

REVIEW



Resmetirom and semaglutide therapy for patients with MAFLD in the MENA region: expert panel recommendations

Yasser Fouad^a, Khalid M. AlNaamani^b, Fatheya Alawadi^c, Abdulla Al Hassani^d, Nawal Alkhalidi^e, Bilal Hotayt^f, Faisal Abaalkhail^g, Samir Rouabhia^h, Maheeba Abdullaⁱ, Munira Y. Altarrah^j, Mohamed Tahiri^{k,l}, Meriam Sabbah^m, Faisal M. Sanaiⁿ, Necati Ormeci^o, Gamal Esmat^p and Mohammed Eslam^q

^aDepartment of Gastroenterology, Hepatology and Endemic Medicine, Faculty of Medicine, Minia University, Minia, Egypt; ^bDepartment of Medicine, Division of Gastroenterology and Hepatology, The Medical City for Military and Security Services, Muscat, Oman; ^cDepartment of Endocrinology, Dubai Academic Health Corporation, Dubai, United Arab Emirates; ^dGastroenterology and Endoscopy Department, Zayed Military Hospital, Abu Dhabi, United Arab Emirates; ^eGastroenterology & Hepatology Teaching Hospital, Medical City, Ministry of Health and Environment, Baghdad, Iraq; ^fGastroenterology Department, Sahel General Hospital, Beirut, Lebanon; ^gDepartment of Medicine, King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia; ^hDepartment of Internal Medicine, University Hospital Center Touhami Benflis, Batna, Algeria; ⁱDepartment of Internal Medicine, Ibn Al Nafees Hospital, Manama, Bahrain; ^jDepartment of Gastroenterology, Department of Internal Medicine, Al Amiri Hospital, Kuwait City, Kuwait; ^kService d'Hépatogastro-Entérologie, CHU Ibn Rochd, Casablanca, Morocco; ^lFaculté de Médecine et de Pharmacie, Université Hassan II, Casablanca, Morocco; ^mDepartment of Gastroenterology, Habib Thameur Hospital, Tunis, Tunisia; ⁿGastroenterology Section, Department of Medicine, King Abdulaziz Medical City, King Abdullah International Medical Research Center, Jeddah, Saudi Arabia; ^oDepartment of Internal Medicine, Istanbul Health and Technology University, Istanbul, Türkiye; ^pDepartement of Endemic Medicine and Hepatogastroenterology, Faculty of Medicine, Cairo University, Cairo, Egypt; ^qStorr Liver Centre, Westmead Institute for Medical Research, Westmead Hospital and University of Sydney, Sydney, NSW, Australia

ABSTRACT

Introduction: Metabolic dysfunction-associated fatty liver disease (MAFLD) affects 25–30% of the global population, with the Middle East and North Africa (MENA) region showing some of the highest prevalence rates, reaching up to 40%. MAFLD is a common cause of cirrhosis and hepatocellular carcinoma and is a leading indication for liver transplantation in this region. Hitherto, there have been no specific pharmacotherapies for MAFLD. However, the recent conditional approval of resmetirom and semaglutide by the FDA for the treatment of non-cirrhotic moderate-to-advanced (fibrosis stages 2 or 3) metabolic-associated steatohepatitis (MASH) offers a much-needed therapeutic option for this largely underserved condition.

Areas covered: An expert panel from the MENA region conducted a comprehensive literature search via PubMed and Google Scholar, focusing on clinical trials and international guidelines for resmetirom and semaglutide. This review identifies the target treatment population, proposes criteria for cessation of therapy, outlines monitoring protocols, and addresses regional knowledge gaps.

Expert opinion: The approval of the first two drugs for MASH is a milestone. Access to and affordability of these therapies will be the crucial determinants of their actual adoption. Future efforts should consider individualized treatment pathways stratified by cost, regulatory status, and healthcare infrastructure, while generating further regional evidence.

ARTICLE HISTORY

Received 19 February 2026
Accepted 29 June 2026

KEYWORDS

Resmetirom; Semaglutide;
MASH; MAFLD; MENA;
fibrosis

1. Introduction

Metabolic dysfunction-associated fatty liver disease (MAFLD) (also known as Metabolic dysfunction-associated steatotic liver disease (MASLD)) is increasingly recognized as a global epidemic, affecting nearly 25–30% of the world's population [1,2]. Despite its widespread impact, the burden of the disease varies significantly across different regions, with the Middle East and Northern Africa (MENA) and the Arab region showing some of the highest prevalence rates [3]. Recent estimates based on the Global Burden of Disease 2021 database indicate that approximately 109.4 million people in the Arab region have MAFLD [3], with prevalence rates reaching as high as 45% in certain countries. MAFLD has become

a leading cause of liver transplantation and hepatocellular carcinoma [4,5]. The escalating burden in the MENA region is primarily driven by a sharp rise in body mass index (BMI) and dysglycemia over the last three decades, which predicts a significant worsening of both the clinical and economic burden of the disease across the region, further compounded by a lack of disease awareness among key stakeholders [6].

The MENA region faces unique demographic and socio-economic challenges shaped by its varied cultures, economies, social factors, histories, and political contexts [7], which significantly influence health outcomes, particularly concerning metabolic diseases. Therefore, formulating regionally tailored

CONTACT Mohammed Eslam  mohammed.eslam@sydney.edu.au  Storr Liver Centre, Westmead Institute for Medical Research, Westmead Hospital and University of Sydney, 176 Hawkesbury Road, Westmead, NSW 2145, Australia

 Supplemental data for this article can be accessed online at <https://doi.org/10.1080/17446651.2026.2698115>

© 2026 The Author(s). Published by Informa UK Limited, trading as Taylor & Francis Group.

This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives License (<http://creativecommons.org/licenses/by-nc-nd/4.0/>), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited, and is not altered, transformed, or built upon in any way. The terms on which this article has been published allow the posting of the Accepted Manuscript in a repository by the author(s) or with their consent.

Article highlights

- The Food and Drug Administration (FDA) recently conditionally approved resmetirom and semaglutide for the treatment of non-cirrhotic moderate-to-advanced (fibrosis stages 2 or 3) metabolic-associated steatohepatitis (MASH), providing a much-needed therapeutic option for this largely underserved population.
- An expert panel from the MENA region provides practical recommendations for determining the target patient population for resmetirom and semaglutide treatment.
- Taking into account regional specifics, the panel outlines a monitoring protocol, establishes criteria for stopping treatment, and identifies crucial regional knowledge gaps.
- Evidence-based monitoring strategies utilizing longitudinal trends in noninvasive tests (NITs) are recommended to assess treatment response and define non-responders in clinical practice.
- The panel emphasizes the need for a multidisciplinary approach to manage comorbidities, specifically addressing the risks of sarcopenia, gallbladder disease, and thyroid function during therapy.
- Affordability will significantly impact the actual adoption of these treatments and recommendations across economically heterogeneous healthcare systems.

effective strategies for curbing the burden of MAFLD is pivotal to reducing liver-related morbidity and mortality [8,9].

With the Food and Drug Administration (FDA) granting expedited approval to resmetirom in March 2024, followed by semaglutide on 15 August 2025, for the treatment of metabolic dysfunction-associated steatohepatitis (MASH), novel therapeutic pathways have emerged. Resmetirom is a first-in-class, orally active, liver-directed, selective agonist of the thyroid hormone receptor-beta (THR- β) [10,11]. In the liver, THR- β is the predominant isoform responsible for regulating lipid metabolism; resmetirom restores impaired THR- β signaling, thereby increasing mitochondrial fatty acid oxidation and reducing lipotoxicity [11]. In contrast, semaglutide is a long-acting glucagon-like peptide-1 receptor agonist (GLP-1 RA). Its primary action involves stimulating glucose-dependent insulin secretion and promoting satiety via central nervous system pathways, leading to substantial weight loss and reducing the delivery of adipose-derived free fatty acids to the liver [12,13].

2. Method

To address the pressing need for region-specific clinical guidance, the writing group, commissioned by the Arab Middle East Alliance for Liver Disease (AMAL) governing board, developed this narrative review and expert recommendation document. Panel members were selected by the governing board based on their established academic output, peer-reviewed publications on fatty liver disease, and their documented impact on shaping regional health policies, medical education, and community healthcare services within the MENA region.

Systematic searches were performed in PubMed and Google Scholar using keywords including Resmetirom, Semaglutide, MASH, and MAFLD. The search was restricted to English-language publications and included the most recent clinical trial data presented at major international liver congresses up to 2026. Following the literature collection, the panel engaged in an iterative, open review process to synthesize the evidence. Rather than employing a formal, rigid

Delphi voting structure or numeric evidence-ranking matrix, consensus was reached through roundtable collaborative discussions. This approach enabled the integration of diverse clinical perspectives that reflect the stark heterogeneity in healthcare across MENA countries. The final recommendations focus on providing practical, straightforward clinical guidance regarding patient selection, treatment response, and the criteria for stopping treatment. This document aims to summarize the available evidence, present practical recommendations, and outline existing gaps in the current literature to encourage further studies that will generate regional data and address outstanding questions regarding the use of new therapies in the management of MAFLD.

3. Whom to treat

The ESSENCE trial, a phase 3, randomized, multicentre trial for semaglutide 2.4 mg weekly, recruited 1,200 adults with biopsy-defined MASH and fibrosis stage 2 or 3 (F2-F3) [12]. There were no specific requirements regarding the number of metabolic comorbidities or noninvasive test (NIT) cutoffs for trial eligibility, and mild alcohol consumption (<20 g/day for females and <30 g/day for males) was permitted. Compared with placebo, semaglutide increased the rate of MASH resolution without worsening liver fibrosis (63% vs. 34%) and reduced liver fibrosis without worsening steatohepatitis (37% vs. 23%).

The MAESTRO-NASH trial for resmetirom [10] included 966 participants with metabolic syndrome (defined as having at least three of the five cardio-metabolic risk factors) along with biopsy-confirmed MASH and stage 1b, 2, or 3 liver fibrosis. Compared with placebo, resmetirom increased the rate of MASH resolution without worsening liver fibrosis (29.9% vs. 9.7%) and reduced liver fibrosis without worsening steatohepatitis (25.9% vs. 14.2%).

Therefore, if approved regionally and based on the labeling, adults with non-cirrhotic MASH who have significant liver fibrosis (F2-3) should be considered for treatment with resmetirom or semaglutide as targeted therapies for MASH. While both trials demonstrated clear efficacy in halting or reversing fibrosis progression, the MAESTRO-NASH trial strictly required a baseline metabolic syndrome profile, whereas the ESSENCE trial focused heavily on overall metabolic weight reduction, illustrating a slight divergence in patient phenotypes that clinicians should consider during baseline evaluation.

Given that a liver biopsy is often not feasible or is impractical for widespread application in patient selection and follow-up among most candidates for these treatments [5,14]. The writing panel recommends that the diagnosis of fibrotic MASH using liver biopsy should not be mandated. Instead, in line with the African Middle East Association of Gastroenterology (AMAGE) guidelines [5], we recommend a testing strategy for ruling in fibrotic MASH based on sequential combinations of tests, including blood-based noninvasive tests (NITs) and imaging modalities, including FIB-4, Enhanced Liver Fibrosis (ELF), liver stiffness measurement (LSM) using vibration-controlled transient elastography (VCTE) and/or magnetic resonance elastography (MRE), depending on their availability in individual practice settings (Figure 1). These modalities are widely utilized in clinical practice, demonstrate reasonable

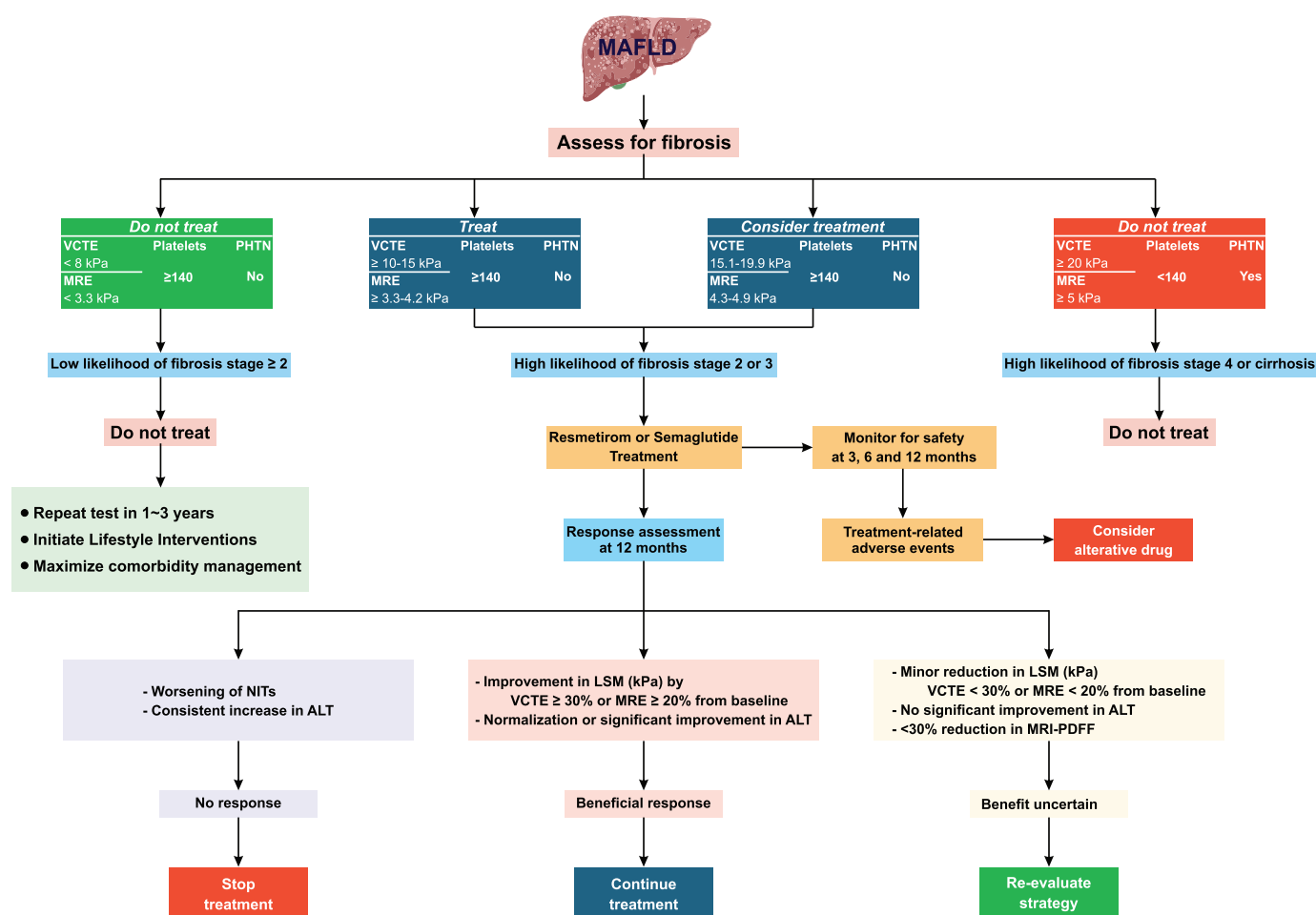


Figure 1. Practical guideline for patient selection, treatment initiation, and response assessment in MAFLD.

accuracy, and could thus be reliably used to identify suitable candidates for therapy. Importantly, FIB-4 should not be relied upon as a standalone diagnostic tool for determining therapy eligibility in patients with MAFLD/MASH [15]. Growing evidence suggests that utilizing multiple NITs can enhance the accuracy of hepatic fibrosis staging and the prediction of clinical outcomes [16-18].

For individuals who have undergone a liver biopsy within the past 6 to 12 months, the fibrosis stage can be assessed from the histological results, provided there has been no significant weight change or decline in metabolic health since the biopsy. However, it is recommended to obtain baseline NITs before initiating treatment with semaglutide or resmetirom to effectively monitor treatment response. If biopsy results indicate MASH with F2-3, treatment initiation can be considered regardless of the NIT results, unless there is clinical or imaging evidence of portal hypertension.

For biopsies that are older than 12 months but within the last 3 years, the same recommendations apply to avoid starting treatment in patients with undiagnosed cirrhosis. If NITs indicate minimal fibrosis, suggesting potential improvement in the disease, it may be necessary to consider either a repeat liver biopsy or collecting updated NITs to obtain a more accurate assessment of liver fibrosis staging.

4. Whom not to treat?

We advise against using either resmetirom or semaglutide for treating patients on both ends of the spectrum – those with no or early fibrosis and those with established cirrhosis, because the metabolism, benefits, and side effects of these medications for this population have not been established [10,12]. Additionally, this group may require different dosing regimens and assessments.

Resmetirom should not be used in cases of concomitant active liver disease, excessive alcohol consumption (more than 20 g per day for women and 30 g per day for men), or active thyroid disease. Concurrently, patients with cachexia, diabetic retinopathy, a personal or family history of medullary thyroid carcinoma, or multiple endocrine neoplasia type 2 (MEN2) should not be treated with semaglutide.

In a small Phase 2b trial involving 71 participants with biopsy-proven compensated MASH cirrhosis, once-weekly semaglutide (2.4 mg) was generally well tolerated and did not result in unexpected adverse events. However, it did not demonstrate a difference in fibrosis improvement or MASH resolution compared with placebo [19]. Observational studies suggest a lower rate of major liver-related outcomes in patients treated with semaglutide, but this evidence is indirect and primarily serves as a hypothesis generator [20]. Another key concern is the potential

worsening of sarcopenia in patients treated with semaglutide, characterized by the loss of skeletal muscle mass, quality, and strength, which is a significant complication in patients with cirrhosis and may be exacerbated by rapid weight loss [21,22]. Overall, these results raise concerns about its overall benefit-risk profile in cirrhosis, and the ability to alter the natural progression of MASH cirrhosis has yet to be well demonstrated and requires dedicated outcome studies. Nonetheless, as per the separate indications for other cardiometabolic diseases, semaglutide can be used in patients with early-stage fibrosis or compensated cirrhosis for its cardiometabolic benefits [13].

For resmetirom, the outcomes of the MAESTRO-NASH-OUTCOMES trial, which is currently evaluating composite clinical outcomes, will be vital for determining the effectiveness and safety of the drug in patients with compensated cirrhosis [23].

5. Which drug to use?

Regardless of whether resmetirom or semaglutide is being utilized, best practices for managing MAFLD should include comprehensive lifestyle modifications – such as nutrition, exercise, and behavioral changes – as well as effective control of comorbid metabolic conditions [1]. Treatment decisions on which of these two drugs to use should be tailored to the patient based on an array of factors and align with the dominant disease phenotype, including fibrosis stage and progression rate, the comorbidity profile, response to prior or ongoing treatment, patient preference and the local availability (Supplementary Table 1).

Resmetirom might be preferred as the first-line treatment when the dominant phenotype is deterioration of liver condition, such as in patients with advanced fibrosis or a rapid rate of fibrosis progression, but with minimal evidence of systemic metabolic dysfunction. In contrast, semaglutide may be a better choice when impaired metabolic health and metabolic risk factors predominate, particularly in patients with comorbid overweight/obesity, type 2 diabetes (T2D), and/or chronic kidney disease, even in individuals with normal BMI and T2D [24,25].

Additionally, semaglutide could be a suitable option for patients with dual etiology of MAFLD and coexisting alcohol-related liver disease (ALD) or alcohol use disorder (AUD), due to its low risk of hepatotoxicity and potential to reduce alcohol cravings and intake [12,26]. Limited data exist on the use of semaglutide and resmetirom together, so their combined use should be considered on a case-by-case basis.

When resmetirom is chosen, dosing should be based on the patient's weight, with a recommended dosage of 100 mg/day for individuals weighing 100 kg or more and 80 mg/day for those weighing less than 100 kg [10].

Semaglutide dose optimization is essential to ensure patient compliance and optimize treatment outcomes. The starting dose is 0.25 mg weekly, and the dose is increased every 4 weeks until the maintenance dose is reached. The 2.4 mg once-weekly regimen is the evidence-based recommended dose for MASH [12]. If patients do not tolerate this dose, the dose can be temporarily decreased to 1.7 mg weekly,

but specific efficacy data for this group in MASH are still unavailable.

6. Monitoring for adverse events and considerations for stopping treatment

Gastrointestinal (GI) adverse events, including nausea, diarrhea, and vomiting, are the most frequently reported side effects for both semaglutide and resmetirom (Supplementary Table 2) [10,12]. In the ESSENCE trial, these symptoms were typically transient, occurring primarily during the 4- to 16-week titration period [12]. Similarly, in resmetirom trials, GI events predominantly occurred within the first 4 to 12 weeks after initiation, with a higher incidence observed at the 100 mg dose [10]. To improve adherence and prevent discontinuation, the panel recommends a gradual dose escalation – potentially extending the titration interval beyond 4 weeks if symptoms persist. If symptoms are severe, the last tolerated dose should be maintained for 1–2 months before any attempt to re-escalate. Patient education is essential; clinicians should provide practical advice, such as consuming smaller, low-fat meals, maintaining proper hydration, and avoiding lying down immediately after eating [27]. Such measures are critical to mitigate GI distress and prevent secondary complications, such as dehydration-induced acute kidney injury. In persistent cases, the use of antiemetics or prokinetics may be considered alongside dose modifications [27].

There are a few additional reported adverse events in patients treated with semaglutide. Cases of acute pancreatitis, including acute necrotizing pancreatitis, have been reported in patients on semaglutide and other glucagon-like peptide-1 receptor agonists (GLP-1 RAs), which may develop within 30 days to 5 weeks after therapy initiation [28]. Although large studies and meta-analyses are yielding conflicting conclusions to date [29,30]. A previous meta-analysis of large randomized controlled trials indicated that incretin-based therapies were associated with an approximately 82% increased risk of acute pancreatitis when compared to conventional drugs [31]. Additionally, an analysis of case series involving patients and data from the Food and Drug Administration's Adverse Event Reporting System (FAERS) also suggested an elevated risk of acute pancreatitis associated with all GLP-1 RAs [32]. However, a recent randomized, placebo-controlled study of semaglutide therapy, which included 34,721 patients, found that semaglutide was not associated with an increased risk of acute pancreatitis, showing an odds ratio of 0.7 [30]. Therefore, semaglutide should be used cautiously in patients with a history of acute pancreatitis. If pancreatitis is suspected, semaglutide must be discontinued promptly, and re-initiation should be avoided following a confirmed incident, regardless of the underlying cause.

The use of GLP-1 RAs is significantly associated with increased risks of gallbladder or biliary diseases, with risks being dose- and treatment duration-dependent [33]. Although a history of gallbladder disease is not an absolute contraindication, caution and patient education on the symptoms of biliary complications are advised.

Additionally, in vitro and in vivo experiments have demonstrated that long-term use of GLP-1 RAs is associated with an

increased risk of the development of thyroid C-cell tumors, including medullary thyroid carcinoma (MTC) [34], resulting in a black box warning for these agents in individuals at risk for this condition. Yet, this association remains controversial, particularly given the species differences in thyroid cell density and GLP-1 receptor expression between rodents and humans [34]. Until further evidence is available, semaglutide should be contraindicated in individuals with a personal or family history of multiple endocrine neoplasia syndrome type 2 (MEN2) or MTC.

Semaglutide is generally associated with a low risk of hypoglycemia on its own, but this risk significantly increases when it is used with other blood glucose-lowering drugs, especially sulfonylureas and insulin, particularly in those with a history of bariatric surgery. It also affects heart rate through GLP-1 receptors in the sinoatrial node; patients should report any palpitations or change in baseline resting heartbeat while resting [35].

Semaglutide reversibly delays gastric emptying, which can lead to gastroparesis symptoms. The rate of gastroparesis among those who were treated with semaglutide was found to be 6.5 events per 1,000 person-years. A gastric motility assessment should be considered for those with preexisting motility disorders. Semaglutide use is contraindicated in severe gastroparesis. There are potential concerns about delayed gastric emptying leading to aspiration risks during anesthesia, but no data support an increased risk [36]. A large analysis found no higher rates of aspiration pneumonia or related complications in those undergoing screening colonoscopy while on GLP-1 RA [37]. It is essential to document GLP-1 RA treatment during pre-procedure evaluations to support safe anesthesia planning, with recommendations tailored to local institutional guidelines.

Semaglutide may increase the risk of complications related to diabetes-associated retinopathy and non-anterior ischemic optic neuropathy (NAION), a rare but potentially serious eye condition that, if untreated, may result in irreversible vision loss with no proven permanent treatment actually exists, particularly in patients with a prior history of this condition, with the risk rising with prolonged use, particularly in older adults [38,39]. In June 2025, the WHO issued a safety alert, noting its advisory committee also found that this risk should be added to semaglutide's risk management plan [40]. Therefore, we recommend that all patients with T2D treated with GLP-1 RAs, regardless of preexisting diabetic retinopathy, should be regularly screened and monitored for potential complications of T2D, including diabetic retinopathy, especially during periods of rapid glycemic changes.

Another major concern is that approximately 40% of the total semaglutide-induced weight reduction is attributed to lean mass loss, with a nearly 10% decrease in muscle volume [41]. This effect is especially pronounced in older adults and individuals with preexisting sarcopenia. Thus, to mitigate risks associated with muscle loss, it is recommended to regularly monitor patients through physical exams, engage in resistance exercises, and ensure adequate protein intake.

Finally, patients receiving semaglutide should be monitored for the emergence or worsening of depression, suicidal thoughts or behaviors, or any unusual changes in mood or

behavior [42]. Semaglutide should not be initiated in individuals with active suicidal ideation and suicidality until the individual receives the appropriate mental health care and is deemed to be stable.

In the resmetirom trials, the most frequently reported adverse events were diarrhea and nausea, which often appeared within 12 weeks of therapy initiation, mainly occurring in the first 4 weeks [10]. The median duration of diarrhea was 15–20 days, with around half of those who experienced diarrhea reporting symptoms lasting longer than 4 weeks [10]. The majority of GI adverse events were associated with the higher dose of 100 mg rather than the lower dose of 80 mg. Additionally, resmetirom was associated with a higher incidence of gallbladder disease, but currently, a history of biliary colic or gallstones is not considered an absolute contraindication.

A case of severe hepatotoxicity was reported in a patient treated with resmetirom, who developed jaundice with bilirubin levels 15 times above normal. A detailed further investigation suggested that the likelihood that resmetirom contributed to the hepatotoxicity was 25% to 50% [10]. Therefore, it is recommended that regular hepatic function tests should be conducted during treatment and therapy should be discontinued if clinically significant hepatotoxicity is identified, defined as an elevation of ALT $\geq 5 \times$ upper limit of normal (ULN); ALP $\geq 2 \times$ ULN; or ALT $\geq 3 \times$ ULN and total bilirubin > 2.5 mg/dL and or international normalized ratio (INR) ≥ 1.5 with elevated liver enzymes [43].

7. Monitoring during treatment and assessing response and futility (non-response) to treatment

Based on a review of the available data [5], the writing panel recommends that a reduction in VCTE LSM of $\geq 30\%$ or MRE LSM of $\geq 20\%$ from baseline, and an ALT level reduction of > 17 U/L or $\geq 20\%$ throughout week 72, indicate a likely beneficial response. By extension, a similar proportional increase in these measures or consistently elevated ALT levels may define meaningful worsening and categorize patients as nonresponders. Responses that fall below these thresholds, or patients who do not fulfil the criteria for continuation or discontinuation after 72 weeks of therapy without showing evidence of worsening or progression to cirrhosis, require individual patient evaluation due to the lack of sufficient available data. These thresholds may also be updated as new evidence emerges.

It is important to note that histologic responses have been observed in some individuals even when there is no improvement in VCTE LSM [44], indicating that it might not be sensitive or precise enough to monitor response to therapy. However, the writing group recognizes that VCTE is validated and most commonly used in clinical practice; therefore, many clinicians and patients will continue to rely on it to inform treatment decisions. To help remedy this, recent data indicate that consistent improvements across multiple NITs, rather than isolated changes in a single biomarker, may provide a more robust indication of meaningful disease improvement [5,14]. Therefore, treatment monitoring should focus on longitudinal trends across complementary fibrosis biomarkers, rather than

relying solely on any single NIT. Similarly, due to high variability in some NITs, we suggest that worsening in at least 2 NITs be considered clinically meaningful and indicative of treatment failure.

For treatment response in clinical practice, we recommend reassessing patients 12 months after initiating resmetirom and 18 months after initiating semaglutide. This timeframe allows for adequate evaluation of efficacy, as it provides time for dose adjustments and a response in fibrosis. An initial assessment, approximately 6 months into treatment, may be appropriate for patients at risk of rapid disease progression. In the absence of noticeable or meaningful improvement, it is essential to conduct a rigorous review of the underlying diagnosis and, if a dual etiology exists, including underreported alcohol intake, lifestyle interventions, adequate drug dosing, and adherence. If there is a partial response or persistent F2-3 fibrosis, intensifying treatment with a combination of resmetirom and semaglutide may be a safe and reasonable strategy, though data supporting this recommendation remain limited. In the phase 3 MAESTRO-NASH trial, 13%–17% of patients in the treatment groups were receiving GLP-1 RAs or sodium-glucose cotransporter-2 inhibitors (SGLT2i), and no interaction between these drugs was noted [10]. Continuous monitoring every 6 to 12 months is vital to assess progress, confirm sustained benefits, and determine whether any necessary adjustments to therapy or combination approaches are required.

8. Concomitant therapy and drug-drug interaction

Pharmacokinetic studies reveal that resmetirom is primarily metabolized by Cytochrome P450 Family 2 Subfamily C Member 8 (CYP2C8) [45]. Thus, when used in combination with CYP2C8 inhibitors, such as gemfibrozil or clopidogrel, it is advisable to reduce the resmetirom dose to 80 mg/day for individuals weighing 100 kg or more and to 60 mg/day for those under 100 kg, with increased monitoring for adverse effects.

In patients with MAFLD, managing cardiovascular risk with statins is crucial [46,47]. Drug – drug interactions are particularly concerning when resmetirom is co-administered with statins (atorvastatin, pravastatin, rosuvastatin, and simvastatin), which can result in increased statin exposure and a heightened risk of adverse reactions [45]. Thus, statin dose adjustment would be required, with the recommended maximum doses for rosuvastatin and simvastatin at 20 mg/d and for atorvastatin and pravastatin at 40 mg/d. Although resmetirom reduced low-density lipoprotein (LDL) levels, whether it confers a cardiovascular protective effect remains unknown.

9. Endocrinology and cardiometabolic considerations

The endocrine consequences of resmetirom are not yet well-defined. Resmetirom has been associated with an increase in sex hormone binding globulin and mild reductions in thyroid-stimulating hormone (TSH) and free thyroxine (T4). The clinical significance of any potential effects of these hormonal changes remains to be established [11]. These findings indicate that any abnormal thyroid function, whether hyperthyroidism or hypothyroidism, should be addressed prior to

initiating resmetirom therapy. Consequently, a thyroid function assessment, including at least TSH, should be performed at baseline or within the past 6 months. Caution is advised when resmetirom is prescribed in patients with preexisting thyroid disease or those on thyroid medication, while maintaining standard clinical monitoring is recommended. Individuals with normal baseline thyroid function do not require routine monitoring. However, training and vigilance regarding potential adverse effects are important, as with any other drug.

Patients with MASH have a higher risk not only of liver-related morbidity and mortality, but also of adverse cardiometabolic outcomes [48,49]. The beneficial effects of semaglutide on various metabolic conditions, such as T2D and obesity, suggest that it may confer cardioprotective effects in patients with MAFLD. However, further evidence is required, specifically in this group of patients.

10. Lean MASH and other special subgroups

Evidence regarding lean MASH is currently limited [50,51], as this subgroup was underrepresented in both the ESSENCE trial (semaglutide) and the MAESTRO-NASH trial (resmetirom). Additionally, neither agent has been prospectively evaluated in this population. Therefore, treatment decisions should be informed by clinical judgment and the predominant phenotype. For example, semaglutide may be the preferred option for individuals with T2DM, even if they are of normal weight. Conversely, resmetirom might be more suitable for those experiencing significant fibrosis (F2-F3) without evident systemic metabolic dysfunction.

Another area that lacks clear evidence concerns the management of patients with a dual MAFLD etiology [52,53]. Common additional diseases to consider in this group include alcohol-associated liver disease, iron overload, viral hepatitis, and autoimmune hepatitis. The initiation of treatment, necessary dosages, and the preferred first-line drug for these patients remain undefined. Semaglutide could be a reasonable therapeutic option in this context due to its low potential for hepatotoxicity and emerging data suggesting that GLP-1 RAs may help reduce alcohol cravings and intake [26], although further evidence is still needed.

11. Financial aspect and access to treatment

The MENA region is characterized by extreme economic heterogeneity, which directly impacts healthcare delivery. It includes high-income nations (e.g. KSA, UAE, and Qatar) with robust health expenditures, alongside middle-income (e.g. Egypt, Tunisia, Lebanon) and low-income nations (e.g. Yemen), where pharmaceutical budgets are severely constrained [54]. Consequently, affordability will significantly influence the actual adoption of these treatments. If the cost of these medications far exceeds the pharmaceutical budget of many healthcare systems, it will be challenging to treat all eligible patients with fatty liver disease. In this case, implementing risk stratification algorithms to determine which patients should be prioritized for treatment and which can safely wait might be needed. On the other hand, it is hoped

that with the widespread use of these drugs, health and financial authorities will be able to negotiate prices with pharmaceutical companies and also find mechanisms to allocate limited resources as equitably as possible [55].

12. Expert opinion

The conditional approval of resmetirom and semaglutide represents a paradigm shift in the management of MAFLD, particularly in the MENA region, where the disease burden is among the highest globally [56]. However, the transition from clinical trials to real-world impact faces significant hurdles. While these therapies offer a path to reducing liver-related mortality, their implementation into clinical practice in the MENA region will require a departure from the traditional biopsy-centric model. We anticipate that the widespread adoption of noninvasive tests (NITs) will not only facilitate earlier diagnosis but also allow for scalable monitoring of treatment response in resource-constrained environments. The primary barrier to this adoption remains the high cost of these medications. Unless regional health authorities can negotiate sustainable pricing or implement strict risk-stratification algorithms to prioritize individuals with advanced fibrosis (F3), the public health impact may be limited to a small subset of the population.

Current challenges in the field include a lack of data on 'Lean MASH' and dual-etiology cases, both of which are clinically significant in our region. Furthermore, the risk of accelerated sarcopenia with GLP-1 receptor agonists necessitates a shift toward a more holistic, multidisciplinary treatment model that incorporates geriatric and nutritional expertise [57]. Methodological limitations, such as the high variability of NITs in patients with high BMIs, still prevent us from having a perfectly accurate 'liquid biopsy.' Further research must focus on head-to-head trials and, more importantly, on the potential of combination therapies (resmetirom plus semaglutide) to simultaneously target different pathophysiological pathways of the disease.

Optimizing treatment adherence is critical for long-term therapeutic success, particularly in the chronic liver disease (CLD) population [58]. Ultimately, future studies are required to define optimized, patient-centric dose-escalation protocols for the CLD population to mitigate the risk of treatment discontinuation due to intolerance.

In the next five to ten years, we expect the field to move toward precision medicine, where genetic markers common in Middle Eastern populations are utilized to predict drug response. The 'standard procedure' will likely evolve from simple weight-loss advice to a sophisticated metabolic protocol where pharmacotherapy is tailored to the patient's specific fibro-inflammatory profile. The ultimate goal is to move beyond simple 'MASH resolution' on a histological slide and toward a measurable reduction in cardiovascular and liver-related events across the population.

13. Future directions

Several clinical nuances remain unresolved, including the impact of structured counseling on adherence, the risk of

biliary complications following rapid weight loss, and the specific monitoring requirements for post-bariatric surgery patients who may face higher hypoglycemia risks. While these factors are clinically significant, there is currently insufficient drug-specific evidence in the MASH/MAFLD population to provide formal recommendations. These subgroups represent a critical frontier for real-world evidence generation in the MENA region, and their outcomes will likely inform the next iteration of clinical guidelines as more data become available.

Acknowledgments

The authors declare that no artificial intelligence-based tools or technologies were used in the preparation, writing, editing, analysis, or interpretation of this manuscript.

Author contributions

CRediT: **Yasser Fouad**: Conceptualization, Data curation, Writing – original draft, Writing – review & editing; **Khalid M. AlNaamani**: Writing – original draft, Writing – review & editing; **Fathey Alawadi**: Writing – original draft, Writing – review & editing; **Abdulla Al Hassani**: Writing – original draft, Writing – review & editing; **Nawal Alkhalidi**: Writing – original draft, Writing – review & editing; **Bilal Hotayt**: Writing – original draft, Writing – review & editing; **Faisal Abaalkhail**: Writing – original draft, Writing – review & editing; **Samir Rouabhia**: Writing – original draft, Writing – review & editing; **Maheeba Abdulla**: Writing – original draft, Writing – review & editing; **Munira Y. Altarrah**: Writing – original draft, Writing – review & editing; **Mohamed Tahiri**: Writing – original draft, Writing – review & editing; **Meriam Sabbah**: Writing – original draft, Writing – review & editing; **Faisal M. Sanai**: Writing – original draft, Writing – review & editing; **Necati Ormeci**: Writing – original draft, Writing – review & editing; **Gamal Esmat**: Writing – original draft, Writing – review & editing; **Mohammed Eslam**: Conceptualization, Project administration, Visualization, Writing – original draft, Writing – review & editing.

Funding

This paper was not funded.

Disclosure statement

M Eslam is on advisory boards and receives honoraria for talks from Pfizer Sanofi, Boehringer Mannheim and Novo Nordisk, outside his participation in this work. The other authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

Reviewer disclosures

A reviewer on this manuscript has disclosed that they served as advisor / consultant to Madrigal Pharmaceuticals and Novo-Nordisk in their drug-development programs for MASH. Peer reviewers on this manuscript have no other relevant financial relationships or otherwise to disclose.

References

Papers of special note have been highlighted as either of interest (*) or of considerable interest () to readers.**

1. Eslam M, Fan JG, Yu ML, et al. The Asian pacific association for the study of the liver clinical practice guidelines for the diagnosis and

- management of metabolic dysfunction-associated fatty liver disease. *Hepatol Int.* **2025**;19(2):261–301. doi: [10.1007/s12072-024-10774-3](https://doi.org/10.1007/s12072-024-10774-3)
2. Chan KE, Koh TJL, Tang ASP, et al. Global prevalence and clinical characteristics of metabolic-associated fatty liver disease: a meta-analysis and systematic review of 10 739 607 individuals. *J Clin Endocrinol Metab.* **2022**;107(9):2691–2700. doi: [10.1210/clinem/dgac321](https://doi.org/10.1210/clinem/dgac321)
 3. Pan Z, Fouad Y, Abaalkhail F, et al. The burden of metabolic diseases in the Arab region, 1990–2021. *Ther Adv Endocrinol Metab.* **2025**;16:20420188251406531.
 4. Pan Z, Al Hassani A, Ismail MH, et al. Changing profile and burden of hepatocellular carcinoma in Arab countries in 1990–2021. *Ann Hepatol.* **2025**;30(2):102104.
 5. Fouad Y, Elwakil R, Sanai FM, et al. The African Middle East association of Gastroenterology (AMAGE) clinical practice guidelines for the diagnosis and management of metabolic dysfunction associated fatty liver disease. *Ann Hepatol.* **2026**;31:102180.
- **This reference provides the regional clinical guidelines that form the foundation for the current expert panel's recommendations in the MENA region.**
6. Younossi ZM, Paik JM, Yilmaz Y, et al. Two-decade trends in MASLD and its complications in the Middle East and North Africa (2010–2021). *Liver Int.* **2025**;45(10):e70342.
 7. Spearman CW, Desalegn H, Ocama P, et al. The sub-saharan Africa position statement on the redefinition of fatty liver disease: from NAFLD to MAFLD. *J Hepatol.* **2021**;74(5):1256–1258. doi: [10.1016/j.jhep.2021.01.015](https://doi.org/10.1016/j.jhep.2021.01.015)
 8. Fouad Y, Ghazinyan H, Alborai M, et al. Joint position statement from the Middle East and North Africa and sub-saharan Africa on continuing to endorse the MAFLD definition. *J Hepatol.* **2024**;80(5):e194–e197. doi: [10.1016/j.jhep.2024.01.033](https://doi.org/10.1016/j.jhep.2024.01.033)
 9. 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(5):1557–1565. doi: [10.1002/hep.29085](https://doi.org/10.1002/hep.29085)
 10. Harrison SA, Bedossa P, Guy CD, et al. A phase 3, randomized, controlled trial of resmetirom in NASH with liver fibrosis. *N Engl J Med.* **2024**;390(6):497–509. doi: [10.1056/NEJMoa2309000](https://doi.org/10.1056/NEJMoa2309000)
- **This pivotal phase 3 trial led to the first FDA approval for a MASH-specific therapy, establishing the efficacy of resmetirom in improving fibrosis and MASH resolution.**
11. Karim G, Bansal MB. Resmetirom: an orally administered, smallmolecule, liver-directed, β -selective THR agonist for the treatment of non-alcoholic fatty liver disease and non-alcoholic steatohepatitis. *touchREVIEWS Endocrinol.* **2023**;19(1):60.
 12. Sanyal AJ, Newsome PN, Kliers I, et al. Phase 3 trial of semaglutide in metabolic dysfunction-associated steatohepatitis. *N Engl J Med.* **2025**;392(21):2089–2099. doi: [10.1056/NEJMoa2413258](https://doi.org/10.1056/NEJMoa2413258)
- **This study provides high-level evidence for the efficacy of semaglutide in achieving MASH resolution and its impact on liver histology.**
13. Deanfield J, Lincoff AM, Kahn SE, et al. Semaglutide and cardiovascular outcomes by baseline and changes in adiposity measurements: a prespecified analysis of the SELECT trial. *Lancet.* **2025**;406(10516):2257–2268. doi: [10.1016/S0140-6736\(25\)01375-3](https://doi.org/10.1016/S0140-6736(25)01375-3)
 14. Alharthi J, Eslam M. Biomarkers of metabolic (dysfunction)-associated fatty liver disease: an update. *J Clin Transl Hepatol.* **2021**;10(1):134. doi: [10.14218/JCTH.2021.00248](https://doi.org/10.14218/JCTH.2021.00248)
 15. Franck M, John K, Rau M, et al. Limitations of guideline-recommended risk stratification in identifying MASLD patients for novel drug treatments. *Liver Int.* **2025**;45(9):e70281. doi: [10.1111/liv.70281](https://doi.org/10.1111/liv.70281)
 16. Lin H, Lee HW, Yip TC, et al. Vibration-controlled transient elastography scores to predict liver-related events in steatotic liver disease. *JAMA.* **2024**;331(15):1287–1297. doi: [10.1001/jama.2024.1447](https://doi.org/10.1001/jama.2024.1447)
 17. Truong E, Gornbein JA, Yang JD, et al. MRI-AST (MAST) score accurately predicts major adverse liver outcome, hepatocellular carcinoma, liver transplant, and liver-related death. *Clin Gastroenterol Hepatol.* **2023**;21(10):2570–2577.e1. doi: [10.1016/j.cgh.2023.02.003](https://doi.org/10.1016/j.cgh.2023.02.003)
 18. Eslam M, Wong G-H, Hashem AM, et al. A sequential algorithm combining ADAPT and liver stiffness can stage metabolic-associated fatty liver disease in hospital-based and primary care patients. *Am J Gastroenterol.* **2021**;116(5):984–993. doi: [10.14309/ajg.0000000000001059](https://doi.org/10.14309/ajg.0000000000001059)
- **This reference is of interest because it details a non-invasive diagnostic algorithm essential for the practical implementation of new therapies in resource-limited settings.**
19. Loomba R, Abdelmalek MF, Armstrong MJ, et al. 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(6):511–522.
- **This reference explores the limits of current therapy by evaluating semaglutide's performance in the more advanced cirrhosis population.**
20. Kuo CC, Chuang MH, Li CH, et al. Semaglutide and the risk of adverse liver outcomes in patients with nonalcoholic fatty liver disease and type 2 diabetes: a multi-institutional cohort study. *Hepatol Int.* **2025**;19(2):395–404. doi: [10.1007/s12072-024-10752-9](https://doi.org/10.1007/s12072-024-10752-9)
 21. Bloomgarden ZT. Monitoring sarcopenia with incretin receptor activator treatment. *J Diabetes.* **2025**;17(6):e70117. doi: [10.1111/1753-0407.70117](https://doi.org/10.1111/1753-0407.70117)
 22. Ren Q, Zhi L, Liu H. Semaglutide therapy and accelerated sarcopenia in older adults with type 2 diabetes: a 24-month retrospective cohort study. *Drug Des Devel Ther.* **2025**;19:5645–5652. doi: [10.2147/DDDT.S531778](https://doi.org/10.2147/DDDT.S531778)
 23. Harrison SA, Ratziu V, Anstee QM, et al. Design of the phase 3 MAESTRO clinical program to evaluate resmetirom for the treatment of nonalcoholic steatohepatitis. *Aliment Pharmacol Ther.* **2024**;59(1):51–63. doi: [10.1111/apt.17734](https://doi.org/10.1111/apt.17734)
 24. Perkovic V, Tuttle KR, Rossing P, et al. Effects of semaglutide on chronic kidney disease in patients with type 2 diabetes. *N Engl J Med.* **2024**;391(2):109–121. doi: [10.1056/NEJMoa2403347](https://doi.org/10.1056/NEJMoa2403347)
 25. Pan Z, Alqahtani SA, Eslam M. MAFLD and chronic kidney disease: two sides of the same coin? *Hepatol Int.* **2023**;17(3):519–521. doi: [10.1007/s12072-023-10526-9](https://doi.org/10.1007/s12072-023-10526-9)
 26. Hendershot CS, Bremmer MP, Paladino MB, et al. Once-weekly semaglutide in adults with alcohol use disorder: a randomized clinical trial. *JAMA Psychiatry.* **2025**;82(4):395–405. doi: [10.1001/jamapsychiatry.2024.4789](https://doi.org/10.1001/jamapsychiatry.2024.4789)
 27. Shu Y, He X, Wu P, et al. Gastrointestinal adverse events associated with semaglutide: a pharmacovigilance study based on FDA adverse event reporting system. *Front Public Health.* **2022**;10:996179. doi: [10.3389/fpubh.2022.996179](https://doi.org/10.3389/fpubh.2022.996179)
 28. Hughes K, Sumaruth YRK, Mohammed E, et al. Acute pancreatitis likely due to Semaglutide. *Cureus.* **2024**;16(9):e69844. doi: [10.7759/cureus.69844](https://doi.org/10.7759/cureus.69844)
 29. Wen J, Nadora D, Bernstein E, et al. Evaluating the rates of pancreatitis and pancreatic cancer among GLP-1 receptor agonists: a systematic review and meta-analysis of Randomised controlled trials. *Endocrino Diabet Metabol.* **2025**;8(5):e70113. doi: [10.1002/edm2.70113](https://doi.org/10.1002/edm2.70113)
 30. Masson W, Lobo M, Barbagelata L, et al. Acute pancreatitis due to different semaglutide regimens: an updated meta-analysis. *Endocrinología, Diabetes y Nutrición.* **2024**;71(3):124–132. doi: [10.1016/j.endinu.2024.01.001](https://doi.org/10.1016/j.endinu.2024.01.001)
 31. Roshanov PS, Dennis BB. Incretin-based therapies are associated with acute pancreatitis: meta-analysis of large randomized controlled trials. *Diabetes Res Clin Pract.* **2015**;110(3):e13–e17. doi: [10.1016/j.diabres.2015.10.014](https://doi.org/10.1016/j.diabres.2015.10.014)
 32. Guo H, Guo Q, Li Z, et al. Association between different GLP-1 receptor agonists and acute pancreatitis: case series and real-world pharmacovigilance analysis. *Front Pharmacol.* **2024**;15:1461398. doi: [10.3389/fphar.2024.1461398](https://doi.org/10.3389/fphar.2024.1461398)
 33. Ramírez-Mejía MM, Ponciano-Rodríguez G, Eslam M, et al. GLP-1 receptor agonists and gallbladder disease risk: insights into molecular mechanisms and clinical implications. *Ther Adv Endocrinol Metab.* **2025**;16:20420188251406456. doi: [10.1177/20420188251406456](https://doi.org/10.1177/20420188251406456)

34. Bezin J, Gouverneur A, Pénichon M, et al. GLP-1 receptor agonists and the risk of thyroid cancer. *Diabetes Care*. 2023;46(2):384–390. doi: 10.2337/dc22-1148
35. Lubberding AF, Veedfald S, Achter JS, et al. Glucagon-like peptide-1 increases heart rate by a direct action on the sinus node. *Cardiovasc Res*. 2024;120(12):1427–1441. doi: 10.1093/cvr/cvae120
36. Aneke-Nash C, Hung KS, Wall-Wieler E, et al. Comparing the risk of gastroparesis following different modalities for treating obesity: semaglutide versus bupropion-naltrexone versus sleeve gastrectomy—a retrospective cohort study. *BMJ Open Gastroenterol*. 2025;12(1):e001704. doi: 10.1136/bmjgast-2024-001704
37. Chhabra P, Bhandari R, Singh R. Unmasking aspiration risks: a Propensity-Matched odyssey of GLP-1 receptor agonists and colonoscopy. *J Gastro Hepatol*. 2025;40(11):2732–2737. doi: 10.1111/jgh.70071
38. Wang F, Mao Y, Wang H, et al. Semaglutide and diabetic retinopathy risk in patients with type 2 diabetes mellitus: a meta-analysis of randomized controlled trials. *Clin Drug Investig*. 2022;42(1):17–28. doi: 10.1007/s40261-021-01110-w
39. Tesfaye H, Paik JM, Wexler DJ, et al. GLP-1RA and the risk of non-arteritic anterior ischaemic optic neuropathy in patients with type 2 diabetes: a population-based study. *Diabetes Obes Metab*. 2025;28(2):1517–1528. doi: 10.1111/dom.70200
40. WHO. The use of semaglutide medicines and risk of non-arteritic anterior ischemic optic neuropathy (NAION). 2025 Jun 27. Available from: <https://www.who.int/news/item/27-06-2025-27-06-2025-semaglutide-medicines-naion>
41. Bikou A, Dermiki-Gkana F, Penteris M, et al. A systematic review of the effect of semaglutide on lean mass: insights from clinical trials. *Expert Opin Pharmacother*. 2024;25(5):611–619. doi: 10.1080/14656566.2024.2343092
42. Agarwal SM, Hahn M. Semaglutide in Psychiatry—opportunities and challenges. *JAMA Psychiatry*. 2024;81(10):955. doi: 10.1001/jamapsychiatry.2024.2412
43. Regev A, Palmer M, Avigan MI, et al. Consensus: guidelines: best practices for detection, assessment and management of suspected acute drug-induced liver injury during clinical trials in patients with nonalcoholic steatohepatitis. *Aliment Pharmacol Ther*. 2019;49(6):702–713. doi: 10.1111/apt.15153
44. Loomba R, Schattenberg J, Taub R, et al. 521 ALT, FibroScan VCTE, and FibroScan Cap as predictive markers of resmetirom biopsy response. *Gastroenterology*. 2024;166(5):S-1550. doi: 10.1016/S0016-5085(24)04014-9
45. Levien TL, Baker DE. Resmetirom. *Hosp Pharm*. 2025;60(1):12–20. doi: 10.1177/00185787241278571
46. Mostafa AM, Pan Z, Yu M-L, et al. MAFLD: a comprehensive review of the link between metabolic dysfunction and cardiovascular risk. *Hepatic Med: Evidence Res*. 2025;Volume 17:75–90. doi: 10.2147/HMER.S506402
47. Pan Z, Shiha G, Esmat G, et al. MAFLD predicts cardiovascular disease risk better than MASLD. *Liver Int*. 2024;44(7):1567–1574. doi: 10.1111/liv.15931
48. Sanyal AJ, Husain M, Diab C, et al. Cardiovascular disease in patients with metabolic dysfunction-associated steatohepatitis compared with metabolic dysfunction-associated steatotic liver disease and other liver diseases: a systematic review. *Am Heart J Plus*. 2024;41:100386. doi: 10.1016/j.ahjo.2024.100386
49. Pan Z, Derbala M, AlNaamani K, et al. MAFLD criteria are better than MASLD criteria at predicting the risk of chronic kidney disease. *Ann Hepatol*. 2024;29(5):101512. doi: 10.1016/j.aohp.2024.101512
50. Pan Z, Khatry MA, Yu M-L, et al. MAFLD: an ideal framework for understanding disease phenotype in individuals of normal weight. *Ther Adv Endocrinol Metab*. 2024;15:20420188241252543. doi: 10.1177/20420188241252543
51. Eslam M, El-Serag HB, Francque S, et al. Metabolic (dysfunction)-associated fatty liver disease in individuals of normal weight. *Nat Rev Gastroenterol Hepatol*. 2022;19(10):638–651. doi: 10.1038/s41575-022-00635-5
52. Zerehpoooshnesfchi S, Lonardo A, Fan J-G, et al. Dual etiology vs. MetALD: how MAFLD and MASLD address liver diseases coexistence. *Metab Target Organ Damage*. 2025;5(1). doi: 10.20517/mtod.2025.04
53. Jiang M, Butt AS, Cua IH, et al. MAFLD vs. MASLD: a year in review. *Expert Rev Endocrinol Metab*. 2025;20(4):267–278. doi: 10.1080/17446651.2025.2492767
54. Katoue MG, Cerda AA, Garcia LY, et al. Healthcare system development in the Middle East and North Africa region: challenges, endeavors and prospective opportunities. *Front Public Health*. 2022;10:1045739. doi: 10.3389/fpubh.2022.1045739
55. Weiskirchen R. Resmetirom and semaglutide in metabolic dysfunction-associated steatohepatitis (MASH): a comparative perspective. *Explor Drug Sci*. 2025;3:1008132. doi: 10.37349/eds.2025.1008132
- This paper is of interest for providing a direct comparative analysis of the two primary pharmacological agents discussed in this review.
56. Sarkoohi Z, Bastan MM, Khajuei Gharaei MA, et al. Epidemiological trends and burden of metabolic dysfunction-associated steatotic liver disease in the Middle East and North Africa region: a 32-year analysis of health impact. *J Health Popul Nutr*. 2025;44(1):207. doi: 10.1186/s41043-025-00973-5
57. Memel Z, Gold SL, Pearlman M, et al. Impact of GLP-1 receptor agonist therapy in patients high risk for sarcopenia. *Curr Nutr Rep*. 2025;14(1):63. doi: 10.1007/s13668-025-00649-w
58. Hayward KL, Weersink RA. Improving medication-related outcomes in chronic liver disease. *Hepatol Commun*. 2020;4(11):1562–1577. doi: 10.1002/hep4.1612