



Metabolic Dysfunction–Associated Steatotic Liver Disease (MASLD) in People With Diabetes: The Need for Screening and Early Intervention. A Consensus Report of the American Diabetes Association

Diabetes Care 2025;48:1057–1082 | <https://doi.org/10.2337/dci24-0094>

Metabolic dysfunction–associated steatotic liver disease (MASLD), formerly referred to as nonalcoholic fatty liver disease (NAFLD), is a growing but often unrecognized medical problem for people with diabetes (particularly type 2 diabetes, especially when associated with obesity). Liver health has not been at the forefront of complications tracked for disease prevention, as traditionally done for diabetic retinopathy, nephropathy, or neuropathy. However, liver steatosis affects approximately two out of three people with type 2 diabetes and places them at an increased risk for metabolic dysfunction–associated steatohepatitis (MASH), cirrhosis, hepatocellular carcinoma (HCC), and overall liver-related mortality. MASLD is also associated with extrahepatic cancers, atherosclerotic cardiovascular disease, and progression from prediabetes to type 2 diabetes and negatively impacts health-related quality of life. However, most individuals and their health care professionals remain unaware of the severe hepatic or extrahepatic health risks associated with MASLD and the need for early identification. In recognition of this knowledge gap and the rising prevalence of MASLD, this consensus report is a call to action to screen for liver fibrosis and risk stratify people with prediabetes or type 2 diabetes, in particular if obesity is also present. This consensus report explains the rationale for the recent MASLD nomenclature change, how to best risk stratify, current treatment and long-term monitoring options, the value of an interprofessional approach to disease management, and the impact of alcohol intake on liver health. More awareness about the health risks associated with MASLD and broad adoption of screening for liver fibrosis as a new standard of care hold promise for a future without cirrhosis for people with prediabetes and type 2 diabetes.

Until recently, liver health has been somewhat overlooked in the context of prediabetes and type 2 diabetes. The growing prevalence and serious health implications of metabolic dysfunction–associated steatotic liver disease (MASLD), formerly referred to as nonalcoholic fatty liver disease (NAFLD), have prompted a call to action

Kenneth Cusi,¹ Manal F. Abdelmalek,² Caroline M. Apovian,³ Kirthikaa Balapattabi,⁴ Raveendhara R. Bannuru,⁴ Diana Barb,¹ Joan K. Bardsley,⁵ Elizabeth A. Beverly,^{6,7} Karen D. Corbin,⁸ Nuha A. ElSayed,^{4,9} Scott Isaacs,¹⁰ Fasiha Kanwal,¹¹ Elizabeth J. Pekas,⁴ Caroline R. Richardson,¹² Michael Roden,^{13,14,15} Arun J. Sanyal,¹⁶ Jay H. Shubrook,¹⁷ Zobair M. Younossi,^{18,19} and Mandeep Bajaj¹¹

¹Division of Endocrinology, Diabetes and Metabolism, University of Florida, Gainesville, FL

²Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN

³Division of Endocrinology, Diabetes and Hypertension, Brigham and Women's Hospital, Boston, MA

⁴American Diabetes Association, Arlington, VA

⁵MedStar Diabetes Institute, Washington, DC

⁶Heritage College of Osteopathic Medicine, Ohio University, Athens, OH

⁷Diabetes Institute, Ohio University, Athens, OH

⁸AdventHealth Translational Research Institute, Orlando, FL

⁹Harvard Medical School, Boston, MA

¹⁰Division of Endocrinology, Metabolism, and Lipids, Emory School of Medicine, Emory University, Atlanta, GA

¹¹Department of Medicine, Baylor College of Medicine, Houston, TX

¹²The Warren Alpert Medical School of Brown University, Providence, RI

¹³Department of Endocrinology and Diabetology, Medical Faculty, and University Hospital Düsseldorf, Heinrich-Heine-University Düsseldorf, Düsseldorf, Germany

¹⁴Institute for Clinical Diabetology, German Diabetes Center - Leibniz Center for Diabetes Research at Heinrich-Heine-University Düsseldorf, Düsseldorf, Germany

¹⁵German Center for Diabetes Research, Partner Düsseldorf, München-Neuherberg, Düsseldorf, Germany

¹⁶Virginia Commonwealth University School of Medicine, Richmond, VA

¹⁷Department of Clinical Sciences and Community Health, College of Osteopathic Medicine, Touro University California, Vallejo, CA

¹⁸The Global NASH Council, Washington, DC

¹⁹Beatty Liver and Obesity Research Program, Inova Health System, Falls Church, VA

Corresponding author: Kenneth Cusi, kenneth.cusi@medicine.ufl.edu

Received 22 October 2024 and accepted 25 March 2025

This article contains supplementary material online at <https://doi.org/10.2337/figshare.28673327>.

by the American Diabetes Association (ADA). The overarching goal of this consensus report is to provide guidance to health care professionals for the care and prevention of liver disease for people with prediabetes or diabetes.

Table 1 summarizes the clinical implications for adults with prediabetes or diabetes of having MASLD. In the U.S., the prevalence of MASLD among people with type 2 diabetes is $\geq 70\%$, with approximately half having the more progressive form with metabolic dysfunction–associated steatohepatitis (MASH) and about one in five having advanced liver fibrosis (1–3). Similar trends are observed worldwide in adults with type 2 diabetes (4–6). The presence of MASH markedly increases the risk of developing liver-related complications such as cirrhosis, hepatocellular carcinoma (HCC), and overall mortality. MASLD is one of the most common indications for liver transplantation in the U.S. (7), and having type 2 diabetes is independently associated with higher posttransplantation mortality, especially after kidney transplantation (8). Having MASLD significantly increases the likelihood of developing type 2 diabetes, cardiovascular disease, and extrahepatic malignancies (6). Finally, MASLD has a major negative impact on health-related quality of life and has become a significant economic burden (9).

Despite these alarming trends, a significant lack of awareness remains among both people at risk and clinicians regarding the health perils associated with MASLD and how best to manage it, often resulting in the condition being overlooked and untreated. There is a pressing need for heightened awareness, early diagnosis, and comprehensive management. This consensus report aims to address this knowledge gap with a clinical care pathway to manage people with prediabetes or diabetes and MASLD. Health care professionals must recognize that an early diagnosis is possible by using noninvasive tests (NITs) to stratify people for their

risk of developing cirrhosis. A timely diagnosis can encourage the adoption of healthier lifestyle habits or the initiation of pharmacological treatments for obesity and type 2 diabetes, which can prevent disease progression and, ultimately, cirrhosis. Numerous medications are currently under development to treat MASH. In 2024 the U.S. Food and Drug Administration approved resmetirom as the first pharmacological agent for people with MASH (10). Improvements in steatohepatitis and liver fibrosis were reported with semaglutide after 72 weeks of treatment in a phase 3 clinical trial, supporting an upcoming indication for MASH (11).

This guidance also covers the best practices for monitoring MASLD once diagnosed or in response to treatment. Because managing both hepatic and extrahepatic conditions associated with diabetes and MASLD is challenging, this guidance recommends the development of interprofessional teams that support the primary care physician and endocrinologist, including professionals such as registered dietitian nutritionists (RDNs), diabetes care and education specialists (DCES), behavioral health specialists, obesity management teams, pharmacists, hepatologists, and other specialists. Currently, numerous health care barriers hinder the delivery of optimal person-centered care for MASLD in primary care settings (12). This guidance also discusses integrating management pathways into electronic medical records (EMRs) to enhance care and the impact of alcohol intake on liver health and provides considerations for managing diabetes in individuals with cirrhosis and HCC.

Cirrhosis from MASLD is preventable in people with diabetes through early diagnosis, proper treatment, and long-term monitoring, similar to the management of care for diabetes-related microvascular complications (retinopathy, nephropathy, or neuropathy) or cardiovascular disease. With increased

clinician awareness and action, individualized education, more effective care models, and robust public health policies (13,14), we aim to catalyze a shift in clinical practice that will improve outcomes and the quality of life of people with diabetes and MASLD.

RESEARCH DESIGN AND METHODS

The ADA convened a technical expert panel of health care professionals who play a key role in the prevention and management of diabetes and MASLD, and an experienced member of the panel was chosen as a chair to lead the development of the report. Panelist inclusion was based on excellence in clinical care, research, leadership, collaboration, and writing and editing; commitment to evidence-based practice; and availability to volunteer (unpaid) for the report development process. The number of panelists was chosen based on consideration of the health care professionals likely to be included as a part of diabetes and MASLD care teams (e.g., primary care physicians, endocrinologists, hepatologists, behavioral health specialists, obesity management specialists, RDNs, DCES, etc.). ADA solicited nominations from the pool of experts on record and from other relevant societies. ADA led the selection process and invited the experts to join this panel. In the event of invited panel members opting not to participate, the subsequent nominee on the list was invited. A preliminary version of this report was presented at the ADA 84th Scientific Sessions, and public feedback received during and after that session was incorporated into the subsequent versions of this report.

Prior to the initiation of evidence review and writing, the panel was convened in a virtual meeting and agreed on the proposed goal, content, methodology, and rigor to be followed for this consensus report. An additional virtual meeting was held for discussion of sub-

This consensus report was reviewed and approved by the American Diabetes Association (ADA) Professional Practice Committee (PPC) in March 2025.

An ADA consensus report is a document on a particular topic that is authored by a technical expert panel under the auspices of ADA. The document does not reflect the official ADA position but rather represents the panel's collective analysis, evaluation, and expert

opinion. The primary objective of a consensus report is to provide clarity and insight on a medical or scientific matter related to diabetes for which the evidence is contradictory, emerging, or incomplete. The report also aims to highlight evidence gaps and to propose avenues for future research. Consensus reports undergo a formal review process, including external peer review and review by the ADA PPC and ADA scientific team, for publication.

This article is featured in a podcast available at diabetescareonair.libsyn.com/site.

© 2025 by the American Diabetes Association. Readers may use this article as long as the work is properly cited, the use is educational and not for profit, and the work is not altered. More information is available at <https://www.diabetesjournals.org/journals/pages/license>.

Table 1—Clinical implications of MASLD in people with prediabetes and diabetes

Adults with prediabetes and type 2 diabetes have the highest risk of developing MASLD	Adults with prediabetes and type 2 diabetes, especially those with obesity, should be risk stratified for having MASLD and liver fibrosis.
Increased risk of severe liver disease	MASLD with clinically significant fibrosis (stage \geq F2) raises the risk of cirrhosis, liver cancer, and overall liver-related mortality.
Leading cause for liver transplantation	Approximately one in five people with type 2 diabetes are at high risk of developing cirrhosis due to MASLD, making it one of the leading reasons for liver transplantation in the U.S.
Higher likelihood of developing a broad spectrum of comorbidities	MASLD increases risk of progression from prediabetes to type 2 diabetes, development of cardiovascular disease, and extrahepatic malignancies.
Negatively impacts quality of life	MASLD significantly impacts health-related quality of life and represents a significant economic burden.
Importance of an early diagnosis	Timely identification and proper management can prevent the progression of fibrosis to cirrhosis in people with MASLD.

sections and writing teams to contribute to the sections of the report. The technical expert panel, with the assistance of a methodologist, conducted literature searches in PubMed and the Cochrane Library using related medical subject headings and terms to identify studies published in English through April 2024. The literature search was updated in November 2024. To identify appropriate evidence, the panel prioritized information from systematic reviews, randomized controlled trials, and observational studies. Questions related to clinical practice and interprofessional team collaboration for the prevention and care of liver disease in people with diabetes or prediabetes provide the foundation of this report. This document includes recent information about nomenclature and clinical definition, epidemiology, diagnosis, treatment, and topics of special consideration (e.g., development of interprofessional teams, cirrhosis, and alcohol intake).

Monthly virtual meetings were held between December 2023 and November 2024 along with email and Web-based collaboration as needed. An in-person meeting was conducted in April 2024 to finalize discussion of evidence, reach consensus on the present guidance, discuss the tables and graphic design elements, and finalize writing content. Meetings were recorded, and meeting summaries were provided to panel members via an online collaboration platform and email.

This consensus guidance was developed under the auspices of ADA and represents the technical expert panel's collective analysis and evaluation. ADA

and the panel were committed to fostering a collaborative environment of respectful communication. Panel members were asked to focus on evidence-based discussion and clinical judgement rather than personal opinions or biases, which warranted supplying supporting evidence for their discussions. ADA scientific team members were present for all discussions and helped ensure that all perspectives were taken into account. These principles were conducive to mitigating conflict, respectful discussion, and consensus building.

The nominal group technique was used to reach consensus on the guidance presented in this document, which was facilitated by the consensus report chair and the ADA scientific team. Topic areas and questions were posed to the full group by the chair and other panel members during virtual and in-person meetings. The panel used discussion in a roundtable or similar fashion to take all ideas into account. These discussions were carried out in detail so as to clarify meaning, resolve questions and/or clarifications, and bring forth new ideas. The technical expert panel collectively finalized the topic areas and reached consensus on the guidance covered in this document in a nonanonymous group setting during the virtual and in-person meetings, where each member "agreed" or "strongly agreed" in a rotating sequence, ensuring that all voices were heard before a decision was made. Verbal responses were aggregated in real time during these meetings and in written fashion from comments on collaborative documents. At the end of each meeting, the panel members were

provided with qualitative summaries, including topic areas for which consensus was reached and topics that required further attention on an ongoing basis.

The nominal group technique presented several strengths and some limitations. This methodology was used to encourage equal participation by all panel members and to facilitate discussion of diverse ideas. This allowed the panel to discuss viewpoints of all members of the interprofessional care team. Though this methodology had its advantages, time periodically posed a concern. Every effort was made to give topics ample time for deliberation. Complex topics were given priority at meetings to allow full discussion of insights and perspectives. The qualitative meeting summaries shared with the panel after each meeting allowed for reflection and opportunity to bring forth further discussion points throughout the development of the report until consensus on these topics was reached.

SECTION 1. CLINICAL DEFINITIONS AND NOMENCLATURE CHANGE FROM NAFLD TO MASLD

Table 2 summarizes the current nomenclature with the most relevant clinical definitions. In Supplementary Table 1, we describe the mortality risk associated with each liver disease stage, the most commonly used NITs, and the optimal setting for health care professionals managing care for people with MASLD.

Three multinational liver associations recently agreed to modify the nomenclature from NAFLD to MASLD (15). MASLD was

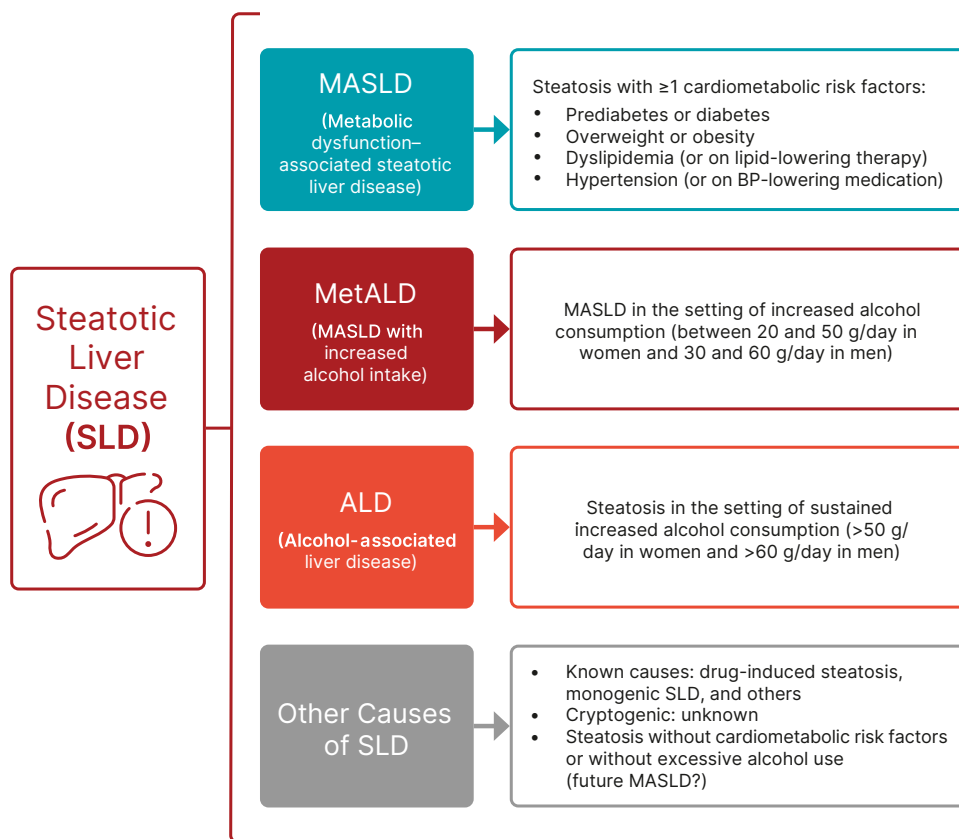


Figure 1—Nomenclature changes in SLD. BP, blood pressure; MetALD, metabolic dysfunction and alcoholic liver disease.

MASLD by virtue of the presence of one of these cardiometabolic risk factors and be aware of alternate causes of steatosis, for many of which specific therapies are available. (See diagnostic considerations in SECTION 3. DIAGNOSIS and Supplementary Table 2). Finally, while recent data confirm that obesity worsens the risk of hepatic fibrosis in young adults (aged 18–44 years) with type 2 diabetes (26), at the other end of the spectrum young adults may have isolated steatosis with insulin resistance without obesity or evident cardiometabolic disease (27). Clinicians should not miss the opportunity for these individuals with presumable “early” MASLD to risk stratify and encourage lifestyle intervention.

The perception of stigma arising from obesity, and in some cases from the term fatty in NAFLD, affects a significant number of people with this disease and is highly variable among affected individuals and their clinicians and across geographic regions (28). While the new nomenclature MASLD may function to reduce stigma, much work remains in eliminating additional contributing factors. Finally, a separate category named

MetALD has been created for individuals with MASLD and an alcohol intake that is greater than that for MASLD classification but less than in alcohol-associated liver disease (ALD) (15) (Fig. 1). Future studies will be needed to help determine its natural history and the impact of lifestyle interventions and pharmacotherapy to prevent cirrhosis from MetALD.

SECTION 2. EPIDEMIOLOGY: MAGNITUDE OF THE PROBLEM

Prevalence of MASLD in Prediabetes and Type 2 Diabetes

MASLD has become the most common cause of chronic liver disease, affecting $>38\%$ (2016–2019) of the world’s adult population and 7%–14% of children and adolescents (6,29). The prevalence of MASH among the general population is estimated at 5%–7%, while the prevalence of MASLD-related cirrhosis is 1.8% (6). These rates are much higher in people with type 2 diabetes, with estimated prevalence of $\sim 70\%$ for MASLD, $\sim 35\%$ for MASH, and $\sim 7\%$ for MASLD-related cirrhosis (1–6,30,31).

Recent data also suggest that the prevalence of MASLD among those with

prediabetes is between $\sim 37\%$ and 50% (32). In fact, people with prediabetes are 2.5 times more likely than those without prediabetes to have MASLD, 8.5 times more likely to have significant fibrosis, and almost 6 times more likely to have advanced fibrosis (32).

Incidence of MASLD in Prediabetes and Type 2 Diabetes

The incidence rate of MASLD has been reported to be 49 per 1,000 person-years (6). The bidirectional association of type 2 diabetes and MASLD is suggested by the twofold higher incidence of type 2 diabetes among those with MASLD (33,34). The most important predictors for prediabetes and type 2 diabetes are having overweight or obesity and MASLD (34).

Additionally, having type 2 diabetes is associated with an increased relative risk of fibrosis progression (35–37), while 15%–38% of people with type 2 diabetes have MASH with clinically significant liver fibrosis or cirrhosis (also known as at-risk MASH [see fibrosis stage definitions in Table 2 and Supplementary Table 1]) (1–6,26,31,38). The presence of MASLD

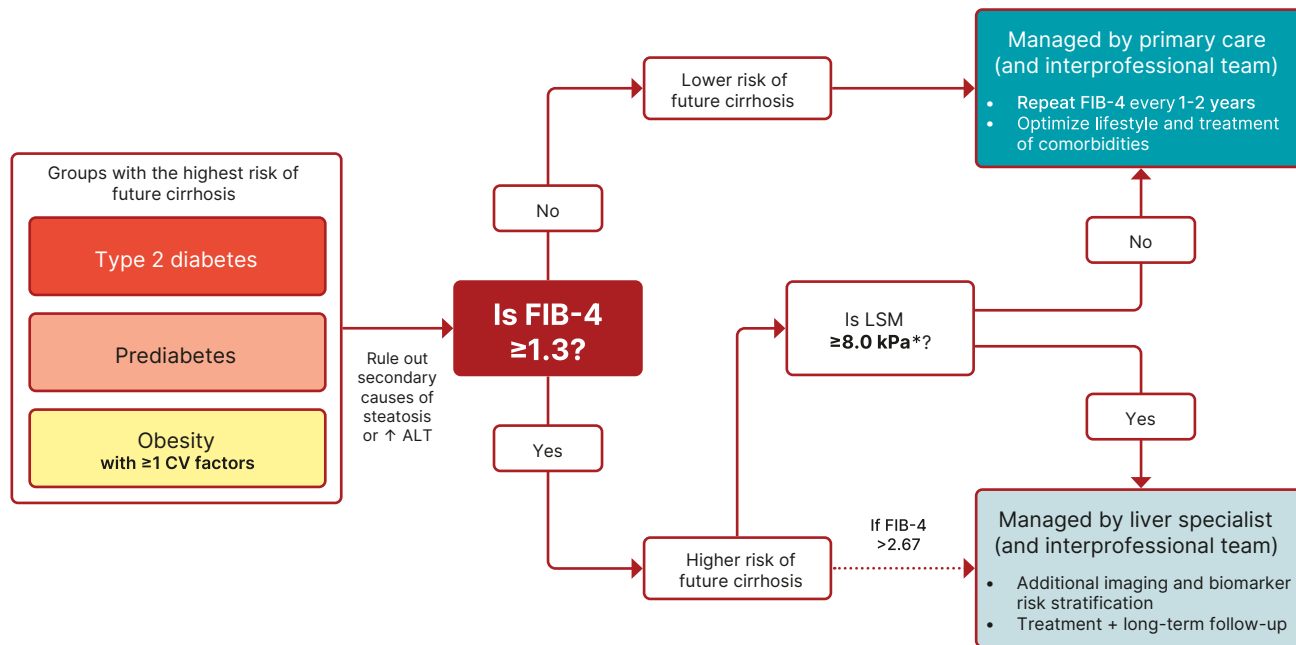


Figure 2—Diagnostic algorithm for risk stratification and the prevention of cirrhosis in individuals with MASLD. *In the absence of LSM, consider the blood-based ELF test as a diagnostic alternative. If ELF score is ≥ 9.8 , a referral to a liver specialist is recommended, as there is a high risk of MASH with advanced liver fibrosis. Adapted from “Standards of Care of Diabetes—2025” (59).

settings) are at increased risk for advanced fibrosis, with a positive predictive value for clinically significant fibrosis ranging from 60% to 80% (81). These individuals can be directly referred (without the need of additional risk stratification at the primary care level) to gastroenterologists and hepatologists to assess for the presence of at-risk MASH or cirrhosis (Fig. 2). Most clinical care pathways endorse the use of liver stiffness measurement

(LSM), most commonly with transient elastography (VCTE), as the second step in the two-tier approach (Fig. 2). A stepwise FIB-4 plus VCTE-based algorithm performed well in stratifying the risk of future liver-related events in a recent multicenter cohort (80). A VCTE-derived LSM of < 8.0 kPa rules out advanced fibrosis accurately most times (81) and is associated with a low risk of liver outcomes (82,83), and people with LSM < 8.0 kPa should

be followed in primary care and endocrinology clinics with repeat surveillance in 1–2 years (see *LONG-TERM MONITORING*). Individuals with LSM > 8.0 kPa should be referred to gastroenterology or hepatology specialists for additional diagnostic testing. Shear wave elastography, point shear wave elastography, and other ultrasound-based methods can also be used for initial risk stratification, but they are not as well validated as VCTE.

Table 4—Preferred tests for the initial (FIB-4) and secondary (VCTE, ELF) liver fibrosis risk stratification of people at high risk for MASLD*

FIB-4	Calculated with the following inputs: age, AST and ALT levels, and platelet count. First-line screening test for clinically significant fibrosis (stage \geq F2). If FIB-4 score is > 1.3 , additional risk stratification is needed. Calculator: https://www.mdcalc.com/calc/2200/fibrosis-4-fib-4-index-liver-fibrosis
VCTE	Imaging technique for LSM, extensively validated with liver histology as a surrogate of liver fibrosis stage. Second-line screening test for clinically significant fibrosis (stage \geq F2). Diagnostic cutoffs:* <ul style="list-style-type: none"> • LSM score > 8 kPa = stage \geqF2 (clinically significant fibrosis) • LSM score > 10 kPa = stage F3 or F4 (advanced fibrosis) • LSM score > 15 kPa = stage F4 (cirrhosis)
ELF	A blood test that helps identify individuals with advanced fibrosis and at risk of developing cirrhosis or liver-related outcomes. A score obtained from three proteins linked to liver fibrosis (hyaluronic acid, amino-terminal propeptide of type III procollagen [PIIINP], and tissue inhibitor of metalloproteinase-1 [TIMP-1]). Second-line screening test for clinically significant fibrosis (stage $>$ F2). Diagnostic cutoffs:* <ul style="list-style-type: none"> • ELF score > 9.8 = stage F3 or F4 (advanced fibrosis) • ELF score > 11.2 = stage F4 (cirrhosis)

*Since NITs have significant interindividual variability and overlapping CIs across fibrosis stages, it is best to consider results in the context of having a “probability” of a given liver disease stage rather than the certainty that only a liver biopsy can provide.

The Enhanced Liver Fibrosis (ELF) test can also be used as a second-tier test (84) (Fig. 2, Supplementary Table 1, and Table 4). ELF is a noninvasive blood-based proprietary test approved for prognostication when advanced fibrosis is suspected, although it can be ordered for secondary risk assessment, particularly because the availability of VCTE may be limited in some settings. The ELF test includes a panel of biomarkers consisting of three components: type III procollagen peptide, hyaluronic acid, and tissue inhibitor of metalloproteinase-1. An ELF score <7.7 is associated with a very low risk of fibrosis, whereas a score ≥ 9.8 helps identify people with MASLD with advanced fibrosis and at increased risk of progression to cirrhosis and liver-related clinical events (85–88). An ELF score >11.3 is associated with the highest risk of hepatic decompensation events, and such cases are best managed in a hepatology setting (89,90). ELF has proven useful in guiding referrals in primary care and diabetes clinic populations (91,92). An ELF score <9.8 suggests a low risk of advanced liver fibrosis, which may be followed in primary care or endocrinology settings with repeat testing at ≥ 2 years. Individuals with ELF score ≥ 9.8 should be referred for secondary assessment due to the increased risk of liver-related events. Of note, the optimal ELF cutoff for use in nonhepatology clinics is evolving; management decisions should be individualized when the ELF score is between 9.2 and 9.7 based on clinical risk (i.e., testing may be needed more often in a high-risk individual with multiple cardiometabolic risk factors).

Referral Guidelines, Overview of Additional Tests by Specialists, and Role of Liver Biopsy

Individuals with a FIB-4 score >1.3 and VCTE-derived LSM ≥ 8.0 kPa or an ELF score ≥ 9.8 should be considered for referral to liver specialty clinics (gastroenterology or hepatology) for additional assessment (Fig. 2). In liver clinic settings, imaging-based methods are usually used for better estimation of the fibrosis stage, including magnetic resonance elastography (MRE) (93) or multiparametric MRI-derived iron-corrected T1 (cT1) (which may identify people with at-risk MASH) (94). In head-to-head comparisons, MRE has higher accuracy in detecting liver fibrosis, especially in

earlier stages, than VCTE (95–97). While MRE may not be the initial choice for risk stratification due to cost and access considerations, it can serve as a valuable tool in specialty clinics, especially in cases of uncertainty or unreliable VCTE results. VCTE-derived LSM >10 kPa and MRE-derived LSM >3.5 kPa suggest advanced fibrosis (i.e., liver fibrosis stages 3 [F3] and 4 [F4]) and a value >15 kPa and MRE values >4.4 kPa are consistent with a high probability of cirrhosis (i.e., stage F4) (98). VCTE-derived LSM >25 kPa (99), VCTE-derived LSM >20 kPa with platelet counts $\leq 150,000/\text{mm}^3$, and MRE-derived LSM >5.7 kPa are all reflective of likely having clinically significant portal hypertension (100) (Supplementary Table 1).

Liver biopsy is generally considered when noninvasive assessments are inconclusive or when alternative diagnoses are suspected. NIT results that may improve identification of advanced fibrosis or cirrhosis among individuals attending liver clinics and decrease the need for liver biopsy include transient elastography-based scores such as Agile 3+ (VCTE-LSM combined with AST-to-ALT ratio, platelet count, sex, diabetes status, and age) or Agile 4 (VCTE-LSM combined with AST-to-ALT ratio and platelet count for diagnosis of cirrhosis) (101–103), MRE-based measures such as MRI-AST (MAST) score (MRE plus AST) or MEFIB index (MRE plus FIB-4) (104,105), and used more recently to identify at-risk MASH, results from blood-based proprietary tests such as NIS2+ score (from a two-biomarker test derived from YKL-40 and miR-34a-5p corrected for sex) (102,103) or Metabolomics-Advanced Steatohepatitis Fibrosis Score (MASEF score) (a metabolomics-driven score) (106) and MRI-derived cT1 (94) (Supplementary Table 1).

Long-term Monitoring

The chronic nature and fluctuating course of MASLD require monitoring of the disease state in affected individuals. There is also a high possibility of de novo development of MASLD in individuals with diabetes, supporting the need for monitoring individuals without MASLD at the initial evaluation. Initiation of therapy also requires follow-up to assess treatment response. The best evidence-based guidance is summarized below.

Long-term Follow-up of Individuals With a FIB-4 Score <1.3 at Initial Evaluation

A growing body of literature indicates that most individuals with a FIB-4 score <1.3 are unlikely to have increased liver-related outcomes or mortality within a 5-year time frame (76,107,108). These individuals may therefore be considered relatively low-risk, and management is usually focused on optimization of body weight, diabetes management, and underlying risk factors. However, there are limited data on how often to repeat FIB-4 testing because the natural history of fibrosis progression in MASH is not fully established and is highly variable among people with type 2 diabetes. In a prospective study from Hong Kong with use of repeated imaging (VCTE), worsening in LSM was found in 12% of participants after 3 years of follow-up (109). Of note, FIB-4 is a low-cost test with acceptable negative predictive value but with modest sensitivity and positive predictive value. With factors taken together, we recommend that individuals with an initial FIB-4 score <1.3 be reassessed with repeat FIB-4 measurements in 1–2 years. Clinically significant fibrosis may be present in some adults with type 2 diabetes and FIB-4 values between 1.0 and 1.3, especially when type 2 diabetes is associated with obesity and multiple cardiometabolic risk factors. For instance, in a recent large phase 3 study with recruitment of people with MASLD with fibrosis stages F2 and F3, often with obesity and type 2 diabetes, the mean \pm SD of the FIB-4 score was 1.4 ± 0.7 (10). This indicates that for some individuals with at-risk MASH FIB-4 score may be <1.3 , especially in the context of obesity and type 2 diabetes. Therefore, a FIB-4 score cutoff of <1.3 should be taken as a general guidance for assessment of having a lower risk of advanced fibrosis, but it does not replace clinical judgement. Case finding with eventual additional testing may be justified with a FIB-4 score between 1.0 and 1.3 in people with type 2 diabetes with obesity or other traditional cardiometabolic risk factors. For these cases transient elastography may also be of benefit as part of risk assessment. The risk of developing MASLD has been independently associated with insulin resistance, weight gain, obesity, and cardiometabolic risk factors (110–112). In contrast, individuals with type 2 diabetes without MASLD often have less

role for busy clinicians in screening implementation for high-risk individuals and improve clinical outcomes.

SECTION 4. TREATMENT

Management of MASLD in adults involves an interprofessional team including but not limited to primary care physicians, endocrinologists, nurses, RDNs, DCES, behavioral health specialists, obesity management teams, pharmacists, and liver and other medical specialists. The comprehensive care plan includes lifestyle modification, weight management, and pharmacological treatment aimed at preventing cardiovascular disease and MASH cirrhosis (59).

Lifestyle Modification

A healthy lifestyle is the foundation of treatment in people with type 2 diabetes and MASLD. Figure 3 summarizes a broad spectrum of useful lifestyle interventions. In people with overweight and obesity, the magnitude of weight loss correlates overall with improved glycemic management, insulin sensitivity, and histological improvement in MASH, including fibrosis (122,123). Among people with MASH, weight loss of $\geq 5\%$ of total body weight decreases steatosis. Weight loss of $>5\%$ usually is needed to reverse steatohepatitis (56,122,124,125). Many studies suggest that even more weight reduction ($\geq 10\%$) is needed to improve

fibrosis and that the response can be highly variable (56,57,122,124). Of note, improvement in liver histology may be seen with lesser degrees of weight loss and, conversely, only modest improvement with significant weight loss.

When lifestyle modification includes individualized nutrition diagnosis, treatment, and behavior modification recommendations, it should be delivered by an RDN. However, all health care team members can reinforce general nutrition guidance. Furthermore, it is essential to use appropriate psychosocial care methods and provide access to diabetes self-management education and support (DSMES) services as a critical part of healthy lifestyle interventions for people with type 2 diabetes and MASLD (126).

Nutrition Plans

Nutrition plans should be tailored to the individual’s social, work, cultural, and financial context and provided in a practical, implementable format. Given that MASLD often clusters in families, and family support is crucial for success, family counseling should be included (69). Evidence suggests that no ideal calorie percentage from carbohydrates, proteins, and fats can be broadly recommended for all people with prediabetes or diabetes (127). However, nutrition plans high in saturated fat and sugar (from sucrose and/or high-fructose corn syrup)

are associated with postprandial hypertriglyceridemia, insulin resistance, and higher risk of MASLD or MASH with fibrosis progression in high-risk individuals (122,128). Increased fructose consumption is associated with fibrosis severity, independent of total caloric intake (128). In macronutrient distribution avoidance of ultraprocessed foods and reduction in saturated fat and simple sugars and fructose consumption should be emphasized, as should an eating pattern enriched with high fiber and unsaturated fats (56,57,126,127).

Various nutritional approaches (e.g., low fat vs. low carbohydrate, Mediterranean diet, Dietary Approaches to Stop Hypertension [DASH] diet, high protein, meal replacement, and intermittent fasting, among others) seem comparable in their ability to improve steatosis (129,130), but their benefit for steatohepatitis and fibrosis have not been adequately studied (122). A (culturally appropriate) Mediterranean eating pattern (rich in fruits, vegetables, whole grains, and heart healthy fats) is preferred due to the best long-term data on beneficial cardiometabolic risk factor reduction and mortality benefit (122,129–131) and is endorsed in current MASLD guidelines (55,56,58,59,122).

Alcohol consumption increases the risk of cirrhosis and HCC (132). It should be avoided in individuals with at-risk MASH. (See SECTION 8. ALCOHOL INTAKE AND LIVER HEALTH.)

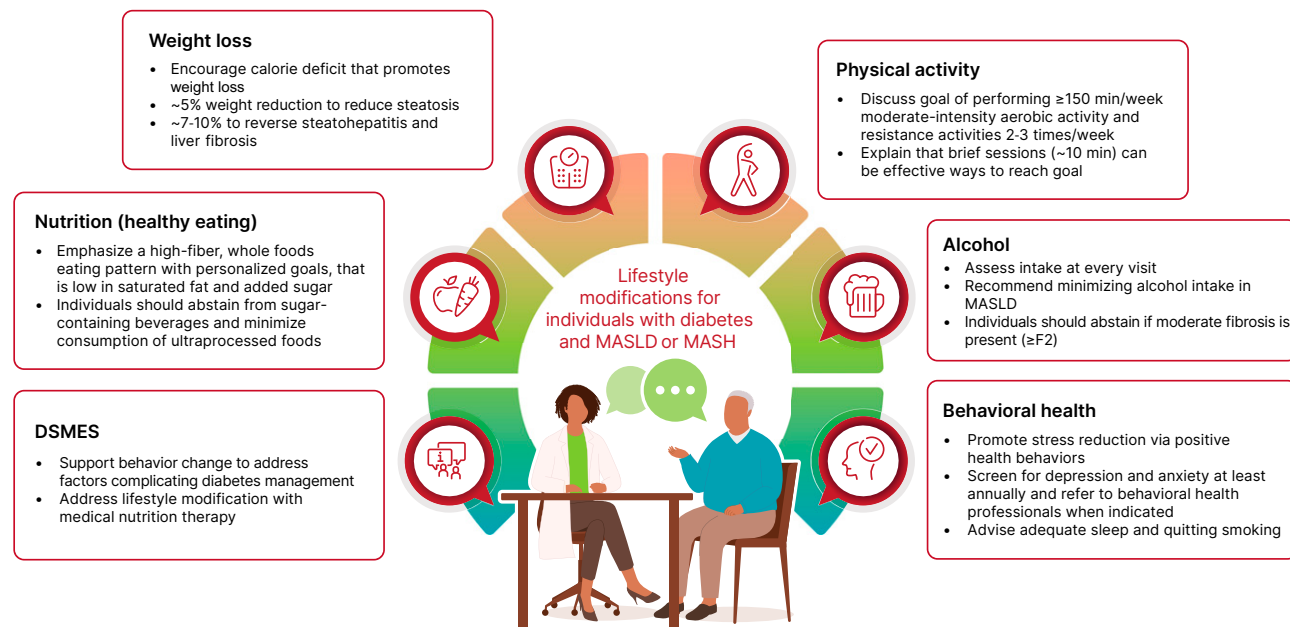


Figure 3—Lifestyle modification for individuals with prediabetes or diabetes and MASLD.

Physical Activity

Structured exercise has been shown to decrease insulin resistance, plasma aminotransferases, and steatosis in individuals with MASLD (133–136). Different exercise types and intensities can produce different outcomes, with aerobic activity potentially offering greater hepatic benefits than other types (133,134) and high-intensity activity improving MASH and fibrosis (137).

Although current guidelines recommend accumulating at least 150 min of moderate- or 75 min of vigorous-intensity activity weekly and performing resistance activities two to three times per week for individuals with diabetes or MASLD or MASH (126,138), care teams should personalize activity plans based on individual needs, goals, and preferences as well as provide resources to support activity self-efficacy and long-term adoption (126). Minimizing sedentary time and engaging in brief sessions (~10 min) of simple activities such as walking with the goal of meeting activity guidelines should be encouraged (126). Resistance training may prevent sarcopenia and functional decline (133,139).

Behavioral Health

Psychosocial care should be provided to all people with type 2 diabetes and MASLD to optimize health-related quality of life. There is a lack of large, high-quality studies for evidence-based best treatment recommendations for depression, anxiety, binge eating disorder, serious

mental illness, or substance use, specifically in MASLD (140). Drawing from the type 2 diabetes literature, evidence-based approaches include cognitive behavioral therapy, mindfulness-based therapy, and/or pharmacotherapy (126). All may be of help to treat mental health issues in adults with diabetes and MASLD that often overlap with obesity and its comorbidities, as well as with the use of obesogenic psychiatric medications. Behavioral health professionals should monitor outcomes systematically to assess progress and ongoing needs.

DSMES

DSMES services provided by a DCES have been shown to support behavior change in people with type 2 diabetes. DSMES should be offered at least annually to people with type 2 diabetes and MASLD (for more details, refer to ADA “Standards of Care in Diabetes—2025” [Standards of Care] [126]). While basic healthy eating guidance is provided during DSMES sessions, coordination with the RDN ensures that specific nutrition therapy related to the person’s liver disease is addressed (141).

Although there are limited data on behavioral weight loss interventions in MASLD (142), structured nutrition and exercise intervention in addition to health education should be offered to all people with MASLD (57,126,143–145). These interventions share similarities with strategies for the management of obesity

and for the prevention and treatment of type 2 diabetes (146). Literacy about fibrosis stage and risk of MASLD progression may improve adherence to lifestyle intervention (147–149).

Pharmacological Treatment of Obesity and Role of Metabolic Surgery in MASLD

Pharmacological Treatment of Obesity in MASLD

Together with lifestyle optimization, pharmacotherapy should always be considered in the management of people with diabetes with overweight or obesity and MASLD. Lifestyle modification alone often is unable to achieve or maintain long-term weight loss of the magnitude usually recommended to reverse steatohepatitis and fibrosis (>10%) (56,57,122).

Pharmacological therapy for obesity in MASLD should be individualized, potential risk-benefit and cost considered, and treatment strategies reassessed often over time. Figure 4 summarizes the management of MASLD in considering the severity of liver disease and the pharmacological options for obesity or type 2 diabetes with potential to reverse steatohepatitis, as well as MASH-specific therapies (i.e., resmetirom). GLP-1RA reduce cardiovascular disease, the main cause of death in MASLD (150), and offer renal protection to people with type 2 diabetes (see ADA Standards of Care [151,152]). Certain GLP-1RA also reduce cardiovascular disease in individuals

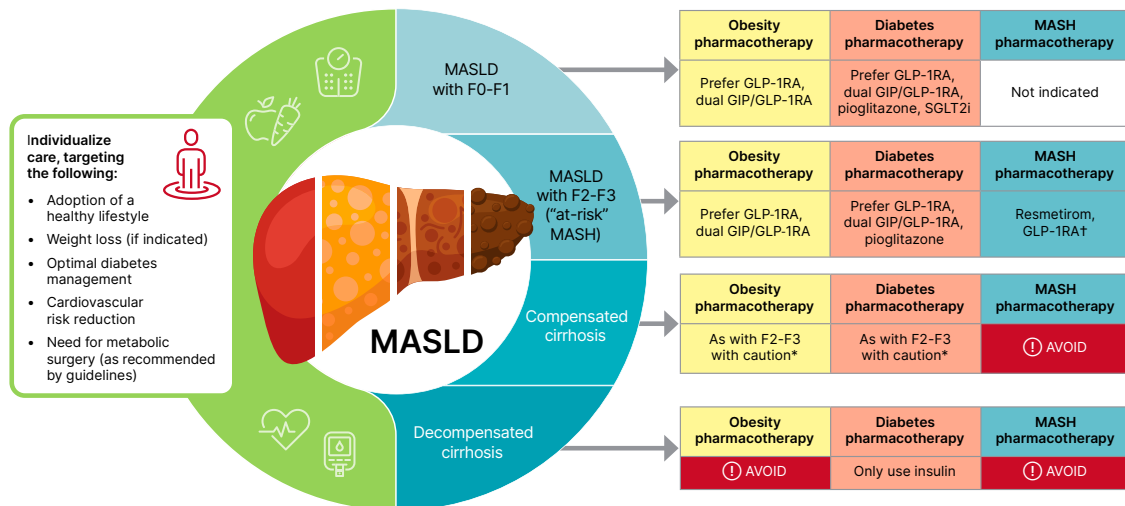


Figure 4—MASLD treatment algorithm for individuals with prediabetes or diabetes. Fibrosis stages: F0 and F1, mild or no liver fibrosis; F2, moderate fibrosis; F3, advanced fibrosis. CV, cardiovascular; SGLT2i, SGLT2 inhibitors. *Individualized care and close monitoring is needed in compensated cirrhosis given limited safety data available. †Only semaglutide among GLP-1RA has been reported to be of benefit in a phase 3 RCT with histological outcomes in MASH. Adapted from “Standards of Care of Diabetes—2025” (59).

diabetes (196,201). Pioglitazone improves left ventricular function (194,202) but may promote heart failure if inadvertently prescribed to individuals with preexisting congestive heart failure. Dose- and time-dependent increases in risk of fractures and bladder cancer have been reported, although the data for bladder cancer remain controversial (203).

Vitamin E may be considered for the treatment of MASH in selected individuals without diabetes (182), with effects significantly impacted by haptoglobin genotype (204), although when used in combination with pioglitazone in adults with diabetes it did not enhance pioglitazone's efficacy in comparison with earlier studies with the thiazolidinedione, and there is not enough evidence at this time for recommendation for people with type 2 diabetes (55–58,205). In a retrospective study in individuals with MASH and advanced fibrosis, it was reported that vitamin E was associated with less disease progression (206). However, controversy remains about a potential increase in hemorrhagic stroke and prostate cancer (207).

In at least six phase 2 RCTs, SGLT2 inhibitors were tested in individuals with type 2 diabetes and MASLD (dapagliflozin, empagliflozin, and canagliflozin, and smaller studies with others), and modest reductions in hepatic steatosis were consistently reported (e.g., mean of ~20% placebo-subtracted relative decrease in intrahepatic triglycerides) (164) (Table 5). Modest benefit was reported in an open-label trial with liver histological outcomes (208), while in another no improvement was noted (209). In a recent prospective study in 237 people with type 2 diabetes from diabetes clinics, with a mean follow up of ~4.5 years, it was reported that use of SGLT2 inhibitors was associated with less fibrosis progression (liver stiffness measured with transient elastography) (210). SGLT2 inhibitors have not been rigorously tested with histological outcomes in MASH, but their cardiometabolic benefits make them an attractive option for people with MASLD.

Glucose-lowering agents other than pioglitazone or GLP-1RA or dual GIP/GLP-1RA can be continued for glycemic management, as clinically indicated, but may not improve MASH (i.e., metformin) (56,57) or have not been tested in MASH

in paired liver biopsy trials (i.e., insulin, sulfonylureas, dipeptidyl peptidase 4 [DPP-4] inhibitors, meglitinides, or acarbose) (Table 5).

The prevalence of MASLD is increasing among people with type 1 diabetes, especially when associated with obesity (211), and weight gain appears to be linked to insulin resistance, hyperglycemia, and more difficult to manage diabetes (212). In one study an only 8% prevalence of steatosis was reported, measured with MRI, in adults with type 1 diabetes predominantly without obesity compared with an eightfold higher prevalence in those with type 2 diabetes (liver fibrosis was not measured) (213). A meta-analysis from 29 studies, including 390 individuals with type 1 diabetes and 10,487 individuals with type 2 diabetes, reported prevalence rates of fibrosis, measured with transient elastography, of 5.2% and 19.8%, respectively (4). The current recommendation is to screen for fibrosis in people with type 1 diabetes only in the context of risk factors for MASLD, in particular obesity, elevated plasma aminotransferases, or steatosis as an incidental finding (56,59). Treatment should focus on lifestyle modification that induces weight loss in individuals with overweight or obesity. Optimizing glycemic management with insulin therapy may reduce steatosis (155,164,214). Other diabetes medications (or resmetirom) have not been tested in this population.

MASH Pharmacotherapy

Resmetirom is a selective thyroid hormone receptor β (THR- β) agonist (215), approved in early 2024 for the treatment of MASH with fibrosis stages F2 and F3. Its THR- β isoform selectivity (a receptor isoform with expression predominately in liver, kidney, pituitary, and brain tissue) minimizes potential undesirable off-target THR- α -related effects in heart and bone tissues. Resmetirom decreases steatosis through not yet fully understood mechanisms such as enhancing mitochondrial function and improving the hepatic conversion of thyroxine (T4) to triiodothyronine. Administration for 52 weeks in 966 adults randomized 1:1:1 to oral resmetirom at a dose of 80 mg or 100 mg or placebo led to MASH resolution in up to 29.9% of participants receiving resmetirom compared with 9.7% on placebo ($P < 0.001$) (10). Fibrosis

improved in up to 25.9% and 14.2%, respectively ($P < 0.001$). Treatment initiation does not require a liver biopsy, and specific guidance has been developed for identification with NITs of adults with MASH with fibrosis stages F2 and F3 (i.e., LSM by imaging with VCTE or MRE) for whom therapy is suitable (216). Main exclusion criteria are compensated or decompensated cirrhosis, active liver diseases (i.e., autoimmune hepatitis or primary biliary cholangitis), suboptimally managed hypothyroidism or hyperthyroidism, or ongoing alcohol consumption of >20 g/day for women or >30 g/day for men. Nausea, vomiting, and diarrhea are the most frequent adverse events with resmetirom therapy. Resmetirom may lower free T4 levels by ~20% and increase two- to threefold sex hormone-binding globulin (SHBG) protein levels (10,216). Increasing SHBG in the setting of borderline or frank hypogonadism has the potential to exacerbate hypogonadism because it may alter the dynamics between bound and free testosterone, resulting in a decrease in biologically active hormone. Also, SHBG can potentially deliver testosterone directly to tissues with unknown biological effects on androgen-dependent organs (63,217). The long-term clinical significance of these hormonal changes remains to be determined (218). Baseline thyroid function testing prior to initiating therapy is recommended by the American Association for the Study of Liver Diseases (AASLD) (216), as hypothyroidism is common in the general population (~12%) and steatosis may be associated with hypothyroidism (55). Monitoring of thyroid function during resmetirom therapy should be based on clinical judgement. Of note, some people during the phase 3 trial had free T4 levels below normal (most often transient), needed resmetirom dose adjustments, or were started on levothyroxine (219). Because hypogonadism develops more often in older adults and in those with MASLD, clinicians should follow current guidelines (56,122,124) that recommend the evaluation of symptomatic individuals for hypogonadism on the basis of a fasting total testosterone and free testosterone concentration (ideally with liquid chromatography–mass spectrometry and equilibrium dialysis, respectively) (220) or consider an endocrinology consult.

There is limited information on combining resmetirom with medications often used for comorbidities in MASLD (e.g., pioglitazone, GLP-1RA, or dual GIP/GLP-1RA). People with obesity and type 2 diabetes should make it a priority to optimize lifestyle and medical management with a GLP-1RA, pioglitazone, or their combination or a dual GIP/GLP-1RA (tirzepatide) with potential benefits for steatohepatitis (59). Addition of resmetirom should be initiated by a hepatologist or gastroenterologist with expertise in MASH and within the context of an interprofessional team approach, cost-benefit assessment, and individual decision sharing. In monitoring resmetirom treatment recent guidance by AASLD should be followed (216).

SECTION 5. THE NEED TO DEVELOP INTERPROFESSIONAL TEAMS

Role of Primary Care

MASLD in type 2 diabetes is best managed by a coordinated health care team with expertise to address prevention, screening, diagnosis, lifestyle interventions, medication, and monitoring, led by the primary care physician (Fig. 5). Depending on the disease stage,

location, and resources in the area, the health care team may vary and even include expertise accessed remotely. Prevention is a critical first step, requiring awareness and expertise in managing diet, exercise, and obesity at the primary care level with support from dietitians, exercise physiologists, and behavioral health care professionals. Pharmacists can help by screening for obesogenic medications and suggesting pharmacologic interventions for obesity if appropriate. Diagnosis of early disease and eventual referral to a gastroenterologist or hepatologist, as per the diagnostic algorithm in Fig. 2, should become a routine component of type 2 diabetes care. A diagnosis of at-risk MASH may motivate behavior change and may be helpful for individuals for obtaining insurance coverage for more intensive behavioral and medical interventions.

Other valuable team members include obesity specialists in established weight loss programs and medical exercise programs, such as for cardiovascular or pulmonary rehabilitation. Mental health treatment and referral to behavioral health specialists can aid people with type 2 diabetes and MASLD who struggle with depression (140), which can hinder behavior change and weight

loss (Fig. 5). Suboptimally managed hyperglycemia should be managed with the combined efforts of an endocrinologist and diabetes educator. Even after an individual progresses to advanced fibrosis or cirrhosis and is under a liver specialist's care, the primary care and interprofessional teams must remain involved for management of behavioral and nutritional care and care for cardiometabolic risk factors and other MASLD-related comorbidities (56,57,59,126).

Role of the Endocrinologist/Diabetes Care Specialist

The endocrinologist/diabetes care specialist is essential in managing MASLD in people with type 2 diabetes (56,57,221). Given the increased risk of cardiometabolic complications (150,222,223) and advanced liver fibrosis in this population (1,21), these professionals are at the front line of recognizing MASLD and treating its comorbidities (224). MASLD is found to occur more often in people attending diabetes clinics in comparison with primary care, possibly because longstanding type 2 diabetes is much more common. Therefore, the endocrinologist is in a unique position to 1) lead efforts to screen and risk stratify people at risk

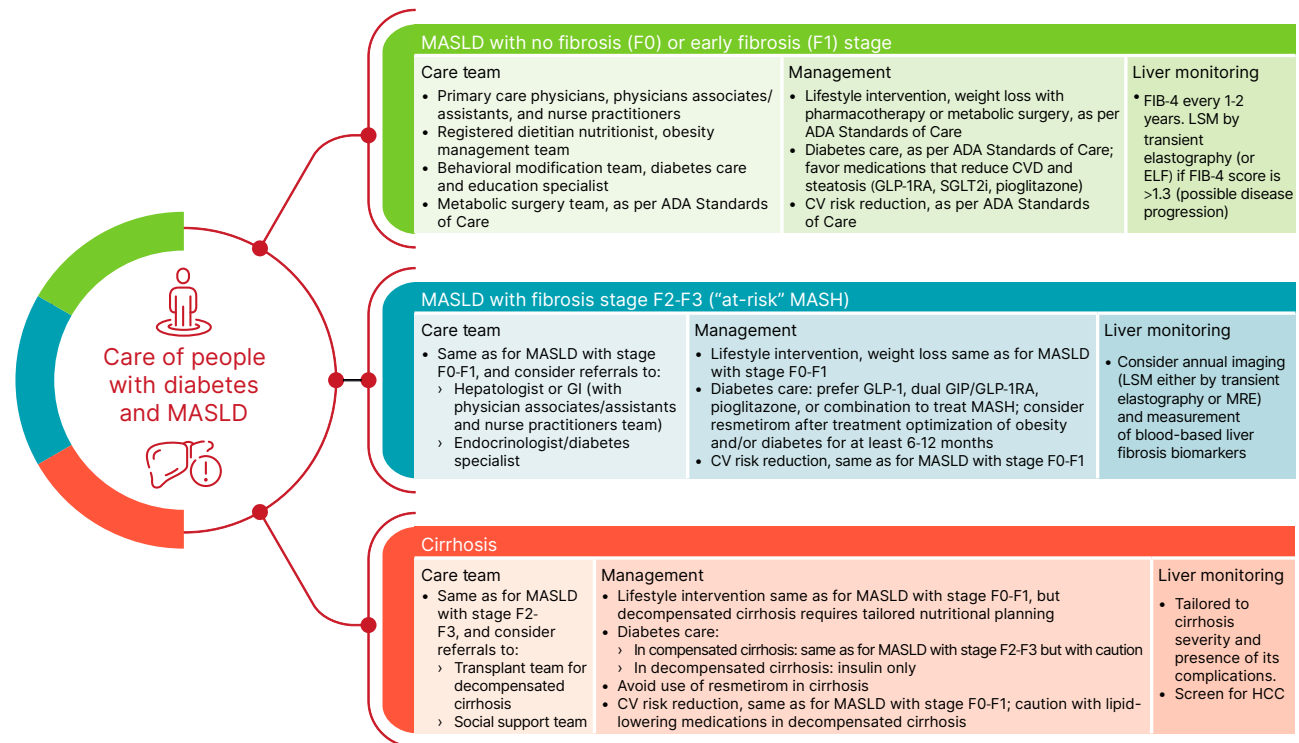


Figure 5—Interprofessional teams, management, and liver monitoring for care of individuals with diabetes and MASLD. CV, cardiovascular; CVD, cardiovascular disease; F0, no fibrosis; F1, mild fibrosis; F3, advanced/severe fibrosis; GI, gastroenterologist; SGLT2i, SGLT2 inhibitors.

SECTION 7. DIABETES AND HCC

In several retrospective and prospective studies, type 2 diabetes is independently associated with a two- to fourfold higher risk for HCC (31,177,253–257). Much of the association between diabetes and HCC may be explained by the development and progression of MASLD.

Although people with both diabetes and MASLD are among the highest-risk groups for HCC, the absolute risk of HCC is low and variable (258). Hence, current guidelines do not recommend screening for HCC in people with diabetes and MASLD unless there is evidence of cirrhosis. People with diabetes complications and/or suboptimal glycemic management, especially if they also have a high FIB-4 score, may be an important subgroup for close monitoring for future risk of cirrhosis (258,259). Duration of diabetes and other comorbid metabolic conditions also increased HCC risk in other studies.

Improved glycemic management to reduce cirrhosis and HCC burden in people with diabetes may hold promise but remains an understudied paradigm. Studies among individuals with type 2 diabetes have shown a reduction in HCC incidence with metformin but an increase with combination of metformin and a sulfonylurea or insulin, or a greater risk of HCC with oral agents combined with insulin therapy (259,260). Adequate glycemic management was associated with a 31% lower risk of HCC (259). The potential preventive effects of newer glucose-lowering medications for HCC are currently unknown, but this question warrants evaluation. While GLP-1RA, SGLT2 inhibitors, and pioglitazone are associated with lower rates of cirrhosis in population-based studies, their ability to prevent HCC is less clear (234,252,261). Overall, there is significant heterogeneity across observational studies, which, together with challenges in adjusting for multiple confounders, calls for caution in interpreting associations between diabetes medications and risk of HCC.

SECTION 8. ALCOHOL INTAKE AND LIVER HEALTH

Initial evaluation of people with cirrhosis includes an assessment of alcohol intake (Supplementary Table 3). In people with preexisting obesity and diabetes, alcohol use has a synergistic effect for worsening insulin resistance, chronic liver

injury, cirrhosis, HCC, and liver-related morbidity and mortality (132). Any alcohol use should be avoided in people with diabetes and chronic liver disease. Mild-to-moderate alcohol intake can serve as a cofactor for the development of steatohepatitis and fibrosis progression. Heavy alcohol intake may increase the risk of type 2 diabetes in genetically predisposed individuals by inducing hepatic and peripheral (i.e., muscle) insulin resistance and promoting a chronic increase in pancreatic β -cell demand. Alcohol intake can be defined as mild if <20 g/day for women and <30 g/day for men, moderate if between 21 and 39 g/day for women and between 31 and 59 g/day for men, or heavy if ≥ 40 g/day for women and ≥ 60 g/day for men. While earlier studies suggested a protective effect of alcohol use on cardiometabolic risk factors (262,263), subsequent studies of moderate alcohol use (defined broadly as >20 g/day) suggest lower odds of MASH resolution and increased risk for cirrhosis, HCC (264,265), and extrahepatic malignancies (266–268). Further, alcohol use may have a negative effect on glycemic management in people with diabetes (269,270), irrespective of the use of antidiabetes medications (271). Understanding of the impact of alcohol use (type, pattern, frequency, duration) in individuals with concomitant diabetes and liver disease is required.

CONCLUSIONS

It is now well established that adults with prediabetes or type 2 diabetes have the highest risk of developing MASLD. Approximately one in five people with type 2 diabetes have clinically significant fibrosis and are at high risk of developing cirrhosis from MASLD (i.e., has at-risk MASH), which is one of the leading reasons for liver transplantation in the U.S. MASLD is also associated with increased risk of HCC as well as extrahepatic malignancies and cardiovascular disease.

Individuals with prediabetes or type 2 diabetes should be risk stratified with a two-tier approach (FIB-4 \pm VCTE-LSM) for assessment of their risk of having at-risk MASH with clinically significant liver fibrosis or cirrhosis. This consensus report delivers the message that timely identification and proper management can prevent the progression of fibrosis to cirrhosis in people with prediabetes

and type 2 diabetes in the same way as already accepted for diabetes-related microvascular complications (retinopathy, nephropathy or neuropathy) or cardiovascular disease. With interprofessional care teams and clinician awareness and action, education, development of proper models of care, and proactive public health policies we hope to catalyze a shift in clinical practice that will improve outcomes and the quality of life of people with diabetes and MASLD.

Acknowledgments. The authors thank Alexandra M. Yacoubian (ADA) for administrative assistance and Michael Bonar (Leicester Diabetes Centre, Leicester, U.K.) and Charlie Franklin (Leicester Diabetes Centre) for figure design.

Funding. This statement was funded by ADA general revenue. C.R.R. has received honoraria for travel and speaker engagements from the ADA. M.B. has received research funding (to institution) from the ADA.

No other entity, including industry, provided support for this statement.

Duality of Interest. K.C. has received research support (to institution) from Boehringer Ingelheim, Echosens, Inventiva, Labcorp, and Perspectum. K.C. has served as a consultant for Aligos Therapeutics, Arrowhead, AstraZeneca, 89bio, Bristol-Myers Squibb, Boehringer Ingelheim, Eli Lilly, GlaxoSmithKline, Novo Nordisk, ProSciento, Sagimet Biosciences, Siemens USA, Zealand Pharma, and Terns Pharmaceuticals. M.F.A. has received research support (to institution) from Madrigal Pharmaceuticals, 89bio, Hanmi Pharmaceutical, Gilead Sciences, and Inventiva. M.F.A. has served as a consultant or advisory board member for Novo Nordisk, Hanmi Pharmaceutical, Inventiva, Madrigal Pharmaceuticals, and 89bio. C.M.A. has served as an advisory board member for Altimmune, BioAge Labs, Biolinq, CinFina Pharma, Cowen and Company, EPG Comm, Vida, Veru, Wave Life Sciences, Form Health, Fractyl Health, Gelesis, Eli Lilly, L-Nutra, NeuroBo Pharmaceuticals, Xeno, Novo Nordisk, Nutrisystem, Optum Rx, Pain Script, Palatin, The Pursuit By You, Redesign Health, and ReShape Lifesciences. D.B. has served as a co-investigator for clinical trials with Inventiva Pharma and Boehringer Ingelheim. D.B. also attended an advisory board meeting for Boehringer Ingelheim and has received honoraria for lectures from Novo Nordisk. K.D.C. has received research funding from BPGbio, Target RWE, and Merck. K.D.C. has served as an advisory board member or instructor/speaker for Target RWE. C.R.R. has been part of a focus group with Dexcom and is part of a steering committee funded by Boehringer Ingelheim and Eli Lilly. M.R. has received funding for travel, is part of a speaker's bureau, or served on advisory board for AstraZeneca, Boehringer Ingelheim, Echosens, Madrigal Pharmaceuticals, Merck Sharp & Dohme, Novo Nordisk, and Target RWE. A.J.S. has received consulting fees from Eli Lilly and has served as a consultant for Echosens, Abbott, Promed, GENFIT,

Satellite Bio, Corcept Therapeutics, Arrowhead, Boston Pharmaceuticals, Variant, Cascade, 89bio, AstraZeneca, Alnylam Pharmaceuticals, Regeneron Pharmaceuticals, Boehringer Ingelheim, Bristol-Myers Squibb, Genentech, Gilead Sciences, Histoindex, Janssen, Lipocine, Madrigal Pharmaceuticals, Merck, GlaxoSmithKline, Novartis, Akero Therapeutics, Novo Nordisk, PathAI, Pfizer, Poxel, Salix Pharmaceuticals, Myovant Sciences, Median Technologies, Sequana Medical, Surrozen, Takeda Pharmaceuticals, Terns Pharmaceuticals, and Zydus Pharmaceuticals. A.J.S. has received grant funding (to institution) from AstraZeneca, Bristol-Myers Squibb, Gilead Sciences, Intercept Pharmaceuticals, Mallinckrodt Pharmaceuticals, Merck, Ocelot, Novartis, and Salix Pharmaceuticals. A.J.S. has received royalties from Elsevier and UpToDate. A.J.S. also has stock options in Duress, GENFIT, Tiziana Life Sciences, and Inversago. J.H.S. has served as a consultant or advisory board member for Abbott, Bayer, Novo Nordisk, Sanofi, Eli Lilly, and Madrigal Pharmaceuticals. Z.M.Y. has received grant funding from Madrigal Pharmaceuticals and has served as a consultant for Madrigal Pharmaceuticals, Novo Nordisk, and Boehringer Ingelheim. No other potential conflicts of interest relevant to this article were reported.

Prior Presentation. Parts of this study were presented at the 84th Scientific Sessions of the ADA, Orlando, FL, 21–24 June 2024.

Handling Editors. The journal editor responsible for overseeing the review of the manuscript was John B. Buse.

References

- Lomonaco R, Godinez Leiva E, Bril F, et al. Advanced liver fibrosis is common in patients with type 2 diabetes followed in the outpatient setting: the need for systematic screening. *Diabetes Care* 2021;44:399–406
- Harrison SA, Gawrieh S, Roberts K, et al. Prospective evaluation of the prevalence of non-alcoholic fatty liver disease and steatohepatitis in a large middle-aged US cohort. *J Hepatol* 2021;75:284–291
- Ciardullo S, Monti T, Perseghin G. High prevalence of advanced liver fibrosis assessed by transient elastography among U.S. adults with type 2 diabetes. *Diabetes Care* 2021;44:519–525
- Ciardullo S, Perseghin G. Prevalence of elevated liver stiffness in patients with type 1 and type 2 diabetes: a systematic review and meta-analysis. *Diabetes Res Clin Pract* 2022;190:109981
- Stefan N, Cusi K. A global view of the interplay between non-alcoholic fatty liver disease and diabetes. *Lancet Diabetes Endocrinol* 2022;10:284–296
- Younossi ZM, Golabi P, Paik JM, Henry A, Van Dongen C, Henry L. The global epidemiology of nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH): a systematic review. *Hepatology* 2023;77:1335–1347
- Younossi ZM, Stepanova M, Al Shabeeb R, 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* 2024;8:e0352
- Stepanova M, Kumar A, Brandt P, et al. Impact of type 2 diabetes on the outcomes of solid organ transplantations in the U.S.: data from a national registry. *Diabetes Care* 2023;46:2162–2170
- Younossi ZM, Henry L. Understanding the burden of nonalcoholic fatty liver disease: time for action. *Diabetes Spectr* 2024;37:9–19
- Harrison SA, Bedossa P, Guy CD, et al.; MAESTRO-NASH Investigators. A phase 3, randomized, controlled trial of resmetirom in NASH with liver fibrosis. *N Engl J Med* 2024;390:497–509
- Sanyal AJ, Newsome PN, Kliers I, et al.; ESSENCE Study Group. Phase 3 trial: semaglutide in metabolic dysfunction-associated steatohepatitis. *N Engl J Med*. 30 April 2025 [Epub ahead of print]. DOI: 10.1056/NEJMoa2413258
- Cusi K, Budd J, Johnson E, Shubrook J. Making sense of the nonalcoholic fatty liver disease clinical practice guidelines: what clinicians need to know. *Diabetes Spectr* 2024;37:29–38
- Lazarus JV, Anstee QM, Hagström H, et al. Defining comprehensive models of care for NAFLD. *Nat Rev Gastroenterol Hepatol* 2021;18:717–729
- Lazarus JV, Mark HE, Anstee QM, et al.; NAFLD Consensus Consortium. Advancing the global public health agenda for NAFLD: a consensus statement. *Nat Rev Gastroenterol Hepatol* 2022;19:60–78
- Rinella ME, Lazarus JV, Ratzliff V, et al.; NAFLD Nomenclature consensus group. A multisociety Delphi consensus statement on new fatty liver disease nomenclature. *Hepatology* 2023;78:1966–1986
- Song SJ, Lai JC-T, Wong GL-H, Wong VW-S, Yip TC-F. Can we use old NAFLD data under the new MASLD definition? *J Hepatol* 2024;80:e54–e56
- 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
- Ciardullo S, Carbone M, Invernizzi P, Perseghin G. Exploring the landscape of steatotic liver disease in the general US population. *Liver Int* 2023;43:2425–2433
- Castera L, Cusi K. Diabetes and cirrhosis: current concepts on diagnosis and management. *Hepatology* 2023;77:2128–2146
- Alexopoulos A-S, Crowley MJ, Wang Y, et al. Glycemic control predicts severity of hepatocyte ballooning and hepatic fibrosis in nonalcoholic fatty liver disease. *Hepatology* 2021;74:1220–1233
- Barb D, Repetto EM, Stokes ME, Shankar SS, Cusi K. Type 2 diabetes mellitus increases the risk of hepatic fibrosis in individuals with obesity and nonalcoholic fatty liver disease. *Obesity (Silver Spring)* 2021;29:1950–1960
- Colomba J, Netedu SR, Lehoux-Dubois C, et al. Hepatic enzyme ALT as a marker of glucose abnormality in men with cystic fibrosis. *PLoS One* 2019;14:e0219855
- Zaharia OP, Strassburger K, Strom A, et al.; German Diabetes Study Group. Risk of diabetes-associated diseases in subgroups of patients with recent-onset diabetes: a 5-year follow-up study. *Lancet Diabetes Endocrinol* 2019;7:684–694
- Cusi K, Younossi Z, Roden M. From NAFLD to MASLD: promise and pitfalls of a new definition. *Hepatology* 2024;79:E13–E15
- Simmons RK, Alberti KGMM, Gale EAM, et al. The metabolic syndrome: useful concept or clinical tool? Report of a WHO Expert Consultation. *Diabetologia* 2010;53:600–605
- Sharma A, Godina Leiva E, Kalavalapalli S, et al. Obesity increases the risk of hepatic fibrosis in young adults with type 2 diabetes mellitus: the need to screen. *Obesity (Silver Spring)* 2024;32:1967–1974
- Parcha V, Heindl B, Kalra R, et al. Insulin resistance and cardiometabolic risk profile among nondiabetic American young adults: insights from NHANES. *J Clin Endocrinol Metab* 2022;107:e25–e37
- Younossi ZM, Alqahtani SA, Alswat K, et al.; Global NASH Council. Global survey of stigma among physicians and patients with nonalcoholic fatty liver disease. *J Hepatol* 2024;80:419–430
- 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
- Younossi ZM, Golabi P, Price JK, et al. The global epidemiology of nonalcoholic fatty liver disease and nonalcoholic steatohepatitis among patients with type 2 diabetes. *Clin Gastroenterol Hepatol* 2024;22:1999–2010.e8
- En Li Cho E, Ang CZ, Quek J, et al. Global prevalence of non-alcoholic fatty liver disease in type 2 diabetes mellitus: an updated systematic review and meta-analysis. *Gut* 2023;72:2138–2148
- Golabi P, Paik JM, Kumar A, 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
- Bell JA, Kivimaki M, Hamer M. Metabolically healthy obesity and risk of incident type 2 diabetes: a meta-analysis of prospective cohort studies. *Obes Rev* 2014;15:504–515
- Cuthbertson DJ, Koskinen J, Brown E, 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
- Pais R, Charlotte F, Fedchuk L, et al.; LIDO Study Group. A systematic review of follow-up biopsies reveals disease progression in patients with non-alcoholic fatty liver. *J Hepatol* 2013;59:550–556
- McPherson S, Hardy T, Henderson E, Burt AD, Day CP, Anstee QM. Evidence of NAFLD progression from steatosis to fibrosing-steatohepatitis using paired biopsies: implications for prognosis and clinical management. *J Hepatol* 2015;62:1148–1155
- Huang DQ, Wilson LA, Behling C, et al.; NASH Clinical Research Network. Fibrosis progression rate in biopsy-proven nonalcoholic fatty liver disease among people with diabetes versus people without diabetes: a multicenter study. *Gastroenterology* 2023;165:463–472.e5
- Castera L, Laouenan C, Vallet-Pichard A, et al.; QUID NASH investigators. High prevalence of NASH and advanced fibrosis in type 2 diabetes: a prospective study of 330 outpatients undergoing liver biopsies for elevated ALT, using a low threshold. *Diabetes Care* 2023;46:1354–1362
- Le MH, Le DM, Baez TC, et al. Global incidence of adverse clinical events in non-alcoholic fatty liver disease: a systematic review and meta-analysis. *Clin Mol Hepatol* 2024;30:235–246
- Paik JM, Henry L, Younossi Y, Ong J, Alqahtani S, Younossi ZM. The burden of nonalcoholic fatty

liver disease (NAFLD) is rapidly growing in every region of the world from 1990 to 2019. *Hepatol Commun* 2023;7:e0251

41. Rich NE, Noureddin M, Kanwal F, Singal AG. Racial and ethnic disparities in non-alcoholic fatty liver disease in the USA. *Lancet Gastroenterol Hepatol* 2021;6:422–424

42. Henry L, Paik J, Younossi ZM. Review article: the epidemiologic burden of non-alcoholic fatty liver disease across the world. *Aliment Pharmacol Ther* 2022;56:942–956

43. Noureddin M, Vipani A, Bressee C, 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

44. Kardashian A, Dodge JL, Terrault NA. Food insecurity is associated with mortality among U.S. adults with nonalcoholic fatty liver disease and advanced fibrosis. *Clin Gastroenterol Hepatol* 2022;20:2790–2799.e4

45. Paik JM, Duong S, Zelber-Sagi S, Lazarus JV, Henry L, Younossi ZM. Food insecurity, low household income, and low education level increase the risk of having metabolic dysfunction-associated fatty liver disease among adolescents in the United States. *Am J Gastroenterol* 2024; 119:1089–1101

46. Orci LA, Sanduzzi-Zamparelli M, Caballol B, et al. Incidence of hepatocellular carcinoma in patients with nonalcoholic fatty liver disease: a systematic review, meta-analysis, and meta-regression. *Clin Gastroenterol Hepatol* 2022;20: 283–292.e10

47. Younossi ZM, Stepanova M, Ong J, 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

48. Younossi ZM, Stepanova M, Saab S, et al. The impact of type 2 diabetes and obesity on the long-term outcomes of more than 85 000 liver transplant recipients in the US. *Aliment Pharmacol Ther* 2014;40:686–694

49. Stepanova M, Henry L, Younossi ZM. Economic burden and patient-reported outcomes of nonalcoholic fatty liver disease. *Clin Liver Dis* 2023;27:483–513

50. Younossi ZM, Golabi P, de Avila L, et al. The global epidemiology of NAFLD and NASH in patients with type 2 diabetes: a systematic review and meta-analysis. *J Hepatol* 2019;71:793–801

51. Kanwal F, Kramer JR, Mapakshi S, et al. Risk of hepatocellular cancer in patients with non-alcoholic fatty liver disease. *Gastroenterology* 2018;155:1828–1837.e2

52. Dulai PS, Singh S, Patel J, et al. Increased risk of mortality by fibrosis stage in nonalcoholic fatty liver disease: systematic review and meta-analysis. *Hepatology* 2017;65:1557–1565

53. Arab JP, Dirchwolf M, Álvares-da-Silva MR, et al. Latin American Association for the study of the liver (ALEH) practice guidance for the diagnosis and treatment of non-alcoholic fatty liver disease. *Ann Hepatol* 2020;19:674–690

54. Eslam M, Sarin SK, Wong VW-S, et al. The Asian Pacific Association for the Study of the Liver clinical practice guidelines for the diagnosis and management of metabolic associated fatty liver disease. *Hepatol Int* 2020;14:889–919

55. Kanwal F, Shubrook JH, Adams LA, et al. Clinical care pathway for the risk stratification

and management of patients with nonalcoholic fatty liver disease. *Gastroenterology* 2021;161:1657–1669

56. Cusi K, Isaacs S, Barb D, 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

57. Rinella ME, Neuschwander-Tetri BA, Siddiqui MS, et al. AASLD practice guidance on the clinical assessment and management of nonalcoholic fatty liver disease. *Hepatology* 2023;77:1797–1835

58. European Association for the Study of the Liver (EASL); European Association for the Study of Obesity (EASO). Clinical practice guidelines on the management of metabolic dysfunction-associated steatotic liver disease (MASLD). *J Hepatol* 2024;81:492–542

59. American Diabetes Association Professional Practice Committee. 4. Comprehensive medical evaluation and assessment of comorbidities: Standards of Care in Diabetes—2025. *Diabetes Care* 2025;48(Suppl. 1):S59–S85

60. Noureddin M, Jones C, Alkhoury N, Gomez EV, Dieterich DT, Rinella ME; NASHNET. Screening for nonalcoholic fatty liver disease in persons with type 2 diabetes in the United States is cost-effective: a comprehensive cost-utility analysis. *Gastroenterology* 2020;159:1985–1987.e4

61. Bril F, Ortiz-Lopez C, Lomonaco R, et al. Clinical value of liver ultrasound for the diagnosis of nonalcoholic fatty liver disease in overweight and obese patients. *Liver Int* 2015;35:2139–2146

62. Heba ER, Desai A, Zand KA, et al. Accuracy and the effect of possible subject-based confounders of magnitude-based MRI for estimating hepatic proton density fat fraction in adults, using MR spectroscopy as reference. *J Magn Reson Imaging* 2016;43:398–406

63. Goldman AL, Bhasin S, Wu FCW, Krishna M, Matsumoto AM, Jasuja R. A reappraisal of testosterone's binding in circulation: physiological and clinical implications. *Endocr Rev* 2017;38: 302–324

64. Mofrad P, Contos MJ, Haque M, et al. Clinical and histologic spectrum of nonalcoholic fatty liver disease associated with normal ALT values. *Hepatology* 2003;37:1286–1292

65. Maximos M, Bril F, Portillo Sanchez P, et al. The role of liver fat and insulin resistance as determinants of plasma aminotransferase elevation in nonalcoholic fatty liver disease. *Hepatology* 2015; 61:153–160

66. Verma S, Jensen D, Hart J, Mohanty SR. Predictive value of ALT levels for non-alcoholic steatohepatitis (NASH) and advanced fibrosis in non-alcoholic fatty liver disease (NAFLD). *Liver Int* 2013;33:1398–1405

67. Connors EE, Panagiotakopoulos L, Hofmeister MG, et al.; Contributors. Screening and testing for hepatitis B virus infection: CDC recommendations - United States, 2023. *MMWR Recomm Rep* 2023; 72:1–25

68. Cartwright EJ, Patel P, Kamili S, Wester C. Updated operational guidance for implementing CDC's recommendations on testing for hepatitis C virus infection. *MMWR Morb Mortal Wkly Rep* 2023;72:766–768

69. Siddiqui MS, Yamada G, Vuppalanchi R, et al.; NASH Clinical Research Network. Diagnostic

accuracy of noninvasive fibrosis models to detect change in fibrosis stage. *Clin Gastroenterol Hepatol* 2019;17:1877–1885.e5

70. McPherson S, Stewart SF, Henderson E, Burt AD, Day CP. Simple non-invasive fibrosis scoring systems can reliably exclude advanced fibrosis in patients with non-alcoholic fatty liver disease. *Gut* 2010;59:1265–1269

71. Unalp-Arida A, Ruhl CE. Liver fibrosis scores predict liver disease mortality in the United States population. *Hepatology* 2017;66:84–95

72. Hagström H, Talbäck M, Andreasson A, Walldius G, Hammar N. Repeated FIB-4 measurements can help identify individuals at risk of severe liver disease. *J Hepatol* 2020;73:1023–1029

73. Cholankeril G, Kramer JR, Chu J, et al. Longitudinal changes in fibrosis markers are associated with risk of cirrhosis and hepatocellular carcinoma in non-alcoholic fatty liver disease. *J Hepatol* 2023;78:493–500

74. Lee J, Vali Y, Boursier J, et al. Prognostic accuracy of FIB-4, NAFLD fibrosis score and APRI for NAFLD-related events: a systematic review. *Liver Int* 2021;41:261–270

75. Kamada Y, Muneke K, Nakahara T, et al.; Japan Study Group of NAFLD (JSG-NAFLD). The FIB-4 index predicts the development of liver-related events, extrahepatic cancers, and coronary vascular disease in patients with NAFLD. *Nutrients* 2022;15:66

76. Sanyal AJ, Munoz B, Cusi K, et al.; TARGET-NASH Investigators. Validation of a clinical risk-based classification system in a large nonalcoholic fatty liver disease real-world cohort. *Clin Gastroenterol Hepatol* 2023;21:2889–2900.e10

77. Anstee QM, Berentzen TL, Nitze LM, et al. Prognostic utility of Fibrosis-4 Index for risk of subsequent liver and cardiovascular events, and all-cause mortality in individuals with obesity and/or type 2 diabetes: a longitudinal cohort study. *Lancet Reg Health Eur* 2024;36:100780

78. Vali Y, Lee J, Boursier J, et al.; Liver Investigation: Testing Marker Utility in Steatohepatitis (LITMUS) consortium investigators. Biomarkers for staging fibrosis and non-alcoholic steatohepatitis in non-alcoholic fatty liver disease (the LITMUS project): a comparative diagnostic accuracy study. *Lancet Gastroenterol Hepatol* 2023;8:714–725

79. Udompap P, Therneau TM, Canning RE, Benson JT, Allen AM. Performance of American Gastroenterological Association Clinical Care Pathway for the risk stratification of patients with nonalcoholic fatty liver disease in the US population. *Hepatology* 2023;77:931–941

80. Boursier J, Hagström H, Ekstedt M, et al. Non-invasive tests accurately stratify patients with NAFLD based on their risk of liver-related events. *J Hepatol* 2022;76:1013–1020

81. Mózes FE, Lee JA, Selvaraj EA, et al.; LITMUS Investigators. Diagnostic accuracy of non-invasive tests for advanced fibrosis in patients with NAFLD: an individual patient data meta-analysis. *Gut* 2022;71:1006–1019

82. Sanyal AJ, Castera L, Wong VW-S. Noninvasive assessment of liver fibrosis in NAFLD. *Clin Gastroenterol Hepatol* 2023;21:2026–2039

83. Lin H, Lee HW, Yip TC-F, et al.; VCTE-Prognosis Study Group. Vibration-controlled transient elastography models to predict liver-related events in steatotic liver disease. *JAMA* 2024; 331:1287–1297

84. Guha IN, Parkes J, Roderick P, et al. Noninvasive markers of fibrosis in nonalcoholic fatty liver disease: validating the European Liver Fibrosis Panel and exploring simple markers. *Hepatology* 2008;47:455–460
85. Lichtiginghagen R, Pietsch D, Bantel H, Manns MP, Brand K, Bahr MJ. The Enhanced Liver Fibrosis (ELF) score: normal values, influence factors and proposed cut-off values. *J Hepatol* 2013;59:236–242
86. Vali Y, Lee J, Boursier J, et al.; LITMUS systematic review team. Enhanced liver fibrosis test for the non-invasive diagnosis of fibrosis in patients with NAFLD: a systematic review and meta-analysis. *J Hepatol* 2020;73:252–262
87. Sanyal AJ, Shankar SS, Yates KP, et al. Diagnostic performance of circulating biomarkers for non-alcoholic steatohepatitis. *Nat Med* 2023;29:2656–2664
88. Pearson M, Nobes J, Macpherson I, et al. Enhanced liver fibrosis (ELF) score predicts hepatic decompensation and mortality. *JHEP Rep* 2024;6:101062
89. Younossi ZM, Anstee QM, Wong VW-S, et al. The association of histologic and noninvasive tests with adverse clinical and patient-reported outcomes in patients with advanced fibrosis due to nonalcoholic steatohepatitis. *Gastroenterology* 2021;160:1608–1619.e13
90. Sanyal AJ, Harrison SA, Ratziu V, et al. The natural history of advanced fibrosis due to nonalcoholic steatohepatitis: data from the simtuzumab trials. *Hepatology* 2019;70:1913–1927
91. Patel P, Hossain F, Horsfall LU, et al. A pragmatic approach identifies a high rate of nonalcoholic fatty liver disease with advanced fibrosis in diabetes clinics and at-risk populations in primary care. *Hepatol Commun* 2018;2:893–905
92. Arai T, Takahashi H, Seko Y, et al.; Japan Study Group of Nonalcoholic Fatty Liver Disease (JSG-NAFLD). Accuracy of the enhanced liver fibrosis test in patients with type 2 diabetes mellitus and its clinical implications. *Clin Gastroenterol Hepatol* 2024;22:789–797.e8
93. Dulai PS, Sirlin CB, Loomba R. MRI and MRE for non-invasive quantitative assessment of hepatic steatosis and fibrosis in NAFLD and NASH: clinical trials to clinical practice. *J Hepatol* 2016;65:1006–1016
94. Andersson A, Kelly M, Imajo K, et al. Clinical utility of magnetic resonance imaging biomarkers for identifying nonalcoholic steatohepatitis patients at high risk of progression: a multicenter pooled data and meta-analysis. *Clin Gastroenterol Hepatol* 2022;20:2451–2461.e3
95. Park CC, Nguyen P, Hernandez C, et al. Magnetic resonance elastography vs transient elastography in detection of fibrosis and noninvasive measurement of steatosis in patients with biopsy-proven nonalcoholic fatty liver disease. *Gastroenterology* 2017;152:598–607.e2
96. Hsu C, Caussy C, Imajo K, et al. Magnetic resonance vs transient elastography analysis of patients with nonalcoholic fatty liver disease: a systematic review and pooled analysis of individual participants. *Clin Gastroenterol Hepatol* 2019;17:630–637.e8
97. Duman S, Kuru D, Gumusoy M, et al. A combination of non-invasive tests for the detection of significant fibrosis in patients with metabolic dysfunction-associated steatotic liver disease is not superior to magnetic resonance elastography alone. *Eur Radiol* 2024;34:3882–3888
98. Liang J-X, Ampuero J, Niu H, et al.; LITMUS Consortium Investigators. An individual patient data meta-analysis to determine cut-offs for and confounders of NAFLD-fibrosis staging with magnetic resonance elastography. *J Hepatol* 2023;79:592–604
99. de Franchis R, Bosch J, Garcia-Tsao G, Reiberger T, Ripoll C; Baveno VII Faculty. Baveno VII - renewing consensus in portal hypertension. *J Hepatol* 2022;76:959–974
100. Pons M, Augustin S, Scheiner B, et al. Noninvasive diagnosis of portal hypertension in patients with compensated advanced chronic liver disease. *Am J Gastroenterol* 2021;116:723–732
101. Sanyal AJ, Foucquier J, Younossi ZM, et al. Enhanced diagnosis of advanced fibrosis and cirrhosis in individuals with NAFLD using FibroScan-based Agile scores. *J Hepatol* 2023;78:247–259
102. Harrison SA, Ratziu V, Magnanensi J, et al. NIS2+, an optimisation of the blood-based biomarker NIS4 technology for the detection of at-risk NASH: a prospective derivation and validation study. *J Hepatol* 2023;79:758–767
103. Sanyal AJ, Magnanensi J, Majid Z, et al. NIS2+, an effective blood-based test for the diagnosis of at-risk nonalcoholic steatohepatitis in adults 65 years and older. *Hepatol Commun* 2023;7:e0223
104. Nouredin M, Truong E, Gornbein JA, et al. MRI-based (MAST) score accurately identifies patients with NASH and significant fibrosis. *J Hepatol* 2022;76:781–787
105. Nouredin N, Ajmera V, Bergstrom J, et al. MEFIB-Index and MAST-Score in the assessment of hepatic decompensation in metabolic dysfunction-associated steatosis liver disease-individual participant data meta-analyses. *Aliment Pharmacol Ther* 2023;58:856–865
106. Nouredin M, Truong E, Mayo R, et al. Serum identification of at-risk MASH: the metabolomics-advanced steatohepatitis fibrosis score (MASEF). *Hepatology* 2024;79:135–148
107. Vieira Barbosa J, Milligan S, Frick A, et al. Fibrosis-4 index as an independent predictor of mortality and liver-related outcomes in NAFLD. *Hepatol Commun* 2022;6:765–779
108. Guan L, Li L, Zou Y, Zhong J, Qiu L. Association between FIB-4, all-cause mortality, cardiovascular mortality, and cardiovascular disease risk among diabetic individuals: NHANES 1999-2008. *Front Cardiovasc Med* 2023;10:1172178
109. Lee HW, Wong GL-H, Kwok R, et al. Serial transient elastography examinations to monitor patients with type 2 diabetes: a prospective cohort study. *Hepatology* 2020;72:1230–1241
110. Targher G, Corey KE, Byrne CD, Roden M. The complex link between NAFLD and type 2 diabetes mellitus - mechanisms and treatments. *Nat Rev Gastroenterol Hepatol* 2021;18:599–612
111. Yuan S, Chen J, Li X, et al. Lifestyle and metabolic factors for nonalcoholic fatty liver disease: Mendelian randomization study. *Eur J Epidemiol* 2022;37:723–733
112. Shang Y, Grip ET, Modica A, et al. Metabolic syndrome traits increase the risk of major adverse liver outcomes in type 2 diabetes. *Diabetes Care* 2024;47:978–985
113. Ortiz-Lopez C, Lomonaco R, Orsak B, et al. Prevalence of prediabetes and diabetes and metabolic profile of patients with nonalcoholic fatty liver disease (NAFLD). *Diabetes Care* 2012;35:873–878
114. Lomonaco R, Bril F, Portillo-Sanchez P, et al. Metabolic impact of nonalcoholic steatohepatitis in obese patients with type 2 diabetes. *Diabetes Care* 2016;39:632–638
115. Singh S, Allen AM, Wang Z, Prokop LJ, Murad MH, Loomba R. Fibrosis progression in nonalcoholic fatty liver vs nonalcoholic steatohepatitis: a systematic review and meta-analysis of paired-biopsy studies. *Clin Gastroenterol Hepatol* 2015;13:643–654.e1-e19; quiz e39–e40
116. Shah AG, Lydecker A, Murray K, Tetri BN, Contos MJ, Sanyal AJ; Nash Clinical Research Network. Comparison of noninvasive markers of fibrosis in patients with nonalcoholic fatty liver disease. *Clin Gastroenterol Hepatol* 2009;7:1104–1112
117. Gawrieh S, Vilar-Gomez E, Wilson LA, et al.; NASH Clinical Research Network. Increases and decreases in liver stiffness measurement are independently associated with the risk of liver-related events in NAFLD. *J Hepatol* 2024;81:600–608
118. Pennisi G, Enea M, Falco V, et al. Noninvasive assessment of liver disease severity in patients with nonalcoholic fatty liver disease (NAFLD) and type 2 diabetes. *Hepatology* 2023;78:195–211
119. Newsome PN, Sasso M, Deeks JJ, et al. FibroScan-AST (FAST) score for the non-invasive identification of patients with non-alcoholic steatohepatitis with significant activity and fibrosis: a prospective derivation and global validation study. *Lancet Gastroenterol Hepatol* 2020;5:362–373
120. Rinella ME, Dufour J-F, Anstee QM, et al. Non-invasive evaluation of response to obeticholic acid in patients with NASH: results from the REGENERATE study. *J Hepatol* 2022;76:536–548
121. Zhang X, Yip TC-F, Wong GL-H, et al. Clinical care pathway to detect advanced liver disease in patients with type 2 diabetes through automated fibrosis score calculation and electronic reminder messages: a randomised controlled trial. *Gut* 2023;72:2364–2371
122. Younossi ZM, Corey KE, Lim JK. AGA clinical practice update on lifestyle modification using diet and exercise to achieve weight loss in the management of nonalcoholic fatty liver disease: expert review. *Gastroenterology* 2021;160:912–918
123. Zelber-Sagi S, Moore JB. Practical lifestyle management of nonalcoholic fatty liver disease for busy clinicians. *Diabetes Spectr* 2024;37:39–47
124. Vilar-Gomez E, Martinez-Perez Y, Calzadilla-Bertot L, et al. Weight loss through lifestyle modification significantly reduces features of nonalcoholic steatohepatitis. *Gastroenterology* 2015;149:367–378.e5; quiz e14–e15
125. Promrat K, Kleiner DE, Niemeier HM, et al. Randomized controlled trial testing the effects of weight loss on nonalcoholic steatohepatitis. *Hepatology* 2010;51:121–129
126. American Diabetes Association Professional Practice Committee. 5. Facilitating positive health behaviors and well-being to improve health outcomes: Standards of Care in Diabetes—2025. *Diabetes Care* 2025;48(Suppl. 1):S86–S127

127. Evert AB, Dennison M, Gardner CD, et al. Nutrition therapy for adults with diabetes or prediabetes: a consensus report. *Diabetes Care* 2019;42:731–754
128. Jensen T, Abdelmalek MF, Sullivan S, et al. Fructose and sugar: a major mediator of non-alcoholic fatty liver disease. *J Hepatol* 2018;68:1063–1075
129. Pugliese N, Plaz Torres MC, Petta S, Valenti L, Giannini EG, Aghemo A. Is there an 'ideal' diet for patients with NAFLD? *Eur J Clin Invest* 2022;52:e13659
130. Properi C, O'Sullivan TA, Sherriff JL, et al. Ad libitum Mediterranean and low-fat diets both significantly reduce hepatic steatosis: a randomized controlled trial. *Hepatology* 2018;68:1741–1754
131. Haigh L, Kirk C, El Gendy K, et al. The effectiveness and acceptability of Mediterranean diet and calorie restriction in non-alcoholic fatty liver disease (NAFLD): a systematic review and meta-analysis. *Clin Nutr* 2022;41:1913–1931
132. Blomdahl J, Nasr P, Ekstedt M, Kechagias S. Moderate alcohol consumption is associated with advanced fibrosis in non-alcoholic fatty liver disease and shows a synergistic effect with type 2 diabetes mellitus. *Metabolism* 2021;115:154439
133. Sargeant JA, Gray LJ, Bodicoat DH, et al. The effect of exercise training on intrahepatic triglyceride and hepatic insulin sensitivity: a systematic review and meta-analysis. *Obes Rev* 2018;19:1446–1459
134. Nam H, Yoo J-J, Cho Y, et al. Effect of exercise-based interventions in nonalcoholic fatty liver disease: a systematic review with meta-analysis. *Dig Liver Dis* 2023;55:1178–1186
135. Stine JG, DiJoseph K, Pattison Z, et al. Exercise training is associated with treatment response in liver fat content by magnetic resonance imaging independent of clinically significant body weight loss in patients with nonalcoholic fatty liver disease: a systematic review and meta-analysis. *Am J Gastroenterol* 2023;118:1204–1213
136. Orzi LA, Gariani K, Oldani G, Delaune V, Morel P, Toso C. Exercise-based interventions for nonalcoholic fatty liver disease: a meta-analysis and meta-regression. *Clin Gastroenterol Hepatol* 2016;14:1398–1411
137. Kistler KD, Brunt EM, Clark JM, Diehl AM, Sallis JF, Schwimmer JB; NASH CRN Research Group. Physical activity recommendations, exercise intensity, and histological severity of nonalcoholic fatty liver disease. *Am J Gastroenterol* 2011;106:460–468; quiz 469
138. Stine JG, Long MT, Corey KE, et al. Physical activity and nonalcoholic fatty liver disease: a roundtable statement from the American College of Sports Medicine. *Med Sci Sports Exerc* 2023;55:1717–1726
139. Hashida R, Kawaguchi T, Bekki M, et al. Aerobic vs. resistance exercise in non-alcoholic fatty liver disease: a systematic review. *J Hepatol* 2017;66:142–152
140. Shea S, Lionis C, Kite C, et al. Non-alcoholic fatty liver disease and coexisting depression, anxiety and/or stress in adults: a systematic review and meta-analysis. *Front Endocrinol (Lausanne)* 2024;15:1357664
141. Powers MA, Bardsley JK, Cypress M, et al. Diabetes self-management education and support in adults with type 2 diabetes: a consensus report of the American Diabetes Association, the Association of Diabetes Care & Education Specialists, the Academy of Nutrition and Dietetics, the American Academy of Family Physicians, the American Academy of PAs, the American Association of Nurse Practitioners, and the American Pharmacists Association. *Diabetes Care* 2020;43:1636–1649
142. Balakrishnan M, Liu K, Schmitt S, et al. Behavioral weight-loss interventions for patients with NAFLD: a systematic scoping review. *Hepatol Commun* 2023;7:e0224
143. Hamman RF, Wing RR, Edelstein SL, et al. Effect of weight loss with lifestyle intervention on risk of diabetes. *Diabetes Care* 2006;29:2102–2107
144. Koutoukidis DA, Astbury NM, Tudor KE, et al. Association of weight loss interventions with changes in biomarkers of nonalcoholic fatty liver disease: a systematic review and meta-analysis. *JAMA Intern Med* 2019;179:1262–1271
145. Wadden TA, Neiberg RH, Wing RR, et al.; Look AHEAD Research Group. Four-year weight losses in the Look AHEAD study: factors associated with long-term success. *Obesity (Silver Spring)* 2011;19:1987–1998
146. American Diabetes Association Professional Practice Committee. 8. Obesity and weight management for the prevention and treatment of type 2 diabetes: Standards of Care in Diabetes—2025. *Diabetes Care* 2025;48(Suppl. 1):S167–S180
147. Carrieri P, Mourad A, Marcellin F, et al. Knowledge of liver fibrosis stage among adults with NAFLD/NASH improves adherence to lifestyle changes. *Liver Int* 2022;42:984–994
148. Haigh L, Bremner S, Houghton D, et al. Barriers and facilitators to Mediterranean diet adoption by patients with nonalcoholic fatty liver disease in Northern Europe. *Clin Gastroenterol Hepatol* 2019;17:1364–1371.e3
149. Zelber-Sagi S, Bord S, Dror-Lavi G, et al. Role of illness perception and self-efficacy in lifestyle modification among non-alcoholic fatty liver disease patients. *World J Gastroenterol* 2017;23:1881–1890
150. Mantovani A, Csermely A, Petracca G, et al. Non-alcoholic fatty liver disease and risk of fatal and non-fatal cardiovascular events: an updated systematic review and meta-analysis. *Lancet Gastroenterol Hepatol* 2021;6:903–913
151. American Diabetes Association Professional Practice Committee. 10. Cardiovascular disease and risk management: Standards of Care in Diabetes—2025. *Diabetes Care* 2025;48(Suppl. 1):S207–S238
152. American Diabetes Association Professional Practice Committee. 11. Chronic kidney disease and risk management: Standards of Care in Diabetes—2025. *Diabetes Care* 2025;48(Suppl. 1):S239–S251
153. Lincoff AM, Brown-Frandsen K, Colhoun HM, et al.; SELECT Trial Investigators. Semaglutide and cardiovascular outcomes in obesity without diabetes. *N Engl J Med* 2023;389:2221–2232
154. Newsome PN, Buchholtz K, Cusi K, et al.; NN9931-4296 Investigators. A placebo-controlled trial of subcutaneous semaglutide in nonalcoholic steatohepatitis. *N Engl J Med* 2021;384:1113–1124
155. Gastaldelli A, Cusi K, Fernández Landó L, Bray R, Brouwers B, Rodríguez Á. Effect of tirzepatide versus insulin degludec on liver fat content and abdominal adipose tissue in people with type 2 diabetes (SURPASS-3 MRI): a substudy of the randomised, open-label, parallel-group, phase 3 SURPASS-3 trial. *Lancet Diabetes Endocrinol* 2022;10:393–406
156. Looma R, Hartman ML, Lawitz EJ, et al.; SYNERGY-NASH Investigators. Tirzepatide for metabolic dysfunction-associated steatohepatitis with liver fibrosis. *N Engl J Med* 2024;391:299–310
157. Armstrong MJ, Gaunt P, Aithal GP, et al.; LEAN trial team. Liraglutide safety and efficacy in patients with non-alcoholic steatohepatitis (LEAN): a multicentre, double-blind, randomised, placebo-controlled phase 2 study. *Lancet* 2016;387:679–690
158. Sanyal AJ, Bedossa P, Fraessdorf M, et al.; 1404-0043 Trial Investigators. A phase 2 randomized trial of survodutide in MASH and fibrosis. *N Engl J Med* 2024;391:311–319
159. Rosenstock J, Frias J, Jastreboff AM, et al. Retatrutide, a GIP, GLP-1 and glucagon receptor agonist, for people with type 2 diabetes: a randomised, double-blind, placebo and active-controlled, parallel-group, phase 2 trial conducted in the USA. *Lancet* 2023;402:529–544
160. Jastreboff AM, Kaplan LM, Frias JP, et al.; Retatrutide Phase 2 Obesity Trial Investigators. Triple-hormone-receptor agonist retatrutide for obesity - a phase 2 trial. *N Engl J Med* 2023;389:514–526
161. Sanyal AJ, Kaplan LM, Frias JP, et al. Triple hormone receptor agonist retatrutide for metabolic dysfunction-associated steatotic liver disease: a randomized phase 2a trial. *Nat Med* 2024;30:2037–2048
162. Wang H, Wang L, Cheng Y, Xia Z, Liao Y, Cao J. Efficacy of orlistat in non-alcoholic fatty liver disease: a systematic review and meta-analysis. *Biomed Rep* 2018;9:90–96
163. Patel Chavez C, Cusi K, Kadiyala S. The emerging role of glucagon-like peptide-1 receptor agonists for the management of NAFLD. *J Clin Endocrinol Metab* 2022;107:29–38
164. Genua I, Cusi K. Pharmacological approaches to nonalcoholic fatty liver disease: current and future therapies. *Diabetes Spectr* 2024;37:48–58
165. Courcoulas AP, Patti ME, Hu B, et al. Long-term outcomes of medical management vs bariatric surgery in type 2 diabetes. *JAMA* 2024;331:654–664
166. Sheng B, Truong K, Spittler H, Zhang L, Tong X, Chen L. The long-term effects of bariatric surgery on type 2 diabetes remission, microvascular and macrovascular complications, and mortality: a systematic review and meta-analysis. *Obes Surg* 2017;27:2724–2732
167. Lafarge J-C, Aron-Wisniewsky J, Pattou F, et al.; ARMMS-T2D Consortium. French National Authority for Health assessment of metabolic surgery for type 2 diabetes remission—a meta-analysis in patients with class I to III obesity. *Diabetes Metab* 2024;50:101495
168. Obeso-Fernández J, Millan-Alanis JM, Sáenz-Flores M, et al. Benefits of metabolic surgery on macrovascular outcomes in adult patients with type 2 diabetes: a systematic review and meta-analysis. *Surg Obes Relat Dis* 2024;20:202–212
169. Fakhry TK, Mhaskar R, Schwitalla T, Muradova E, Gonzalo JP, Murr MM. Bariatric surgery improves nonalcoholic fatty liver disease: a contemporary systematic review and meta-analysis. *Surg Obes Relat Dis* 2019;15:502–511

- clinical impact, and mechanisms. *Endocr Rev* 2018;39:629–663
212. Bailey R, Calhoun P, Garg SK. Weight gain and glycemic control in adults with type 1 diabetes in the T1D Exchange Registry. *Diabetes Technol Ther* 2024;26:156–160
213. Cusi K, Sanyal AJ, Zhang S, et al. Non-alcoholic fatty liver disease (NAFLD) prevalence and its metabolic associations in patients with type 1 diabetes and type 2 diabetes. *Diabetes Obes Metab* 2017;19:1630–1634
214. Cusi K, Sanyal AJ, Zhang S, et al. Different effects of basal insulin peglispro and insulin glargine on liver enzymes and liver fat content in patients with type 1 and type 2 diabetes. *Diabetes Obes Metab* 2016;18(Suppl. 2):50–58
215. Hatzigelaki E, Paschou SA, Schön M, Psaltopoulou T, Roden M. NAFLD and thyroid function: pathophysiological and therapeutic considerations. *Trends Endocrinol Metab* 2022;33:755–768
216. Chen VL, Morgan TR, Rotman Y, et al. Resmetirom therapy for metabolic dysfunction-associated steatotic liver disease: October 2024 updates to AASLD practice guidance. *Hepatology* 2025;81:312–320
217. Guzelce EC, Galbiati F, Goldman AL, Gattu AK, Basaria S, Bhasin S. Accurate measurement of total and free testosterone levels for the diagnosis of androgen disorders. *Best Pract Res Clin Endocrinol Metab* 2022;36:101683
218. Cusi K. Selective agonists of thyroid hormone receptor beta for the treatment of NASH. *N Engl J Med* 2024;390:559–561
219. Center for Drug Evaluation and Research. Application Number: 217785Orig1s000. NDA 217785: REZDIFFRA (Resmetirom): Integrated Review. U.S. Food & Drug Administration. Accessed 16 August 2024. Available from https://www.accessdata.fda.gov/drugsatfda_docs/nda/2024/217785Orig1s000IntegratedR.pdf
220. Bhasin S, Brito JP, Cunningham GR, et al. Testosterone therapy in men with hypogonadism: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab* 2018;103:1715–1744
221. Kanwal F, Shubrook JH, Younossi Z, et al. Preparing for the NASH epidemic: a call to action. *Metabolism* 2021;122:154822
222. Muzurović E, Peng CC-H, Belanger MJ, Sanoudou D, Mikhailidis DP, Mantzoros CS. Nonalcoholic fatty liver disease and cardiovascular disease: a review of shared cardiometabolic risk factors. *Hypertension* 2022;79:1319–1326
223. Long MT, Zhang X, Xu H, et al. Hepatic fibrosis associates with multiple cardiometabolic disease risk factors: the Framingham Heart Study. *Hepatology* 2021;73:548–559
224. Cusi K. Nonalcoholic fatty liver disease in diabetes: a call to action. *Diabetes Spectr* 2024;37:5–7
225. Younossi ZM, Henry L, Isaacs S, Cusi K. Identification of high-risk patients with nonalcoholic fatty liver disease in endocrinology clinics. *Endocr Pract* 2023;29:912–918
226. Academy Quality Management Committee. Academy of Nutrition and Dietetics: revised 2017 scope of practice for the registered dietitian nutritionist. *J Acad Nutr Diet* 2018;118:141–165
227. Wlazlo N, Beijers HJBH, Schoon EJ, Sauerwein HP, Stehouwer CDA, Bravenboer B. High prevalence of diabetes mellitus in patients with liver cirrhosis. *Diabet Med* 2010;27:1308–1311
228. Lee WG, Wells CI, McCall JL, Murphy R, Plank LD. Prevalence of diabetes in liver cirrhosis: a systematic review and meta-analysis. *Diabetes Metab Res Rev* 2019;35:e3157
229. Makol A, Kanthaje S, Dhiman RK, Kalra N, Chawla YK, Chakraborti A. Association of liver cirrhosis severity with type 2 diabetes mellitus in hepatocellular carcinoma. *Exp Biol Med (Maywood)* 2018;243:323–326
230. Chhabra S, Singh SP, Singh A, et al. Diabetes mellitus increases the risk of significant hepatic fibrosis in patients with non-alcoholic fatty liver disease. *J Clin Exp Hepatol* 2022;12:409–416
231. Mota M, Banini BA, Cazanave SC, Sanyal AJ. Molecular mechanisms of lipotoxicity and glucotoxicity in nonalcoholic fatty liver disease. *Metabolism* 2016;65:1049–1061
232. Ferdous S-E, Ferrell JM. Pathophysiological relationship between type 2 diabetes mellitus and metabolic dysfunction-associated steatotic liver disease: novel therapeutic approaches. *Int J Mol Sci* 2024;25:8731
233. Gancheva S, Roden M, Castera L. Diabetes as a risk factor for MASH progression. *Diabetes Res Clin Pract* 2024;217:111846
234. Khanmohammadi S, Habibzadeh A, Kamrul-Hasan ABM, Schuermans A, Kuchay MS. Glucose-lowering drugs and liver-related outcomes among individuals with type 2 diabetes: a systematic review of longitudinal population-based studies. *Diabet Med* 2024;41:e15437
235. American Diabetes Association Professional Practice Committee. 2. Diagnosis and classification of diabetes: Standards of Care in Diabetes—2025. *Diabetes Care* 2025;48(Suppl. 1):S27–S49
236. American Diabetes Association Professional Practice Committee. 7. Diabetes technology: Standards of Care in Diabetes—2025. *Diabetes Care* 2025;48(Suppl. 1):S146–S166
237. Lee J-Y, Kim Y-E, Han K, et al. Analysis of severe hypoglycemia among adults with type 2 diabetes and nonalcoholic fatty liver disease. *JAMA Netw Open* 2022;5:e220262
238. Yen F-S, Hou M-C, Liu J-S, Hsu C-C, Hwu C-M. Severe hypoglycemia in patients with liver cirrhosis and type 2 diabetes. *Front Med (Lausanne)* 2022;9:962337
239. American Diabetes Association Professional Practice Committee. 6. Glycemic goals and hypoglycemia: Standards of Care in Diabetes—2025. *Diabetes Care* 2025;48(Suppl. 1):S128–S145
240. Tuo S, Yeo YH, Chang R, et al. Prevalence of and associated factors for sarcopenia in patients with liver cirrhosis: a systematic review and meta-analysis. *Clin Nutr* 2024;43:84–94
241. Costa D, Lourenço J, Monteiro AM, et al. Clinical performance of flash glucose monitoring system in patients with liver cirrhosis and diabetes mellitus. *Sci Rep* 2020;10:7460
242. Honda F, Hiramatsu A, Hyogo H, et al. Evaluation of glycemic variability in chronic liver disease patients with type 2 diabetes mellitus using continuous glucose monitoring. *PLoS One* 2018;13:e0195028
243. Macías-Rodríguez RU, Illaraza-Lomelí H, Ruiz-Margáin A, et al. Changes in hepatic venous pressure gradient induced by physical exercise in cirrhosis: results of a pilot randomized open clinical trial. *Clin Transl Gastroenterol* 2016;7:e180
244. Berzigotti A, Albillos A, Villanueva C, et al.; Ciberehd SportDiet Collaborative Group. Effects of an intensive lifestyle intervention program on portal hypertension in patients with cirrhosis and obesity: the SportDiet study. *Hepatology* 2017;65:1293–1305
245. Locklear CT, Golabi P, Gerber L, Younossi ZM. Exercise as an intervention for patients with end-stage liver disease: systematic review. *Medicine (Baltimore)* 2018;97:e12774
246. Piguat A-C, Saran U, Simillion C, et al. Regular exercise decreases liver tumors development in hepatocyte-specific PTEN-deficient mice independently of steatosis. *J Hepatol* 2015;62:1296–1303
247. Zamanian-Azodi M, Khatoun Hajisayah S, Razzaghi M, Rezaei-Tavirani M. Introducing physical exercise as a potential strategy in liver cancer prevention and development. *Gastroenterol Hepatol Bed Bench* 2021;14:317–322
248. American Diabetes Association Professional Practice Committee. 9. Pharmacologic approaches to glycemic treatment: Standards of Care in Diabetes—2025. *Diabetes Care* 2025;48(Suppl. 1):S181–S206
249. Loomba R, Abdelmalek MF, Armstrong MJ, et al.; NN9931-4492 Investigators. Semaglutide 2.4 mg once weekly in patients with non-alcoholic steatohepatitis-related cirrhosis: a randomised, placebo-controlled phase 2 trial. *Lancet Gastroenterol Hepatol* 2023;8:511–522
250. Lawitz EJ, Fraessdorf M, Neff GW, et al.; NCT05296733 Investigators. Efficacy, tolerability and pharmacokinetics of survodutide, a glucagon/glucagon-like peptide-1 receptor dual agonist, in cirrhosis. *J Hepatol* 2024;81:837–846
251. Kawamori R, Kadowaki T, Onji M, Seino Y, Akanuma Y, PRACTICAL Study Group. Hepatic safety profile and glycemic control of pioglitazone in more than 20,000 patients with type 2 diabetes mellitus: postmarketing surveillance study in Japan. *Diabetes Res Clin Pract* 2007;76:229–235
252. Kanwal F, Kramer JR, Li L, et al. GLP-1 receptor agonists and risk for cirrhosis and related complications in patients with metabolic dysfunction-associated steatotic liver disease. *JAMA Intern Med* 2024;184:1314–1323
253. El-Serag HB, Hampel H, Javadi F. The association between diabetes and hepatocellular carcinoma: a systematic review of epidemiologic evidence. *Clin Gastroenterol Hepatol* 2006;4:369–380
254. Simon TG, King LY, Chong DQ, et al. Diabetes, metabolic comorbidities, and risk of hepatocellular carcinoma: results from two prospective cohort studies. *Hepatology* 2018;67:1797–1806
255. Zoppini G, Fedeli U, Gennaro N, Saugo M, Targher G, Bonora E. Mortality from chronic liver diseases in diabetes. *Am J Gastroenterol* 2014;109:1020–1025
256. Llovet JM, Willoughby CE, Singal AG, et al. Nonalcoholic steatohepatitis-related hepatocellular carcinoma: pathogenesis and treatment. *Nat Rev Gastroenterol Hepatol* 2023;20:487–503
257. Huang DQ, Nouredin N, Ajmera V, et al. Type 2 diabetes, hepatic decompensation, and hepatocellular carcinoma in patients with non-alcoholic fatty liver disease: an individual participant-level data meta-analysis. *Lancet Gastroenterol Hepatol* 2023;8:829–836

258. Ye F, Chen L, Zheng X. Diabetes and the risk of cirrhosis and HCC: an analysis of the UK Biobank. *Hepatol Commun* 2023;7:e0280
259. Kramer JR, Natarajan Y, Dai J, et al. Effect of diabetes medications and glycemic control on risk of hepatocellular cancer in patients with nonalcoholic fatty liver disease. *Hepatology* 2022;75:1420–1428
260. Singh S, Singh PP, Singh AG, Murad MH, Sanchez W. Anti-diabetic medications and the risk of hepatocellular cancer: a systematic review and meta-analysis. *Am J Gastroenterol* 2013;108:881–891; quiz 892
261. Wester A, Shang Y, Toresson Grip E, Matthews AA, Hagström H. Glucagon-like peptide-1 receptor agonists and risk of major adverse liver outcomes in patients with chronic liver disease and type 2 diabetes. *Gut* 2024;73:835–843
262. Gepner Y, Golan R, Harman-Boehm I, et al. Effects of initiating moderate alcohol intake on cardiometabolic risk in adults with type 2 diabetes: a 2-year randomized, controlled trial. *Ann Intern Med* 2015;163:569–579
263. Baliunas DO, Taylor BJ, Irving H, et al. Alcohol as a risk factor for type 2 diabetes: a systematic review and meta-analysis. *Diabetes Care* 2009;32:2123–2132
264. Yuan J-M, Govindarajan S, Arakawa K, Yu MC. Synergism of alcohol, diabetes, and viral hepatitis on the risk of hepatocellular carcinoma in blacks and whites in the U.S. *Cancer* 2004;101:1009–1017
265. Hassan MM, Hwang L-Y, Hatten CJ, et al. Risk factors for hepatocellular carcinoma: synergism of alcohol with viral hepatitis and diabetes mellitus. *Hepatology* 2002;36:1206–1213
266. Agabio R, Madeddu C, Contu P, et al. Alcohol consumption is a modifiable risk factor for breast cancer: are women aware of this relationship? *Alcohol Alcohol* 2022;57:533–539
267. Bongaerts BWC, de Goeij AFPM, van den Brandt PA, Weijnenberg MP. Alcohol and the risk of colon and rectal cancer with mutations in the K-ras gene. *Alcohol* 2006;38:147–154
268. Ortolá R, Sotos-Prieto M, García-Esquinas E, Galán I, Rodríguez-Artalejo F. Alcohol consumption patterns and mortality among older adults with health-related or socioeconomic risk factors. *JAMA Netw Open* 2024;7:e2424495
269. Mekary RA, Rimm EB, Giovannucci E, et al. Joint association of glycemic load and alcohol intake with type 2 diabetes incidence in women. *Am J Clin Nutr* 2011;94:1525–1532
270. Murata C, Suzuki Y, Muramatsu T, et al. Inactive aldehyde dehydrogenase 2 worsens glycemic control in patients with type 2 diabetes mellitus who drink low to moderate amounts of alcohol. *Alcohol Clin Exp Res* 2000;24:55–115
271. Ye Q, Ouyang X, Qin Z, et al. The association between alcohol drinking and glycemic management among people with type 2 diabetes in China. *J Diabetes Investig* 2024;15:237–244