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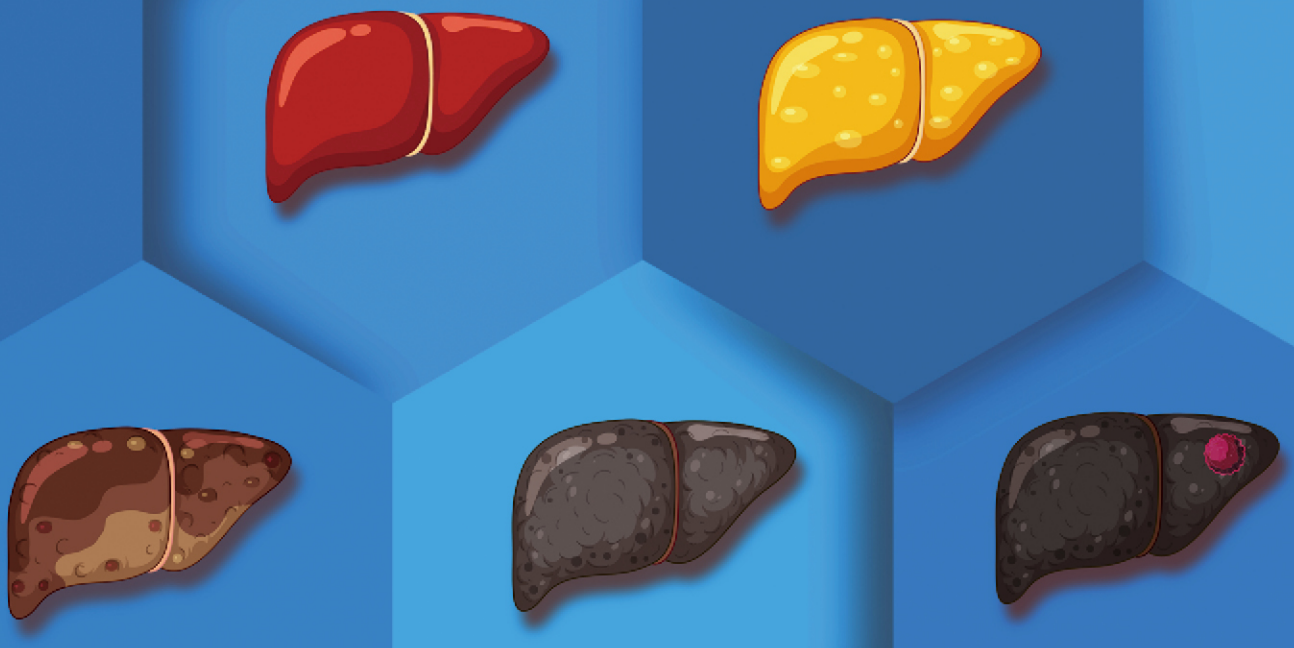

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Review

Epidemiology of metabolic dysfunction-associated steatotic liver disease

Zobair M. Younossi[1,2,3], Markos Kalligeros[4], and Linda Henry[1,2,3]

[1]The Global NASH Council, Washington DC, USA; [2]Beatty Liver and Obesity Program, Inova Health System, Falls Church, VA, USA; [3]Center for Outcomes Research in Liver Disease, Washington DC, USA; [4]Beth Israel Deaconess Medical Center, Harvard University, Cambridge, MA, USA

As the rates of obesity and type 2 diabetes (T2D) continue to increase globally, so does the prevalence of metabolic dysfunction–associated steatotic liver disease (MASLD). Currently, 38% of all adults and 7–14% of children and adolescents have MASLD. By 2040, the MASLD prevalence rate for adults is projected to increase to more than 55%. Although MASLD does not always develop into progressive liver disease, it has become the top indication for liver transplant in the United States for women and those with hepatocellular carcinoma (HCC). Nonetheless, the most common cause of mortality among patients with MASLD remains cardiovascular disease. In addition to liver outcomes (cirrhosis and HCC), MASLD is associated with an increased risk of developing *de novo* T2D, chronic kidney disease, sarcopenia, and extrahepatic cancers. Furthermore, MASLD is associated with decreased health-related quality of life, decreased work productivity, fatigue, increased healthcare resource utilization, and a substantial economic burden. Similar to other metabolic diseases, lifestyle interventions such as a heathy diet and increased physical activity remain the cornerstone of managing these patients. Although several obesity and T2D drugs are available to treat co-morbid disease, resmetirom is the only MASH-targeted medication for patients with stage 2–3 fibrosis that has approved by the Food and Drug Administration for use in the United States. This review discusses MASLD epidemiology and its related risk factors and outcomes and demonstrates that without further global initiatives, MASLD incidence could continue to increase. **(Clin Mol Hepatol 2025;31(Suppl):S32-S50)**

Keywords: MASLD; Insulin resistance; Type 2 diabetes; Metabolic syndrome

INTRODUCTION

The history of fatty liver dates back to 1836 when it was first described by Addison,[1,2] but it wasn't until 1980 when the term nonalcoholic steatohepatitis (NASH) was first used to describe a progressive form of fatty liver that histologically resembled alcohol-related steatohepatitis but was found in patients who denied alcohol misuse.[3] This terminology was extended to children in 1983, and in 1986, the term nonalcoholic fatty liver (NAFLD) was introduced (Fig. 1).[4,5]

In parallel, metabolic syndrome (MetS) and its components were also being identified and discussed. In 1999, investigators described the metabolic conditions associated with NAFLD: hyperinsulinemia, insulin resistance (IR), and hypertriglyceridemia.[1,3,6,7] Additionally, investigators described the association between MetS components and

Corresponding author : **Zobair M. Younossi**
The Global NASH Council, Center for Outcomes Research in Liver Diseases, 2411 I Street, Washington DC 20023, USA
Tel: (202) 530-6199, Fax: 703-776-2540, E-mail: Zobair.younossi@cldq.org
https://orcid.org/0000-0001-9313-577X

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the presence of liver steatosis, fibrosis, and cirrhosis.[1,3,6-8] In 1999, the clinicopathologic spectrum of NAFLD was described and aroused intense interest in this disease.[9] In fact, in 2002, the first single-topic conference on NAFLD was held in the United States.[10] Although most of the data suggested that NAFLD is predominantly found in people who are overweight or obese and those with type 2 diabetes (T2D), in 2008, NAFLD was also described in an individual with normal weight, leading to the term lean NAFLD.[11] Lean NAFLD was still associated with IR, but it had lower rates of the other components of MetS.[11]

Given the close association between NAFLD and MetS, researchers have long tried to connect both diseases to an underlying cause. In 2020, it was proposed that the name NAFLD should be changed to indicate what it is, rather than what it is not. Metabolic-associated fatty liver disease (MAFLD) was the term proposed to replace NAFLD.[12] That name change was associated with changes in the definition to allow more liberal use of alcohol and remove the subcategory of steatohepatitis.[12] Additionally, many felt that the use of fatty in the name was associated with stigma that could be associated with the low public awareness of NAFLD and the hesitancy of healthcare workers to discuss this disease with their patients. Those factors led to the creation of a multi-society effort to develop consensus about a new name to more appropriately describe this disease and reduce the potential stigma associated with the terminology.[13]

In 2023, those efforts culminated in a new name, metabolic dysfunction–associated steatotic liver disease (MASLD). At the same time, experts introduced the broad umbrella term steatotic liver disease (SLD) to encompass

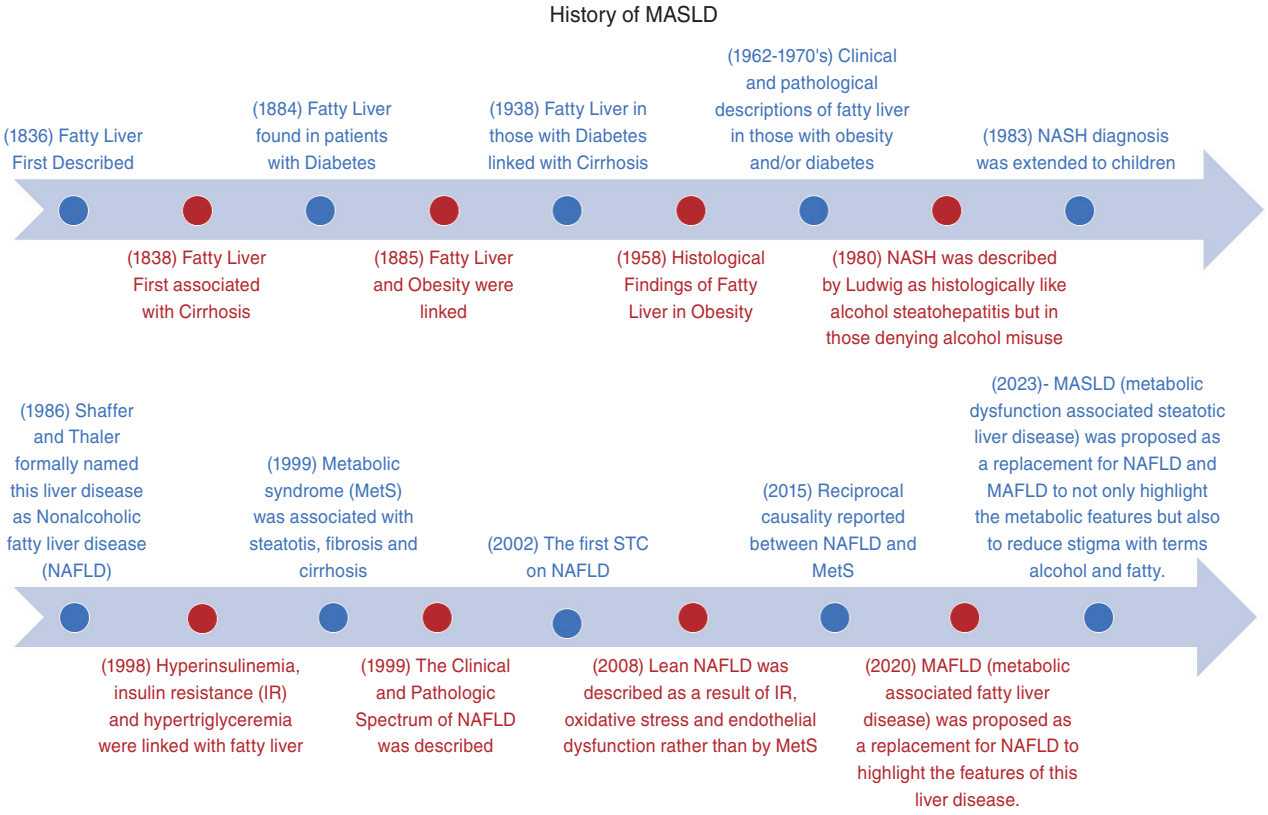

Figure 1. Timeline for the evolution of metabolic dysfunction–associated steatotic liver disease (MASLD). NASH, nonalcoholic steatohepatitis.

Abbreviations:

CKD, chronic kidney disease; CVD, cardiovascular disease; HCC, hepatocellular carcinoma; HRQL, health related quality of life; IR, insulin resistance; MASH, metabolic dysfunction-associated steatohepatitis; MASLD, metabolic dysfunction-associated steatotic liver disease; PreD, prediabetes; PRO, patient reported outcomes; T2D, type 2 diabetes

both metabolic- and alcohol-based fatty liver disease. As an umbrella term, SLD allows for a continuum of alcohol ingestion to more adequately quantify its role in the progression of liver disease.[13]

The definitions for these three terms (NAFLD, MASLD, MAFLD) are very similar but not identical. NAFLD excludes the use of excessive alcohol and other liver diseases.[14] Although 95% of NAFLD patients have clinically overt metabolic abnormalities, about 5% have no cardiometabolic risk (CMR) factors, despite having hepatic steatosis.[15] In contrast, MASLD requires at least one CMR to connect hepatic steatosis with clinically overt metabolic abnormality. On the other hand, MAFLD requires both a metabolic abnormality and the use of alcohol, which can lead to the inclusion of some patients with hepatic steatosis who could be categorized with Met-alcohol-associated liver disease (ALD) or even ALD under the new nomenclature.[13] One study comparing MAFLD with NAFLD suggested that alcohol was the most important predictor of disease-related mortality among MAFLD patients, whereas IR was the most important predictor of disease-related mortality among patients with NAFLD.[16] Given those differences, research comparing the outcomes of different liver diseases will need to continue to determine whether these terms are truly interchangeable.

One systematic review compared MASLD with NAFLD and found very high concordance and almost identical outcomes, suggesting that these two diseases are basically identical, although approximately 5% of those with NAFLD would not have met the criteria for MASLD. In this case, further study will be needed to determine whether those NAFLD patients develop MASLD over time.[15] Additionally, whether the term MASLD actually reduces stigma will need to be determined in future research. In summary, MASLD seem to be an appropriate term for identifying patients whose liver disease is caused exclusively by metabolic abnormalities, whereas the term MAFLD introduces the additional influence of alcohol. Furthermore, MASLD addresses the issue of stigma, and MAFLD and NAFLD both continue to contain the word fatty, which can be stigmatizing for

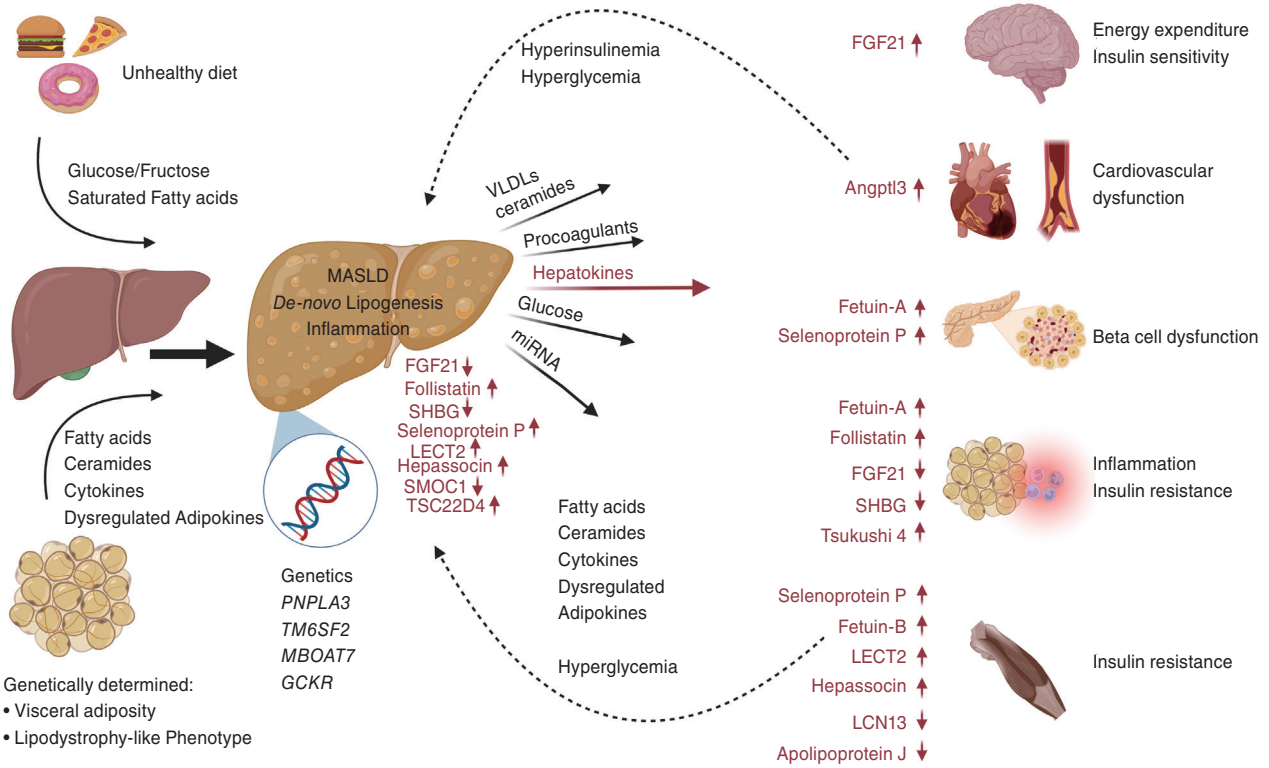

Figure 2. Role of hepatokines and other factors in the development of insulin resistance and cardiovascular disease. MASLD, metabolic dysfunction-associated steatotic liver disease. Adopted and modified from the article of Stefan et al.[22] (Cell Metab 2023;35:236-252) with permission from creative commons.

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some patients.

Irrespective of the nomenclature, MASLD is recognized as the most common cause of chronic liver disease (CLD), with the most recent meta-analysis suggesting that more than 38% of the world's adult population and between 7% and 14% of children are affected.[17,18] Although the burden of MASLD is increasing around the world, in the many countries where viral hepatitis remains endemic, resources and efforts to treat and reduce that disease must continue to be prioritized.[19]

This review summarizes the most recent data on the epidemiology of MASLD.

BRIEF OVERVIEW OF THE INTERACTION BETWEEN METABOLIC FACTORS AND MASLD

MASLD has often been called the hepatic manifestation of MetS due to the close association between the factors of MetS and MASLD. In fact, the more metabolic components that are present, the higher the risk for advanced fibrosis and MASLD-related mortality.[20] However, the interaction between the components of MetS and MASLD is complex and potentially bi-directional. It involves the liver, pancreas, adipose tissue, and muscles; occurs through hepatokine-mediated communication pathways; and leads to a pro-inflammatory state. This pro-inflammatory environment produces metabolic derangements that in turn increase the risk of several metabolic diseases (Fig. 2).[21,22] Given the close associations between metabolic risk factors and obesity, the current global epidemic of obesity is expected to drive this vicious cycle.[23]

Additionally, IR and its severity continuum play a major role in the development of MASLD and its outcomes. A recent study used data generated from the National Health and Nutrition Examination Survey (NHANES) to compare mortality rates among individuals with a spectrum of IR and reported that compared with a metabolically healthy cohort, those with T2D had 11-fold increased risk of MASLD, and people with prediabetes and those who were considered metabolically unhealthy had a 4-fold and 3.4-fold increased risk of MASLD, respectively.[24] Although the subjects with MASLD had a significantly higher age-adjusted mortality rate than those without MASLD, the presence of MASLD and T2D was associated with the highest rate of all-cause and cause-specific mortality, followed by the presence of prediabetes, non-diabetics who were metabolically unhealthy, and then those considered metabolically healthy.[24]

Given the associations among MASLD, obesity, and metabolic abnormalities, most interventions focus on managing lifestyle. In this context, lifestyle interventions include weight loss through a healthy diet, decreased consumption of ultra-processed and fructose-laden foods such as sugar-sweetened beverages, and increasing physical activity.[25] These interventions have been shown to reverse some aspects of MASLD.[26] As such, lifestyle intervention is the recommended first-line treatment, even in the presence of medications for obesity, T2D, and the first liver-targeted drug for MASH, Rezdiffra (resmetirom; Madrigal Pharmaceutical, West Conshohocken, PA, USA), which was recently approved for use in the United States (US) by the US Food and Drug Administration.[26-29] Optimal management of CMRs according to their respective guidelines is also recommended. This is an especially important point as MASLD's CMR's are closely associated with the CMRs for cardiovascular disease, the most common cause of death among those with MASLD.26-29 This combined approach is one of the main avenues to decreasing the disease burden of MASLD (Fig. 3).[26-31]

EPIDEMIOLOGY OF MASLD

MASLD

In the most recent meta-analysis, 38% of adults around the world were shown to have MASLD (years 2016–2019), which was an increase of 50% since 1990–2006.[17] The prevalence seems to be highest in Latin America (44.4%) and lowest in Western Europe (25.1%). These trends are expected to grow, and the global prevalence of MASLD is forecast to reach 55.4% by 2040.[32]

However, the Northern Africa and Middle East (MENA) region and Asia are experiencing rapid growth in the MASLD risk factors of obesity and T2D.[33,34] As a result, the prevalence of MASLD in those areas is also expected to grow. In fact, growth within the MENA region was evident when a study reported that in 2020, the pooled estimated

prevalence of MASLD was 39.43% in the general population and 68.71% among T2D patients.[35] The MENA countries expected to have the highest number of MASLD cases are Egypt, followed by Türkiye and Iran.[35]

Another study used the Global Burden of Disease database from 2019 and estimated that in that year, 170,000 incident cases of liver cancer (LC) occurred globally among people with MASLD (LC-MASLD), accounting for 6.6% of incident LC cases caused by all CLDs. In addition, 168,969 deaths were related to LC-MASLD, accounting for 8.6% of LC deaths from all CLDs. When the data were analyzed by region, Asia accounted for 48.3% of the global incidence of LC-MASLD and 46.2% of deaths attributable to LC-MASLD, whereas MENA accounted for 8.9% of LC-MASLD cases and 8.6% of deaths attributable to LC-MASLD. Both Asia and MENA also experienced an increase in disability-adjusted life years (DALYs) from 2009–2019 due to LC-MASLD. The predictors for increased DALYs were similar for Asia and MENA; however, in Asia, smoking was related to increased DALYs, whereas in MENA, it was low levels of physical activity.[36]

Several other recent studies have provided further evidence of the growing burden of MASLD. In a recent systematic review and meta-analysis of 63 studies from mostly Asian countries (China/Hong Kong [n=26], South Korea [n=22], Japan [n=14], Sri Lanka [n=1] and Israel [n=1]), investigators reported an incidence rate of 46.13 new cases per 1,000 person-years (PY).[37] The incidence rate was found to be higher in smokers than non-smokers and obese or overweight persons than normal-weight persons; China had the highest incidence rates, and Japan had the lowest incidence rates. The finding that China is experiencing a sharply increasing rate of MASLD has also been featured in several other recent reports, which noted that the aging of the Chinese population could be one contributor to that increase. Geographic variability within China has been noted, with higher prevalences in the North, Northwest, and East.[38,39]

Another meta-analysis of data from Asia, which included 237 published articles from 16 countries/regions (Mainland China: 93, South Korea: 61, Japan: 29, Taiwan: 15, Iran: 9, India: 7, Hong Kong: 6, Sri Lanka: 3, Malaysia: 3, Pakistan: 3, Bangladesh: 2, Indonesia: 2, Israel: 1, Singapore: 1, Thailand: 1, Saudi Arabia: 1) reported that the NAFLD incidence rate was 50.01 per 1,000 PY, with an annual HCC incidence rate of 1.8 cases per 1,000 PY among those with NAFLD and an overall mortality rate of 5.3 deaths per 1,000 PY. However, in that meta-analysis, most of the study participants came from South Korea (n=11,323,296; 93.2%) followed by Mainland China (n=607,253; 5.0%). They also found that the rate of NAFLD increased from 25% in 1995–2005 to 34% in 2012–2017.[40]

A recent modeling study of four Asian regions (Hong Kong, Singapore, South Korea, and Taiwan) adds further information about the adverse outcomes that could occur by 2030 without intervention. Those investigators reported that the MASLD prevalence will increase between 6% and 20%, MASH prevalence will increase 20–35%, and new cases of HCC, decompensated cirrhosis, and CLD-related mortality could increase by anywhere from 65% to 100%.[41] We suspect that these trends might be underestimated because they were based only on the trending data for obesity; T2D is the most significant predictor of adverse outcomes, and it was not accounted for in that modeling study.[42] Nonetheless those findings highlight the significant burden of MASLD in Asia. A similar study conducted in Saudi Arabia, Kuwait, and the United Arab Emirates also reported substantial increases in the prevalence of MASLD, MASH, and the adverse outcomes of advanced fibrosis, cirrhosis, decompensated cirrhosis, and liver-related mortality. These findings highlight the need to treat MASLD as a public health emergency.[43]

Children and adolescents

Almost one in 10 children/adolescents have MASLD, with a higher prevalence among children considered obese.[44,45] However, those data are relatively old, so the actually prevalence of MASLD among children is probably closer to 15–20%. In fact, in a global study, the 15–29-year-old age group accounted for 17.2% (0.29 billion) of CLD prevalent cases, 11.2% (n=232,072) of CLD incident cases, and 3.8% (n=55,515) of CLD deaths.[18] Furthermore, the CLD prevalence rates were determined to be increasing as a result of increasing rates of MASLD. When CLD-related deaths were analyzed, the researchers reported that deaths due to hepatitis B virus (HBV) were decreasing, and MASLD- and hepatitis C virus (HCV)-related deaths were increasing.[18] A recent meta-analysis conducted for the years 1997–2023 reported that the prevalence of MASLD in chil-

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dren (≤18 years old) was 13% in the general population (15% in males and 10% in females) and 47% in obese children, with a higher prevalence noted among males. The prevalence of MASLD among the general population and the obese population was higher in studies from Asia (15% and 53%, respectively), than in studies from non-Asian countries (11% and 39%, respectively). The prevalence of MASLD was also noted to increase with age, regardless of obesity, although the rates were highest in obese persons, with a pattern of increasing disease prevalence as weight increased.[46]

These data suggest that the current epidemiologic burden of MASLD is enormous and continuing to grow. In fact, it appears that MASLD is becoming the dominant liver disease in most regions of the world but especially in Asia. Additionally, as better treatments and prevention of HBV have become more globally available, deaths due to HBV are decreasing, whereas MASLD- and HCV-related deaths are increasing. MASLD-related LC is also increasing, with Asia experiencing the largest number of incident cases and deaths.[18]

DISEASE BURDEN AND PROJECTED ISSUES

Obesity

The increase in MASLD appears to be occurring in parallel with increasing rates of obesity and T2D, both strong risk factors associated with MASLD (Fig. 4). In 2016, the World Health Organization suggested that 650 million adults (≥18 years old, 13% of the global population) were obese, and more than 340 million children (aged 5–19 years) were found to be either overweight or obese. In 2023, the World Obesity Federation reported that without any change, 1 in 4 people (nearly 2 billion people) would have obesity by 2035 and that childhood obesity could more than double by 2035, with rates among young males increasing 100% to 208 million and rates among young females increasing by 125% to 175 million. Lower-income countries are also facing rapid increases in obesity prevalence: 9 of the top 10 countries with the greatest expected increases in obesity are low or lower-middle income countries in Asia or Africa.[23,33,34]

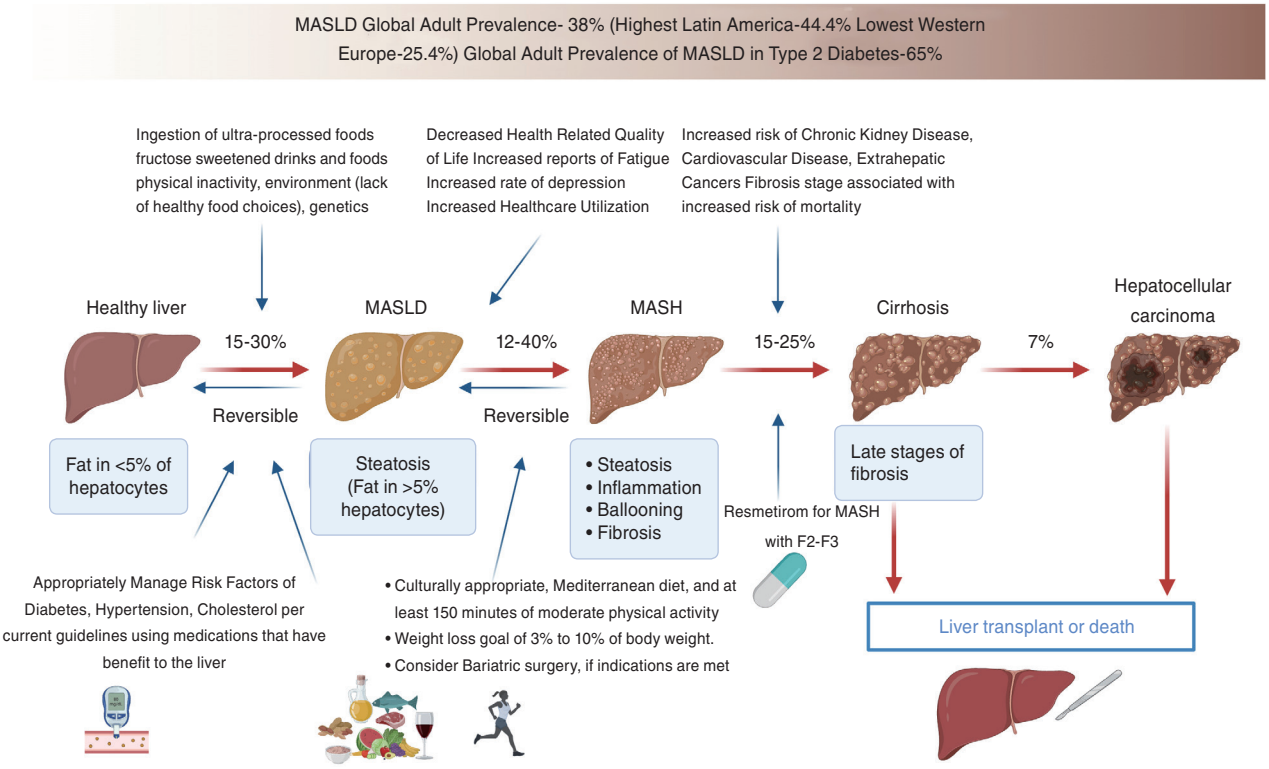

Figure 3. Current understanding of the progression and regression of metabolic dysfunction–associated steatotic liver disease (MASLD). MASH, metabolic dysfunction-associated steatohepatitis.

These are distressing numbers in the context of MASLD and the high prevalence rates associated with being overweight or obese. A recent meta-analysis conducted among 101,028 individuals considered overweight or obese helped to quantify the large negative impact of obesity on MASLD.[47] The investigators reported that the pooled prevalence of MASLD in the overweight and obese populations was 70% and 75%, respectively, and the prevalence of progressive disease, MASH, was 34% in both the overweight and obese populations. The prevalence of fibrosis stages F2–F4, the most significant risk factor for CLD-related mortality, was 20% in the overweight group and 22% in the obese group, with 7% of both the overweight and obese groups having advanced fibrosis (F3–F4).[47-49]

Type 2 diabetes

T2D is expected to affect nearly 600 million people globally by 2035, but the prevalence rates vary around the globe.[50,51] As previously mentioned, MASLD and T2D appear to share a bidirectional relationship, with increases in T2D increasing the prevalence of MASLD and vice versa.[52,53] In a recent meta-analysis of MASLD prevalence among those with T2D, the investigators determined that the MASLD prevalence for 2016–2021 was 68.8%, an increase of 13% from 1990–2004 (55.6%).[50] The highest MASLD prevalence among T2D patients was observed in Eastern Europe (80.6%) followed by the Middle East (71.2%), with the lowest rate in Africa (53.1%). Among patients with liver biopsy data, the global pooled prevalence of NASH/MASH was 66.4%, of significant fibrosis was 40.8%, and of advanced fibrosis was 15.5%. Those investigators also provided pooled all-cause and cause-specific mortality rates, which were 16.8 per 1,000 PY for all-cause mortality, 4.2 per 1,000 PY for cardiac-specific mortality, 6.1 per 1,000 PY for extrahepatic cancer–specific mortality, and 2.2 per 1,000 PY for liver-specific mortality.[50]

In another recent meta-analysis of 20 studies, wherein 117,020 patients were followed for a median period of 5 years, MASLD was noted to be associated with an almost 2-times increase in the risk of developing incident T2D.[52] This association could indicate a genetic link between MASLD and T2D.[53,54] In fact, in a genetic study that used a bidirectional Mendelian randomization approach, the researchers found a causal link between MASLD and T2D.[54] Using differential gene expression analyses, other investi-

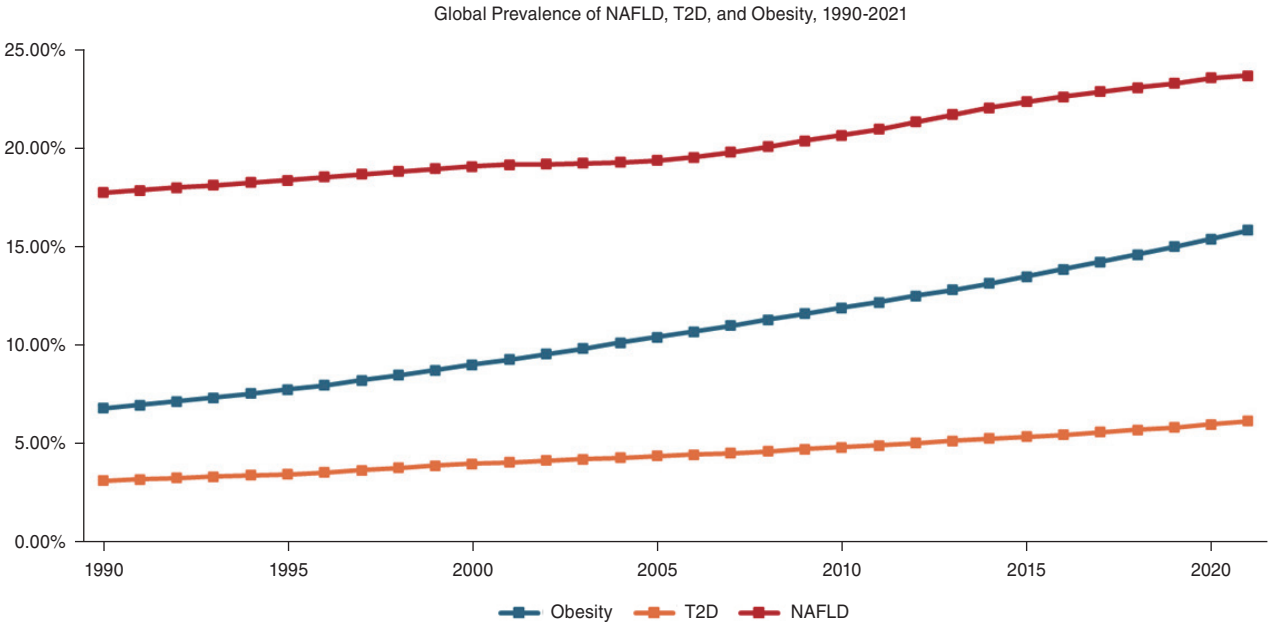

Figure 4. Parallel increases in obesity, diabetes, and NAFLD from 2013 to 2020. NAFLD, nonalcoholic fatty liver disease; T2D, type 2 diabetes.

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gators determined that 15 core genes are linked to both T2D and MASLD. Those findings have provided a platform for further research into genetic and pathogenic connections between MASLD and T2D.[54]

Insulin resistance

IR appears to be the pathophysiological link connecting obesity, T2D, and MASLD.[55,56] In a study from the United States, investigators determined that approximately 40% of young adults (18–44 years old) had IR, and IR was more prevalent in those with a higher body mass index (BMI), those with hypertension or hypercholesteremia, and those of Mexican-American ethnicity.[57,58] In other studies, the prevalence of IR was estimated to be the lowest among European adults, with a prevalence of 15.5%, and higher in countries such as Thailand (23.3%), Lebanon (44.6%), and Venezuela (46.5%).[59,60] It is estimated that 80% of individuals with MASLD have IR, including those who have a normal BMI.[61,62]

The role of insulin in the development of MASLD might be related to the presence of single nucleotide polymorphisms (SNPs) in the patatin-like phospholipase domain containing protein 3 (PNPLA3). It is postulated that PNPLA3 creates an insulin-sensitive environment. On the other hand, a recent study concluded that the presence of IR was necessary for the development of MASLD irrespective of PNPLA3 status.[55] These findings suggest that people with both MASLD and the PNPLA3 SNP are insulin resistant and might experience more adverse liver outcomes due to their increased susceptibility to the effects of obesity and diabetes. Therefore, this population might need earlier and more aggressive treatment than other groups with MASLD.[56]

Metabolic syndrome

Early studies suggested that MASLD was the liver manifestation of MetS because of its close relationship with the metabolic abnormalities noted within the definition of MetS.[63-68] In fact, more recent studies have shown that as the number of MetS conditions increases so does the risk for MASLD-related mortality.[69] The prevalence of MASLD in those with MetS has been reported to be approximately 73%, but the prevalence of MetS among those with MASLD is only 43%.[65,66] When MetS is present, the prevalence of advanced fibrosis is almost doubled, and when all five MetS criteria are present, the prevalence of advanced fibrosis can reach 30%.[67]

On the other hand, there is evidence that the presence of MASLD increases the risk of MetS, similar to the risk for T2D.[70] In a meta-analysis of 81,411 patients who were followed for a median of 4.5 years (range 3–11 years), investigators determined that MASLD was associated with an increased relative risk for incident MetS of 1.80 (95% confidence interval [CI] 1.72–1.89).[70]

Prediabetes

The prevalence of prediabetes among those with MASLD ranges between 20% and 25%.[24] In one study conducted using data from the Cardiovascular Risk in Young Finns Study, researchers found that among young adults (mean age 31 years; n=2,020), 25% developed prediabetes over the course of 10 years. Those who were either overweight or obese and had a higher fatty liver index (FLI≥60) at the start of the study were more likely to develop prediabetes than those who were overweight or obese but had a low FLI (<60).[65] In fact, the presence of a high FLI was associated with a 2-fold higher risk of developing prediabetes, demonstrating, as noted above, that fat in the liver can lead to metabolic abnormalities.[68] In another study using data from NHANES, 25% of the participants with MASLD had prediabetes. The odds of developing MASLD were 4 times higher in those with prediabetes than in those considered metabolically healthy. In addition, among those with MASLD, the presence of prediabetes increased the risk of all-cause mortality during follow up by three times, and it raised the risk of cardiovascular-related mortality by more than 10 times, compared with those who were metabolically healthy.[24] As such, prediabetes is not a benign condition, and it requires careful follow-up to prevent the development of MASLD and related outcomes.

Cardiovascular disease

As noted above, MASLD is associated with an increased risk of cardiovascular disease (CVD). Importantly, cardiovascular disease (CVD) is the number one cause of mortality followed by non-hepatic cancers as the number two

cause of mortality among those with MASLD, while HCC is the number one cause of liver-related mortality.[71-74] The exact pathophysiological mechanism linking MASLD and CVD has yet to be fully elucidated. Nonetheless, these two diseases share common metabolic abnormalities that could interact synergistically to increase the risk of both heart disease and liver disease.[75] In this case, it appears that the ectopic fat deposition that occurs as MASLD develops also occurs in the epicardium. Combined with the systematic inflammation present in MASLD, these factors increase endothelial dysfunction and intramyocardial inflammation and accelerate atherogenesis, leading to coronary artery disease, an increased risk of left ventricular diastolic dysfunction and hypertrophy, cardiac valvular calcification, arrhythmias (mainly permanent atrial fibrillation), and heart failure.[76-83]

Studies have reported that 40–60% of persons with MASLD have hypertension.[65] Importantly, though, the prevalence and incidence of hypertension increase by fibrosis stage, with the highest prevalence and incidence rates found in those with F4 fibrosis (cirrhosis).[71] A similar pattern was noted for cardiac events: those with MASLD and F3 or F4 fibrosis had a 2.2-fold higher risk of a cardiac event than those with MASLD and F0–F2 fibrosis, along with a 1.35-fold higher risk of hypertension.[71] A recent meta-analysis provided a pooled rate of 4.20 per 1,000 PY for cardiac-specific mortality.[17]

On the other hand, a recent study that investigated cardiovascular events among those with MASLD as defined with the new nomenclature criteria determined that once CMRs, age, and sex were accounted for, MASLD was no longer correlated with CVD-related mortality.[84] Although more research, especially using the new MASLD criteria, is needed to determine the actual relationship between MASLD and CVD, awareness that MASLD and CVD can coexist is necessary, and when it is present, CVD requires appropriate assessment and treatment.[85-87]

This suggestion is particularly important because of the association between CVD and CLD in the presence of the increased alcohol consumption allowed under the MASLD continuum. A study conducted in Korea using the MAFLD definition, which allows for increased alcohol consumption, reported that among almost 9 million individuals aged 40–64 years who had undergone a health screening and were followed for a median of 10 years, the risk of a CVD event (myocardial infarction, ischemic stroke, heart failure, or CVD-related death) was 34% higher in those with MAFLD (adjusted hazard ratio [aHR] 1.43; 95% CI 1.41–1.45) than in those with NAFLD (aHR 1.09; 95% CI 1.03–1.15), suggesting that alcohol could increase the risk of CVD events and deaths.[88] However, as noted, this suggestion needs further study and validation using the new terminology. Additionally, given these findings, a recent study suggested that use of elevated liver enzymes in those with MASLD may assist practitioners in identifying individuals who may be at even higher risk for adverse CVD related outcomes and helps to validate the current guidelines that all individuals should be screened for CMRs and appropriate treatments initiated where appropriate.[89]

Chronic kidney disease

Liver-driven, chronic, systemic, low-grade inflammation appears to contribute not only to CVD, but also to chronic kidney disease (CKD).[90-93] In a Cox regression, investigators confirmed a significant association between NAFLD and CKD, with a hazard ratio (HR) of 1.80 (95% CI 1.73–1.86; $P<0.001$).[88] Subgroup analyses revealed that that association was most pronounced in the 18–50-year age group (HR 2.13; 95% CI 1.91–2.37; $P<0.001$) and among female MASLD patients (HR 1.85; 95% CI 1.76–1.95; $P<0.001$).[88] A recent meta-analysis confirmed that MASLD was an independent predictor for the development of CKD.[90] That large meta-analysis indicated that MASLD was significantly associated with a 1.45-fold increase in the long-term risk of incident CKD stage ≥3.[90] On the other hand, there is a paucity of data on the relationships among MASLD, CKD, and mortality. One small study from Scotland reported that the mortality rate was 5-fold higher in those with MASLD, fibrosis, and CKD when compared to those with MASLD without fibrosis or CKD.[92] Understanding of MASLD and CKD will continue to evolve, especially as the new terminology and associated outcomes are studied. Nonetheless, the potential for the development of CKD and its adverse outcomes suggest that monitoring renal function in patients with MASLD is important and should be part of routine assessments.[93]

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Extrahepatic cancers

The chronic state of inflammation associated with MASLD is also suspected to increase the risk of extrahepatic cancers.[94] In a retrospective review study of the Swedish National Patient Registry (1987–2016) that analyzed data for approximately 8,500 individuals with NAFLD but without cancer over a median of six years, the risk of developing cancer was 22% higher in those with NAFLD than in those without NAFLD, and the rate of cancer development was significantly higher in those with NAFLD than in those without NAFLD (9.7 cases vs. 8.6 cases per 1,000 PY). By specific cancer and compared with those without NAFLD, those with NAFLD were at a 38% higher risk for colorectal cancer, a 2-fold higher risk for kidney cancer, a 2.5-fold higher risk for bladder cancer, and a 78% higher risk for uterine cancer.[95] In a study conducted in the United States over a median of 8 years (range 1–21 years), the findings were similar but more pronounced: NAFLD was associated with a 90% higher risk of cancer development, especially for cancers of the gastrointestinal tract, liver, and uterus.[96] A study conducted in Korea also reported an increased risk of extrahepatic cancer for those with NALFD, with the highest risks noted for HCC, colorectal cancer in males, and breast cancer in females. This sex distinction in the development of extrahepatic cancer in the Korean population is somewhat different from what has been reported before, especially the association with breast cancer.[97]

One meta-analysis conducted on extrahepatic cancers in patients with MASLD determined that MASLD was associated with a 1.2-fold to 1.5-fold increased risk of developing lung, breast, gynecological, or urinary system cancers.[98] Yet another meta-analysis reported that the pooled extrahepatic cancer incidence rate was 10.58 per 1,000 PY (95% CI 8.14–13.02; I^2=97.1%), with the most frequently occurring extrahepatic cancers being uterine, breast, prostate, colorectal, and lung.[99] Importantly, the extrahepatic cancer incidence rates were not associated with the presence of any stage of fibrosis. The differences in these reports on the incidence and type of extrahepatic cancers associated with MASLD can most likely be attributed to the different inclusion/exclusion criteria of each study, which affected the size of the patient populations. Nonetheless, it is evident that MASLD is associated with an increased risk of extrahepatic cancer that appears to be higher than the risk of liver-related mortality, which was reported to be only 0.92 per 1,000 PY.[99] As such, it is essential to follow current cancer screening guidelines for patients with MASLD.

Hepatocellular carcinoma

HCC in MASLD usually occurs only when cirrhosis is present. However, among those with MASLD, a small percentage can develop HCC when cirrhosis is not present.[100] A meta-analysis reported that the current pooled MASLD-related HCC incidence rate was 1.25 per 1,000 PY overall, but in those with MASLD and advanced fibrosis, the HCC incidence rate was 14.46 per 1,000 PY.[101] In a recent study of almost 300,000 veterans, among whom 823 developed HCC, the reported 1-, 3- and 5- year mortality rates were 47.0%, 69.6%, and 74.6%, respectively.[102] Using a competing risk analysis, the investigators determined that HCC was the most prominent cause of death, accounting for more than 70% of the deaths that occurred in the first year after diagnosis and still accounting for the majority of deaths at 3 and 5 years. However, among those aged 75 years and older, other causes of death were more frequent than HCC.[102] Additionally, a recent study looked across the continuum of MASLD, (MASLD, Met-ALD, and ALD) to investigate the risk of cirrhosis and HCC in 129,802 individuals from Taiwan who had participated in a health screening program between 1997 and 2013. Within that cohort, 39.1% had SLD, of whom 81% had MASLD, 7% had Met-ALD, and 8.8% had ALD (4% had cryptogenic SLD). After a mean follow up of 16 years, 4,458 cases of cirrhosis and 1,392 cases of HCC occurred in the entire cohort, for an incidence rate of 86.1 and 26.8 per 100,000 PY, respectively. Importantly, the investigators found that as the amount of alcohol consumed increased, as allowed per the new terminology (although due to the differences in alcohol metabolism between Asians and Caucasians, the amount allowed was adjusted down), the ALD group had the highest incidence rate for cirrhosis and HCC, followed by the Met-ALD, MASLD, and then non-SLD groups, with a similar pattern for cirrhosis.[103] Interestingly, the rates and hazard ratios for developing HCC and cirrhosis were even higher when compared with people with SLD who had no CMR factors, suggesting that although the presence and amount of alcohol consumption play a significant role in the development of HCC and cirrhosis, the presence of CMR factors

must also be addressed.[103]

Despite the fact that HCC can occur in people who do not have cirrhosis, the incidence rates justify routine HCC screening only in those with cirrhosis. However, the presence of certain risk factors, including a family history, can prompt clinicians to individualize screening for individuals with MASLD but without cirrhosis.[102]

LIVER TRANSPLANTATION

As previously noted, MASH is the number one cause of HCC among liver transplant candidates, and it is now the number one cause for liver transplantation among women. However, MASH might soon be the number one reason for liver transplantation among other subgroups if the current estimates for the increase in MASH remain unabated.[104-108]

SARCOPENIA

Sarcopenia has recently been identified as more prevalent in those with MASLD than in those without it, despite their BMI, and it is associated with higher rates of adverse outcomes among these patients.[109,110]

HEALTH-RELATED QUALITY OF LIFE, FATIGUE, AND ECONOMIC BURDEN

MASLD affects not only clinical outcomes, but also patient-reported outcomes. The presence of MASLD is associated with decreased health-related quality of life, especially in the domain of physical activity and the ability to carry out activities of daily living.[111,112] One reason for such a decrement in this domain is the reported presence of fatigue.[113] Fatigue in those with CLD is a state of tiredness that is not resolved with rest and is believed to occur when the liver disease triggers inflammatory and hormonal pathways that travel from the liver to the brain and cause fatigue. Those same pathways are also associated with decreased cognitive functioning and depression, both of which can play an important role in the inability to be active, the high rates of depression noted among those with MASLD, and their reported work productivity impairment. impairment.[111-115] The economic burden of MASLD is high as a result of increased healthcare utilization and the decreased quality of years lived.[116-119]

AWARENESS AND STIGMA

Despite the significant negative effects of MASLD on clinical outcomes and patient-reported outcomes, awareness of this disease remains low, probably due to factors such as stigma and lack of knowledge about the burden of MASLD.[120-122] Nevertheless, now that treatments other than lifestyle interventions are coming into clinical practice, it is imperative to implement strategies to increase awareness. Two such interventions are currently underway. The first, as mentioned above, was the name change from NAFLD to MASLD.[13] This name change was made to identify what this liver disease is rather than what it is not, as well as to better align the terminology for use in children and in cultures that forbid alcohol consumption. The use of steatosis was also found to be less stigmatizing than the term fatty, which could ease communication about MASLD with patients. Second, risk stratification algorithms have been developed by several major professional organizations to help practitioners identify patients at high risk for MASLD and MASLD with fibrosis and provide non-invasive diagnostic tools that can be easily implemented at the bedside to assist in clinical decision making and treatment.[26-29]

LEAN MASLD

Although obesity, as discussed previously, is one of the most common metabolic comorbidities present in those with MASLD, individuals can also have what has been termed lean MASLD, where the BMI falls within the normal range but SLD is present. In patients with a normal BMI, the abnormal distribution of body fat, which is a precursor to the pathogenesis of metabolic comorbidities, can be evident. Specifically, abdominal fat might play a key role in the development of MASLD because of its strong association with IR and its potential as a source of free fatty acids.[123,124] Furthermore, waist circumference has been shown to predict mortality among MASLD patients.[125] Therefore, many advocate for the use of waist circumference rather than

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BMI when assessing patients for risk factors.[125] Additionally, it has been found that those with lean NAFLD can also have the same liver disease progression and outcomes as patients who are not lean.[126,127]

In this context, the change to the new nomenclature of MASLD will require specific research about lean NAFLD due to the potential lack of overt metabolic abnormality required for the MASLD diagnosis.[15] This point was recently highlighted in several studies. Once such study compared the concordance between MASLD and NAFLD and reported that it was high, but 5–7% of individuals who would have been classified as NAFLD did not meet the criteria for MASLD.[15]

Several recent meta-analyses have validated those findings by reporting that the prevalence of metabolic features increased significantly as the individual's weight increased, indicating that those with lean NAFLD might be overlooked when testing for MASLD.[126,128,129] This is an especially important issue for individuals from Asia, where lean NAFLD/MASLD is quite prevalent but can remain undiagnosed because of the new metabolic criteria requirement.[126,128,129]

It is quite important to note that in Asian countries where the prevalence of lean MASLD is high, the prevalence of viral hepatitis is also very high.[130] This fact has multiple implications. First, providers in Asian countries who predominantly focus on viral hepatitis should also consider MASLD in their practice, either alone or superimposed on viral hepatitis. In this context, it is possible that lean MASLD combined with viral hepatitis can be more aggressive and lead to higher rates of cirrhosis and HCC.[130-133] Furthermore, given the relatively low BMI and alcohol consumption common in Asian populations, addressing these specific issues and conducting more studies in Asia would be beneficial to policy development and the allocation of resources.[132]

FUTURE PERSPECTIVES FOR MASLD

Although understanding of the natural history of MASLD has come a long way since it was first discovered, changing the terminology and definition of this SLD to better align with its manifestation has introduced new questions and concerns into the field. First, in the realm of clinical care, awareness remains low in the general practice healthcare field, as well as in the general public; therefore, bringing awareness to this liver disease remains a priority, especially because a new drug for MASLD with fibrosis stage 2 or 3 has been approved for use in the United States.[134] It is important to write clear and concise guidelines to help general practitioners identify those most at risk for having MASLD and those at high risk for disease progression. New society guidelines are currently being released to help address this need.[135-137] However, research will be needed to determine whether these new guidelines and the name change improve awareness. Years of work have gone into developing and understanding the performance of non-invasive tests (NITs) in those with NAFLD.[138] Fortunately, several studies have shown that the most commonly used NITs perform similarly well in those with MASLD.[15] However, data are lacking as to whether those same NITs are valid for the identification of high-risk Met-ALD. The same type of research is needed to determine which NITs are most appropriate for monitoring disease progression and regression in those with Met-ALD.[139,140] Furthermore, GLP-1 inhibitors, newer diabetic agents, have now been approved to treat obesity, so research is needed to determine how the use of those medications in patients with both MASLD and obesity will change the course of both diseases.[141] Past research has shown that having both NAFLD and HBV may offer some protection against disease progression, but a recent study discerned that having both MASLD and HBV or HCV was associated with a higher risk of mortality.[131] Further research into this discrepancy is urgently needed, as is understanding of the long-term outcomes of people who would be diagnosed with NAFLD but would not be diagnosed with MASLD because they do not meet the MASLD CMR criteria. This particular area could be of great concern in Asian countries where most of those with NAFLD but not MASLD are lean.[142]

SUMMARY

MASLD prevalence is growing, and it already affects more than 38% of the global adult population. Although prevalence varies around the world, with the highest rates in Latin America, MENA, and Asia, in most global areas, one of every four adults has MASLD. Given rapid growth in the rates of obesity and T2D, two of the major risk factors for MASLD, the prevalence of MASLD is projected to con-

tinue increasing. MASLD is not a benign disease; it is associated with cirrhosis, HCC, and liver mortality. Furthermore, CVD remains the number one cause of death for those with MASLD, most likely through a complex communication pathway between the liver and the heart that promotes dyslipidemia, atherosclerotic plaques, and other metabolic abnormalities. MASLD is now the most common cause of liver transplantation in the US among those who are listed for HCC. MASLD is related to decreased health-related quality of life and increased healthcare and societal costs. With the name change to MASLD and the release of NIT based risk stratification and treatment algorithms, the hope is that awareness of the detrimental effects of MASLD will increase and more interventions targeted at both prevention and treatment will occur.

Authors' contribution

ZY manuscript writing and critical revision; MK critical review and editing and figure development; LH manuscript writing and critical revision.

Conflicts of Interest

ZM Younossi has received research funding and/or serve as consultant to Intercept, Cymabay, Boehringer Ingelheim, Ipsen, BMS, GSK, NovoNordisk, Siemens, Madridgal, Merck, Akero and Abbott. All other authors have not received any funding.

REFERENCES

1. Lonardo A, Leoni S, Alswat KA, Fouad Y. History of nonalcoholic fatty liver disease. Int J Mol Sci 2020;21:5888.
2. Addison T. Observations on fatty degeneration of the liver. Guys Hosp Rep 1836;1:476-485.
3. Ludwig J, Viggiano TR, McGill DB, Oh BJ. Nonalcoholic steatohepatitis: Mayo Clinic experiences with a hitherto unnamed disease. Mayo Clin Proc 1980;55:434-438.
4. Batman PA, Scheuer PJ. Diabetic hepatitis preceding the onset of glucose intolerance. Histopathology 1985;9:237-243.
5. Schaffner F, Thaler H. Nonalcoholic fatty liver disease. Prog Liver Dis 1986;8:283-298.
6. Cortez-Pinto H, Camilo ME, Baptista A, De Oliveira AG, De Moura MC. Non-alcoholic fatty liver: another feature of the metabolic syndrome? Clin Nutr 1999;18:353-358.
7. Lonardo A. Fatty liver and nonalcoholic steatohepatitis. Where do we stand and where are we going? Dig Dis 1999;17:80-89.
8. Musso G, Gambino R, Bo S, Uberti B, Biroli G, Pagano G, et al. Should nonalcoholic fatty liver disease be included in the definition of metabolic syndrome? A cross-sectional comparison with Adult Treatment Panel III criteria in nonobese nondiabetic subjects. Diabetes Care 2008;31:562-568.
9. Matteoni CA, Younossi ZM, Gramlich T, Boparai N, Liu YC, McCullough AJ. Nonalcoholic fatty liver disease: a spectrum of clinical and pathological severity. Gastroenterology 1999;116:1413-1419.
10. Neuschwander-Tetri BA, Caldwell SH. Nonalcoholic steatohepatitis: summary of an AASLD Single Topic Conference. Hepatology 2003;37:1202-1219. Erratum in: Hepatology 2003;38:536.
11. Chen CH, Huang MH, Yang JC, Nien CK, Yang CC, Yeh YH, et al. Prevalence and risk factors of nonalcoholic fatty liver disease in an adult population of Taiwan: metabolic significance of nonalcoholic fatty liver disease in nonobese adults. J Clin Gastroenterol 2006;40:745-752.
12. Eslam M, Sanyal AJ, George J; International Consensus Panel. MAFLD: a consensus-driven proposed nomenclature for metabolic associated fatty liver disease. Gastroenterology 2020;158:1999-2014.e1.
13. Rinella ME, Lazarus JV, Ratziu V, Francque SM, Sanyal AJ, Kanwal F, et al; NAFLD Nomenclature consensus group. A multisociety Delphi consensus statement on new fatty liver disease nomenclature. J Hepatol 2023;79:1542-1556.
14. Chalasani N, Younossi Z, Lavine JE, Charlton M, Cusi K, Rinella M, et al. The diagnosis and management of nonalcoholic fatty liver disease: practice guidance from the American Association for the Study of Liver Diseases. Hepatology 2018;67:328-357.
15. Younossi ZM, Paik JM, Stepanova M, Ong J, Alqahtani S, Henry L. Clinical profiles and mortality rates are similar for metabolic dysfunction-associated steatotic liver disease and non-alcoholic fatty liver disease. J Hepatol 2024;80:694-701.
16. Younossi ZM, Paik JM, Al Shabeeb R, Golabi P, Younossi I, Henry L. Are there outcome differences between NAFLD and metabolic-associated fatty liver disease? Hepatology 2022;76:1423-1437.
17. 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

https://doi.org/10.3350/cmh.2024.0431

systematic review. Hepatology 2023;77:1335-1347.
18. Paik JM, Kabbara K, Eberly KE, Younossi Y, Henry L, Younossi ZM. Global burden of NAFLD and chronic liver disease among adolescents and young adults. Hepatology 2022;75: 1204-1217.
19. Lee MH, Chen YT, Huang YH, Lu SN, Yang TH, Huang JF, et al. Chronic viral hepatitis B and C outweigh MASLD in the associated risk of cirrhosis and HCC. Clin Gastroenterol Hepatol 2024;22:1275-1285.e2.
20. Golabi P, Otgonsuren M, de Avila L, Sayiner M, Rafiq N, Younossi ZM. Components of metabolic syndrome increase the risk of mortality in nonalcoholic fatty liver disease (NAFLD). Medicine (Baltimore) 2018;97:e0214.
21. Ke Y, Xu C, Lin J, Li Y. Role of hepatokines in non-alcoholic fatty liver disease. J Transl Int Med 2019;7:143-148.
22. Stefan N, Schick F, Birkenfeld AL, Häring HU, White MF. The role of hepatokines in NAFLD. Cell Metab 2023;35:236-252.
23. World Health Organization. Obesity and overweight. WHO web site, <https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight>. Accessed 3 Jnue 2024.
24. Golabi P, Paik JM, Kumar A, Al Shabeeb R, Eberly KE, Cusi K, et al. Nonalcoholic fatty liver disease (NAFLD) and associated mortality in individuals with type 2 diabetes, pre-diabetes, metabolically unhealthy, and metabolically healthy individuals in the United States. Metabolism 2023;146:155642.
25. Cusi K, Isaacs S, Barb D, Basu R, Caprio S, Garvey WT, et al. American Association of Clinical Endocrinology Clinical Practice Guideline for the diagnosis and management of nonalcoholic fatty liver disease in primary care and endocrinology clinical settings: co-sponsored by the American Association for the Study of Liver Diseases (AASLD). Endocr Pract 2022;28:528-562.
26. Kanwal F, Shubrook JH, Adams LA, Pfotenhauer K, Wai-Sun Wong V, Wright E, et al. Clinical care pathway for the risk stratification and management of patients with nonalcoholic fatty liver disease. Gastroenterology 2021;161:1657-1669.
27. American Diabetes Association. Diabetes care. Standards of care in diabetes – 2023. ADA web site, <https://diabetesjournals.org/care/issue/46/Supplement_1>. Accessed 3 Jnue 2024.
28. Rinella ME, Neuschwander-Tetri BA, Siddiqui MS, Abdelmalek MF, Caldwell S, Barb D, et al. AASLD Practice Guidance on the clinical assessment and management of nonalcoholic fatty liver disease. Hepatology 2023;77:1797-1835.
29. European Association for the Study of the Liver (EASL); European Association for the Study of Diabetes (EASD); European Association for the Study of Obesity (EASO). EASL-EASD-EASO Clinical Practice Guidelines for the management of non-alcoholic fatty liver disease. J Hepatol 2016;64: 1388-1402.
30. Allen AM, Lazarus JV, Younossi ZM. Healthcare and socioeconomic costs of NAFLD: a global framework to navigate the uncertainties. J Hepatol 2023;79:209-217.
31. Hossain MJ, Al-Mamun M, Islam MR. Diabetes mellitus, the fastest growing global public health concern: early detection should be focused. Health Sci Rep 2024;7:e2004.
32. Le MH, Yeo YH, Zou B, Barnet S, Henry L, Cheung R, et al. Forecasted 2040 global prevalence of nonalcoholic fatty liver disease using hierarchical bayesian approach. Clin Mol Hepatol 2022;28:841-850.
33. NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in underweight and obesity from 1990 to 2022: a pooled analysis of 3663 population-representative studies with 222 million children, adolescents, and adults. Lancet 2024;403: 1027-1050.
34. World Obesity Federation. World obesity atlas 2023. World Obesity Federation web site, < https://www.worldobesity.org/resources/resource-library/world-obesity-atlas-2023>. Accessed 15 Jan 2024.
35. Younossi ZM, Golabi P, Paik J, Owrangi S, Yilmaz Y, El-Kassas M, et al. Prevalence of metabolic dysfunction-associated steatotic liver disease in the Middle East and North Africa. Liver Int 2024;44:1061-1070.
36. Golabi P, Paik JM, AlQahtani S, Younossi Y, Tuncer G, Younossi ZM. Burden of non-alcoholic fatty liver disease in Asia, the Middle East and North Africa: data from global burden of disease 2009-2019. J Hepatol 2021;75:795-809.
37. Le MH, Le DM, Baez TC, Wu Y, Ito T, Lee EY, et al. Global incidence of non-alcoholic fatty liver disease: a systematic review and meta-analysis of 63 studies and 1,201,807 persons. J Hepatol 2023;79:287-295.
38. Zhou F, Zhou J, Wang W, Zhang XJ, Ji YX, Zhang P, et al. Unexpected rapid increase in the burden of NAFLD in China from 2008 to 2018: a systematic review and meta-analysis. Hepatology 2019;70:1119-1133.
39. Zhou J, Zhou F, Wang W, Zhang XJ, Ji YX, Zhang P, et al. Epidemiological features of NAFLD from 1999 to 2018 in China. Hepatology 2020;71:1851-1864.
40. Li J, Zou B, Yeo YH, Feng Y, Xie X, Lee DH, et al. Prevalence, incidence, and outcome of non-alcoholic fatty liver

disease in Asia, 1999-2019: a systematic review and meta-analysis. Lancet Gastroenterol Hepatol 2019;4:389-398.
41. Estes C, Chan HLY, Chien RN, Chuang WL, Fung J, Goh GB, et al. Modelling NAFLD disease burden in four Asian regions-2019-2030. Aliment Pharmacol Ther 2020;51:801-811.
42. Adams LA, Lymp JF, St Sauver J, Sanderson SO, Lindor KD, Feldstein A, et al. The natural history of nonalcoholic fatty liver disease: a population-based cohort study. Gastroenterology 2005;129:113-121.
43. Sanai FM, Al Khathlan A, Al Fadhli A, Jazzar AS, Hashim AM, Mansour E, et al. Clinical and economic burden of nonalcoholic steatohepatitis in Saudi Arabia, United Arab Emirates and Kuwait. Hepatol Int 2021;15:912-921.
44. Smith SK, Perito ER. Nonalcoholic liver disease in children and adolescents. Clin Liver Dis 2018;22:723-733.
45. Anderson EL, Howe LD, Jones HE, Higgins JP, Lawlor DA, Fraser A. The prevalence of non-alcoholic fatty liver disease in children and adolescents: a systematic review and meta-analysis. PLoS One 2015;10:e0140908.
46. Lee EJ, Choi M, Ahn SB, Yoo JJ, Kang SH, Cho Y, et al. Prevalence of nonalcoholic fatty liver disease in pediatrics and adolescents: a systematic review and meta-analysis. World J Pediatr 2024;20:569-580.
47. Quek J, Chan KE, Wong ZY, Tan C, Tan B, Lim WH, et al. Global prevalence of non-alcoholic fatty liver disease and non-alcoholic steatohepatitis in the overweight and obese population: a systematic review and meta-analysis. Lancet Gastroenterol Hepatol 2023;8:20-30.
48. Dulai PS, Singh S, Patel J, Soni M, Prokop LJ, Younossi Z, et al. Increased risk of mortality by fibrosis stage in nonalcoholic fatty liver disease: systematic review and meta-analysis. Hepatology 2017;65:1557-1565.
49. Ekstedt M, Hagström H, Nasr P, Fredrikson M, Stål P, Kechagias S, et al. Fibrosis stage is the strongest predictor for disease-specific mortality in NAFLD after up to 33 years of follow-up. Hepatology 2015;61:1547-1554.
50. Younossi ZM, Golabi P, Price JK, Owrangi S, Gundu-Rao N, Satchi R, et al. The global epidemiology of nonalcoholic fatty liver disease and nonalcoholic steatohepatitis among patients with type 2 diabetes. Clin Gastroenterol Hepatol 2024:S1542-3565(24)00287-8.
51. World Health Organization. Diabetes. WHO web site, <https://www.who.int/news-room/fact-sheets/detail/diabetes>. Accessed 22 July 2024.
52. Ballestri S, Zona S, Targher G, Romagnoli D, Baldelli E, Nascimbeni F, et al. Nonalcoholic fatty liver disease is associated with an almost twofold increased risk of incident type 2 diabetes and metabolic syndrome. Evidence from a systematic review and meta-analysis. J Gastroenterol Hepatol 2016;31:936-944.
53. Tan Y, He Q, Chan KHK. Identification of shared genetic architecture between non-alcoholic fatty liver disease and type 2 diabetes: a genome-wide analysis. Front Endocrinol (Lausanne) 2023;14:1050049.
54. Liu N, Wang G, Liu C, Liu J, Huang S, Zhou Y, et al. Nonalcoholic fatty liver disease and complications in type 1 and type 2 diabetes: a Mendelian randomization study. Diabetes Obes Metab 2023;25:365-376.
55. Li M, Chi X, Wang Y, Setrerrahmane S, Xie W, Xu H. Trends in insulin resistance: insights into mechanisms and therapeutic strategy. Signal Transduct Target Ther 2022;7:216.
56. Bril F, Kalavalapalli S, Lomonaco R, Frye R, Godinez Leiva E, Cusi K. Insulin resistance is an integral feature of MASLD even in the presence of PNPLA3 variants. JHEP Rep 2024;6:101092.
57. Parcha V, Heindl B, Kalra R, Li P, Gower B, Arora G, et al. Insulin resistance and cardiometabolic risk profile among nondiabetic american young adults: insights from NHANES. J Clin Endocrinol Metab 2022;107:e25-e37.
58. Raygor V, Abbasi F, Lazzeroni LC, Kim S, Ingelsson E, Reaven GM, et al. Impact of race/ethnicity on insulin resistance and hypertriglyceridaemia. Diab Vasc Dis Res 2019;16:153-159.
59. Fahed M, Abou Jaoudeh MG, Merhi S, Mosleh JMB, Ghadieh R, Al Hayek S, et al. Evaluation of risk factors for insulin resistance: a cross sectional study among employees at a private university in Lebanon. BMC Endocr Disord 2020;20:85.
60. Kodama K, Tojjar D, Yamada S, Toda K, Patel CJ, Butte AJ. Ethnic differences in the relationship between insulin sensitivity and insulin response: a systematic review and meta-analysis. Diabetes Care 2013;36:1789-1796.
61. Feldman A, Eder SK, Felder TK, Kedenko L, Paulweber B, Stadlmayr A, et al. Clinical and metabolic characterization of lean Caucasian subjects with non-alcoholic fatty liver. Am J Gastroenterol 2017;112:102-110.
62. Nogueira JP, Cusi K. Role of insulin resistance in the development of nonalcoholic fatty liver disease in people with type 2 diabetes: from bench to patient care. Diabetes Spectr 2024;37:20-28.
63. Grander C, Grabherr F, Moschen AR, Tilg H. Non-alcoholic

https://doi.org/10.3350/cmh.2024.0431

fatty liver disease: cause or effect of metabolic syndrome. Visc Med 2016;32:329-334.
64. Goyal A, Arora H, Arora S. Prevalence of fatty liver in metabolic syndrome. J Family Med Prim Care 2020;9:3246-3250.
65. Younossi ZM, Koenig AB, Abdelatif D, Fazel Y, Henry L, Wymer M. Global epidemiology of nonalcoholic fatty liver disease-Meta-analytic assessment of prevalence, incidence, and outcomes. Hepatology 2016;64:73-84.
66. Jinjuvadia R, Antaki F, Lohia P, Liangpunsakul S. The association between nonalcoholic fatty liver disease and metabolic abnormalities in the United States population. J Clin Gastroenterol 2017;51:160-166.
67. Elsaid MI, Bridges JFP, Li N, Rustgi VK. Metabolic syndrome severity predicts mortality in nonalcoholic fatty liver disease. Gastro Hep Adv 2022;1:445-456.
68. Cuthbertson DJ, Koskinen J, Brown E, Magnussen CG, Hutri-Kähönen N, Sabin M, et al. Fatty liver index predicts incident risk of prediabetes, type 2 diabetes and non-alcoholic fatty liver disease (NAFLD). Ann Med 2021;53:1256-1264.
69. Golabi P, Paik JM, Arshad T, Younossi Y, Mishra A, Younossi ZM. Mortality of NAFLD according to the body composition and presence of metabolic abnormalities. Hepatol Commun 2020;4:1136-1148.
70. Hua S, Qi Q, Kizer JR, Williams-Nguyen J, Strickler HD, Thyagarajan B, et al. Association of liver enzymes with incident diabetes in US Hispanic/Latino adults. Diabet Med 2021;38:e14522.
71. Sanyal AJ, Van Natta ML, Clark J, Neuschwander-Tetri BA, Diehl A, Dasarathy S, et al; NASH Clinical Research Network (CRN). Prospective study of outcomes in adults with nonalcoholic fatty liver disease. N Engl J Med 2021;385:1559-1569.
72. Adams LA, Anstee QM, Tilg H, Targher G. Non-alcoholic fatty liver disease and its relationship with cardiovascular disease and other extrahepatic diseases. Gut 2017;66:1138-1153.
73. Labenz C, Huber Y, Michel M, Nagel M, Galle PR, Kostev K, et al. Impact of NAFLD on the incidence of cardiovascular diseases in a primary care population in Germany. Dig Dis Sci 2020;65:2112-2119.
74. Wong VW, Ekstedt M, Wong GL, Hagström H. Changing epidemiology, global trends and implications for outcomes of NAFLD. J Hepatol 2023;79:842-852.
75. Targher G, Byrne CD, Tilg H. MASLD: a systemic metabolic disorder with cardiovascular and malignant complications. Gut 2024;73:691-702.
76. Roderburg C, Krieg S, Krieg A, Vaghiri S, Mohr R, Konrad M, et al. Non-alcoholic fatty liver disease (NAFLD) and risk of new-onset heart failure: a retrospective analysis of 173,966 patients. Clin Res Cardiol 2023;112:1446-1453.
77. Stefan N, Häring HU, Cusi K. Non-alcoholic fatty liver disease: causes, diagnosis, cardiometabolic consequences, and treatment strategies. Lancet Diabetes Endocrinol 2019;7:313-324.
78. Sao R, Aronow WS. Association of non-alcoholic fatty liver disease with cardiovascular disease and subclinical atherosclerosis. Arch Med Sci 2018;14:1233-1244.
79. Al Rifai M, Silverman MG, Nasir K, Budoff MJ, Blankstein R, Szklo M, et al. The association of nonalcoholic fatty liver disease, obesity, and metabolic syndrome, with systemic inflammation and subclinical atherosclerosis: the Multi-Ethnic Study of Atherosclerosis (MESA). Atherosclerosis 2015;239:629-633.
80. Lonardo A, Nascimbeni F, Mantovani A, Targher G. Hypertension, diabetes, atherosclerosis and NASH: cause or consequence? J Hepatol.2018;68:335-352.
81. Byrne CD, Targher G. Ectopic fat, insulin resistance, and nonalcoholic fatty liver disease: implications for cardiovascular disease. Arterioscler Thromb Vasc Biol 2014;34:1155-1161.
82. Bugianesi E, Moscatiello S, Ciaravella MF, Marchesini G. Insulin resistance in nonalcoholic fatty liver disease. Curr Pharm Des 2010;16:1941-1951.
83. Toth PP. Epicardial steatosis, insulin resistance, and coronary artery disease. Heart Fail Clin 2012;8:671-678.
84. Semmler G, Wernly S, Bachmayer S, Leitner I, Wernly B, Egger M, et al. Metabolic dysfunction-associated fatty liver disease (MAFLD)-rather a bystander than a driver of mortality. J Clin Endocrinol Metab 2021;106:2670-2677.
85. Semmler G, Balcar L, Wernly S, Völkerer A, Semmler L, Hauptmann L, et al. Insulin resistance and central obesity determine hepatic steatosis and explain cardiovascular risk in steatotic liver disease. Front Endocrinol (Lausanne) 2023;14:1244405.
86. Ciardullo S, Cannistraci R, Mazzetti S, Mortara A, Perseghin G. Nonalcoholic fatty liver disease, liver fibrosis and cardiovascular disease in the adult US population. Front Endocrinol (Lausanne) 2021;12:711484.
87. Mellemkjær A, Kjær MB, Haldrup D, Grønbæk H, Thomsen KL. Management of cardiovascular risk in patients with metabolic dysfunction-associated steatotic liver disease. Eur J Intern Med 2024;122:28-34.
88. Lee H, Lee YH, Kim SU, Kim HC. Metabolic dysfunction-

associated fatty liver disease and incident cardiovascular disease risk: a nationwide cohort study. Clin Gastroenterol Hepatol 2021;19:2138-2147.e10.
89. Chen YT, Chen TI, Yin SC, Huang CW, Huang JF, Lu SN, et al. Prevalence, proportions of elevated liver enzyme levels, and long-term cardiometabolic mortality of patients with metabolic dysfunction-associated steatotic liver disease. J Gastroenterol Hepatol 2024;39:1939-1949.
90. Mantovani A, Petracca G, Beatrice G, Csermely A, Lonardo A, Schattenberg JM, et al. Non-alcoholic fatty liver disease and risk of incident chronic kidney disease: an updated meta-analysis. Gut 2022;71:156-162.
91. Roderburg C, Krieg S, Krieg A, Demir M, Luedde T, Kostev K, et al. Non-alcoholic fatty liver disease (NAFLD) is associated with an increased incidence of chronic kidney disease (CKD). Eur J Med Res 2023;28:153.
92. Gurun M, Brennan P, Handjiev S, Khatib A, Leith D, Dillon JF, et al. Increased risk of chronic kidney disease and mortality in a cohort of people diagnosed with metabolic dysfunction associated steatotic liver disease with hepatic fibrosis. PLoS One 2024;19:e0299507.
93. Bilson J, Mantovani A, Byrne CD, Targher G. Steatotic liver disease, MASLD and risk of chronic kidney disease. Diabetes Metab 2024;50:101506.
94. Kalligeros M, Henry L, Younossi ZM. Metabolic dysfunction-associated steatotic liver disease and its link to cancer. Metabolism 2024;160:156004.
95. Björkström K, Widman L, Hagström H. Risk of hepatic and extrahepatic cancer in NAFLD: a population-based cohort study. Liver Int 2022;42:820-828.
96. Allen AM, Hicks SB, Mara KC, Larson JJ, Therneau TM. The risk of incident extrahepatic cancers is higher in non-alcoholic fatty liver disease than obesity - A longitudinal cohort study. J Hepatol 2019;71:1229-1236.
97. Kim GA, Lee HC, Choe J, Kim MJ, Lee MJ, Chang HS, et al. Association between non-alcoholic fatty liver disease and cancer incidence rate. J Hepatol 2017:S0168-8278(17)32294-8.
98. Mantovani A, Petracca G, Beatrice G, Csermely A, Tilg H, Byrne CD, et al. Non-alcoholic fatty liver disease and increased risk of incident extrahepatic cancers: a meta-analysis of observational cohort studies. Gut 2022;71:778-788.
99. Thomas JA, Kendall BJ, Dalais C, Macdonald GA, Thrift AP. Hepatocellular and extrahepatic cancers in non-alcoholic fatty liver disease: a systematic review and meta-analysis. Eur J Cancer 2022;173:250-262.
100. Vitale A, Svegliati-Baroni G, Ortolani A, Cucco M, Dalla Riva GV, Giannini EG, et al; Italian Liver Cancer (ITA.LI.CA) group. Epidemiological trends and trajectories of MAFLD-associated hepatocellular carcinoma 2002-2033: the ITA.LI.CA database. Gut 2023;72:141-152.
101. Behari J, Gougol A, Wang R, Luu HN, Paragomi P, Yu YC, et al. Incidence of hepatocellular carcinoma in nonalcoholic fatty liver disease without cirrhosis or advanced liver fibrosis. Hepatol Commun 2023;7:e00183.
102. Chu J, Cholankeril G, Yu X, Rana A, Natarajan Y, El-Serag HB, et al. Clinical course and outcomes of patients with non-alcoholic fatty liver disease-related hepatocellular cancer (NAFLD-HCC). Dig Dis Sci 2023;68:1060-1070.
103. Chen YT, Chen TI, Yang TH, Yin SC, Lu SN, Liu XR, et al. Long-term risks of cirrhosis and hepatocellular carcinoma across steatotic liver disease subtypes. Am J Gastroenterol 2024;119:2241-2250.
104. Stepanova M, Kabbara K, Mohess D, Verma M, Roche-Green A, AlQahtani S, et al. Nonalcoholic steatohepatitis is the most common indication for liver transplantation among the elderly: data from the United States Scientific Registry of Transplant Recipients. Hepatol Commun 2022;6:1506-1515.
105. Younossi ZM, Stepanova M, Ong J, Trimble G, AlQahtani S, Younossi I, et al. Nonalcoholic steatohepatitis is the most rapidly increasing indication for liver transplantation in the United States. Clin Gastroenterol Hepatol 2021;19:580-589.e5.
106. Younossi ZM, Stepanova M, Al Shabeeb R, Eberly KE, Shah D, Nguyen V, et al. The changing epidemiology of adult liver transplantation in the United States in 2013-2022: the dominance of metabolic dysfunction-associated steatotic liver disease and alcohol-associated liver disease. Hepatol Commun 2023;8:e0352.
107. Koh JH, Ng CH, Nah B, Tan DJH, Loomba R, Huang DQ; Nash HCC Transplant Collaborative. NASH is the leading cause of hepatocellular carcinoma in liver transplant candidates. Clin Gastroenterol Hepatol 2024;22:197-199.e3.
108. Noureddin M, Vipani A, Bresee C, Todo T, Kim IK, Alkhouri N, et al. NASH leading cause of liver transplant in women: updated analysis of indications for liver transplant and ethnic and gender variances. Am J Gastroenterol 2018;113:1649-1659.
109. Van Dongen C, Paik JM, Harring M, Younossi Y, Price JK, Kabbara K, et al. Sarcopenia, healthy living, and mortality in patients with chronic liver diseases. Hepatol Commun 2022;6:3140-3153.

https://doi.org/10.3350/cmh.2024.0431

110. Harring M, Golabi P, Paik JM, Shah D, Racila A, Cable R, et al. Sarcopenia among patients with nonalcoholic fatty liver disease (NAFLD) is associated with advanced fibrosis. Clin Gastroenterol Hepatol 2023;21:2876-2888.e5.
111. Younossi ZM, Yilmaz Y, Yu ML, Wai-Sun Wong V, Fernandez MC, Isakov VA, et al; Global NASH Council. Clinical and patient-reported outcomes from patients with nonalcoholic fatty liver disease across the world: data from the global non-alcoholic steatohepatitis (NASH)/non-alcoholic fatty liver disease (NAFLD) registry. Clin Gastroenterol Hepatol 2022;20:2296-2306.e6.
112. Stepanova M, Henry L, Younossi ZM. Economic burden and patient-reported outcomes of nonalcoholic fatty liver disease. Clin Liver Dis 2023;27:483-513.
113. Younossi ZM, Stepanova M, Myers RP, Younossi I, Henry L. The potential role of fatigue in identifying patients with NASH and advanced fibrosis who experience disease progression. Clin Gastroenterol Hepatol 2023;21:970-977.e1.
114. Younossi ZM, Paik JM, Golabi P, Younossi Y, Henry L, Nader F. The impact of fatigue on mortality of patients with nonalcoholic fatty liver disease: data from National Health and nutrition examination survey 2005-2010 and 2017-2018. Liver Int 2022;42:2646-2661.
115. Weinstein AA, De Avila L, Kannan S, Paik JM, Golabi P, Gerber LH, et al. Interrelationship between physical activity and depression in nonalcoholic fatty liver disease. World J Hepatol 2022;14:612-622.
116. Younossi ZM, Paik JM, Henry L, Yang J, Fernandes G, Stepanova M, et al. The growing economic and clinical burden of nonalcoholic steatohepatitis (NASH) in the United States. J Clin Exp Hepatol 2023;13:454-467.
117. Paik JM, Eberly KE, Kabbara K, Harring M, Younossi Y, Henry L, et al. Non-alcoholic fatty liver disease is associated with greater risk of 30-day hospital readmission in the United States (U.S.). Ann Hepatol 2023;28:101108.
118. Golabi P, Owrangi S, Younossi ZM. Global perspective on nonalcoholic fatty liver disease and nonalcoholic steatohepatitis - prevalence, clinical impact, economic implications and management strategies. Aliment Pharmacol Ther 2024;59 Suppl 1:S1-S9.
119. Younossi ZM, Tampi RP, Racila A, Qiu Y, Burns L, Younossi I, et al. Economic and clinical burden of nonalcoholic steatohepatitis in patients with type 2 diabetes in the U.S. Diabetes Care 2020;43:283-289.
120. Younossi ZM, Ong JP, Takahashi H, Yilmaz Y, Eguc Hi Y, El Kassas M, et al; Global Nonalcoholic Steatohepatitis Council. A global survey of physicians knowledge about nonalcoholic fatty liver disease. Clin Gastroenterol Hepatol 2022;20:e1456-e1468.
121. Alqahtani SA, Paik JM, Biswas R, Arshad T, Henry L, Younossi ZM. Poor awareness of liver disease among adults with NAFLD in the United States. Hepatol Commun 2021;5:1833-1847.
122. Younossi ZM, Alqahtani SA, Alswat K, Yilmaz Y, Keklikkiran C, Funuyet-Salas J, et al; Global NASH Council. Global survey of stigma among physicians and patients with nonalcoholic fatty liver disease. J Hepatol 2024;80:419-430.
123. Eguchi Y, Eguchi T, Mizuta T, Ide Y, Yasutake T, Iwakiri R, et al. Visceral fat accumulation and insulin resistance are important factors in nonalcoholic fatty liver disease. J Gastroenterol 2006;41:462-469.
124. Nabi O, Lapidus N, Boursier J, de Ledinghen V, Petit JM, Kab S, et al. Lean individuals with NAFLD have more severe liver disease and poorer clinical outcomes (NASH-CO Study). Hepatology 2023;78:272-283.
125. Shao C, Ye J, Li F, Feng S, Wang W, Zhong B. Different predictors of steatosis and fibrosis severity among lean, overweight and obese patients with nonalcoholic fatty liver disease. Dig Liver Dis 2019;51:1392-1399.
126. Tang A, Ng CH, Phang PH, Chan KE, Chin YH, Fu CE, et al. Comparative burden of metabolic dysfunction in lean NAFLD vs non-lean NAFLD - A systematic review and meta-analysis. Clin Gastroenterol Hepatol 2023;21:1750-1760.e12.
127. Younes R, Govaere O, Petta S, Miele L, Tiniakos D, Burt A, et al. Caucasian lean subjects with non-alcoholic fatty liver disease share long-term prognosis of non-lean: time for reappraisal of BMI-driven approach? Gut 2022;71:382-390.
128. Ye Q, Zou B, Yeo YH, Li J, Huang DQ, Wu Y, et al. Global prevalence, incidence, and outcomes of non-obese or lean non-alcoholic fatty liver disease: a systematic review and meta-analysis. Lancet Gastroenterol Hepatol 2020;5:739-752.
129. Lu FB, Zheng KI, Rios RS, Targher G, Byrne CD, Zheng MH. Global epidemiology of lean non-alcoholic fatty liver disease: a systematic review and meta-analysis. J Gastroenterol Hepatol 2020;35:2041-2050.
130. Wong MCS, Huang JLW, George J, Huang J, Leung C, Eslam M, et al. The changing epidemiology of liver diseases in the Asia-Pacific region. Nat Rev Gastroenterol Hepatol 2019;16:57-73.
131. Makuza JD, Jeong D, Binka M, Adu PA, Cua G, Yu A, et al.

Impact of hepatitis B virus infection, non-alcoholic fatty liver disease, and hepatitis C virus co-infection on liver-related death among people tested for hepatitis B virus in British Columbia: results from a large longitudinal population-based cohort study. Viruses 2022;14:2579.
132. Sarin SK, Kumar M, Eslam M, George J, Al Mahtab M, Akbar SMF, et al. Liver diseases in the Asia-Pacific region: a Lancet Gastroenterology & Hepatology Commission. Lancet Gastroenterol Hepatol 2020;5:167-228. Erratum in: Lancet Gastroenterol Hepatol 2020;5:e2.
133. Yang M, Wei L. Impact of NAFLD on the outcome of patients with chronic hepatitis B in Asia. Liver Int 2022;42:1981-1990.
134. Le MH, Yeo YH, Cheung R, Wong VW, Nguyen MH. Ethnic influence on nonalcoholic fatty liver disease prevalence and lack of disease awareness in the United States, 2011-2016. J Intern Med 2020;287:711-722.
135. European Association for the Study of the Liver (EASL); European Association for the Study of Diabetes (EASD); European Association for the Study of Obesity (EASO); European Association for the Study of the Liver (EASL). EASL-EASD-EASO Clinical Practice Guidelines on the management of metabolic dysfunction-associated steatotic liver disease (MASLD). J Hepatol 2024;81:492-542.
136. Kanwal F, Neuschwander-Tetri BA, Loomba R, Rinella ME. Metabolic dysfunction-associated steatotic liver disease: update and impact of new nomenclature on the American Association for the Study of Liver Diseases practice guidance on nonalcoholic fatty liver disease. Hepatology 2024;79:1212-1219.
137. Wattacheril JJ, Abdelmalek MF, Lim JK, Sanyal AJ. AGA clinical practice update on the role of noninvasive biomarkers in the evaluation and management of nonalcoholic fatty liver disease: expert review. Gastroenterology 2023;165:1080-1088.
138. Sanyal AJ, Castera L, Wong VW. Noninvasive assessment of liver fibrosis in NAFLD. Clin Gastroenterol Hepatol 2023;21:2026-2039. Erratum in: Clin Gastroenterol Hepatol 2024;22:676.
139. Abdelhameed F, Kite C, Lagojda L, Dallaway A, Chatha KK, Chaggar SS, et al. Non-invasive scores and serum biomarkers for fatty liver in the era of metabolic dysfunction-associated steatotic liver disease (MASLD): a comprehensive review from NAFLD to MAFLD and MASLD. Curr Obes Rep 2024;13:510-531.
140. Hsu CL, Loomba R. From NAFLD to MASLD: implications of the new nomenclature for preclinical and clinical research. Nat Metab 2024;6:600-602.
141. Newsome PN, Ambery P. Incretins (GLP-1 receptor agonists and dual/triple agonists) and the liver. J Hepatol 2023;79:1557-1565.
142. Gao Y, Zhao T, Song S, Duo Y, Gao J, Yuan T, et al. Lean nonalcoholic fatty liver disease and risk of incident type 2 diabetes mellitus: A literature review and meta-analysis. Diabetes Res Clin Pract 2023;200:110699.

https://doi.org/10.3350/cmh.2024.0431