Liver disease in diabetes

NIPCDOS Conference

25th September 2025

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Aims

- Metabolic dysfunction-associated steatotic liver disease (MASLD)
- Liver function tests and their interpretation
- Treatment, including CVD prevention
- When to refer
- Liver transplant

Clinical Practice Guidelines

JOURNAL
OF HEPATOLOGY

EASL–EASD–EASO Clinical Practice Guidelines on the management of metabolic dysfunction-associated steatotic liver disease (MASLD)☆

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)

Which risk factors and comorbidities have the greatest impact on the natural history of hepatic disease including hepatocellular carcinoma in MASLD?

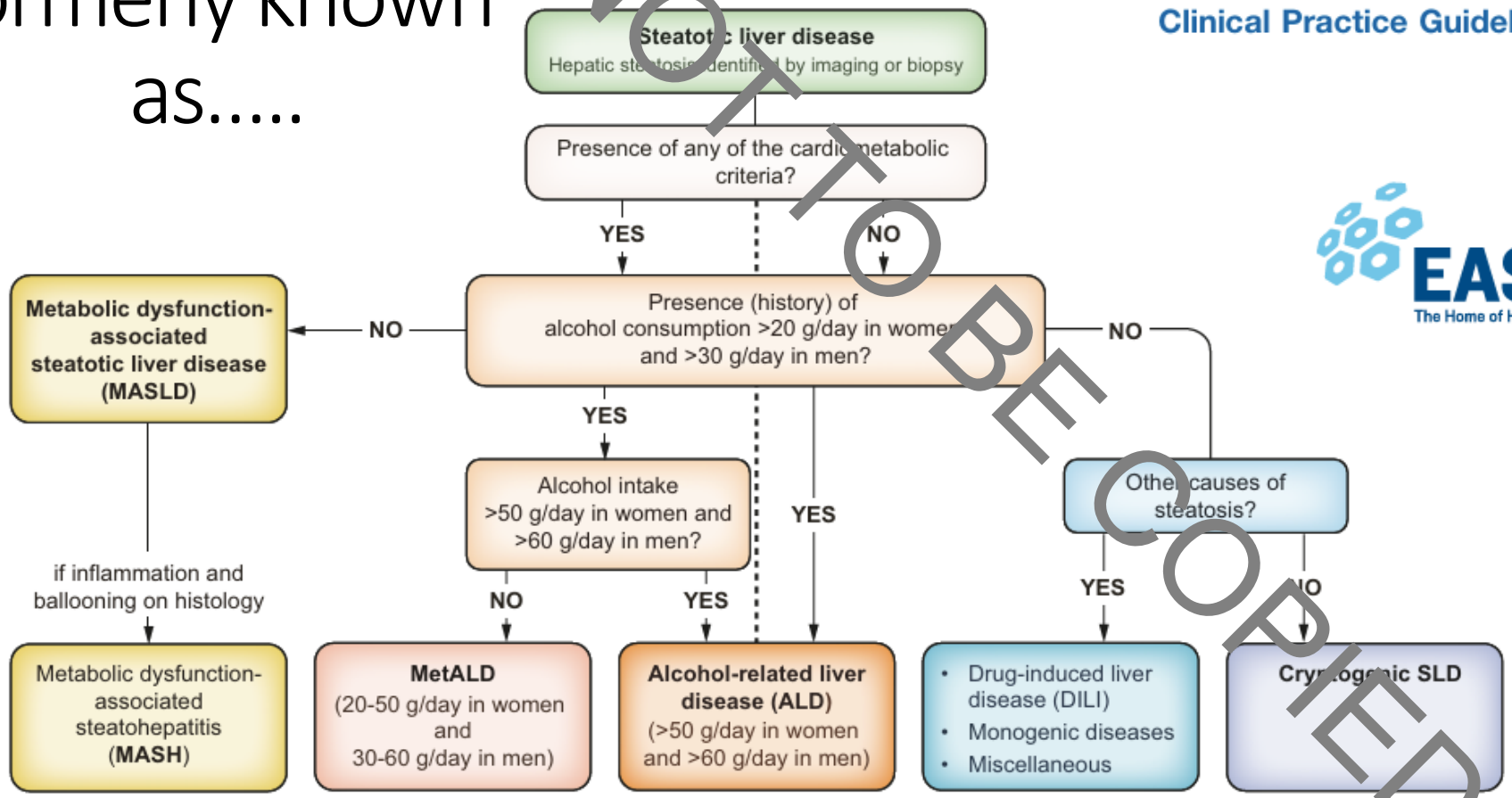
Statements

- Type 2 diabetes and obesity (particularly abdominal obesity) are the metabolic diseases with the strongest impact on the natural history of MASLD, including progression to MASLD/MASH-related advanced fibrosis, cirrhosis and hepatocellular carcinoma (**LoE 2, strong consensus**).
- Males aged >50 years, postmenopausal women, and individuals with multiple cardiometabolic risk factors are at increased risk of progressive fibrosis and the development of cirrhosis and its complications (**LoE 2, strong consensus**).

The artist formerly known as…..

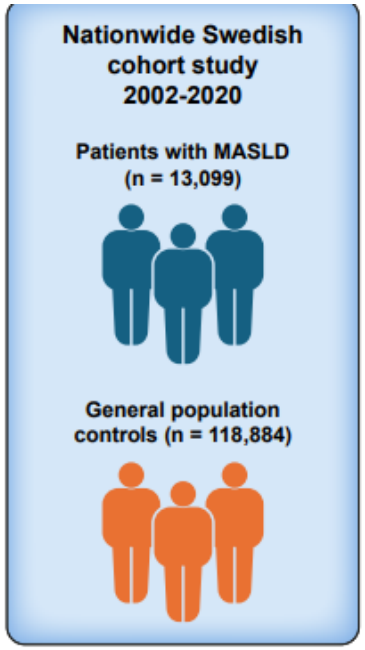
Clinical Practice Guidelines

EASL™ The Home of Hepatology



Why is diabetes important in MASLD?

- One of the major risk factors for fibrosis progression
  - Paired liver biopsy study of MASLD patients with and without DM → higher rate of progression in diabetic cohort
- Poor outcomes in patients with biopsy-proven MASH cirrhosis
  - 4-fold increased risk of death and 2-fold increased risk of liver-related outcomes including HCC over 5 years
- T2DM strongest independent risk factor for development of HCC in large European study (136,703 patients with MASLD and low fibrosis rates)



Mortality rates

All-cause, HR = 1.85
Liver, HR = 26.9
HCC, HR = 35
Non-HCC cancer,
CVD, HR = 1.54
Infection, HR = 1.79
Gastrointestinal, HR = 2.73
Respiratory disease, HR = 1.65
External causes, HR = 1.88
Mental health, HR = 1.03
Endocrine disorders, HR = 3.86
Other, HR = 1.71

Research Article
MASLD and Alcohol-Related Liver Diseases

JOURNAL OF HEPATOLOGY

Cause-specific mortality in 13,099 patients with metabolic dysfunction-associated steatotic liver disease in Sweden

Highlights

- All-cause mortality rate was nearly doubled in MASLD *vs.* the general population.
- Liver- and HCC-related mortality were highest in relative terms.
- Non-HCC cancer and cardiovascular disease mortality were highest in absolute terms.
- Earlier multidisciplinary care might be needed to reduce premature mortality.

2 X all cause mortality

Major cause of death
- Cardiovascular disease
- Non-HCC cancer

NB 95% MASLD population non-cirrhotic

Why risk-stratify?

LIVER	HEART
Simple steatosis – address risk factors	Cardiac risk factors – address risk factors
Fibrosis (asymptomatic) – potentially reversible	Angina – warning signs but no permanent damage yet
Cirrhosis – established and permanent damage (often still asymptomatic) – address risk factors, screen for HCC +/- varices	Myocardial infarction – established damage

Liver "function" tests

- Bilirubin & albumin (and coagulation)
- AST and ALT (+/- GGT)
- ALP and GGT

LIVER FUNCTION TEST Cumulative « Show Older | Show Newer »

	Number	1 of 2	LATEST 2 of 2	Ref. Range (Units)
☐	Collected	15-Jun-2 17:4	11-Sep-25 14:45	
	Source	[1] BHSCT	[2] BHSCT	
☐	**Albumin**	**43**	**4**	35 - 50 (g/L)
☐	**Total Bilirubin**	**6**	**6**	0 - 21 (u ol/L)
☐	**ALP**	**84**	**100**	30 130 (U/L)
☐	**ALT**	*** 89**	*** 72**	0 - 33 (U/L)
☐	**AST**	*** 59**	*** 52**	0 - 32 (U/L)
☐	**Gamma-glutamyl transferase activity**	*** 185**	*** 151**	6 - 42 (U/L)

Graph No tests selected

HAEMOGLOBIN A1C (IFCC) Cumulative « Show Older | Show Newer »

	Number	LATEST 1 of 1	Ref. Range (Units)
☐	Collected	11-Sep-25 14:45	
	Source	[1] BHSCT	
☐	**Haemoglobin A1c (IFCC)**	*** 57.0**	20 - 41 (mmol/mol)

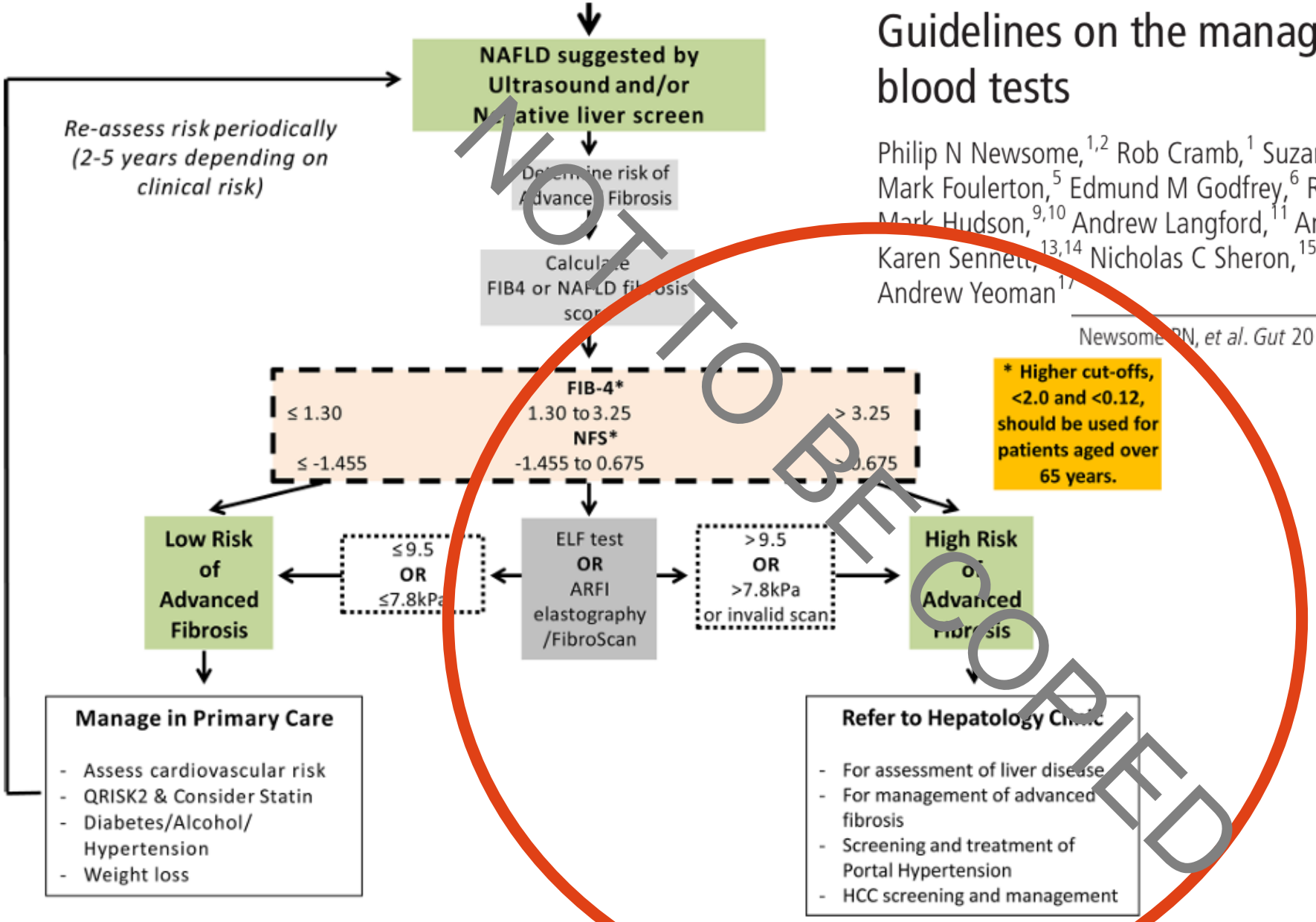
LIPID PROFILE Cumulative « Show Older | Show Newer »

	Number	LATEST 1 of 1	Ref. Range (Units)
☐	Collected	11-Sep-25 14:45	
	Source	[1] BHSCT	
☐	**Cholesterol**	*** 7.4**	2.8 - 5.0 (mmol/L)
☐	**High density lipoprotein (HDL) cholesterol**	1.3	1.00 - 2.50 (mmol/L)
☐	**Triglyceride**	*** 4.15**	0.40 - 1.70 (mmol/L)
☐	**LDL Cholesterol**	*** 4.2**	<3.0 (mmol/L)
☐	**Cholesterol:HDL Ratio (Chol/HDL)**	*** 5.7**	2 - 5
☐	**Non HDL Cholesterol (Chol-HDL)**	6.1	(mmol/L)

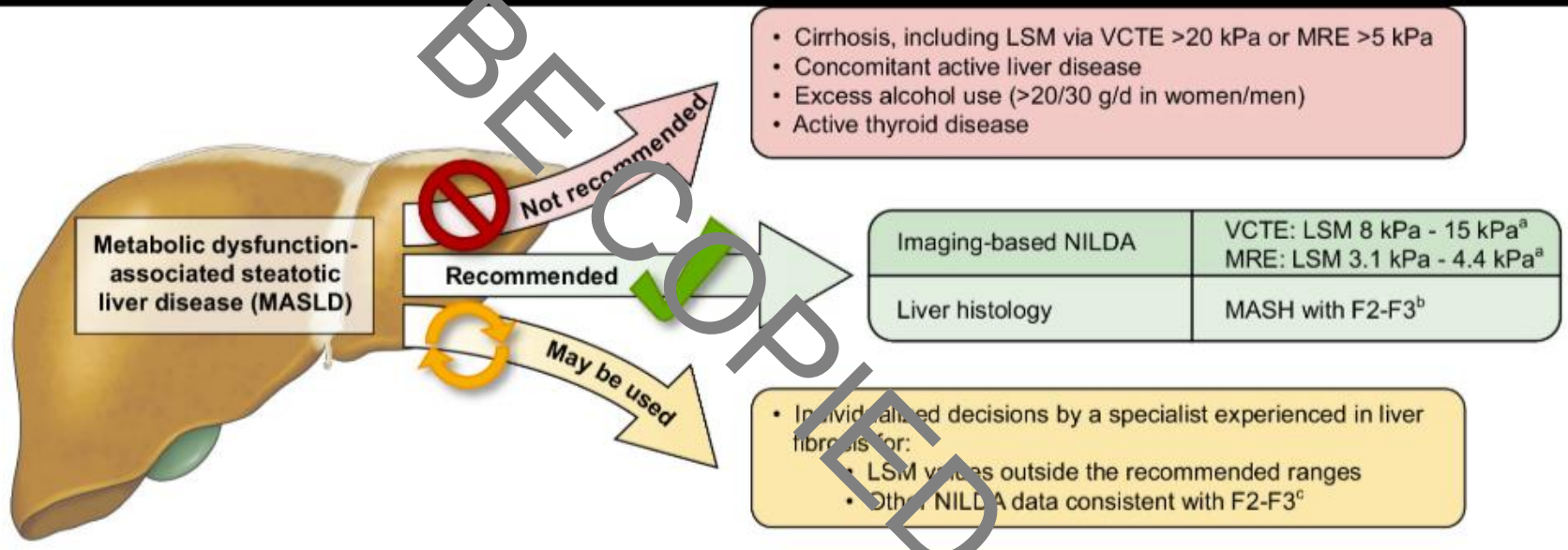
Guidelines on the management of abnormal liver blood tests

Philip N Newsome,[1,2] Rob Cramb,[1] Suzanne M Davison,[3] John F Dillon,[4] Mark Foulerton,[5] Edmund M Godfrey,[6] Richard Hall,[7] Ulrike Harrower,[8] Mark Hudson,[9,10] Andrew Langford,[11] Anne Mackie,[8] Robert Mitchell-Thain,[12] Karen Sennett,[13,14] Nicholas C Sheron,[15] Julia Verne,[8] Martine Walmsley,[16] Andrew Yeoman[17]

Newsome PN, *et al*. *Gut* 2017;**0**:1–14. doi:10.1136/gutjnl-2017-314924



Conclusions: Both the 80-mg dose and the 100-mg dose of resmetirom were superior to placebo with respect to NASH resolution and improvement in liver fibrosis by at least one stage. (Funded by Madrigal Pharmaceuticals; MAESTRO-NASH ClinicalTrials.gov number, NCT03900429.).



Modified from the AASLD NILDA guidelines.[5]
Liver biopsy is not routinely recommended for staging of MASH.
Imaging-based NILDA is preferred, eg, shear wave elastography (applying local standards for F2-F3) versus enhanced liver fibrosis score (9.2-10.4).
The latter range is based on the interquartile range from the MAESTRO trial data; no recommendations are available from the AASLD NILDA guidelines.[6]

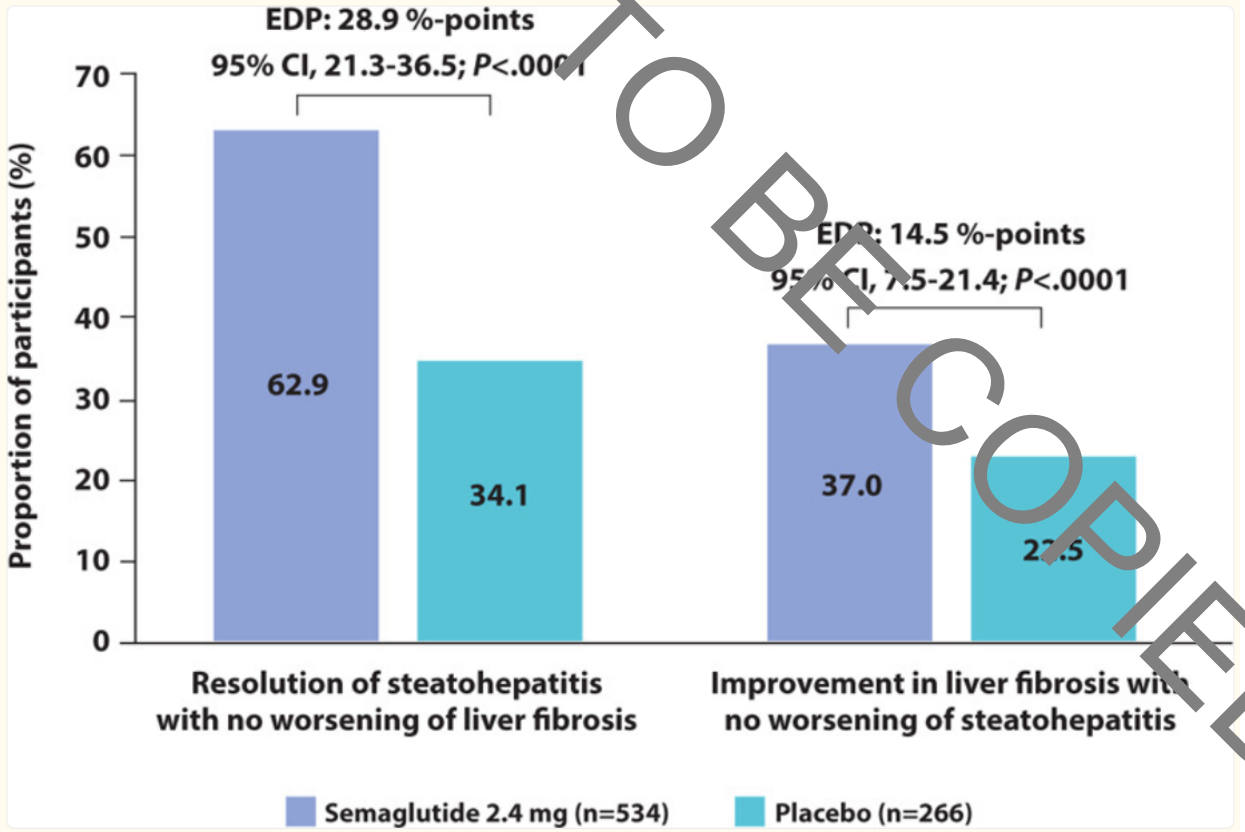
NOVO NORDISK

Company announcement

12:13 1 November 2024

Announcement.pdf

Novo Nordisk A/S: Semaglutide 2.4 mg demonstrates superior improvement in both liver fibrosis and MASH resolution in the ESSENCE trial



FDA Approval
August 2025 USA

ORIGINAL ARTICLE

Phase 3 Trial of Semaglutide in Metabolic Dysfunction–Associated Steatohepatitis

Authors: Arun J. Sanyal, M.D., Philip N. Newsome, M.B., Ch.B., Ph.D., Ines Kliers, M.D., Laura Harms Østergaard, M.Sc., Michelle T. Long, M.D., Mette Skalshøi Kjær, M.D., Ph.D., Anna M.G. Cali, M.D., Elisabetta Bugianesi, M.D., Ph.D., Mary E. Rinella, M.D., Michael Roden, M.D., and Vlad Ratziu, M.D., Ph.D., for the ESSENCE Study Group* Author Info & Affiliations

Published April 30, 2025 | N Engl J Med 2025;392:2089-2099 | DOI: 10.1056/NEJMoa2413258 | VOL. 392 NO. 21

Semaglutide 2.4mg weekly versus placebo

- Resolution of steatohepatitis without worsening of fibrosis occurred in 62.9% of the 534 patients in the semaglutide group and in 34.3% of the 266 patients in the placebo group (p<0.001)
- A reduction in liver fibrosis without worsening of steatohepatitis was reported in 36.8% of the patients in the semaglutide group and in 22.4% of those in the placebo group (p<0.001)

Secondary outcomes

1. Resolution of steatohepatitis and improvement in fibrosis Semaglutide>Placebo P<0.001
2. Change in body weight Semaglutide>Placebo P<0.001
3. Change in pain scores - NS

Nurse led MASLD service

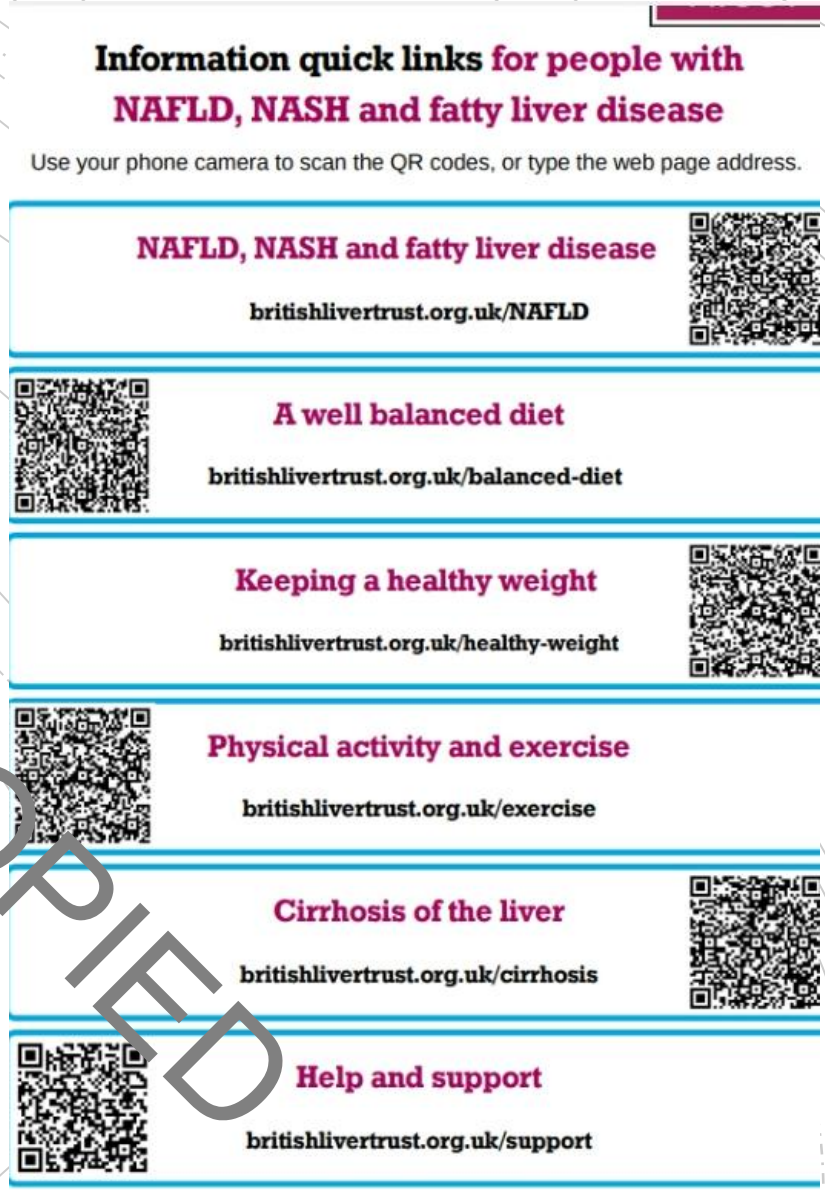
- Service commenced in October 2023.
- Referrals via the consultants & GP Pilot scheme (3 Belfast practices)
- 3 independent clinics a week with 6 patients in each session
- 30 minute appointment
- 1 stop shop for Belfast Trust MASLD patients

NL MASLD appointment

- Risk factor assessment
- Fibroscan
- Vitals & BMI
- Dietary education - balanced diet, Lean protein, lower in carbs, reduced salt intake, plenty of fruit & veg and reduced sugary snacks & drinks
- Exercise – setting sensible goals (20-30mins daily)
- Weight loss - target of 5-10% over 6 months as per BLT guidelines
- BLT information barcode advice leaflet

Smart phrase:

.QRCODEMASLD



Information quick links for people with NAFLD, NASH and fatty liver disease

Use your phone camera to scan the QR codes, or type the web page address.

NAFLD, NASH and fatty liver disease
britishlivertrust.org.uk/NAFLD

A well balanced diet
britishlivertrust.org.uk/balanced-diet

Keeping a healthy weight
britishlivertrust.org.uk/healthy-weight

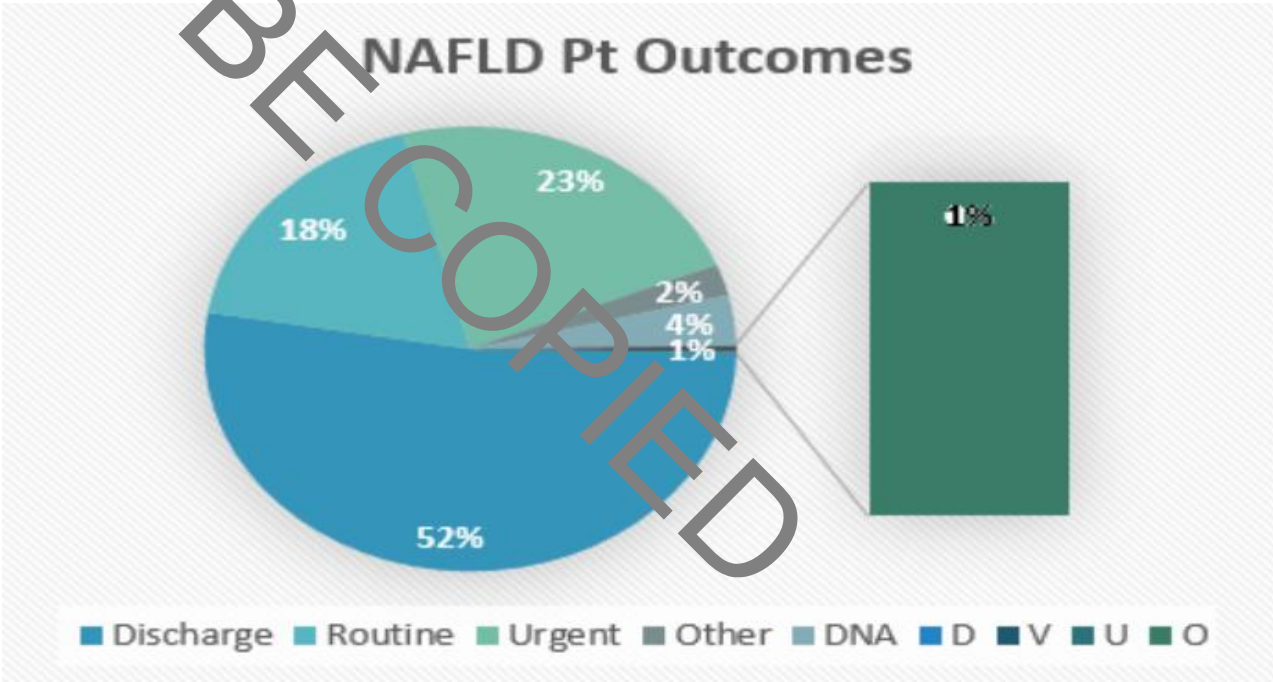
Physical activity and exercise
britishlivertrust.org.uk/exercise

Cirrhosis of the liver
britishlivertrust.org.uk/cirrhosis

Help and support
britishlivertrust.org.uk/support

Outcomes

- 460 patients offered appointments to date
- 52% of patients suitable for discharge back to primary care due to Liver stiffness score <8kPa, with lifestyle advice and asked to contact their GP in 3 years time for bloods & FIB-4 recalculation

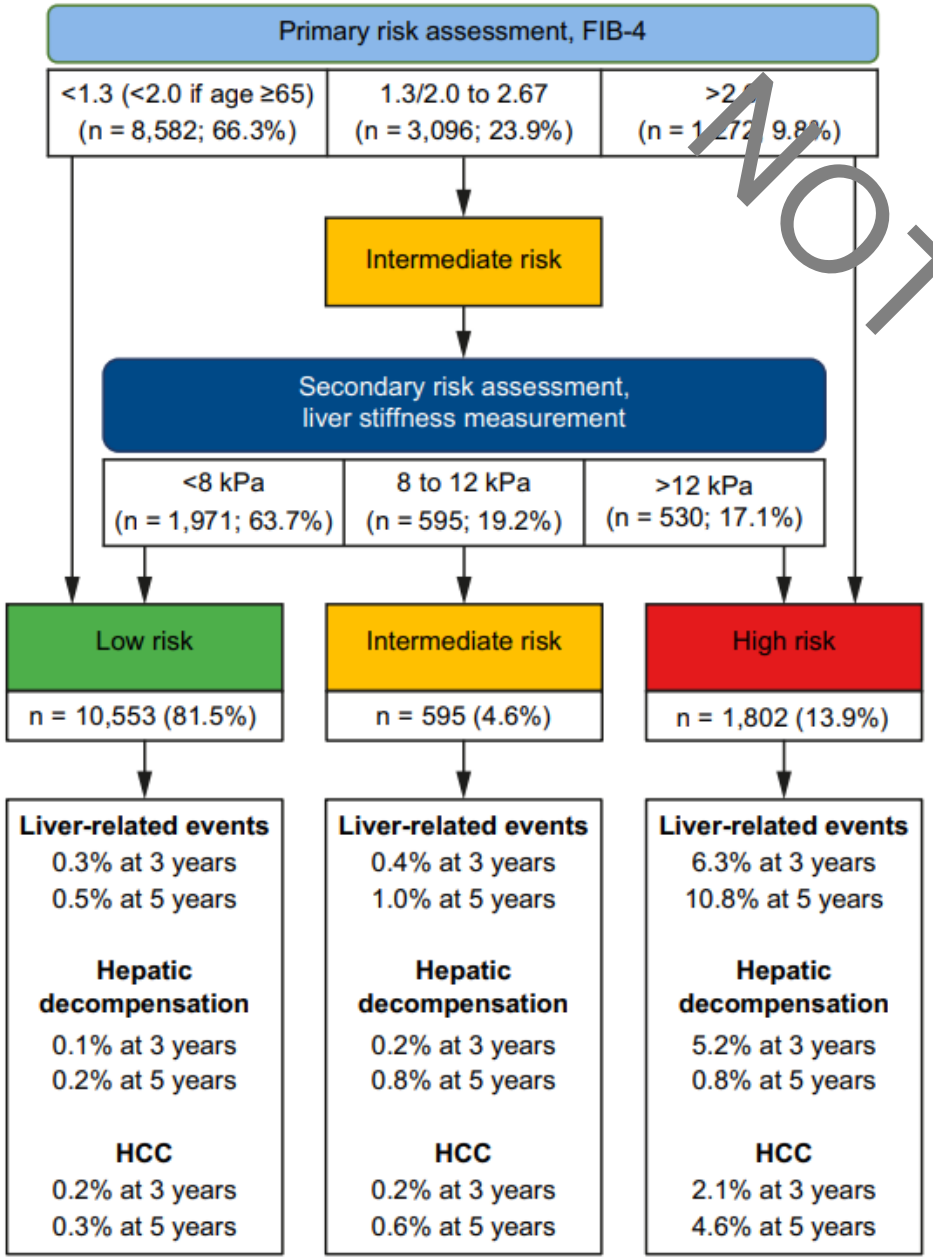


MASH outcomes

- 23% =100 patients require urgent consultant review appointments (ideally within 3 months) due to LSM >11
- This patient group are also added to the HCC screening programme & if LSM is >20 they are considered for OGD
- 18% patients had evidence of early scarring (LSM 8-11) requiring routine consultant follow up within 6 months and a repeat Fibroscan in 2 years
- Others - review no longer required or Pt declined offer
- DNA's - 4%

Service Impacts

- 182 consultant clinic appointments saved in 2024 following NL MASLD discharge criteria
- Reduced the number of patients identified with MASLD at triage from being adding to the Routine/Urgent Fibroscan waiting lists, which has allowed improvement in waiting times.
- 326 patients scanned at NL MASLD clinic in 2024



Research Article
MASLD and Alcohol-Related Liver Diseases

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Prognostic performance of the two-step clinical care pathway in metabolic dysfunction-associated steatotic liver disease

This 58 y.o. female underwent assessment of Metabolic dysfunction-associated steatotic Liver disease (MASLD) following referral with metabolic syndrome features and an indeterminate FIB-4.

Metabolic Risk Factors:

Diabetes	Yes	New
Hypertension	No	None
Hyperlipidaemia	Yes	QRISK3 5.4%
Alcohol	AUDIT-C - 0	None
Smoking Status	Non-Smoker	None

Visit Vital Signs

BP	117/78
Pulse	88
Ht	1.65 m
Wt	62.4 kg
BMI	22.92 kg/m^2
BSA	1.71 m^2

emains in the ideal category based on today's weight & BMI.

Imaging: Confirmed steatosis on recent imaging Yes ; US in April 2023

Exercise: We have discussed the importance of exercise to improve liver health and I have provided examples of the types of Aerobic exercises that they may find beneficial to their overall health.

Diet: I have explained that research has shown eating a Mediterranean type diet can improve liver health. We have discussed the sub sections of leaner proteins, increasing fruit & vegetables intake & adding fibre by switching to wholemeal breads, pasta and rice. I have also advised reduced consumption of salt and sugar. Brief advice was offered and abstinence from alcohol recommended.

Fibroscan:

Lab Test Results

Component	Value	Date
EKPA	6.1	11/09/2025
IQRMED	23	11/09/2025
CAP	291	11/09/2025

The elevated CAP score confirms significant fatty deposits within the liver, however, the Liver Stiffness score (LSM) is reassuringly normal suggesting no evidence of fibrosis.

Diabetes pre-liver transplant

- Cardiovascular risk profile
- Cerebrovascular risk profile
- NG feeding
- Predictive of post-transplant CKD

Investigations
Bloods
He is **Blood Group O Positive.** Current bloods show bilirubin 159um[illegible]/L (conjugated 145umol/L), ALP 149U/L, ALT 49U/L, AST 78U/L, GGT 103U/L and albumin 34g/L. INR is 1.2. Sodium is 137mmol/L, urea 3.2mmol/L, creatinine 65umol/L. AFP last week was 16.3 (5.4 in June - he had an MRI liver two weeks ago which did not show any focal liver lesions. Liver auto antibodies continue to show a strongly positive AMA and IgM is raised at 4.43. HbA1c is normal.

Respiratory investigations
Arterial blood gas on room air shows a pH of 7.44, p02 11.3KPA, lactate 0.8, bicarbonate 25.
Pulmonary function tests:-
FEV1 is 2.96, FVC3.66 with a ratio of 0.81.

Cardiac Investigations
Echocardiogram shows normal LV and RV size and systolic function. There is some impaired diastolic dysfunction of the left ventricle. Left atrium is dilated with a volume of 40.1mls per metre squared. There is no significant valvular stenosis or regurgitation. Bubble study is negative for the presence of shunting.

CPEX - he exercised for 10 minutes and 32 seconds and stopped due to leg fatigue. Effort was good. V02 peak was 23.3mls per kilo per minute. Peak power 156watts with a peak heart rate of 130bpm and no significant ST changes. Anaerobic threshold was 12.7mls per kilo per minute. It was noted that his V02 max has actually improved since his initial transplant assessment in 2022.

Imaging
CT chest, abdomen and pelvis was completed in September and shows no evidence of any malignancy. There is a cirrhotic configuration of the liver with no free fluid in the abdomen. He has since undergone two MRI's of his liver which show established cirrhosis, no evidence of HCC and mild longstanding CBD dilatation but no evidence of choledocholithiases or other biliary tract obstructing lesion. Portal vasculature is patent.

Nutritional Assessment

Physiotherapy: 6 minute walk test - this gentleman managed 669 metres with a V02 max of 20.34 and speed of 1.9 metres per second and he was found to be robust on the 4th percentile. DASI score is 58.2. Mets max is 9.89 and he was found to live a very active life as a civil engineer and a part time farmer. His grip strength is 44.7kilos which is above average for a man of his age.

Dietician Assessment
Weight is 94.8kilos and height is 1.7metres giving a BMI of 32.8kgs per metre squared. Left mid-upper arm circumference is 33.5cms (between the 25th to 50th centile) and left grip strength at that time was 50.2 kilos. He was found to eat three balance meals a day and there is no evidence of nutritional concern. He has been given advice to help him maintain his muscle mass.

HbA1c, lipids

Cardiovascular risk profile

Arterial calcification

Physical condition

Diabetes post-liver transplant

- Peri-operative infections
- Steroid use
- Calcineurin inhibitor
- Metabolic syndrome

Chronic Kidney Disease in Liver Transplant Recipients

Andrew Wiley[1], Rebecca O'Kane[2], Mhairi Orr[3], Christopher Hughes[4], James Stout[1]

High Prevalence but Low Risk of End-Stage Kidney Disease in Contemporary Practice

Background

- Studies report **5–15%** of LT recipients develop **ESKD** within 10 years post-transplantation
- CKD independently drives **cardiovascular disease** (CVD) risk in LT patients
- CKD may be caused by
  - Pre-existing disease
  - Perioperative complications
  - Use of Calcineurin inhibitors
- There is limited recent data on renal function post LT

Aim

Evaluate the incidence and risk factors for CKD stage 3 or higher among LT recipients in Northern Ireland

Methods

Retrospective analysis of:

- **216 patients** with LT
- Between Jan 2010 – Dec 2019
- Within the regional Liver Unit in NI

Renal function at most recent assessment

Stage 5 – 1.4%

CKD Stage 4 – 4.6%

CKD Stage 3b – 11.1%

CKD Stage 3a – 49.5%

No CKD – 34.3%

Results

- **48 patients** died during study period
- Median follow up time – **8 years**
- Median time to CKD stage 3+ in those without pre-transplant CKD - **7.7 years**
- Risk factors for CKD
  - Pre-transplant diabetes
  - Older age at transplant

Risk Factor	Odds Ratio (95% CI)	p-value
Age at transplant (per year)	1.04 (1.03-1.08)	**0.001**
Pre-transplant diabetes	3.23 (1.44-5.19)	**0.019**
Hypertension pre-transplant	0.93 (0.37-2.5)	0.879
Hepatorenal syndrome pre-transplant	2.37 (0.26-4.12)	0.445
eGFR one month pre-transplant (per ml/min/1.73m²)	0.99 (0.97-1.01)	0.434

Conclusions

- Previously reported high rates of ESKD after LT may not reflect contemporary clinical practice
- CKD is still highly prevalent and proactive management is vital to reduce patient morbidity and mortality

1) Regional Nephrology and Transplant Unit, Belfast City Hospital, Belfast
2) Gastroenterology Unit, Altnagelvin Hospital, Derry
3) Centre for Public Health, Queen's University Belfast. Belfast
4) Regional Liver Unit, Royal Victoria Hospital, Belfast

Questions?