JEUDI D'UNISANTÉ

MASLD

Metabolic dysfunction-associated steatotic liver disease

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02 juillet 2026

Terminology and diagnosis criteria

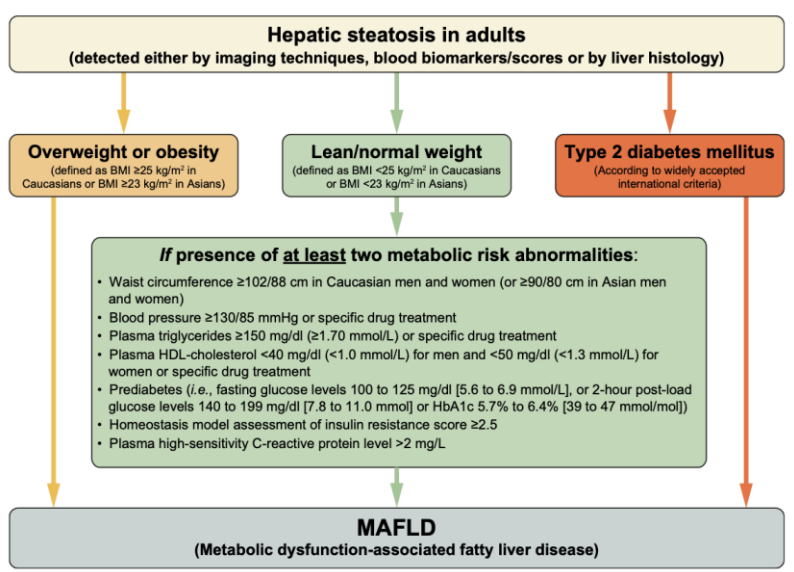
Nomenclature evolution

1980

NAFLD and NASH

1980 by Ludwig et al

Liver steatosis + no alcohol + related with obesity and diabetes



2023

MASLD

Multisociety Delphi Consensus Statement

Liver steatosis + metabolic risk factor + no other cause

> Mayo Clin Proc. 1980 Jul;55(7):434-8.

Nonalcoholic steatohepatitis: Mayo Clinic experiences with a hitherto unnamed disease

J Ludwig, T R Viggiano, D B McGill, B J Oh

PMID: 7382552

Abstract

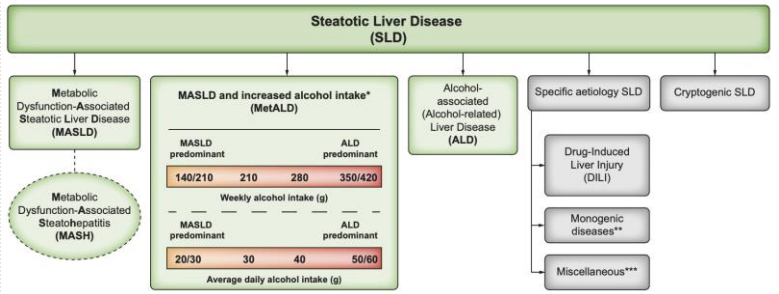
Nonalcoholic steatohepatitis is a poorly understood and hitherto unnamed liver disease that histologically mimics alcoholic hepatitis and that also may progress to cirrhosis. Described here are findings in 20 patients with nonalcoholic steatohepatitis of unknown cause. The biopsy specimens were characterized by the presence of striking fatty changes with evidence of lobular hepatitis, focal necroses with mixed inflammatory infiltrates, and, in most instances, Mallory bodies; Evidence of fibrosis was found in most specimens, and cirrhosis was diagnosed in biopsy tissue from three patients. The disease was more common in women. Most patients were moderately obese, and many had obesity-associated diseases, such as diabetes mellitus and cholelithiasis. Presence of hepatomegaly and mild abnormalities of liver function were common clinical findings. Currently, we know of no effective therapy.

2020

MAFLD

International Expert Consensus Statement

Liver steatosis + metabolic risk factor. **"Positive" diagnosis**, regardless of alcohol consumption of other concomitant liver diseases



2024 : EASL CGP update

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)

Key shift: from a diagnosis ***of exclusion*** → to a ***positive diagnosis*** requiring metabolic dysfunction.

NAFLD vs MAFLD vs MASLD : High concordance

Hagström et al. 99% of patients with NAFLD meet MASLD criteria and natural history is therefore identical J Hep, 2024: 80, e51–e91

The new framework: Steatotic Liver Disease (SLD)

STEATOTIC LIVER DISEASE (SLD)

Hepatic steatosis on imaging or biopsy

MASLD

Metabolic Dysfunction-Associated Steatotic Liver Disease

≥1 cardiometabolic risk factor; no "at risk" alcohol intake

Replaced NAFLD

MetALD

MASLD and increased alcohol intake

MASLD + increased alcohol (♀ 20–50 / ♂ 30–60 g/day)

New category!

ALD

Alcohol-Associated (alcohol-related) Liver Disease

Alcohol-related disease (♀ > 50 / ♂ > 60 g/day)

Replaced Alcoholic Liver Disease

Specific aetiology

Drug-induced, Monogenic diseases, miscellaneous

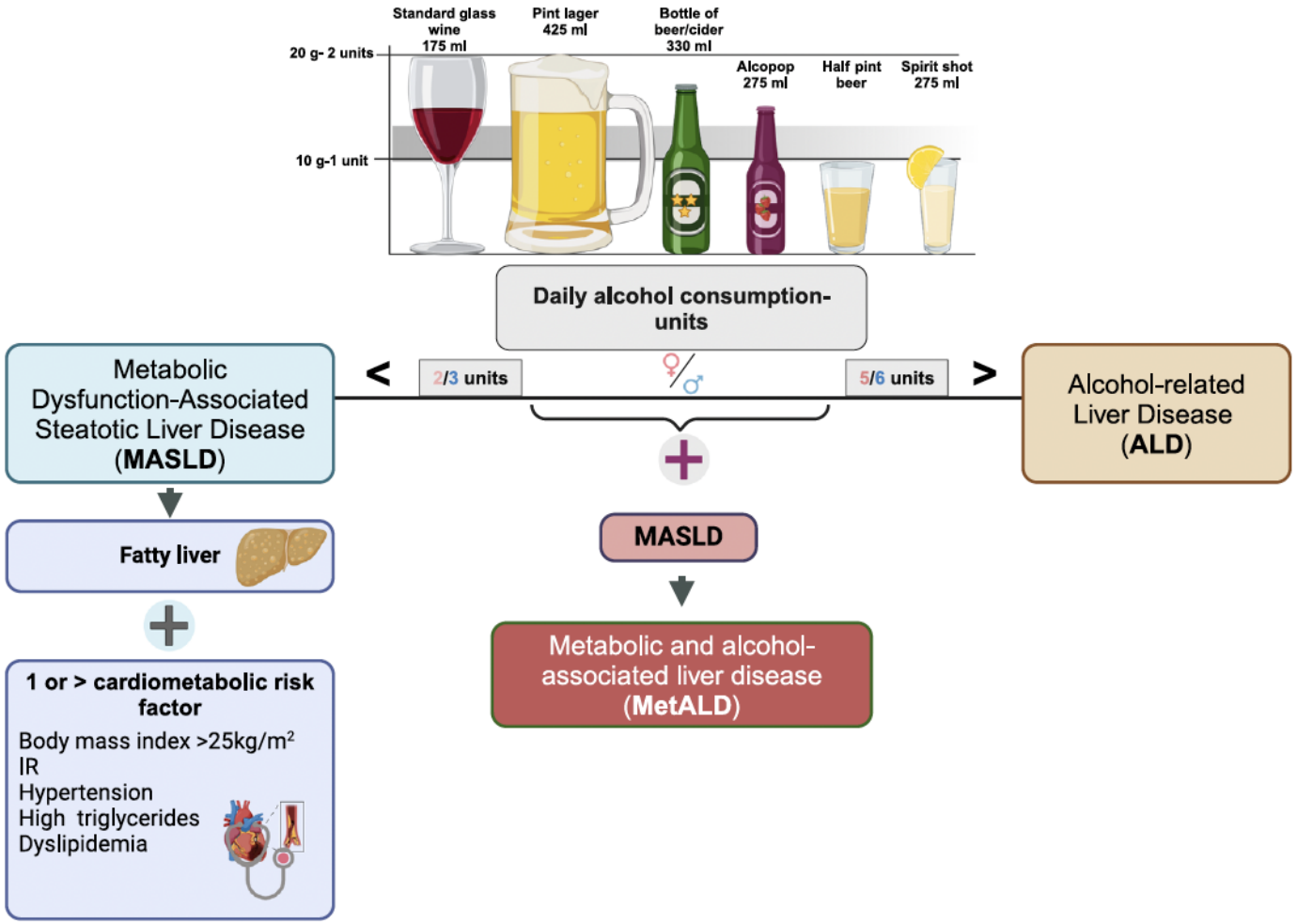
Cryptogenic

No cause and no metabolic criteria identified

Not all steatosis is MASLD

Rinella ME et al. A multisociety Delphi consensus statement on new fatty liver disease nomenclature. Hepatology 2023 Dec 1;78(6):1966-1986

Defining MASLD



Cardiometabolic risk factors

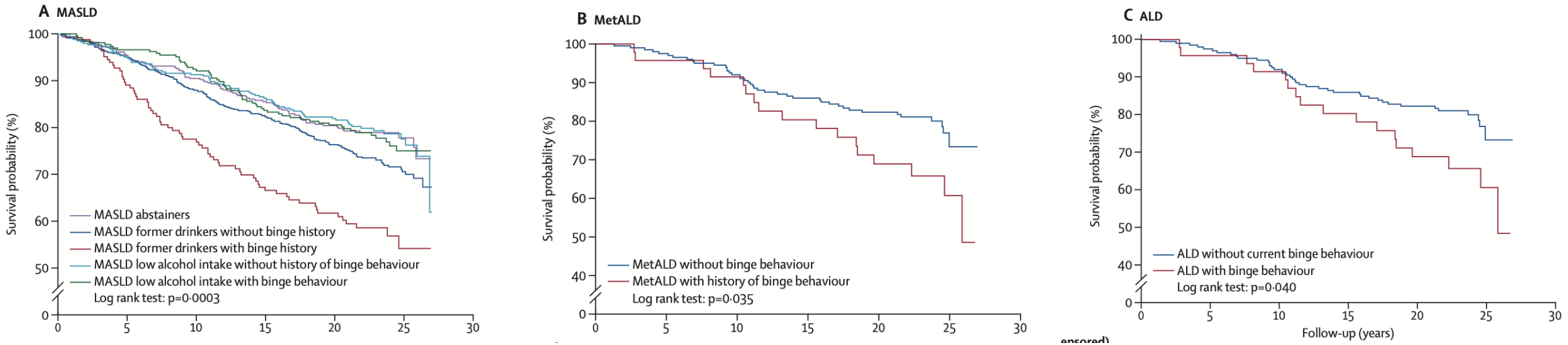
Adult Criteria

At least 1 out of 5:

- ☐ BMI ≥ 25 kg/m² [23 Asia] **OR** WC > 94 cm (M) 80 cm (F) **OR** ethnicity adjusted
- ☐ Fasting serum glucose ≥ 5.6 mmol/L [100 mg/dL] **OR** 2-hour post-load glucose levels ≥ 7.8 mmol/L [≥140 mg/dL] **OR** HbA1c ≥ 5.7% [39 mmol/L] **OR** type 2 diabetes **OR** treatment for type 2 diabetes
- ☐ Blood pressure ≥ 130/85 mmHg **OR** specific antihypertensive drug treatment
- ☐ Plasma triglycerides ≥ 1.70 mmol/L [150 mg/dL] **OR** lipid lowering treatment
- ☐ Plasma HDL-cholesterol ≤ 1.0 mmol/L [40 mg/dL] (M) and ≤ 1.3 mmol/L [50 mg/dL] (F) **OR** lipid lowering treatment

EASL-EASD-EASO Clinical Practice Guidelines on the management of metabolic dysfunction-associated steatotic liver disease (MASLD). J Hepatol 2024 Sep;81(3):492-542
Rinella ME et al. A multisociety Delphi consensus statement on new fatty liver disease nomenclature. Hepatology 2023 Dec 1;78(6):1966-1986

MASLD – MetALD - ALD



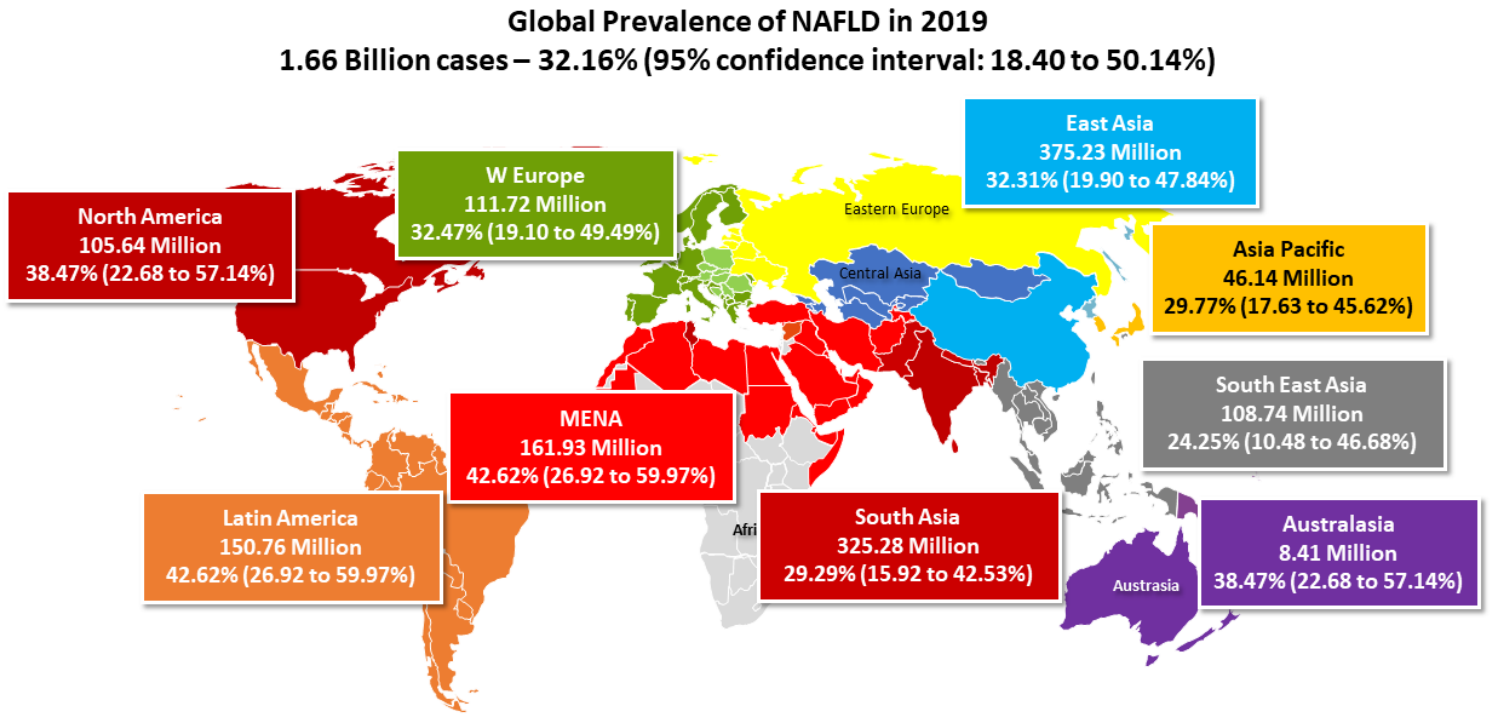
- ✓ **Mortality rates were highest in ALD (HR 2·21), followed by MetALD (HR 1·45)** and MASLD (HR 1·39) vs abstainers without SLD
- ✓ T2DM was the strongest metabolic predictor of MASLD mortality
- ✓ Binge drinking was the dominant driver in MetALD and ALD
- ✓ The greatest mortality risks were among those with binge drinking coexisting with type 2 diabetes or hypertension

Zobair Y et al. Binge drinking, metabolic dysfunction, and the spectrum of steatotic liver disease in the USA: a cross-sectional and longitudinal analysis. Lancet Hepatol Gastrology 2026.

Epidemiology and Natural History of MASLD

Epidemiology

MASLD represents a global health crisis affecting one-third of the world's population



NASH PREVALENCE

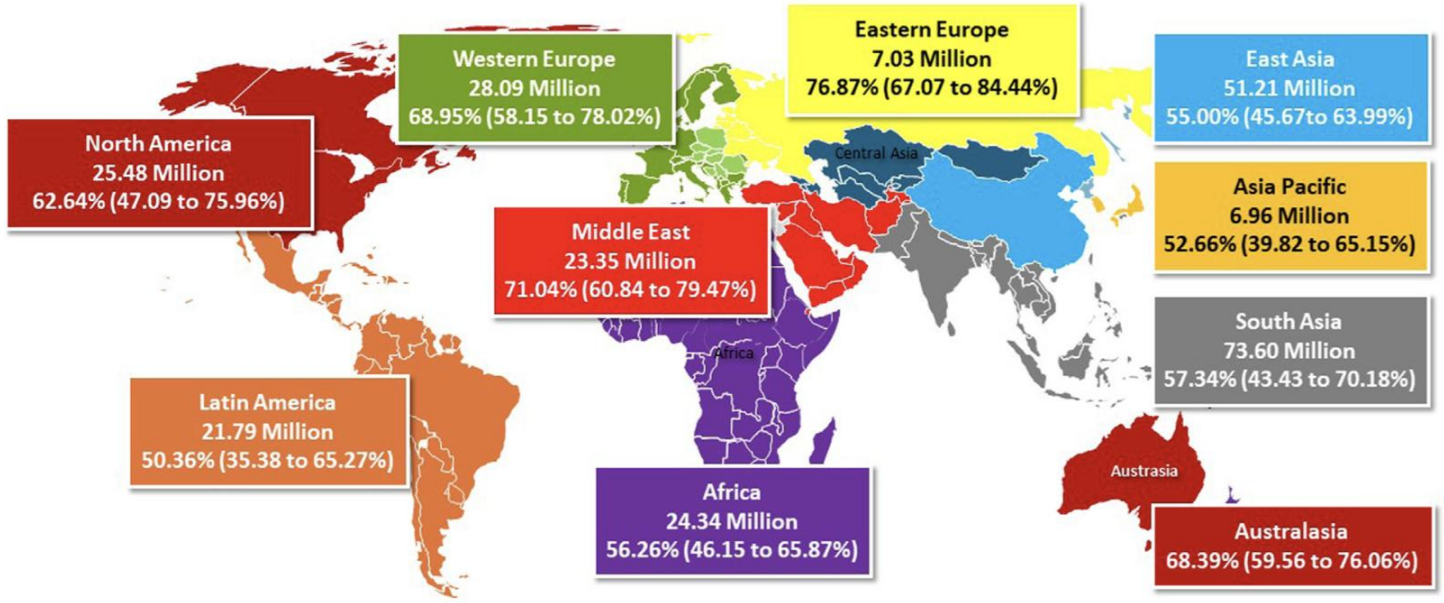
5.27%

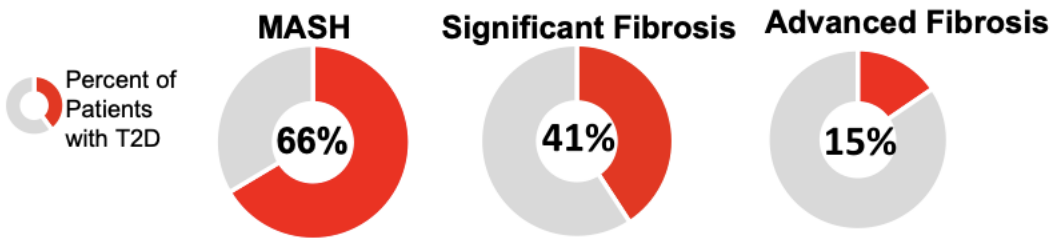
± 2.63 (global pooled estimate)

Younossi ZM et al. Hepatology 2023;77:1335-1347
Riazi K et al. Lancet Gastroenterol Hepatol 2022;7(9):851-861

Epidemiology

MASLD Prevalence in T2DM: 65% (95% confidence interval: 56.6 to 72.5%)



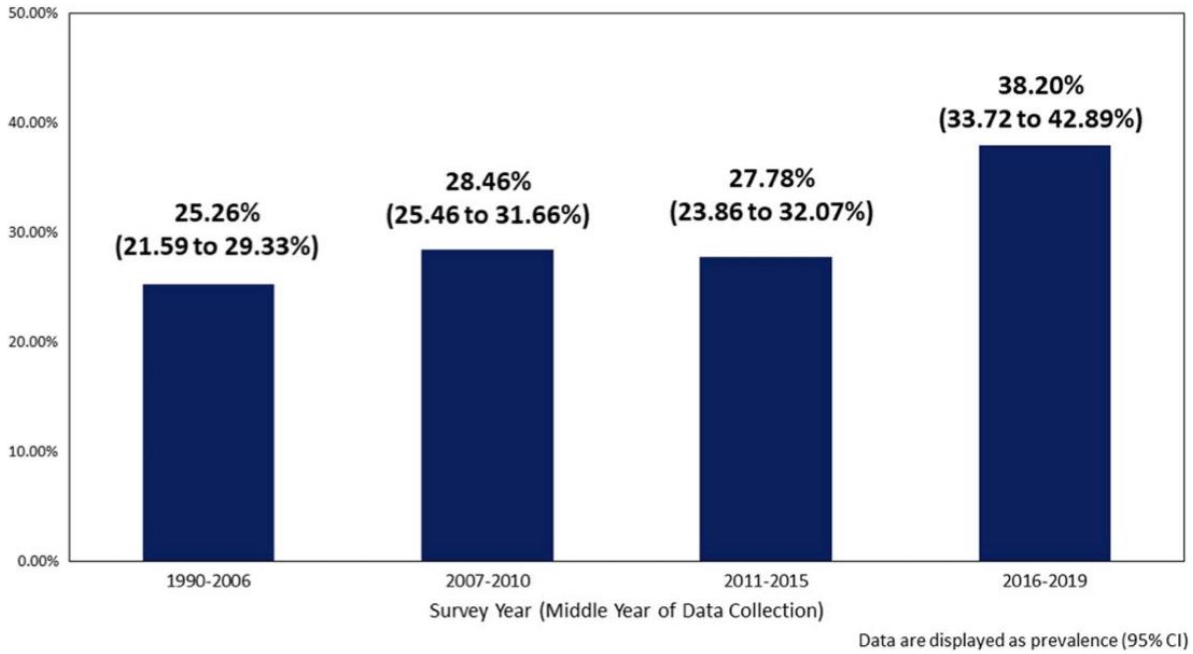


Younossi ZM et al. The Global Epidemiology of Nonalcoholic Fatty Liver Disease and Nonalcoholic Steatohepatitis Among Patients With Type 2 Diabetes. Clinical Gastroenterology and Hepatology 2024;22:1999–2010

Alarming trend

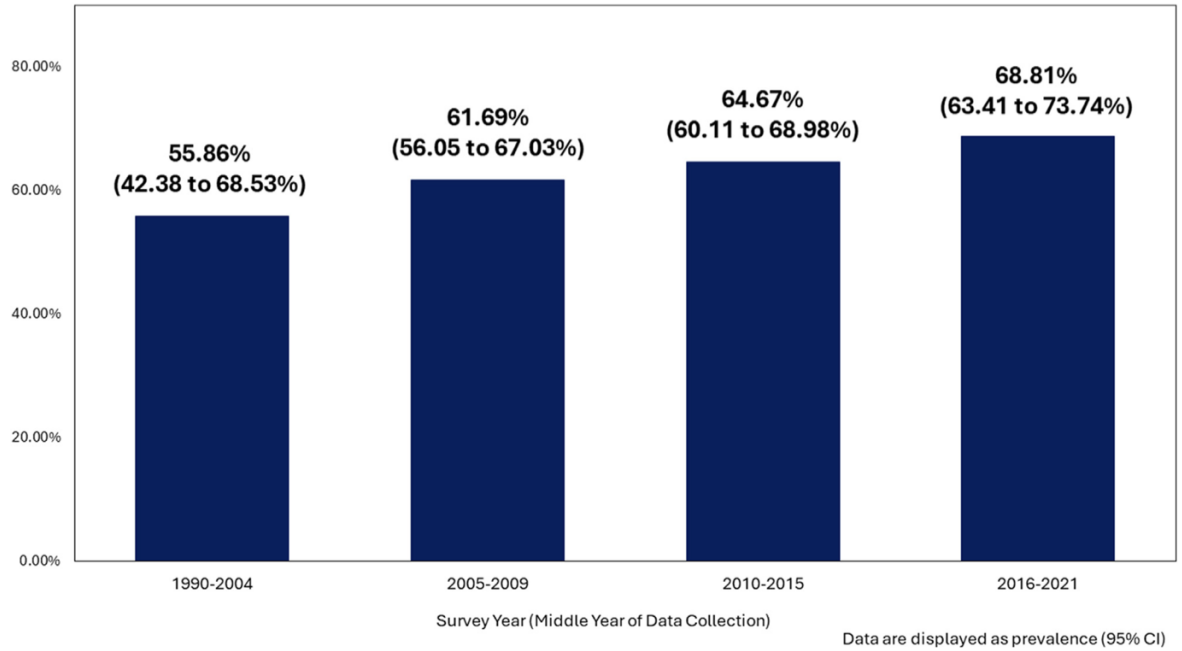
General population

Prevalence increased from 25% (before 2006) to 38% (2016 and beyond)



T2DM

Prevalence increased from 56% (before 2006) to 69% (2016 and beyond)



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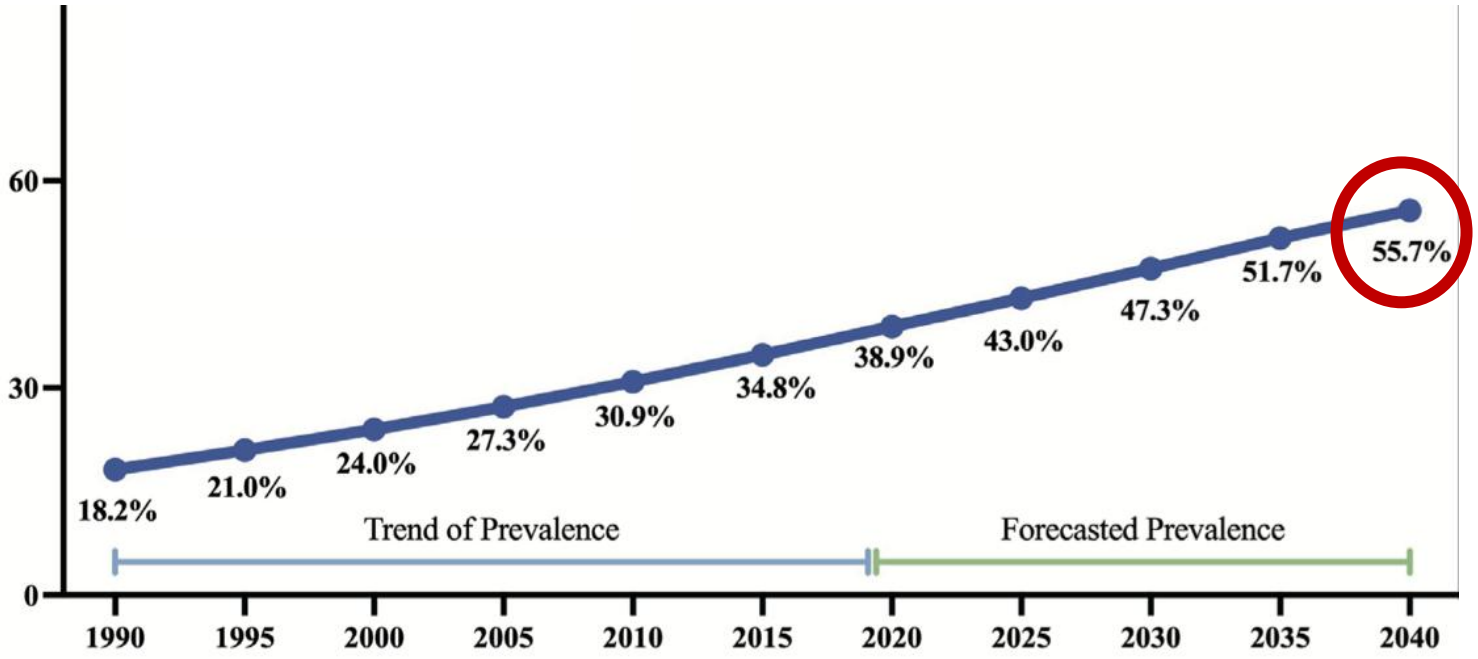
In the future …

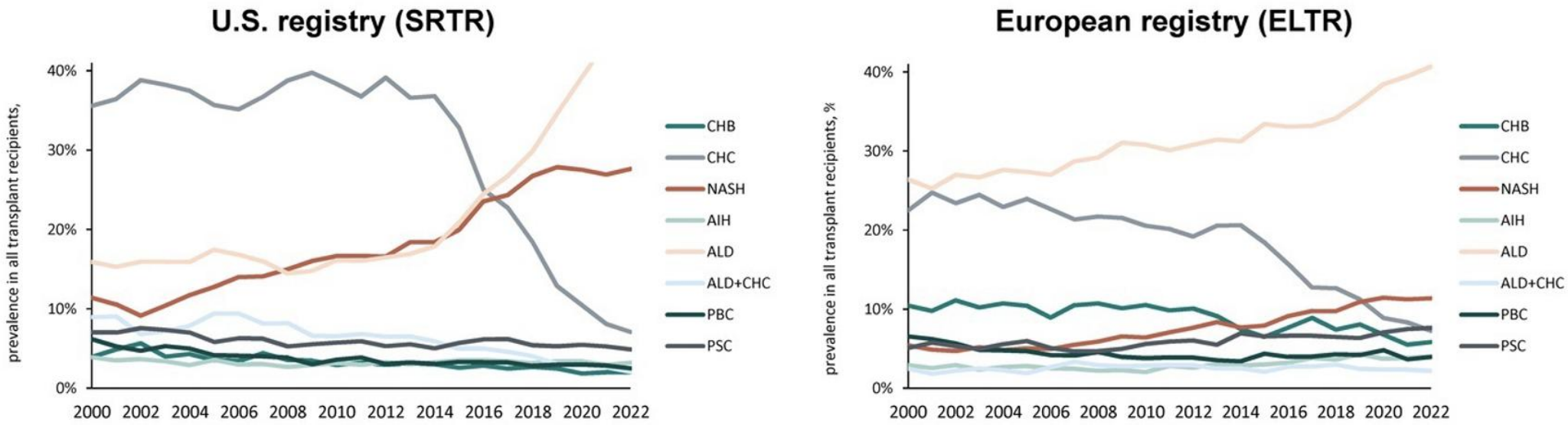
Forecast to 2040 — systematic review of 202 studies, 2,425,860 patients



Le MH et al. Forecasted 2040 global prevalence of NAFLD. Clin Mol Hepatol 2022;28:841-850

Clinical burden of SLD

Clinical burden : Increase of liver transplantation in MASH

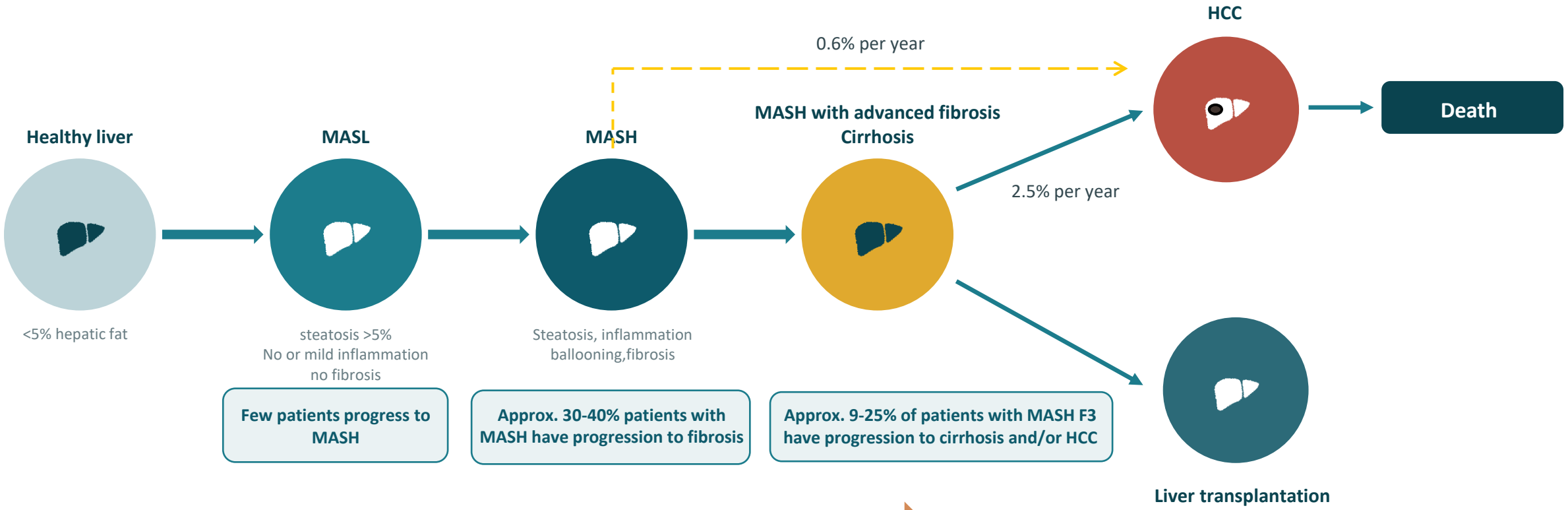


- ✓ **NASH/MASH increased in both registries although faster in SRTR**
- ✓ In non-HCC, the most common chronic liver disease were ALD followed by NASH/MASH
- ✓ In HCC, NASH/MASH is the most common etiology in SRTR and ALD was the most common in ELTR

Zobair Y et al. Steatotic liver disease is the dominant indication for liver transplantation in both Europe and the United States: Trends and outcomes in the past 2 decades. Liver Transplantation 2026, 32(4) 549-557

Natural history of MASLD

Most common cause of death



Fibrosis develops slowly and regression may be easier

Fibrosis is harder to reverse

Post-transplant recurrent / de novo MASLD–MASH (20-40%)

RISK FACTORS

- ✓ BMI
- ✓ Post-LT diabetes mellitus
- ✓ Genetics

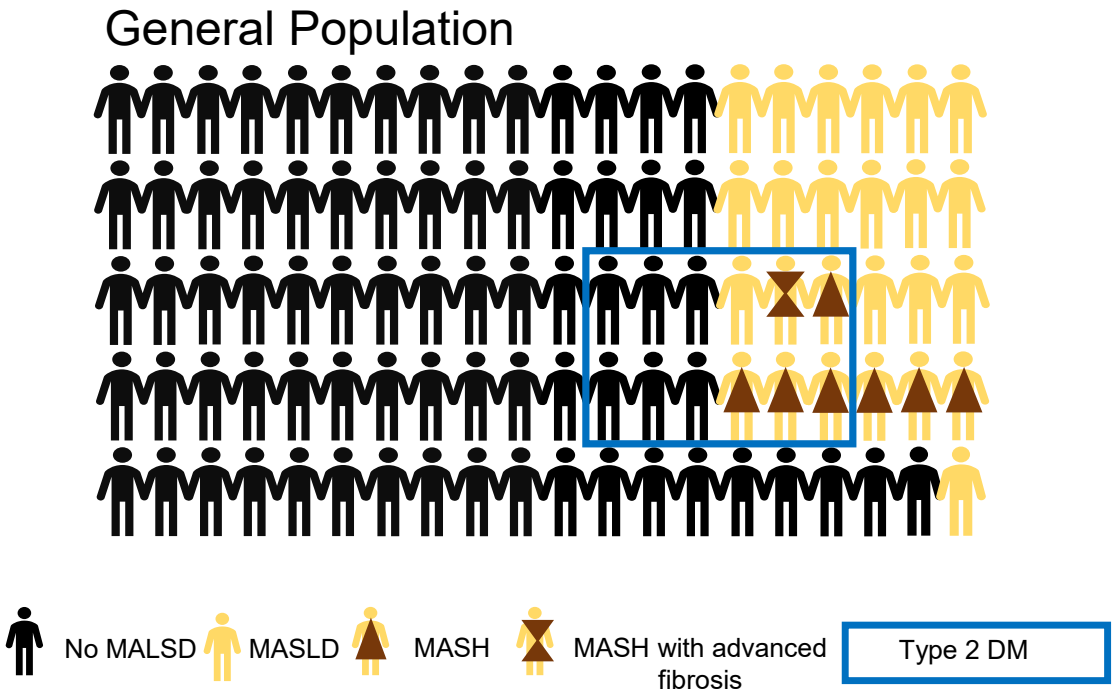
Younossi ZM et al. Hepatology 2018;68:9-360 & 68:361-371

Diagnosis, screening & risk factors

Challenges in MASLD diagnosis

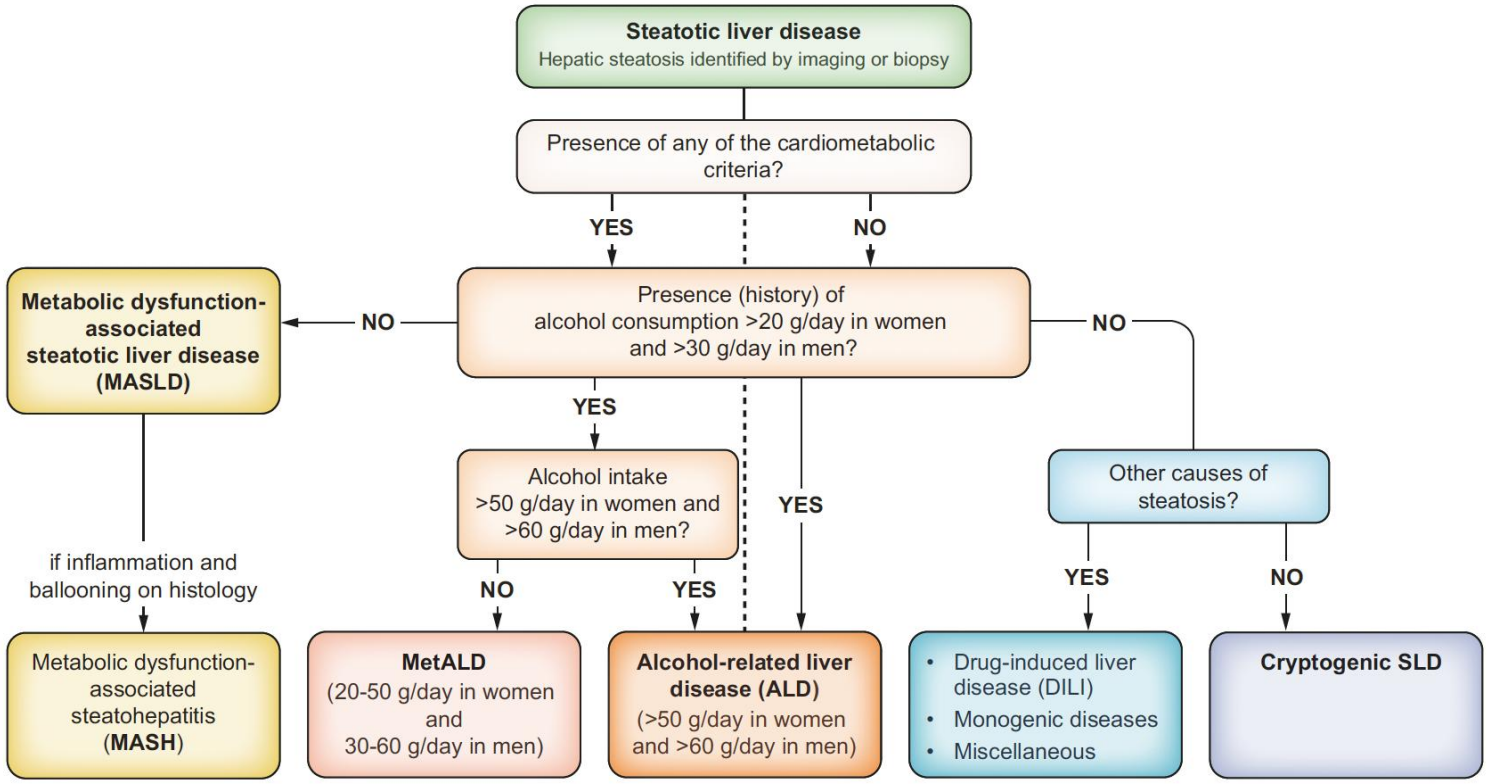
- MASLD is a highly prevalent disease – ***needs to be identified by primary doctors***
- Despite MASLD being a prevalent disease in the general population (and thus, in primary care), only a minority of patients (1/3 of patients) with MASLD have a MASH and advanced liver fibrosis and are at high-risk of developing liver-related complications – ***needs an easy way to screen and triage patients***
- Asymptomatic until very late stage - ***presenting to specialists too late***

Risk stratification
is therefore crucial for the appropriate referral of high-risk minority to specialists



Vieira Barbosa J et al, Hepatology Communications, 2021. 5(2):158-167

SLD and cardiometabolic risk factors



Adult Criteria

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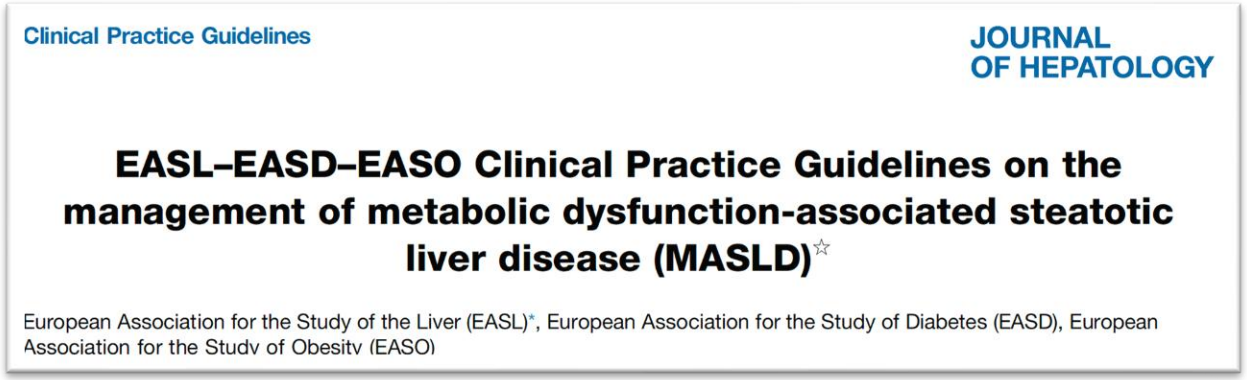
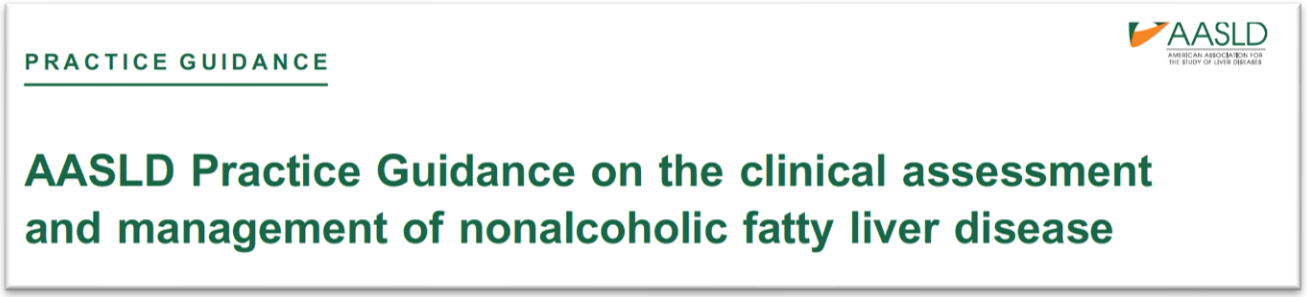
Should we screen general population? What do guidelines say



Healthcare providers should look for MASLD with liver fibrosis either in individuals with (A) ***type 2 diabetes*** *or (B)* ***abdominal obesity and >1 additional metabolic risk factor(s)*** *or (C)* ***abnormal liver function tests****.*
Early diagnosis of fibrosis and subsequent appropriate management can potentially prevent progression to cirrhosis and its complications and may justify screening in these populations at risk.



Screening in ***high-risk populations****, such as those with T2DM, obesity with metabolic complications, a* ***family history of cirrhosis****, or* ***significant alcohol*** *use, may identify those with asymptomatic but clinically significant fibrosis.*
Early identification of such at-risk patients allows for interventions that may prevent.

EASL-EASD-EASO Clinical Practice Guidelines on the management of metabolic dysfunction-associated steatotic liver disease (MASLD). J Hepatol 2024 Sep;81(3):492-542
AASLD Practice Guidance on the clinical assessment and management of nonalcoholic fatty liver disease. Hepatology 2023 May 1;77(5):1797-1835

Should we screen general population? What do guidelines say

Metabolic Dysfunction–Associated Steatotic Liver Disease (MASLD) in People With Diabetes: The Need for Screening and Early Intervention. A Consensus Report of the American Diabetes Association

Diabetes Care 2025;48:1057–1082 | https://doi.org/10.2337/dci24-0094

4. Comprehensive Medical Evaluation and Assessment of Comorbidities: Standards of Care in Diabetes—2025

Diabetes Care 2025;48(Suppl. 1):S59–S85 | https://doi.org/10.2337/dc25-S004

*Screen adults with **type 2 diabetes or with prediabetes**, particularly those with **obesity or other cardiometabolic risk factors or established cardiovascular disease**, for their risk of having or developing cirrhosis related to metabolic dysfunction–associated steatohepatitis (MASH) using a calculated fibrosis-4 index (FIB-4), **even if they have normal liver enzymes***

Assessing risk of diabetes complications

- ASCVD and heart failure history
- ASCVD risk factors and 10-year ASCVD risk assessment
- Staging of chronic kidney disease (see **Table 11.2**)
- Hypoglycemia risk (see Section 6, "Glycemic Targets and Hypoglycemia Prevention")
- Assessment for retinopathy
- Assessment for neuropathy
- Assessment for MASLD and MASH

Cusi K et al. Metabolic Dysfunction–Associated Steatotic Liver Disease (MASLD) in People With Diabetes: The Need for Screening and Early Intervention. A Consensus Report of the American Diabetes Association. Diabetes Care 2025;48(7):1057–1082
4. Comprehensive Medical Evaluation and Assessment of Comorbidities: Standards of Care in Diabetes—2025. Diabetes Care 2025 48(Suppl. 1):S59–S85

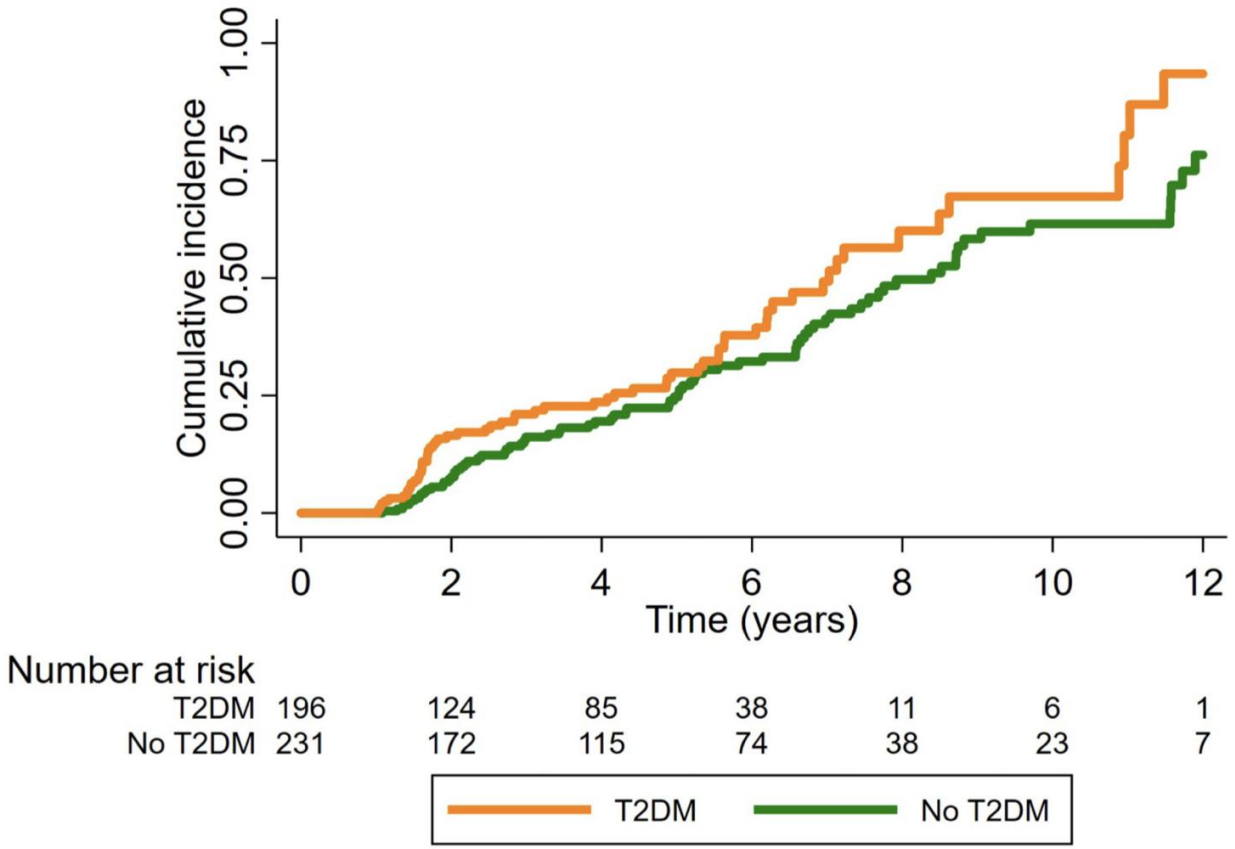
High risk population- T2DM

T2DM is the strongest risk factor for the development of MASH, advanced fibrosis/cirrhosis, HCC and CV and liver-related morbidity and mortality

T2DM patients had a **significantly higher cumulative incidence of fibrosis progression** (p =0.005)

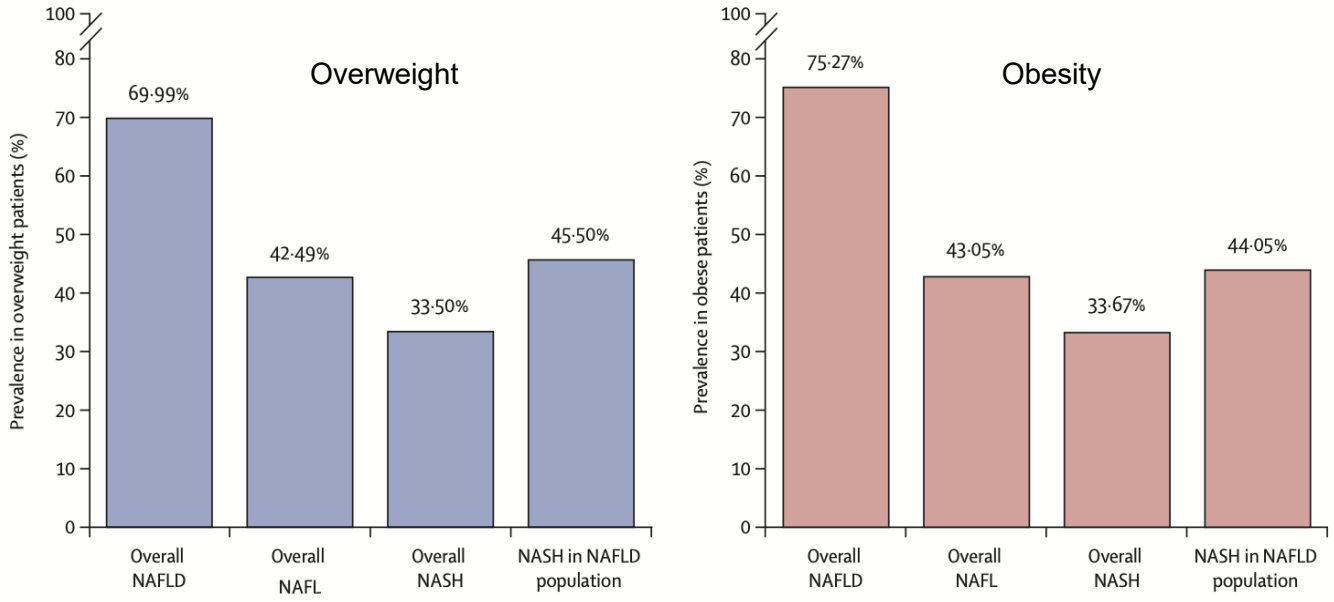
- 4-years (24% vs 20%)
- 8-years (60% vs 50%)
- 12-years (93% vs 76%)

T2DM is independent predictor of fibrosis progression (adjusted HR 1.69, 95%CI 1.17 – 2.43, p =0.005).



Huang DQ, et al. NASH Clinical Research Network. Fibrosis progression rate in biopsy-proven nonalcoholic fatty liver disease among people with diabetes versus people without diabetes: a multicenter study. Gastroenterology 2023;165:463–472.e5

High risk population- Obesity

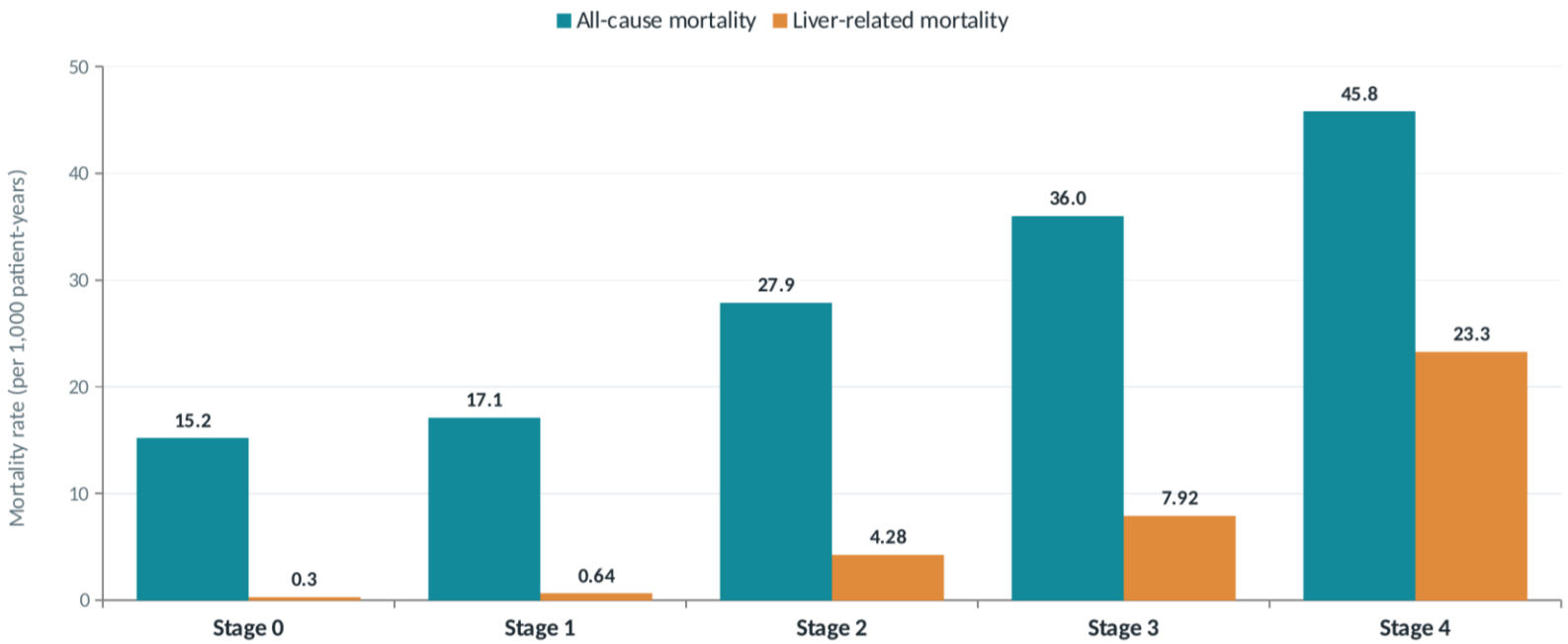


	Overweight population					Obese population				
	Studies	Sample size	Prevalence (95% CI)	I^2	p value	Studies	Sample size	Prevalence (95% CI)	I^2	p value
NAFLD										
Fibrosis stage F1	12	1939	14·89% (6·17–31·76)	96·00%	<0·0001*	12	1604	13·85% (5·83–29·44)	97·00%	<0·0001*
Fibrosis stage F2	12	1939	13·39% (5·52–29·02)	93·00%	..	12	1604	14·05% (5·68–30·76)	94·00%	..
Fibrosis stage F3	13	2136	5·07% (3·10–8·19)	58·00%	..	13	1801	5·15% (2·82–9·22)	83·00%	..
Fibrosis stage F4	13	2151	2·46% (1·62–3·73)	0·00%	..	13	1816	2·06% (1·02–4·12)	72·00%	..
Fibrosis stages F1–4	20	2870	46·56% (26·56–67·74)	97·00%	<0·0001*	20	2472	50·21% (27·67–72·66)	97·00%	<0·0001*
Clinically significant fibrosis (F2–4)	19	3227	20·27% (11·32–33·62)	93·00%	..	19	2829	21·60% (11·47–36·92)	95·00%	..
Advanced fibrosis (F3–4)	13	2197	6·65% (4·35–10·01)	58·00%	..	13	1862	6·85% (3·85–11·90)	90·00%	..

Quek J et al. Global prevalence of non-alcoholic fatty liver disease and non-alcoholic steatohepatitis in the overweight and obese population: a systematic review and meta-analysis. Lancet Gastroenterol Hepatol 2023 Jan;8(1):20-30

Fibrosis is key prognostic factor in MASLD

The severity of liver fibrosis is the strongest histological risk factor for all- cause mortality and development of severe liver disease



Hagstrom H, et al. Fibrosis stage but not NASH predicts mortality and time to development of severe liver disease in biopsy-proven NAFLD. J Hepatol 2017 Dec;67(6):1265-1273
Dulai PS et al. Increased risk of mortality by fibrosis stage in nonalcoholic fatty liver disease: Systematic review and meta-analysis. Hepatology 2017 May;65(5):1557-1565
Angulo P, Kleiner DE, Dam-Larsen S, et al. Liver fibrosis, but no other histologic features, is associated with long-term outcomes of patients with nonalcoholic fatty liver disease. Gastroenterology. 2015;149:389–e39710

Risk stratification & Non-invasive diagnostic tests (NITs)

Why non-invasive tests replace routine biopsy

Liver biopsy is no longer required for routine management

Liver biopsy — the historical reference

- Invasive, costly, with risk of pain and bleeding
- Sampling error: ~1/50,000 of the organ examined
- Substantial inter-observer variability in staging
- Impractical for screening a huge at-risk population

Non-invasive tests (NITs)

- Safe, repeatable, and scalable for case-finding
- Excellent at ruling OUT advanced fibrosis (high NPV)
- Enable longitudinal monitoring of progression
- Recommended first-line by both EASL and AASLD

Biopsy remains essential for definitive MASH diagnosis, resolving discordant tests, and excluding co-existing liver disease.

Steatosis vs Fibrosis

NITs assess two distinct domains

Steatosis (liver fat)

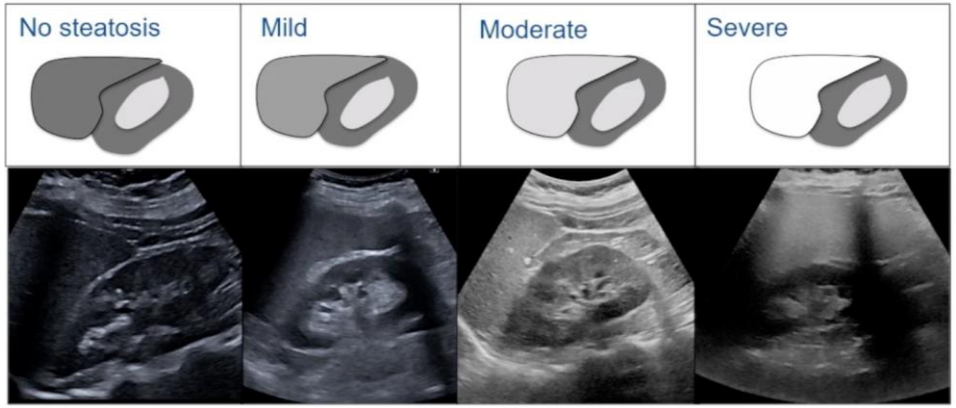
Ultrasound, CAP (FibroScan), MRI-PDFF — quantifies fat but does not stage fibrosis.

Fibrosis (the prognostic domain)

FIB-4, ELF (blood) and elastography: VCTE, pSWE, 2D-SWE, MRE.

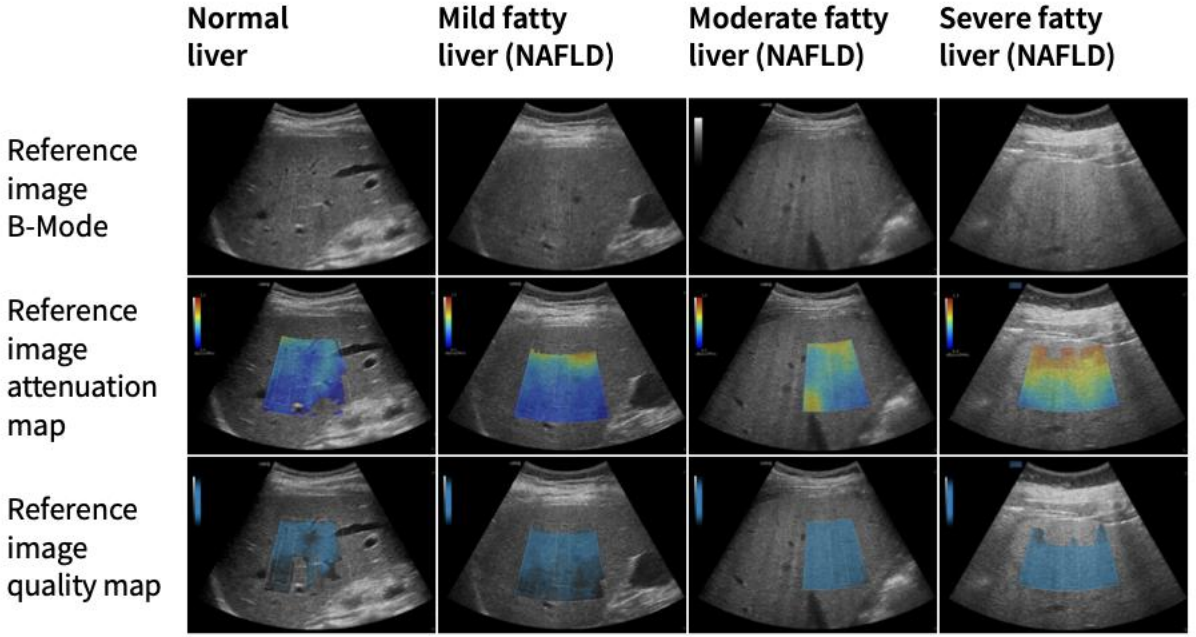
Steatosis

Fat quantification with ultrasound



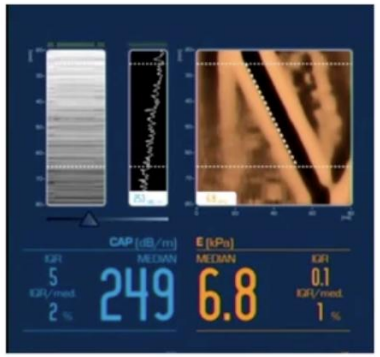
- ✓ Low sensitivity for mild steatosis
- ✓ Sensitivity of 85% for moderate-to-severe steatosis
- ✓ Operator dependent

Ultrasound-Guided Attenuation Parameter (UGAP)



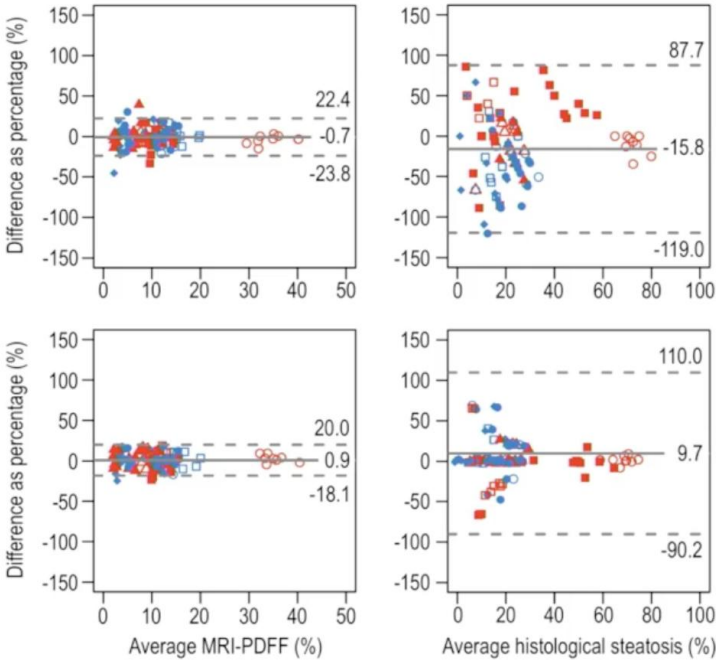
Steatosis

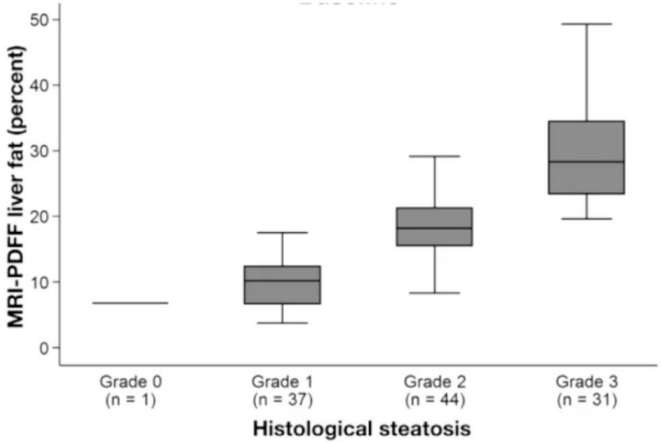
Controlled Attenuation Parameter (CAP)



- ✓ Etiology, diabetes, and BMI should be integrated in the CAP interpretation
- ✓ Examiner variability
- ✓ Ascites anatomic barriers

MRI-PDFF





grade 0 vs 1–2–3	AUROC 0.98
grade 0–1 vs 2–3	AUROC 0.91
grade 0–2 vs grade 3	AUROC 0.92

- ✓ Reference method for fat quantification

FIB-4 - Recommended primary NIT

$$\text{FIB-4} = \frac{\text{Age (yrs)} \times \text{AST}}{\text{Platelets} \times \sqrt{\text{ALT}}}$$

Uses four routine parameters — free, instantly available in any setting, extensively validated.

Cut-offs for advanced fibrosis (F3–F4)

< 1.3	1.3 – 2.67	> 2.67
Rule OUT (low risk)	Indeterminate	Rule IN (high risk)

Age > 65 yrs: raise the lower cut-off to 2.0 to preserve specificity (per EASL & AASLD).

Strengths

- **High negative predictive value — excellent rule-out tool**
- Zero added cost; ideal for primary care & endocrinology
- Validated for repeat testing to track progression

Limitations

- Large indeterminate “grey zone” (1.3–2.67)
- Lower accuracy at age extremes — more false positives in the elderly, poor sensitivity in young adults
- Lower accuracy in isolated T2DM
- Insensitive to significant (F2) fibrosis — may miss it

EASL-EASD-EASO Clinical Practice Guidelines on the management of metabolic dysfunction-associated steatotic liver disease (MASLD). J Hepatol 2024 Sep;81(3):492-542

VCTE / FibroScan & ultrasound elastography

Fibrosis stiffens the liver. Elastography sends a mechanical or acoustic pulse into the tissue and measures how fast the resulting **shear wave** propagates — faster waves mean a stiffer, more fibrotic liver. Stiffness is reported in **kilopascals (kPa)** as a surrogate for histological fibrosis stage.

VCTE

Vibration-controlled transient elastography

- FibroScan® device; mechanical 50 Hz pulse
- Not image-guided (A/M-mode)
- Adds CAP for steatosis
- Most evidence & defined cut-offs

pSWE

Point shear-wave (ARFI)

- Built into a standard US scanner
- Single operator-placed ROI
- B-mode guidance avoids vessels
- Result in kPa or m/s

2D-SWE

Two-dimensional shear-wave

- Real-time colour stiffness map
- Larger sampling region
- Integrated in diagnostic US
- Useful when VCTE limited

MRE

Magnetic resonance elastography

- Highest diagnostic accuracy
- Whole-liver assessment
- Costly, limited availability
- Reserved for selected cases

FibroScan® / VCTE in clinical practice

Two measurements, one probe (M or XL)

LSM (kPa) — liver stiffness → fibrosis stage
CAP (dB/m) — controlled attenuation parameter → steatosis (range ~100–400)

Liver stiffness cut-offs in MASLD

< 8 kPa	8–12 kPa	> 12 kPa
Advanced fibrosis unlikely	Indeterminate (grey zone)	Advanced fibrosis likely → refer

Reliable exam: median of ≥10 valid shots, IQR/median ≤ 30%; select M vs XL probe by body habitus.

Why it is the reference

- Point-of-care, rapid, well standardised cut-offs
- Simultaneous fibrosis (LSM) and fat (CAP) read-out
- Largest evidence base; embedded in both guidelines

Pitfalls & confounders

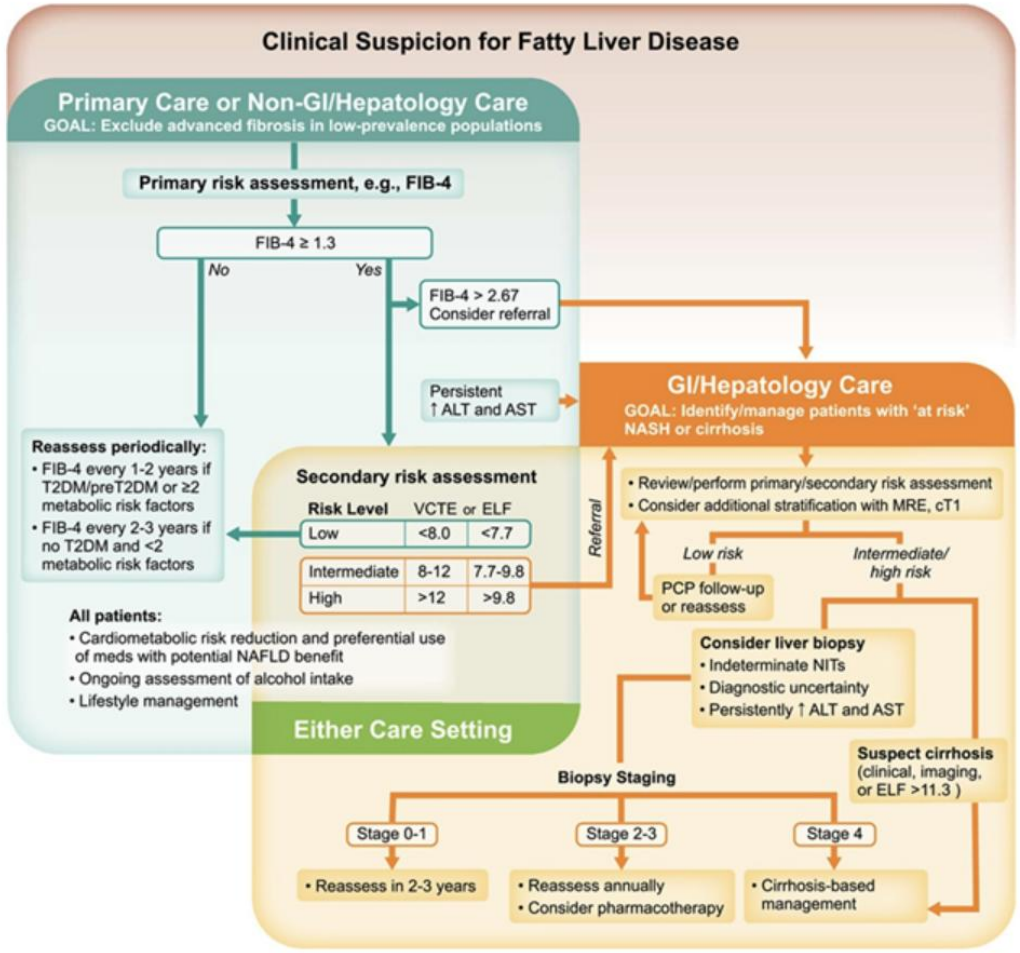
- Failure / unreliable scans with obesity, narrow rib space
- Patient must fast ≥ 3 h — food falsely raises stiffness
- Ascites prevents measurement; use XL probe if BMI high
- Acute hepatitis, congestion, cholestasis inflate values

VCTE (FibroScan) LSM:
< 8.0 kPa → advanced fibrosis unlikely; intensify comorbidity management & re-assess.
≥ 8.0 kPa → hepatology referral for full work-up.

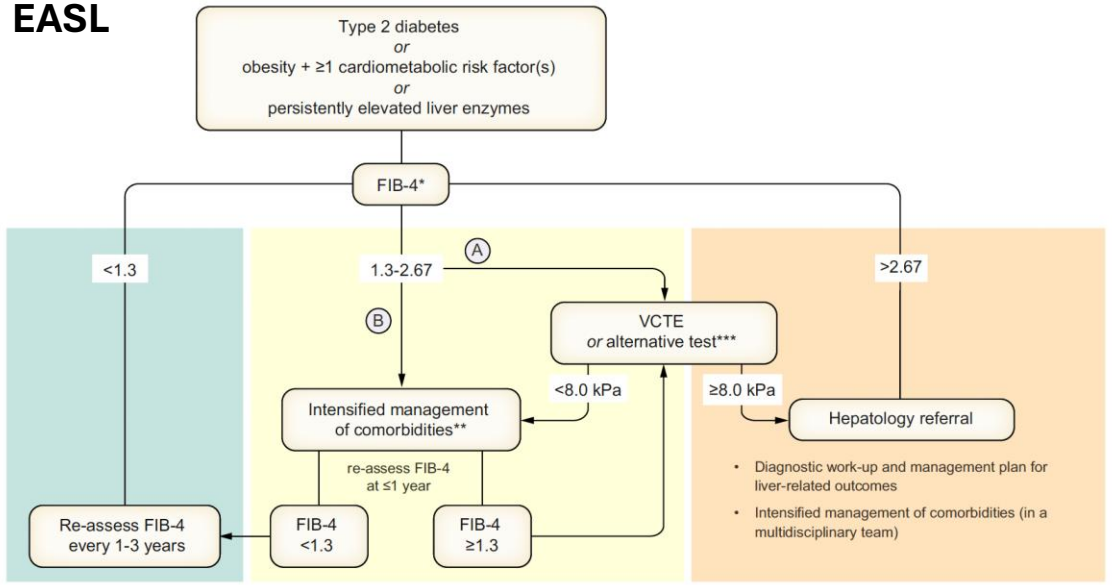
Major guidelines, one pathway

Strategy: **blood-based scores** are best at **ruling OUT** advanced fibrosis; **elastography** is better at **ruling IN**.
None can assess ballooning or lobular inflammation.

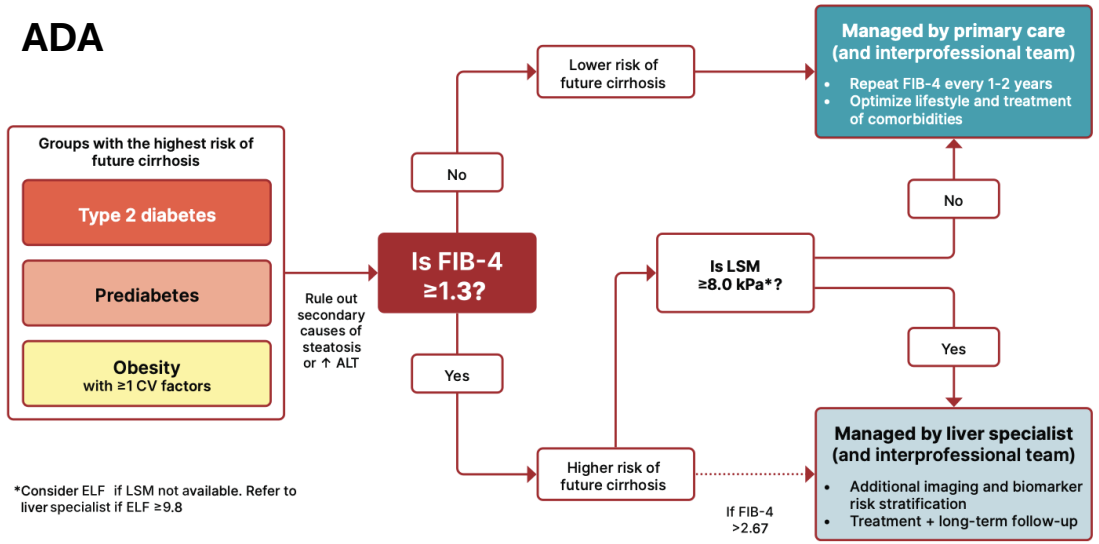
AASLD



EASL

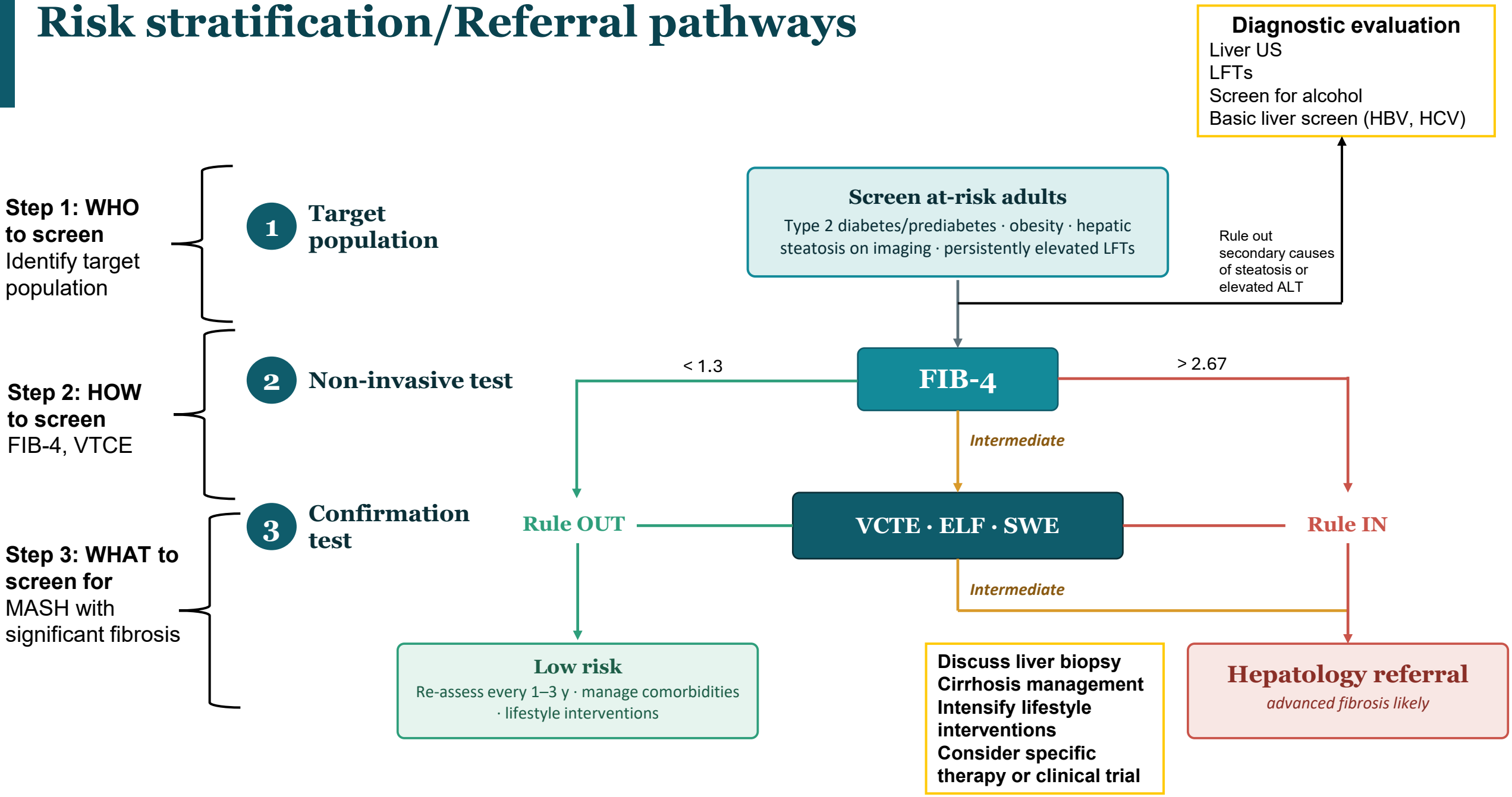


ADA



EASL–EASD–EASO Clinical Practice Guidelines · J Hepatol 2024;81:492–542

Risk stratification/Referral pathways



FIB-4 as the 1st step in risk evaluation

High NPV but poor PPV - best used to rule out rather than to rule in advanced fibrosis

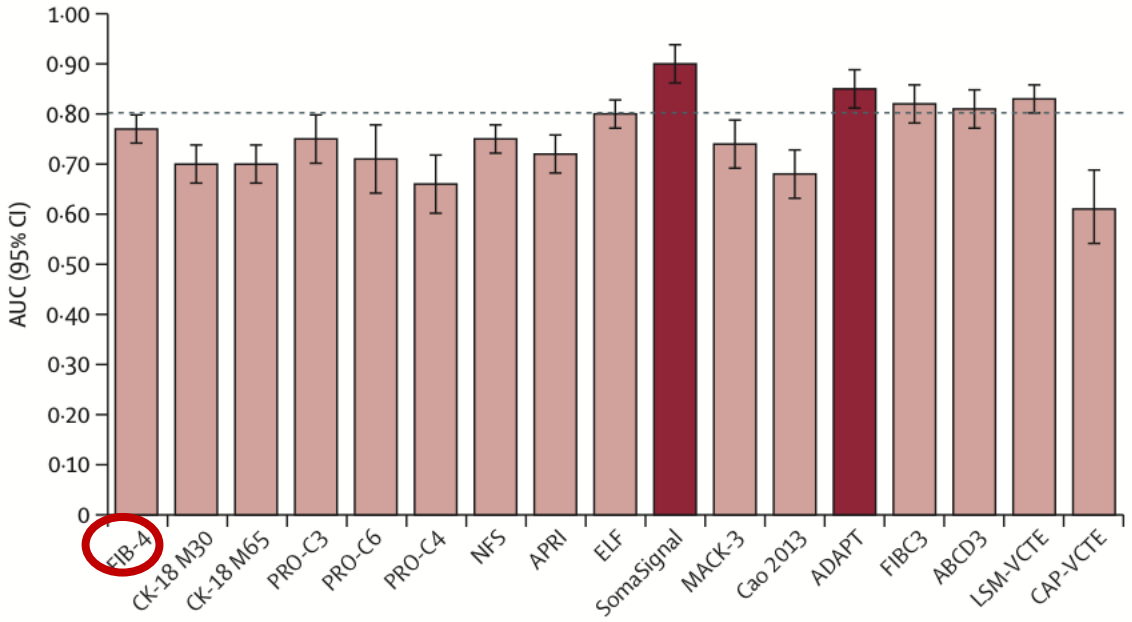


Table 2—Diagnostic accuracy of NITs for detection of high risk of AF using literature-suggested threshold

	AUROC (95% CI)	Sensitivity	Specificity	PPV	NPV	Uncertainty area, %
NFS	0.71 (0.64–0.79)					63.04
<−1.455		89.8	23	10.7	95.1	
>0.676		35.6	87	22	92.9	
FIB-4 score	0.78 (0.72–0.84)					41.46
<1.30		84.7	58	17.1	97.2	
>2.67		16.9	96.9	35.7	91.9	
MAF-5	0.77 (0.71–0.84)					8.0
<0		100	2.8	9.5	95.1	
≥1		100	11.5	10.4	98.7	

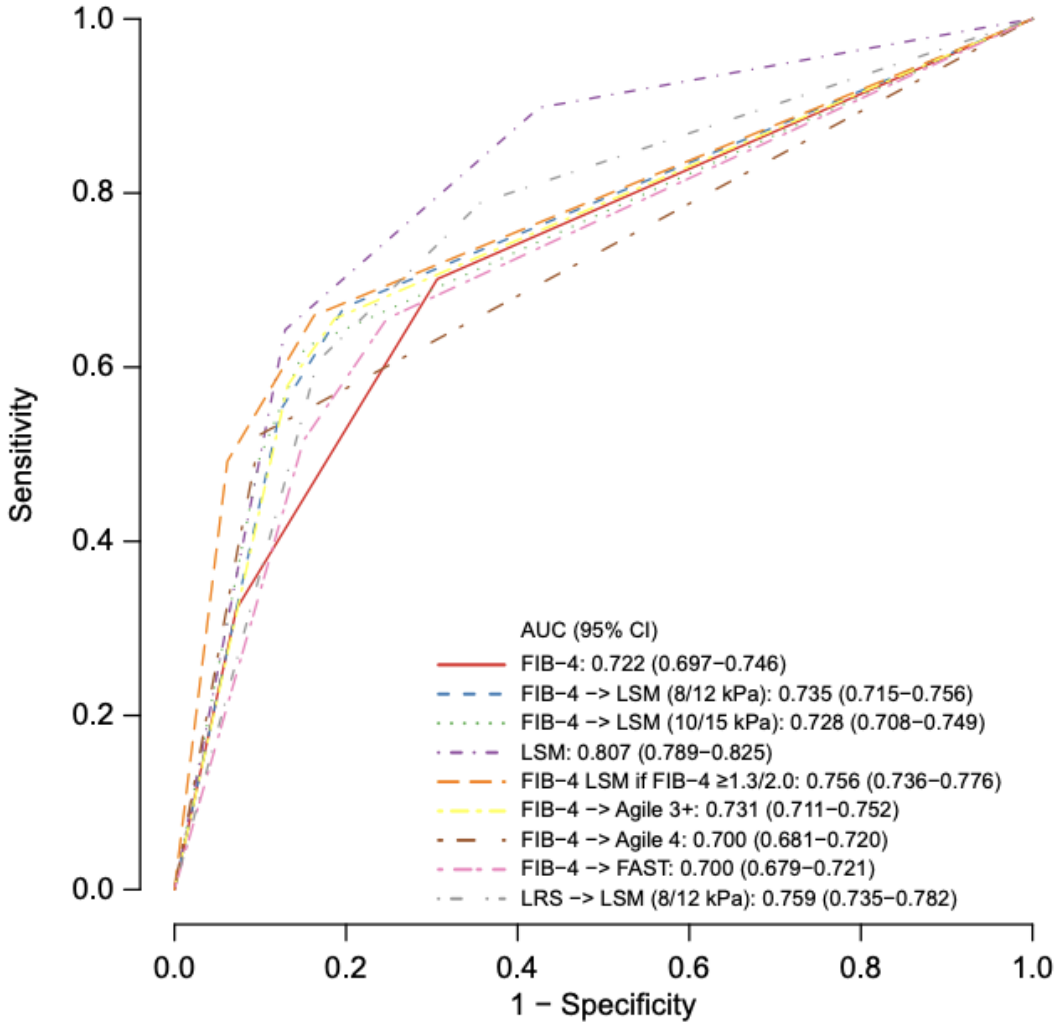
Caussy C et al. Screening for Metabolic Dysfunction–Associated Steatotic Liver Disease–Related Advanced Fibrosis in Diabetology: A Prospective Multicenter Study. Diabetes Care 2025 Jun; 48:877

Vali Y et a. Biomarkers for staging fibrosis and non-alcoholic steatohepatitis in non-alcoholic fatty liver disease (the LITMUS project): a comparative diagnostic accuracy study. Lancet Gastroenterol Hepatol 2023; 8(8):714-725

Two-step approach: FIB-4/LSM

- In a subgroup of 1,587 patients with liver biopsy together with all scores available, the median (P25-P75) FIB-4 and LSM were 1.29 (0.79-2.10) and 8.9 (6.4-13.8), respectively.

- The two-step approach achieved an AUC of 0.735 (95% CI 0.715-0.756) in diagnosing F3-F4 fibrosis



Yip TC-F et al. Prognostic performance of the two-step clinical care pathway in metabolic dysfunction-associated steatotic liver disease. J Hep 2025:83, 304–314

Transaminases “normal range”

- ALT “problem”
  - Most lab “normal” ALT range inaccurate; true normal ALT <= 19 U/l for women, <= 30 U/l for men
  - Normal ALT does NOT preclude MASLD or severe disease; ALT can normalize after progression to cirrhosis (“burnt out” liver)

McPherson S, et al. Gut 2010; 59:1265-1269

Treatment

Lifestyle management

Overweight/obesity NAFLD

Weight reduction

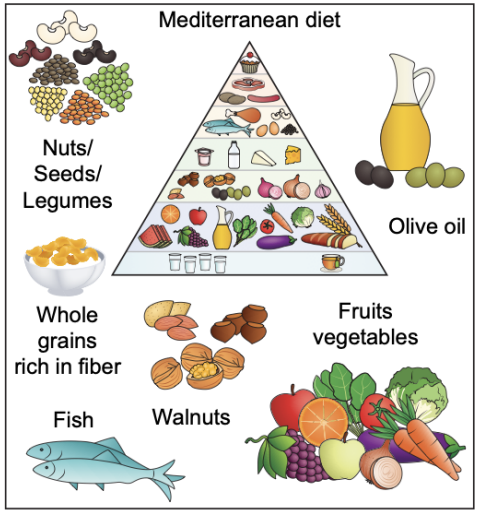
- The more severe the liver disease is, the higher the goals are in terms of weight loss
- Healthy diet with caloric restriction tailored for your preferences

Non-obesity NAFLD

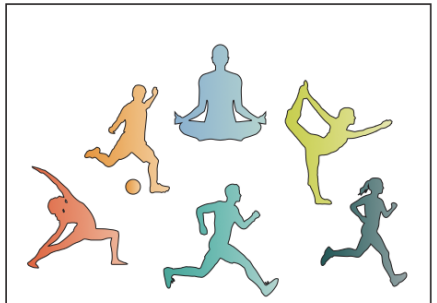
- 3-5% reduction of weight even within the normal BMI range (especially if recent weight gain occurred or if abdominal obesity is present)

Lifestyle advice for ALL patients with NAFLD

Recommended foods

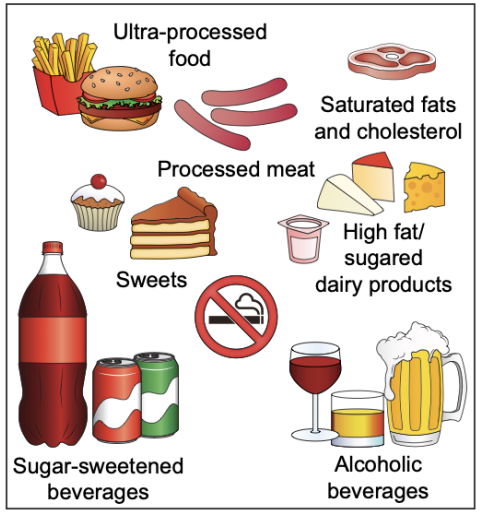


Recommended activity



- Mental well being management
- Aerobic exercise ≥3 days/week (≥150 min/week moderate intensity)
- Resistance exercise ≥2 days/week
- Reduce sedentary behaviour

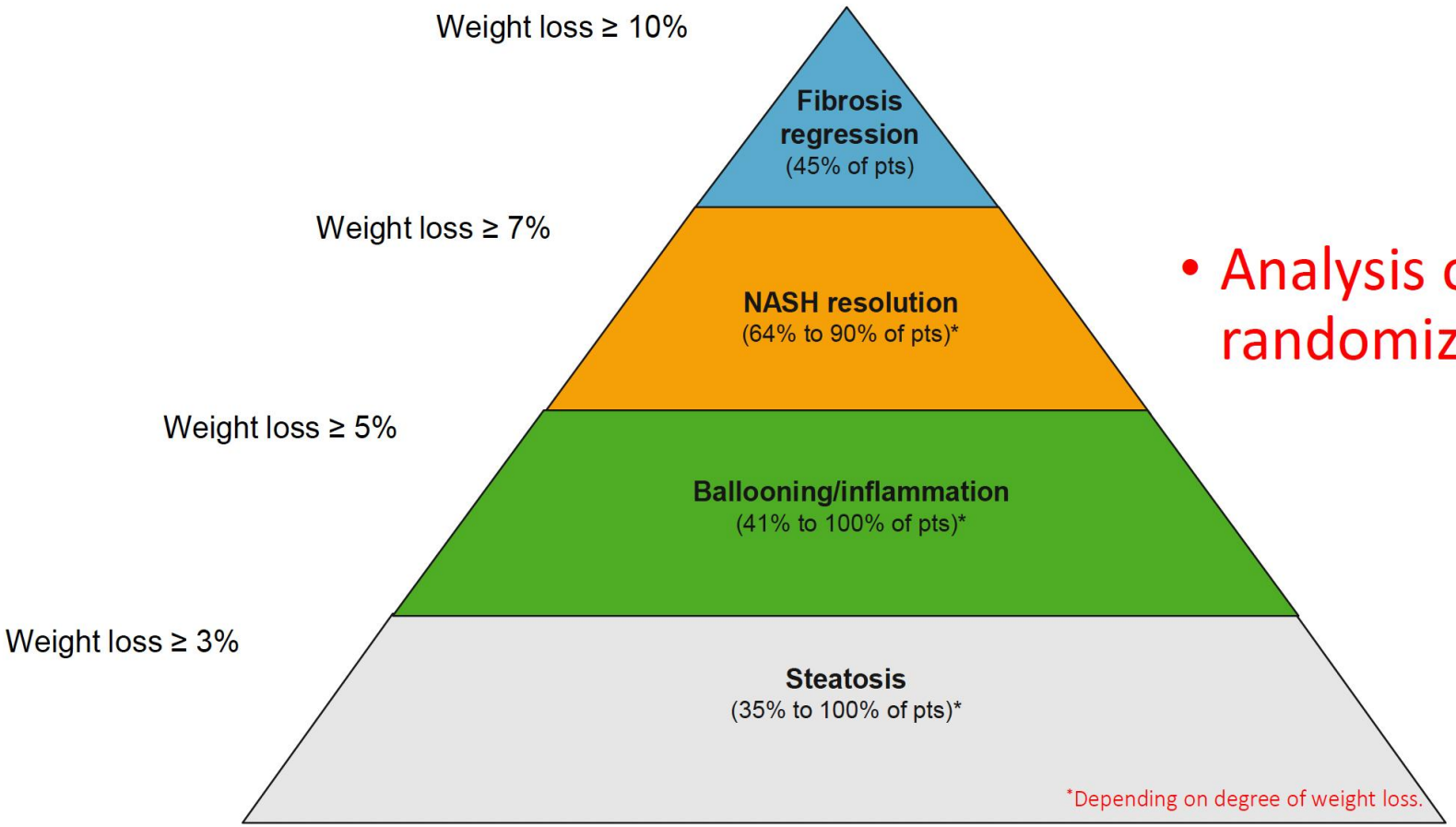
Non-recommended foods/ Minimize consumption



- Reduce added sugar (*e.g.* by reducing sweets, processed foods, sugared dairy products, *etc.*)
- Avoid sugar-sweetened beverages
- Reduce saturated fat and cholesterol (*e.g.* by eating low fat meat and low fat dairy products)
- Increase n-3 fatty acids found in fish, and walnuts; utilize olive oil over other oils more often
- Minimize "fast food" and ultra-processed food
- Home-cooked meals are preferable
- Try to follow the Mediterranean dietary pattern

Francque SV et al. Non-alcoholic fatty liver disease: A patient guideline. JHEP Rep 2021 Sep 17;3(5):100322

Weight loss



- Analysis of data from 4 randomized studies

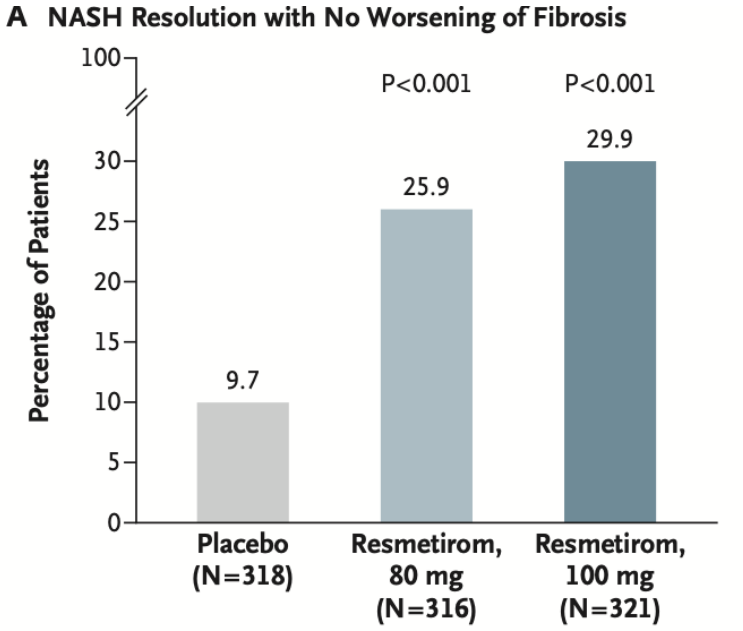
Hannah WN, et al. Clin Liver Dis. 2016;20:339-350

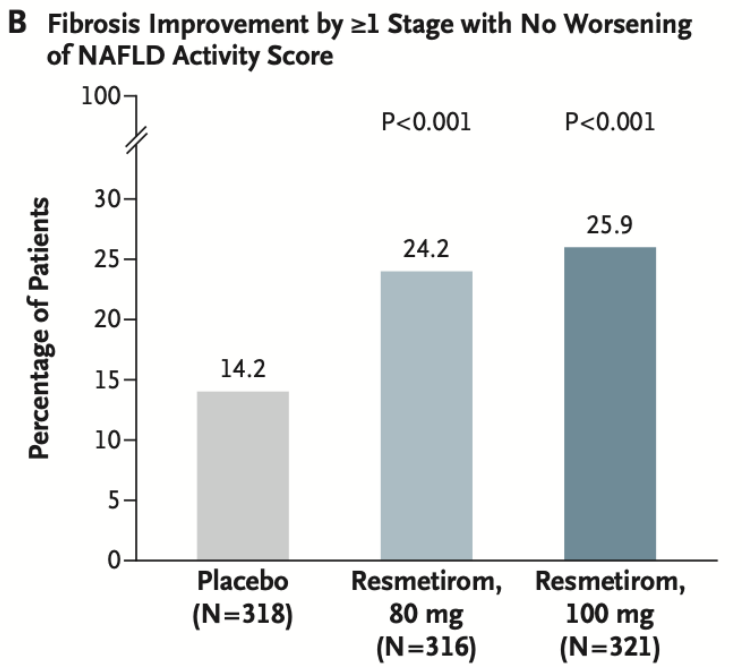
Resmetirom

The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 FEBRUARY 8, 2024 VOL. 390 NO. 6

A Phase 3, Randomized, Controlled Trial of Resmetirom in NASH with Liver Fibrosis

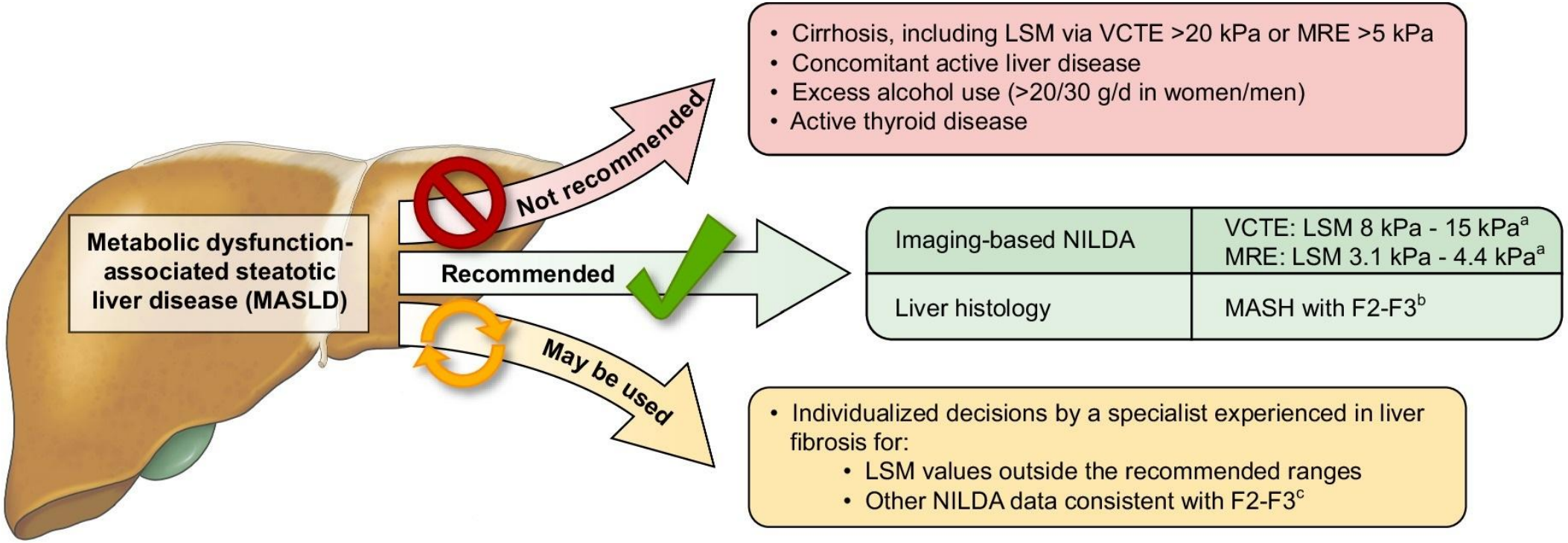
- Oral, liver-directed, thyroid hormone receptor beta (THR-β)- selective agonist
- Randomly assigned in a 1:1:1 ratio to receive once-daily resmetirom at a dose of 80 mg or 100 mg or placebo
- **Inclusion:** NASH with F1-F3
- **Exclusion:** Active hyperthyroidism or non treated hypothyroidism
- **Primary endpoint**: 52-week liver biopsy read blindly
- 966 patients included
  - 5% F1, 33% F2 et 62% F3
- **Secondary effects:** Diarrhea and nausea
- Weight stable





Harrison SA et al. A Phase 3, Randomized, Controlled Trial of Resmetirom in NASH with Liver Fibrosis. N Engl J Med 2024 Feb 8;390(6):497-509

Resmetirom



MASH with moderate to advanced liver fibrosis (consistent with F2-F3)

- Noninvasive liver disease assessment—preferably imaging-based test results—consistent with MASH with F2-F3, or
- Historical liver biopsy demonstrating MASH with F2-F3 (and without evidence of concomitant, histologically active autoimmune liver disease).

NOT for cirrhosis!

AASLD, Resmetirom therapy for metabolic dysfunction-associated steatotic liver disease: October 2024 updates to AASLD Practice Guidance Hepatology 2025:81(1), 312-321

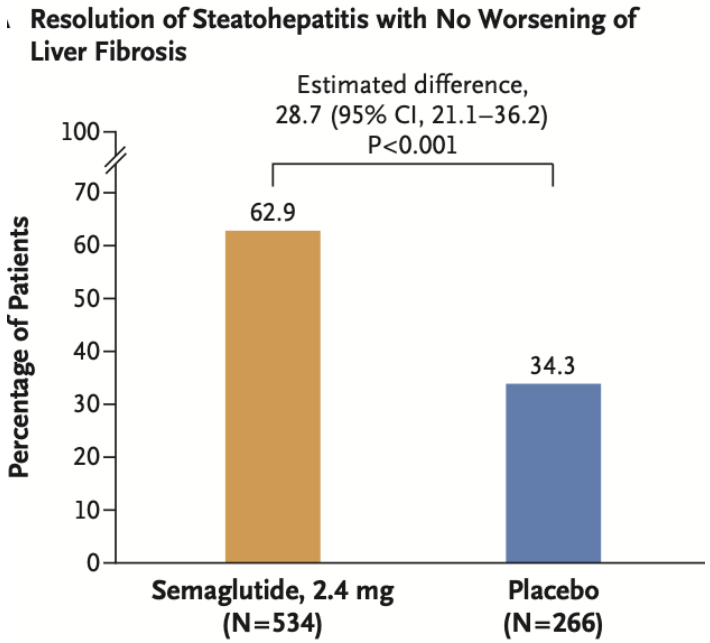
Semaglutide

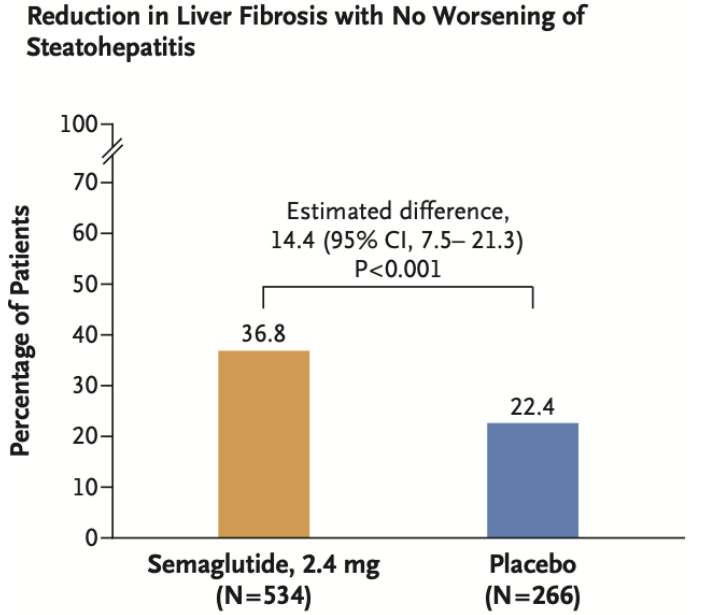
The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 JUNE 5, 2025 VOL. 392 NO. 21

Phase 3 Trial of Semaglutide in Metabolic Dysfunction–Associated Steatohepatitis

- Glucagon-like peptide-1 receptor agonist
- Randomly assigned in a 2:1 ratio to receive once-weekly subcutaneous Semaglutide at a dose of 2.4 mg or placebo for 240 weeks.
- **Inclusion:** MASH with F2-F3, NAS >= 4
- **Exclusion:** history of acute pancreatitis
- **Primary endpoint**: 72-week liver biopsy
- 800 patients included
  - 150 patients F2, 550 patients F3
- **Side effects:** GI adverse events
- Weight loss: - 10.5% vs -2.0%

Part 2 ongoing: clinical outcomes at 240 weeks





Sanyal AJ et al. Phase 3 Trial of Semaglutide in Metabolic Dysfunction-Associated Steatohepatitis. N Engl J Med 2025 Jun 5;392(21):2089-2099

Treatment

Drugs	**FDA approval for MASH + fibrosis**	**EMA approval for MASH + fibrosis**	**Switzerland approval for MASH + fibrosis**	**Available in Switzerland**
Resmetiron	Oui (03/24)	Oui (8/25)	Non	Non
Semaglutide	Oui (8/2025)	Oui (04/26)	Non	Yes (T2DM, obesity)

EASL CONGRESS Barcelona Spain 27–30 May 2026

EASL The Home of Hepatology

EASD European Association for the Study of Diabetes

EASO European Association for the Study of Obesity

EASL-EASD-EASO Guidance for the use of Resmetirom and Semaglutide as MASH-Targeted Therapy

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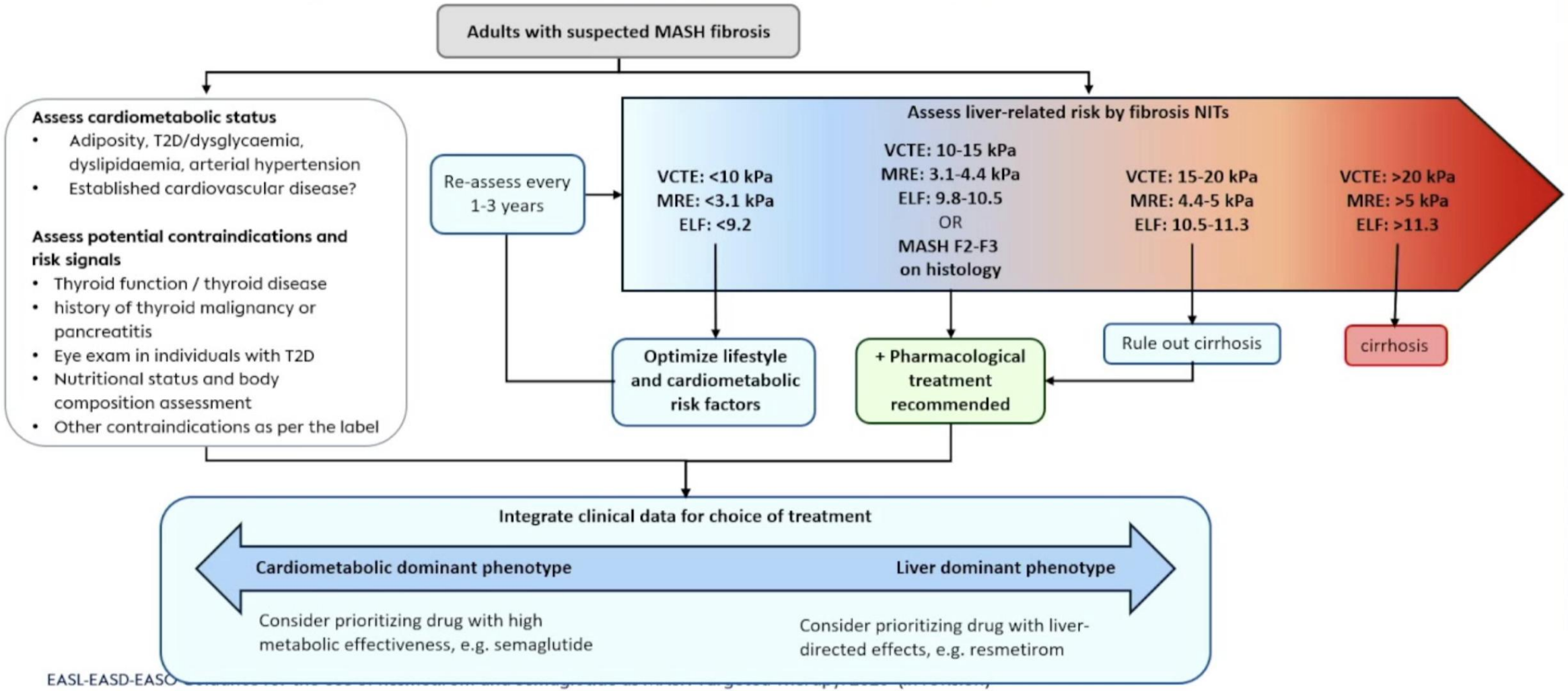
CHARITÉ UNIVERSITÄTSMEDIZIN BERLIN

EASL multisociety initiatives: PSVD, MASH Guidance

EASL Congress 2026, Barcelona, Spain, May 30, 2026

General strategy for MASH-targeted pharmacotherapy



EASL-EASD-EASO

CHARITÉ | Hepatology & Gastroenterology, Prof. Dr. Frank Tacke, email: frank.tacke@charite.de

Clinical scenarios favouring Resmetirom or Semaglutide for MASH-pharmacotherapy

Resmetirom

- Normal-weight or non-obese individuals
- Individuals already on a GLP-1 RA for another indication
- Prominent atherogenic dyslipidaemia (e.g. Lp(a)↑)
- Preference for oral administration
- Presence or high risk of sarcopenia

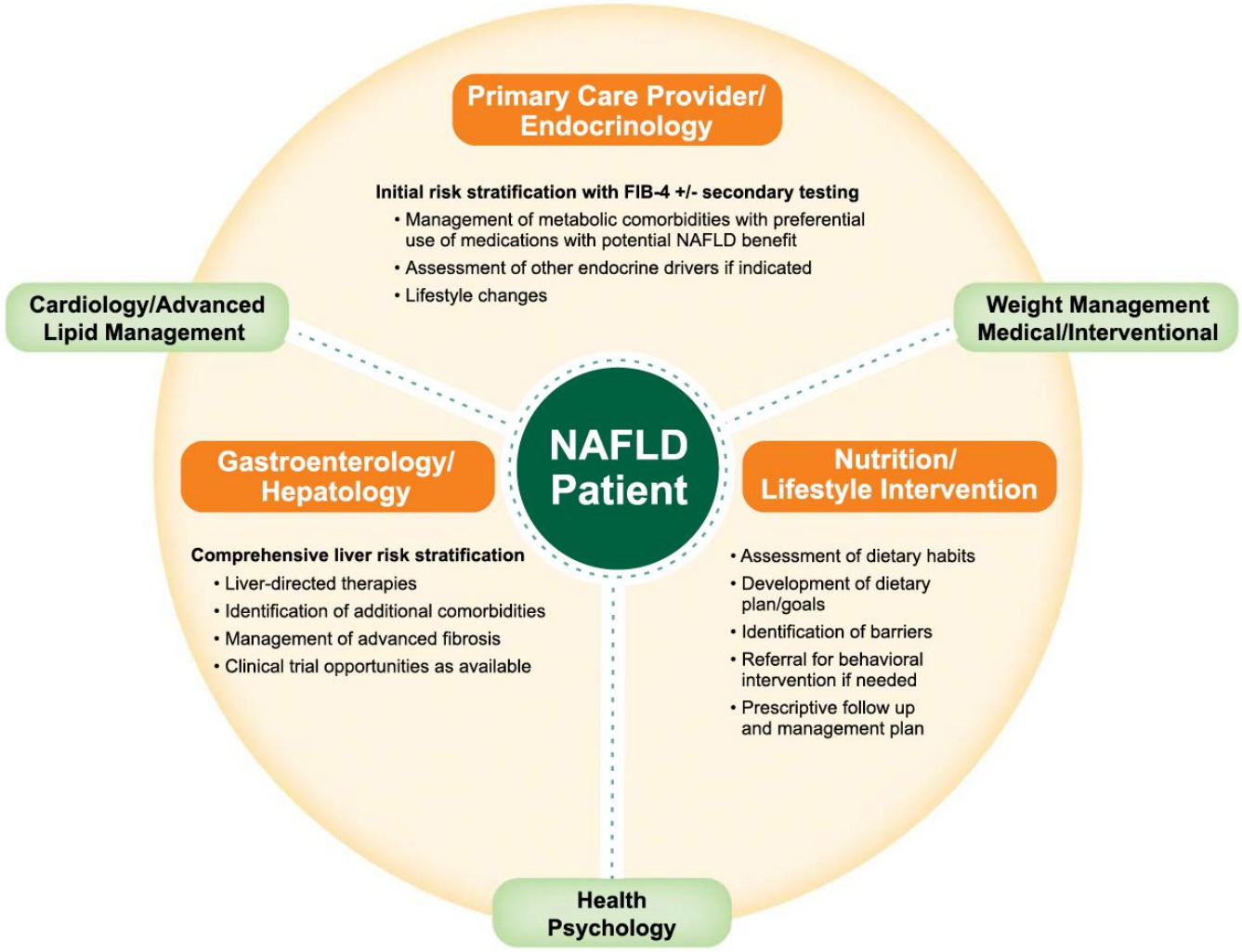
Semaglutide

- Obesity or overweight with weight-related comorbidities
- Insufficiently controlled type 2 diabetes
- Established cardiovascular disease or high CV risk
- Chronic kidney disease with overweight/obesity and/or T2D

EASL-EASD-EASO Guidance for the Use of Resmetirom and Semaglutide as MASH-Targeted Therapy. 2026 (*in revision*)

CHARITÉ | Hepatology & Gastroenterology, Prof. Dr. Frank Tacke, email: frank.tacke@charite.de

Conclusion



- ✓ **Multidisciplinary team!**
- ✓ **Patient navigators (specialized nurses)**
- ✓ **Identification of high-risk patients**
- ✓ **Risk stratification**
- ✓ **Specialized care to patients with significant fibrosis/cirrhosis**
- ✓ **Nutrition**
- ✓ **MASH-specific treatment**

Thank you