Ensuring people with MASH and liver fibrosis get access to drug therapy

30-second summary:

The European Association for the Study of the Liver, European Association for the Study of Diabetes and European Association for the Study of Obesity have added to their existing 2024 guideline on diagnosis, risk stratification and lifestyle management of people with metabolic dysfunction-associated steatotic liver disease and steatohepatitis (MASLD and MASH), adding guidance on use of the newly licensed resmetirom and semaglutide 2.4 mg in people with non-cirrhotic MASH with stage 2 or 3 fibrosis. Direct comparison of interim trial results with these two drugs is not possible, as studies differed. Resmetirom targets the liver, with little metabolic effect elsewhere, so it may be prioritised in individuals without obesity or type 2 diabetes, if treatment with a GLP-1 receptor agonist is already in place for another indication, or if a GLP-1 RA is not tolerated or there is a preference for oral therapy. Semaglutide 2.4 mg has significant cardiometabolic effects but little or no direct intrahepatic effects, so it may be prioritised in people with obesity or overweight with weight-related comorbidities; type 2 diabetes with glycaemia outside target range; established or high risk of cardiovascular disease; or chronic kidney disease with overweight, obesity and/or type 2 diabetes. If recommended by NICE, these drugs are likely to be initiated by specialist teams, but the important role of finding those with MASLD at high risk of fibrosis, and supporting them with lifestyle and behaviour change and cardiovascular risk reduction, will need to take place in primary care. It is hoped that this important work will be recognised and funded.



Pam Brown
GP in Swansea

The existing guideline from the European Association for the Study of the Liver (EASL), European Association for the Study of Diabetes (EASD) and European Association for the Study of Obesity (EASO), published in 2024, provides detailed guidance on diagnosis, risk stratification and lifestyle management of people with metabolic dysfunction-associated steatotic liver disease and steatohepatitis (MASLD and MASH). Since then, significant publications have highlighted the important role that primary care teams play in using Fibrosis-4 scoring to identify high-risk individuals with MASLD who require further investigation, as well as facilitating the following:

- Access to non-invasive testing (Extended Liver Fibrosis blood test or vibration-controlled transient elastography) to confirm and stage fibrosis or cirrhosis.
- Education around the associated health risks and benefits of weight loss, in order to reduce progression of adverse liver outcomes, including fibrosis, cirrhosis and hepatocellular cancer.
- Optimisation of cardio–kidney–metabolic risk factors and reducing risk of cardiovascular events and cancers.

In the near future, these activities may also identify people who are eligible for fibrosis-modifying drugs for treatment of MASH and stage 2 or 3 fibrosis.

Resmetirom and semaglutide: Supplemental guidance

As a result of recent drug licensing, the EASL, EASD and EASO have published new joint guidance on the use of resmetirom – an orally administered, liver-directed agonist of thyroid hormone receptor-beta – and injectable semaglutide 2.4 mg once weekly as MASH-targeted therapy. This guidance is designed to supplement but not replace their 2024 guidance.

Citation: Brown P (2026) Diabetes Distilled: Ensuring people with MASH and liver fibrosis get access to drug therapy. *Diabetes & Primary Care* **28**: [Early view publication]

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The ADA/EASD type 2 diabetes consensus 2026: What's new?

Updated consensus aims for more holistic management of type 2 diabetes, its complications and associated long-term conditions, including MASLD and MASH.

Diabetes & Primary Care **28**: 207–10

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The guidance, published in the *Journal of Hepatology*, makes the following recommendations.

Non-invasive tests for fibrosis

The guideline recommends using the Fibrosis-4 (Fib-4) index for initial fibrosis assessment in individuals at risk, including those with type 2 diabetes, obesity with additional cardiometabolic risk, or persistently elevated liver enzymes. Fib-4 should be used primarily as an initial risk-stratification tool, however, with other non-invasive tests recommended to assess for suitability to receive MASH treatment.

People with a Fib-4 score of ≥1.3, or ≥2.0 if over 65 years of age, should undergo confirmatory non-invasive testing. Test thresholds for significant or advanced liver fibrosis (associated with major adverse liver-related outcomes) include the following:

- Vibration-controlled transient elastography (VCTE): liver stiffness 10–20 kPA – confirmed by repeat testing (see below) or other non-invasive testing.
- Magnetic resonance elastography: liver stiffness 3.1–5.0 kPa.
- Extended Liver Fibrosis (ELF) score of 9.8–11.3 – ideally confirmed by another non-invasive test.
- Liver stiffness by point-shear or 2-dimensional wave elastography likely carries the same diagnostic support, but thresholds are less defined, with differences between machines.

Agreement of two or more specific non-invasive tests for fibrosis increases confidence in accuracy for identifying stage 2 and 3 fibrosis.

The ELF test uses three blood-based biomarkers of liver fibrosis and is available in primary care in some parts of the UK, where it can be used to triage those who require referral for VCTE. ELF scores >9.8 stratify risk of all-cause and liver mortality, development of cirrhosis, and hospitalisation for liver decompensation.

Liver stiffness by VCTE is a good negative predictor for excluding advanced fibrosis. However, more than one-third of people with high liver stiffness on initial VCTE may have normal measurements on repeat and are unlikely to have advanced fibrosis; therefore, a repeat scan on another day is recommended, with the lower of the two scores used to reflect fibrosis status.

Pharmacological therapy

Consider resmetirom or subcutaneous semaglutide 2.4 mg therapy (assuming regulatory approval) in the following groups:

- Adults with MASLD and non-invasive tests suggestive of significant or advanced liver fibrosis with increased risk of major adverse liver events, in the absence of evidence of cirrhosis.
- Adults with biopsy-proven steatohepatitis and stage 2 or 3 fibrosis.

Non-invasive tests are preferred for identifying people eligible for treatment; liver biopsy is not required for treatment initiation and is considered unnecessary for most individuals due to an unfavourable risk-to-benefit ratio.

The choice of drugs for initiation in specialist settings should be based on expected hepatic and non-hepatic benefits versus the risks and side-effects of the drugs. Comprehensive lifestyle modification and structured behaviour therapy is recommended alongside drug therapy, as this remains the cornerstone of MASLD/MASH management.

Licences for both drugs are based on interim trial analyses demonstrating significant superiority over placebo on MASH resolution and fibrosis improvement on sequential liver biopsies (semaglutide at 18 months' treatment, resmetirom at 12 months' treatment), for use alongside currently recommended lifestyle interventions. Direct comparison of trial results is not possible, as inclusion and exclusion criteria and placebo event rates differed. However, practical differences between the two drugs are listed in *Table 1*.

- Resmetirom is liver-targeted, with little metabolic effect elsewhere, so it may be prioritised in individuals without obesity or type 2 diabetes, if treatment with a GLP-1 receptor agonist is already in place for another indication, or if a GLP-1 RA is not tolerated or there is a preference for oral therapy.
- Semaglutide 2.4 mg has significant cardiometabolic effects but little or no direct intrahepatic effects, so it may be prioritised in individuals with obesity or overweight with weight-related comorbidities; type 2 diabetes with glycaemia outside target range; established or high risk of cardiovascular disease; or chronic kidney disease with overweight, obesity and/or type 2 diabetes.

Resmetirom or semaglutide should not be used as MASH-targeted therapy in adults with MASH-related compensated cirrhosis (Child–Pugh score A), but semaglutide can be used for type 2 diabetes and weight management.

A detailed baseline assessment is recommended in specialist care prior to initiating drug therapy, and this will include adherence to lifestyle options, alcohol intake and cardiometabolic assessment. Safety assessment relevant to the planned drug will include:

- **Resmetirom:** Thyroid function, drug–drug interactions, gall bladder disease.
- **Semaglutide:** Thyroid C-cell tumours/MEN2, diabetes eye disease, history of pancreatitis, sarcopenia, kidney function, gall bladder disease, gastroparesis.

If worsening of fibrosis occurs or there is evidence of cirrhosis, these treatments should be stopped, but semaglutide may be continued if beneficial for cardiometabolic effects. Other practical points for prescribing are:

- Cardiometabolic therapies should be continued when starting treatment for MASH-related fibrosis.
- People already on GLP-1-based therapy who meet criteria for anti-MASH therapy should switch to high-dose semaglutide or add resmetirom.
- Resmetirom can be used in people on stable doses of SGLT2 inhibitors or GLP-1 RAs.
- In people with type 2 diabetes, resmetirom can be used alongside all glucose-lowering and antihypertensive drugs, but statin doses may need reduction and clopidogrel dose should be reduced.

There is no evidence for first-line combination therapy with both drugs together. Long-term effects of these drugs are currently unknown.

Table 1. Key differences between resmetirom and subcutaneous semaglutide 2.4 mg.

	Resmetirom	Semaglutide 2.4 mg
Administration	Oral, once daily	Subcutaneous injection, once weekly
Lipids	Reductions in LDL, lipoprotein (a), apolipoprotein B, non-HDL	Improves HDL and triglycerides
Glycaemia	No effect	Improves glycaemia and insulin resistance
Weight loss	No change; consider if sarcopenia or high risk	10.5% vs 2.0% placebo
Gastrointestinal tolerability	Mild/moderate diarrhoea, nausea (early weeks)	Nausea, vomiting, constipation, diarrhoea (dose-dependent)
Treatment discontinuation rates due to adverse effects	6.8% (100 mg) and 1.9% (80 mg), vs 2.2% placebo	2.6% vs 3.3% placebo
Key drug interactions	CYP2C8 – reduce clopidogrel dose, reduce statin dose (rosuvastatin/simvastatin maximum 20 mg; pravastatin/atorvastatin maximum 40 mg)	Minimal hepatic drug interactions; may slow gastric emptying, affecting drug absorption
Gall bladder risk	Increased cholelithiasis and cholecystitis	Increased gallbladder events

Implications for practice

Resmetirom (June 2026) and semaglutide 2.4 mg (July 2026) are both licensed to treat non-cirrhotic MASH with stage 2–3 fibrosis; however, their use in the UK awaits the NICE Technology Appraisals for both drugs, which are expected soon.

It is hoped that primary care teams will be motivated to use Fib-4 scores to actively identify people who may be at high risk of MASH and fibrosis, and to use the ELF test where available, and when appropriate, to refer for VCTE/FibroScan to confirm the diagnosis of MASH and stage 2 or 3 fibrosis to meet the criteria for pharmacotherapy. However, it was recognised in the feedback to NICE that expecting primary care to undertake this work will involve a significant capacity challenge, that identification and treatment initiation is likely to take longer than the 90-day timeframe usually allocated, and that a funding variation will likely also be needed to cope with treatment costs.

Even with diligent calculation of Fib-4 scores, in high-risk populations, such as those with type 2 diabetes for example, some people will not be correctly identified as having high risk of advanced fibrosis and, thus, may miss out on further imaging, diagnosis and drug therapy. Some of these people will have elevated liver enzymes, however, and we can refer them for further investigation.

Diagnosis of MASH fibrosis and initiation of pharmacotherapy with resmetirom or semaglutide 2.4 mg is likely to take place in specialist hepatology or gastroenterology services, and it is not clear whether longer-term shared-care prescribing will be implemented, with

EASL–EASD–EASO guidance on the use of resmetirom and semaglutide as MASH-targeted therapy

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liver monitoring and follow-up undertaken in specialist settings.

We will have an important role in encouraging ongoing lifestyle and behaviour changes in people with MASLD, MASH and fibrosis, with weight loss and cardiovascular risk reduction being important primary care interventions, including when awaiting VCTE to confirm liver status. Since people with MASLD and obesity are at increased risk of common cancers, including breast and colon, we can encourage non-attenders to take part in screening programmes.

Most would agree that the licensing of drugs for MASH with stage 2 or 3 fibrosis and the impending NICE Technology Appraisals make it important to help identify those who will qualify for drug treatment even if there has previously been reluctance to take on this extra workload. People with type 2 diabetes appear to be at greater risk of progression to fibrosis, and since they already have regular blood tests, we can add AST, ALT and platelets to our routine diabetes monitoring. In some areas, laboratories calculate the Fib-4 scores, flagging up those who need further investigation. The weight loss and lifestyle guidance is similar to that provided for type 2 diabetes, making it easy to incorporate in clinics, even if the individual does not qualify for treatment with anti-MASH drugs.

Most guidelines agree that only primary care teams have the opportunity to identify and refer people at high risk of MASH fibrosis. At my practice, we have been successfully incorporating MASLD screening in routine diabetes reviews for more than 2 years, using Fib-4 scores to identify and refer those requiring VCTE/FibroScan, despite long waiting lists. I hope that the availability of drug therapy will finally encourage more consistent UK-wide action and resources to identify and manage those who will benefit from drug treatment. And let's hope that our important primary care roles, as described here, will be recognised and funded.

European Association for the Study of the Liver (EASL); European Association for the Study of Diabetes (EASD); European Association for the Study of Obesity (EASO); European Association for the Study of Obesity (EASO) (2026) EASL–EASD–EASO guidance on the use of resmetirom and semaglutide as MASH-targeted therapy. *J Hepatol* **85**: 1176–97

Practice points

1. Resmetirom and subcutaneous semaglutide 2.4 mg are both approved in the UK for treatment of non-cirrhotic MASH with stage 2–3 fibrosis; however, NICE guidance is awaited and may be subject to a funding variation.
2. The advent of these drugs should encourage primary care to use Fibrosis-4 scores to identify people at high risk of MASH and fibrosis, and to use or refer for non-invasive tests to determine eligibility for these therapies in secondary care.
3. People with type 2 diabetes are at greater risk of progression to fibrosis, and since they already have regular blood tests, we can add AST, ALT and platelets to our routine diabetes monitoring to allow calculation of Fibrosis-4 score.
4. Lifestyle modification remains the mainstay of MASLD treatment, alongside cardiovascular risk reduction, and this will continue to take place in primary care.