FibroScan in the Metabolic Clinic: Simple Pathways, Big Impact

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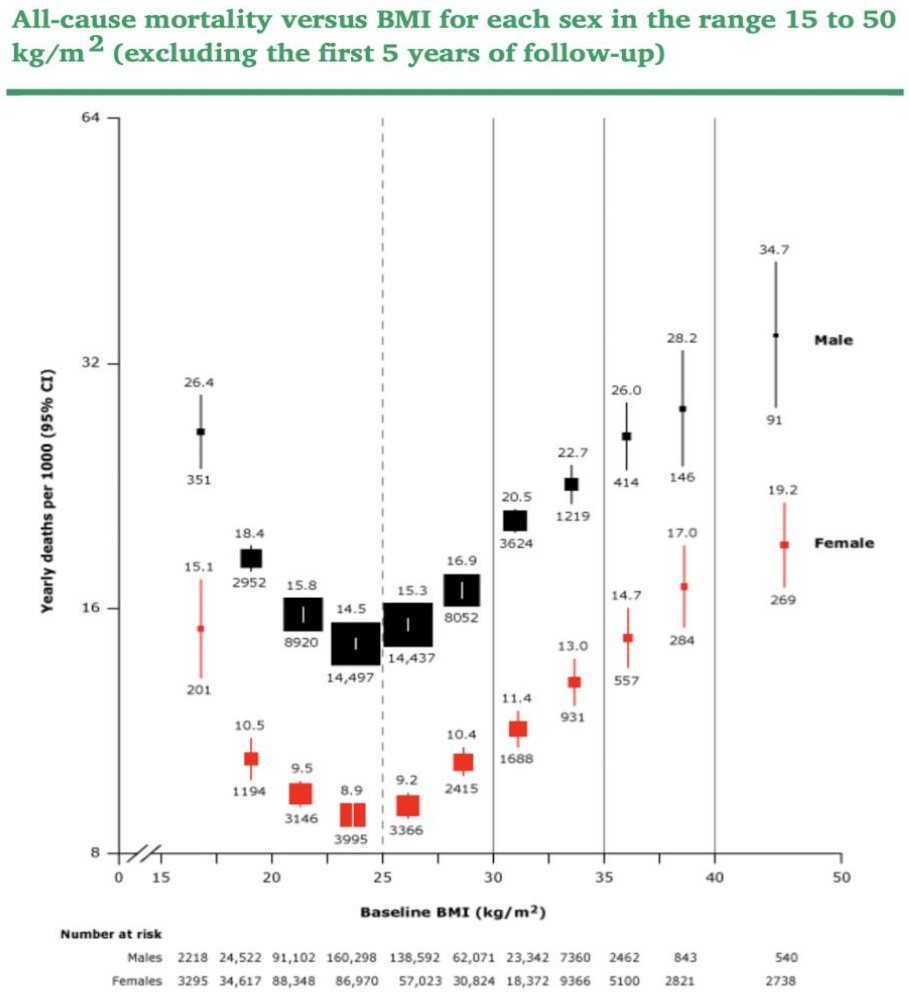
Obesity

- Obesity – known in medicine for over 2500 years
- Defined as BMI ≥ 30 kg/m^2
- Associated with increased mortality and morbidity
- Forecasts estimate that by 2050, 3.8 billion adults worldwide will be considered overweight or obese.



Lancet 2025; 405:813

Metabolic syndrome

- Metabolic syndrome: co-occurrence of metabolic risk factors for T2DM and cardiovascular disease
- Most widely accepted definition – by NCEP ATP III panel:
  - 3 of any of the following traits:

Abdominal obesity

Serum triglycerides ≥ 150 mg/dL or treatment for elevated TGs

HDL < 40 mg/dL in males and < 50 mg/dL in females

Blood pressure ≥ 130/85 mmHg or drug treatment for elevated blood pressure

Fasting plasma glucose ≥ 100 mg/dL or drug treatment for elevated BG

Paradigm shift!!!

No longer about being “obese”, overweight or have a certain BMI class

Chronic, life-long metabolic condition

Almost 40% of people have metabolic syndrome by the 6th decade of their lives

Likely under-reported!

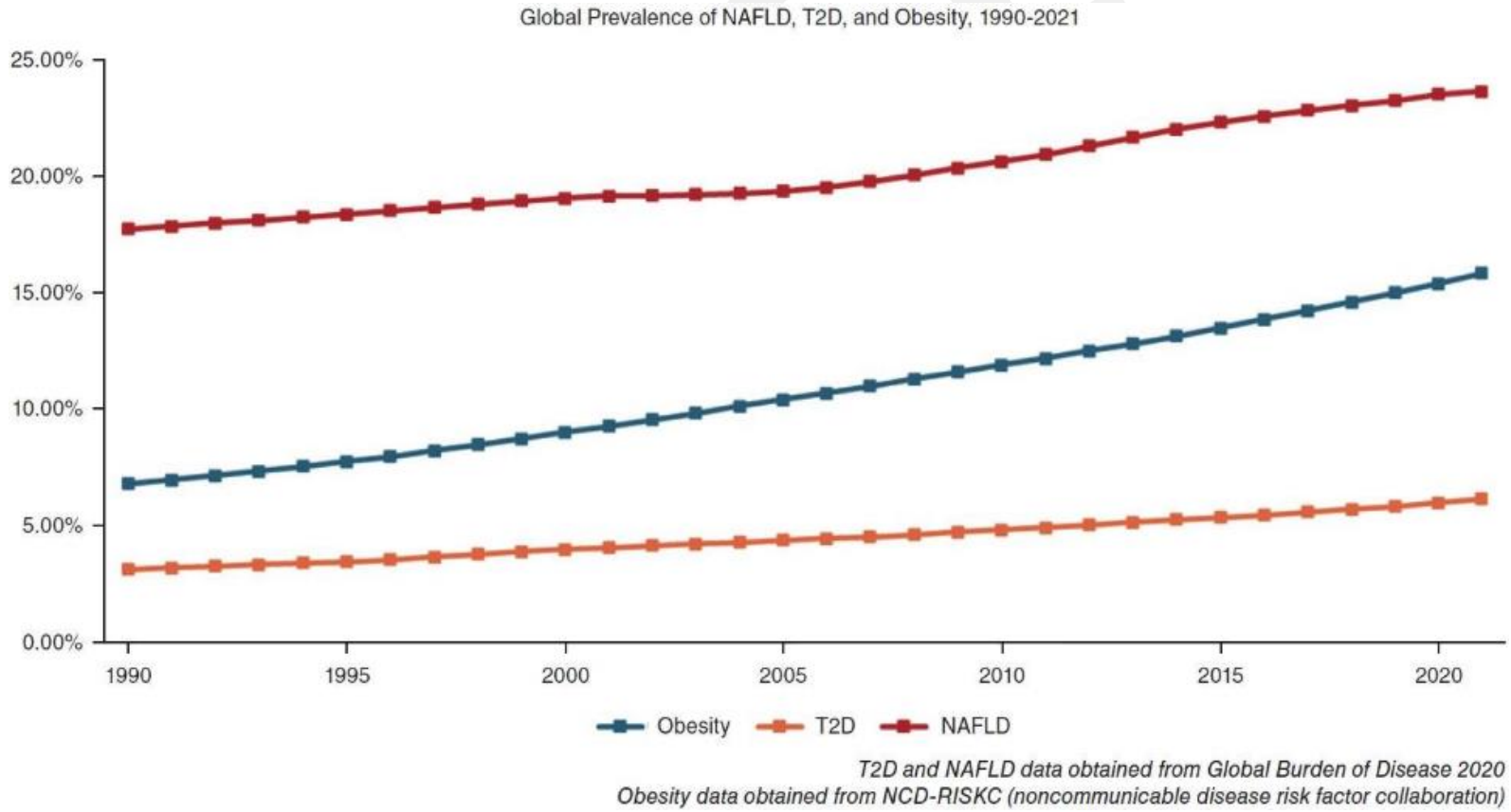
Arterioscler Thromb Vasc Biol. 2008 Apr;28(4):629-36

Question.. Who is our target patient population?

EVERYONE!

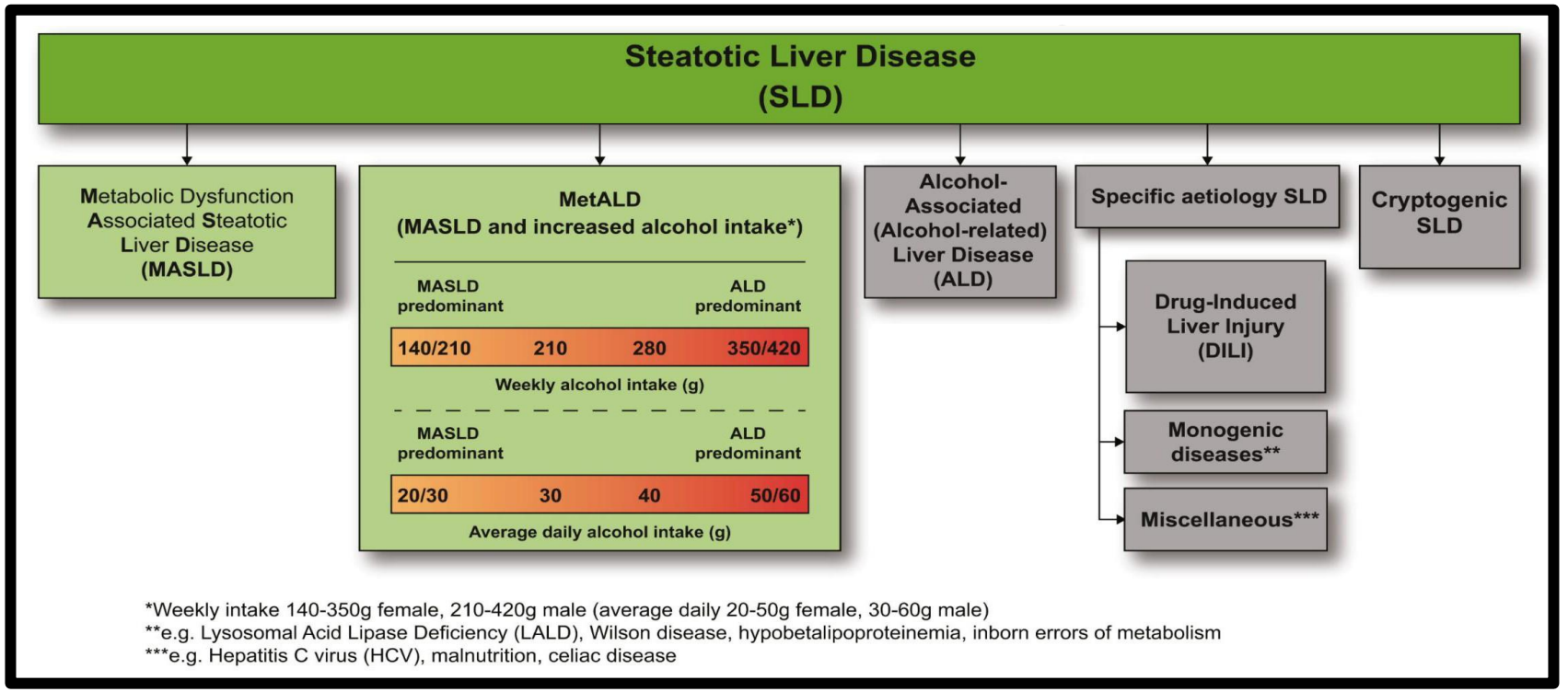
Who is our target patient population?

- Everyone!!!
- Majority of the adult population has some degree of metabolic dysfunction



Metabolic dysfunction-associated steatotic liver disease (MASLD)

Hepatology 2023 1;78(6):1966-1986



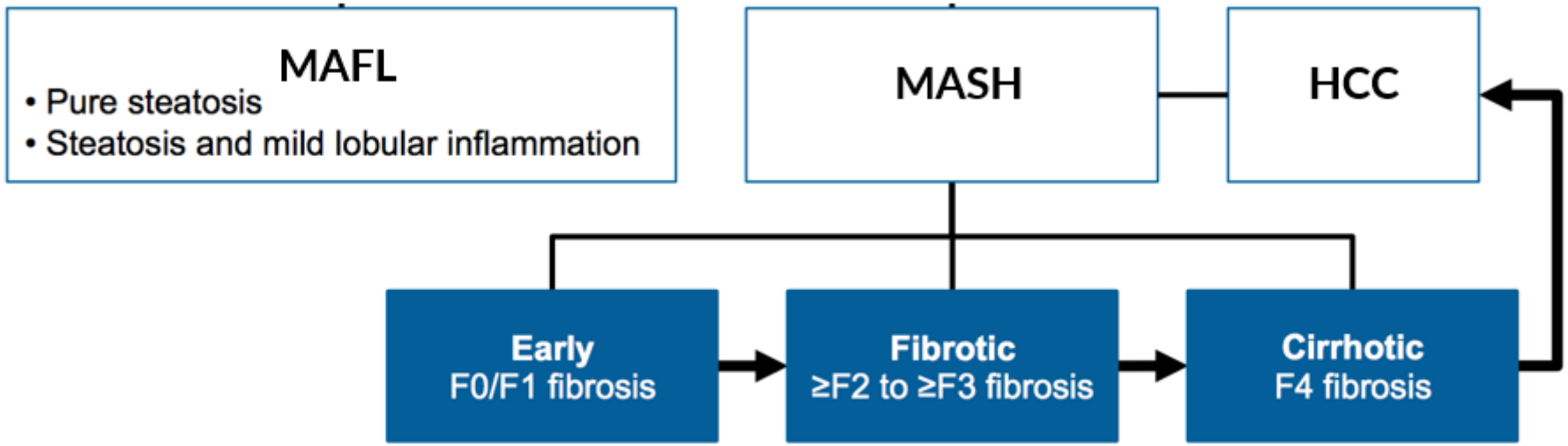
Steatotic Liver Disease diagnosed histologically or by imaging

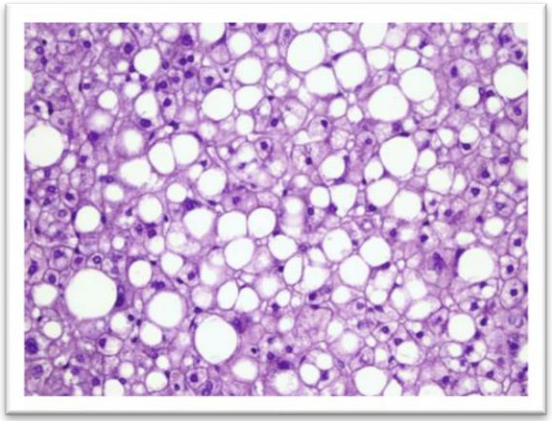
MASLD: Defined as presence of hepatic steatosis in conjunction with one CMRF and no other discernible cause

MetALD: There is a continuum across spectrum in which the contribution of MASLD and ALD will vary

Multiple aetiologies of steatosis can coexist: MASLD + autoimmune hepatitis or viral hepatitis

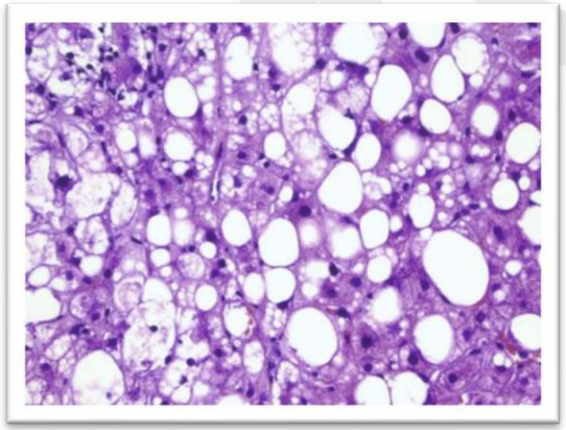
MASLD: Spectrum of Disease





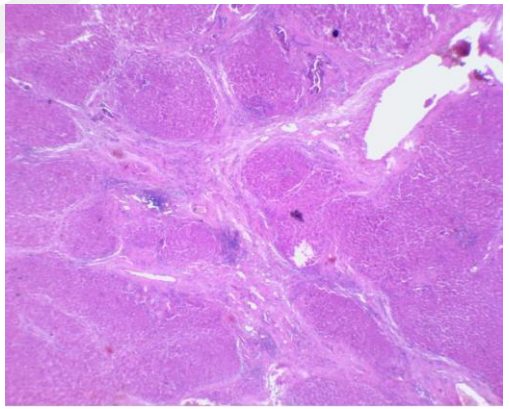
MAFL

Diffuse macro-vesicular steatosis >5% of hepatocytes



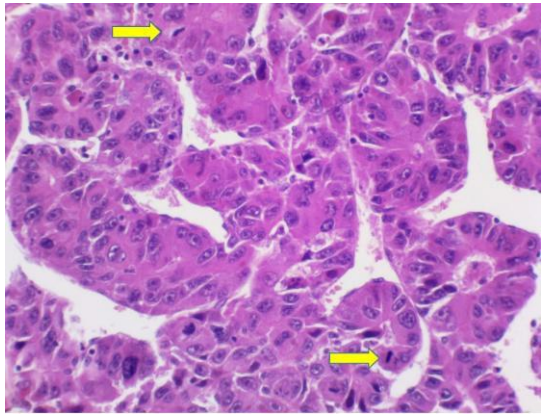
MASH

MAFL + lobular inflammation, hepatocyte ballooning, necrosis



Cirrhosis

Variably sized regenerative nodules surrounded by fibrous septa
Loss of steatosis



HCC

Thickened trabeculae of pleomorphic hepatocytes
Large irregular nuclei with conspicuous mitotic activity

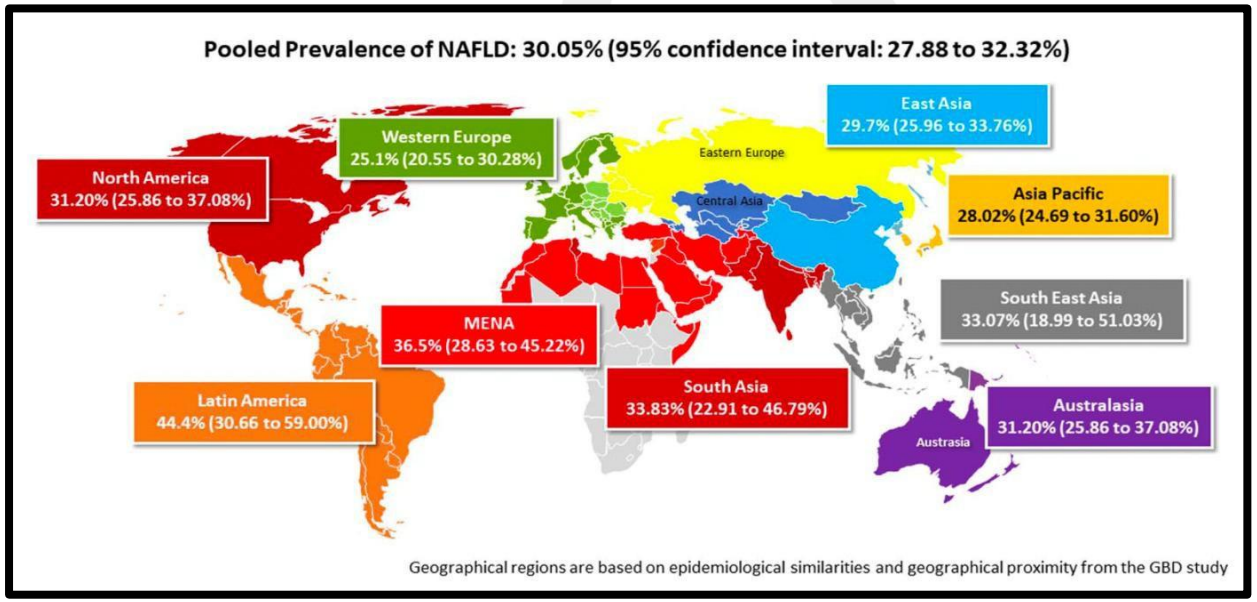
J Hepatol 2016; 64:1388

Global Epidemiology of MASLD

MASLD is the leading global cause of chronic liver disease

Estimated to **affect approximately 38.0% (33.71-42.49) of world's population: 1.66 billion (0.95–2.59)**

- Global NASH prevalence is 5.27% (SE: 2.63)
- Prevalence of **MASH among MASLD patients is 16.02% (3.24% - 52.08%)**
- Underestimate → Esp rising prevalence of obesity & type 2 diabetes

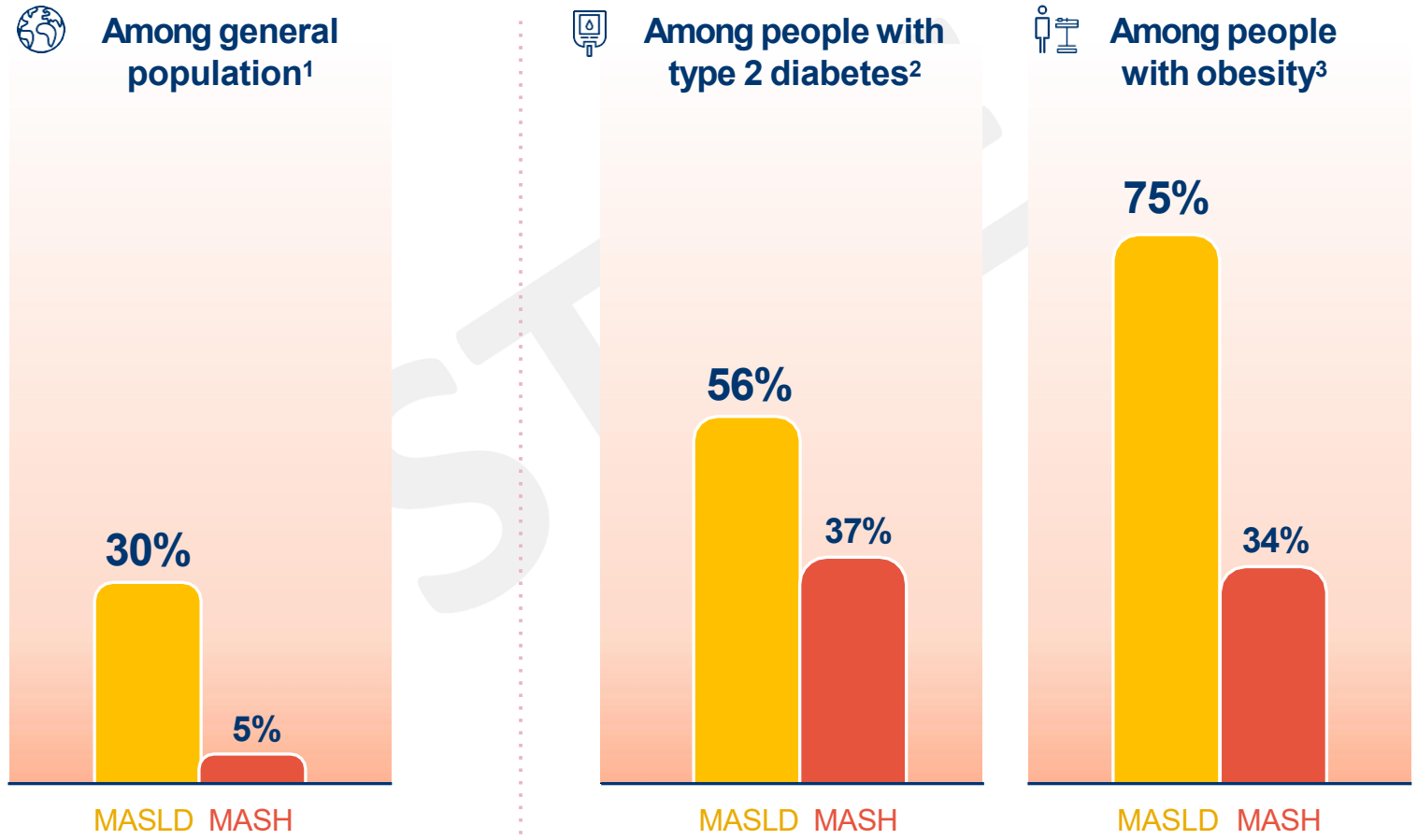


NAFLD Prevalence: 2019 GBD

- **Latin America: 44.4%**
- **MENA: 36.5%**
- **South Asia: 33.8%**
- **South-East Asia: 33.1%**
- **North America 31.2%**
- **East Asia: 29.7%**
- **Asia Pacific: 28.0%**
- **Western Europe: 25.1%**

Hepatology 2023;77:1335; Nat Rev Gastroenterol Hepatol 2018; 15: 11
Lancet Gastroenterol Hepatol 2022;7:851

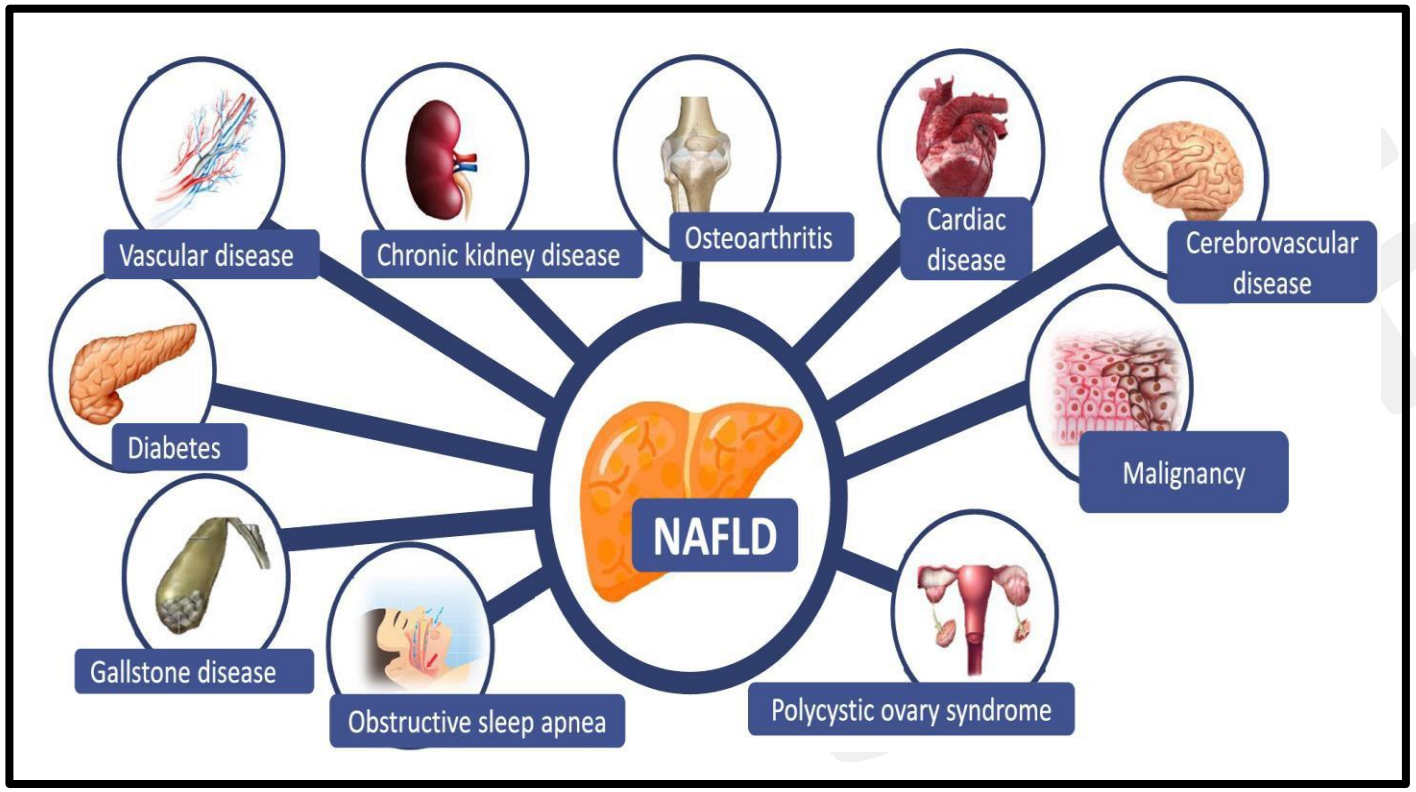
MASH is more prevalent in people with T2D and obesity than in general population



NAFLD, non-alcoholic fatty liver disease; NASH, non-alcoholic steatohepatitis.

1. Younossi ZM et al. Hepatology. 2023;10.1097/HEP.0000000000000004; 2. Younossi ZM et al. J Hepatol. 2019;71:793-801; 3. Quek J, et al. Lancet Gastroenterol Hepatol. 2023;8:20-30.

Extrahepatic Manifestations with MASLD



Pooled mortality rates per 1000 PY for MASLD

- **12.60: All-cause mortality**
- **4.20: Cardiac-specific mortality**
- 2.83: Extrahepatic cancer-specific mortality
- 0.92: Liver-specific mortality

- Although liver-related mortality is increased**, cardiovascular disease remains the leading cause of death** in patients with MASLD and liver fibrosis stages F3 or F4
- **HCC can occur in the absence of cirrhosis**

Lancet Gastroenterol Hepatol 2021; 6: 578; Hepatology 2023;77:1335

What is the solution?

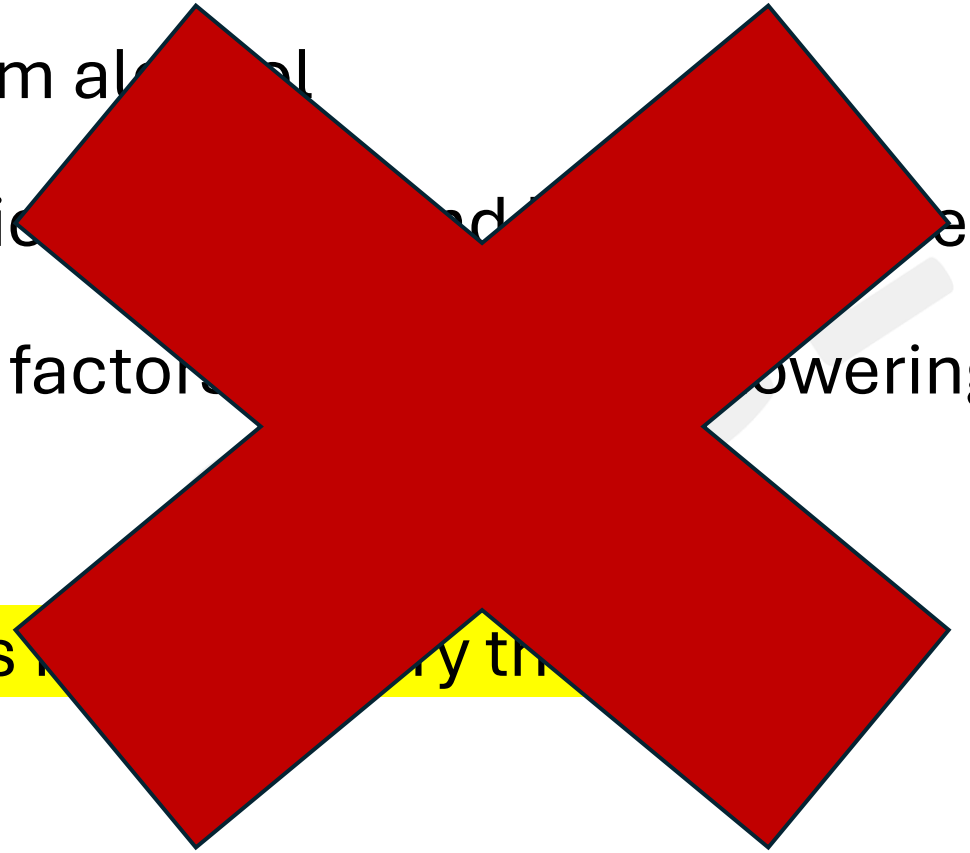
What options do we have?

General management

- ✓Abstain from alcohol
- ✓Immunizations – hep A and hep b vaccines
- ✓Modify risk factors for CVD – lipid-lowering therapy, blood glucose control
- ✓Weight loss is the primary therapy

General management

- ✓Abstain from al l
- ✓Immunizatio d es
- ✓Modify risk factor owering th control
- ✓Weight loss y th



We need to change the way we approach this..

Bariatric surgery – for who?

- NOT a last resort?
- Systemic reviews and meta-analyses of RCTs comparing bariatric surgery with nonsurgical treatment of obesity (diet, exercise, weight-reducing drug, behavior therapy) → bariatric surgery resulted in greater weight loss and higher remission rates of type 2 diabetes

Hormonal changes (ghrelin, GLP-1)

Change in intestinal glucose absorption and utilization

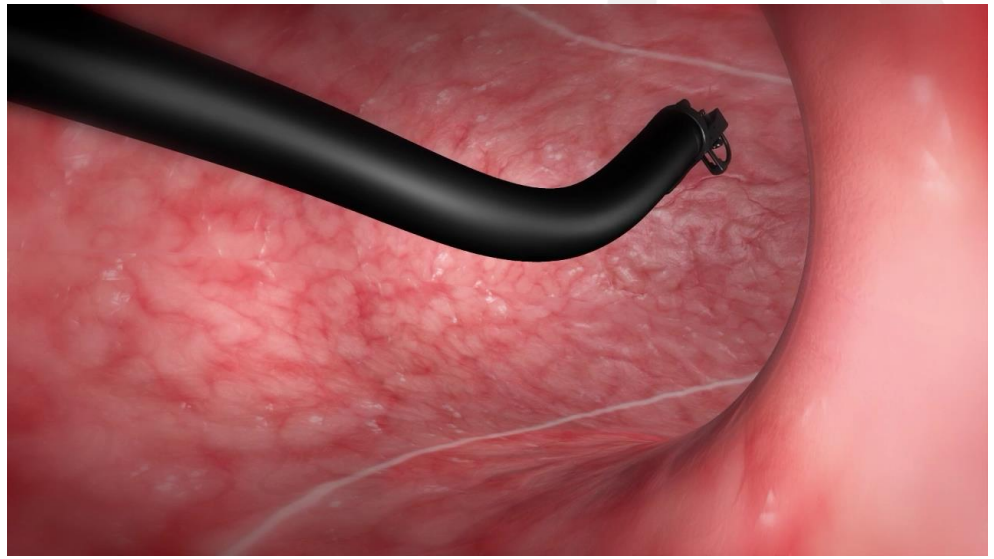
Improved immune function

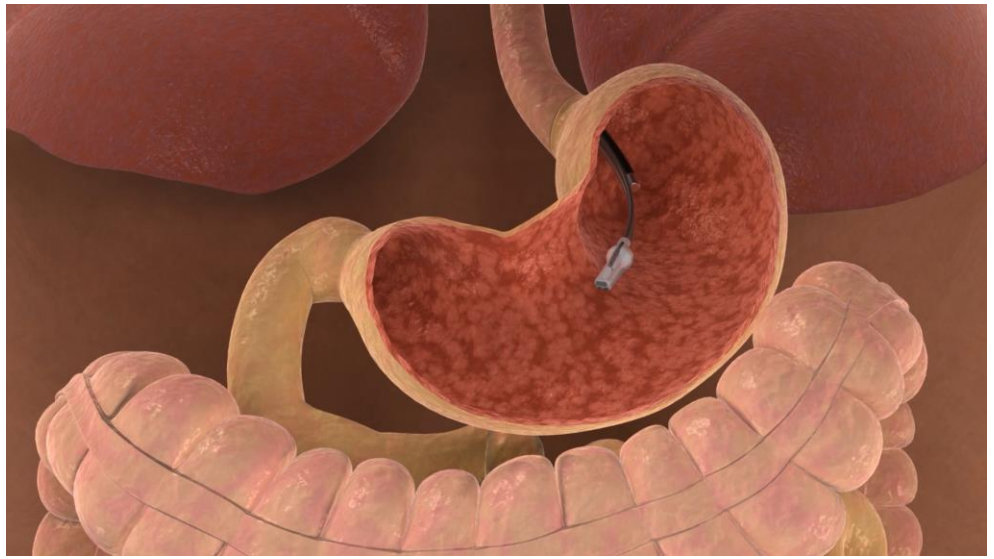
Change in bile acid pool

Positive change to the microbiome including inc. in Bacteroidetes and dec. in Firmicutes

Endoscopic gastric remodeling

- Includes endoscopic sleeve gastrectomy or endoscopic gastric plication
- According to several systematic reviews and meta-analyses, the pooled total weight loss at 12 months was 10.5 percent in randomized trials and 17.3 percent in observational studies.





Surgical management

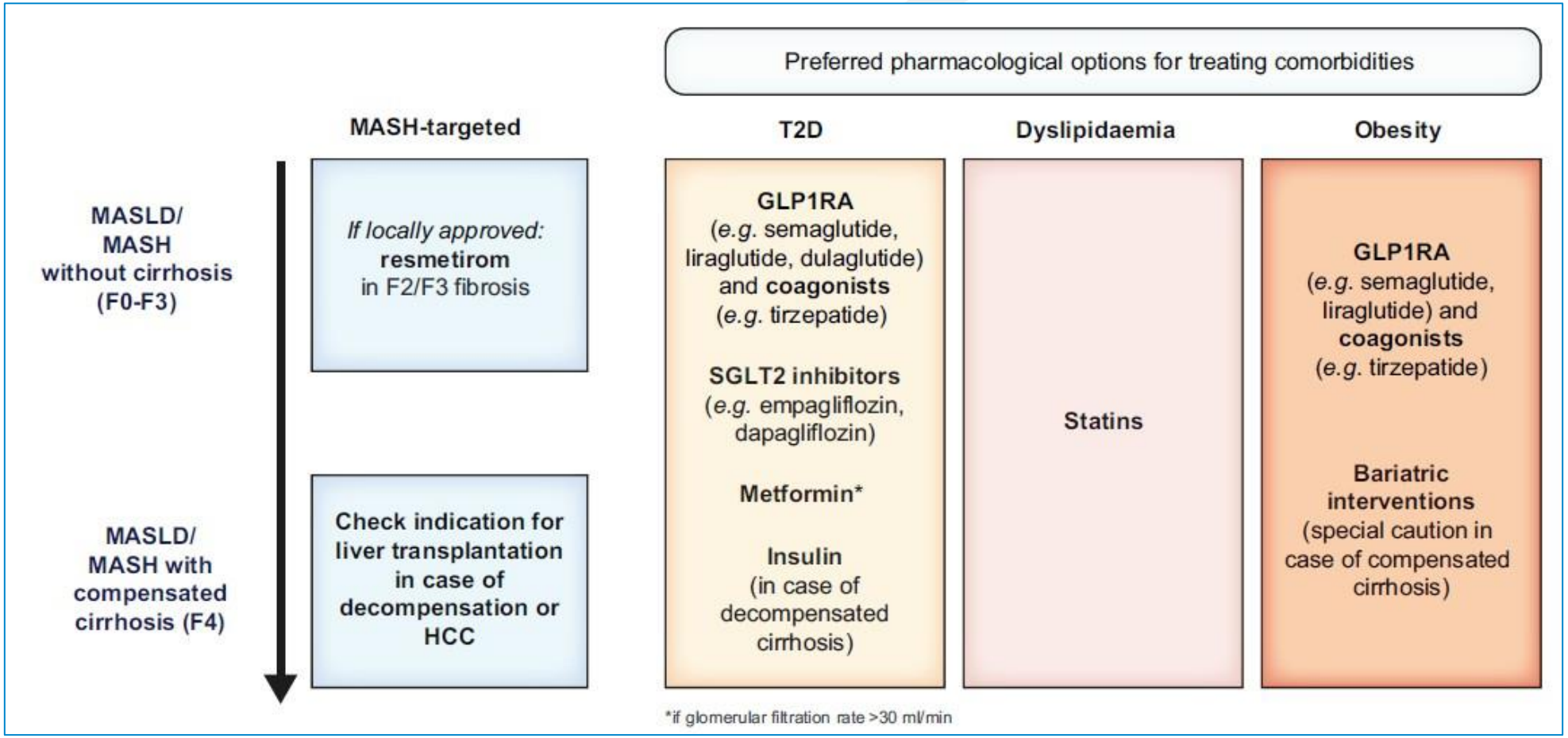
- Sleeve gastrectomy → at two years, expected weight loss is 25-30% of a patient's total body weight.
- Roux-en-Y gastric bypass → at two years, expected weight loss is 30-35%

Again, we are looking to work on the metabolic dysfunction → weight loss follows

Ann Surg. 2011;254(3):410.
Surg Endosc. 2006;20(6):859.
Br J Surg. 2014 May;101(6):661-8.

MASH Treatment options

As per the EASL-EASD-EASO Guidelines 2024



Pharmacological therapy

- NO longer just “weight loss” drugs as previously believed..

FDA Approves Treatment for Serious Liver Disease Known as ‘MASH’

Action Will Provide New Therapy for Growing Public Health Issue

Action

The U.S. Food and Drug Administration has approved Wegovy (semaglutide) injection to treat metabolic-associated steatohepatitis (MASH) in adults with moderate-to-advanced fibrosis (excessive scar tissue in the liver). MASH, also known as nonalcoholic steatohepatitis, is a serious liver disease. Wegovy, which was first approved in 2017, is also approved for obesity or overweight and to reduce cardiovascular events, such as heart attacks, in individuals at high risk of these events. Approximately 6% of U.S. adults (14.9 million people) have MASH, and its prevalence is expanding.

Pharmacological therapy

Table 2 Anti-diabetic medications in MASLD and MASH

Medication	Liver enzymes	Hepatic steatosis	Liver stiffness	MASH	Fibrosis progression	Fibrosis regression
Tirzepatide[71 72]	Beneficial	Beneficial	Beneficial	Beneficial	Possible benefit	Possible benefit
GLP-1 RA[62–66 68 69]	Beneficial	Beneficial	Beneficial	Beneficial	Possible benefit*	Possible benefit*
Pioglitazone[44 46–51]	Beneficial	Beneficial	Beneficial	Beneficial	Possible benefit	Neutral
SGLT2 inhibitors[92–101]	Beneficial	Beneficial	Beneficial	Unknown	Unknown	Unknown
Insulin[102–104]	Beneficial	Beneficial	Unknown	Unknown	Unknown	Unknown
Metformin[105–107]	Beneficial	Neutral	Neutral	Neutral	Neutral	Neutral
DPP-4 Inhibitors[105–107]	Neutral	Unknown	Unknown	Unknown	Unknown	Unknown
Sulfonylureas[13]	Neutral	Unknown	Unknown	Unknown	Unknown	Unknown

*Histological evidence for semaglutide.[68]

GLP-1 RA, glucagon-like peptide-1 receptor agonists; MASH, metabolic dysfunction-associated steatohepatitis; MASLD, metabolic dysfunction-associated steatotic liver disease; SGLT2, sodium-glucose transporter 2.

*Isaacs SD, Farrelly FV, Brennan PN. Role of anti-diabetic medications in the management of MASLD. Frontline Gastroenterology 2025;**16:**239-249.*

GLP-1 based and other drug therapies

- In patients with significant fibrosis (stage ≥ 2) + failed lifestyle modifications
- GLP-1 based therapy – Semaglutide (Ozempic, Wegovy)
  - Improves liver histology in patients with MASH with stage 2 or 3 fibrosis
  - Interim analysis of a phase 3 trial of 800 patients with biopsy-proven MASH (stage 2/3 fibrosis), semaglutide 2.4 mg weekly for 72 weeks improved liver fibrosis without worsening of steatohepatitis compared with placebo (in 36.8 versus 22.4 percent of patients, 95% CI 8-21)

N Engl J Med 2025; 392:2089.

GLP-1 based and other drug therapies

- GLP-1 based therapy – Tirzepatide (Mounjaro)
  - Improves liver histology in patients with MASH with stage 2 or 3 fibrosis
  - Phase 2 trial (n = 190 patients) with biopsy-proven MASH (stage 2 or 3 fibrosis), tirzepatide (5 mg, 10 mg, or 15 mg) weekly for 52 weeks resulted in resolution of MASH without worsening of fibrosis in 44 to 62 percent of patients (depending on the dose), compared with 10 of patients in the placebo

N Engl J Med 2024; 391:299.

Again.. Question.. Who is our target patient population?

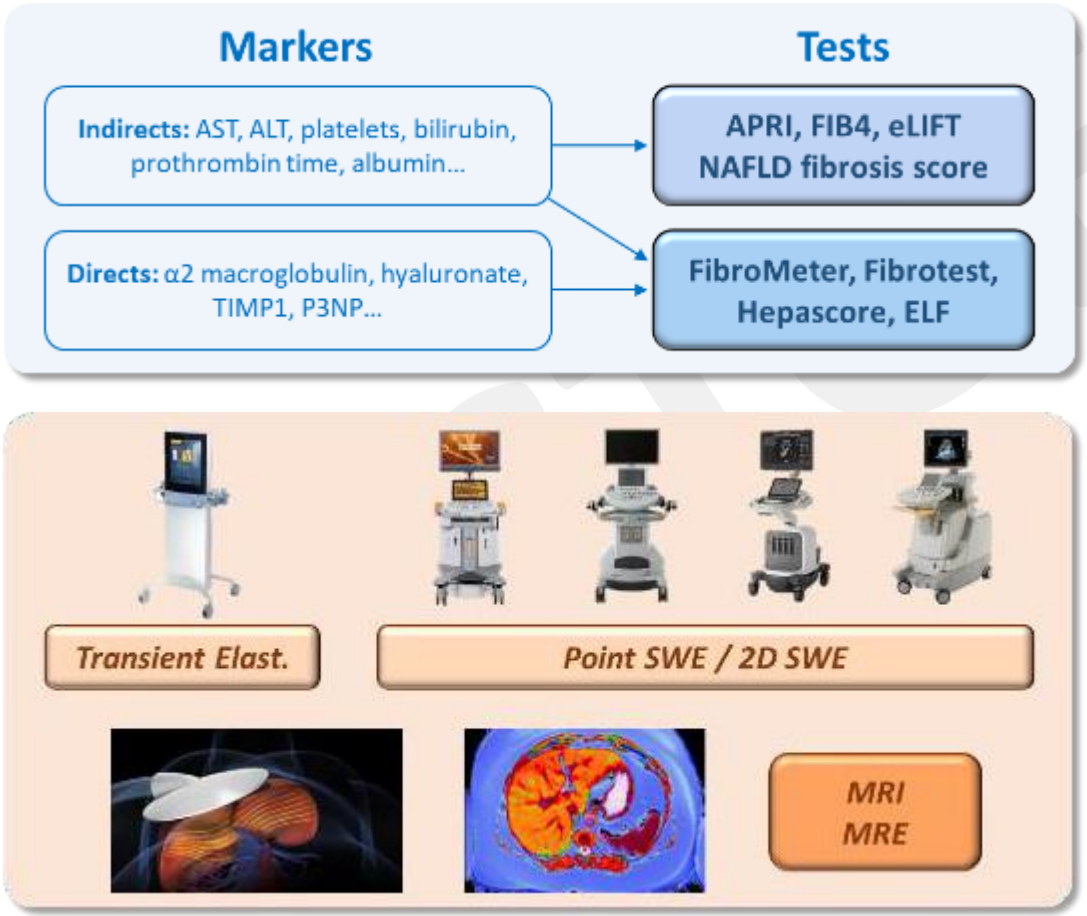
EVERYONE!

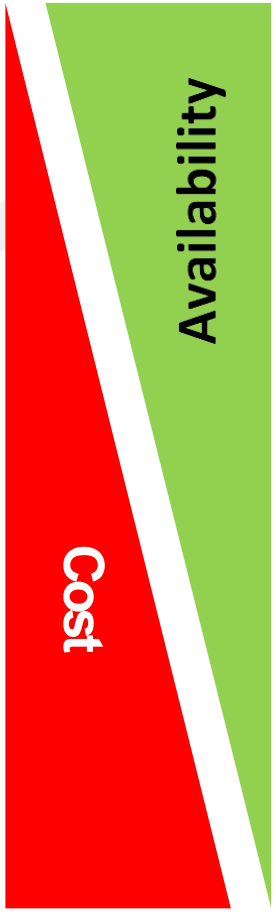
We need to find a way to stratify patients.. Who is high risk? Who is improving on management?

Role of non-invasive tests in management

BLOOD

IMAGING





Primary care centre

Secondary care centre

A solution?

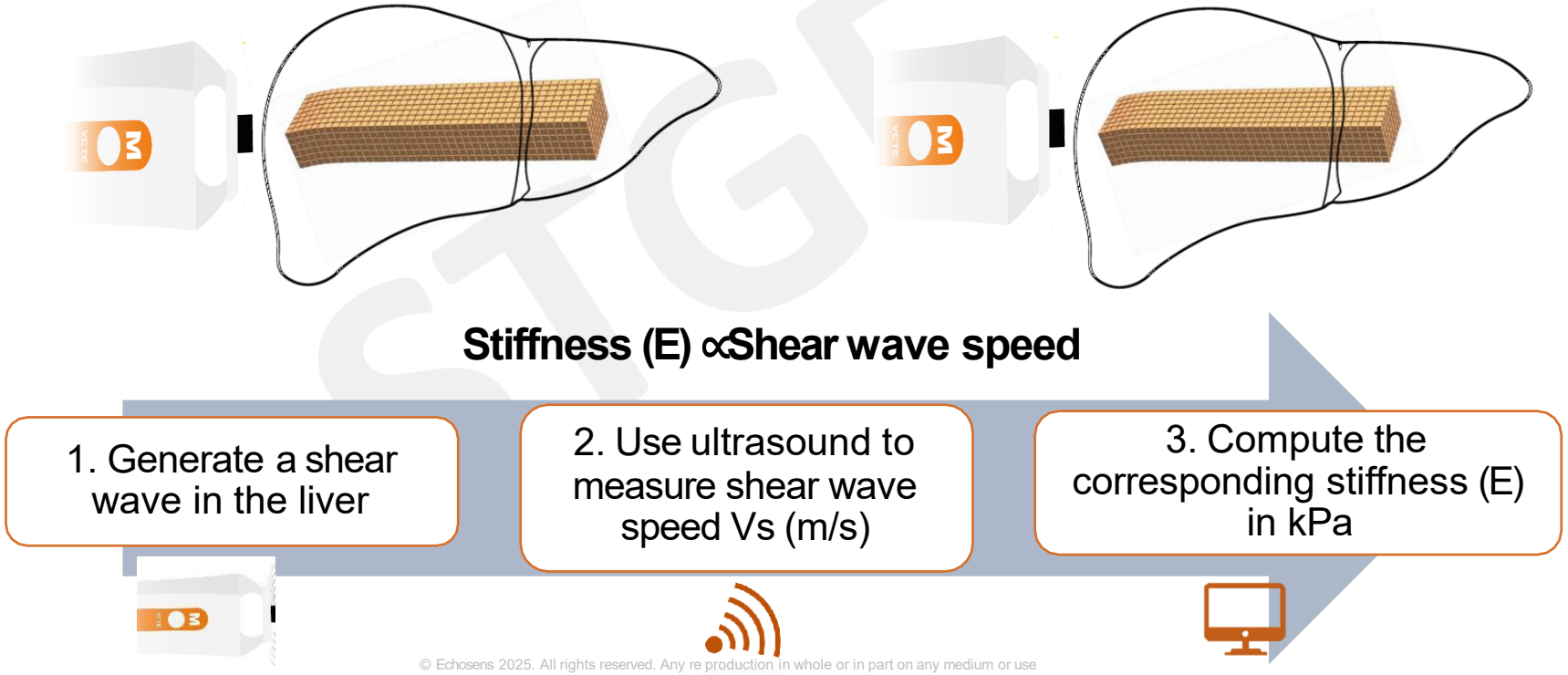
FibroScan® by echosens

A solution?

FAT SCAN®
by echoens

How to measure Stiffness ?

- In soft tissues, stiffness is related to the velocity of elastic waves called **shear waves**.
- The faster the shear waves, the stiffer the medium



FibroScan® by echosens

3 quantitative biomarkers available on FibroScan

Liver Stiffness *by VCTE™*

4.2 kPa

Marker of liver fibrosis[1]
Measurement of **liver stiffness (LSM)** (in kPa) at 50Hz shear wave frequency. Relevant for management of all types of chronic liver diseases.

Liver CAP™

224 dB/m

Marker of liver steatosis[2]
Measurement of **ultrasound attenuation** (in dB/m). Relevant for metabolic and alcoholic related liver diseases (*MASLD, MetALD, ALD*…)

Spleen Stiffness* *by VCTE™*

18.6 kPa

Marker of portal hypertension[3]
Measurement of **spleen stiffness** (in kPa) at 100Hz shear wave frequency. Used for risk stratification and non-invasive assessment **of portal hypertension**

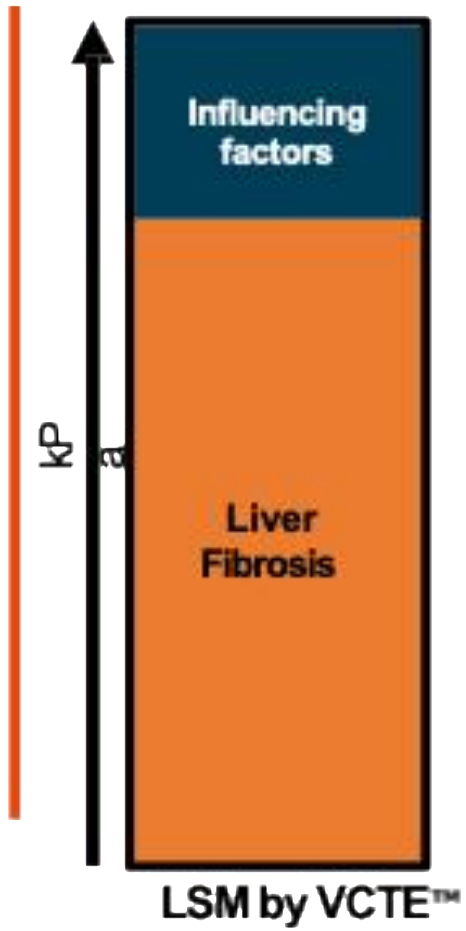
1 - Friedrich Rust et al., *Gastroenterology* 2008,
2 - Sasso et al. *Journal of Viral Hepatitis* 2011
3- Stefanescu et al. *Liver International 2019*

* Only available on FibroScan 630 Expert Model

FibroScan by echosens

Liver stiffness influencing factors

Any single FibroScan Liver Stiffness Measurement results from the sum of factors and not only fibrosis



Know liver enzymes (ALT, AST levels)

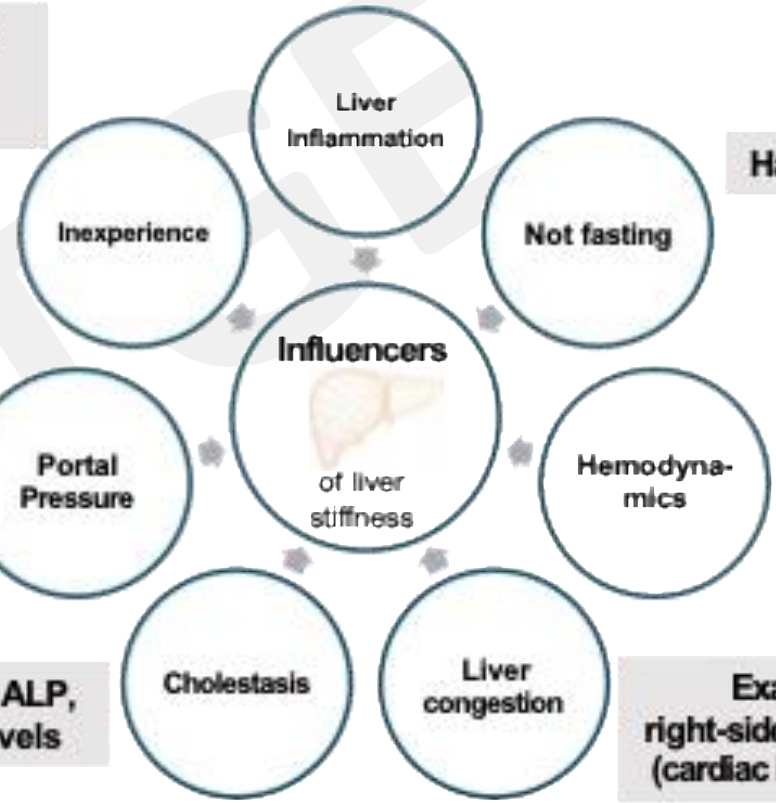
Proficient & trained operators (≥50 exams)

Have patients fast for ≥3 hours

5 minutes resting time prior to examination

Examine for right-sided heart failure (cardiac insufficiency)

Know GGT, ALP, bilirubin levels



Adapted from:
2015-Tapper-24909907; EASL CPG Guidelines 2015; 2009–Mueller-24367208

echosens

Diagnostic performance of LSM and CAP in clinical studies in patients with MASH: Landmark studies

LSM kPa

Fibrosis stage	Ref.	Prevalence	AUROC	Cut-off* (kPa)	Se/Sp	NPV/PPV
F0–F1 vs. F2–F4	1	0.51	0.79	8.6	0.66/0.80	0.70/0.78
	2	0.60	0.77	8.2	0.71/0.70	0.61/0.78
F0–F2 vs. F3–F4	1	0.32	0.83	8.6	0.80/0.74	0.89/0.59
	2	0.38	0.80	9.7	0.71/0.75	0.81/0.63
F0–F3 vs. F4	1	0.09	0.93	13.1	0.89/0.86	0.99/0.39
	2	0.09	0.89	13.6	0.85/0.79	0.98/0.29

- Performances of LSM are consistent between the two studies
- LSM by VCTE is very good at ruling our cirrhosis (high NPV)

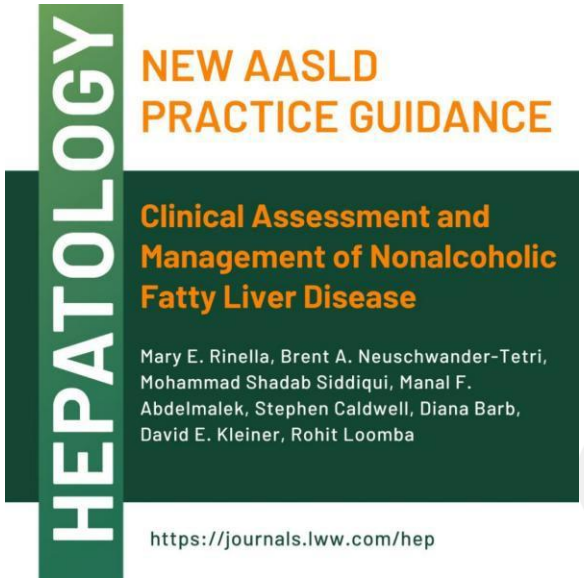
CAP dB/m

	AUROC (95%CI)	Cutoff (dB/m)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Primary analysis: MRI-PDFF ≥ 5%						
CAP (dB/m)						
Optimal threshold	**0.80 (0.70–0.90)**	**288**	**75.0**	**77.1**	**88.7**	**56.2**
Threshold for 100% sensitivity		128	100	0	70.6	0
Threshold for 100% specificity		369	8.3	100	100	31.2
Secondary analysis: MRI-PDFF ≥ 10%						
CAP (dB/m)						
Optimal threshold	**0.87 (0.80–0.94)**	**306**	**78.6**	**82.5**	**80.0**	**81.2**
Threshold for 100% sensitivity		250	100	38.1	58.9	100
Threshold for 100% specificity		369	12.5	100	100	56.2

- CAP is good at ruling in the presence of steatosis using PDFF as reference tool.

1. Siddiqui, Mohammad S. et al. Clinical Gastroenterology and Hepatology, Volume 17, Issue 1, 156 - 163.e2
2. Caussy C, Alquiraish MH, Nguyen P, Hernandez C, Cepin S, Fortney LE, Ajmera V, Bettencourt R, Collier S, Hooker J, Sy E, Rizo E, Richards L, Sirlin CB, Loomba R. Optimal threshold of controlled attenuation parameter with MRI-PDFF as the gold standard for the detection of hepatic steatosis. Hepatology. 2018 Apr;67(4):1348-1359.

AASLD Recognizes CAP as a Solution to Identify Hepatic Steatosis at Point-of-Care



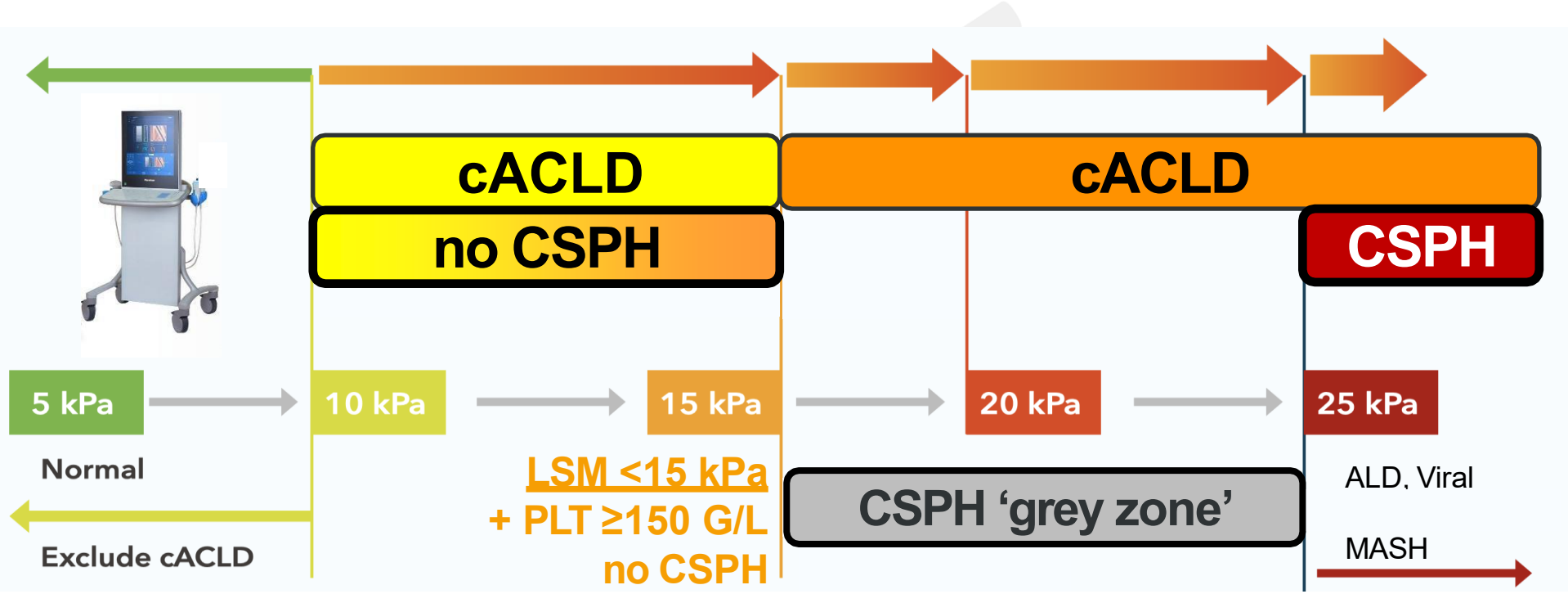
Liver CAP™

CAP [dB/m] – Correlated Marker of Hepatic Steatosis[1] Range [100-400 dB/m]	
Presence of steatosis	≥288 dB/m

Steatosis Assessment Guidance

- Conventional B-mode ultrasound imaging is not recommended to identify hepatic steatosis due to low sensitivity.
- CAP may be used to identify & semi-quantify hepatic steatosis at the point of care
- MRI-PDFF may be used to identify & quantify hepatic steatosis but is constrained by patient access and cost.

The Baveno VII Consensus Guidelines – How to stratify patients



De Franchis – Baveno VII Guidelines (J Hepatol 2022)

Role of FibroScan guiding management

- **Resmetirom** – for stage 2 or 3 fibrosis
  - Thyroid hormone receptor-beta agonist
  - Data suggests resmetirom improved MASH and stage of liver fibrosis

N Engl J Med. 2024;390(6):497.

Patient selection

Updated recommendations based on the 52 Weeks follow up data from the ongoing Maestro-NASH Trial

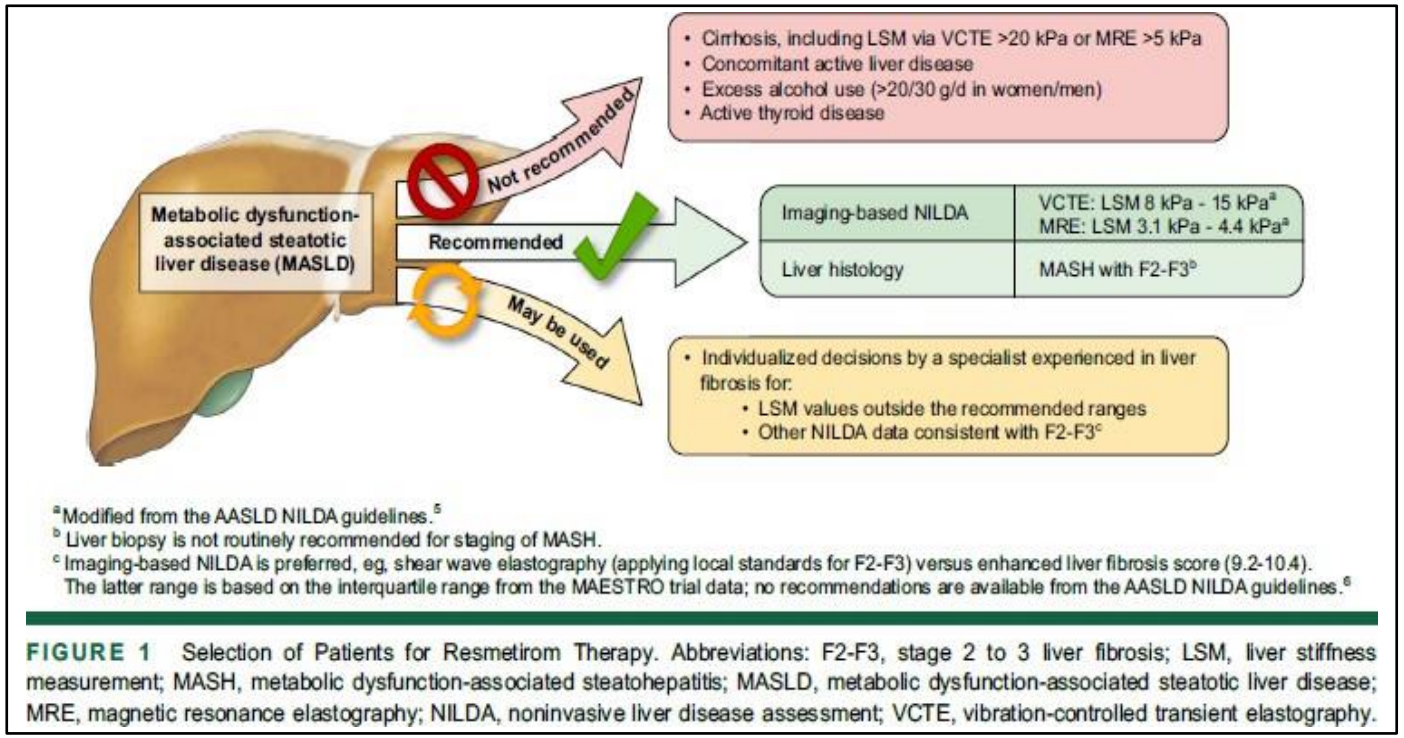
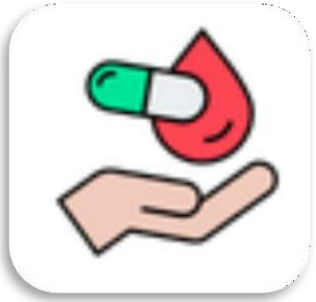


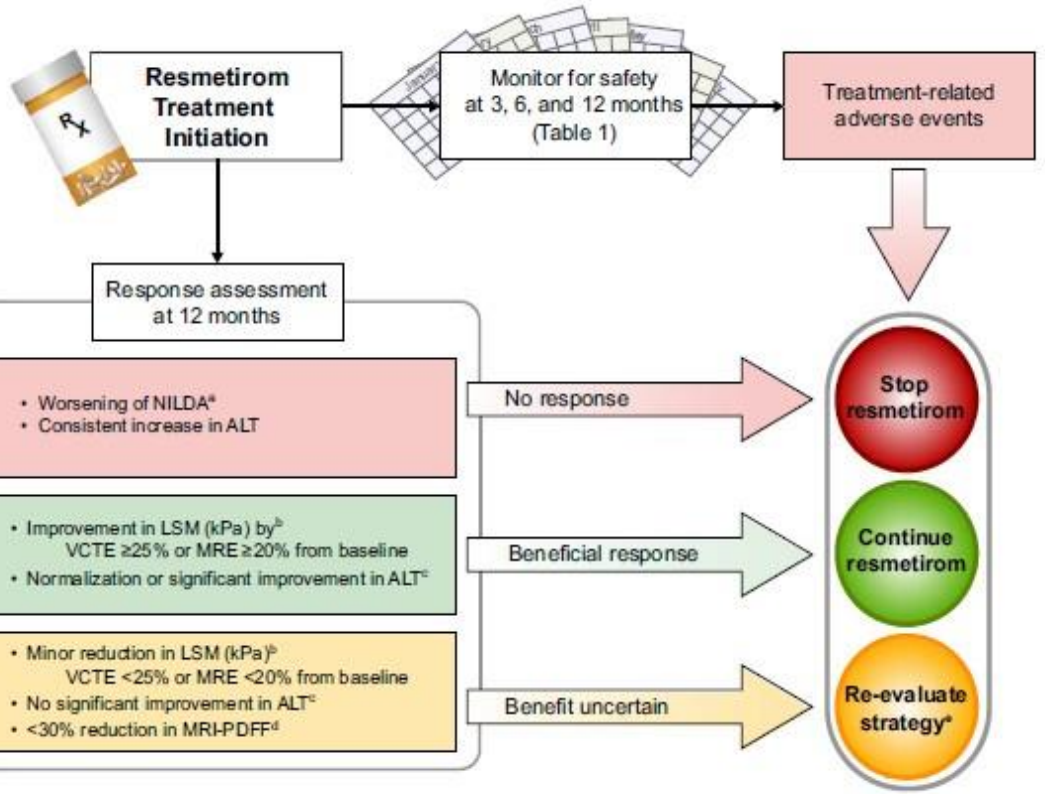
FIGURE 1 Selection of Patients for Resmetirom Therapy. Abbreviations: F2-F3, stage 2 to 3 liver fibrosis; LSM, liver stiffness measurement; MASH, metabolic dysfunction-associated steatohepatitis; MASLD, metabolic dysfunction-associated steatotic liver disease; MRE, magnetic resonance elastography; NILDA, noninvasive liver disease assessment; VCTE, vibration-controlled transient elastography.



Key Takeways:

- **LSM by VCTE™ and MRE are the preferred Non Invasive Test** mentioned in the guidelines for selecting patients candidates for Resmetirom treatment, **with specific cut-offs for both modalities**
- Other tests (*ELF, 2D-SWE*) are only mentioned as second line tests when VCTE ™ or MRE are outside recommended ranges

Assesment of treatment response



[a] Assess based on the same imaging-based or blood-based markers used to determine treatment eligibility.
[b] LSM improvement thresholds of VCTE ≥25% or MRE ≥20% are based on assay characteristics and not specifically validated for clinical decisions in resmetirom treatment patients. There are currently no comparable data to determine response in blood-based NILDAs.
[c] Applies to patients with elevated ALT at baseline. No specific ALT response cutoffs are available from the MAESTRO trial.
[d] MRI-PDFF reduction by >30% does not necessarily correlate with histologic response.
[e] Options may include re-optimizing lifestyle interventions and considering other therapy, with or without stopping resmetirom.

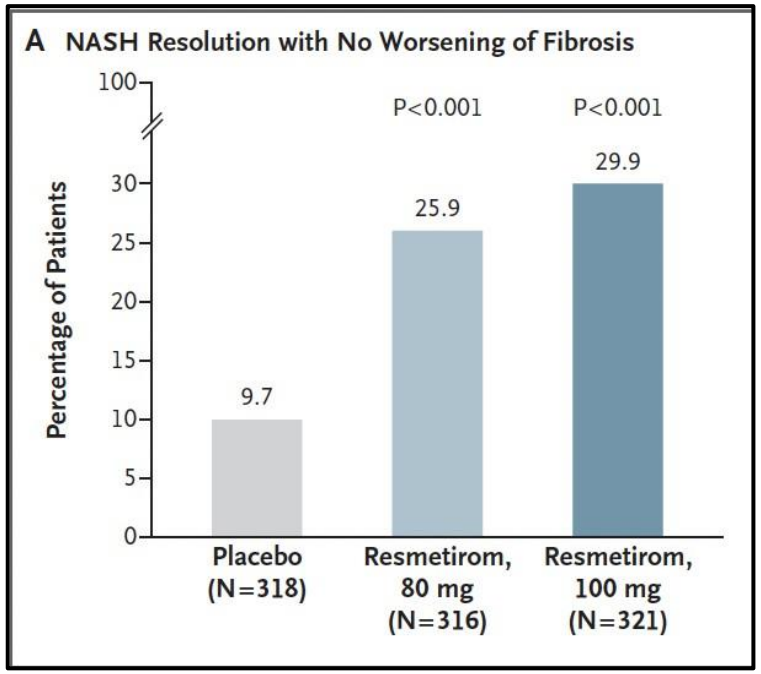
FIGURE 2 Assessment for Treatment Outcome in Patients Receiving Resmetirom. Abbreviations: ALT, alanine aminotransferase; LSM, liver stiffness measure; MRE, magnetic resonance elastography; MRI-PDFF, magnetic resonance imaging proton density fat fraction; NILDA, noninvasive liver disease assessment; VCTE, vibration-controlled transient elastography.

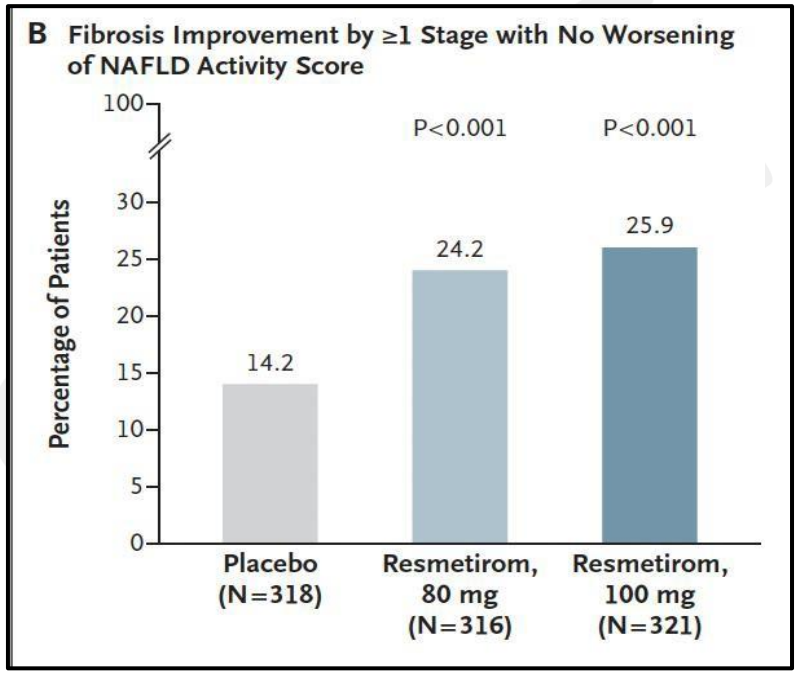
KEY TAKEWAYS

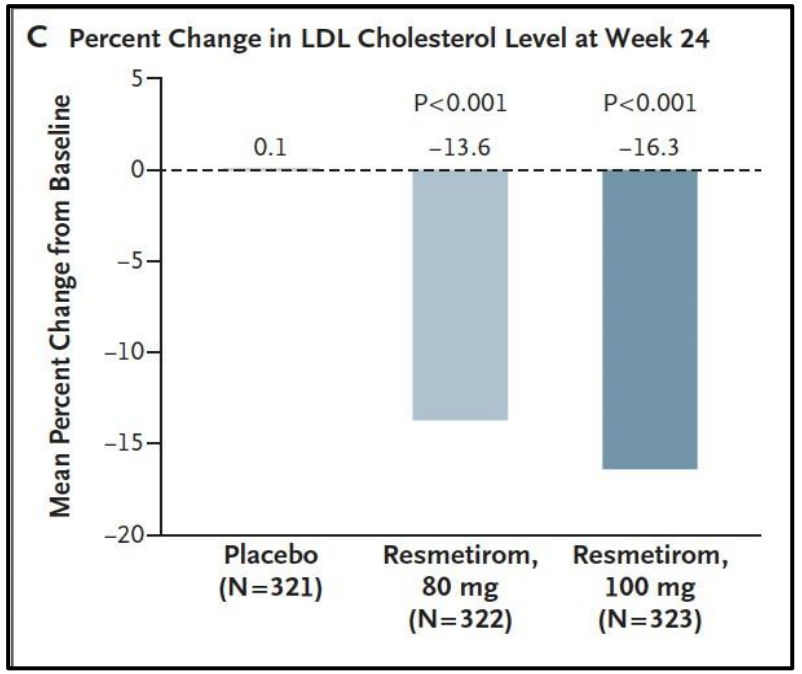
- Treatment response shall be assessed **at 12 months**
- **LSM by VCTE™** and MRE are the only imaging tests recommended for monitoring treatment response
- Improvement of **LSM by VCTE™≥25%** van be used to characterize beneficial response*

Resmetirom: Phase 3 RCT: Biopsy proven NASH with Liver Fibrosis

966 patients: 52 weeks: 80-mg Resmetirom: 322, 100-mg Resmetirom: 323 and placebo



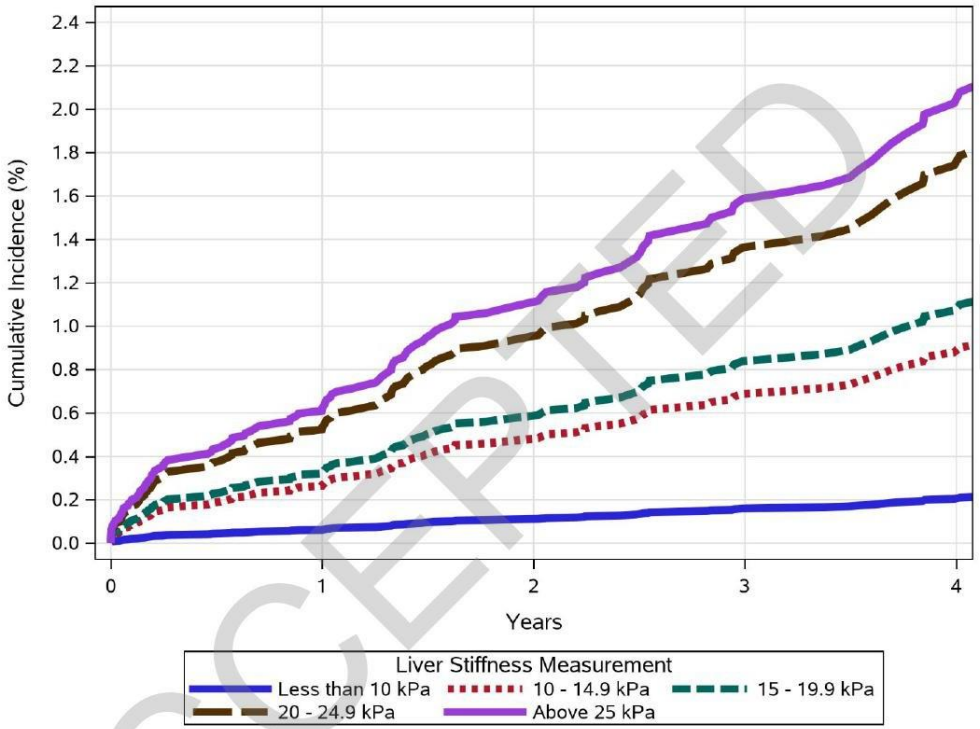




- Diarrhoea and nausea more frequent with resmetirom than with placebo
- **18/3/2024: FDA granted accelerated approval for Rezdiffra (resmetirom)** in conjunction with **diet and exercise** for treatment of adults with noncirrhotic NASH with moderate to advanced liver fibrosis (F2 to F3)

Role of FibroScan in HCC surveillance

Cohort of US Veterans with MASLD – 30414 participants (VALID Study)



Cumulative incidence Rate of HCC in patients with MASLD by categories of liver stiffness measurement

John et al. Hepatology 2025

- Guidelines recommend HCC Surveillance in MASLD for patients with HCC-Risk of 1-1.15 per persons/years
- HCC risk increased by 18% with every 5 kPa increase in LSM
- Non-cirrhotic MASLD patients **with diabetes and LSM ≥10 kPa** had annual HCC rates of 0.46 per 100 person-years, and can be considered for HCC Surveillance
- LSM therefore may serve as a useful tool to identify HCC risk in patients **who would not traditionally qualify for surveillance** based on cirrhosis status alone

FibroScan may help to predict short term & long term outcomes in patients with HCC after curative resection

401 patients with HCC undergone hepatectomy and per-operative LSM measurements by FibroScan

- Patients with higher pre-operative LSM (>12 kPa) **had significantly worse short-term and long-term outcomes** with lower 5-year overall survival rate (57.3% vs 75.1%, p < 0.001) and 5-year disease free survival rate (26.7% Vs 45.8%, p < 0.001).
- Higher LSM is also **the only predictive factor for late recurrence of HCC** (OR 2.04, p = 0.048).
- Implementing FibroScan liver stiffness measurement value in every patient undergoing hepatectomy **may help estimate the complication risk, recurrence risk and aid the overall treatment plan.**

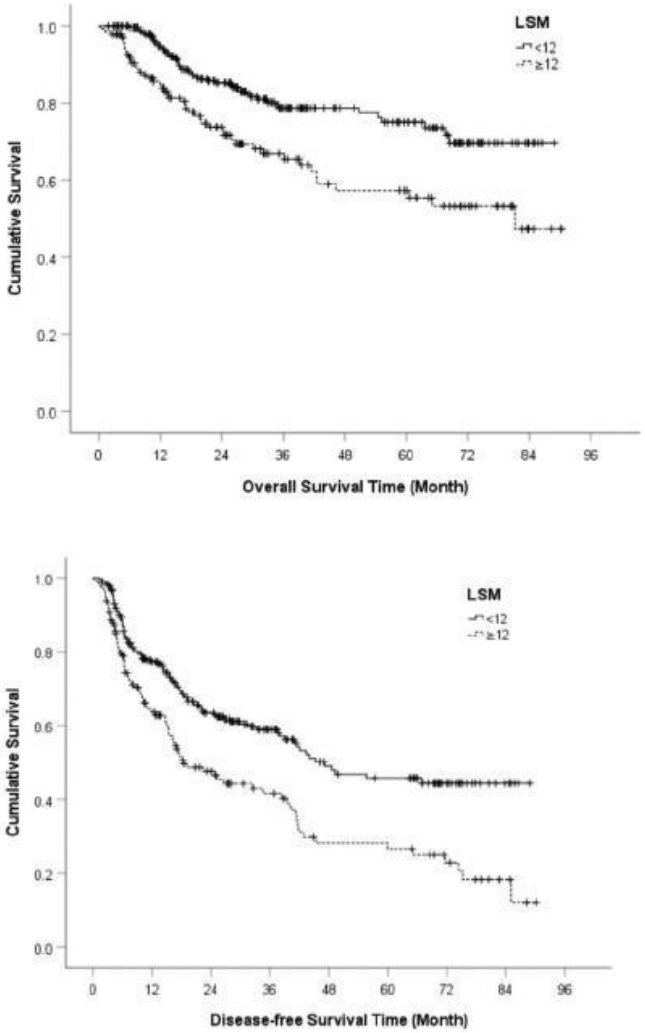
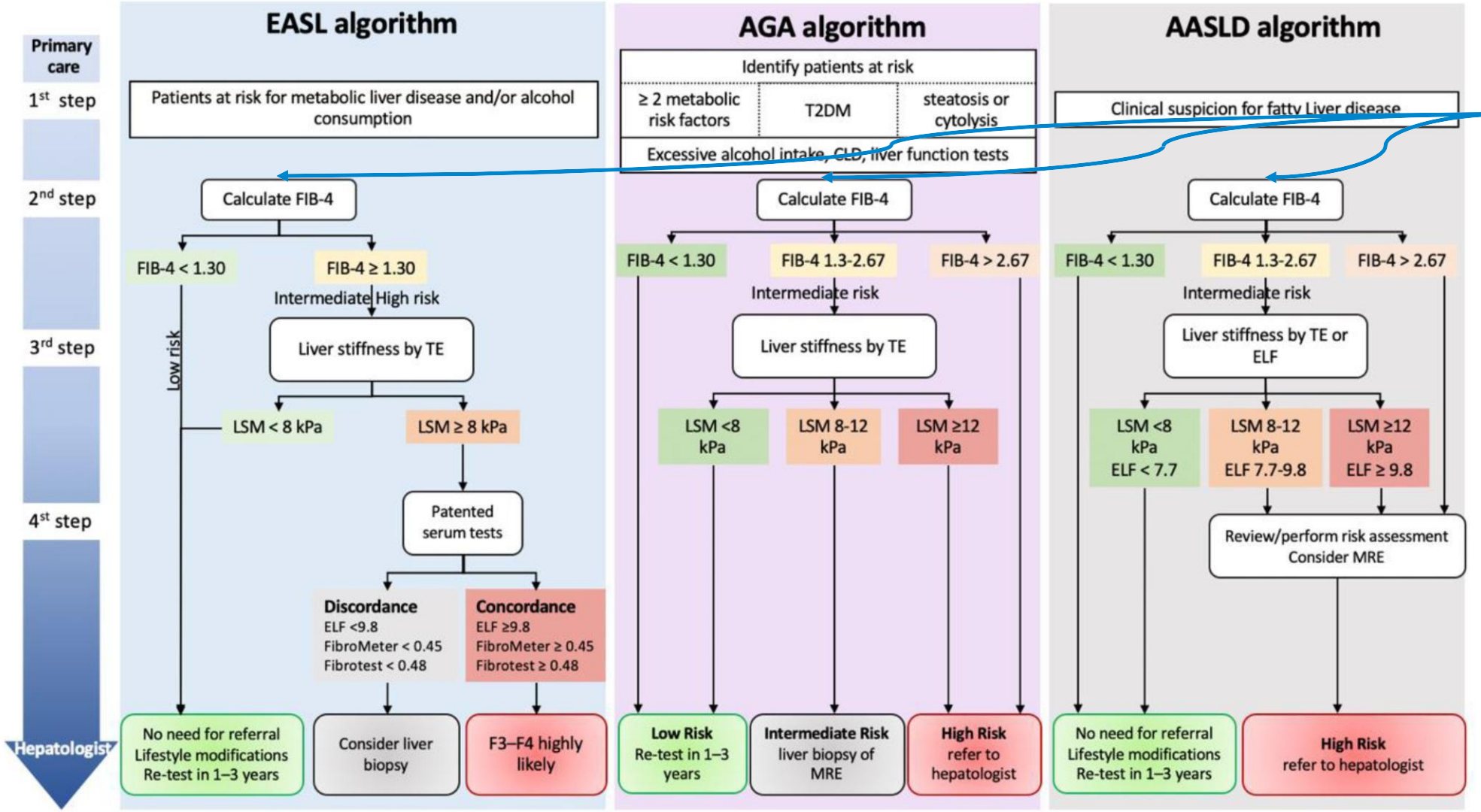


Fig. 2 – Kaplan–Meier curve of overall and disease free survival.

Lau et al. The Surgeon 2021

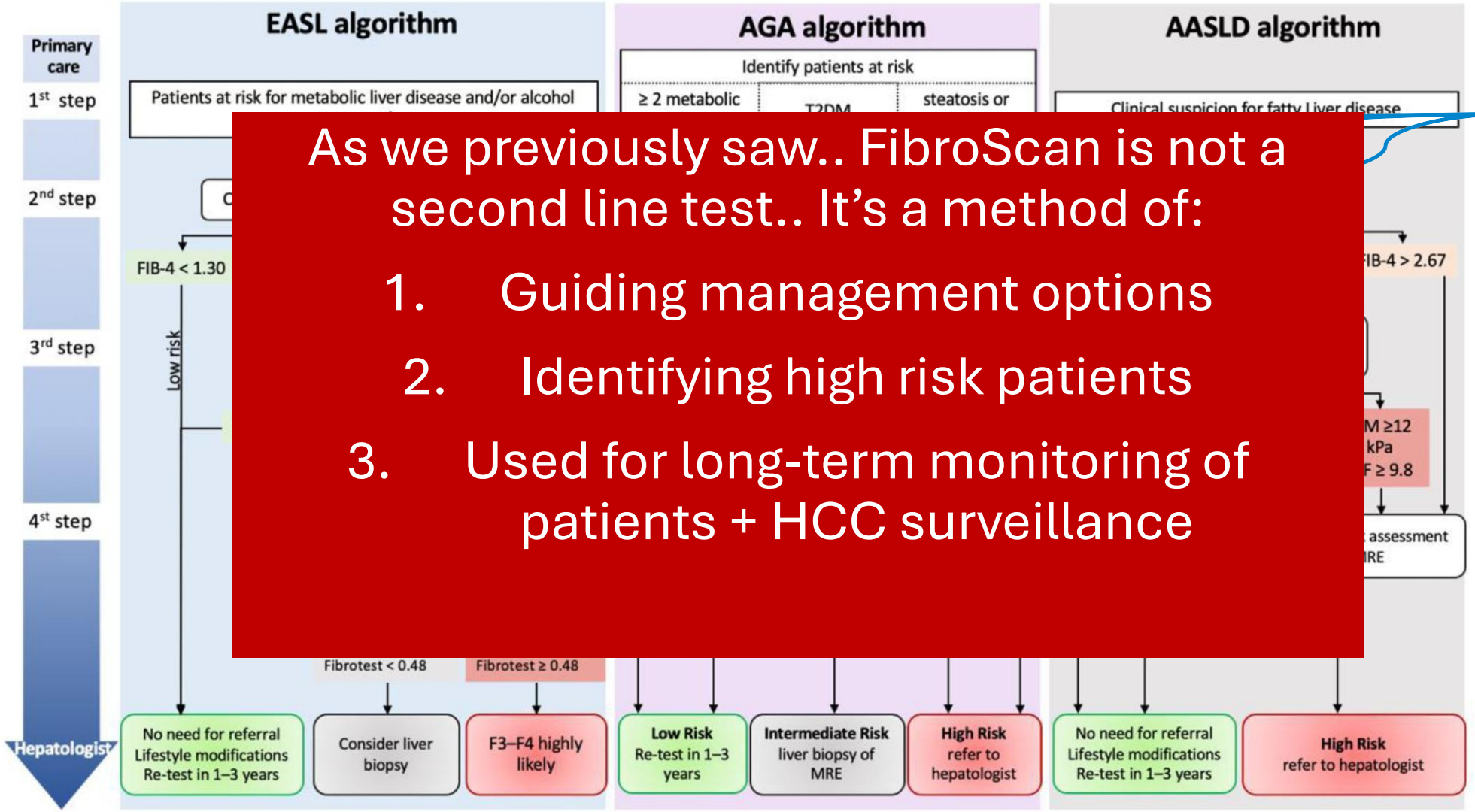
Guideline recommendations



Simple test (**FIB-4**) as a first line test

FibroScan as a second line test

Guideline recommendations



As we previously saw.. FibroScan is not a second line test.. It's a method of:

1. Guiding management options
2. Identifying high risk patients
3. Used for long-term monitoring of patients + HCC surveillance

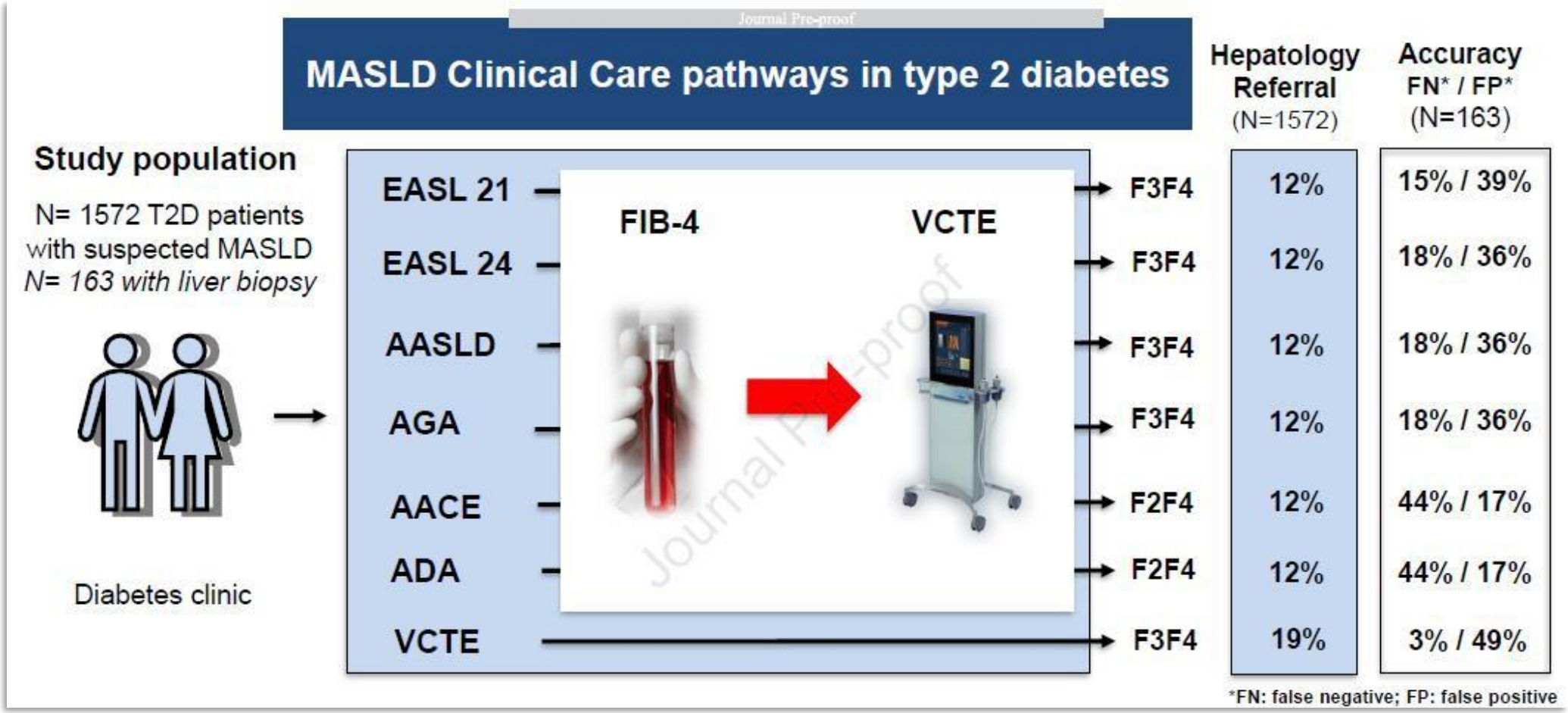
Simple test (**FIB-4**) as a first line test

Fib … as a sec… test

How do the pathways perform ?

Evaluation in clinical practice

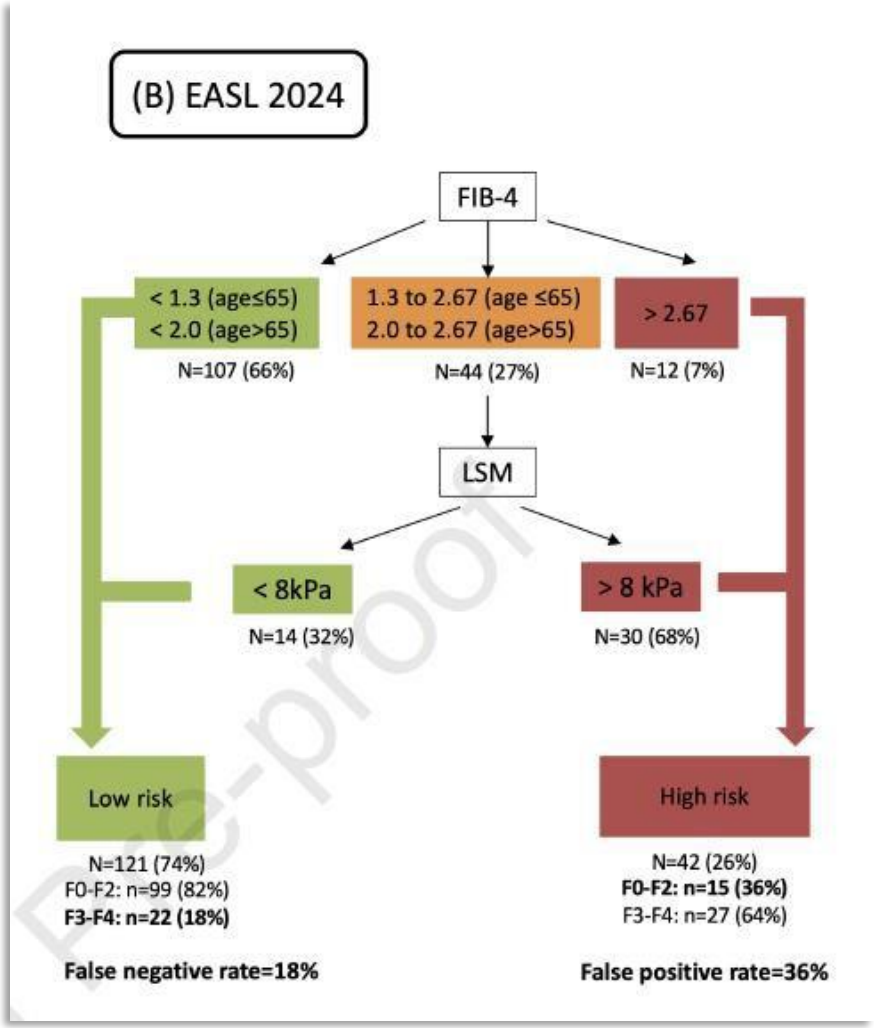
Numerous pathways have been proposed to screen patients at risk for MASLD and fibrosis in T2D patients. What is their performance in real clinical practice ?



Vidal Trecan et al. CGH 2025

How do the pathways perform ?

Evaluation in real clinical practice



- The percentage of T2D patients in diabetes clinics **requiring referral to hepatology (12%) was similar across the six pathways** using the FIB-4/VCTE sequential algorithm
- When used alone at first line, VCTE **led to a higher referral rate (19%)**, with **a low false negative rate (3%)** for advanced fibrosis
- Higher referrals numbers than those reported in the general population, highlighting **the urgent need for screening of these patients**

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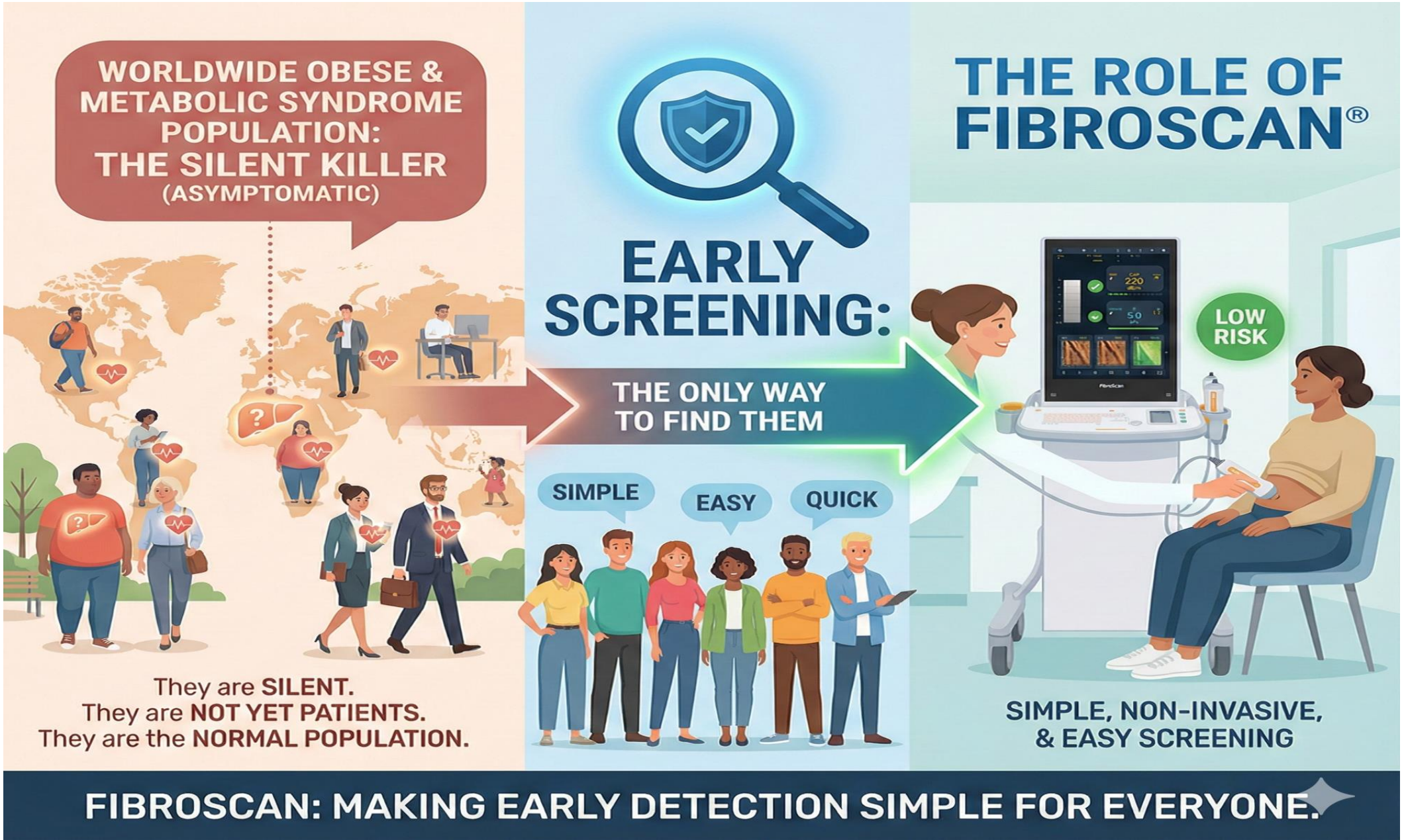
Take home message



Take home message

Thank you