fatty liver outside hepatology, enabling primary care and other specialists to initiate timely lifestyle or pharmacologic management of metabolic dysfunction [19].

RISK STRATIFICATION AND COMORBIDITIES

By requiring metabolic dysfunction, MAFLD inherently identifies patients with a greater cardiometabolic burden.Compared to NAFLD, MAFLD patients more often present with obesity, type 2 diabetes, hypertriglyceridemia, and low HDL – all risk factors for cardiovascular disease[xxi]. Reflecting this, MAFLD cohorts exhibit higher rates of extrahepatic complications. For instance, a large analysis found MAFLD was associated with significantly more chronic kidney disease (CKD) than NAFLD, and that MAFLD status independently predicted higher CKD risk[xxii]. These findings indicate that MAFLD criteria capture a higher-risk subset, informing more proactive monitoring for cardiovascular, renal, and diabetic complications.

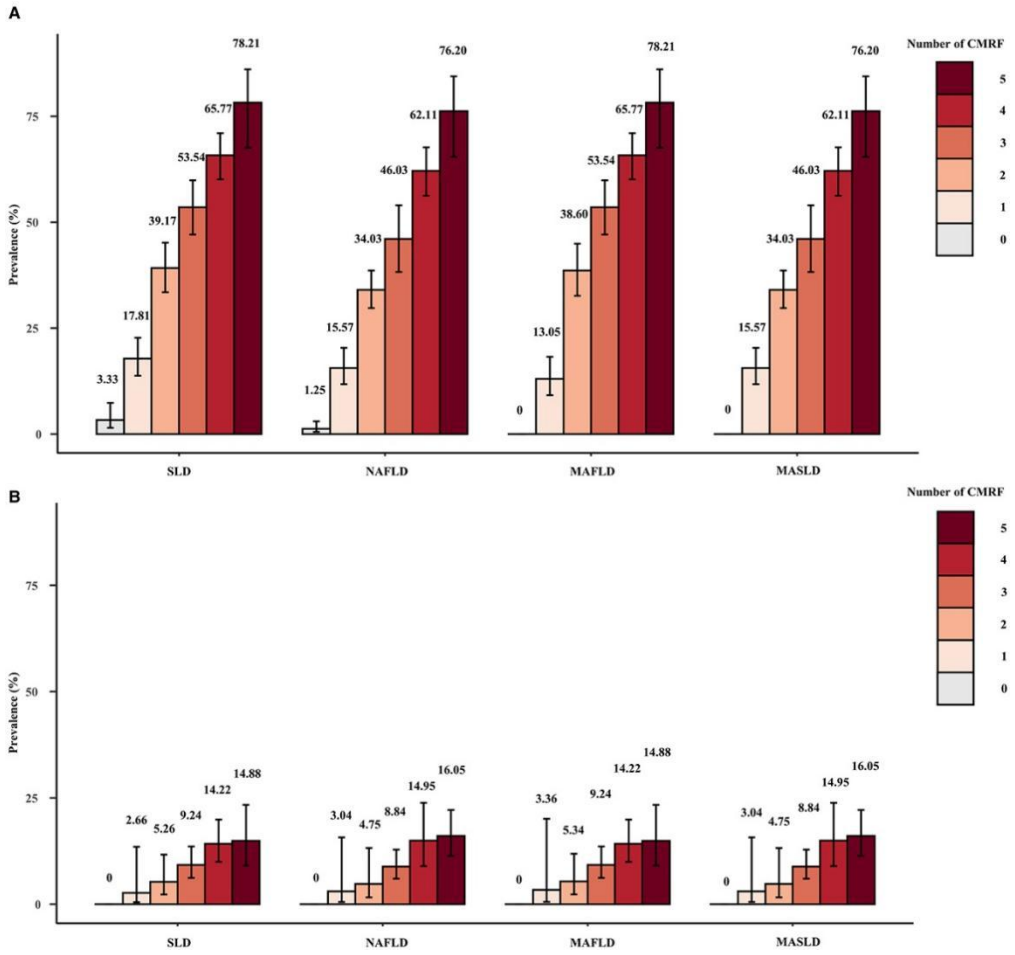

FIGURE 3. DISTRIBUTION OF CARDIO-METABOLIC RISK FACTORS (CMRFS) IN SLD, NAFLD, MAFLD, AND MASLD POPULATIONS.

Panel A shows the proportion of individuals in each diagnostic category carrying 0–5 cardiometabolic risk factors, while Panel B presents corresponding data among patients with significant alcohol-related fatty liver (ALF). MAFLD and MASLD groups consistently demonstrate higher clustering of multiple CMRFs, supporting their association with a greater systemic metabolic burden[xxiii]

PROGNOSTIC DIFFERENCES

Evidence shows that patients meeting MAFLD criteria have, on average, worse prognoses than those defined only by NAFLD. In one cohort, 43.6% of MAFLD-only patients (those with metabolic fatty liver who would have been excluded under NAFLD's definition) had significant liver fibrosis versus 15.9% of NAFLD-only patients, indicating a greater risk of progressive liver disease[xxiv]. Likewise, meta-analyses confirm that MAFLD is associated with higher rates of adverse outcomes. One systematic review found that MAFLD carries a significantly higher all-

cause mortality risk than NAFLD[xxv], and other cohort studies have shown greater cardiovascular mortality in MAFLD-defined groups[xxvi]. Thus, the MAFLD label tends to identify a sicker patient population, warranting closer follow-up and counseling.

IMPACT ON CLINICAL TRIALS

The terminology shift also impacts research. The inclusive MAFLD criteria (allowing concurrent liver etiologies if metabolic dysfunction exists) could broaden clinical trial eligibility, accelerate recruitment, and capture more representative patient cohorts [25]. This may enrich trials with higher-risk subjects, potentially enhancing the detection of treatment effects. Conversely, experts warn that changing definitions mid-study could confuse trial design and endpoints. Redefining a disease name and criteria (for example, altering a "NASH resolution" endpoint) may complicate ongoing trials and regulatory assessments[xxvii]. Notably, major liver societies are deliberating the nomenclature change to ensure it does not impede drug development or regulatory approval[25]. Thus, while the new terminology might improve trial inclusion, careful transition planning is needed to avoid disrupting existing studies.

MULTIDISCIPLINARY RELEVANCE

This nomenclature change carries significance across specialties. For hepatologists, it underscores managing metabolic comorbidities as part of liver care. For endocrinologists, diabetologists, and internists, MAFLD highlights fatty liver as an important complication of obesity and diabetes that merits screening and intervention. Cardiologists, too, should be vigilant, since MAFLD's cardiovascular risks have often been underestimated. An international MAFLD consensus recently convened experts in hepatology, endocrinology, cardiology, and primary care, reinforcing the need for multidisciplinary management[xxviii].

CHALLENGES AND CONTROVERSIES

Key challenges and controversies surrounding the NAFLD to MAFLD transitionare given as:

OPPOSITION FROM SOME EXPERTS, CONTINUED USE OF NAFLD

Many experts question whether renaming NAFLD to MAFLD yields clinical benefits. They argue the MAFLD definition can exclude patients without metabolic risk who still develop severe fatty liver, e.g., metabolically healthy lean NAFLD,[xxix] and note little evidence that the name change improves patient outcomes or drug development efforts[xxx]. Consequently, some guidelines and practitioners continue to use the established "NAFLD" terminology.

COMPATIBILITY ISSUES WITH HISTORICAL DATA

The definitional shift complicates comparisons with prior NAFLD research. MAFLD includes

cases NAFLD would exclude (e.g., concurrent alcohol or viral hepatitis) and omits some that NAFLD would include. An estimated ~25% of MAFLD patients do not meet the old NAFLD criteria. Thus, existing epidemiologic data and trial cohorts require re-evaluation to ensure comparability post-renaming [29].

REGULATORY LANGUAGE AND ICD CODING CONFUSION

Official classifications have not yet caught up with the new nomenclature. No specific ICD-10/11 code exists for MAFLD, so clinicians must still code diagnoses as NAFLD[xxxi]. In a 2024 global survey, over 80% of experts supported updating ICD-11 to incorporate MAFLD terminology[xxxii]. Aligning nomenclature in coding systems is critical to avoid confusion in clinical care and reporting

NEED FOR UPDATED GLOBAL CONSENSUS

A unified global consensus on nomenclature remains urgently needed. The emergence of parallel terms (MAFLD vs the alternative MASLD) reflects disagreement between scientific groups and confuses. In response, over 1000 specialists across 135 countries signed an open letter endorsing the MAFLD definition to encourage worldwide alignment[xxxiii]. Ongoing international dialogue is crucial to resolve nomenclature differences and ensure consistent disease recognition globally.

RESEARCH, CLINICAL PRACTICE, AND POLICY PERSPECTIVES

RESEARCH PERSPECTIVE

The redefinition of NAFLD to MAFLD requires researchers to adjust study design and inclusion criteria. MAFLD uses positive diagnostic criteria based on metabolic dysfunction, in contrast to NAFLD's exclusion of other liver diseases. This inclusive approach captures patients with fatty liver plus metabolic dysfunction who would have been missed by the NAFLD definition [7]. Studies indicate that MAFLD criteria identify high-risk individuals (with metabolic disorders and advanced fibrosis),but NAFLD is overlooked[xxxiv]. Consequently, clinical trials and studies are broadening eligibility to include these patients, which may improve risk stratification. The shift is expected to enhance study power by reducing heterogeneity; NAFLD's exclusionary definition contributed to variable cohorts and high trial failure rates in the past. Multiple analyses have demonstrated the superior utility of MAFLD criteria in identifying patients at greater risk of fibrosis and cardiometabolic complications[xxxv]. By adopting MAFLD definitions, researchers can more effectively target metabolically at-risk patients in future investigations.

CLINICAL PRACTICE PERSPECTIVE

Clinicians must adapt to the NAFLD-to-MAFLD paradigm shift through ongoing re-education

efforts and improved patient communication. The new terminology emphasizes that fatty liver disease is a manifestation of metabolic dysfunction, so healthcare providers need updated training to diagnose MAFLD and manage its metabolic comorbidities [34]. Lack of awareness of MAFLD among physicians has been associated with misdiagnoses and underestimation of disease severity, underscoring the importance of education on the revised criteria[xxxvi]. In terms of patient communication, dropping the "non-alcoholic" label may reduce stigma. The term NAFLD inadvertently stigmatized patients by implying an alcohol-related cause, which led to misconceptions and hindered effective provider–patient dialogue [7].By adopting the MAFLD nomenclature, clinicians can focus discussions on metabolic health without the judgmental undertones, improving patient understanding and engagement. Surveys already report high acceptance of the MAFLD name among patients and health professionals, suggesting this change can increase disease awareness and trust [36].

POLICY PERSPECTIVE

The NAFLD-to-MAFLD paradigm shift has broad public health implications. Health authorities worldwide should update disease classification and coding systems to adopt the MAFLD definition. Screening strategies are needed to detect MAFLD in high-risk groups (e.g., people with obesity or type 2 diabetes), given their markedly higher disease prevalence[xxxvii]. Policymakers must acknowledge MAFLD as a critical non-communicable disease: it is projected to become a leading cause of cirrhosis and liver cancer within the next decade [36]. Yet countries remain unprepared – a 102-country review found no nation with a NAFLD/MAFLD strategy, and one-third had no policy at all [37]. Fatty liver disease is still largely absent from national health agendas and global NCD initiatives, and the lack of reliable epidemiological data (especially in low- and middle-income countries) impedes effective action[xxxviii]. These gaps underscore an urgent need for dedicated funding, better surveillance, and integration of MAFLD into public health programs worldwide.

OPPORTUNITIES AND FUTURE DIRECTIONS

Looking ahead, future MAFLD management is expected to emphasize personalized, metabolism-focused therapeutics and holistic, cross-disciplinary care. Therapeutic approaches should be strongly tailored to individual patient features and disease drivers[xxxix]. Accordingly, diverse metabolic pathways are being targeted by new pharmacotherapies (FXR and PPAR agonists, GLP-1 analogues) to address the heterogeneity of MAFLD[xl]. Given MAFLD's close ties to metabolic syndrome, clinical guidelines across specialties must become better integrated.

Endocrinology and diabetes societies now recommend routine NAFLD screening and fibrosis risk assessment in patients with type 2 diabetes[xli], and cardiology guidelines stress aggressive cardiovascular risk management in NAFLD patients[xlii]. However, obesity and diabetes guidelines have only recently begun acknowledging NAFLD, signaling a need for multi-specialty consensus[xliii].

Advanced computational tools also offer new opportunities: artificial intelligence (AI) and big-data models can enhance risk stratification and personalize MAFLD care. Future AI advancements promise to improve early detection and treatment optimization[xliv]. Finally, better population screening tools are needed, as current policies endorse only high-risk screening using noninvasive fibrosis tests due to uncertain cost-effectiveness. Developing cost-efficient screening strategies and user-friendly risk stratification tools – alongside greater provider awareness – is a priority for the next phase of MAFLD care [43].

CONCLUSION

In conclusion, this review aimed to critically examine the paradigm shift from NAFLD to MAFLD in light of the global fatty liver disease epidemic and its implications. Renaming NAFLD as MAFLD emphasizes metabolic dysfunction as the key driver of fatty liver disease, moving away from an exclusion-based definition. This shift better captures patients with coexisting metabolic risk factors or dual liver etiologies, improving diagnostic inclusivity and highlighting those at higher risk of advanced fibrosis and comorbidities. The MAFLD framework encourages holistic management by integrating liver health with metabolic care and engaging multiple specialties in care. However, challenges remain: some experts oppose the new terminology, historical data and coding systems need adaptation, and consensus is still evolving. Despite these hurdles, the transition to MAFLD represents an important advancement in understanding and treating fatty liver disease. Aligning nomenclature with pathogenesis, it provides a clearer focus for research, more tailored patient care, and a stronger platform for public health strategies and policies.

REFERENCES

[i]Younossi ZM, Golabi P, Paik JM, Henry A, Van Dongen C, Henry L. The global epidemiology of nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH): a systematic review. *Hepatology*. 2023;77(4):1335–1347.

[ii]Eslam M, Newsome PN, Sarin SK, Anstee QM, Targher G, Romero-Gomez M, Zelber-Sagi S, Wong VW, Dufour JF, Schattenberg JM, Kawaguchi T. A new definition for metabolic dysfunction-associated fatty liver disease: an international expert consensus statement. *J Hepatol.* 2020;73(1):202–9.

[iii] Targher G. What's past is prologue: history of nonalcoholic fatty liver disease. Metabolites. 2020 Oct;10(10):397. doi:10.3390/metabo10100397.

[iv] Zhou XD, Cai J, Targher G, Byrne CD, Zheng MH. Metabolic dysfunction-associated fatty liver disease and implications for cardiovascular risk and disease prevention. *Cardiovasc Diabetol.* 2022;21:270. doi:10.1186/s12933-022-01697-0

[v] Kaya E, Zedginidze A, Bechmann L, Canbay A. Metabolic dysfunction-associated fatty liver disease (MAFLD) and non-alcoholic fatty liver disease (NAFLD): distinct fatty liver entities with different clinical outcomes? *Hepatobiliary Surg Nutr.* 2022;11(2):299–301. doi:10.21037/hbsn-21-548

[vi] Ruan S, Huang L, Song J, Zhao W, Chen Y. Global burden trends and forecasts for MAFLD in adolescents and young adults from 1990 to 2021. *Sci Rep.* 2025;15:13534. doi:10.1038/s41598-025-98489-9

[vii] Habibullah M, Jemmieh K, Ouda A, Haider MZ, Malki MI, Elzouki AN. Metabolic-associated fatty liver disease: a selective review of pathogenesis, diagnostic approaches, and therapeutic strategies. *Front Med (Lausanne).* 2024;11:1291501. doi:10.3389/fmed.2024.1291501

[viii] Zerehpooshnesfchi S, Lonardo A, Fan JG, Elwakil R, Tanwandee T, Altarrah MY, Örmeci N, Eslam M. Dual etiology vs. MetALD: how MAFLD and MASLD address liver diseases coexistence. *Metab Target Organ Damage.* 2025;5(1):15. doi:10.20517/mtod.2025.04

[ix] Veskovi ć M, Šutulovi ć N, Hrnči ć D, Stanojlovi ć O, Macut D, Mladenovi ć D. The interconnection between hepatic insulin resistance and metabolic dysfunction-associated steatotic liver disease— the transition from an adipocentric to liver-centric approach. *Curr Issues Mol Biol.* 2023;45(11):9084–9102. doi:10.3390/cimb45110570

[x] Noureddin M, Sanyal AJ. Pathogenesis of NASH: the impact of multiple pathways. *Curr Hepatol Rep.* 2018;17(4):350–360. doi:10.1007/s11901-018-0425-7.

[xi] Xian YX, Weng JP, Xu F. MAFLD vs. NAFLD: shared features and potential changes in epidemiology, pathophysiology, diagnosis, and pharmacotherapy. *Chin Med J (Engl).* 2020;134(1):8–19. doi:10.1097/CM9.0000000000001263

[xii] Dai YN, Xu CF, Pan HY, Huang HJ, Chen MJ, Li YM, Yu CH. Metabolic dysfunction is associated with steatosis but no other histologic features in nonalcoholic fatty liver disease. *World J Clin Cases*. 2022;10(13):4097–4109. doi:10.12998/wjcc.v10.i13.4097

[xiii] Huang SC, Su HJ, Kao JH, Tseng TC, Yang HC, Su TH, Chen PJ, Liu CJ. Clinical and histologic features of patients with biopsy-proven metabolic dysfunction-associated fatty liver disease. *Gut Liver*. 2021 May 15;15(3):451–458. doi:10.5009/gnl20218. PMID: 33431715; PMCID: PMC8129653

[xiv] Fouad Y, Esmat G, Elwakil R, Zakaria S, Yosry A, Waked I, El-Razky M, Doss W, El-Serafy M, Mostafa E, Anees M, Sakr MA, AbdelAty N, Omar A, Zaki S, Al-Zahaby A, Mahfouz H, Abdalla M, Albendary M, Hamed AK, Gomaa A, Hasan A, Abdel-Baky S, El Sahhar M, Shiha G, Attia D, Saeed E, Kamal E, Bazeed S, Mehrez M, Abdelaleem S, Gaber Y, Abdallah M, Salama A, Tawab DA, Nafady S. The Egyptian clinical practice guidelines for the diagnosis and management of metabolic associated fatty liver disease. *Saudi J Gastroenterol*. 2022;28(1):3–20. doi:10.4103/sjg.sjg_357_21. PMID:35083973; PMCID:PMC8919931

[xv] Wang X, Chen H, Wang L, Sun W. Machine learning for predicting all-cause mortality of metabolic dysfunction-associated fatty liver disease: a longitudinal study based on NHANES. *BMC Gastroenterol*. 2025;25:376. doi:10.1186/s12876-025-03946-4

[xvi] Alomari M, Rashid MU, Chadalavada P, Ragheb J, Zafar H, Suarez ZK, Khazaaleh S, Gonzalez AJ, Castro FJ. Comparison between metabolic-associated fatty liver disease and nonalcoholic fatty liver disease: from nomenclature to clinical outcomes. *World J Hepatol*. 2023 Apr 27;15(4):477–496. doi:10.4254/wjh.v15.i4.477. PMID:37206648; PMCID:PMC10190689

[xvii]Chen YL, Li H, Li S, et al. Prevalence of and risk factors for metabolic associated fatty liver disease in an urban population in China: a cross-sectional comparative study. *BMC Gastroenterol*. 2021;21:212. doi:10.1186/s12876-021-01782-w

[xviii]Sumida Y, editor. Metabolic associated fatty liver disease: a new definition [special issue]. *Int J Mol Sci*. 2021;1422-0067. Section Molecular Endocrinology and Metabolism

[xix]Gofton C, Upendran Y, Zheng MH, George J. MAFLD: how is it different from NAFLD? Clin Mol Hepatol. 2023;29(Suppl):S17–S31. doi:10.3350/cmh.2022.0367.

[xx] Zhang X, Zheng M-H, Liu D, Lin Y, Song SJ, Chu E-SH, Liu D, Singh S, Berman M, Lau H C-H, Gou H, Wong G L-H, Zhang N, Yuan H-Y, Loomba R, Wong V W-S, Yu J. A

blood-based biomarker panel for non-invasive diagnosis of metabolic dysfunction-associated steatohepatitis. *Cell Metab.* 2025;37(1):59–68.e3. doi:10.1016/j.cmet.2024.10.008.

[xxi] Szymala-Pędzik M, Piersiak M, Pachana M, Lindner-Pawłowicz K, Szczepaniak W, Sobieszczańska M. MAFLD as a cardiovascular risk factor: an extended retrospective study with a control group. *J Clin Med.* 2025;14(12):4181. doi:10.3390/jcm14124181

[xxii] Sun DQ, Jin Y, Wang TY, Zheng KI, Rios RS, Zhang HY, Targher G, Byrne CD, Yuan W-J, Zheng MH. MAFLD and risk of CKD. *Metabolism.* 2021;115:154433. doi:10.1016/j.metabol.2020.154433.

[xxiii] Zou H, Ma X, Pan W, Xie Y. Comparing similarities and differences between NAFLD, MAFLD, and MASLD in the general U.S. population. *Front Nutr (Lausanne).* 2024;11:1411802. doi:10.3389/fnut.2024.1411802.

[xxiv] Hong SM, Hong ZB, Hao YW, Sun LP, Wei H. Metabolic dysfunction–associated fatty liver disease indicates more hepatic fibrosis than nonalcoholic fatty liver disease. *Med (Baltimore).* 2025;104(6):e41455. doi:10.1097/MD.0000000000041455.

[xxv] Vaz K, Clayton-Chubb D, Majeed A, Lubel J, Simmons D, Kemp W, et al. Current understanding and future perspectives on the impact of changing NAFLD to MAFLD on global epidemiology and clinical outcomes. *Hepatol Int.* 2023;17(5):1082–1097. doi:10.1007/s12072-023-10568-z.

[xxvi] Wen W, Li H, Wang C, Chen C, Tang J, Zhou M, et al. Metabolic dysfunction-associated fatty liver disease and cardiovascular disease: a meta-analysis. *Front Endocrinol (Lausanne).* 2022;13:934225. doi:10.3389/fendo.2022.934225.

[xxvii] García-Compeán D, Jiménez-Rodríguez AR. NAFLD vs MAFLD: the evidence-based debate has come. Time to change? *Ann Hepatol.* 2022 Nov–Dec;27(6):100765. doi:10.1016/j.aohep.2022.100765.

[xxviii] Zhou XD, Targher G, Byrne CD, Somers V, Kim SU, Chahal CAA, et al. An international multidisciplinary consensus statement on MAFLD and the risk of CVD. *Hepatol Int.* 2023;17(4):773–791. doi:10.1007/s12072-023-10543-8.

[xxix] Zeng M, Chen L, Li Y, Mi Y, Xu L, et al. Problems and challenges associated with renaming non-alcoholic fatty liver disease to metabolic associated fatty liver disease. *Infect Dis Immun.* 2023;3(3):105–113. doi:10.1097/ID9.0000000000000085.

[xxx] Huang Q, Zou X, Wen X, Zhou X, Ji L. NAFLD or MAFLD: which has closer association with all-cause and cause-specific mortality? Results from NHANES III. *Front Med (Lausanne).* 2021;8:693507. doi:10.3389/fmed.2021.693507.

[xxxi] Hagström H, Adams LA, Allen AM, Byrne CD, Chang Y, Duseja A, et al. The future of International Classification of Diseases coding in steatotic liver disease: an expert panel Delphi consensus statement. *Hepatology Commun.* 2024;8(2):e0386. doi:10.1097/HC9.0000000000000386.

[xxxii] Zhang H, Targher G, Byrne CD, Kim SU, Wong VWS, Valenti L, et al. A global survey on the use of the international classification of diseases codes for metabolic dysfunction-associated fatty liver disease. *Hepatol Int.* 2024;18(4):1178–1201. doi:10.1007/s12072-024-10702-5.

[xxxiii] Fouad Y. Metabolic-associated fatty liver disease: new nomenclature and approach with hot debate. *World J Hepatol.* 2023;15(2):123–128. doi: 10.4254/wjh.v15.i2.123

[xxxiv] Liu Q, Zhao G, Li Q, Wang L, Zhang X, Chen L, et al. A comparison of NAFLD and MAFLD diagnostic criteria in contemporary urban healthy adults in China: a cross-sectional study. BMC Gastroenterol. 2022;22:471. doi:10.1186/s12876-022-02576-4

[xxxv] Fouad Y, Palmer M, Chen M, Regev A, Banerjee R, Myers R, et al. Redefinition of fatty liver disease from NAFLD to MAFLD through the lens of drug development and regulatory science. J Clin Transl Hepatol. 2022;10(2):374–82. doi:10.14218/JCTH.2021.00408

[xxxvi] Méndez-Sánchez N, Díaz-Orozco LE, Cordova J. Redefinition of fatty liver disease from NAFLD to MAFLD raised disease awareness: Mexican experience. J Hepatol. 2021;75(1):e15–6. doi:10.1016/j.jhep.2021.04.021

[xxxvii] Lazarus JV, Mark HE, Villota-Rivas M, Palayew A, Carrieri P, Colombo F, et al. The global NAFLD policy review and preparedness index: Are countries ready to address this silent public health challenge? J Hepatol. 2022;76(4):771–80. doi:10.1016/j.jhep.2021.10.025

[xxxviii] Lazarus JV, Mark HE, Anstee QM, Arab JP, Batterham RL, Cusi K, et al. Advancing the global public health agenda for NAFLD: a consensus statement. Nat Rev Gastroenterol Hepatol. 2022;19:60–78. doi:10.1038/s41575-021-00523-4

[xxxix] Lonardo A, Arab JP, Arrese M. Perspectives on precision medicine approaches to NAFLD diagnosis and management. *Adv Ther.* 2021 May;38(5):2130-2158. doi:10.1007/s12325-021-01690-1. PMID: 33829368; PMCID: PMC8107169.

[xl] Bhopale KK, Srinivasan MP. Therapeutics for metabolic dysfunction-associated fatty liver disease (MAFLD). *Livers.* 2023 Dec;3(4):597–617. doi:10.3390/livers3040040

[xli] Ciardullo S, Vergani M, Perseghin G. Nonalcoholic fatty liver disease in patients with type 2 diabetes: screening, diagnosis, and treatment. *J Clin Med.* 2023 Aug 27;12(17):5597. doi:10.3390/jcm12175597. PMID: 37685664; PMCID: PMC10488336.

[xlii] Millán-Rodríguez C, Palacios Castelló C, Caballero-Valderrama MR, Esquivias GB. Clinical management of non-alcoholic steatohepatitis and the role of the cardiologist. *Eur Cardiol Rev.* 2023 Dec 22;18:e64. doi:10.15420/ecr.2023.22. PMID: 38213666; PMCID: PMC10782421.

[xliii] Forlano R, Sigon G, Mullish BH, Yee M, Manousou P. Screening for NAFLD—current knowledge and challenges. *Metabolites.* 2023 Apr 9;13(4):536. doi:10.3390/metabo13040536. PMID: 37110194 (PMC10144613)

[xliv] Gao YN, Chen ML, Li WM, Liu Q, Jiao Y. Advancing the diagnosis and treatment of metabolic-associated steatotic liver disease: the transformative role of artificial intelligence. *Artif Intell Gastroenterol.* 2025 Jun 8;6(1):107105. doi:10.35712/aig.v6.i1.107105