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?

- There has been recent international consensus to rename non-alcoholic fatty liver disease (NAFLD) to improve awareness and patient identification and reduce stigma⁽¹⁾
- NAFLD is now termed metabolic dysfunctionassociated steatotic liver disease (MASLD)^[1]

 MASLD encompasses individuals who have hepatic steatosis and at least one cardiometabolic risk factor^[2]
- Metabolic dysfunction-associated steatohepatitis (MASH) replaces non-alcoholic steatohepatitis (NASH).^[2] MASH is defined by inflammation of hepatocytes and carries a risk of progression to fibrosis, cirrhosis, and hepatocellular carcinoma (HCC)
- **MetALD** describes individuals with MASLD who consume more than recommended amounts of alcohol per week (around 17.5 units/week for women and 26 units/week for men)
- MASLD is primarily a metabolic disease heavily influenced by lifestyle factors, and is the liver's manifestation of the metabolic syndrome (MetS) alongside hypertension, insulin resistance and dysglycaemia, dyslipidaemia, and obesity/ increased waist circumference.^{[4][5]}

How Common and Serious is MASLD?

- 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^{(6)[7]}
 MASH has been estimated to affect up to 5% of
 - the UK population^[6]
- MASLD (specifically the progressive MASH) is the fastest growing indication for liver transplantation in Western countries^[6]
- MASLD is also associated with an increased prevalence and incidence of cardiovascular disease (CVD)⁽⁹⁾
 - $^{\rm o}$ CVD is a more common cause of death than liver disease in MASLD^{[9]}
- MASLD is highly prevalent in people living with type 2 diabetes (T2D); the global prevalence of MASLD in T2D is 67%.



Cardiometabolic Risk Factors

- $BMI \ge 25 \text{ kg/m}^2$ (23 kg/m² if high-risk ethnic minority) or waist circumference >94 cm for men (>90 cm if high-risk ethnic minority) or >80 cm for women (all ethnicities)
- HbA_{1c} 42–47mmol/mol or established type 2 diabetes
- Blood pressure ≥130/85 mmHg or antihypertensive drug treatment
- Plasma triglycerides ≥1.70 mmol/l or lipid-lowering treatment
- Plasma HDL-cholesterol ≤1.0mmol/l or lipid-lowering treatment
- Adapted from: Alberti K, Eckel R, Grundy S et al. Harmonizing the Metabolic Syndrome. *Circulation*, 2009; **120** (16).

Secondary Causes of Hepatic Steatosis

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

Screening for MASLD in Primary Care

- The appearance of steatosis on abdominal ultrasound (USS) are operatordependent and a normal USS does not rule out MASLD^[15]
- Consider screening all individuals with steatosis (e.g. incidentally found on USS) for features of MetS, **independent of liver blood tests**
- Consider screening for MASLD with liver blood tests and/or USS in people living with obesity or MetS
- In high-risk individuals (aged >50 years, T2D, MetS) active case finding for advanced disease (that is, MASH) is recommended (see below).

Assessing People with MASLD and Stratifying Their Risk of Progression to Advanced Fibrosis

- Check body mass index, waist circumference and blood pressure^[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!^[16]
- See the NICE Clinical Knowledge Summary on NAFLD for further guidance on arranging blood tests, but consider the following in the first instance:^{116]}
 - liver blood tests
 - lipid profile
 - ° glycated haemoglobin A_{1c} (HbA_{1c}); see the Primary Care Hack, <u>Type 2 Diabetes Cardiovascular Renal Metabolic Review Checklist</u>
 - ° hepatitis serology
 - full blood count
 - 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 non-invasive scoring system such as the <u>Fibrosis-4 (FIB-4) score.</u>⁽¹⁶⁾ FIB-4 is calculated by the laboratory using age, AST, ALT, and platelets, and stages disease severity⁽¹⁷⁾
- The British Society of Gastroenterology (BSG) has produced an <u>algorithm for the diagnosis of NAFLD and non-invasive assessment of liver</u> <u>fibrosis</u>.⁽¹¹⁶⁾

Diagnosis of MASLD Using the FIB-4 Non-invasive Scoring System^{[17][18]}

FIB-4 Score (Aged ≤65 Years)	Risk Status for Liver Fibrosis	Recommended Action
<1.30	Low risk for fibrosis	Consider monitoring every 2 years in primary care
1.30–3.25	Intermediate risk for fibrosis	Second-line non-invasive testing to rule out advanced fibrosis, for example, ELF test, FibroTest, or Fibroscan. If advanced fibrosis excluded, individuals can be treated as low risk and monitored in primary care as above
>3.25	High risk for advanced fibrosis	Consider referral to hepatology

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

ELF=enhanced liver fibrosis; **FIB-4**=Fibrosis-4

Managing MASLD in Primary Care

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: weight loss 3–5% reduces hepatic steatosis, ≥5–7% can lead to resolution of MASH, and ≥10% improves hepatic fibrosis^[19]
- Aim for moderate-intensity exercise training for 150-200 minutes per week in 3-5 sessions where possible
- 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 <u>QRISK3</u>, 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!

• there is evidence brewing that coffee is good for liver health, and decreases the risk of fibrosis, cirrhosis, and HCC in chronic liver disease, including MASLD^[23]

- no specific recommendations have been made; however, a moderate intake of coffee of 3–5 cups a day may be beneficial^[24]
- There are no current licensed drug therapies for MASLD/MASH, however there is emerging and compelling evidence for <u>pioglitazone</u>, <u>sodium</u>glucose cotransporter-2 inhibitors, glucagon-like peptide-1 (GLP-1) receptor agonists, and the dual GLP-1 and glucose-dependent insulinotropic polypeptide receptor agonist, tirzepatide^{[25][26]}
 - NICE and EASL guidance suggest that pioglitazone can be used off-label in those without T2D for MASH
- Follow up in primary care:
 - o if identified as intermediate or high risk, consider referral to secondary care gastroenterology 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 the <u>BSG guidance</u>.

Useful Resources

- The British Liver Trust:
 - <u>Coffee consumption and the liver the potential health benefits</u>
 - <u>NAFLD, NASH and fatty liver disease</u>
- The European Association for the Study of the Liver:
 <u>Non-alcoholic fatty liver disease (NAFLD): How you can reduce the risk for your liver and for other health issues?</u>

For references, and to view this Primary Care Hack online, visit medscape-uk.co/Hack-MASLD