*Liver International*

WILEY

Liver INTERNATIONAL

ORIGINAL ARTICLE OPEN ACCESS

# Metabolic Dysfunction–Associated Steatohepatitis Diagnosis and Management in Germany: Insights From an Expert Consensus Panel

Yestle Kim[1] | Peter Rydqvist[1] | Thomas Ramezani[1] | Jennifer S. Haas[2] | Heike Bantel[3] | Peter Buggisch[4] | Andreas Geier[5] | Wolf-Peter Hofmann[6] | Stefan Mauss[7] | Elke Roeb[8] | Jörn M. Schattenberg[9] | Karl-Georg Simon[10] | Norbert Stefan[11] | Katja Deterding[3] | Johannes Wiegand[12] | Anita Pathil[13] | Frank Tacke[14]

[1]Health Economics and Outcomes Research, Madrigal Pharmaceuticals Inc, West Conshohocken, Pennsylvania, USA | [2]EU Real World Evidence, PharmaLex GmbH (former Xcenda GmbH), Hannover, Germany | [3]Department of Gastroenterology, Hepatology, Infectious Diseases and Endocrinology, Hannover Medical School, Hannover, Germany | [4]Medical Care Center (MVZ) Ifi-Institut, Asklepios Clinic St. Georg, Hamburg, Germany | [5]Department of Medicine II – Hepatology, University Hospital Würzburg, Würzburg, Germany | [6]Gastroenterology Medical Center at Bayerischer Platz, Berlin, Germany | [7]Medical Care Center, Düsseldorf, Germany | [8]Gastroenterology, Medical Clinic II, University Hospital Gießen, Gießen, Germany | [9]Department of Internal Medicine II, Saarland University Hospital, Homburg, Germany | [10]Leverkusen Gastroenterology Group Practice (Medical Care Center (MVZ) Gastroenterologie Leverkusen GbR), Leverkusen-Schlebusch, Germany | [11]Department of Internal Medicine IV – Diabetology, Endocrinology, Nephrology, University Hospital Tübingen, Tübingen, Germany | [12]Department of Oncology, Gastroenterology, Hepatology and Pneumology, University Hospital Leipzig, Leipzig, Germany | [13]Medical Clinic 1, University Hospital Frankfurt, Frankfurt am Main, Germany | [14]Medical Department, Division of Hepatology and Gastroenterology, Charité - Universitätsmedizin Berlin, Campus Virchow-Klinikum (CVK) and Campus Charité Mitte (CCM), Berlin, Germany

**Correspondence:** Yestle Kim (ykim@madrigalpharma.com)

**Received:** 30 April 2025 | **Revised:** 30 June 2025 | **Accepted:** 7 July 2025

**Handling Editor:** Luca Valenti

**Funding:** Madrigal Pharmaceuticals Inc. provided the funding for this research, which was conducted by PharmaLex GmbH (former Xcenda GmbH), part of Cencora Inc. H.B., P.B., A.G., W.-P.H., S.M., E.R., J.M.S., K.-G.S., N.S., K.D., J.W., A.P.-W. as well as F.T. have received consulting fees from Madrigal Pharmaceuticals Inc.

**Keywords:** MASH | MASLD | NAFLD | NASH | non-invasive tests

## ABSTRACT

**Background:** Metabolic dysfunction–associated steatotic liver disease (MASLD) is a major cause of chronic liver disease. Metabolic dysfunction-associated steatohepatitis (MASH), a progressive form of MASLD, can lead to fibrosis and cirrhosis. The incidence and burden of MASH in Germany are expected to double by 2030, while diagnostic and management challenges persist. Expert consensus on diagnostic strategies and treatment modalities in MASLD and MASH is required.

**Objectives:** The panel aimed to gather insights and consensus on the diagnostic pathway and current treatment modalities for MASH in Germany.

**Abbreviations:** AASLD, American Association for the Study of Liver Diseases; BARD, BMI-AST/ALT-Ratio-Diabetes Score; CAP, controlled attenuation parameter; CT, computed tomography; DGVS, Deutsche Gesellschaft für Gastroenterologie, Verdauungs- und Stoffwechselkrankheiten; EASD, European Association for the Study of Diabetes; EASL, European Association for the Study of the Liver; EASO, European Association for the Study of Obesity; ELF, enhanced liver fibrosis; FDA, U.S. Food and Drug Administration; FIB4, Fibrosis-4 Index; GIP, gastric inhibitory polypeptide; GLP-1, glucagon-like peptide-1; HCC, hepatocellular carcinoma; HRQoL, health-related quality of life; LFT, liver function test; LSM, liver stiffness measurement; MASH, metabolic dysfunction–associated steatohepatitis; MASL, metabolic dysfunction–associated steatotic liver; MASLD, metabolic dysfunction–associated steatotic liver disease; MRE, magnetic resonance elastography; MRI, magnetic resonance imaging; NAFLD, nonalcoholic fatty liver disease; NAS, NAFLD activity score; QOL, quality of life; SAF, steatosis activity and fibrosis; SGLT-2, sodium glucose transporter-2; VCTE, vibration controlled transient elastography.

**Methods:** A three-round web-based survey, integrating Delphi panel methodology with a standard survey, was conducted from February to May 2024 to reach consensus on predefined questions. The survey involved 12 gastroenterology, diabetology and/or hepatology specialists in Germany.

**Results:** The Delphi panel revealed that ~75% of MASH patients in Germany remain undiagnosed. Non-invasive measures, such as fibrosis scores (values from clinical and imaging tests to assess fibrosis), liver enzyme tests and liver stiffness measurement, were primary methods for diagnosing and monitoring MASH patients. Lifestyle modifications were the primary management strategy, given the absence of approved pharmacological treatments for MASH. The panel also highlighted significant challenges in managing MASH, including the lack of approved medications and the difficulty in sustaining lifestyle changes.

**Conclusions:** The survey underscores the substantial underdiagnosis of MASH and the reliance on non-invasive diagnostic methods in Germany. The lack of approved treatments necessitates a focus on lifestyle modifications and comorbidity management. The Delphi panel's insights call for enhanced screening, early detection and standardised algorithms to improve patient outcomes.

**Summary**

- Metabolic dysfunction–associated steatotic liver disease (MASLD) is a leading cause of chronic liver disease globally and is closely linked to metabolic issues like obesity and type 2 diabetes.
- This study highlights the challenges in diagnosing and managing MASLD, particularly its severe form, MASH, in Germany.
- Using a web-based survey integrating the Delphi panel methodology, the research identifies a critical need for standardised diagnostic criteria and treatment strategies as there are currently no approved medications, and most management relies on lifestyle changes.
- The findings emphasise the importance of early detection to prevent progression to more severe liver conditions.

## 1 | Introduction

Metabolic dysfunction–associated steatotic liver disease (MASLD) is the most prevalent cause of chronic liver disease worldwide [1]. The condition is defined by the presence of hepatic steatosis, with at least one cardiometabolic risk factor and no other cause of liver steatosis. MASLD encompasses various forms, including isolated liver steatosis (metabolic dysfunction-associated steatotic liver, MASL) and metabolic dysfunction-associated steatohepatitis (MASH) [2, 3][1]. MASH is a progressive form of MASLD characterised by hepatocellular ballooning and lobular inflammation, associated with liver fibrosis, cirrhosis, and hepatocellular carcinoma (HCC) and intrahepatic cholangiocellular carcinoma upon progression [2, 4, 5]. The global prevalence of MASLD is around 30% [6], with a prevalence in Germany of approximately 23% for MASLD and 4% for MASH as of 2016, based on Markov projections [7].

MASLD and MASH have a bidirectional relationship with metabolic comorbidities such as obesity, type 2 diabetes, hyperlipidaemia and metabolic syndrome, creating a substantial burden on patients and healthcare systems [5, 8–10], with the majority of costs being attributed to later disease stages of MASH [8]. Among the various forms of MASLD, patients with MASH are prone to progressive liver disease, with approximately 20% of these patients potentially progressing to end-stage liver disease. Specifically, the disease can progress to cirrhosis, HCC, liver transplantation, and death, highlighting the importance of early diagnosis and treatment [11, 12].

In recent years, MASLD and MASH have emerged as a leading cause of liver transplantation, particularly for women, individuals over 55 years of age and patients with diabetes [12–14]. Patients with MASLD and MASH report higher levels of fatigue, anxiety, and depression compared to the general population. Further, patients' disease burden is compounded by a diminished health-related quality of life (HRQoL), especially in advanced disease stages [12].

Liver fibrosis serves as a key prognostic marker for MASH, increasing the risk of mortality as patients with advanced fibrotic stages are more susceptible to complications such as HCC [15]. MASLD, MASH, as well as fibrosis in MASLD often remain unrecognised in clinical practice, which can lead to a delayed diagnosis of serious complications [16, 17]. This highlights the critical need for early detection of advanced fibrosis in MASLD patients.

While liver biopsy is generally not required for the clinical management of MASLD patients according to current treatment guidelines, it remains the reference standard for confirming MASH diagnosis and fibrosis staging and ruling out other potential liver conditions [2]. Concurrently, there is growing recognition of non-invasive procedures such as liver stiffness measurement (LSM) by vibration controlled transient elastography (VCTE) to clarify the stage of fibrosis in patients with MASLD/MASH [18].

As there are no pharmacological treatments for MASH approved in Germany, lifestyle modification has been the primary management method [2]. Guidelines recommend optimising pharmacological therapy for comorbidities, such as type 2 diabetes and obesity [2, 3, 5].

Given the substantial burden of MASLD and MASH, alongside the complexities in diagnosing and managing these conditions, there is a critical need to establish a consensus on diagnostic criteria and current treatment modalities. Despite the increasing prevalence of MASLD and MASH, a significant gap in standardised diagnostic

approaches and therapeutic strategies remains in Germany. Furthermore, the absence of approved pharmacological treatments for MASH underscores the necessity for clear guidance and expert recommendations to optimise patient care.

To address these challenges, we conducted a Delphi panel involving experts in the field. The objective of this study was to generate insights into the diagnostic criteria and current treatment modalities for MASH in Germany. The Delphi method, known for its systematic and iterative process to achieve consensus among experts, was deemed particularly suitable to navigate the complexities and diverse perspectives in MASH management.

## 2 | Materials and Methods

### 2.1 | Delphi Method

A three-round web-based survey, combining methodologies of a Delphi panel with a standard expert survey, was conducted to achieve consensus on predefined study questions (Figure 1). The survey allowed panellists to participate online, ensuring convenience and broad accessibility. The study period extended from February 2024 to May 2024.

### 2.2 | Participants

Seventeen specialists who practise in Germany were identified and invited to participate via email. In total, 12 physicians from various specialties (gastroenterology, diabetology, hepatology) agreed to participate. These experts were identified in consultation with a thought leader.

### 2.3 | Questionnaire

A structured questionnaire, comprising 36 questions, was developed and presented to the experts in German (Data S1). The survey covered a range of MASH-related topics, including definitions, epidemiology, diagnosis, current treatments, comorbidity management, pharmaceutical therapy and patient education. Additionally, panellists were requested to provide information about their workplace and number of treated patients.

The terminology used in this manuscript is based on the questions provided to participants during the Delphi panel (see Data S1). To avoid any confusion and ensure consistency between the survey instrument and the manuscript, the same terminology has been retained throughout the text.

The panellists provided their responses based on personal estimates, reflecting their individual expertise and experience in the field.

### 2.4 | Consensus

Consensus was defined as achieving 75% participant agreement. Out of the questions posed, four were consensus questions. Results from each round were analysed by calculating the arithmetic mean of all responses. Questions that did not reach the 75% agreement threshold proceeded to the third round. In this final round, a new mean value, derived from the second-round responses, was presented. Participants were then asked to either agree or disagree with this new mean value, providing an alternative value if they disagreed.

## 3 | Results

### 3.1 | Participants

The twelve participating specialists were distributed across Germany, with eight hospital-based and four office-based participants. Each participant treated an average of 1825 patients annually, with approximately 62.5% of these patients having some

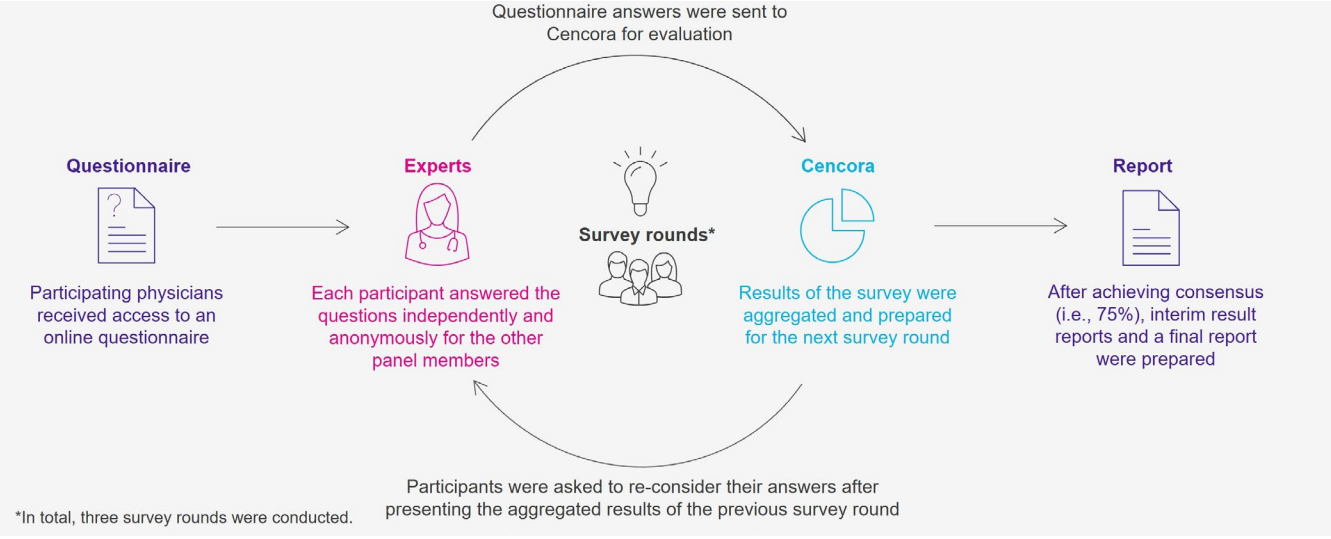


**FIGURE 1** | Flow chart presenting the process of the Delphi method with experts participating anonymously in three rounds of survey. Results were prepared by Cencora for the respective next round and results were provided in interim and final report(s).

**TABLE 1** | Number of patients treated by experts per year and proportions of patients with liver diseases and MASH.

| Number of treated patients | Mean/% | SD | Minimum | Median | Maximum |
|---|---|---|---|---|---|
| Overall number of patients treated per year | 1825 | 1459.7 | 350 | 1650 | 6000 |
| Thereof, proportion of patients with liver diseases (in %) | 62.5% | 28.5% | 20.0% | 70.0% | 100.0% |
| Of patients with liver diseases, proportion of MASH patients (in %) | 25.8% | 19.9% | 5.0% | 20.0% | 75.0% |

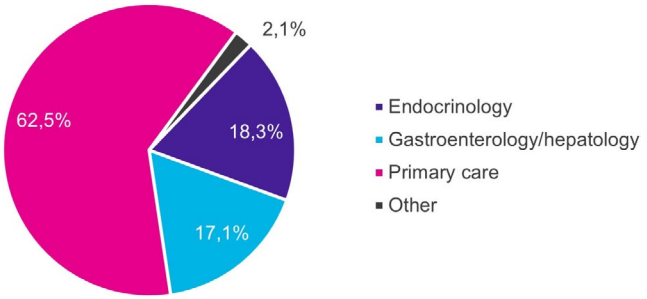


**FIGURE 2** | Pie chart showing the average proportions of referral routes of MASH patients to experts' clinics or offices: 62.5% general practitioners (primary care), 18.3% endocrinologists, 17.1% gastroenterologists/hepatologists and 2.1% others.

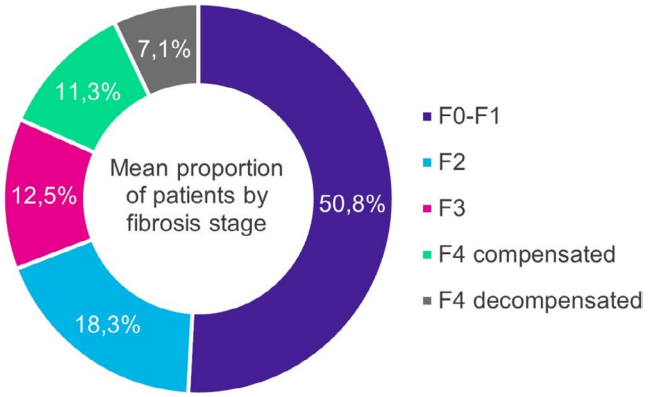


**FIGURE 3** | Pie chart showing the estimated fibrosis stages of patients with MASLD including MASH in experts' clinics/practices: 50.8% in stages F0 to F1, 18.3% in F2, 12.5% in F3, 11.3% in F4 compensated and 7.1% in F4 decompensated.

form of liver disease. Out of these, 25.8% are diagnosed with MASH (Table 1).

Almost all participants (91.7%) are involved in diagnosing and treating MASH. More than half (58.3%) actively manage comorbid conditions such as diabetes and cardiovascular symptoms. However, the proportion of cases with underlying comorbidities managed by the panellists themselves varied depending on the specific comorbidity. For example, when treating type 2 diabetes, experts referred the patient to a specialist colleague or back to the referring healthcare provider in 72.5% of cases on average. In contrast, experts reported managing 55.4% of obesity cases themselves without any referrals.

### 3.2 | Epidemiology and MASH Diagnosis

In the first panel round, experts estimated that approximately 75.0% of MASH patients in Germany remain undiagnosed. In the second round, this mean value was confirmed by 83.3% of the specialists. On average, 62.5% of the experts' patients are referred by general practitioners. Referral rates from endocrinologists and gastroenterologists/hepatologists are similar, at 18.3% and 17.1%, respectively (Figure 2). The primary reason for referral to the experts' clinics/practices, accounting for an average of 73.3% of referrals, is the observation of elevated or abnormal liver function test (LFT) results.

The estimated fibrosis stages of MASH patients in clinics and practices of the participating experts reveal a clear distribution across different stages on average. Patients with fibrosis stages F0 to F1 constitute the largest group, potentially indicating a high proportion of MASL only, with an average proportion of 50.8% (median: 50%) and a range from 10% to 80%, reflecting significant variability. For fibrosis stage F2, the mean proportion is 18.3% (median: 20%) and a narrower range of 10%–30%, indicating a more consistent distribution. Patients at fibrosis stage F3 represent an average proportion of 12.5% (median: 10%, range: 5%–30%). For those at fibrosis stage F4 compensated, the average proportion is 11.3% (median: 10%, range: 5%–20%). Finally, patients with fibrosis stage F4 decompensated form the smallest group, with an average proportion of 7.1% (median: 5%, range: 0%–20%) (Figure 3).

The participating physicians were asked to rank the likelihood of a confirmed MASH diagnosis for a broad range of methods/procedures for diagnosing MASH in clinical practice. Consensus was reached, as 75.0% of experts agreed to liver biopsy being the most important approach in the second panel round. This was followed by imaging procedures, such as computed tomography (CT), magnetic resonance imaging (MRI), ultrasonography and proton magnetic resonance spectroscopy. The third rank included fibrosis scores referring to NAFLD fibrosis score, FibroTest, BARD-Score, FIB4 Index and enhanced liver fibrosis (ELF) panel (Table 2).

Another question referred to approaches important to diagnose MASH patients in clinical practice. The survey results indicate that fibrosis scores (values from clinical and imaging tests to assess liver fibrosis such as NAFLD fibrosis score, FibroTest, BARD-Score, FIB4 Index, Enhanced Liver Fibrosis (ELF) panel), liver enzyme tests, other serological tests and LSM by VCTE are unanimously regarded as important diagnostic approaches for diagnosing MASH (100% agreement). Imaging procedures are also highly valued, with 91.7% of experts considering them important, though 8.3% reported limited availability. Biopsy evaluation scores NAFLD Activity score (NAS), Steatosis Activity and Fibrosis (SAF) score, are important to 75.0% of experts, while 25.0% do not prioritise them. The expert opinions on liver biopsy were divided,

with 50.0% viewing it as important and 50.0% as not important. Controlled Attenuation Parameter (CAP) is considered important by 66.7% of experts, with 25.0% not finding it important and 8.3% citing accessibility issues. Magnetic resonance elastography (MRE) is deemed important by only 16.7% of experts, with 41.7% not finding it important and another 41.7% reporting it as unavailable or inaccessible. Lastly, steatosis and activity scores (referring to SteatoTest and ActiTest) are not considered important by any experts, with 58.3% finding them not important and 41.7% indicating no availability or accessibility (Figure 4a).

**TABLE 2** | Ranking of selected approaches for diagnosing a MASH patient.

| Procedure | Rank |
|---|---|
| Liver biopsy[a] | 1 |
| Imaging procedures | 2 |
| Fibrosis scores | 3 |
| LSM by VCTE | 4 |
| CAP | 5 |
| Liver enzyme tests | 6 |
| Biopsy evaluation scores | 7 |
| Other serological tests | 8 |
| Steatosis and activity scores | 9 |
| Magnetic resonance elastography | 10 |
| Bio-electrical impedance analyser | 11 |

[a]Liver biopsy was pre-specified as Rank 1.

Only 16.7% of the panellists considered liver biopsy as important for monitoring MASH patients (Figure 4b). Furthermore, participating specialists provided information on the proportion of patients with suspected MASH (stages F0 to F3) in whom they perform liver biopsy. On average, they conduct biopsies in 22.5% of such cases. However, responses varied widely, with one expert performing biopsies in 0% of these cases and one expert in up to 80.0%.

When asked to provide the main reasons for not performing a liver biopsy, 83.3% stated possible complications from biopsies (e.g., risk of bleeding and infection) as the primary factor. Other reasons such as negative impact on patient QOL, procedural/capacity issues or financial constraints were indicated by two to three experts.

## 3.3 | Current Treatment Options

Current treatment strategies emphasise lifestyle modifications (such as weight reduction, nutrition and exercise) and the

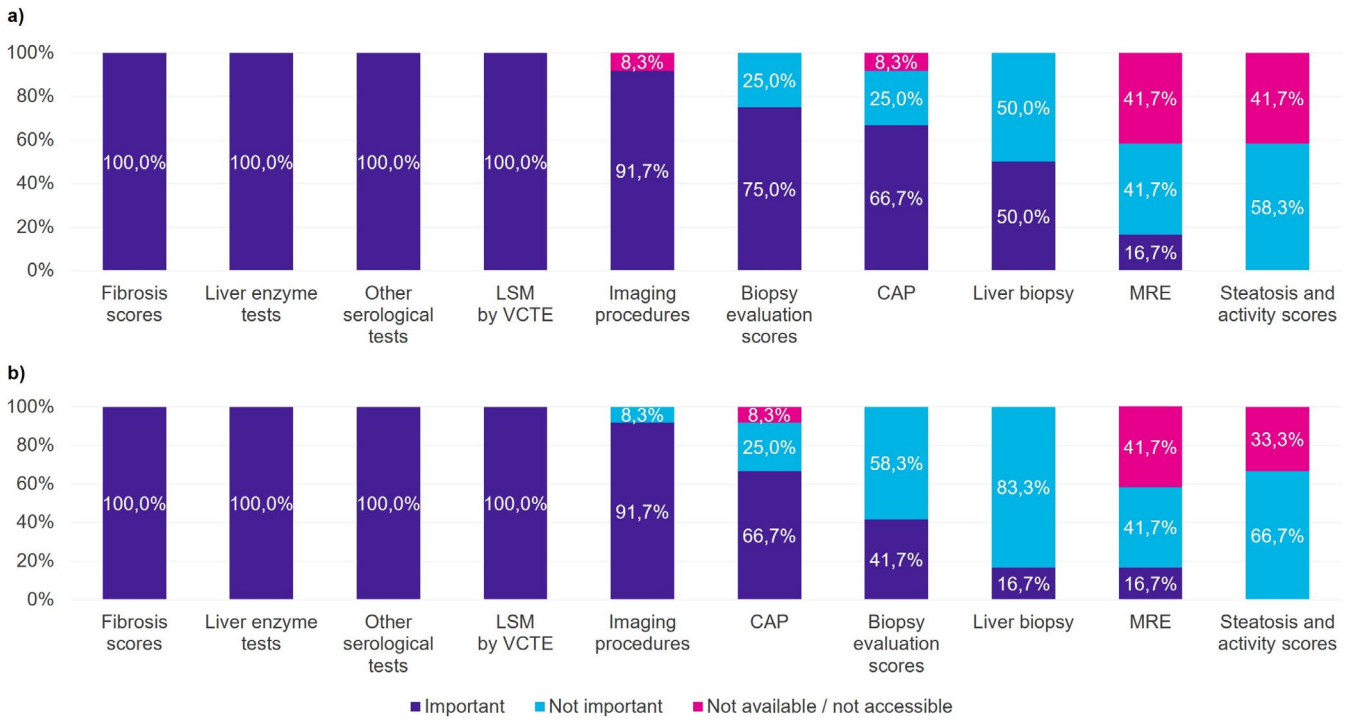


**FIGURE 4** | Visualisation of the importance of selected approaches (a) to diagnose MASH patients in clinical practice; bar chart showing fibrosis scores, liver enzyme tests, other serological tests and LSM by VCTE as the most important approaches (100%) (b) to monitor MASH patients in clinical practice; bar chart showing fibrosis scores, liver enzyme tests, other serological tests and LSM by VCTE as the most important approaches (100%). Fibrosis scores: NAFLD fibrosis score, FibroTest, BARD-Score, FIB4 Index, Enhanced Liver Fibrosis (ELF) panel; Imaging procedures: computed tomography (CT), magnetic resonance imaging (MRI), ultrasonography, proton magnetic resonance spectroscopy; liver enzyme tests: aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), γ-glutamyltransferase (GGT); other serological tests: INR ratio, serum albumin, total bilirubin, platelets, serological tests that show absence of hepatitis; steatosis and activity scores: SteatoTest, ActiTest; biopsy evaluation scores: NAFLD Activity score (NAS), Steatosis Activity and Fibrosis (SAF) score.

management of comorbidities such as diabetes and cardiovascular diseases, with all panellists (100%) endorsing this approach assumed due to the limited availability of pharmaceutical options and the lack of approved medications for MASH. 75.0% of the experts reported having access to surgical options (mainly bariatric surgery), while 50.0% had access to experimental options through clinical trials. Specifically for treating MASH, 41.7% had access to pharmaceutical treatment options, including therapies for optimising lipid metabolism disorders and diabetes/obesity medications.

When asked about the main challenges or unmet needs they faced in managing MASH, 50.0% of experts pointed out that the absence of approved or payer-covered medications is a significant issue, while 33.3% mentioned that addressing causal factors such as poor diet and unhealthy lifestyle, or the addictive nature of the eating disorder, remains a major challenge.

### 3.4 | Comorbidity Management

A significant proportion of MASH patients suffered from comorbidities, including overweight/obesity (82.1%), metabolic syndrome (66.3%), hypertension (63.8%) and type 2 diabetes (57.1%). Lifestyle management primarily targeted these comorbidities, reflecting current treatment guidelines. Additionally, 75% of the experts agreed that 20% of patients suffer from coronary heart disease and 10% from pain syndromes, while 91.7% reached a consensus that 10.8% of patients have depression.

In the absence of MASH-specific treatments, experts primarily target comorbidities such as type 2 diabetes (100%), obesity (91.7%), metabolic syndrome (91.7%) and dyslipidaemia (83.3%). For MASH patients with type 2 diabetes, GLP-1 (glucagon-like peptide-1) receptor agonists, GLP-1/GIP (gastric inhibitory polypeptide) receptor agonists, metformin, lifestyle changes and sodium glucose transporter-2 (SGLT-2) inhibitors are considered standard of care. For those without type 2 diabetes, lifestyle changes and comorbidity management are standard, while opinions on utilisation of GLP-1/GIP receptor agonists in these patients are divided.

## 4 | Discussion

### 4.1 | Overview

The Delphi panel provided valuable insights into the current state of diagnosing and treating MASH in Germany. The panel comprised 12 MASH experts participating in all survey rounds. This process yielded several key findings that highlight both the challenges and potential strategies for improving MASH management.

### 4.2 | Underdiagnosis of MASH

A critical issue identified by the experts is the substantial underdiagnosis of MASH, with an estimated 75.0% of patients in Germany remaining undiagnosed. In contrast, Stahmeyer and colleagues [19] report an even lower diagnosis rate of 0.09% for 2018 based on German claims data. This consensus underscores the necessity for enhanced awareness and diagnostic efforts in clinical practice. The high rate of underdiagnosis aligns with existing literature from other countries suggesting that many patients with MASLD/MASH remain undiagnosed until they present with advanced liver disease [20, 21].

Complications associated with advanced liver disease are associated with a significant impact on HRQOL as well as increased morbidity and mortality [22, 23]. Therefore, early intervention and improved patient outcomes, as well as reducing costs for the healthcare system, are essential. In their cost of illness study, Schattenberg et al. showed that economic costs for end-stage liver disease patients were considerably higher in a range of countries when compared to early stages [8]. This demonstrates that the management of these advanced conditions not only affects QOL but also places a substantial burden on healthcare resources and ultimately healthcare costs.

### 4.3 | Diagnostic Methods

The panel confirmed that while liver biopsy remains the reference standard for diagnosing MASH, its utilisation is limited mainly due to unspecified clinical reasons, an invasive procedure with a risk of complications as well as costs [24, 25]. Only 22.5% of suspected cases (F0–F3) undergo biopsy confirmation on average. Instead, non-invasive methods such as imaging procedures, fibrosis scores (e.g., NAFLD fibrosis score, FibroTest), liver enzyme tests and LSM by VCTE are widely used in both diagnosis and monitoring.

This reliance on non-invasive approaches highlights a critical need for consistent guidelines to be implemented in clinical practice. Current guidelines, such as those from the European Association for the Study of the Liver (EASL), the American Association for the Study of Liver Diseases (AASLD) and the German treatment guideline (Deutsche Gesellschaft für Gastroenterologie, Verdauungs- und Stoffwechselkrankheiten, DGVS), show some variations in the recommended non-invasive tests and the cut-offs to use [2, 3, 5, 26]. These inconsistencies can lead to variability in clinical practice and hinder the effective diagnosis and monitoring of patients. Therefore, harmonising these guidelines in line with the national refinancing of the health insurance funds would help ensure more reliable and universally applicable results.

In terms of monitoring, experts also favoured non-invasive assessments over liver biopsy. Over 90% relied on liver blood panels and weight control/waist size measurements as primary indicators. Liver biopsy was seldom used (8.6%) in routine monitoring.

### 4.4 | Current Treatment

In the absence of approved treatments for MASH in Germany, experts unanimously resort to non-pharmaceutical interventions, including lifestyle modifications such as weight management, dietary adjustments and physical activity. However, maintaining weight loss strictly through lifestyle changes is

challenging and often unsustainable, highlighting the limitations of this approach [27, 28]. Given that weight loss is believed to be beneficial primarily in early stages of MASH, this underscores the urgent need to identify and develop suitable alternatives in more advanced disease stages [21].

### 4.5 | Comorbidities

The Delphi panel results provide a comprehensive overview of the comorbidities frequently associated with MASH and the challenges in managing these conditions. It is important to note that the participating experts had varying specialisations, which may influence their approaches to managing these comorbidities.

The participating experts indicated that a substantial proportion of MASH patients suffer from various comorbid conditions. Overweight/obesity was the most prevalent comorbidity, affecting 82.1% of patients, followed by metabolic syndrome (66.3%), hypertension (63.8%), type 2 diabetes (57.1%) and dyslipidaemia (56.3%). These findings are comparable to what was reported in the literature review by Sheka et al. for the MASH population, with a prevalence of obesity (81.8%), metabolic syndrome (70.7%), hypertension (68.0%), type 2 diabetes (43.6%) and dyslipidaemia (72.1%) [29]. However, in a recent systematic analysis of data from 123 studies, the global pooled prevalence of MASLD among patients with type 2 diabetes was 65.3% [30].

Management of these comorbid conditions is a critical component of MASH treatment strategy, and all of the panellists targeted type 2 diabetes (100%). In the absence of an approved drug specifically indicated for MASH, this is largely in line with relevant treatment guidelines [2, 5, 26].

### 4.6 | Implications for Practice

The current EASL-EASD-EASO treatment guidelines as well as the German S2k guideline for MASLD recommend targeted case-finding strategies using non-invasive tests for MASLD/presumed MASH with liver fibrosis, especially focusing on individuals with cardiometabolic risk factors, abnormal liver enzymes or radiological signs of hepatic steatosis. These strategies aim to identify high-risk patients to reduce hepatic complications of MASLD [2, 3, 5].

Correspondingly, the results of the panel highlight the need for enhanced screening in patients with a high risk of MASLD/MASH as indicated by the high proportion of undiagnosed cases. There should be increased efforts to identify MASLD/MASH patients early through routine screening using validated non-invasive methods, reflecting the challenges of implementing the current guidelines in daily clinical practice.

As treatment guidelines continue to evolve, the future may see the development and implementation of a clearer set of guidelines for improved diagnosis and management of MASLD/MASH. These guidelines could enhance risk stratification as well as screening and monitoring processes, ensuring that high-risk patients are identified earlier and more accurately.

While at the time of the study's initiation in February 2024 until publication, no medication was approved for the treatment of MASH in Germany. In March 2024, resmetirom was conditionally approved by the U.S. Food and Drug Administration (FDA) for the treatment of adults with noncirrhotic MASH with moderate to advanced fibrosis in the United States. This development addresses a significant gap that was highlighted by the Delphi panel, where experts primarily relied on non-pharmaceutical interventions. The potential future may see more treatments becoming available, facilitating the sustainable management of MASLD/MASH patients.

Overall, the integration of new pharmaceutical treatments, alongside existing non-pharmaceutical interventions, would provide a more holistic approach to managing MASLD/MASH. This comprehensive strategy could lead to better patient outcomes, as healthcare providers would be equipped with a structured framework for the effective prevention, detection and management of the disease.

### 4.7 | Limitations

Our study has several limitations that should be acknowledged. While the Delphi method is a valuable tool for reaching consensus among experts, it has inherent limitations. Although our Delphi panel was conducted online with full anonymity, which reduces the risk of dominant panellist bias and enhances the objectivity of responses, the method relies on expert opinions, which can introduce subjective biases and does not replace empirical data.

While all questions targeted MASH, some options were not exclusively referring to MASH only but also included MASLD. Further distinction would have been important as it could have enhanced the accuracy of the questionnaire and overall study findings. Additionally, panellists were asked to provide the main reasons for not performing a liver biopsy. One response option was 'clinical reasons' which was not specified further. This lack of specificity may have led to variability in interpretation among the respondents, potentially affecting the consistency and clarity of the data collected. As a result, the category 'clinical reasons' could encompass a wide range of factors, making it difficult to draw precise conclusions about the specific clinical considerations influencing the decision to forgo a liver biopsy.

Furthermore, the panel consisted solely of physicians, providing a comprehensive medical perspective on MASH. However, as only 12 physicians were included, this cannot be considered representative for Germany. While the relatively small panel size aligns with the methodological requirements of a Delphi study, it inherently limits the generalisability of the findings. Further, the absence of patient perspectives is a limitation. Including patients could have provided valuable insights into the lived experiences and priorities of those directly affected by MASH, potentially leading to more holistic and patient-centred recommendations.

Lastly, as the field continues to evolve with potential new pharmacotherapies on the horizon, the recommendations presented here may require future updates to remain aligned with emerging evidence and therapeutic advancements.

## 5 | Conclusions

The Delphi panel has underscored key areas needing attention within MASH management—from addressing underdiagnosis to optimising diagnostic tools and treatment monitoring strategies in Germany. By focusing on these areas through education, policy updates and technological advancements, we can improve early detection rates and overall patient care outcomes in MASH management.

### Author Contributions

Conceptualization: Peter Rydqvist, Thomas Ramezani, Jennifer S. Haas, Frank Tacke; Methodology: Peter Rydqvist, Thomas Ramezani, Jennifer S. Haas; Data evaluation: Jennifer S. Haas; Writing – original draft preparation: Peter Rydqvist, Thomas Ramezani, Jennifer S. Haas, Frank Tacke; Writing – review and editing: Heike Bantel, Peter Buggisch, Andreas Geier, Wolf-Peter Hofmann, Stefan Mauss, Elke Roeb, Jörn M. Schattenberg, Karl-Georg Simon, Norbert Stefan, Katja Deterding, Johannes Wiegand, Anita Pathil, Frank Tacke.

### Acknowledgements

The contributions of the survey panellists were invaluable to this research. Additionally, we would like to thank Jesse Fishman who played a significant role in the study design.

### Consent

This article does not contain any studies with human subjects.

### Conflicts of Interest

Y.K., P.R. and T.R. are employees of Madrigal Pharmaceuticals Inc. and own stock. J.S.H. is an employee of PharmaLex GmbH (former Xcenda GmbH). PharmaLex GmbH (former Xcenda GmbH) received consulting fees for the execution of the study and for the manuscript preparation from Madrigal Pharmaceuticals Inc. H.B. received consultancy fees from Advanz Pharma, Echosens, Gilead Sciences, GSK, Intercept, Ipsen, Roche and received speaker honoraria from Falk Foundation, Gilead, Advanz and GSK. W.-P.H. receives consultancy fees from AbbVie, Gilead Sciences, Ipsen Pharma, Falk Pharma and Madrigal Pharmaceuticals Inc. E.R. has received honoraria for consulting or lectures from AbbVie, Amgen, Intercept, Madrigal, Medac, Merz, Norgine, Falk Foundation, Gilead, Pfizer, Repha and Takeda. J.M.S. receives consultancy fees from Akero, Alentis, Alexion, Altimmune, AstraZeneca, 89Bio, Bionorica, Boehringer Ingelheim, Gilead Sciences, GSK, HistoIndex, Ipsen, Inventiva Pharma, Madrigal Pharmaceuticals, Kríya Therapeutics, Lilly, MSD Sharp & Dohme GmbH, Novartis, Novo Nordisk, Pfizer, Roche, Sanofi and Siemens Healthineers; speaker honorarium from AbbVie, Boehringer Ingelheim, Gilead Sciences, Ipsen, Novo Nordisk and Madrigal Pharmaceuticals. Stockholder options: Hepta Bio. N.S. receives consultancy fees from Boehringer Ingelheim, Madrigal Pharmaceuticals Inc., Pfizer and Lilly. K.D. receives a consultancy fee, travel support and a research grant from Gilead and lecture fees from Alnylam. F.T.'s lab has received research grants (funding to the institution) from AstraZeneca, MSD and Gilead. F.T. has received honoraria for consulting or lectures from Madrigal, Gilead, AbbVie, Falk, AstraZeneca, Boehringer, MSD, GSK, Ipsen, Pfizer, Novartis, Novo Nordisk and Sanofi. J.W. is a lecturer and advisory board member for AbbVie, Gilead, Intercept/Advanz Pharma, GSK, Ipsen and Novo Nordisk; research grants from AbbVie and Gilead. A.G. reports support from the IMI2 LITMUS project; research grants from Novartis, Falk and Intercept; consulting or speaker's fees from AbbVie, Advanz, Albireo, Alexion, AstraZeneca, Bayer, BMS, Boehringer, Burgerstein, CSL Behring, Eisai, Falk, Gilead, Heel, Intercept, Ipsen, Merz, MSD, Novartis, Novo Nordisk, Orphalan, Pfizer, Roche and Sanofi-Aventis; and travel/meeting support from Intercept, Gilead, AbbVie and Falk. A.P. participates in advisory boards for AbbVie, Gilead, Xcenda and Madrigal, as well as speaker fees from AbbVie, BMS, Gilead, MSD and Novo Nordisk. A.G. is an advisory board or steering committee member for AbbVie, Advanz, Albireo, Alexion, AstraZeneca, Bayer, Bristol Myers Squibb, CSL Behring, Eisai, Falk, Gilead, Heel, Intercept, Ipsen, Merz, MSD, Novartis, Novo Nordisk, Pfizer, Roche, Sanofi-Aventis and Sequana, and a speaker for Orphalan. K.-G.S. received consultancy fees from AbbVie, Gilead and Falk.

### Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

### Endnotes

[1] The term 'MASH' (metabolic dysfunction-associated steatohepatitis) is used throughout this manuscript to align with evolving nomenclature, while 'NASH' (non-alcoholic steatohepatitis) is retained in the Data S1 to reflect the original phrasing of the Delphi panel questionnaire.

### References

1. S. Cheemerla and M. Balakrishnan, "Global Epidemiology of Chronic Liver Disease," *Clinical Liver Disease* 17, no. 5 (2021): 365–370.

2. F. Tacke, P. Horn, V. Wai-Sun Wong, et al., "EASL–EASD–EASO Clinical Practice Guidelines on the Management of Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD)," *Journal of Hepatology* 81 (2024): 492–542.

3. E. Roeb, A. Canbay, H. Bantel, et al., "Amendment 'Neue Nomenklatur zur MASLD (Metabolic Dysfunction Associated Steatotic Liver Disease; Metabolische Dysfunktion Assoziierte Steatotische LEBERERKRANKUNG)' Zur S2k-Leitlinie 'Nicht-Alkoholische Fettlebererkrankung' (v.2.0/April 2022) der Deutschen Gesellschaft für Gastroenterologie Verdauungs- und Stoffwechselkrankheiten (DGVS)," *Zeitschrift Für Gastroenterologie* 62, no. 7 (2024): 1077–1087.

4. European Association for the Study of the Liver, European Association for the Study of Diabetes, and European Association for the Study of Obesity, "EASL-EASD-EASO Clinical Practice Guidelines for the Management of Non-Alcoholic Fatty Liver Disease," *Journal of Hepatology* 64, no. 6 (2016): 1388–1402.

5. E. Roeb, A. Canbay, H. Bantel, et al., "Aktualisierte S2k-Leitlinie Nicht-Alkoholische Fettlebererkrankung der Deutschen Gesellschaft für Gastroenterologie, Verdauungs- und Stoffwechselkrankheiten (DGVS) – April 2022 – AWMF-Registernummer: 021–025," *Zeitschrift für Gastroenterologie* 60, no. 9 (2022): 1346–1421.

6. Z. M. Younossi, P. Golabi, J. M. Paik, A. Henry, C. Van Dongen, and L. Henry, "The Global Epidemiology of Nonalcoholic Fatty Liver Disease (NAFLD) and Nonalcoholic Steatohepatitis (NASH): A Systematic Review," *Hepatology* 77, no. 4 (2023): 1335–1347.

7. C. Estes, Q. M. Anstee, M. T. Arias-Loste, et al., "Modeling NAFLD Disease Burden in China, France, Germany, Italy, Japan, Spain, United Kingdom, and United States for the Period 2016–2030," *Journal of Hepatology* 69, no. 4 (2018): 896–904.

8. J. M. Schattenberg, J. V. Lazarus, P. N. Newsome, et al., "Disease Burden and Economic Impact of Diagnosed Non-Alcoholic Steatohepatitis in Five European Countries in 2018: A Cost-of-Illness Analysis," *Liver International* 41, no. 6 (2021): 1227–1242.

9. N. Stefan and K. Cusi, "A Global View of the Interplay Between Non-Alcoholic Fatty Liver Disease and Diabetes," *Lancet Diabetes and Endocrinology* 10, no. 4 (2022): 284–296.

10. G. Targher, C. D. Byrne, and H. Tilg, "MASLD: a Systemic Metabolic Disorder With Cardiovascular and Malignant Complications," *Gut* 73, no. 4 (2024): 691–702.

11. E. E. Powell, V. W. Wong, and M. Rinella, "Non-Alcoholic Fatty Liver Disease," *Lancet* 397, no. 10290 (2021): 2212–2224.

12. Z. M. Younossi and L. Henry, "Understanding the Burden of Nonalcoholic Fatty Liver Disease: Time for Action," *Diabetes Spectrum: A Publication of the American Diabetes Association* 37, no. 1 (2024): 9–19.

13. M. Noureddin, A. Vipani, C. Bresee, et al., "NASH Leading Cause of Liver Transplant in Women: Updated Analysis of Indications for Liver Transplant and Ethnic and Gender Variances," *American Journal of Gastroenterology* 113, no. 11 (2018): 1649–1659.

14. X. Wang, "Challenges and Opportunities in Nonalcoholic Steatohepatitis," *Medical Review* 2, no. 4 (2021): 328–330.

15. A. J. Sanyal, M. L. Van Natta, J. Clark, et al., "Prospective Study of Outcomes in Adults With Nonalcoholic Fatty Liver Disease," *New England Journal of Medicine* 385, no. 17 (2021): 1559–1569.

16. M. Alexander, A. K. Loomis, J. Fairburn-Beech, et al., "Real-World Data Reveal a Diagnostic Gap in Non-Alcoholic Fatty Liver Disease," *BMC Medicine* 16, no. 1 (2018): 130.

17. E. M. Nielsen, K. P. Anderson, J. Marsden, J. Zhang, and A. D. Schreiner, "Nonalcoholic Fatty Liver Disease Underdiagnosis in Primary Care: What Are We Missing?," *Journal of General Internal Medicine* 37, no. 10 (2022): 2587–2590.

18. M. A. Tincopa and R. Loomba, "Non-Invasive Diagnosis and Monitoring of Non-Alcoholic Fatty Liver Disease and Non-Alcoholic Steatohepatitis," *Lancet Gastroenterology and Hepatology* 8, no. 7 (2023): 660–670.

19. J. T. Stahmeyer, M. Hemmerling, B. Burger, et al., "Frequency of Diagnosed Non-Alcololic Fatty Liver Disease (NAFLD) in the German Population – An Analysis Based on Health Insurance Data," *Zeitschrift für Gastroenterologie* 59, no. 8 (2021): 851–858.

20. J. M. Fraile, S. Palliyil, C. Barelle, A. J. Porter, and M. Kovaleva, "Non-Alcoholic Steatohepatitis (NASH) – A Review of a Crowded Clinical Landscape, Driven by a Complex Disease," *Drug Design, Development and Therapy* 15 (2021): 3997–4009.

21. B. Zhu, S. L. Chan, J. Li, et al., "Non-Alcoholic Steatohepatitis Pathogenesis, Diagnosis, and Treatment," *Frontiers in Cardiovascular Medicine* 8 (2021): 742382.

22. J. G. Orr, T. Homer, L. Ternent, et al., "Health Related Quality of Life in People With Advanced Chronic Liver Disease," *Journal of Hepatology* 61, no. 5 (2014): 1158–1165.

23. I. C. Perez, F. J. Bolte, W. Bigelow, Z. Dickson, and N. L. Shah, "Step by Step: Managing the Complications of Cirrhosis," *Hepatic Medicine: Evidence and Research* 13 (2021): 45–57.

24. S. Di Mauro, A. Scamporrino, A. Filippello, et al., "Clinical and Molecular Biomarkers for Diagnosis and Staging of NAFLD," *International Journal of Molecular Sciences* 22, no. 21 (2021): 11905.

25. V. A. Piazzolla and A. Mangia, "Noninvasive Diagnosis of NAFLD and NASH," *Cells* 9, no. 4 (2020): 1005.

26. M. E. Rinella, B. A. Neuschwander-Tetri, M. S. Siddiqui, et al., "AASLD Practice Guidance on the Clinical Assessment and Management of Nonalcoholic Fatty Liver Disease," *Hepatology* 77, no. 5 (2023): 1797–1835.

27. A. B. Evert and M. J. Franz, "Why Weight Loss Maintenance Is Difficult," *Diabetes Spectrum: A Publication of the American Diabetes Association* 30, no. 3 (2017): 153–156.

28. H. Gupta, "Barriers to and Facilitators of Long Term Weight Loss Maintenance in Adult UK People: A Thematic Analysis," *International Journal of Preventive Medicine* 5, no. 12 (2014): 1512–1520.

29. A. C. Sheka, O. Adeyi, J. Thompson, B. Hameed, P. A. Crawford, and S. Ikramuddin, "Nonalcoholic Steatohepatitis: A Review," *Journal of the American Medical Association* 323, no. 12 (2020): 1175–1183.

30. Z. M. Younossi, P. Golabi, J. K. Price, et al., "The Global Epidemiology of Nonalcoholic Fatty Liver Disease and Nonalcoholic Steatohepatitis Among Patients With Type 2 Diabetes," *Clinical Gastroenterology and Hepatology* 22, no. 10 (2024): 1999–2010.

**Supporting Information**

Additional supporting information can be found online in the Supporting Information section.