

MASTERCLASS FOR PRIMARY CARE

Liver disease and diabetes

Metabolic dysfunction-associated steatotic liver disease (MASLD): why it matters, how to find it and how to treat it

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NHS West Yorkshire Integrated Care Board

45-minute session · September 2026

2 in 3

people with type 2 diabetes
have MASLD

Declarations of interest 2026/27



Pharmaceutical and device industry

I have worked with and/or had discussions with the following companies. I have not received any direct payments from pharmaceutical companies.

- Lilly
- AstraZeneca
- Boehringer Ingelheim
- Novo Nordisk
- Abbott
- Dexcom
- Roche
- Sanofi
- Daiichi Sankyo
- Menarini
- GSK
- Amgen
- Novartis
- Insulet
- Medtronic
- Ypsomed
- AbbVie
- Bayer
- Senseonics
- Tandem
- Ascensia



Roles

- Chair, Cardio-Renal and Metabolic Medicine Expert Reference Group, West Yorkshire ICB
- Chair, Diabetes UK Healthcare Professional Advisory Group
- Trustee, Novo Nordisk Research Foundation
- Trustee, Primary Care Diabetes and Obesity Society
- Advisor, UKCPO
- Member, Kidney Research UK College of Experts



Academic

Aligned to the University of Leeds for my NIHR Pre-Doctoral Fellowship. I work with the University of Leeds and the Leeds Beckett University Obesity Institute on ongoing obesity work.



Paid education and consultancy

TREND UK · iHeed · Omniamed · PCDOS · Soar Beyond · YHRA · PCPA · Clinilink



External providers in diabetes and obesity

Middleton and Hunslet PCN · LS25/26 PCN · Cognitant · HCI · Optum · IQVIA · York Health Economics Consortium · All About Obesity · Healthya · Leeds GP Confederation · Leeds Community Services · Leeds Teaching Hospitals

What we will cover in 45 minutes

By the end of this session you will be able to:

- 1 Explain the MASLD nomenclature and why fibrosis, not fat, drives outcomes
- 2 Interpret liver blood tests and calculate FIB-4 in people with diabetes
- 3 Apply a primary care pathway, including when and how urgently to refer
- 4 Choose therapies that support liver health and explain how emerging MASH treatments work

01

Why is MASLD important yet under-recognised?

8 min

02

Liver function tests: interpretation and when to refer

11 min

03

Treatments, current and future

12 min

04

Case studies: three patients you may already know

10 min

Plus 2 minutes of introduction and 2 minutes for take-home messages and questions

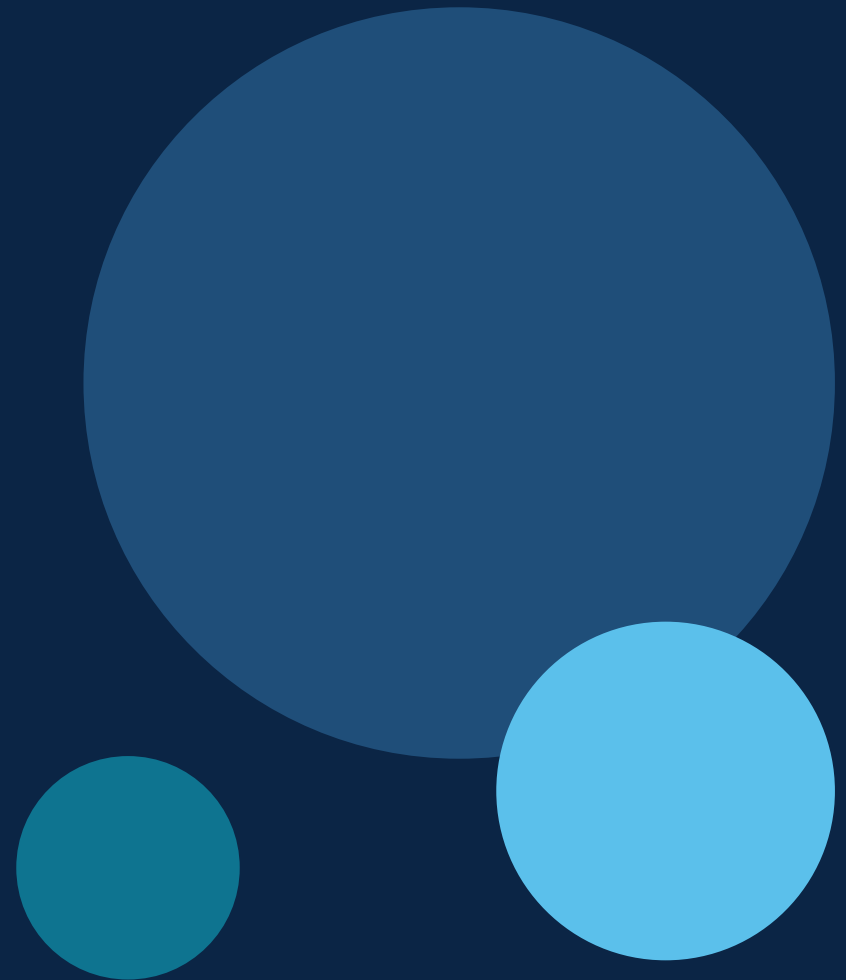
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01

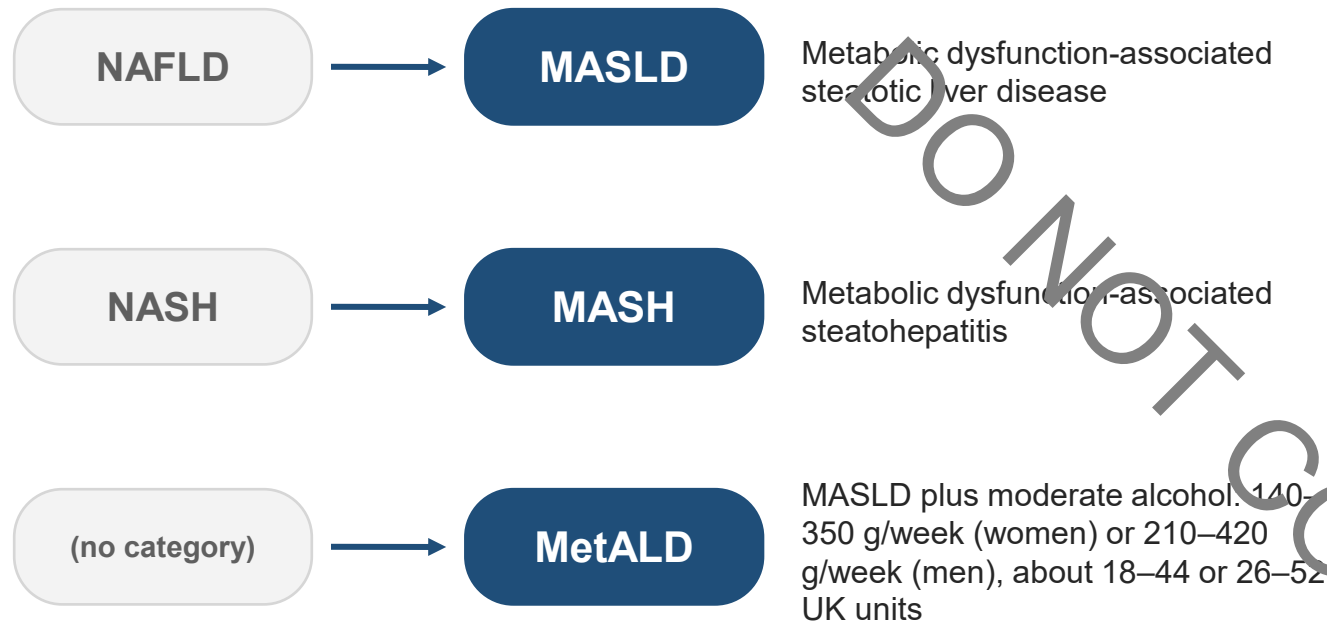
Why is MASLD important yet under-recognised?

New names, the scale of the problem, prognosis and the diagnostic gap

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From NAFLD to MASLD: new names, same patients

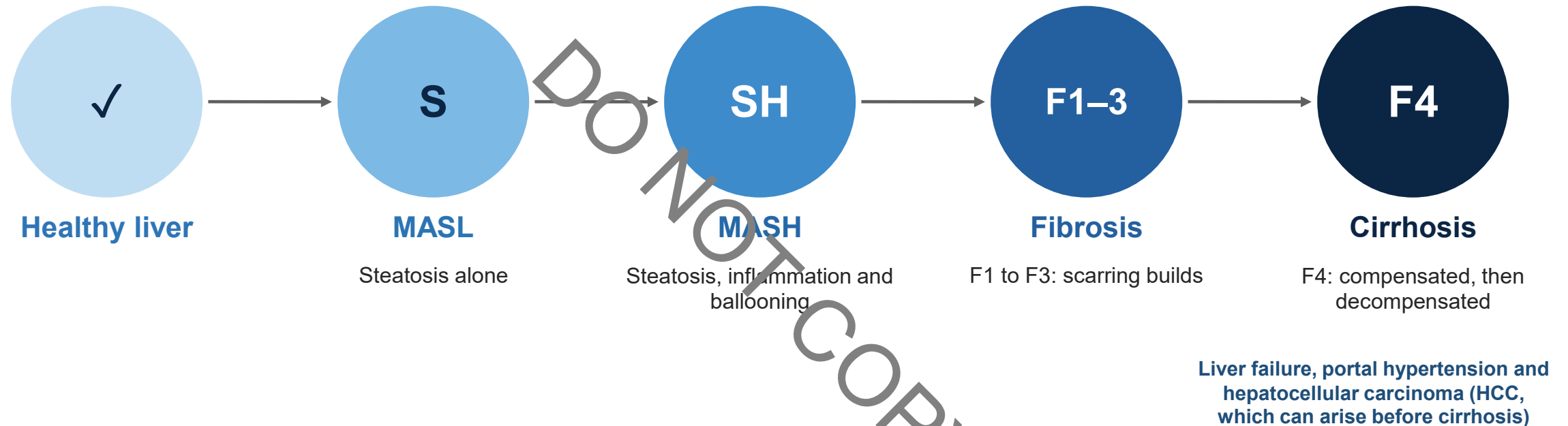


MASLD = steatosis + at least one of five cardiometabolic criteria + no other cause

- 1 BMI ≥ 25 kg/m² (≥ 23 in Asian populations) or raised waist circumference
- 2 Fasting glucose ≥ 5.6 mmol/L, HbA1c ≥ 39 mmol/mol, type 2 diabetes or treatment
- 3 Blood pressure $\geq 130/85$ mmHg or treatment
- 4 Triglycerides ≥ 1.7 mmol/L or treatment
- 5 HDL cholesterol ≤ 1.0 mmol/L (men) or ≤ 1.3 mmol/L (women) or treatment

What about MAFLD? MAFLD was proposed in 2020 with different criteria. The 2023 multisociety Delphi consensus adopted MASLD, and NICE renamed NG49 to MASLD in July 2026. Almost everyone labelled NAFLD meets MASLD criteria, so the existing evidence still applies.

A spectrum where fibrosis is the milestone that matters



Slow, but not benign

Fibrosis progresses about one stage every 14 years with steatosis alone and every 7 years with MASH, faster in type 2 diabetes.



It moves both ways

MASH and fibrosis can regress with weight loss and metabolic treatment, which is why finding people early matters.



The liver is not the main killer

Cardiovascular disease is the most common cause of death in MASLD, followed by extrahepatic cancers and then liver disease.

The scale: common, silent and concentrated in diabetes clinics

1 in 3

adults worldwide have
MASLD

Younossi, Hepatology 2023

65%

of people with type 2
diabetes have MASLD,
rising to 69% in 2021

*Younossi, Clin Gastroenterol Hepatol
2024*

1 in 5

people with type 2
diabetes have advanced
fibrosis

*Wongtrakul, J Gastroenterol Hepatol
2024*

>80%

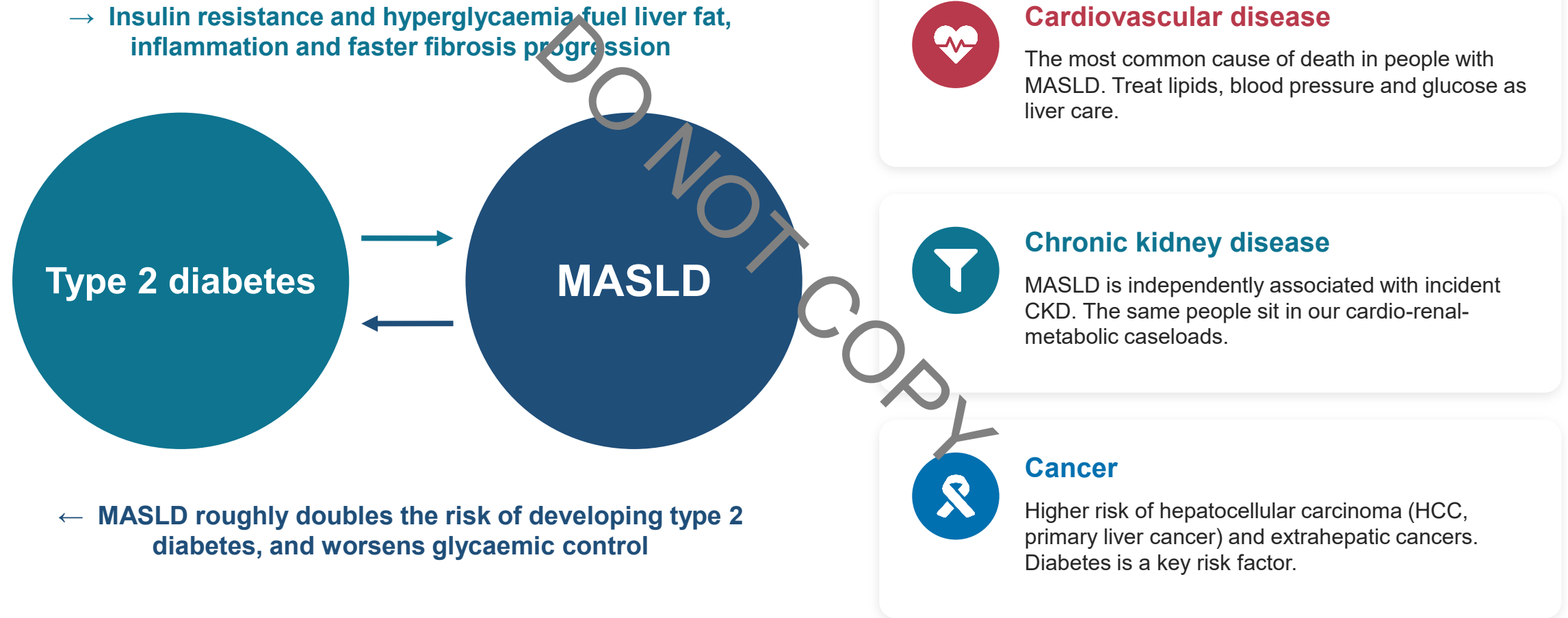
of people with MASLD
have normal routine liver
blood tests

NICE NG49

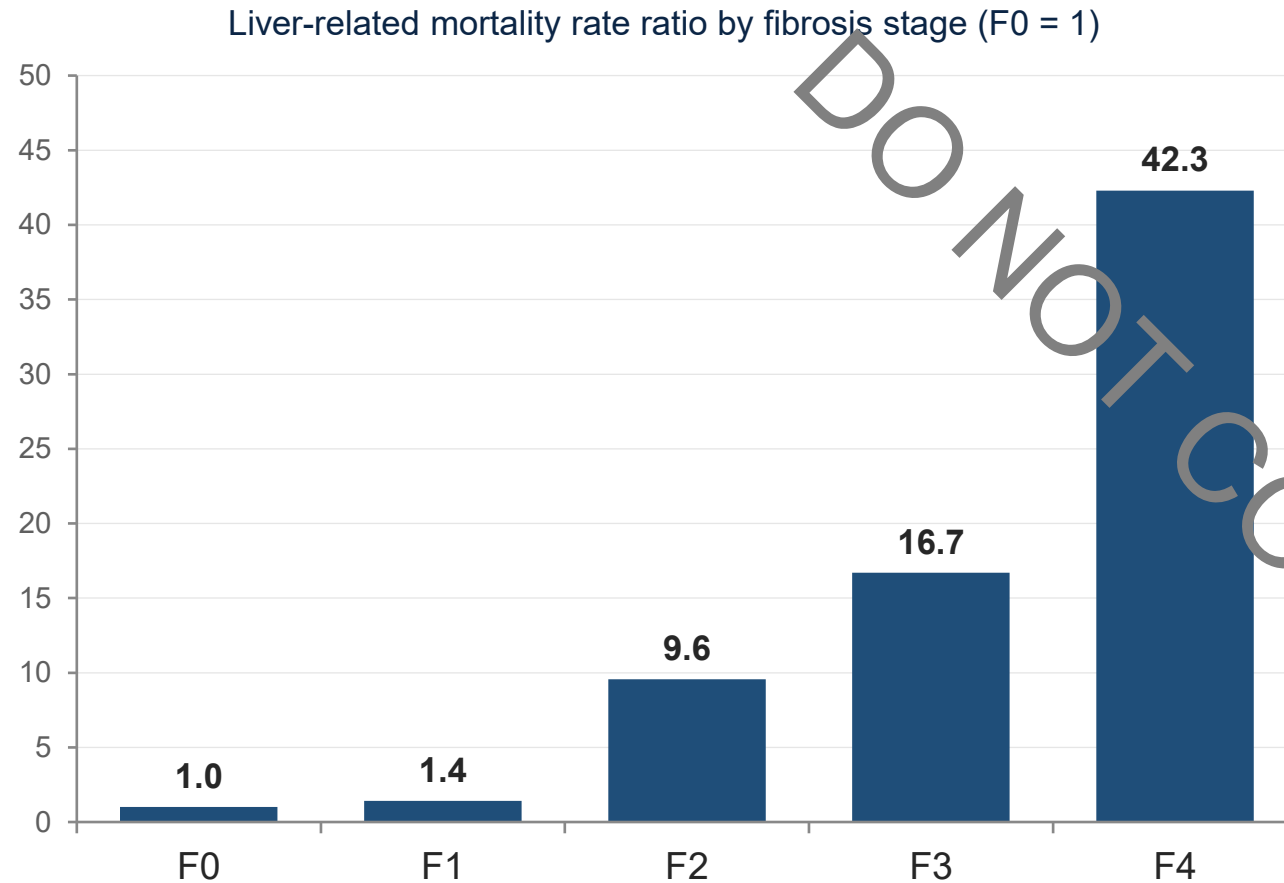


Around three quarters of people with liver disease in the UK are diagnosed at a late stage. In a typical practice list of 10,000 patients with around 700 people with diabetes, several hundred will have MASLD and many will have advanced fibrosis that nobody has looked for.

Liver disease and diabetes: a two-way street



Prognosis: fibrosis stage, not fat, predicts outcomes



42×

higher liver-related mortality at F4 than F0

All-cause mortality rises too: about 2.5× at F2, 3.5× at F3 and 6.4× at F4 compared with no fibrosis.

Fibrosis stage, not the presence of MASH, is the strongest predictor of mortality and severe liver disease in long-term cohorts.

Our job in primary care: find fibrosis, not fat.

Six reasons we miss it



Silent until late

Usually no symptoms until cirrhosis or decompensation. Fatigue and right upper quadrant discomfort are non-specific.



Reassuring blood tests

Most people have normal ALT, and ALT often falls as fibrosis advances. Normal does not mean healthy.



'Just a fatty liver'

Ultrasound reports of steatosis are filed without action. Ultrasound shows fat but cannot stage fibrosis.



Not in the review

Liver health sits outside the diabetes annual review, QOF and most local templates, so FIB-4 is rarely calculated.



'Nothing to offer'

Therapeutic nihilism discourages testing, yet lifestyle, metabolic medicines, surveillance and specialist care all change outcomes.



Stigma and patchy pathways

Blame-laden language and variable access to ELF and FibroScan create postcode differences in who gets diagnosed.

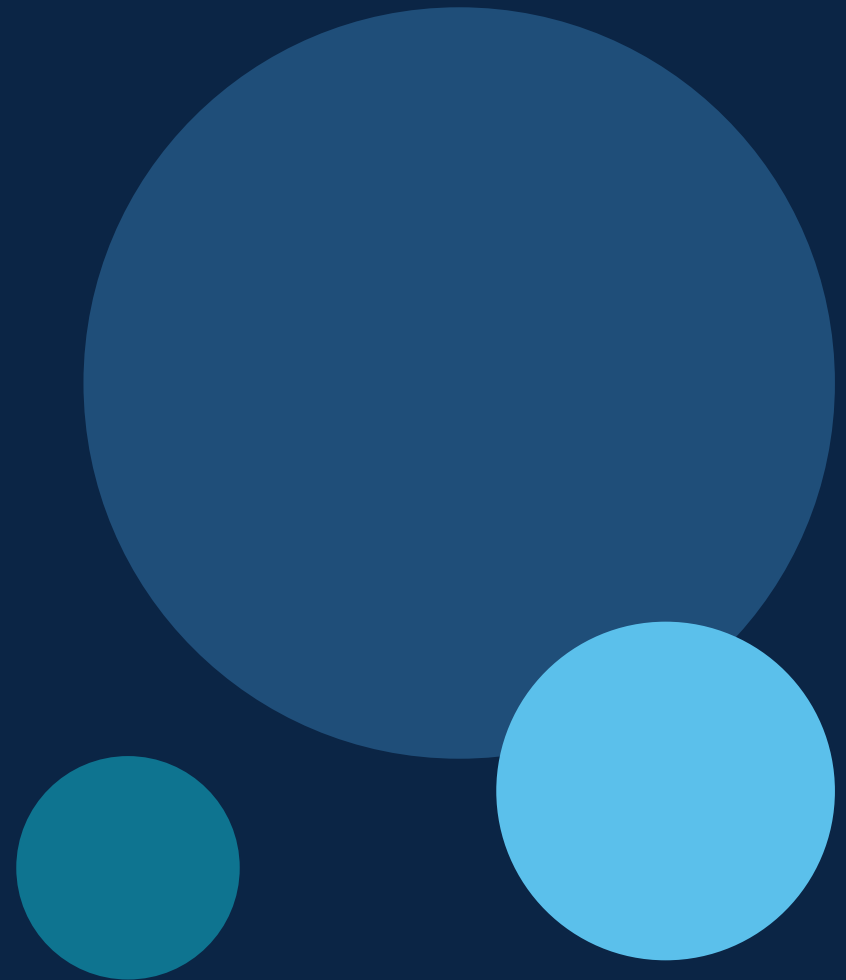
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02

Liver function tests: interpretation and when to refer

Reading the panel, staging fibrosis and choosing the right referral route

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Reading the liver blood test panel

Test	What it mainly tells you	Watch out for
ALT	Hepatocellular injury; the most liver specific enzyme	Normal ALT does not exclude MASLD or advanced fibrosis; laboratory upper limits are often above healthy values
AST	Hepatocellular injury (also muscle, heart and red cells)	AST higher than ALT suggests alcohol or advanced fibrosis
ALP	Cholestasis or biliary obstruction	Also raised by bone disease, growth and pregnancy; check GGT to confirm a liver source
GGT	Sensitive marker of liver or biliary stress	Raised by alcohol, MASLD and enzyme-inducing medicines; poor specificity on its own
Bilirubin	Excretory function	Isolated unconjugated rise with normal enzymes is usually Gilbert's syndrome
Albumin	Synthetic function (changes slowly)	Also low in acute illness, malnutrition and kidney protein loss
Platelets	Portal hypertension, through splenic sequestration	Below $150 \times 10^9/L$ with chronic liver disease: think cirrhosis
PT or INR	Synthetic function (changes quickly)	Affected by warfarin and vitamin K deficiency

Patterns, and three pitfalls in people with diabetes

Hepatocellular pattern

ALT and AST predominate

- MASLD and MetALD
- Alcohol-related liver disease
- Viral hepatitis B or C
- Medicines and supplements
- Autoimmune hepatitis
- Haemochromatosis

Cholestatic pattern

ALP with GGT predominates

- Gallstones and biliary obstruction
- Primary biliary cholangitis
- Primary sclerosing cholangitis
- Medicines such as co-amoxiclav and flucloxacillin
- Infiltration, including malignancy

Severity signals

Regardless of enzyme levels

- Platelets below $150 \times 10^9/L$
- Albumin low without another cause
- Bilirubin or INR raised
- AST higher than ALT
- Splenomegaly or ascites on imaging

1

Normal enzymes do not mean a healthy liver. Stage fibrosis in everyone at risk.

2

The size of the ALT rise does not reflect fibrosis stage. Use FIB-4, not ALT, to judge risk.

3

Do not stop a statin for transaminases below 3 times the upper limit of normal (NICE NG238).

Abnormal liver blood tests: a structured work-up

1 History and examination

- Alcohol intake: AUDIT-C score and units per week (see next slide)
- Metabolic risk: weight, waist, diabetes, blood pressure, lipids
- Viral risk factors and country of birth
- Family history of liver disease
- Signs of chronic liver disease

2 Standard liver aetiology screen

- Abdominal ultrasound
- Hepatitis B surface antigen and hepatitis C antibody
- Anti-mitochondrial, anti-smooth muscle and antinuclear antibodies
- Serum immunoglobulins
- Ferritin and transferrin saturation
- Consider coeliac serology, alpha-1 antitrypsin and caeruloplasmin (younger adults)

3 Medicines review

- Steatosis: corticosteroids, tamoxifen, methotrexate, amiodarone, sodium valproate, some antipsychotics and antiretrovirals
- Drug-induced liver injury: co-amoxiclav, flucloxacillin, nitrofurantoin, NSAIDs
- Herbal and dietary supplements, including turmeric and green tea extract

British Society of Gastroenterology advice: complete the aetiology screen rather than repeating the test and waiting. Then, if MASLD is likely, calculate FIB-4.

AUDIT-C: the alcohol history in three questions

Question	0	1	2	3	4
How often do you have a drink containing alcohol?	Never	Monthly or less	2 to 4 times a month	2 to 3 times a week	4 or more times a week
How many units of alcohol do you drink on a typical drinking day?	1 to 2	3 to 4	5 to 6	7 to 9	10 or more
How often do you have 6 or more units (women) or 8 or more units (men) on one occasion?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily

What the total score means

0 to 4

Lower risk drinking. Record the weekly units and reinforce the UK guideline of no more than 14 units a week.

5 or more

Increasing or higher risk. Go on to the remaining 7 questions of the full AUDIT.

Full AUDIT (0 to 40): 8 to 15 increasing risk, give brief advice; 16 to 19 higher risk, brief advice and referral; 20 or more possible dependence, refer to specialist alcohol services.

Using it in MASLD

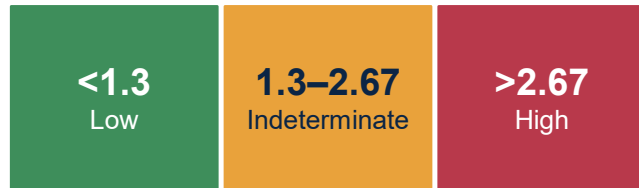
- Record weekly units too: units decide whether this is MASLD, MetALD or alcohol-related liver disease
- Under-reporting is common. Ask without judgement and ask again at review
- Advise abstinence once advanced fibrosis or cirrhosis is confirmed
- If dependence is possible, do not advise stopping abruptly: withdrawal can be dangerous

Staging fibrosis without a biopsy

FIB-4

First line, from routine bloods

$$(\text{age} \times \text{AST}) \div (\text{platelets} \times \sqrt{\text{ALT}})$$



- Use a lower cut-off of 2.0 in people aged 65 and over
- Less reliable under 35 years
- Free, and available in most GP systems and online calculators

ELF test

Second line, blood test

$$\text{HA} + \text{PIIINP} + \text{TIMP-1}$$

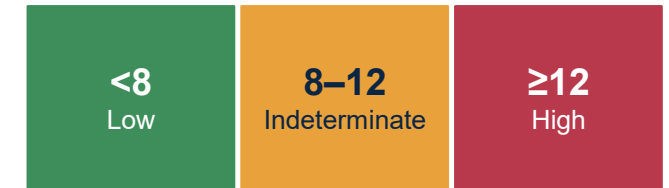


- Enhanced Liver Fibrosis score from three markers of scar turnover
- NICE NG49 uses 10.51 for advanced fibrosis; many UK pathways refer from 9.5 or 9.8

FibroScan (VCTE)

Second line, transient elastography

Liver stiffness in kilopascals



- 15 kPa or more suggests compensated advanced chronic liver disease; 25 kPa or more suggests portal hypertension
- Fast for 2 to 3 hours; inflammation, cholestasis and heart failure can overestimate stiffness

What makes up the ELF score?

Three direct markers of scar turnover in one blood sample

HA

Hyaluronic acid

Made by activated stellate cells and normally cleared by liver sinusoidal cells, so it rises with both scar formation and impaired clearance.

PIIINP

Procollagen III N-terminal peptide

Cut from procollagen as new type III collagen is laid down. A marker of active scar formation.

TIMP-1

Tissue inhibitor of metalloproteinase 1

Blocks the enzymes that break down scar tissue. High levels mean the balance has tipped towards scar accumulation.

$$\text{ELF} = 2.278 + 0.851 \ln(\text{HA}) + 0.751 \ln(\text{PIIINP}) + 0.394 \ln(\text{TIMP-1})$$

Calculated automatically by the laboratory. The original research algorithm also included age; the commercial test does not.

Interpreting the score

≥11.3

Cirrhosis

9.8–11.29

Severe fibrosis

7.7–9.79

Moderate fibrosis

<7.7

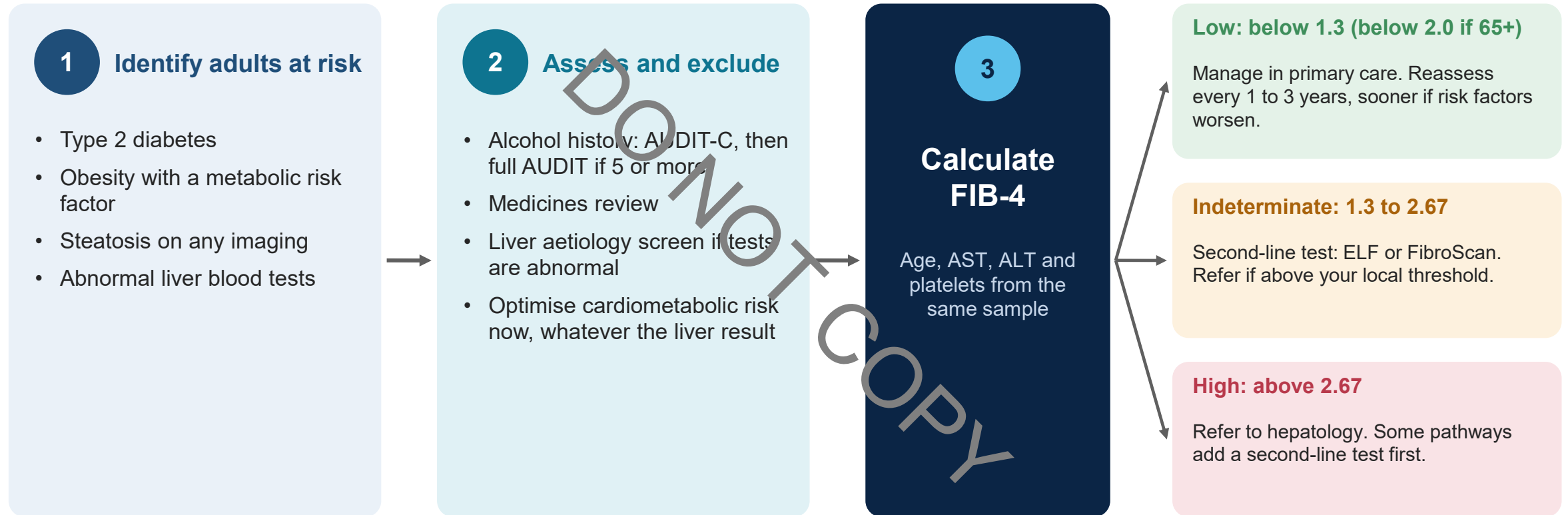
None to mild fibrosis

NICE NG49: 10.51 or above indicates advanced fibrosis. Many local pathways refer from 9.5 or 9.8.

Pitfalls

- Not liver-specific: raised by other fibrotic or inflammatory conditions, such as lung fibrosis, systemic sclerosis and arthritis
- Rises with age, so false positives are more likely in older adults

A primary care pathway for MASLD



Does it work? A FIB-4 then ELF pathway in Camden and Islington increased detection of advanced fibrosis and cirrhosis around fivefold and reduced unnecessary hepatology referrals by around 80%.

Matching urgency to the clinical picture



Same day

Urgent medical assessment

- Jaundice with systemic illness, confusion or raised INR
- Ascites, encephalopathy or gastrointestinal bleeding in known or suspected liver disease
- Very high transaminases suggesting acute liver injury
- Suspected paracetamol overdose



Suspected cancer

Urgent referral pathway

- Jaundice in adults aged 40 and over (NICE NG12)
- Liver mass or lesion on imaging suspicious of cancer
- Aged 60 and over with weight loss and new-onset diabetes: consider urgent CT (NICE NG12)



Hepatology

Routine referral

- FIB-4 above 2.67, or second-line test above local threshold
- Features of cirrhosis: platelets below 150, AST higher than ALT, low albumin
- Hepatitis B or C (or local treatment network), positive autoimmune screen
- Transferrin saturation above 45% on a repeat fasting sample
- Persistently abnormal tests with no cause found

Once cirrhosis is confirmed: 6-monthly ultrasound surveillance for hepatocellular carcinoma (HCC), portal hypertension assessment and vaccination, shared with specialist services.

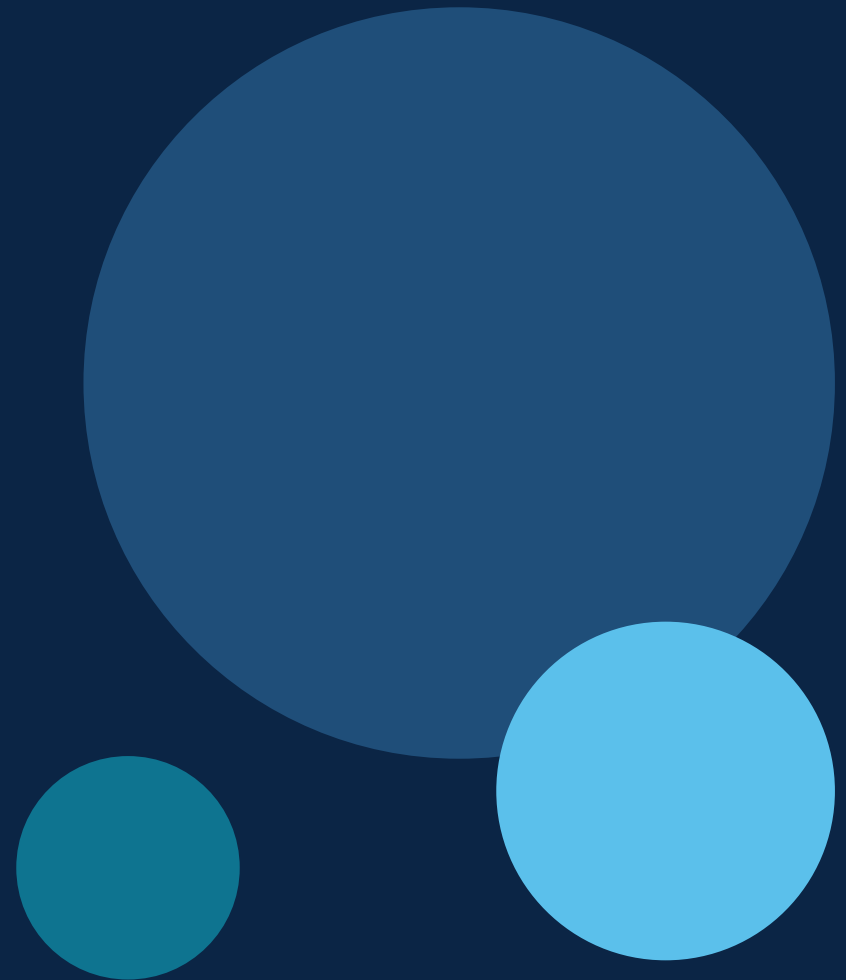
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03

Treatments, current and future

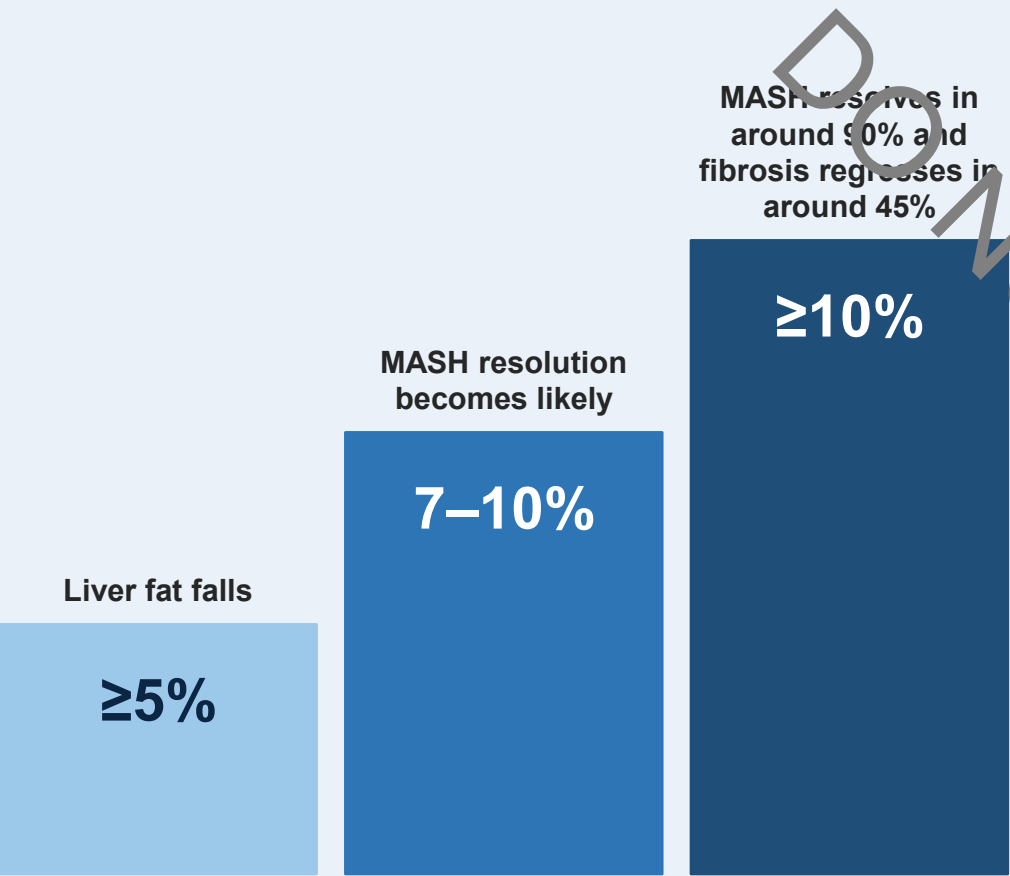
Lifestyle, metabolic medicines, licensed MASH therapy, mechanisms and the pipeline

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Weight loss is the dose; lifestyle is the foundation

Sustained weight loss and liver response



Diet

Mediterranean-style pattern with an energy deficit. Cut ultra-processed foods and sugar-sweetened drinks.



Activity

150 to 300 minutes of moderate activity a week plus resistance training. Liver fat falls even without weight loss.



Alcohol

Less is better in MASLD. Advise abstinence with advanced fibrosis or cirrhosis.



Support to succeed

NHS Type 2 Diabetes Path to Remission, weight management services, obesity medicines and metabolic surgery where eligible.

In the landmark lifestyle study, only around 1 in 10 people reached 10% weight loss. That gap is why medicines and surgery matter.

Choosing glucose-lowering therapy with the liver in mind

Medicine	Liver evidence	Diabetes, heart and kidney	Practical points
GLP-1 receptor agonist (semaglutide)	MASH resolution in phase 3; MHRA licensed for MASH with F2–F3 fibrosis (July 2026)	Lowers HbA1c and weight; cardiovascular and kidney benefit	Titrate slowly for GI effects; preconception planning
Tirzepatide	MASH resolution and fibrosis improvement in phase 2; phase 3 ongoing	Largest HbA1c and weight reductions	Not licensed for MASH; oral contraceptive advice at initiation and dose increases
SGLT2 inhibitor	Reduces liver fat and ALT; limited histology data	Heart failure and CKD protection	Safe in MASLD; sick day rules
Pioglitazone	Improves MASH histology; NICE NG49 supports use in secondary care for advanced fibrosis	Lowers HbA1c; cardiovascular benefit in some trials	Weight gain and oedema; avoid in heart failure; fracture risk
Metformin	No histological benefit	First line; weight neutral	Continue in compensated cirrhosis if kidney function allows
Sulfonylurea, insulin, DPP-4 inhibitor	No liver benefit	Sulfonylureas and insulin cause weight gain	Hypoglycaemia risk rises in cirrhosis

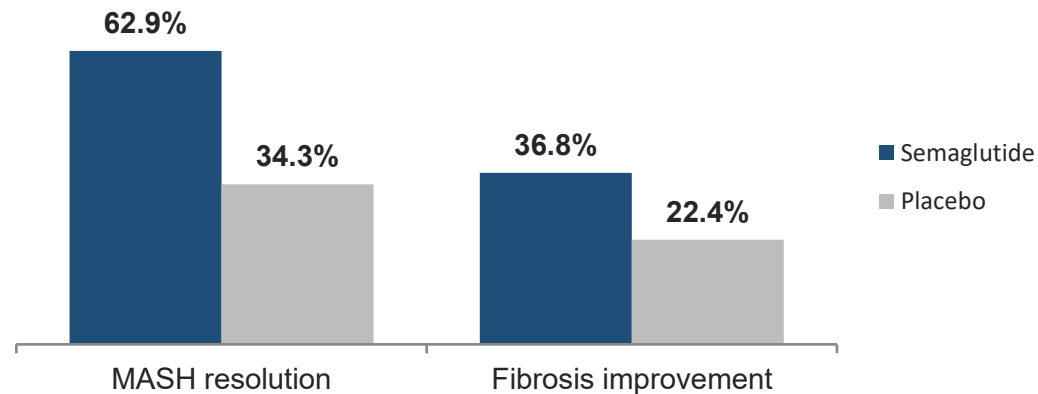
Statins: safe in MASLD and compensated cirrhosis and reduce cardiovascular events. Do not withhold or stop them for transaminases below 3 times the upper limit of normal.

Licensed MASH-specific therapy: where are we in the UK?

Semaglutide 2.4 mg weekly (Wegovy)

GLP-1 receptor agonist · ESSENCE phase 3 · 72 weeks

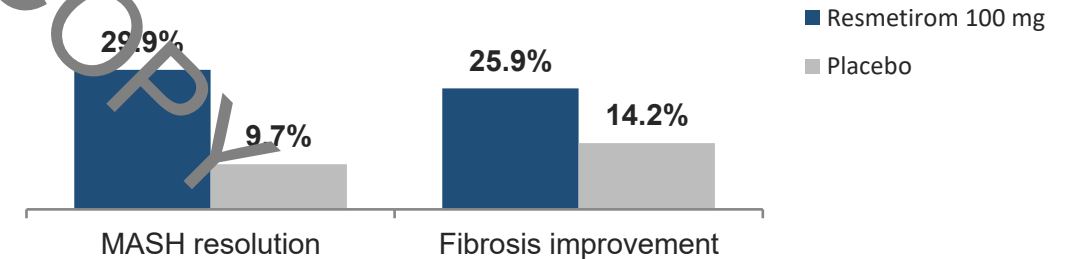
- MHRA conditional marketing authorisation, 3 July 2026
- FDA accelerated approval, August 2025
- NICE appraisal in progress: not yet NHS funded for MASH



Resmetirom 80 or 100 mg daily (Rezdiffra)

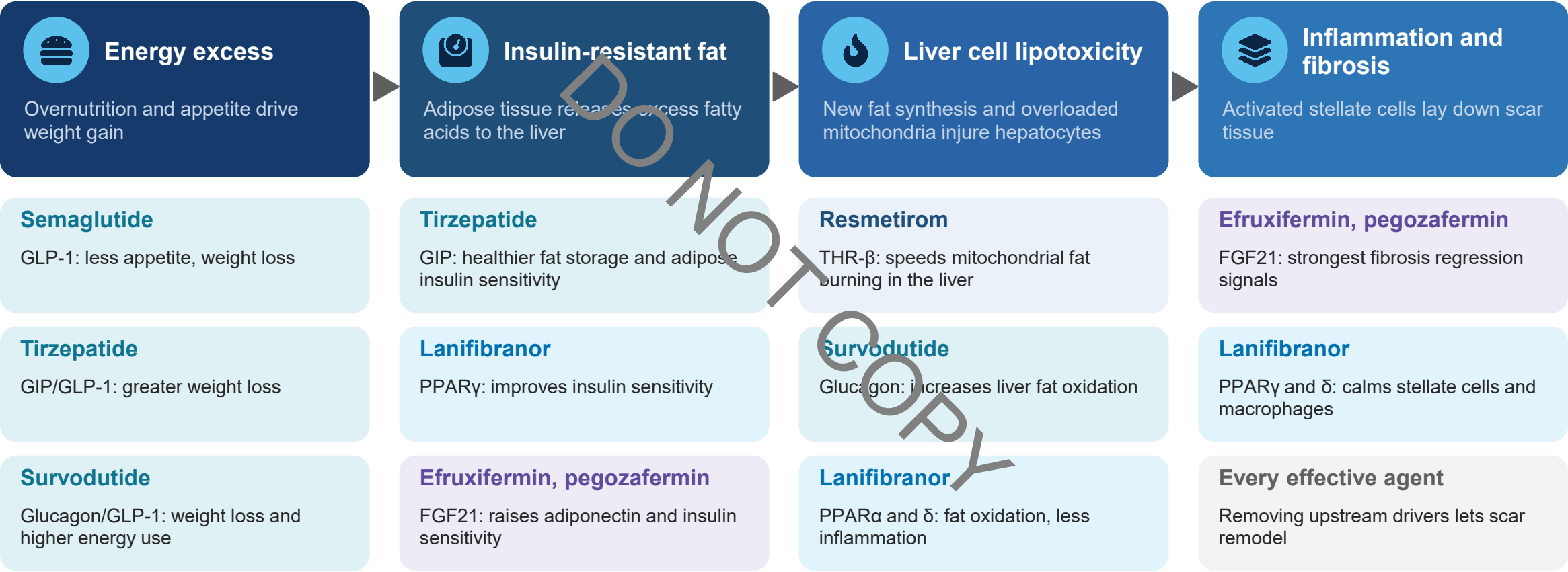
Oral thyroid hormone receptor β agonist · MAESTRO-NASH · 52 weeks

- FDA accelerated approval March 2024; EU conditional approval 2025
- NICE draft guidance June 2026: not recommended
- Final NICE decision expected December 2026



Interpret with care: different trials, populations and durations, so no cross-trial comparison. Both rest on biopsy surrogates while outcome data are awaited. Both are specialist-initiated for non-cirrhotic MASH with F2–F3 fibrosis.

How MASH medicines work: matching mechanism to driver



Direct or indirect? Hepatocytes carry few GLP-1 receptors, so GLP-1 benefit is mainly through weight and metabolism. Glucagon, THR- β , PPAR and FGF21 agents also act on the liver itself.

Mechanisms in more detail

Agent	Target	How it helps	Liver action	Watch-outs
Semaglutide (licensed)	GLP-1 receptor	Reduces appetite and weight, improves glycaemia and lowers adipose inflammation	Mainly indirect	GI effects; gallstones; pregnancy planning
Tirzepatide; retatrutide	GIP and GLP-1 receptors (retatrutide adds glucagon)	Greater weight loss; GIP improves adipose fat storage and insulin sensitivity, cutting fatty acid flow to the liver	Mainly indirect	GI effects; oral contraception advice with tirzepatide
Survodutide	Glucagon and GLP-1 receptors	GLP-1 drives weight loss; glucagon acts on hepatocytes to increase fat oxidation and energy expenditure	Direct and indirect	GI effects; rise in heart rate
Efruxifermin; pegozafermin	FGF21 analogues (FGF receptors with β -Klotho)	Mimic a metabolic hormone: improve insulin sensitivity, raise adiponectin, reduce fat synthesis and dampen stellate cell activation	Direct and indirect	GI effects; injection site reactions; long-term bone safety under study
Lanifibranor	PPAR α , δ and γ (oral)	α increases fat oxidation, δ reduces inflammation, γ improves insulin sensitivity and calms stellate cells	Direct and indirect	Weight gain and oedema from PPAR γ
Resmetirom	Liver-selective thyroid hormone receptor β (oral)	Speeds mitochondrial fat oxidation; lowers LDL cholesterol, triglycerides and lipoprotein(a); spares heart and bone receptors	Direct	Diarrhoea, nausea; CYP2C8 interactions; statin dose limits

The pipeline: where the trial evidence stands

Incretin-based

Tirzepatide

GIP/GLP-1 agonist · weekly injection

Phase 2 SYNERGY-NASH: MASH resolution in up to 73% vs 13%, and fibrosis improvement in 54 to 59% vs 33%, at 52 weeks. Phase 3 SYNERGY-Outcomes under way.

Incretin-based

Survodutide

Glucagon/GLP-1 agonist · weekly injection

Phase 3 SYNCHRONIZE-MASLD: 84% achieved at least 30% liver fat reduction vs 24%, and liver fat normalised in 61% at 48 weeks. LIVERAGE trials in F2–F3 and cirrhosis ongoing.

FGF21 analogue

Efruxifermin

Weekly injection · now Novo Nordisk

Phase 2b data show fibrosis regression, with longer-term signals in compensated cirrhosis. Phase 3 SYNCHRONY programme covers F2–F3 and F4.

FGF21 analogue

Pegozafermin

Injection · now Roche

Phase 3 ENLIGHTEN trials in F2–F3 fibrosis and compensated cirrhosis, building on phase 2b fibrosis improvement.

Liver-directed metabolic

Lanifibranor

Oral pan-PPAR agonist

Phase 3 NATiV3: 1,009 adults with F2–F3 fibrosis have completed 72 weeks. Topline results expected in the final quarter of 2026.

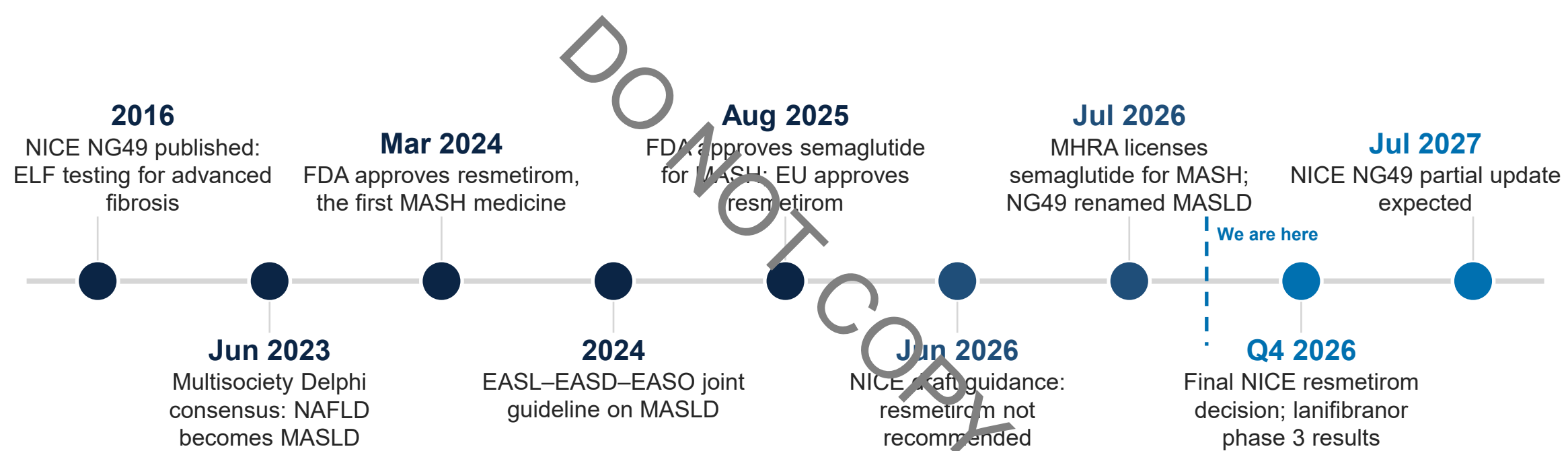
Liver-directed metabolic

Resmetirom in cirrhosis

Oral thyroid hormone receptor β agonist

MAESTRO-NASH OUTCOMES tests whether resmetirom prevents decompensation in compensated MASH cirrhosis. Two-year data show falling liver stiffness.

Key milestones, 2016 to 2027



NICE is also appraising semaglutide for MASH (ID6458). Dates are correct at September 2026; check the NICE website for updates.

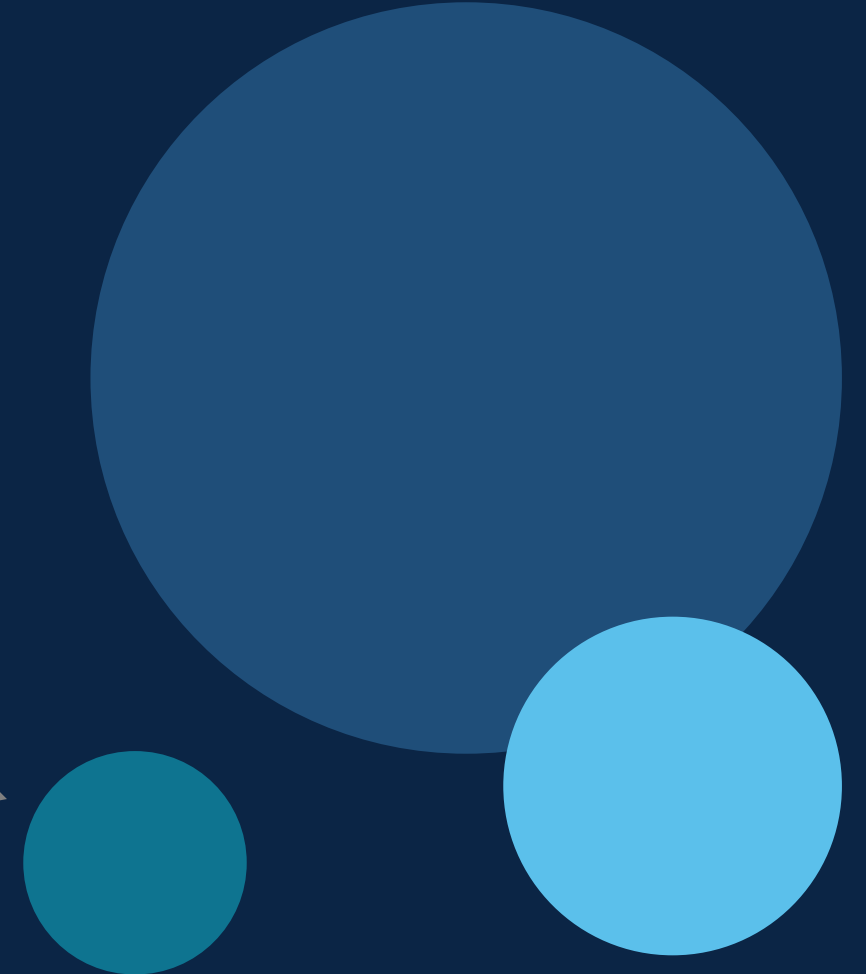
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04

Case studies

Three patients you may already know

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Graham, 58: 'His liver tests are normal'

Background

Type 2 diabetes for 8 years and hypertension. BMI 33 kg/m². Drinks about 14 units a week, mostly at weekends. An ultrasound for suspected gallstones 2 years ago reported 'fatty liver'; no further action was taken.

Medicines

Metformin 1 g twice daily, gliclazide 80 mg twice daily, ramipril 10 mg daily, atorvastatin 20 mg daily.

Results

HbA1c	64 mmol/mol	ALT	28 U/L
AST	31 U/L	ALP	88 U/L
Bilirubin	12 µmol/L	Albumin	42 g/L
Platelets	168 × 10 ⁹ /L	Blood pressure	142/86 mmHg
eGFR	78 mL/min	uACR	4.2 mg/mmol

Questions for the room

1

Is Graham's liver 'normal'?

2

Calculate his FIB-4. What does it mean?

3

What would you change at today's review?

Graham: normal enzymes, likely advanced fibrosis

$$\text{FIB-4} = (58 \times 31) \div (168 \times \sqrt{28}) = 2.02$$



Second-line test: ELF 10.6, above the NICE threshold of 10.51 for advanced fibrosis. Refer to hepatology.

Key learning

Normal ALT plus steatosis on imaging is a prompt to stage fibrosis, not a reassurance. The ultrasound two years ago was a missed opportunity.



Refer

Hepatology for likely advanced fibrosis; specialist review may consider licensed MASH therapy in future.



Glucose-lowering

Replace gliclazide with a GLP-1 receptor agonist for glucose, weight and liver benefit. Consider an SGLT2 inhibitor for uACR 3 to 30 (NICE NG28).



Cardiovascular risk

Continue atorvastatin and check non-HDL reduction; intensify if below 40%. Blood pressure above target: optimise.



Alcohol and weight

14 units a week is below MetALD thresholds, but advise cutting down and abstaining if advanced fibrosis is confirmed. Aim for at least 10% weight loss.

Priya, 46: 'Should we stop her statin?'

Background

Type 2 diabetes for 3 years and polycystic ovary syndrome. British Indian heritage. BMI 29 kg/m², waist 96 cm. Does not drink alcohol. Hopes to have another baby in the next 1 to 2 years.

Medicines

Metformin 1 g twice daily; combined oral contraceptive pill; atorvastatin 20 mg started 3 months ago (ALT before starting: 88 U/L).

Results

HbA1c	58 mmol/mol	ALT	96 U/L
AST	58 U/L	GGT	110 U/L
ALP	74 U/L	Platelets	262 × 10 ⁹ /L
Ferritin	520 µg/L	Transferrin sat.	31%
Liver screen	Otherwise negative	Ultrasound	Steatosis only

Questions for the room

- 1 Is the statin the cause, and should it be stopped?
- 2 How do you interpret the ferritin?
- 3 What is her fibrosis risk, and how would you treat her given her pregnancy plans?

Priya: high ALT, low fibrosis risk, and a preconception plan



The statin: keep it

ALT was already 88 before the statin and is now below 3 times the upper limit. NICE NG238 advises not stopping for this. Statins are safe in MASLD.



Ferritin: a metabolic signal

Raised ferritin with transferrin saturation below 45% is common in MASLD and insulin resistance, and does not suggest iron overload. HFE testing is not needed.



Fibrosis risk: low

$\text{FIB-4} = (46 \times 58) \div (262 \times \sqrt{96}) = 1.04$. Manage in primary care and reassess every 1 to 3 years. High ALT reflects activity, not fibrosis stage.



Treatment and pregnancy plans

Aim for 7 to 10% weight loss; check Path to Remission eligibility. A GLP-1 receptor agonist helps glucose, weight and liver: stop semaglutide at least 2 months before conception. Start folic acid 5 mg and review the statin before trying to conceive.

Key learning: ALT reflects activity; FIB-4 reflects risk. If tirzepatide is chosen, advise non-oral or additional barrier contraception at initiation and each dose increase.

Margaret, 67: 'The low platelets nobody mentioned'

Background

Type 2 diabetes for 15 years, NSTEMI in 2019, CKD G2a and knee osteoarthritis. BMI 36 kg/m². Drinks about 6 units a week. Two overnight hypoglycaemic episodes in the last month.

Medicines

Insulin glargine 38 units at night, metformin 500 mg twice daily, dapagliflozin 10 mg, ramipril, bisoprolol, atorvastatin 80 mg, aspirin 75 mg, omeprazole 20 mg, and ibuprofen 400 mg bought over the counter.

Results

HbA1c	50 mmol/mol	ALT	34 U/L
AST	52 U/L	GGT	88 U/L
Bilirubin	22 µmol/L	Albumin	34 g/L
Platelets	118 × 10⁹/L	Haemoglobin	118 g/L
eGFR	48 mL/min	uACR	8 mg/mmol

Questions for the room

1

What do the platelets, AST to ALT ratio and albumin suggest?

2

Can you trust her HbA1c?

3

Which medicines need reviewing, and why?

Margaret: probable cirrhosis changes her medicines

What is going on?

FIB-4 = 5.06: high risk
 $(67 \times 52) \div (118 \times \sqrt{34})$

FibroScan 26 kPa
Compensated advanced chronic liver disease with probable portal hypertension (Baveno VII)

HbA1c may read falsely low
Shortened red cell survival and hypersplenism. Use capillary glucose or continuous glucose monitoring, and relax targets.

Hepatology referral
Hepatocellular carcinoma surveillance every 6 months, portal hypertension management, vaccination, nutrition

Medicine	Action	Why
Ibuprofen	Stop; paracetamol at standard doses	Kidney injury, fluid retention and bleeding risk in cirrhosis
Insulin glargine	Reduce dose; review hypoglycaemia	Cirrhosis impairs glucose production and glycogen stores
Metformin	Continue while compensated and eGFR ≥30	Stop if decompensation develops: lactic acidosis risk
Dapagliflozin	Continue with sick day rules	Kidney and cardiovascular protection
Atorvastatin	Continue	Safe in compensated cirrhosis; secondary prevention
Aspirin and omeprazole	Review with hepatology	Bleeding risk if varices; long-term proton pump inhibitors linked to infection and encephalopathy

Key learning: platelets and FIB-4 are primary care super-tools. Avoid prolonged fasting, offer a late evening snack and protect muscle during weight loss.

Five things to do on Monday

1

Think liver at every diabetes review

MASLD affects around two in three people with type 2 diabetes.

2

Look for fibrosis, not fat

Calculate FIB-4. Do not be reassured by normal liver enzymes, or alarmed by a raised ALT alone.

3

Use the pathway

Second-line ELF or FibroScan for indeterminate results; refer high-risk results and features of cirrhosis.

4

Treat the whole metabolic person

Weight loss, liver-friendly glucose-lowering choices, statins, blood pressure and alcohol.

5

Watch this space

Semaglutide is now licensed for MASH in the UK, NICE decisions are due and more agents are coming.

Abbreviations: the liver, its tests and disease terms

Disease terms

ALD alcohol-related liver disease

MASL metabolic dysfunction-associated steatotic liver (steatosis alone)

MASLD metabolic dysfunction-associated steatotic liver disease

MASH metabolic dysfunction-associated steatohepatitis

MetALD MASLD with increased alcohol intake

MAFLD metabolic dysfunction-associated fatty liver disease (2020 term, superseded)

NAFLD non-alcoholic fatty liver disease (former term for MASLD)

NASH non-alcoholic steatohepatitis (former term for MASH)

HCC hepatocellular carcinoma, primary liver cancer

F0 to F4 fibrosis stages, from none to cirrhosis

Blood tests and alcohol screening

ALT alanine aminotransferase

AST aspartate aminotransferase

ALP alkaline phosphatase

GGT gamma-glutamyl transferase

INR international normalised ratio

PT prothrombin time

HFE the gene tested in hereditary haemochromatosis

U/L units per litre

AUDIT Alcohol Use Disorders Identification Test

AUDIT-C the three consumption questions of AUDIT

Fibrosis assessment

FIB-4 Fibrosis-4 index, from age, AST, ALT and platelets

ELF Enhanced Liver Fibrosis score

HA hyaluronic acid, an ELF component

PIIINP procollagen III N-terminal peptide, an ELF component

TIMP-1 tissue inhibitor of metalloproteinase 1, an ELF component

VCTE vibration-controlled transient elastography, the FibroScan technique

kPa kilopascal, the unit of liver stiffness

Abbreviations: treatments, conditions and organisations

Drug targets and classes

GLP-1 glucagon-like peptide-1
GIP glucose-dependent insulintropic polypeptide
FGF21 fibroblast growth factor 21
PPAR peroxisome proliferator-activated receptor
THR-β thyroid hormone receptor beta
SGLT2 sodium-glucose co-transporter 2
DPP-4 dipeptidyl peptidase-4
PPI proton pump inhibitor
NSAID non-steroidal anti-inflammatory drug
CYP2C8 cytochrome P450 enzyme 2C8, a route of drug interactions
SmPC summary of product characteristics

Conditions and measures

BMI body mass index
CKD chronic kidney disease
eGFR estimated glomerular filtration rate
uACR urine albumin-to-creatinine ratio
HbA1c glycated haemoglobin
CGM continuous glucose monitoring
HDL high-density lipoprotein cholesterol
NSTEMI non-ST-elevation myocardial infarction
PCOS polycystic ovary syndrome
GI gastrointestinal

Organisations and guidance

NICE National Institute for Health and Care Excellence
NG NICE guideline, as in NG49
MHRA Medicines and Healthcare products Regulatory Agency
FDA US Food and Drug Administration
EASL European Association for the Study of the Liver
EASD European Association for the Study of Diabetes
EASO European Association for the Study of Obesity
AASLD American Association for the Study of Liver Diseases
BSG British Society of Gastroenterology
ICB integrated care board
PCN primary care network
QOF Quality and Outcomes Framework
QALY quality-adjusted life year

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THANK YOU

Questions and discussion

Find fibrosis, not fat. Treat the whole metabolic person.

Useful resources

NICE NG49 · EASL–EASD–EASO MASLD guideline 2024 · BSG abnormal liver blood tests guideline · British Liver Trust

