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The role of dietary modification in the prevention and management of metabolic dysfunction-associated fatty liver disease: An international multidisciplinary expert consensus

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Abbreviations: AHEI, Alternate Healthy Eating Index diet; BMI, body mass index; CAP, controlled attenuation parameter; CVD, cardiovascular disease; DASH, Dietary Approaches to Stop Hypertension; DII, Dietary Inflammatory Index; DNL, de novo lipogenesis; GLP-1, glucagon-like peptide-1; HCC, hepatocellular carcinoma; HEI, Healthy Eating Indices; LoE, levels of evidence; MAFLD, metabolic dysfunction-associated fatty liver disease; MASH, metabolic dysfunction-associated steatohepatitis; MASLD, metabolic dysfunction-associated steatotic liver disease; MED, Mediterranean diet; *PNPLA3*, patatin-like phospholipase domain-containing protein 3; PUFAs, polyunsaturated fatty acids; RCT, randomized clinical trial; SFAs, saturated fatty acids; TE, transient elastography; TFA, trans fatty acids; TLR9, toll-like receptor-9.

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ABSTRACT

Metabolic dysfunction-associated fatty liver disease (MAFLD) or metabolic dysfunction-associated steatotic liver disease (MASLD), has become the leading cause of chronic liver disease worldwide. Optimal dietary intervention strategies for MAFLD are not standardized. This study aimed to achieve consensus on prevention of MAFLD through dietary modification. A multidisciplinary panel of 55 international experts, including specialists in hepatology, gastroenterology, dietetics, endocrinology and other medical specialties from six continents collaborated in a Delphi-based consensus development process. The consensus statements covered aspects ranging from epidemiology to mechanisms, management, and dietary recommendations for MAFLD. The recommended dietary strategies emphasize adherence to a balanced diet with controlled energy intake and personalized nutritional interventions, such as calorie restriction, high-protein, or low-carbohydrate diets. Specific dietary advice encouraged increasing the consumption of whole grains, plant-based proteins, fish, seafood, low-fat or fat-free dairy products, liquid plant oils, and deeply colored fruits and vegetables. Concurrently, it advised reducing the intake of red and processed meats, saturated and trans fats, ultra-processed foods, added sugars, and alcohol. Additionally, maintaining the Mediterranean or DASH diet, minimizing sedentary

behavior, and engaging in regular physical activity are recommended. These consensus statements lay the foundation for customized dietary guidelines and proposing avenues for further research on nutrition and MAFLD.

1. Introduction

Metabolic dysfunction-associated fatty liver disease (MAFLD) or metabolic dysfunction-associated steatotic liver disease (MASLD), has become the most common cause of chronic liver disease worldwide, affecting over 30 % of the global adult population [1,2]. MAFLD encompasses a histological spectrum of liver conditions ranging from isolated steatosis to metabolic dysfunction-associated steatohepatitis (MASH), cirrhosis, and hepatocellular carcinoma (HCC) [3]. The increasing global prevalence of MAFLD parallels the rise in the prevalence of obesity and metabolic dysfunction, with conditions such as type 2 diabetes mellitus and cardiovascular disease frequently coexisting [4,5]. The development of MAFLD is strongly influenced by the combined effects of low physical activity levels and net positive energy balance. This imbalance, along with nutritional deficiencies and unhealthy diets, plays a key role in disease progression [6]. Moreover, strong interactions between genetic factors, obesity, environment and acquired lifestyle factors induce a faster progression of MAFLD from isolated steatosis to MASH, cirrhosis, and HCC [7].

Pharmaceutical agents, such as resmetirom, which target diverse molecular pathways, are currently in development or undergoing testing for the treatment of MAFLD [8,9]. Resmetirom is the only MASH-targeting drug that has shown positive results in a registration phase III clinical trial [10]. Given the anticipated evolution of MASH-targeted treatment options in coming years, the EASL-EASD-EASO Clinical Practice Guidelines recommended lifestyle modification and optimal management of comorbidities for patients with type 2 diabetes or obesity in MAFLD [11]. Comprehensive lifestyle interventions, including hypocaloric diets and increased physical activity remain the cornerstone of MAFLD/MASH treatment [12,13]. While the reduction of liver fat content is the primary objective in the treatment of MAFLD, gradual weight loss is often employed as a strategic pathway to achieve this goal. The optimal nutritional management plan remains limited [14,15]. Dietary energy restriction is a crucial strategy for weight loss. However, patient adherence to lifestyle interventions for weight loss is influenced by a complex interplay of factors, including self-management, neurobiological, environmental, and physiological factors. The interplay of these factors often poses challenges for the success of dietary interventions [16]. Limited evidence has led to differences in global practices, with variations among individual clinicians, primary healthcare, and countries [17]. Therefore, in the context of MAFLD, different nutritional intervention options have been explored.

To guide the development of standardized dietary management methods, a multidisciplinary expert panel used a two-round Delphi survey to provide quality standard recommendations for managing individuals with MAFLD. The consensus statements aim to elucidate current perspectives on nutrition and MAFLD, covering aspects ranging from epidemiology to pathogenesis, management, and treatment.

2. Methods

2.1. Study design

The Delphi method is a scientific approach to achieve expert consensus through a structured process (Fig. 1). Through two rounds of online surveys, this study utilized an improved Delphi process to reach expert consensus on the association between MAFLD and dietary patterns. To ensure professionalism and regional representation of the expert panel, we selected active researchers with knowledge in the field of nutrition and MAFLD or who published articles on fatty liver and nutrition from each of the six continents, namely Asia, Europe, North America, South America, Africa, and Oceania. Experts were included if they replied, citing interest in involvement. We informed the experts of our purpose through emails and provided a secure link using Google Forms. The study included two rounds, the link for the Round 1 survey was: https://forms.gle/8x313TVAJBvUWhJQ7, and the link for the Round 2 was: https://forms.gle/rh7dw1gZ6w7fnAjM8.

In the first phase, by systematically reviewing the relevant literature on nutrition in MAFLD published until 31 August 2023, we developed a structured questionnaire covering five domains and 32 draft statements in the Round 1 survey. Participants rated each statement on a four-point scale (“agree”/”somewhat agree”/”somewhat disagree”/”disagree”), and each domain of questions ended with a free-text comment section. Disagree or somewhat disagree domains required an explanation. The

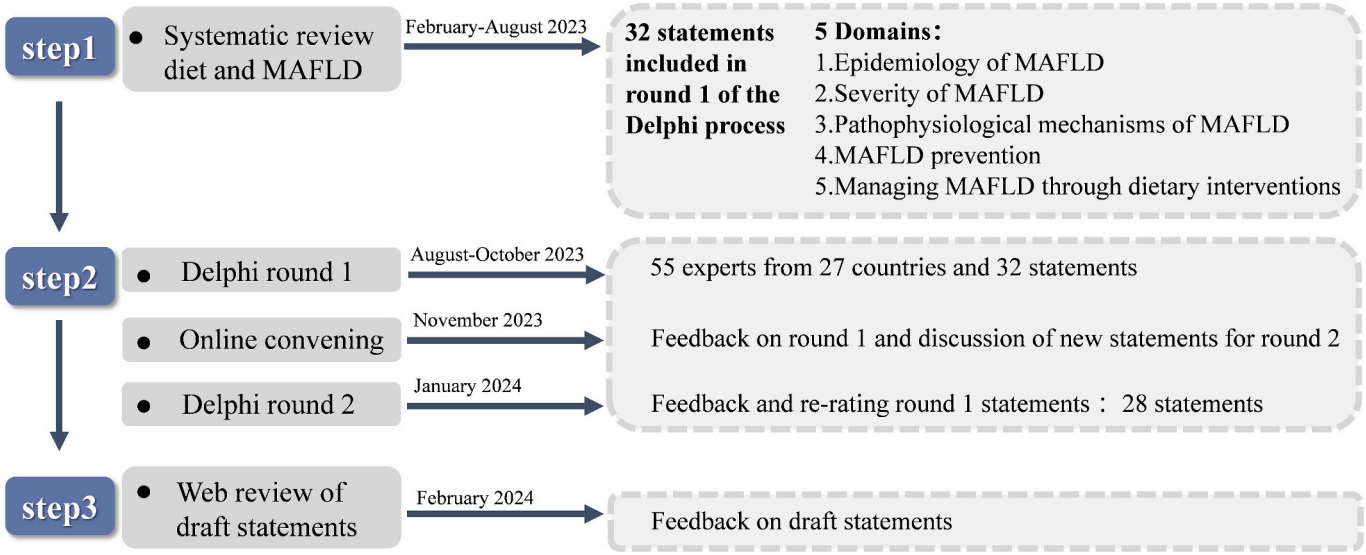

Fig. 1. Flowchart of the Delphi procedure adopted for developing consensus statements of dietary modification in the prevention and management of MAFLD.

data collection period for the Round 1 survey lasted 8 weeks, concluding in October 2023. The second phase, completed by 30th January 2024, included the Round 2 survey, which contained a structured questionnaire in which the experts evaluated and re-evaluated statements until consensus was achieved. The Round 2 survey focused on controversial items identified by analyzing the Round 1 survey results and opinions. Statements with agreement of ≥80 % were accepted. When consensus was not achieved in the Round 1 survey (<80 %), re-voting was carried out in the Round 2 survey after presenting the available evidence. The levels of evidence (LoE) were established using the system developed by the Oxford Centre for Evidence-based Medicine [18] (Table 1). Expert consensus statements were created and graded to reflect the level of agreement. The degree of consensus for each statement was grading scale: 'U' for unanimous (100 %) agreement, 'A' for 90–99 % agreement, 'B' for 78–89 % agreement, and 'C' for 67–77 % agreement. The grading scale is designed to represent statements that show unanimous or nearly unanimous agreement (grades U and A), strong agreement with minimal variance (grade B), or a consensus statement that reflects a balance of diverse opinions (grade C). Based on the comments and suggestions, the consensus steering committee decided on the final statements and composed the first draft manuscript. Some experts changed their responses as they deemed appropriate (Table 2).

2.2. Findings

For this consensus statement, we received responses from 55 healthcare providers from 27 countries and report the final consensus statements, as well as a summary of the broader relevant literature. Across the two rounds of Delphi surveys, there was an increase in consensus for all proposed statements. The mean percentage of "agree" responses increased from 63.49 % to 83.25 %, and "agree" or "somewhat agree" responses rose from 91.53 % in the Round 1-survey to 98.12 % in the Round 2-survey (Fig. 2). The exact percentages of consensus are detailed in the Supplementary Tables. Overall, a grade of 'U' (unanimous, 100 %) was given for 11/28 statements and a grade of 'A' (90–99 % agreement) for 17/28 statements (Table 3). There were 5 domains composing 28 total statements related to nutrition and MAFLD (Fig. 3).

2.3. Consensus statements and recommendations

2.3.1. Domain and statements

1. Epidemiology of MAFLD

1.1 Compared to the non-MAFLD population, MAFLD is associated with an increased prevalence of overweight/obesity. (LoE 2, grade A)

1.2 Compared to the non-MAFLD population, MAFLD is associated with an increased incidence of overweight/obesity. (LoE 2, grade A)

Chronic overnutrition leads to overweight/obesity, which is a well-established risk factor for MAFLD and other metabolic diseases. Overweight/obesity is associated with increased visceral adiposity, adipose tissue dysfunction, insulin resistance, and systemic low-grade inflammation, further aggravating liver inflammation and fibrosis [19]. A meta-analysis of 116 observational studies (2,667,052 participants) reported that the global prevalence of MAFLD was 50.7 % (95 % CI, 46.9–54.4 %) among adults with overweight/obesity [20]. An observational study involving 2,083,984 Chinese adult participants from 2009 to 2017 showed that patients with MAFLD had a high prevalence of overweight/obesity and type 2 diabetes [21]. From the Shanghai Birth Cohort Study databases, children with MAFLD had significantly higher body mass index (BMI) and indices of body fat distribution (waist circumference, hip circumference, waist-to-height ratio, and waist-to-hip ratio) than non-MAFLD children [22]. Given limited evidence on the incidence of MAFLD, particularly in adults, MAFLD might be associated with an increased prevalence of overweight/obesity.

1.3 Compared to the non-MAFLD population, MAFLD is associated with an increase in all-cause mortality. (LoE 2, grade A)

Substantial evidence links MAFLD with an increased risk of all-cause mortality. For example, a longitudinal cohort study involving 32,683 individuals with overweight or obesity found an increased risk of various adverse clinical outcomes, including all-cause mortality and cardiovascular disease (CVD) in individuals with MAFLD compared to non-MAFLD individuals [23]. Kim et al. analyzing data from 7761 participants from the NHANES-III database showed that MAFLD was associated with a higher risk of all-cause mortality than in those without MAFLD or NAFLD (HR 1.66, 95 % CI 1.19–2.32) [24]. Similarly, Nguyen et al. reported that the MAFLD-only status identified a group of individuals with higher all-cause mortality than those without MAFLD or NAFLD (HR 2.4, 95 % CI 1.2–4.6) [25]. A large meta-analysis of 17 observational studies also reported that MAFLD was associated with a higher risk of all-cause mortality (HR 1.24, 95 % CI 1.13–1.34), CVD-related mortality (HR 1.28, 95 % CI 1.03–1.53), nonfatal CVD events (HR 1.49, 95 % CI 1.34–1.64) and stroke (HR 1.55, 95 % CI 1.37–1.73) [26]. In a community-based cohort study of 8919 individuals, Moon et al. confirmed that MAFLD predicted the risk of all-cause mortality, even after adjustment for common cardiometabolic risk factors (HR 1.36, 95 % CI 1.08–1.73) [27].

1.4 Overnutrition (overweight and obesity) in early life stages (childhood and adolescence) is associated with an increased risk of MAFLD in adulthood. (LoE 3, grade U)

Early-life nutrition is a critical period for human development and has long-term effects on adult health [28]. Excessive caloric intake during development may alter the brain and stimulate binge eating in adults [29]. Calorie overconsumption leads to overweight/obesity and metabolic disorders, which are known risk factors for MAFLD [19]. Unsurprisingly, early-life chronic overnutrition is associated with an

Table 1
Level of Evidence based on the Oxford Centre for Evidence-based Medicine (adapted).

Level	Criteria
1	Randomized controlled trial (RCT) or meta-analysis of RCTs
2	Prospective (cohort or outcomes) study with an internal control group or meta-analysis or prospective, controlled studies
3	Retrospective (case-control) study with an internal control group or a meta-analysis of retrospective, controlled studies
4	Case series without an internal control group, retrospective reviews, uncontrolled cohort studies
5	Expert opinion (mechanism-based reasoning)

Table 2
Demographic composition of the expert panel.

Characteristics	Round 1	Round 2
Surveys sent, n	65	55
Total respondents, %	84.6 (55/65)	100 (55/55)
Participant type, %		
Dietician/Nutritional Scientist	23.6	
Hepatologist or Gastroenterologist	56.4	
Endocrinologist or Diabetologist	12.7	
Other	7.3	
Age group, %		
<40 years	23.6	
40-65 years	72.7	
>65 years	3.6	
Sex, %		
Female	65.5	
Male	34.5	
Region of practice, %		
Asia	49.1	
North America	10.9	
South America	5.5	
Europe	27.3	
Africa	3.6	
Oceania	3.6	

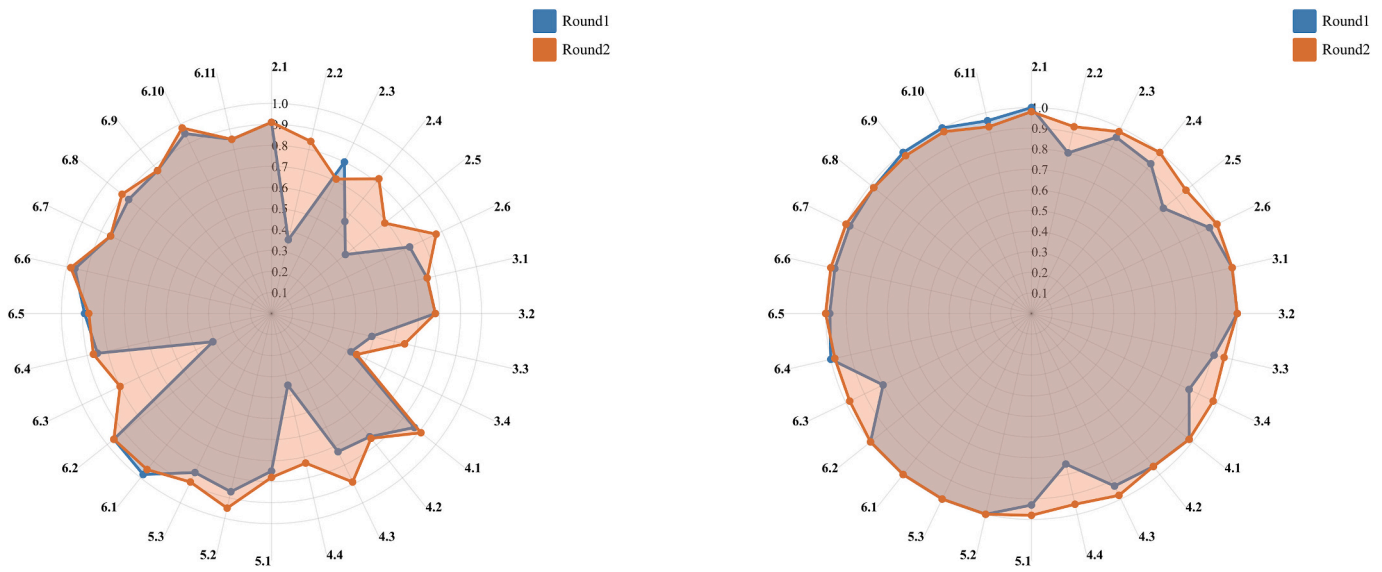

Fig. 2. Scores for agreement during the consensus development process. (A) Scores for agreement by experts in Round 1 and Round 2 surveys. (B) Total scores for "agree" and "somewhat agree" by experts in Round 1 and Round 2 surveys.

increased risk of MAFLD in adulthood [30]. For example, a prospective study reported that weight gain between ages 7 and 13 was related to the severity of MAFLD histological features in adulthood. For each unit increase in BMI z-score during childhood, the risk of adult cirrhosis increased by nearly 15 % [31]. Similarly, weight gain in late adolescence increased the risk of developing adult MAFLD [31]. A study of MAFLD participants from the ALSPAC database [where MAFLD was assessed by transient elastography (TE) and controlled attenuation parameter (CAP)] showed that abdominal obesity and BMI in adolescence were stronger predictors of MAFLD and MAFLD-related fibrosis in adulthood than standard clinical indicators [32]. In addition, review articles also supported the notion that obesity persistence from childhood to adulthood significantly affects the natural course of MAFLD [33,34]. Therefore, avoiding chronic overnutrition in early life is important for preventing MAFLD in adulthood [35].

1.5 Chronic overnutrition is associated with higher hepatic steatosis risk. (LoE 3, grade U)

1.6 Chronic overnutrition is associated with higher hepatic fibrosis risk. (LoE 3, grade U)

Chronic overnutrition can result in hepatic steatosis and fibrosis. Liver inflammation is a known player for liver steatosis/fibrosis, while diet and systemic inflammation are tightly linked [36]. A long-term high-calorie diet rich in saturated fatty acids (SFAs) significantly increased hepatic fat content by 50 %, whereas polyunsaturated fatty acids (PUFAs) reduced hepatic fat content in overweight individuals [37]. An experimental study by Charlton and colleagues reported that a "fast food diet" (i.e., a diet mainly based on high cholesterol, high saturated fat and high fructose) was able to replicate with high fidelity the human condition of fibrosing MASH in mice [38] and these results were supported by Yang and colleagues [39]. Consistently, in a 52-week prospective study conducted by Vilar-Gomez et al. in 293 adult patients with MASH, weight loss following a hypocaloric diet strongly correlated with improvement in all MASH-related histological features. In particular, among MASH patients with weight loss ≥10 %, 90 % of them achieved resolution of MASH, and 45 % experienced fibrosis regression [40]. Another study, utilizing proton magnetic resonance spectroscopy (1H-MRS) to define liver fat content, reported similar results. It demonstrated that a 12-month intensive lifestyle intervention, involving a diet of 1200–1500 kcal/day for individuals weighing <114 kg and 1500–1800 kcal/day for those over 114 kg, significantly improved hepatic steatosis by 50.8 % and reduced glycated hemoglobin by 0.7 % compared to the diabetes support and education group [41]. In another dietary intervention study (1000–1200 kcal/day if baseline weight < 200 lb. or 1200–1500/day if baseline weight > 200 lb), participants who achieved the weight loss goal (≥7 %) as compared to those with weight loss <7 %, exhibited improvements in hepatic steatosis, lobular inflammation, ballooning, and histologic NAFLD activity score [42]. Weight loss induced by lifestyle changes was also associated with the level of improvement in MASH, with fibrosis regression [40]. Overall, these intervention studies demonstrate the adverse effect of calorie overconsumption on liver lipid metabolism, highlighting the clinical importance of reducing calorie intake and incorporating healthier fats in the prevention and treatment of MAFLD/MASH.

2. Severity of MAFLD

*2.1 Diet quality is associated with severity and progression of MA*FLD. (LoE 2, grade U)

Diet quality is evaluated through indices reflecting adherence to food patterns in terms of how closely they align with national dietary guidelines and how diverse the variety of healthy choices is within core food groups or equivalent international groupings [43]. Diet quality also includes healthy eating patterns, with the aim of bringing about lasting improvements in individual and population health. Studies have shown that adherence to high-quality dietary pattern scores, such as the Healthy Eating Indices (HEI), Alternate Healthy Eating Index diet (AHEI), Mediterranean diet (MED), Dietary Approaches to Stop Hypertension (DASH) and Dietary Inflammatory Index (DII), is significantly associated with a reduced risk of MAFLD [44,45]. For example, in the NHANES 2017–2018 database, maintaining a high-quality diet was significantly associated with a lower risk of MAFLD phenotypes [44]. A multiethnic cohort study with diet quality assessed by established indices (HEI-2010, AHEI-2010, aMED, DASH) reported that maintaining a high-quality diet during mid-to-late adulthood reduced liver fat, visceral adipose tissue, and total body fat [46]. Other studies support the notion that adherence to a healthy dietary pattern may also decrease the risk of HCC [47,48]. Similar results were reported in other cohort studies [49]. Collectively, the epidemiological evidence underscores the important role of diet quality in influencing the severity and progression of MAFLD. By periodically assessing dietary quality indices, researchers and policymakers can identify trends, evaluate the effectiveness of interventions, and inform the development of targeted nutritional policies

Table 3
Consensus statements of dietary modification in the prevention and management of MAFLD (using a Delphi method).

Domain and statements	Grade[a]
1. Epidemiology of MAFLD	
1.1 Compared to the non-MAFLD population, MAFLD is associated with an increased prevalence of overweight/obesity.	A
1.2 Compared to the non-MAFLD population, MAFLD is associated with an increased incidence of overweight/obesity.	A
1.3 Compared to the non-MAFLD population, MAFLD is associated with an increased all-cause mortality.	A
1.4 Overnutrition (overweight and obesity) in early life stages (childhood and adolescence) is associated with an increased risk of MAFLD in adulthood.	U
1.5 Chronic overnutrition is associated with higher hepatic steatosis risk.	U
1.6 Chronic overnutrition is associated with higher hepatic fibrosis risk.	U
2. Severity of MAFLD	
2.1 Diet quality is associated with severity and progression of MAFLD.	U
2.2 Excess caloric intake is associated with severity and progression of MAFLD.	U
2.3 Compared to simple steatosis, MASH is associated with a higher prevalence of overweight/obesity.	A
2.4 Compared to MAFLD without advanced fibrosis, MAFLD with advanced fibrosis (stage F3/4) is associated with a higher prevalence of overweight/obesity.	A
3. Pathophysiological mechanisms of MAFLD	
3.1 MAFLD and dietary patterns share multiple underlying risk factors such as chronic inflammation, metabolic dysregulation and insulin resistance.	A
3.2 The gut microbiota-liver axis is one of the potential mechanistic links between nutrition and MAFLD.	A
3.3 Energy/macronutrients imbalance and alterations in metabolic demands may contribute to MAFLD.	A
3.4 Interaction between the *PNPLA3* genetic variant and MAFLD.	A
4. MAFLD prevention	
4.1 Regular self-monitor of body weight is important for patients with MAFLD.	A
4.2 Providing education is essential to reinforce healthy lifestyles in patients with MAFLD.	U
4.3 In MAFLD risk assessment, chronic overnutrition should be considered an additional risk factor.	U
5. Managing MAFLD through dietary interventions	
5.1 Dietitian are integral team members for interventions targeting MAFLD.	U
5.2 Adherence to a balanced diet (including adjustment of energy intake and expenditure) should be considered for patients with MAFLD to achieve and maintain healthy body weight.	U
5.3 Use of personalized nutritional interventions (such as calorie restrict diet, high protein diet, low carbohydrate diets/very low carbohydrate diets, or intermittent energy restriction) under the guidance of a dietitian should be considered for patients with MAFLD.	A
5.4 Advice to eat foods made mostly from whole grains rather than refined grains.	A
5.5 Advice to eat healthy sources of protein (mostly plants); regular intake of fish and seafood; low-fat or fat-free dairy products; and if meat or poultry is desired, advice to choose lean cuts and unprocessed forms.	U
5.6 Advice to reduce red/processed meats, saturated fats, trans fatty acids, ultra-processed foods, and added sugar for patients with MAFLD.	U
5.7 Encouragement to eat deeply colored fruits and vegetables and choosing a variety of foods.	U
5.8 Advice to cook with liquid plant oils rather than saturated or hydrogenated oils/fats (coconut, palm, and palm kernel), animal fats (butter, ghee and lard), or hydrogenated fats.	A
5.9 Advice to greater adherence to the Mediterranean or DASH pattern diet to improve MAFLD and reduce risk.	A
5.10 Reduce sedentary lifestyles and maintain a moderate physical activity level (at least 150 min per week) to support maintenance of muscle mass, physical function and metabolic health.	A
5.11 Advice to alcohol avoidance (of any type or amount) should be encouraged in patients with MAFLD.	A

[a] Grade: U = unanimous (100 %) agreement; A = 90–99 % agreement; B = 78–89 % agreement, and C = 67–77 % agreement.

and programs for MAFLD.

2.2 Excess caloric intake is associated with severity and progression of MAFLD. (LoE 2, grade U)

Excessive caloric intake and dietary patterns rich in saturated fat, carbohydrates, and sugar-sweetened beverages have been implicated in the development and progression of MAFLD. Carbohydrates may lead to rapid hepatic depletion of ATP and accumulation of AMP, which is subsequently converted into uric acid. This process can increase oxidative stress and contribute to the subsequent development of metabolic disorders [50]. When the process of hepatic fatty acid disposal through beta-oxidation or the generation of fatty acids is high, lipotoxic substances originating from fatty acids can lead to endoplasmic reticulum stress, oxidative stress, and activation of inflammatory pathways [51]. Specifically, poor dietary compositions (e.g. SFAs and fructose) are closely related to the development and progression of MAFLD. The overconsumption of SFAs leads to increased hepatic gluconeogenesis, insulin resistance, and hepatic lipid accumulation [52]. This may trigger endoplasmic reticulum stress and alter the interaction between the endoplasmic reticulum and mitochondria in hepatocytes, contributing to hepatocellular damage, inflammation and the progression from steatosis to MASH [53]. Similarly, high fructose intake increases hepatic fat accumulation, as well as hepatic mRNA expression of fructokinase, and fatty acid synthase [54]. Additionally, fructose is involved in oxidative damage through increased production of uric acid, reduction in antioxidant defense, and increase in the production of reactive oxygen species, resulting in hepatic necroinflammation [55].

2.3 Compared to simple steatosis, MASH is associated with a higher prevalence of overweight/obesity. (LoE 3, grade A)

2.4 Compared to MAFLD without advanced fibrosis, MAFLD with advanced fibrosis (stage F3/4) is associated with a higher prevalence of overweight/obesity. (LoE 3, grade A)

MASH a more severe form of liver disease compared to simple steatosis, is often linked with a higher prevalence of overweight and obesity. High-calorie diets and sedentary lifestyles lead to obesity and can increase hepatic fat accumulation, thereby triggering MASH. A recent meta-analysis of 239 prospective studies showed that after adjusting for multiple confounding factors, individuals with overweight and obesity had a higher all-cause mortality rate than those of normal weight [56]. Studies have also shown that patients with MAFLD and metabolically healthy obesity who have one or more traditional risk factors for metabolic syndrome (such as insulin resistance, high blood pressure, and dyslipidemia) and a BMI > 30 kg/m^2, have a high risk of progressing to significant liver fibrosis [57]. Furthermore, being overweight/obese or having metabolic dysfunction are independent risk factors for MAFLD and adverse cardiovascular and metabolic outcomes [58].

In patients with MAFLD, the incidence of metabolic complications also increases in parallel with the severity of liver fibrosis. Specifically, compared to patients with MAFLD and mild liver fibrosis, those with severe fibrosis (F3/4 stage) often have a higher prevalence of overweight/obesity [59]. This observation is consistent with the multisystem nature of MAFLD, highlighting that MAFLD is not only caused by changes in the liver but is a disease affecting multiple organs and systems [60]. Moreover, it is well known that MAFLD is associated with an increased risk of adverse cardiovascular events, and obesity is a known risk factor for cardiovascular disease [61]. The interconnection between MASH/advanced fibrosis and overweight/obesity is further emphasized by the fact that treatment for MAFLD/MASH almost always involves weight management strategies, underscoring the clinical importance of addressing excess adiposity in managing this common and burdensome liver disease.

3. Pathophysiological mechanisms of MAFLD

3.1 MAFLD and dietary patterns share multiple underlying risk factors, such as chronic inflammation, metabolic dysregulation and insulin resistance. (LoE 2, grade A)

A diet rich in sugars and SFAs (from high fat dairy products, red and processed meats, and coconut/palm oils) leads to accumulation of fatty acids that contribute to the development of systemic low-grade

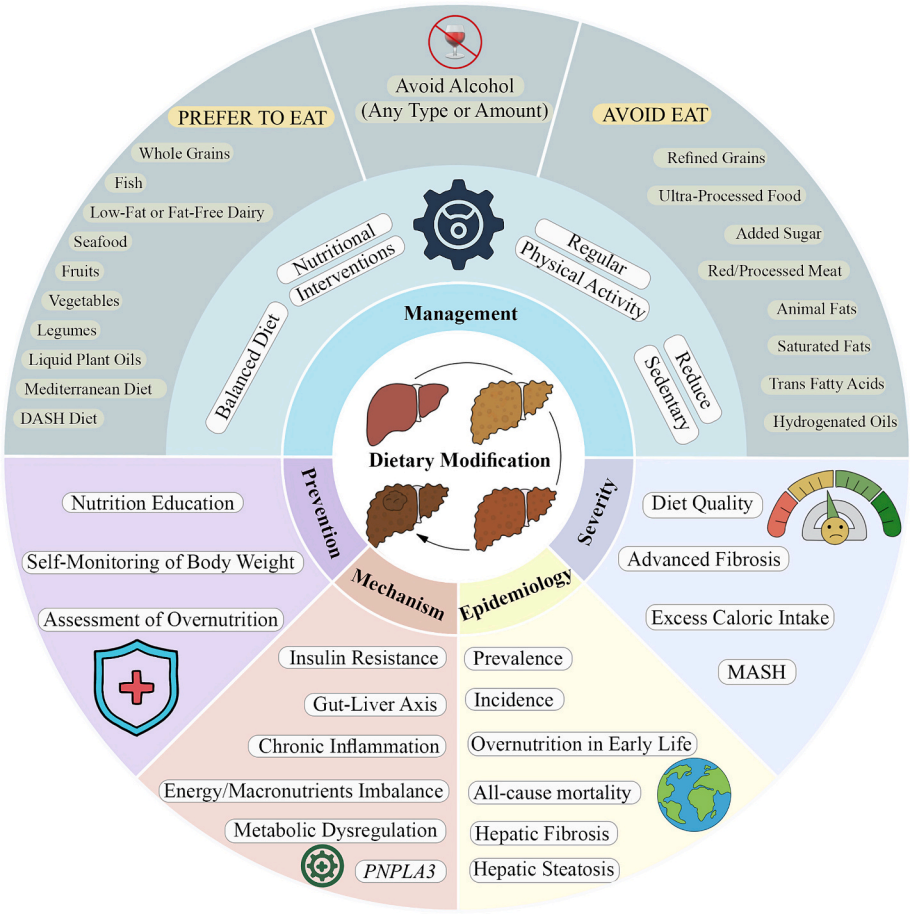

Fig. 3. 5 Domains of dietary modification in the prevention and management of MAFLD.

inflammation, insulin resistance and metabolic dysregulation. These are important risk factors for developing chronic diseases such as MAFLD and are crucial targets in dietary intervention strategies for disease prevention [62]. Toll-like receptor-9 (TLR9) regulates inflammatory responses by recognizing and responding to endogenous mitochondrial DNA. In conditions of obesity and chronic overnutrition, damaged liver cells release more mitochondrial DNA which activates TLR9, thus exacerbating the inflammatory response [63]. Prospective cohort studies report that the Mediterranean-style diet decreases BMI and improves hepatic fat content, liver damage biomarkers (serum liver enzymes, and cytokeratin-18), and proinflammatory status (decreasing the dietary inflammatory index, interleukin-1, and interleukin-6) [64,65]. Second, diets with high content of fructose or sucrose can lead to metabolic alterations related to endoplasmic reticulum stress in the liver, contributing to liver fat accumulation and inflammation [66]. Chronic overnutrition also disrupts normal metabolic processes, leading to altered lipid metabolism, increased hepatic fat accumulation, changes in glycerophospholipid and sphingolipid levels, and dysregulation of fatty acid metabolism [67]. Lastly, increased de novo lipogenesis (DNL) is a characteristic feature of MAFLD and stems from insulin resistance and/or compensatory hyperinsulinemia [68]. Moreover, an intervention study by Cohen and colleagues has reported a reduction of DNL within 8 weeks of dietary sugar restriction in MAFLD adolescents [69].

3.2 The gut microbiota-liver axis is one of the potential mechanistic links between nutrition and MAFLD. (LoE 2, grade A)

The gut microbiota-liver axis is a crucial pathway by which nutrients may influence the development of MAFLD. Gut microbial metabolites are also essential for maintaining energy and glucose homeostasis and immunity. Dietary composition is the leading cause of intestinal dysbiosis in MAFLD. Tateda et al. reported that reported that there was significant decrease in the abundance of nine bacterial genera in individuals with MAFLD, with a particularly low relative abundance of *Blautia* [70]. It has also been demonstrated that high fructose corn syrup increased butyrate-producing bacteria and the *Firmicutes/Bacteroidetes* ratio [71]. A higher ratio of *Firmicutes/Bacteroidetes* has been associated with the development of MAFLD [72]. Conversely, some studies have shown that nuts, polyphenols in green tea, coffee, and plant oils increase the abundance of probiotic *Bifidobacterium*, and *Lactobacillus*, and decrease the amount of *Clostridium* and *Escherichia coli* in the gut, thus suggesting potential long-term hepatoprotective effects [73,74]. A Mediterranean-style diet enriched with antioxidants, including flavonoids and terpenes, may beneficially modulate gut microbiota composition in people with MAFLD [75].

3.3 Energy/macronutrients imbalance and alterations in metabolic demands may contribute to MAFLD. (LoE 3, grade A)

Energy/macronutrients imbalance and alterations in metabolic demands are key contributors to the development of obesity, which in turn is a powerful clinical risk factor for MAFLD. Excessive nutrient intake, metabolic dysregulation and insulin resistance lead to hepatic accumulation of lipids from free fatty acids released from fat, causing hepatic lipotoxicity, overwhelming organ repair capacity, promoting inflammatory pathways, cellular dysfunction, and apoptosis [76]. Nutrient excess in MetS and obesity also warrants exaggerated mesenteric oxygen demand, reducing portal vein oxygen and hepatic oxygen delivery [77]. Furthermore, chronic overnutrition leads to TLR9 overactivation, driving inflammation and MASH development [78]. The complex interplay between dietary habits and metabolic alterations underscores the multifaceted nature of the effects of these conditions on MAFLD.

3.4 Interaction between the PNPLA3 genetic variant and MAFLD. (LoE 3, grade A)

Patatin-like phospholipase domain-containing protein 3 (*PNPLA3*) is the most studied genetic determinant of liver fat and is closely associated with increased susceptibility to MAFLD, MASH and HCC [79,80]. Obesity exacerbates the effect of the *PNPLA3* rs738409 variant, increasing its effect size [81]. Therefore, it is not surprising that the interaction between the *PNPLA3* genetic variant and overnutrition is associated with MAFLD. Vilar-Gomez et al. reported that individuals carrying the *PNPLA3* rs738409 variant had increased susceptibility to high carbohydrate consumption and higher risk of liver fibrosis severity [82]. Interestingly, these authors found that individuals carrying the *PNPLA3* G-allele exhibited increased severity of MAFLD when carbohydrate intake is high. Nobili et al. reported that the interaction between the *PNPLA3* rs738409 variant and carbohydrate intake was associated with the development of MAFLD in at-risk adolescents [83]. Other studies reported a gene-diet interaction between the *PNPLA3* rs738409 G-allele and dietary nutrients, influencing the risk of liver fibrosis in MAFLD [82]. In addition, in a study where participants were treated with omega-3 fatty acids (460 mg of EPA and 380 mg of DHA daily) for 15–18 months, individuals carrying the *PNPLA3* 148 M/M gene variant had less increase in DHA levels in their tissues and lower hepatic fat levels [84]. In a study of 18,921 individuals with obesity from Scotland and Sweden, the *PNPLA3* rs738409 was associated with obesity, greater insulin resistance, higher serum liver enzymes, and lower plasma lipids. This genetic variation makes it harder for the liver to eliminate fat, causing hepatic fat accumulation. Experimental studies consistently reported that the expression of the *PNPLA3* gene is strongly regulated by changes in energy balance, affecting MAFLD progression [85]. The possible reason appears to be that the protein encoded by the *PNPLA3* gene has a structure similar to enzymes involved in triglyceride hydrolysis (ATGL/PNPLA2), thus increasing hepatic triglyceride content [86]. Therefore, individuals carrying the *PNPLA3* rs738409 variant may be prone to increased sensitivity to hepatic stress when exposed to excessive calorie intake [79,87].

4. MAFLD prevention

4.1 Regular self-monitoring of body weight is important for individuals with MAFLD. (LoE 2, grade A)

As reported previously, patients with MAFLD are typically overweight or obese. Regular weighing may be a straightforward strategy for weight loss, which may be effective by boosting motivation [88]. A study showed that compared to those who never weigh themselves or weigh only once a week, individuals who weigh themselves daily had more weight loss within 1 year [89]. In a randomized clinical trial (RCT) involving participants with a BMI of 23 to <30 kg/m^2, dietary intervention, including wheat bran combined with daily self-monitoring of body weight, significantly reduced body weight and visceral adipose tissue [90]. Self-monitoring of physical activity and diet, and recording weight via smartphone applications may be helpful for achieving weight loss. This approach can be utilized anywhere, irrespective of the user's residence [91]. One study suggested that self-weighing contributes to better glycemic control, which is an essential aspect of managing conditions like diabetes that is often associated with MAFLD [92]. While these studies do not specifically address MAFLD, they do suggest that regular self-monitoring of body weight should be a component of interventions that may improve dietary behavior, body weight, and potentially other health outcomes. Notably, while self-monitoring of body weight can be an effective tool for weight management, it is crucial to be aware of potential negative psychological effects, such as hyperawareness, psychological burden, body image issues, and development of obsessive or compulsive behavior.

4.2 Providing education is essential to reinforce healthy lifestyles in individuals with MAFLD. (LoE 1, grade U)

Nutrition education for MAFLD should be aimed at decreasing fat mass and improving adipose tissue function. By providing targeted nutrition education, individuals gain knowledge and skills to make informed dietary choices for their health and well-being. Research has shown that nutrition education interventions significantly impact patient's knowledges, attitudes, and behaviors towards food and nutrition. For instance, one study reported significant increases in self-efficacy, attitude, and intention to drink water, alongside a decrease in sugary drinks, snacks, and meat consumption in the intervention group [93]. Similarly, a study found that cognitive-behavioral skills-building resulted in significant improvements in healthy lifestyle beliefs and behaviors [94]. The Integrated Nutrition Education with eHealth Intervention review highlighted the effectiveness of integrating nutrition education with eHealth-based technology for improving anthropometric measures and behavioral outcomes in obese adults [95]. Finally, nutrition education interventions for the public can extend to the implementation of a nutritional front-of-package labeling system. The nutrition facts label reports the levels of saturated fat, added sugars and sodium, to help consumer understanding and use of these specific nutrients in making healthier food choices. The sugar labeling policy study demonstrated that the disclosure of added sugar and inclusion of a percent daily value on nutrition facts labels can have positive effects on consumer awareness and understanding of the role of added sugar in packaged food products [96]. It is important to highlight that nutritional information and education should be always provided by nutritional specialists, such as a dietician, for quality assurance reasons.

4.3 In MAFLD risk assessment, nutrition should be considered an additional risk factor. (LoE 3, grade U)

Studies have shown a strong association between overnutrition and the prevalence of MAFLD in both children and adults [97]. Chronic overnutrition contributes to the development of MAFLD by disrupting metabolic homeostasis, promoting low-grade inflammation, and directly influencing hepatic fat accumulation through various pathways [19]. Overnutrition not only exacerbates hepatic steatosis but also increases the risk of developing liver fibrosis and other hepatic and extrahepatic clinical complications associated with MAFLD [38]. Research has also highlighted that excess caloric intake is a risk factor for MAFLD, even in non-obese individuals, thus emphasizing the importance of considering dietary habits and nutrient intake in assessing MAFLD risk [98].

5. Managing MAFLD through dietary interventions

5.1 Dietitians are integral team members for interventions targeting MAFLD. (LoE 3, grade U)

While evidence demonstrates that lifestyle interventions can effectively manage MAFLD/MASH, and clinical guidelines advocate for such lifestyle changes, a significant disparity exists between these recommendations and their implementation in clinical practice [99]. Sustaining lifestyle modifications represents a challenge for patients with MAFLD [100]. Moreover, sustained promotion of reducing intake of a single macronutrient may result in nutrient deficiencies, exacerbating digestive or metabolic dysfunctions if neglected in MAFLD patients [14]. Many clinicians advocate for a multidisciplinary approach to effectively manage MAFLD, encompassing various lifestyle intervention strategies to facilitate the sustainability of long-term behavioral changes [101]. Dietitians play a pivotal role as key members of the multidisciplinary team, and follow the nutrition care process model or a scientific way of providing care and support to patients with MAFLD [102]. The model consists of four interrelated steps: (1) nutrition assessment, which Utilizing a combination of anthropometric, dietary, biochemical, clinical, and functional data, along with validated assessment tools like subjective global assessment (SGA) and patient-generated subjective global assessment (PG-SGA), provides a comprehensive evaluation of nutritional status; (2) nutrition diagnosis, where the dietitian formulates a scientific statement to determine nutritional diagnosis, clearly identifying the problem, etiology, and signs and symptom; (3) nutrition intervention, which involves developing personalized dietary plans, encompassing daily caloric intake, macronutrient composition, meal timing arrangements, and specific dietary recommendations. These

interventions should be adjusted according to the patient's preferences, culture, and economic status; (4) nutrition monitoring and evaluation. A continuous process of tracking progress, reassessing the client's nutritional needs, and adjusting the intervention plan as necessary to achieve the desired outcomes [103]. Such continuous support is clinically mandatory for fostering enduring lifestyle change essential for managing MAFLD and associated metabolic complications (e.g., obesity, insulin resistance, and dyslipidemia). Hence, the role of dietitians in the multidisciplinary team addressing interventions for MAFLD is essential and mandatory.

5.2 Adherence to a balanced diet (including adjustment of energy intake and expenditure) should be considered for patients with MAFLD to achieve and maintain a healthy body weight. (LoE 2, grade U)

Guidelines from the American Gastroenterological Association strongly recommend reducing weight by at least 5 % to decrease hepatic steatosis, whereas a 10 % weight loss is needed for reversing liver fibrosis. Additionally, weight loss of ≥7 % can lead to resolution of MASH [104]. Among adult individuals with MAFLD without overweight or obesity, weight loss of 3–5 % is strongly encouraged [40,104]. Treatment for individuals with MAFLD should initially concentrate on limiting daily energy intake, recommending that patients reduce their daily caloric intake by 500–1000 kcal (25–30 kcal/kg/day) to facilitate a gradual body weight reduction [104]. Studies have shown that an adequate total energy restriction (−500 kcal/day, resulting in ~1500 kcal/day for women and ~ 1800 kcal/day for men) leads to a decrease in body weight, visceral adipose tissue, hepatic fat content, and serum liver enzymes, regardless of the type of caloric restriction employed [105,106]. Weight loss attained through a healthy diet has been shown to reduce serum liver enzymes, hepatic inflammation, and fibrosis in a dose-dependent manner [107]. A commonly recommended healthy diet includes non-starchy vegetables, whole fruits, legumes, fish, whole grains, nuts, seeds, and low-fat dairy products. At the same time, it advocates minimizing the consumption of red meat, processed meats, sugary beverages, trans fats, sweets, refined grains, and processed foods [108]. Based on these nutritional principles, the Mediterranean-style dietary pattern has been advocated as the fundamental dietary pattern or approach for other healthy diets [109].

5.3 Use of personalized nutritional interventions (such as calorie restricted diet, high protein diet, low carbohydrate diets/very low carbohydrate diets, or intermittent energy restriction) under the guidance of a dietitian should be considered for individuals with MAFLD. (LoE 3, grade A)

Improving MAFLD and achieving weight loss can be challenging in clinical practice. Researchers have investigated various diets, such as calorie restricted diets [105], low carbohydrate diets (defined as <40 % or < 60 g/day carbohydrate) [110,111], high protein diets [112], and intermittent energy restriction [113]. Each has been shown to offer benefits in the short term for treating patients with MAFLD. Intermittent dietary approaches, such as the 5:2 diet, alternate-day fasting, and time-restricted eating involve cycling between calorie restriction and normal intake, which may help counter circadian disruptions linked to MAFLD [114]. A prospective observational trial found intermittent fasting in adults with MAFLD resulted in a significant improvement in BMI and hepatic steatosis (assessed by the fatty liver index) [115]. However, it's important to note that no single dietary method has been consistently effective across all studies, indicating the need for more research to identify the most optimal dietary plans for long-term outcomes and acceptability among MAFLD patients. Any dietary approach should be personalized, taking into account health status, individual and cultural preferences, health goals, the ability to adhere to recommendations, and ultimately food access and nutritional security [116]. Sustained guidance from a multidisciplinary care team, including dietitians, is needed to support long-term dietary behavioral change for management of people with MAFLD.

5.4 Advice to eat foods mostly from whole grains rather than refined grains. (LoE 2, grade A)

Whole grain foods are distinguished by their higher dietary fiber. Whole grain foods may exhibit a lower energy density than their refined grain counterparts. A meta-analysis of observational cohort studies examining the association between whole grains and the risk of MAFLD reported that whole grain consumption is associated with a significantly lower risk of MAFLD [117]. In a case-control study of Chinese adults, the biomarker 3,5-dihydroxyphenylpropionic acid, derived from consuming whole grain wheat and rye, was associated with a lower risk of MAFLD [118]. In a double-blind, parallel, randomized trial involving 50 overweight men aged 45–70, a whole grain intervention (98 g/day) resulted in lower circulating levels of liver acute-phase proteins, serum amyloid A, and C-reactive protein, compared to a refined grain intervention (98 g/day) [119]. Data from observational studies and food substitution analyses suggests that replacing refined grains with whole grains is inversely associated with MAFLD [120]. Consumption of whole grains, as opposed to refined grains, has been shown to improve metabolic risk factors associated with MAFLD [121]. Studies indicate that whole grains may also contribute to relieving constipation and enhancing gut microbiota quality [122]. Nevertheless, a RCT featuring two dietary interventions found that compared to a refined grains diet, a whole grain diet for 8 weeks reduced body weight and systemic low-grade inflammation in individuals with metabolic syndrome, although no significant changes in insulin resistance and gut microbiota were observed [123]. Further research is required to confirm the beneficial effects of whole grains on the gut microbiome in people with MAFLD.

5.5 Advice to eat healthy sources of protein (primarily plants); regular intake of fish and seafood; low-fat or fat-free dairy products; and if meat or poultry is desired, advice to choose lean cuts and unprocessed forms. (LoE 2, grade U)

Legumes (soybeans, lentils, chickpeas, beans) and nuts/seeds (almonds, chia, flaxseed, hemp) are outstanding plant protein sources rich in fiber, which are key dietary factors for promoting healthy digestion and weight management critical to MAFLD. Evidence suggests that legumes may significantly reduce liver disease risk [124]. Nuts have also been inversely associated with MAFLD prevalence [125]. Evidence demonstrates that swapping animal-sourced proteins for these nutrient-dense plant whole foods can benefit liver health while simultaneously lowering the carbon footprint of dietary patterns [126]. However, the short- and long-term health effects of popular ultra-processed plant-based meat alternatives remain limited [127].

Dietary patterns higher in fish and seafood are associated with a lower risk of MAFLD. A systematic review also showed that higher versus lower fish intake is linked to reduced risk of HCC [128]. Researchers have proposed substituting fish/seafood as protein sources instead of red/processed meats and full-fat dairy to help reduce chronic disease burden - attributing benefits to the concentrated omega-3 fatty acid content [129]. It is important to note that frying, in particular, is not the preferred cooking method for preserving the health benefits of fish and seafood. Current guidelines advise 2–3 servings of varied cooked fish/seafood weekly [130].

Low-fat and nonfat dairy products make up one component of the DASH diet pattern. Substantial evidence indicates an association between the consumption of low-fat dairy items and specific health markers in the MAFLD population. For example, a RCT reported a significant reduction in serum liver enzyme levels after 6 weeks of prescribed low-fat dairy (milk, yogurt, cheese) [131]. Another RCT in individuals with obesity reinforced these findings when low-fat dairy was fortified with vitamin D_3 supplementation [132]. However, the proposed superiority of low-fat over full-fat dairy remains controversial based on mixed evidence from reviews and cohort studies [133,134]. Emerging data hints at potential metabolic benefits from fermented dairy like yogurt for liver health, potentially mediated through improved gut microbiome. However, research in this area is still limited.

5.6 Advice to reduce red/processed meats, saturated fats, trans fatty acids, ultra-processed foods, and added sugar for individuals with MAFLD. (LoE 2, grade U)

Dietary patterns high in red and processed meats are associated with

an increased risk of MAFLD and related mortality, as well as higher BMI and greater insulin resistance. Epidemiological evidence shows a dose-response relationship between greater red and processed meat consumption and the risk of MAFLD and hepatic steatosis [135,136]. Potential drivers for the adverse effect of red meat on MAFLD are the higher saturated fat and heme iron content, as well as the metabolism of compounds like L-carnitine and phosphatidylcholine by gut microbiota [137]. Processed meats are products preserved through smoking, curing, salting or added chemical preservatives like nitrites. Examples include sausages, hot dogs, pepperoni, salted fish, charred meats and specific preparations of red meats. Concerns do exist around nitrites forming carcinogenic N-nitrosamines [138]. Processed meats are also high in sodium, saturated fat, cholesterol, heme iron, and other compounds such as polycyclic aromatic hydrocarbons, which are influenced by processing.

Higher SFA intake than unsaturated fats may increase hepatic fat accumulation and worsen insulin resistance in patients with MAFLD, especially in the context of excess calories. Substantial evidence supports a link between high consumption of SFA and TFA (trans fatty acids) and the development and progression of MAFLD [37,139]. Despite scientific guidelines limiting SFA intake to <10 % of daily total calories, average U.S. intake remains around 12 %, significantly exceeding the recommendations [140]. Ultra-processed foods are a primary dietary source of total fat, sugars, and SFA/TFA. Accumulating evidence associates ultra-processed food consumption with a higher risk of developing overweight/obesity, diabetes, MAFLD and with increased overall mortality [141,142]. Meta-analyses of observational studies show that higher consumption of ultra-processed food is associated with MAFLD in a dose-response manner [143]. Consequently, dietary guidelines advise limiting ultra-processed foods and choosing lean proteins, low-fat dairy and unsaturated plant oils over solid fats to reduce SFA/TFA intake [144].

Added sugars refer to sugars and syrups added to foods or beverages during processing or consumption. Common added sugars include glucose, maple, honey and corn syrups, maltodextrin, and glucose/dextrose [145]. These added sugars contribute to the overall sugar content and are associated with a higher risk of obesity, type 2 diabetes, and MAFLD if excessively consumed [146]. Dietary guidelines recommend limiting added sugars to below 10 % of the daily energy intake [147]. Substituting added sugars with low-energy sweeteners from natural sugars can be a valuable alternative to added sugar in everyday diets. Considering healthier alternatives, like low-abundance mono- and disaccharides, can help individuals make more informed choices for a balanced and nutritious diet while reducing the risks associated with excessive added sugar consumption. However, the long-term effect of these sugars is equivocal on satiety, food cravings, gut microbiota, and long-term health outcomes [149].

5.7 Encouragement to eat deeply colored fruits and vegetables and choosing a variety of foods. (LoE 2, grade U)

Extensive and consistent research has demonstrated that dietary patterns high in fruits and vegetables are associated with a lower risk of MAFLD [150–152]. Daily dietary recommendations advise for 1.5–2 cup-equivalents of fruits and 2–3 cup-equivalents of vegetables daily [153]. Deeply colored fruits and vegetables (e.g., leafy greens and berries), which are rich in antioxidants and vitamins, typically have a higher nutrient density than lighter colored foods [154]. Deeply colored fruits and vegetables typically contain abundant phytonutrients like chlorophyll, lutein, lycopene, and anthocyanins, which aid in antioxidant, anti-inflammatory, and immune-regulating physiological functions [154]. Compared to juice, whole fruits and vegetables may provide more dietary fiber and a stronger sense of satiety while avoiding excessive sugar intake and loss of plant nutrients [153]. Consuming whole fruits and vegetables, rather than juice, is preferable to reduce the risk of MAFLD [146]. If consuming juices, ensuring their composition is 100 % pure juice, devoid of added sugars is highly recommended. Concurrently, when procuring canned fruits, preference should be given to options characterized by the minimal presence of added sugars [144]. Vegetables and fruits, irrespective of their form (fresh, canned, dried, or frozen), should be consumed without adding solid fats, sugars, sodium, or syrup to maintain their nutritional integrity. All forms of fruits and vegetables should be included in healthy dietary patterns for MAFLD [155].

5.8 Advice to cook with liquid plant oils rather than saturated or hydrogenated oils/fats (coconut, palm, and palm kernel), animal fats (butter, ghee and lard), or hydrogenated fats. (LoE 2, grade A)

Evidence from observational studies has shown that unsaturated fats (polyunsaturated and monounsaturated fats) may be beneficial for MAFLD, particularly when they substitute SFA/TFA. Liquid plant oils (olive oil, fish oil, canola oil, corn oil, etc.) rich in monounsaturated and polyunsaturated fatty acids helps to lower plasma LDL cholesterol levels and increase HDL cholesterol levels, thereby reducing the risk of cardiovascular disease and MAFLD. Foods rich in saturated and trans fatty acids have been linked to hepatic steatosis and inflammation [156]. Conversely, monounsaturated fats and omega-3 polyunsaturated fats reduce hepatic fat accumulation by decreasing fat production in the liver [75,157]. A systematic review and meta-analysis of RCTs indicated that consumption of plant-based omega-3 polyunsaturated fatty acids is associated with weight loss and lower levels of transaminases and triglycerides in patients with MAFLD [158]. Specifically, virgin olive oil which contain both a healthy lipid matrix and high content of biophenols. Of note, emerging evidence suggest an important role of biophenols in counteracting inflammatory and oxidative processes which are very important in obesity and MAFLD [159] Collectively, for a healthy dietary pattern, it is highly recommended that individual increase the intake of liquid plant oils, especially virgin olive oil, and decrease consumption of saturated fats (coconut, palm, and palm kernel), animal fats (butter, ghee, and lard), and hydrogenated fats.

5.9 Advice to greater adherence to the Mediterranean or DASH dietary pattern to improve MAFLD risk. (LoE 1, grade A)

The Mediterranean and the DASH dietary patterns emphasize on increasing the intake of plant-based foods (including vegetables, fruits, whole grains, and legumes), and of high-quality proteins. While the DASH-pattern is a low fat one emphasizing on an intake below 28 % of total energy intake from fat and on reduction of saturated fatty acids and an increase in polyunsaturated fatty acids, the Mediterranean dietary patterns is a high fat one emphasizing on mono-unsaturated fat intake from virgin olive oil [160,161]. Evidence is accumulating that both DASH and the Mediterranean pattern diet are associated with a lower risk of MAFLD in the overweight/obese population, with stronger evidence supporting the Mediterranean-style diet rather than DASH diet. Some RCTs have demonstrated that the DASH diet may effectively reduce body weight and metabolic risk profiles, including serum liver enzymes, triglycerides, insulin resistance, and inflammatory biomarkers in overweight or obese individuals with MAFLD [150,151]. Compared to a regular diet, the Mediterranean-style diet significantly improves insulin resistance, plasma lipid profile and hepatic fat in overweight/weight individuals with MAFLD [152]. The EASL-EASD-EASO Clinical Practice guidelines recommend adhering to the Mediterranean diet to manage people with MAFLD, regardless of the weight status [162].

5.10 Reduce sedentary lifestyles and maintain a moderate physical activity level (at least 150 min *per week) to support maintenance of muscle mass, physical function and metabolic health.* (LoE 1, grade A)

Physical activity has proven benefits for improving MAFLD and should be included in clinical care for most patients across the liver disease spectrum [12,162]. Guidelines strongly recommend at least 150 min of moderate-intensity physical activity weekly for most individuals with MAFLD [162]. Meta-analyses confirm physical exercise is associated with significant reductions in hepatic fat content and serum liver enzymes, especially among those with overweight or obesity [163,164]. However, most patients with MAFLD are sedentary, with women being more sedentary than men [165]. There is a significant relationship between television viewing time and the presence of MAFLD in Finnish

adults [166], and additionally, the duration of computer/mobile device use was closely associated with MAFLD in Chinese adults [167]. Intermittent physical activity breaks may help attenuate rises in postprandial plasma glucose and insulin levels, with greater benefit in those with overweight or obesity [168]. Notably, combining physical exercise with dietary interventions may lead to greater reductions in hepatic fat and serum liver enzymes, assist in mitigating losses of lean mass associated with overall weight loss, than exercise alone in people with MAFLD [169].

5.11 Advice to avoid alcohol (of any type or amount) should be encouraged in patients with MAFLD. (LoE 3, grade A)

The role of alcohol intake in MAFLD has attracted increasing attention. Heavy alcohol consumption is strongly associated with an increased risk of MAFLD. However, there is controversy regarding whether light-to-moderate alcohol consumption is harmful or beneficial. Some studies suggested moderate alcohol intake reduces metabolic dysfunction, benefiting cardiovascular health and mortality. However, recent evidence indicates even small amounts of alcohol can worsen steatosis, liver fibrosis and increase the risk of liver cancer [170]. A systematic review found that any alcohol consumption, even within the recommended limits, worsens liver-related outcomes in MAFLD. This suggests that alcohol consumption, regardless of its daily amount, can damage the liver in patients with MAFLD [171]. The presumed protective effects of moderate alcohol intake against obesity-related issues may not outweigh its harm to the liver. A Mendelian randomization analysis suggest no safe alcohol level for liver health in MAFLD [172]. Overall, more high-quality studies are needed to determine if moderate or low alcohol intake is safe for non-obese individuals with MAFLD [173]. Current evidence advises individuals with MAFLD to abstain from alcohol.

2.4. Study strengths and limitations

One key strength of the Delphi method is its ability to enhance consistency in each subsequent round, enabling the recognition of whether feedback improves statements at each step, increases the degree of consensus, and aids in reaching agreement. In the two rounds of our surveys, several international experts had the opportunity to provide detailed comments on each draft statement, and the integration of feedback into the new statements resulted in a growing level of agreement on consensus statements. The increasing rates of participation observed in these two rounds [84.6 % (55/65) in the Round 1 survey and 100 % (55/55) in the Round 2 survey] further enhances confidence in the observed results. Another significant strength of our study is its success in garnering consensus statements endorsed by representative experts from 27 countries across six continents and different medical disciplines. Coverage of multiple areas, including Dietetics, Hepatologists or Gastroenterologists, Endocrinologist/Diabetologists, and other medical Specialists with extensive research and clinical expertise, testifies to the global relevance and interdisciplinary applicability. We have incorporated risk factors into our preliminary findings and transformed them into a Delphi survey report. Experts were strongly encouraged to revise their previous answers based on feedback provided by other group members. Numerous public comments have been received across all five data collection components.

However, while the Delphi method is a structured communication technique, it also has limitations that should be mentioned. Due to the wide geographic spread of the panel experts, we conducted the surveys online and communicated drafts via email rather than in person. We acknowledge that combining face-to-face and written feedback might lead to more comprehensive contributions, facilitating consensus formation. Although there is an overlap between NAFLD and MAFLD populations, healthcare professionals can reach agreement on dietary strategies through consensus, laying the foundation for continuous improvements in knowledge and effectively managing MAFLD and its related long-term hepatic and extrahepatic complications. The lack of specific information on certain vitamins (such as Vitamin D and Vitamin E), minerals (such as selenium and zinc), antioxidants/phytochemicals (like polyphenols), and the role of consumption of herbal supplements, coffee, and tea on MAFLD is a limitation. While cross sectional studies suggest that these components play a role in liver health, no prospective randomized trials have been undertaken to verify their effectiveness. Future research should focus on exploring the effects of these nutrients and substances on MAFLD progression and prevention.

3. Conclusion

In a consensus statement based on the Delphi method, international experts from various countries formulated and endorsed a series of statements addressing the epidemiology, pathophysiological mechanisms, and management of MAFLD. The statements can form the basis for developing dietary guidelines and guiding the direction of future research.

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CRediT authorship contribution statement

Xu-Fen Zeng: Writing – original draft, Investigation, Formal analysis, Data curation. **Krista A. Varady:** Writing – review & editing. **Xiang-Dong Wang:** Writing – review & editing. **Christopher D. Byrne:** Writing – review & editing, Supervision, Resources, Project administration, Conceptualization. **Reema Tayyem:** Writing – review & editing. **Giovanni Latella:** Writing – review & editing, Supervision, Project administration, Conceptualization. **Ina Bergheim:** Writing – review & editing. **Rodrigo Valenzuela:** Writing – review & editing. **Jacob George:** Writing – review & editing. **Carolyn Newberry:** Writing – review & editing. **Ju-Sheng Zheng:** Writing – review & editing. **Elena S. George:** Writing – review & editing. **C. Wendy Spearman:** Writing – review & editing. **Meropi D. Kontogianni:** Writing – review & editing. **Danijela Ristic-Medic:** Writing – review & editing. **Wilza Arantes Ferreira Peres:** Writing – review & editing. **Gamze Yurtdaş Depboylu:** Writing – review & editing. **Wanshui Yang:** Writing – review & editing. **Xu Chen:** Writing – review & editing. **Fredrik Rosqvist:** Writing – review & editing. **Christos S. Mantzoros:** Writing – review & editing. **Luca Valenti:** Writing – review & editing. **Hannele Yki-Järvinen:** Writing – review & editing. **Antonella Mosca:** Writing – review & editing. **Silvia Sookoian:** Writing – review & editing. **Anoop Misra:** Writing – review & editing, Conceptualization. **Yusuf Yilmaz:** Writing – review & editing. **Won Kim:** Writing – review & editing. **Yasser Fouad:** Writing – review & editing. **Giada Sebastiani:** Writing – review & editing. **Vincent Wai-Sun Wong:** Writing – review & editing. **Fredrik**

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Declaration of competing interest

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Data availability

Not applicable.

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None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.metabol.2024.156028.

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