MASLD/MASH and the Role of the PCP

10th Annual Essentials of Clinical Medicine CME Conference

Saturday, June 13, 2026 · 10:00 a.m. EST

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Financial Disclosures

No financial relationships to disclose.

Learning Objectives

At the end of this educational activity, participants will be able to:

Identify patients at highest risk for MASLD using epidemiologic data, with emphasis on relevant comorbidities.

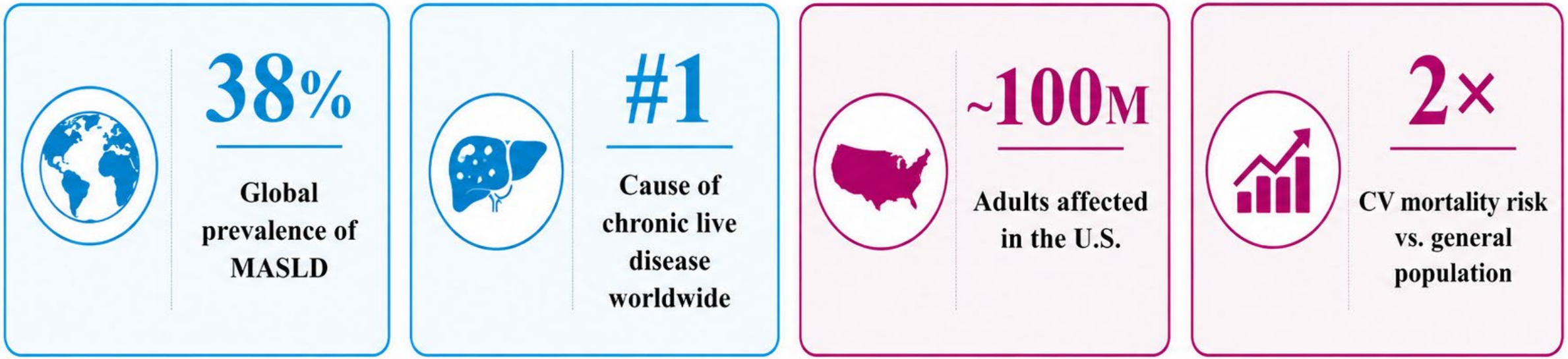
Apply noninvasive screening and fibrosis staging tools for patients with suspected MASLD, per current guidelines

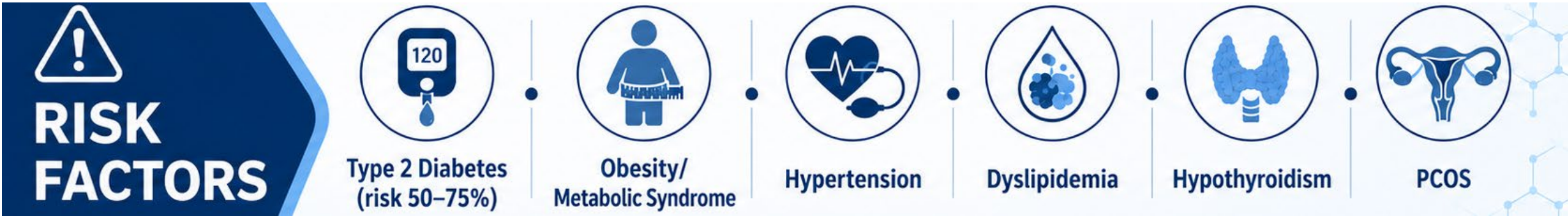
Build a management plan including lifestyle modification, cardiometabolic risk optimization, and evidence-based pharmacotherapy

Establish appropriate follow-up interval and metrics to track treatment response over time in patients with MASLD

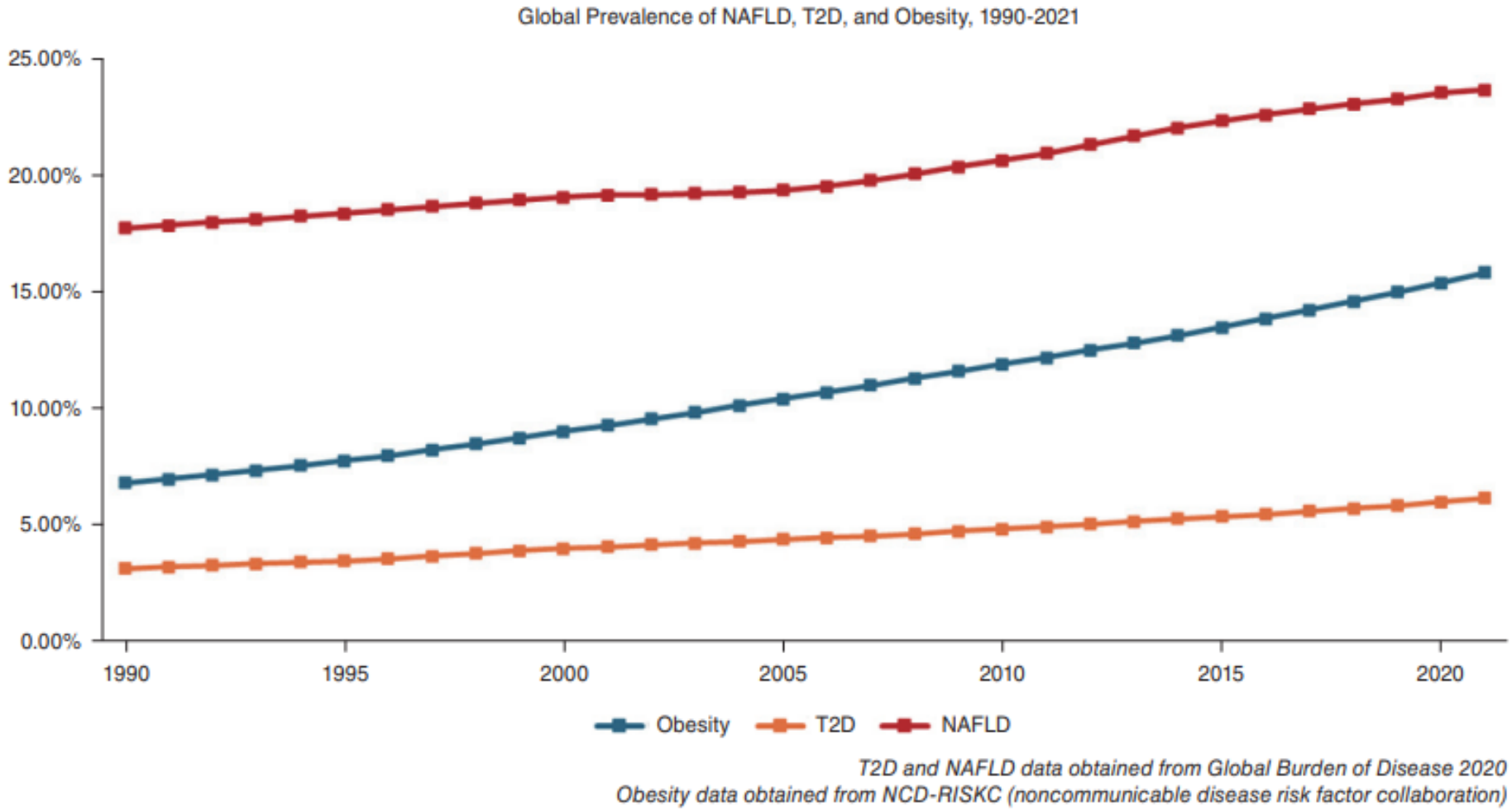
Know when to refer — use fibrosis stage and treatment response to determine the threshold for gastroenterology or hepatology referral

Epidemiology: Why This Matters





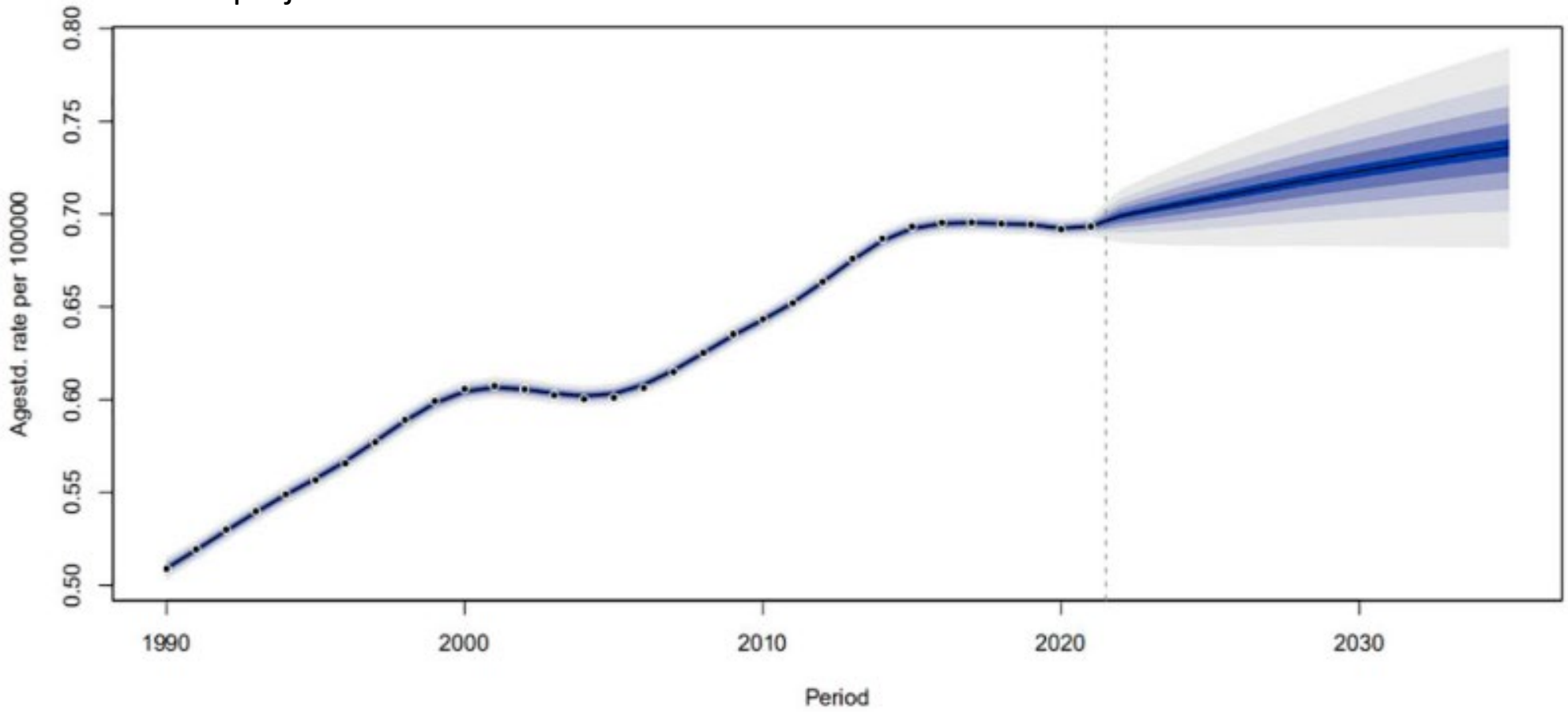
Epidemiology: Why This Matters



MASLD Prevalence Trend Younossi ZM et al., *Clin Mol Hepatol* 2025;31(Suppl):S32–S50

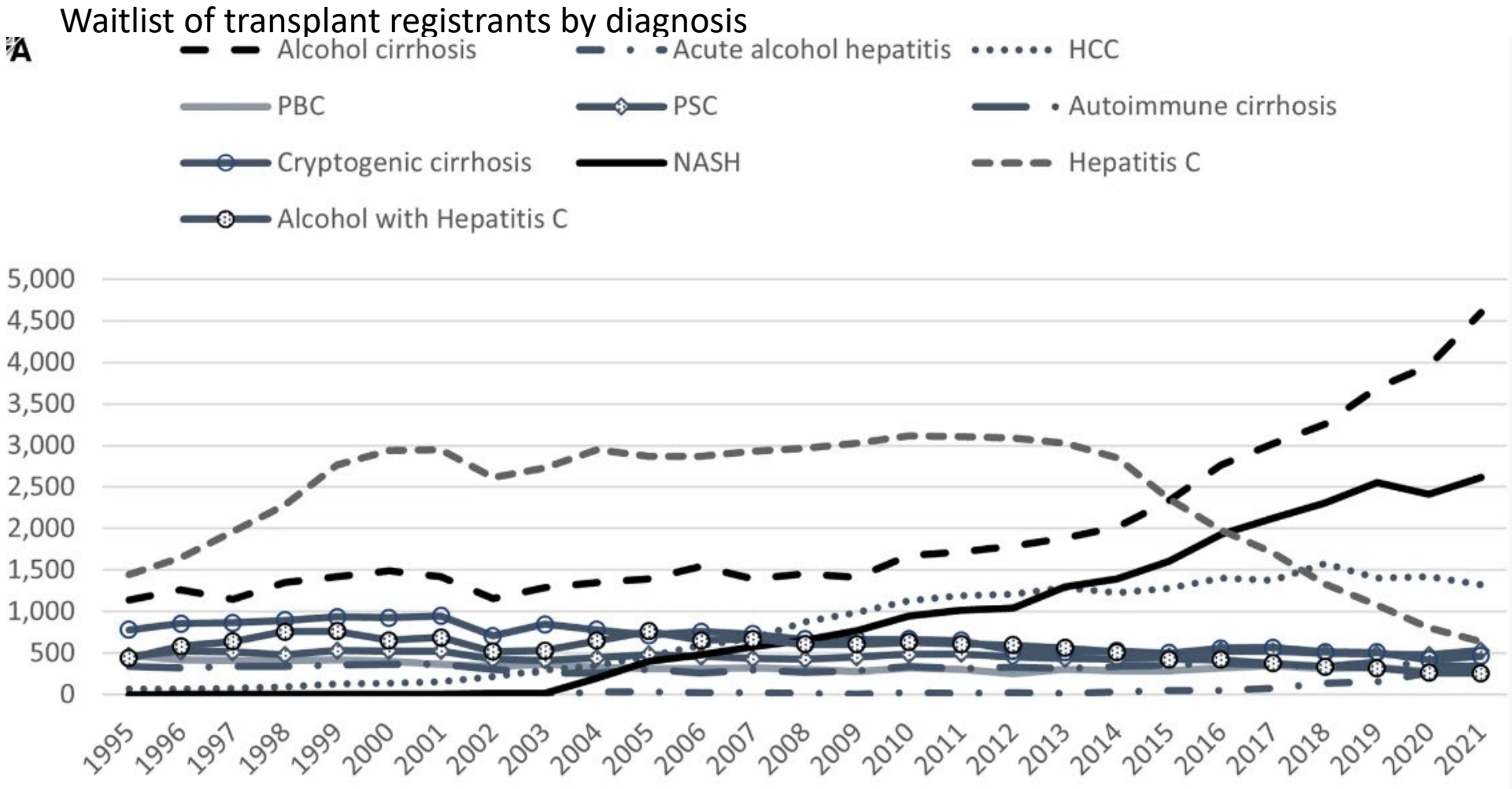
Epidemiology: Why This Matters

Global projections of incidence of HCC in MASLD Patients



MASLD-Related HCC Rising Cui T et al., *Front Oncol* 2026. doi:10.3389/fonc.2025.1623789

Epidemiology: Why This Matters



NASH as Rising Transplant Indication Andreoni KA et al., *Front Transplant* 2024. doi:10.3389/frtra.2024.1449407

What Is MASLD? Understanding the New Nomenclature

Old Name		New Name
NAFLD	→	MASLD
NASH	→	MASH

- Renamed in 2023 by multi-society consensus to:
- Reduce stigma
- Emphasize metabolic etiology
- Align with cardiometabolic* disease framework
  - BMI >25 (>23 in Asian populations)
  - T2DM or prediabetes
  - Hypertension
  - Hypertriglyceridemia
  - Dyslipidemia

MASLD Disease Spectrum

Steatosis only
Fat >5% hepatocytes, no inflammation

MASH
Steatosis + inflammation + ballooning

MASH + Fibrosis
F1–F4 staging; F3–F4 = advanced

Cirrhosis
Decompensation risk; portal hypertension

Hepatocellular Carcinoma (HCC)
Can occur WITHOUT cirrhosis in MASLD

Key clinical point: MASH is a histological diagnosis requiring biopsy.
Without biopsy, the correct term is simply **MASLD** — regardless of clinical suspicion.

* Cardiometabolic risk factors

Communicating with Patients: Language & Stigma

How We Talk About MASLD Matters — Frame It as a Metabolic Disease, Not a Lifestyle Failure

DO SAY / DO

- ✓ **Use "metabolic liver disease"** — less stigmatizing than "fatty liver"
- ✓ **Connect it to diabetes/heart disease** — a framework patients know
- ✓ **Emphasize treatability** — lifestyle + medications can reverse early disease
- ✓ **Set weight loss goals:** "Losing 10% of your body weight can significantly help your liver"
- ✓ **Use teach-back:** "Can you tell me what you'll do differently this week?"
- ✓ **Address food insecurity** and **social determinants of health**

AVOID

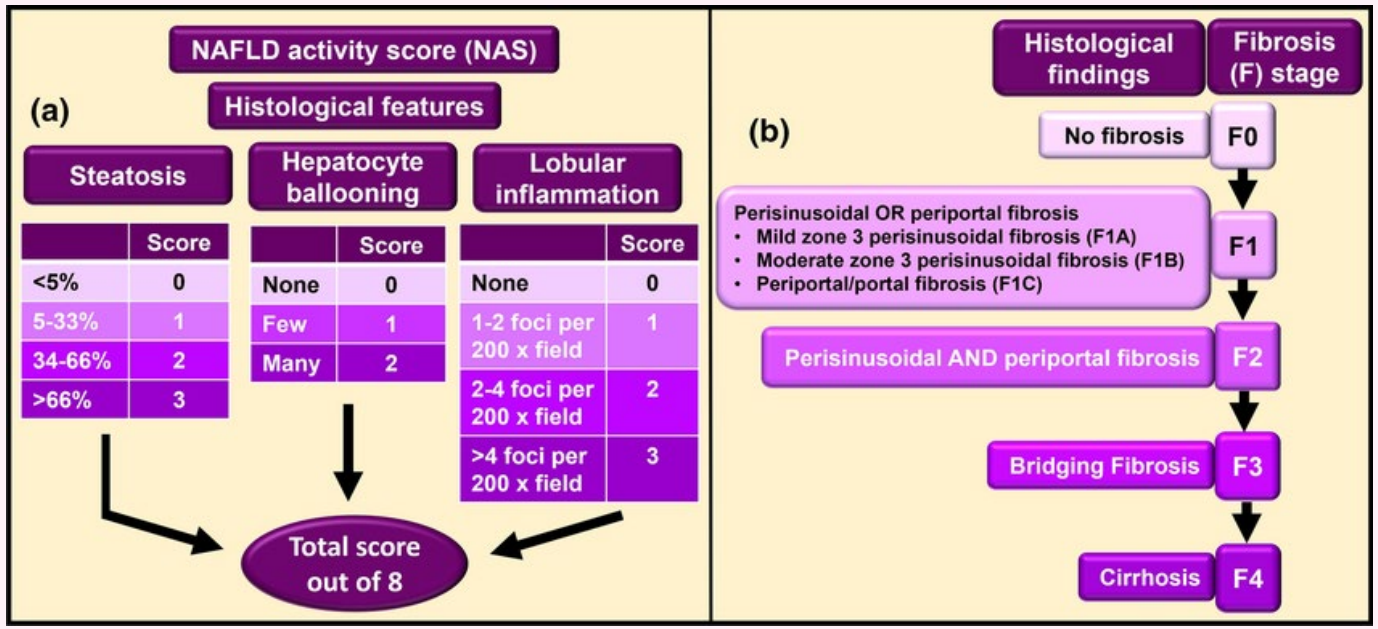
- ✗ **Avoid "you did this to yourself"** framing
- ✗ **Don't rely solely on ALT** — "your liver tests are normal" can be falsely reassuring
- ✗ **Don't delay treatment** while waiting for biopsy confirmation
- ✗ **Don't conflate MASLD** with alcohol-related liver disease in patient language
- ✗ **Avoid "just lose weight"** without actionable steps and support
- ✗ **Don't dismiss fatigue/symptoms** — quality of life matters

MASH: A Histological Diagnosis

MASH vs MASLD

What MASH Requires (by definition)

Liver biopsy — there is no other way to formally diagnose MASH



How to Document

MASLD — steatosis with ≥1 cardiometabolic risk factor, without biopsy

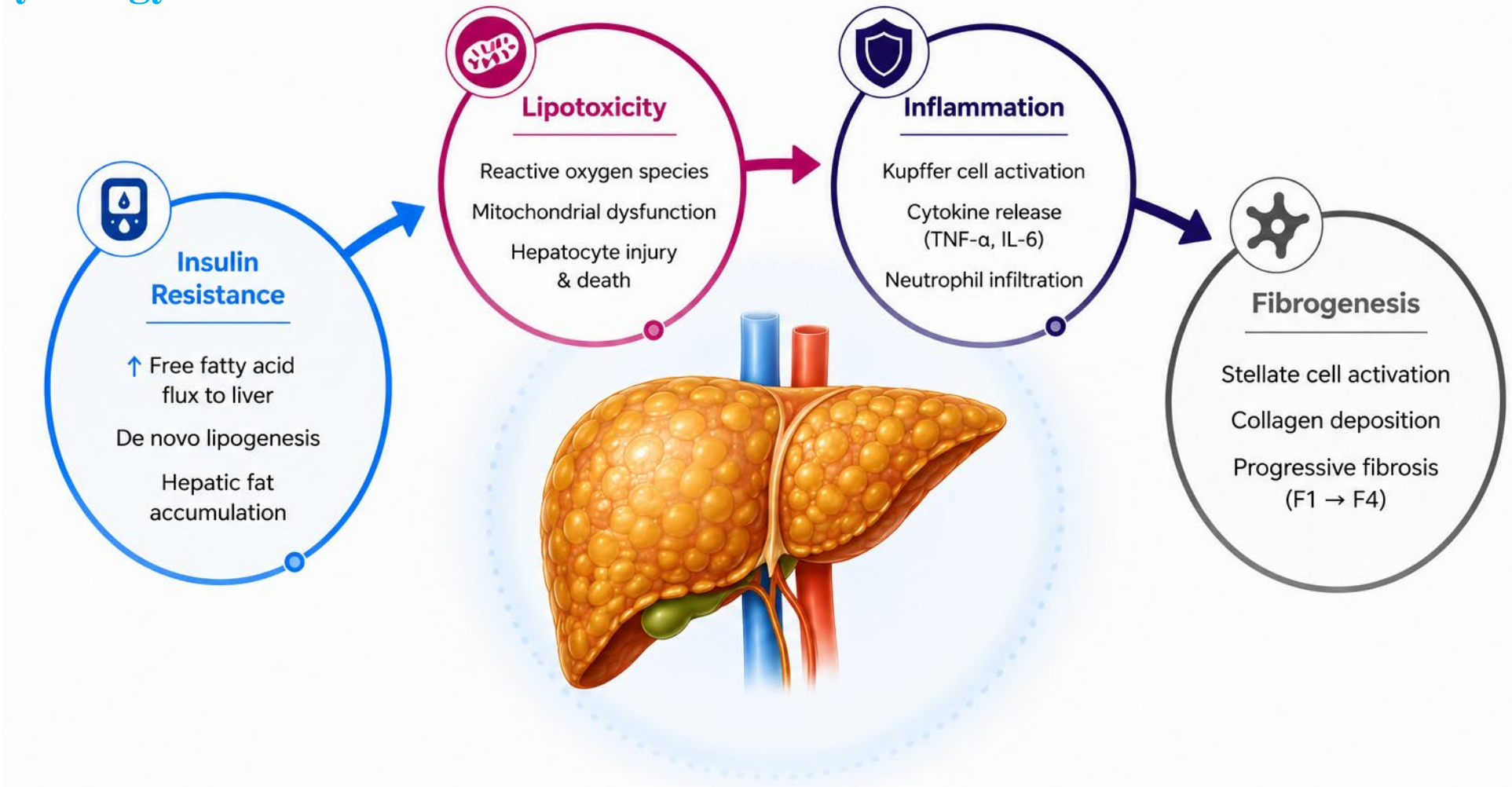
Presumed MASH — clinical suspicion based on elevated LFTs, high FIB-4, or indeterminate NIT is appropriate to note but MASH cannot be confirmed

Fibrosis staging via NIT (FIB-4, VCTE) — can and should risk-stratify even without biopsy

ICD-10 codes:
K76.0 — MASLD / hepatic steatosis
K75.81 — MASH (only after biopsy confirmation)

Takeaway: If your patient hasn't had a biopsy, code K76.0 and treat aggressively.

Pathophysiology: The Metabolic-Liver Axis



Key Insight: Insulin resistance is the central driver — treating metabolic comorbidities IS treating MASLD. GLP-1 agonists and SGLT2 inhibitors address the root mechanism.

MASLD vs MetALD

ALCOHOL USE
Degree of Use

Severity	Women ♀	Men ♂
Moderate / Low-Risk	Up to 1 drink/day (< 10g)	Up to 2 drinks/day (< 20g)
At-Risk / Heavy Drinking	> 3 drinks/day (> 40g) or > 7 drinks/week	> 4 drinks/day (> 50–60g) or > 14 drinks/week
Binge Drinking	4+ drinks (56g) in ~2 hours	5+ drinks (70g) in ~2 hours
MetALD Threshold	140 g/week (avg. ~10 drinks/week)	210 g/week (avg. ~15 drinks/week)
Severe ALD / Cirrhosis Risk	≥ 350 g/week (avg. ~25 drinks/week)	≥ 420 g/week (avg. ~30 drinks/week)

Each drink below = one U.S. standard drink = 14 grams or 0.6 fl oz. of pure ethanol

METALD vs. MASLD

MASLD requires ≥1 cardiometabolic risk factor AND no significant alcohol use (<140g/wk ♀, <210g/wk ♂).

Concurrent alcohol use = **MetALD** — a distinct category.

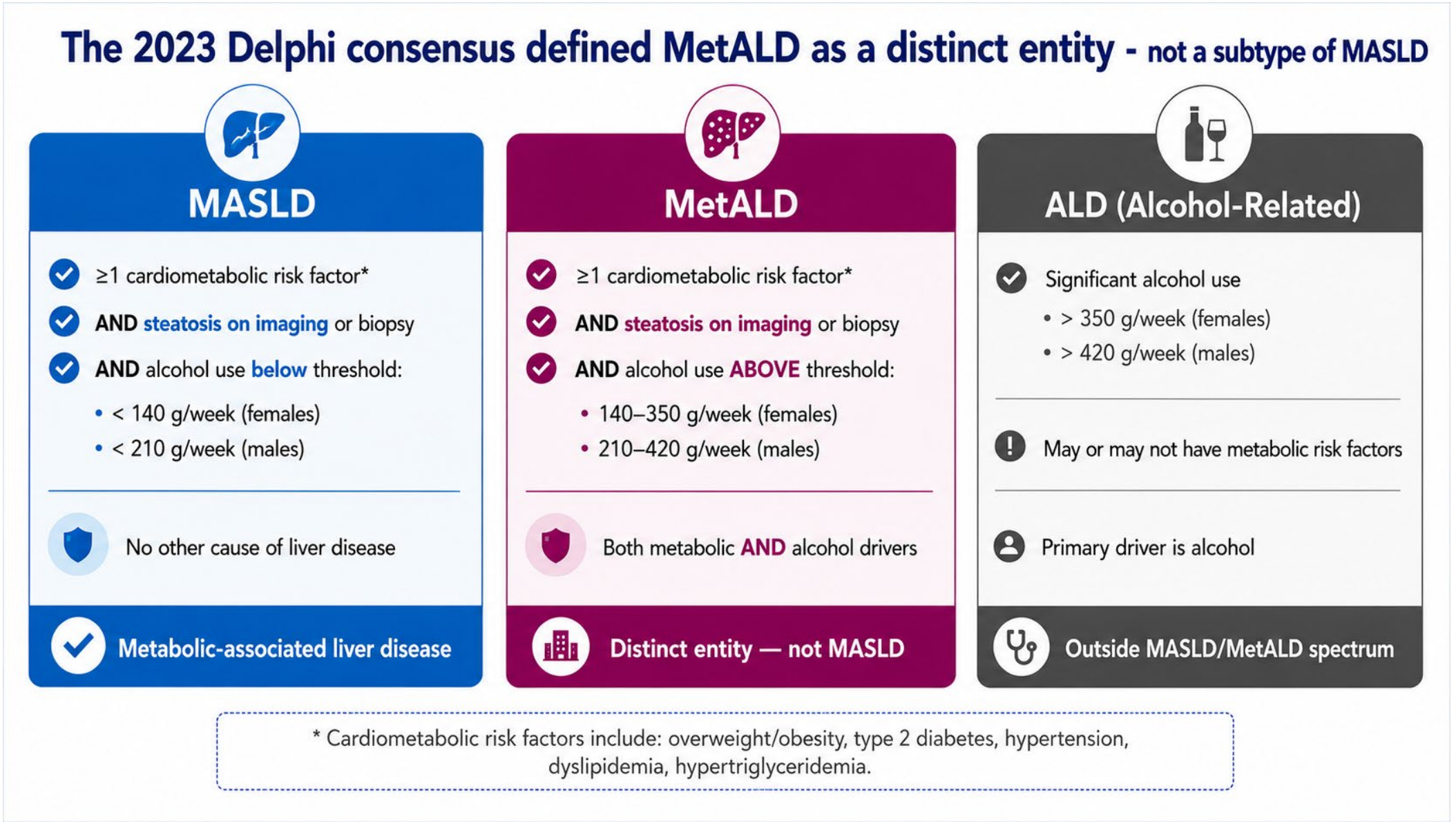
<140 g/week

Alcohol threshold

<210 g/week

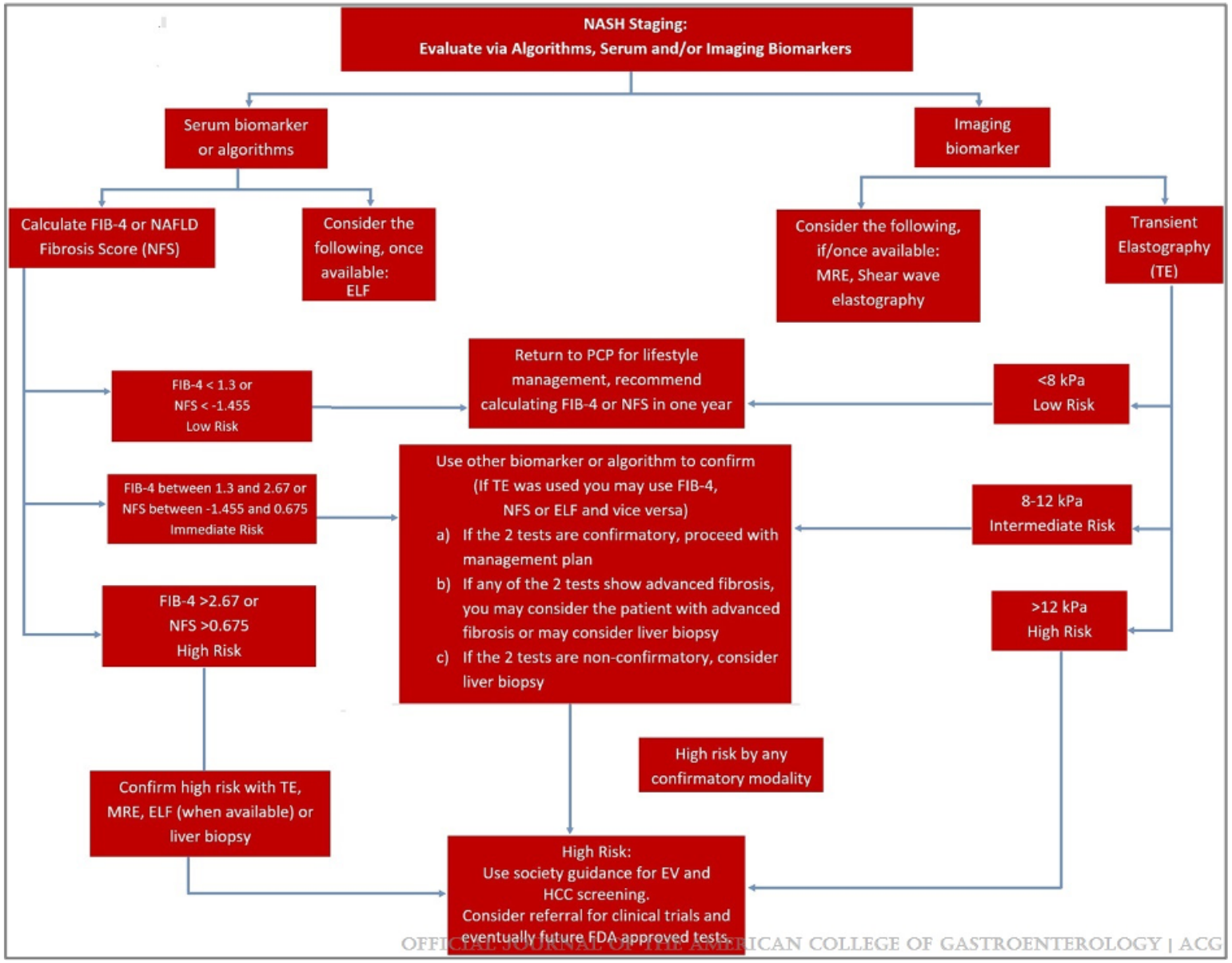
Alcohol threshold

MetALD: Diagnostic Criteria & Distinguishing from MASLD



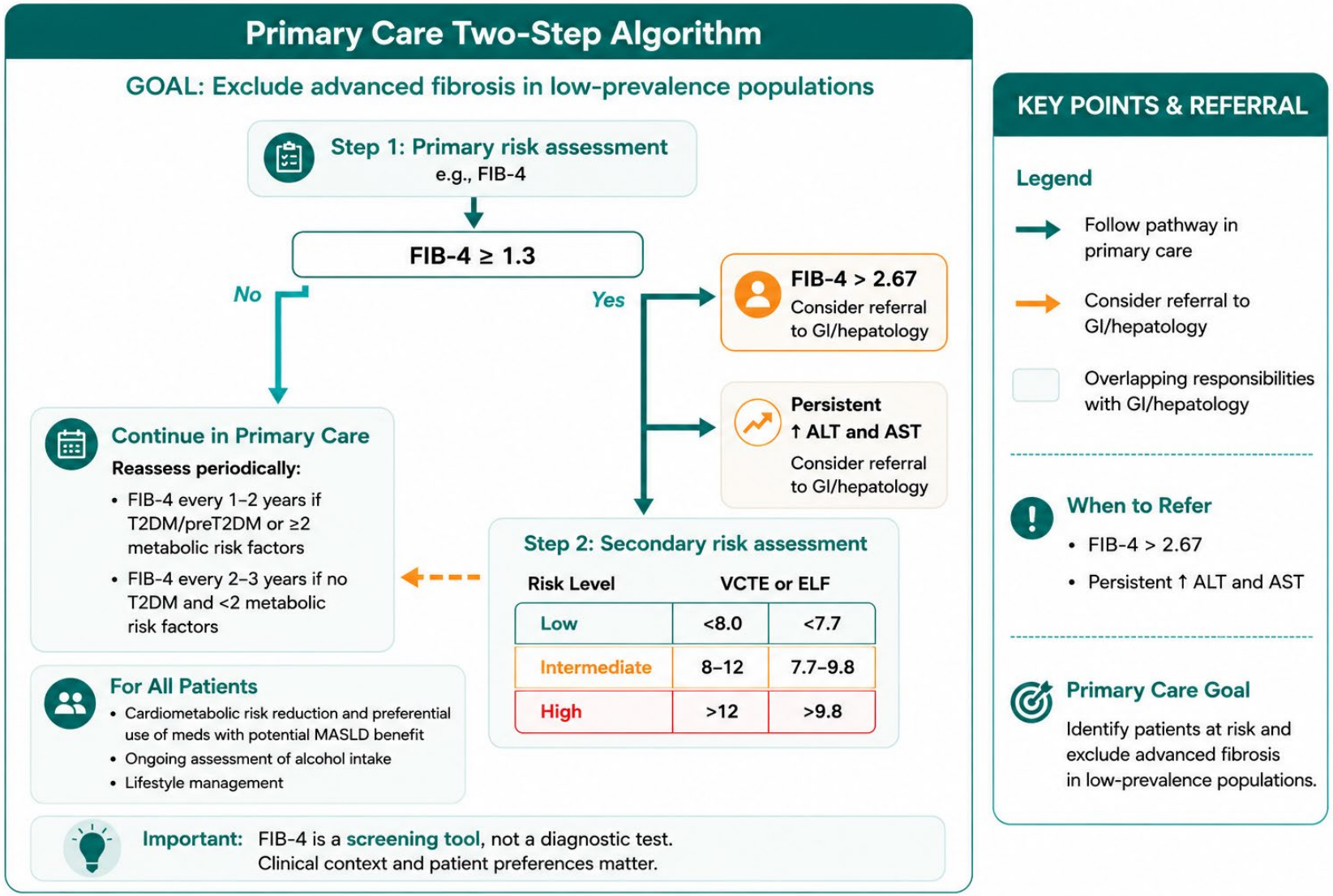
Non-Invasive Testing Algorithm

"Role of Noninvasive Tests in Clinical Gastroenterology Practices," published in *The American Journal of Gastroenterology* February 2021;116(2):254–262, produced by hepatologists from the American College of Gastroenterology and the Chronic Liver Disease Foundation.



Non-Invasive Testing Algorithm

Rinella ME, et al. AASLD Practice Guidance on the clinical assessment and management of nonalcoholic fatty liver disease. Hepatology. 2023;77(5):1797–1835.



Screening: Fishing for Fibrosis

Who Should Be Screened?

Strong indications to screen:

- Type 2 Diabetes Mellitus
- Metabolic Syndrome (≥3 criteria)
- Obesity (BMI ≥30) with elevated ALT
- Persistently elevated AST/ALT
- Incidental steatosis on imaging
- Family history of cirrhosis or HCC

How Should We Screen?

Routine LFTs are NOT enough:

- ALT can be normal even in advanced fibrosis
- Use age-adjusted ALT thresholds:
  >19 U/L (♀) or >30 U/L (♂) = abnormal

Once you identify a patient to screen:

- Order CBC, CMP, fasting lipids, HbA1c
- Calculate FIB-4 from those results
- FIB-4 is your first-line risk stratification tool

Early identification and risk stratification can lead to earlier intervention and better outcomes.

FIB-4 Index: How to Calculate and Interpret It

$$\text{FIB-4} = \text{Age (yr)} \times \text{AST (U/L)} \div [\ \text{Platelets } (\times 10^9/\text{L}) \times \sqrt{\text{ALT (U/L)}}\ ]$$

Example Case

Patient: 58F, AST 52, ALT 68, Platelets 178

$$\text{FIB-4} = 58 \times 52 \div (178 \times \sqrt{68})$$
$$= 3{,}016 \div (178 \times 8.25)$$
$$= 3{,}016 \div 1{,}468.5$$
$$\approx 2.05 \rightarrow \text{Indeterminate}$$

Interpreting FIB-4

< 1.30 Low risk	Reassure. Reassess in 1–2 years. No further fibrosis testing needed.
1.30–2.67 Indeterminate	Order VCTE (FibroScan) or ELF. Age-adjusted: ≥ 65 yr use < 2.0 as low cutoff.
> 2.67 High risk	Refer to hepatology. High probability of advanced fibrosis (F3–F4).

Important: FIB-4 was validated in HIV/HCV cohorts and has limitations in MASLD — use it as a screening tool, not a definitive diagnosis. A normal FIB-4 in a high-risk patient should still prompt clinical vigilance.

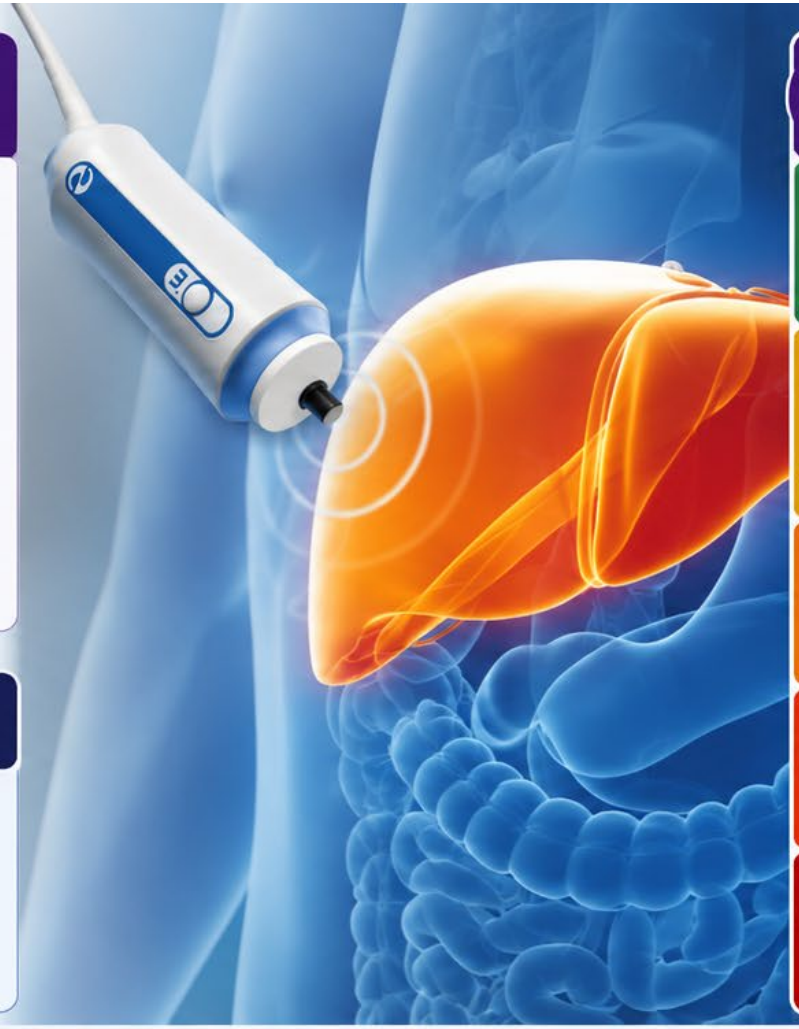
FibroScan (VCTE)

WHAT IS FIBROSCAN®?

- **Vibration-Controlled Transient Elastography (VCTE)**
- Uses a small probe on the right side of the abdomen
- Sends a low-frequency vibration through the liver
- Measures liver stiffness (LSM) in kilopascals (kPa)
- Also measures CAP score — quantifies steatosis grade
- Takes ~10 minutes; painless; no radiation; fasting preferred

COUNSEL YOUR PATIENT BEFORE REFERRAL

- Fast for at least 2 hours before the test
- "It's like an ultrasound but measures liver stiffness"
- BMI >40 may reduce accuracy — flag for hepatology
- Results will come back to me and we'll review together



INTERPRETING LSM RESULTS (kPa)

< 8 kPa F0–F1	**No / minimal fibrosis** Reassure. Recheck in 1–2 yr if risk factors persist.
8–12 kPa F2–F3	**Significant fibrosis** Treat aggressively. Consider Wegovy/ resmetirom eligibility. Co-manage with hepatology.
12–15 kPa F3	**Advanced / bridging fibrosis** High priority referral. Wegovy eligible range. Biopsy may be considered.
> 15–20 kPa F3–F4	**Probable cirrhosis** Refer now. HCC surveillance discussion. Consider biopsy.
> 20 kPa F4	**Cirrhosis likely** Urgent hepatology referral. Semaglutide **NOT** indicated as sole MASH therapy.

FibroScan® helps identify fibrosis early, guide management, and improve outcomes.

Monitoring: What to Track and How Often

Fibrosis Progression Monitoring

Parameter	Low Risk (FIB-4 <1.30)	Intermediate/High Risk
FIB-4 Index	Every 1–2 years	Every 6–12 months (or after referral)
LFTs (AST, ALT, GGT)	Annually	Every 3–6 months
Metabolic panel (lipids, HbA1c, BMI)	Annually	Every 3–6 months
Imaging (ultrasound)	Not routine if FIB-4 low	Every 6 months if cirrhosis (HCC screen)
VCTE / ELF	Not indicated	As directed by hepatology
Response to GLP-1 / lifestyle Rx	Weight, HbA1c, LFT trend	Weight, HbA1c, LFT + NIT at 1 yr

Documentation Tip: Code MASLD (K76.0) or MASH (K75.81) in the problem list. This flags the patient for monitoring and supports referral authorization.

Management: Lifestyle Modification (First-Line for All Patients)

Weight Loss

- ≥5% body weight loss improves steatosis
- ≥7–10% improves MASH histology
- ≥10% can reverse fibrosis
- **Goal:** sustained loss, not rapid cycling
- Address obesity as a disease — pharmacotherapy if needed

Diet

- Mediterranean diet: strongest evidence
- Reduce saturated fat & simple sugars
- Limit fructose (especially liquid)
- Avoid ultra-processed foods
- No specific macro ratio required — adherence > perfection

Exercise

- 150 min/week moderate aerobic activity
- Resistance training adds benefit
- Reduces hepatic fat independent of weight loss
- Even mild activity helps — start where patient is
- Sedentary behavior is an independent risk factor

Counseling Pearl: Frame lifestyle changes as treatment — not just advice. Document MASLD in the problem list to justify referrals to nutrition, obesity medicine, and exercise physiology.

Weight Loss Is Medicine: Dose-Response Data & the Wegovy Approval

≥ 3–5%	**Steatosis reduction** Hepatic fat begins to clear
≥ 7–10%	**MASH resolution** Inflammation & ballooning improve; NAS score drops
≥ 10%	**Fibrosis regression** F3 → F2 or better documented on biopsy/elastography
≥ 15–20%	**Cirrhosis reversal possible** Emerging data; significant fibrosis regression in advanced disease

Wegovy (Semaglutide 2.4mg) — FDA Approval

August 2025: FDA approves Wegovy for F2–F3 fibrotic MASH

Second FDA-approved MASH therapy (accelerated approval)

ESSENCE Trial (NEJM 2025):

- N = 800 patients with biopsy-confirmed MASH F2–F3
- Semaglutide 2.4mg SC weekly × 72 weeks

Key Results:

- 62.9% MASH resolution (vs 34.3% placebo)
- 36.8% fibrosis improvement ≥1 stage (vs 22.4%)
- Mean weight loss –10.5% vs –2.0% placebo

PCP Role:

- Initiate semaglutide for T2DM/obesity NOW — liver benefit is a bonus
- Wegovy for MASH indication: co-manage with hepatology
- Weight loss goal of 10% is achievable — counsel accordingly

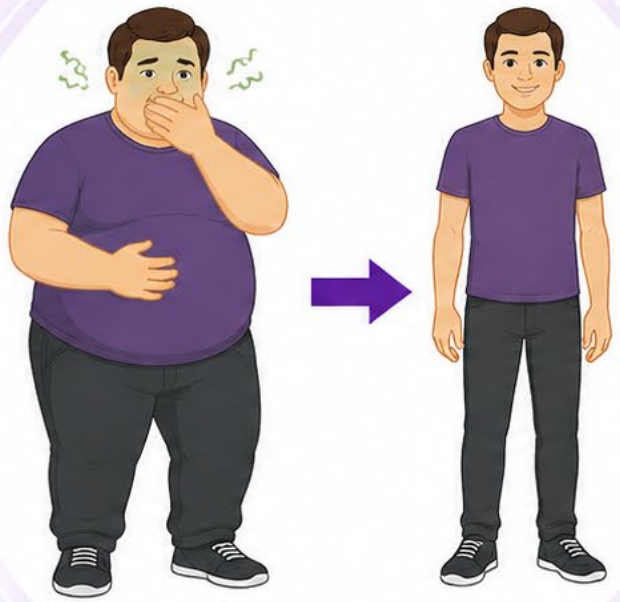
Discuss Risks and How to Mitigate

Counseling Patients Starting GLP-1 Receptor Agonists — Set Expectations Early

- **GI side effects are expected, not a reason to stop:** nausea, vomiting, constipation most common —typically dose-dependent and improve over weeks.

- **Mitigate with dose escalation:** We start low and go slow — your body needs time to adjust. This is by design, not a problem.

- **Eat smaller, lower-fat meals:** counsel to avoid large portions and high-fat foods, especially early in treatment.



- **Injection site rotation:** rotate sites to minimize reactions; store pen correctly.

- **Rare but important — pancreatitis:** counsel to report severe, persistent abdominal pain; hold medication and evaluate.

- **Contraindications to review upfront:** personal/family history of MTC or MEN2 — screen before prescribing.

Pharmacotherapy: How to Maximize Fibrosis Regression

Optimize Cardiometabolic Comorbidities — Many Treatments Overlap with MASLD Management

GLP-1 Receptor Agonists

Semaglutide, Liraglutide | **T2DM, Obesity, MASH (Wegovy FDA Aug 2025)**

- **ESSENCE:** 62.9% MASH resolution
- 36.8% fibrosis improvement
- −10.5% weight loss

SGLT2 Inhibitors

Empagliflozin, Dapagliflozin | **T2DM, HFrEF, CKD**

- Reduces hepatic fat & inflammation
- Bonus: CV & renal protection

Pioglitazone (TZD)

Thiazolidinedione class | **T2DM (non-obese MASH)**

- Improves MASH histology
- Weight gain limits use

Resmetirom (Rezdiffra™)

THR-β agonist | **1st MASH-specific Rx — FDA March 2024**

- Improves fibrosis & MASH resolution
- For F2–F3 MASH — hepatology-led

Statins

Atorvastatin, Rosuvastatin | **Dyslipidemia (safe in MASLD)**

- Do NOT avoid — hepatotoxicity risk is a myth in MASLD
- May reduce fibrosis progression

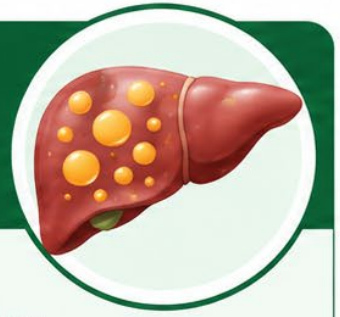
Vitamin E (800 IU/day)

Antioxidant therapy | **Non-diabetic MASH (AASLD)**

- Modest histologic benefit
- Long-term safety uncertain
- Not first-line in PCPs

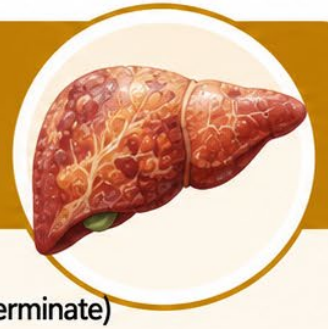
When to Refer: Thresholds for Hepatology / GI

MANAGE IN PRIMARY CARE



- FIB-4 < 1.30 (low risk)
- LSM < 8 kPa (no advanced fibrosis)
- Steatosis only, no metabolic syndrome
- Optimize metabolic comorbidities (GLP-1, SGLT2i, statins)
- Lifestyle counseling + weight management
- Recheck FIB-4 in 1–2 years

CONSIDER REFERRAL



- FIB-4 1.30–2.67 (indeterminate) + no local NIT access
- LSM 8–15 kPa (F2–F3 range; Wegovy eligible)
- MASH confirmed with progressive disease despite treatment
- Candidate for resmetirom (Rezdiffra) — F2–F3 MASH
- Diagnostic uncertainty — biopsy consideration
- Rapid AST/ALT rise without clear cause

REFER NOW

- FIB-4 > 2.67 (confirmed high risk)
- LSM > 15 kPa on VCTE (cirrhosis range)
- Suspected cirrhosis (low platelets, splenomegaly, ascites)
- Thrombocytopenia with other signs of portal hypertension
- Jaundice or hepatic decompensation
- HCC screening needed (established cirrhosis)

What Hepatology Sees: How to Make Referrals More Valuable

Some Referral Patterns We See

1 

Incidental steatosis on imaging

CT or ultrasound done for unrelated reason — no follow-up workup sent with referral

2 

Elevated LFTs, unclear etiology

AST/ALT trending up — viral hepatitis, autoimmune, thyroid, and alcohol sometimes not yet excluded

3 

FIB-4 flagged by lab system

Auto-calculated FIB-4 > 1.30 triggers referral — sometimes sent before clinical context is reviewed

4 

Known MASLD, now worsening labs

Patient followed for years without NIT — referred when AST/ALT spikes or platelets drop

5 

GLP-1/bariatric patient

Rapid weight loss raises concern — hepatology asked to assess baseline fibrosis before or after

Add Value to MASLD Referral First Visit

Labs (within 6 months)

- ✓ CBC with platelets
- ✓ CMP (AST, ALT, ALP, GGT, bilirubin, albumin)
- ✓ Fasting lipid panel + HbA1c
- ✓ TSH
- ✓ Hepatitis B sAg, sAb, cAb • Hepatitis C Ab

Clinical context

- ✓ Alcohol use history (AUDIT-C or equivalent)
- ✓ Current medications (especially steroids, MTX, amiodarone)
- ✓ Prior liver-related diagnoses or family history of liver disease

Calculated values

- ✓ FIB-4 index (document in referral)
- ✓ BMI and weight trend over 6–12 months

Imaging

- ✓ Most recent abdominal ultrasound, CT, or MRI with date
- ✓ Note any prior mention of steatosis, splenomegaly, or ascites

BONUS POINTS

PETH (phosphatidylethanol) lab testing

- ✓ Helps objectively assess alcohol use and guide clinical management

Scenario 1: MASLD Screening in Primary Care — What Would You Do?

58-year-old woman with T2DM (HbA1c 8.2%), HTN, BMI 34. Routine labs show AST 52, ALT 68, PLT 178k. No alcohol use. Ultrasound from 3 years ago noted "echogenic liver."

Discussion — What would you do?

1. What is the FIB-4 and how do you interpret it?	→ *FIB-4 = 58 × 52 ÷ (178 × √68) ≈ 2.2 → Indeterminate range*
2. What is your next step in risk stratification?	→ *Refer for VCTE (FibroScan) or order ELF panel if available*
3. What pharmacologic changes would you make today?	→ *Consider GLP-1 agonist — addresses T2DM + MASLD simultaneously*
4. Does she need hepatology referral now?	→ *Not urgently — reassess after VCTE; refer if LSM >8 kPa or FIB-4 rises*

Scenario 2: GLP-1 Agonist Side Effects — What Would You Do?

52-year-old man with T2DM, BMI 38, MASLD (FIB-4 1.8 — indeterminate). You initiate semaglutide 0.25mg weekly. At his 4-week follow-up he reports nausea and vomiting, has missed 3 doses, and says "I don't think this medication is for me." He's lost 4 lbs.

Discussion — What would you do?

1. Is this a reason to stop semaglutide?

→ *No — GI side effects at dose escalation are expected and typically transient. This is dose-dependent nausea at week 4 of the starting dose.*

2. What do you do about the missed doses?

→ *Reassure and re-educate. If missed <5 days, take as soon as remembered. If >5 days, skip and resume next scheduled weekly dose to avoid double-dose.*

3. What practical strategies do you offer?

→ *Smaller meals, avoid high-fat/spicy foods, eat slowly, stay upright after eating, consider ondansetron short-term if severe. Delay escalation if needed — staying at 0.25mg longer is acceptable.*

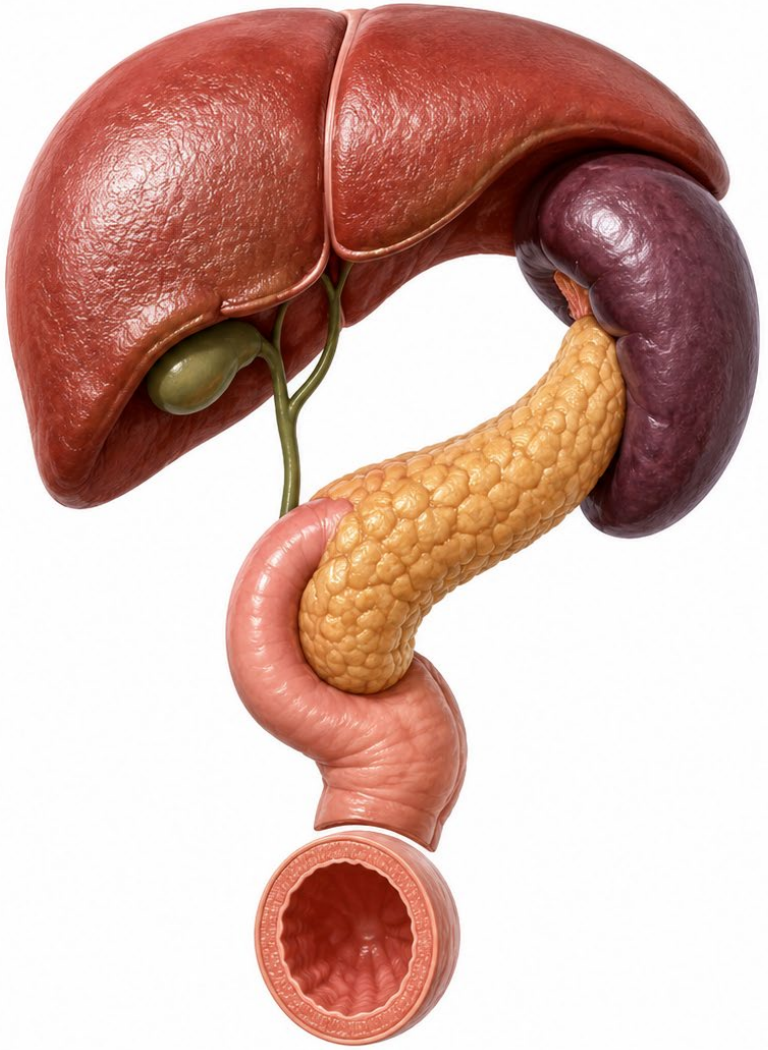
4. He asks: "Should I be worried about pancreatitis?" How do you respond?

→ *Counsel that risk is real but low (~0.2%). Symptoms to watch: severe persistent mid-epigastric pain radiating to back. If that occurs, hold medication and go to ED. Distinguish from typical GI side effects.*

Key Takeaways

1. MASLD is extremely common — screen any patient with T2DM, metabolic risk factors, or unexplained elevated LFTs.
2. FIB-4 is your first tool — it's free, calculated from routine labs, and stratifies risk for advanced fibrosis.
3. Normal ALT does not rule out MASLD — use age-adjusted ALT thresholds and FIB-4 together.
4. GLP-1 agonists and SGLT2 inhibitors treat metabolic disease and MASLD simultaneously — leverage your existing toolkit.
5. Refer to hepatology for FIB-4 >2.67, LSM >15 kPa, suspected cirrhosis, or candidates for resmetirom or Wegovy (semaglutide) for F2–F3.

Questions?



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