Identification and Management of People with MASLD and MASH in Primary Care

Medscape UK X Guidelines
Primary Care Hacks

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What Is MASLD?[1–7]

- There has been recent international consensus to rename nonalcoholic fatty liver disease (NAFLD) to improve awareness and patient identification and reduce stigma;[1] using this terminology, the EASL, the EASD, and the EASO produced an updated guideline in 2024[2]
- NAFLD is now termed **metabolic dysfunction-associated steatotic liver disease (MASLD)**[1]
  - MASLD encompasses individuals who have **hepatic steatosis and at least one cardiometabolic risk factor**[3]
- **Metabolic dysfunction-associated steatohepatitis (MASH)** replaces nonalcoholic steatohepatitis (NASH).[3] MASH is defined by inflammation of hepatocytes and carries a risk of progression to fibrosis, cirrhosis, and HCC[3,4]
- **MetALD** describes individuals with MASLD who consume more than recommended amounts of alcohol per week (defined as 3.75–7.50 units/day [30–60 g/day] in men and 2.50–6.25 units/day [20–50 g/day] in women)[2]
  - for all adults in the UK, the recommended alcohol intake is ≤14 units/week (i.e. 112 g/week, or 2.0 units/day [16 g/day]), best spread evenly over ≥3 days[5]
- **MASLD is primarily a metabolic disease heavily influenced by lifestyle factors, and is the liver's manifestation of the MetS alongside hypertension, insulin resistance and dysglycaemia, dyslipidaemia, and obesity/increased waist circumference.**[6,7]

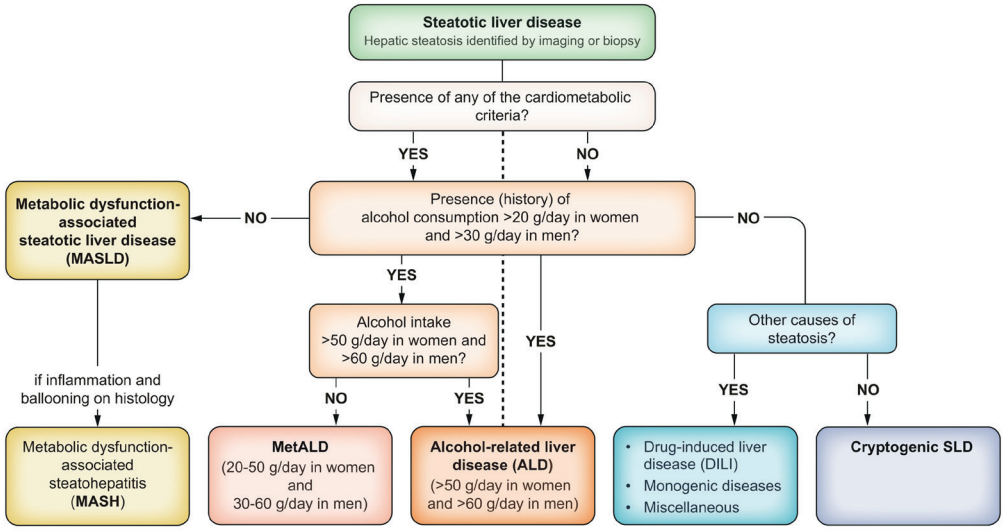
Cardiometabolic Risk Factors[2,8,9]

- BMI ≥25 kg/m² (23 kg/m² if high-risk ethnic minority) or waist circumference ≥94 cm (37.0 inches) for men (≥90 cm [35.4 inches] in men of South Asian or Chinese ethnicity, or ≥85 cm [33.5 inches] in men of Japanese ethnicity) or ≥80 cm (31.5 inches) for women of all ethnicities
- HbA_{1c} 39–47 mmol/mol, fasting plasma glucose of 5.6–6.9 mmol/l (100–125 mg/dl), or 2-hour plasma glucose during OGTT of 7.8–11 mmol/l (140–199 mg/dl), or established T2D
- BP ≥130/85 mmHg or antihypertensive drug treatment
- Plasma triglycerides ≥1.70 mmol/l or lipid-lowering treatment
- Plasma HDL-cholesterol ≤1.0 mmol/l in men, ≤1.30 mmol/l in women, or lipid-lowering treatment.

Secondary Causes of Hepatic Steatosis[2,8,10]

- Drug-induced liver injury, e.g. amiodarone, methotrexate, tamoxifen, and corticosteroids
- Endocrine disorders, such as hypothyroidism, PCOS, panhypopituitarism, or growth hormone deficiency
- Nutrient deficiency or malnutrition, such as from acute weight loss due to bariatric surgery or fasting, total parenteral nutrition, or small intestinal bacterial overgrowth
- Chronic hepatitis C virus infection.

Flowchart for SLD and Its Subcategories[2]



Note: 50 g of alcohol equates to 6.25 units, and 60 g equates to 7.5 units.

How Common and Serious Is MASLD?[2,11–13]

- MASLD is now the most common liver disorder in Western countries, and has been estimated to affect up to 30% of adults in the UK[11,12]
  - MASH has been estimated to affect up to 5% of the UK population[11]
- MASLD (specifically progressive MASH) is the fastest growing indication for liver transplantation in Western countries[13]
- MASLD is also associated with an increased prevalence and incidence of CVD[2]
  - CVD is a more common cause of death than liver disease in MASLD[2]
- MASLD is highly prevalent in people living with T2D.[2]

Screening for MASLD in Primary Care[2,14]

- The appearance of steatosis on abdominal USS is operator-dependent and a normal USS does not rule out MASLD[14]
- Consider case-finding strategies for MASLD with liver fibrosis in those who have abnormal liver enzymes, cardiometabolic risk factors, and/or incidental radiological signs of hepatic steatosis[2]
- The EASL, the EASD, and the EASO recommend looking for MASLD with liver fibrosis in individuals with one or more of the following:[2]
  - T2D
  - abdominal obesity and ≥1 additional metabolic risk factor
  - abnormal liver blood test results.

Useful Resources

- The British Liver Trust:
  - *Coffee consumption and the liver—the potential health benefits*
  - *MASLD, NAFLD, and fatty liver disease*
- The EASL:
  - *Non-alcoholic fatty liver disease (NAFLD): how you can reduce the risk for your liver and for other health issues?*

Assessing People With MASLD and Stratifying Their Risk of Progression to Advanced Fibrosis[2,8,15–19]

- Check BMI, waist circumference, waist-to-height ratio (a ratio of 0.4–0.49 is considered low risk, 0.50–0.59 moderate risk, and ≥0.6 high risk; no adjustment for ethnicity required), and BP[2,15,16]
- Check bloods to exclude coexisting liver disease (if there are abnormal liver blood tests) and metabolic conditions depending on clinical judgement. Not everyone needs a full liver screen![2,8,15,17]
- Various blood tests may be required depending on clinical presentation, but consider the following in the first instance:[2,8,15,17]
  - liver blood tests; see the Primary Care Hack, *Interpreting Liver Blood Tests in Primary Care*
  - fasting lipid profile
  - HbA_{1c}; see the Primary Care Hack, *Type 2 Diabetes Cardiovascular Renal Metabolic Review Checklist*
  - hepatitis serology
  - FBC
  - iron studies (see the Primary Care Hack on *Interpreting Iron Studies in Primary Care*)
  - autoantibodies and immunoglobulins
- Assess the risk of advanced liver fibrosis using a noninvasive scoring system such as the FIB-4 score.[15,18,19] FIB-4 is calculated by the laboratory using age, AST, ALT, and platelets, and is a way of staging disease severity[18]
- Figure 2 in the EASL–EASD–EASO guideline on MASLD details a strategy for noninvasive assessment of liver fibrosis risk (also see *Assessment of MASLD Using the FIB-4 Non-invasive Scoring System*, below).[2]

Assessment of MASLD Using the FIB-4 Non-invasive Scoring System[2,18]

FIB-4 Score (Aged ≤65 Years)	Risk Status for Liver Fibrosis	Recommended Action
<1.30	Low risk for fibrosis	Consider reassessing every 1–3 years in primary care
1.30–2.67	Intermediate risk for fibrosis	Depending on clinical context, medical history, and the resources available locally, consider referring the patient for a VCTE (a non-invasive ultrasound-based technique that measures liver stiffness, e.g. FibroScan) or an equivalent second-line test, e.g. ELF (a blood test that reflects severity of any liver fibrosis) or MRE (an MRI-based technique to assess liver stiffness) • If VCTE ≥8.0 kPa, treat as 'high risk' for advanced fibrosis • If VCTE <8.0 kPa or second-line testing is not carried out, conduct intensified management of comorbidities (see *Managing MASLD in Primary Care*, below) and reassess after ≤1 year o If FIB-4 score remains ≥1.30, test VCTE (or equivalent) o If FIB-4 score is now <1.30, treat as 'low risk' for fibrosis
>2.67	High risk for advanced fibrosis	Refer to hepatology

Note: For individuals >65 years of age, FIB-4 score <2.0 suggests low risk for liver fibrosis. This table draws on EASL–EASD–EASO guidance and FIB-4 cut-offs. Healthcare professionals should refer to their own local pathways where they exist.

Managing MASLD in Primary Care[2,20–25]

What Can We Do in Primary Care for Those With MASLD to Lower Their Risk of Advanced Fibrosis?

- Strongly encourage and facilitate weight loss where possible: a weight loss target of ≥5% is recommended to reduce liver fat, with 7–10% improving liver inflammation and ≥10% improving fibrosis[2]
- Recommend physical activity and exercise tailored to the individual's situation and preference, ideally amounting to >150 minutes of moderate-intensity exercise or >75 minutes of vigorous exercise per week; also recommend that patients minimise sedentary time[2]
- The EASL recommends a Mediterranean diet,[20] which can reduce liver fat even without weight loss
- Active management of any coexisting features of MetS, for example, dysglycaemia/T2D, hypertension, dyslipidaemia, and abdominal obesity/increased waist circumference
- Ideally, alcohol abstinence is advised; otherwise, maintain alcohol intake within recommended limits
- Assess CV risk using QRISK3, and consider statin therapy, including those with abnormal baseline liver blood tests. Statins can be initiated as long as liver blood tests are <3x ULN[21]
  - there is emerging evidence that statin use is associated with a reduction in liver cancer risk[22]
- Coffee might help!
  - consumption of coffee (both caffeinated and not) has been associated with improvements in liver damage and reduced liver-related clinical outcomes in adults with MASLD[2,23]
  - a moderate intake of coffee of ≥3 cups a day may be beneficial[2,23]
- Consider incretin-based weight loss drugs or bariatric procedures in those living with overweight or obesity[2]
- There are no currently licensed drug therapies for MASLD/MASH in the UK, but certain drugs are sometimes used off label
  - resmetirom is the first MASH therapy to be approved by the US FDA,[24] and can be considered for the treatment of noncirrhotic MASH with significant liver fibrosis when it has been approved locally[2]
  - there is emerging, compelling evidence of the benefits in MASH of GLP-1 RAs, tirzepatide, survodutide (a dual GLP-1 and glucagon agonist), and retatrutide (a triple GLP-1, GIP, and glucagon RA), but the EASL–EASD–EASO guideline only recommends GLP-1 RAs in patients with MASH **for their respective indications** (i.e. T2D, obesity);[2,25] not enough current evidence was found to recommend SGLT2 inhibitors, incretin mimetics, or pioglitazone as MASH-targeted therapies[2]
- Follow up in primary care:
  - if identified as intermediate or high risk, consider referral to secondary care hepatology for transient elastography (FibroScan)
  - ensure those with MASLD found to have a low risk of advanced fibrosis are under recall and reviewed regularly in primary care, using clinical judgement and Figure 2 in the EASL–EASD–EASO guideline.

ALT=alanine transaminase; **AST**=aspartate aminotransferase; **BMI**=body mass index; **BP**=blood pressure; **BSG**=British Society of Gastroenterology; **CV**=cardiovascular; **CVD**=cardiovascular disease; **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; **FBC**=full blood count; **FDA**=Food and Drug Administration; **FIB-4**=Fibrosis-4; **GIP**=glucose-dependent insulinotropic polypeptide; **GLP-1**=glucagon-like peptide-1; **HbA_{1c}**=glycated haemoglobin; **HCC**=hepatocellular carcinoma; **HDL**=high-density lipoprotein; **MASLD**=metabolic dysfunction-associated steatotic liver disease; **MASH**=metabolic dysfunction-associated steatohepatitis; **MetALD**=metabolic alcohol-related liver disease; **MetS**=metabolic syndrome; **MRE**=magnetic resonance elastography; **MRI**=magnetic resonance imaging; **NAFLD**=nonalcoholic fatty liver disease; **NASH**=nonalcoholic steatohepatitis; **OGTT**=oral glucose tolerance test; **PCOS**=polycystic ovary syndrome; **RA**=receptor agonist; **SGLT2**=sodium–glucose co-transporter-2; **SLD**=steatotic liver disease; **T2D**=type 2 diabetes; **ULN**=upper limit of normal; **USS**=ultrasound scan; **VCTE**=vibration-controlled transient elastography