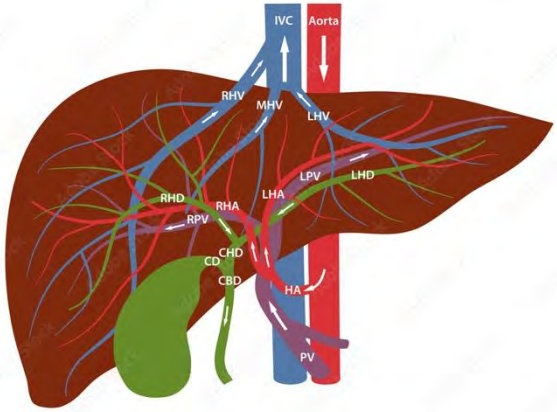

MASLD in Type 2 Diabetes

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MCT2D
MICHIGAN COLLABORATIVE FOR TYPE 2 DIABETES

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ADA MASLD
consensus statement

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

ANNALS OF FAMILY MEDICINE

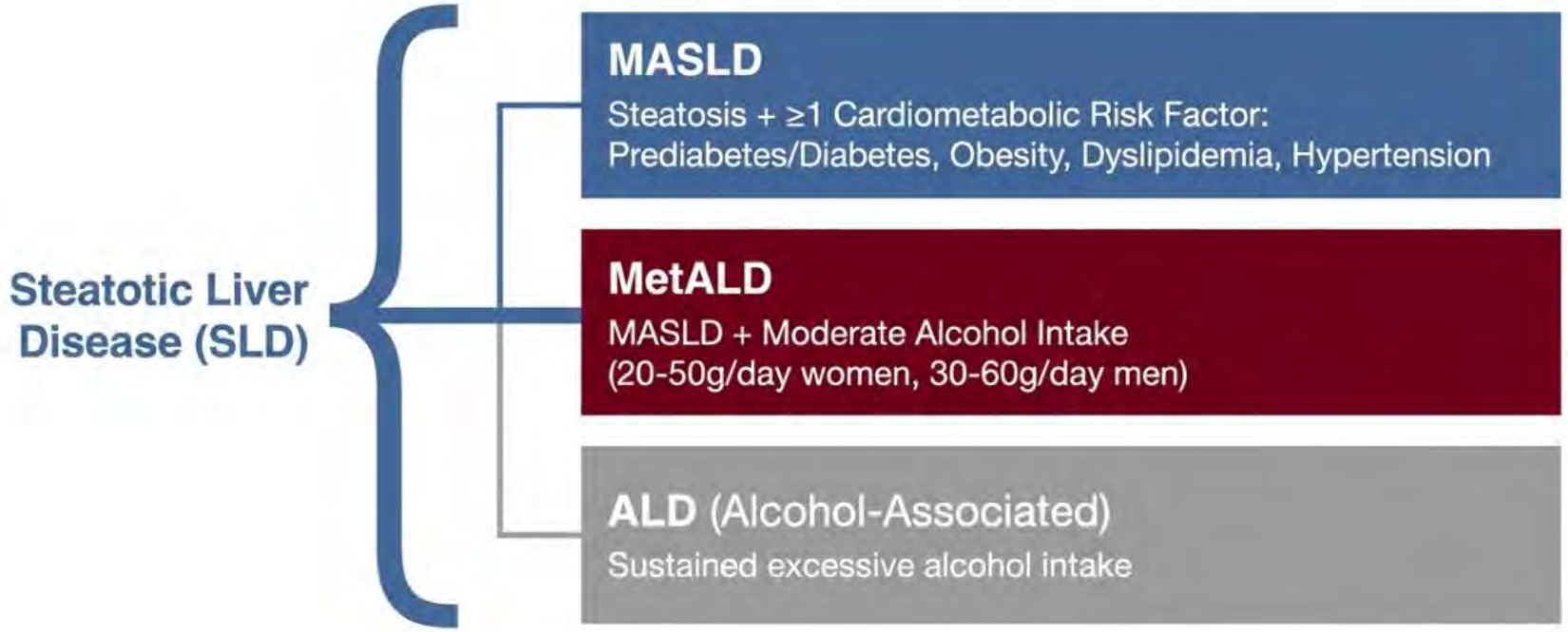
Editor of *Annals of Family Medicine*

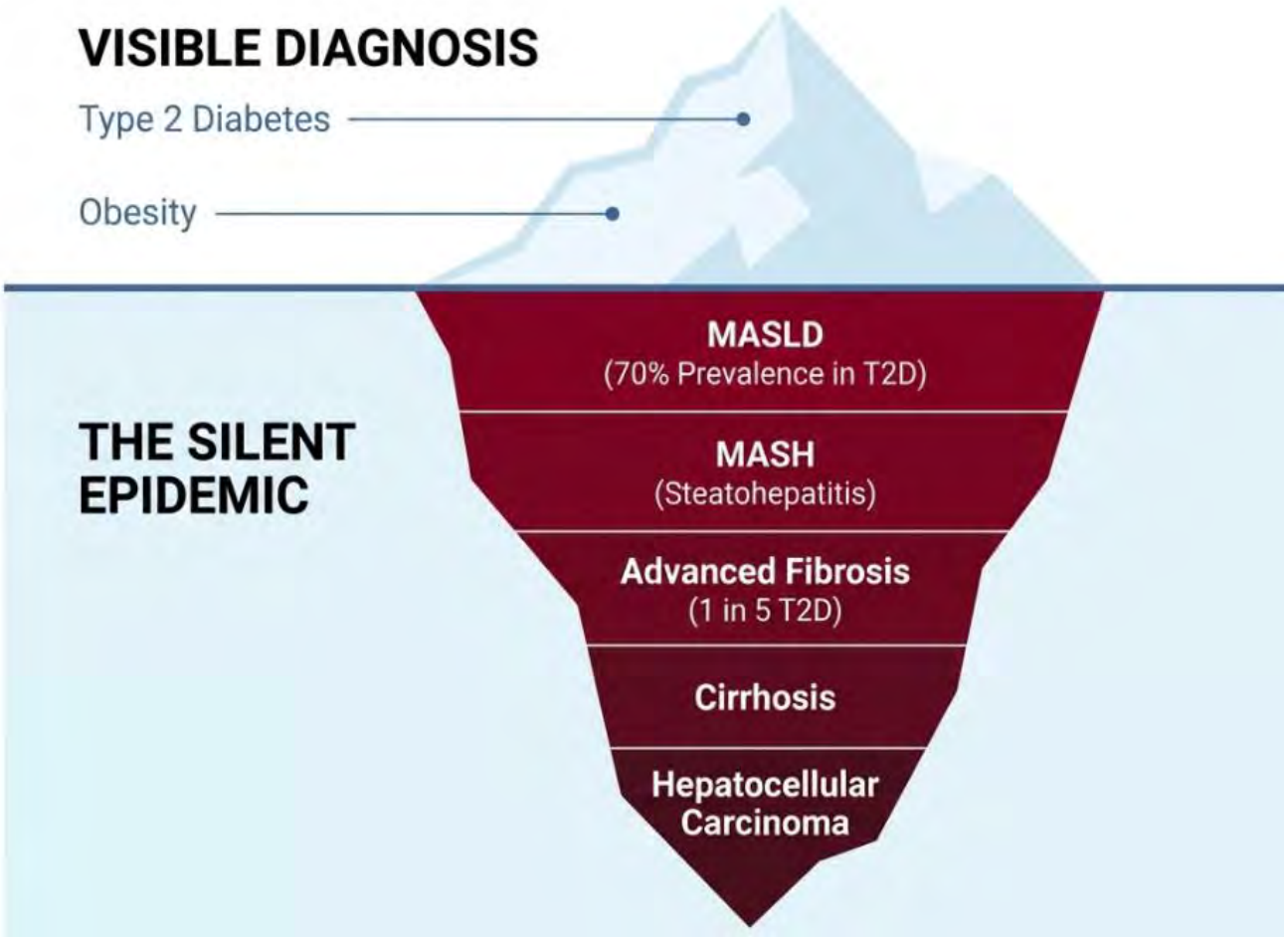
Founding Director of MCT2D

MCT2D
MICHIGAN COLLABORATIVE FOR TYPE 2 DIABETES

Decoding the Alphabet Soup

From NAFLD to MASLD: A shift toward precision and destigmatization





- 70% of people with Type 2 DM have MASLD

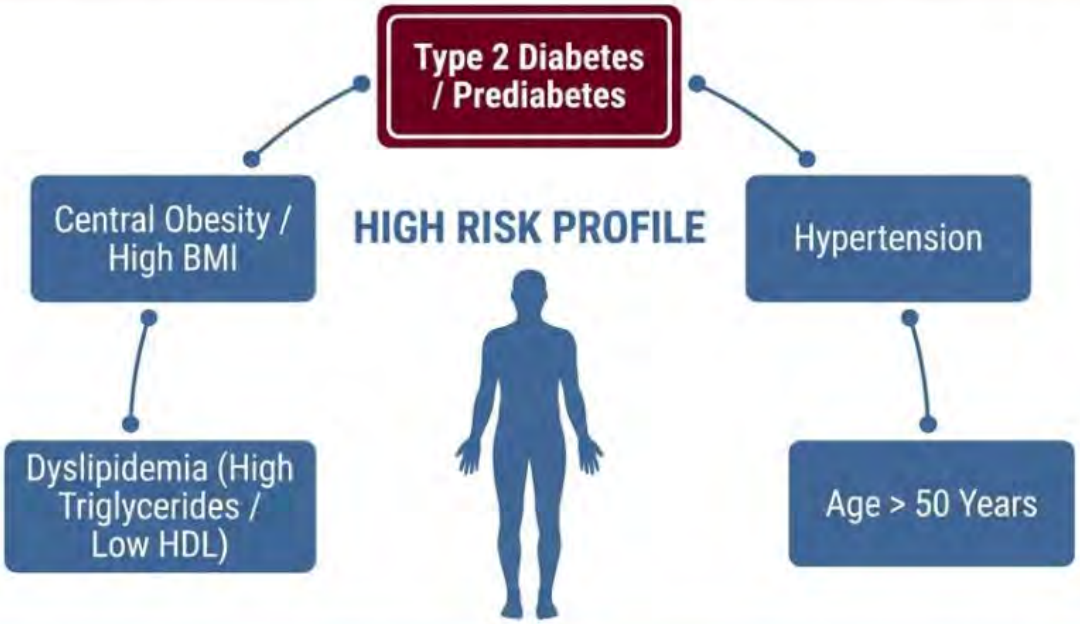
- Alcohol and MASLD are main causes of liver transplant and death from liver failure in the US.

Annual rates

- 12,000 transplants
- 30,000 HCC cancers
- 52,000 liver failure deaths

- About 2 to 3 liver related deaths in 1000 person years with T2D.

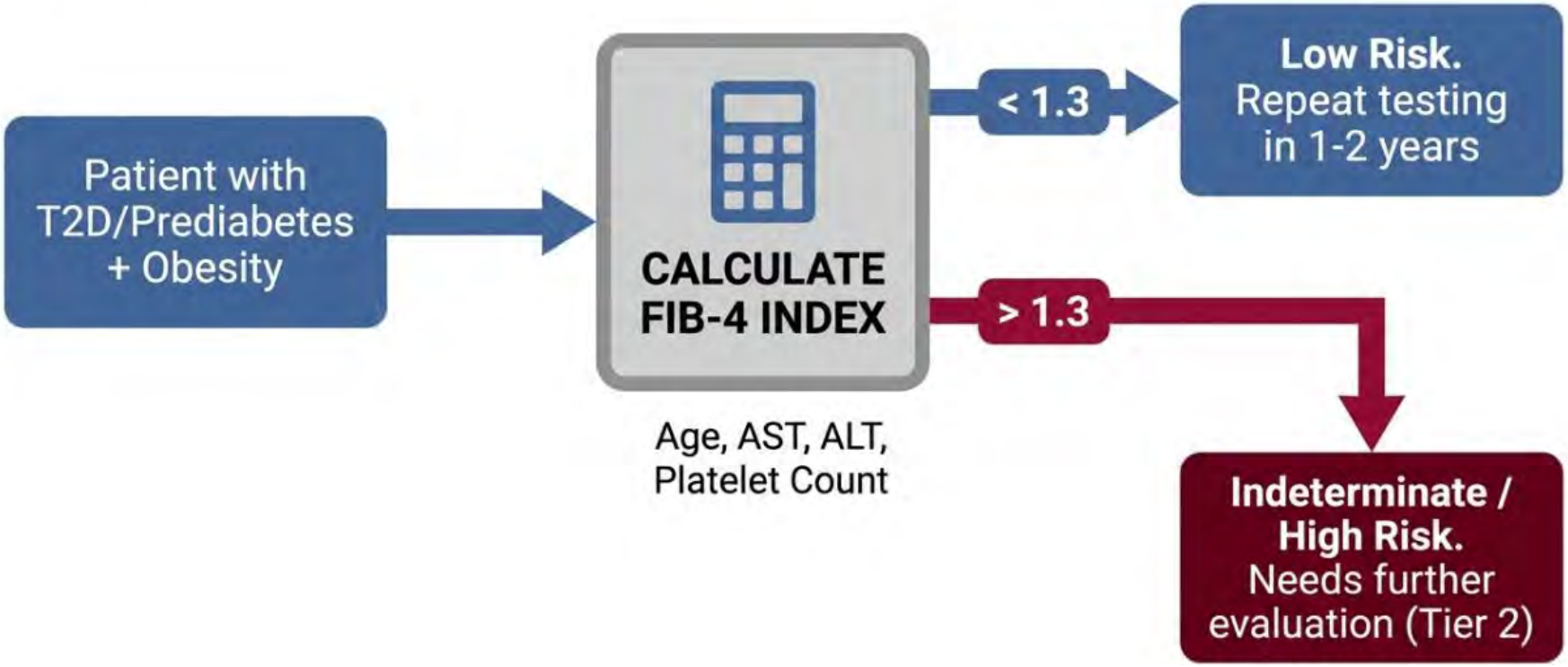
The High-Risk Profile: Who Needs Screening?



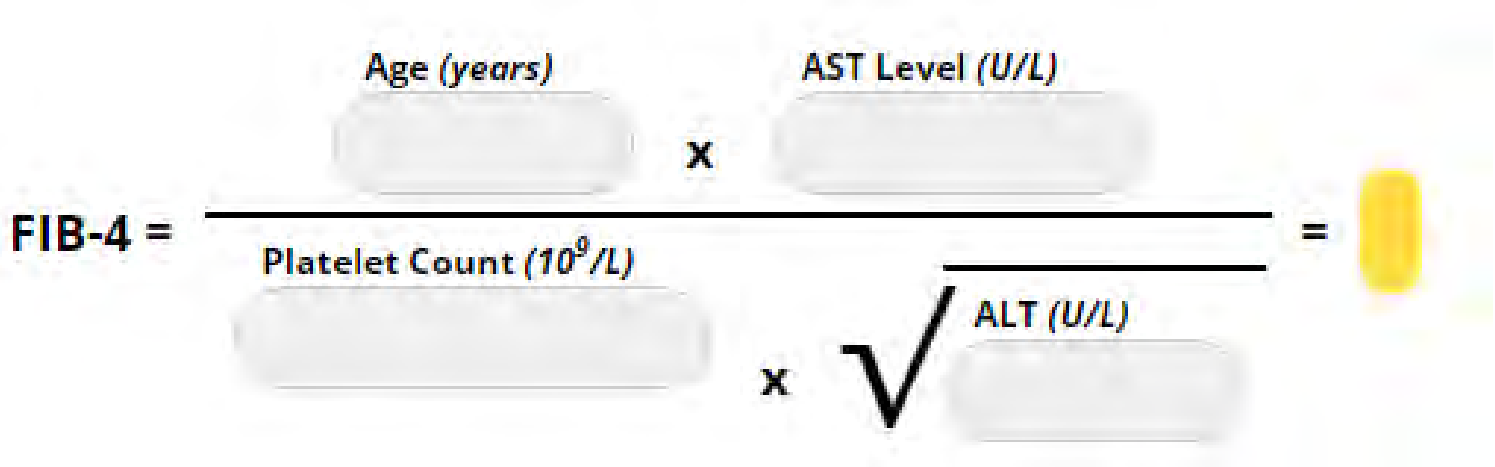
The Bidirectional Threat: T2D doubles the risk of liver fibrosis, while MASLD doubles the risk of developing T2D.

Screening for LIVER FIBROSIS

Step 1: The FIB-4 First Strategy



FIB-4 Calculation



Order – CBC, LFTs or Comp

MD CALC FIB-4

Fibrosis-4 (FIB-4) Index for Liver Fibrosis

Noninvasive estimate of liver scarring in HCV and HBV patients, to assess need for biopsy.

When to Use | Pearls/Pitfalls | Why Use

Age
Use with caution in patients <35 or >65 years old, as the score has been shown to be less reliable in these patients
years

AST
Aspartate aminotransferase
Norm: 15 - 41 U/L

ALT
Alanine aminotransferase
Norm: 1 - 35 U/L

Platelet count
Norm: 150 - 350 $\times 10^3/\mu L$

Result:
Please fill out required fields.

» Next Steps | Evidence | Creator Insights

EPIC FIB-4 flowsheet

	Office Visit from 2/16/2 2/16/2026 0001
FIB4 Components	
AST	21
ALT	21
Platelets	303
Recalculate FIB-4?	Yes
FIB-4 Calculator	
FIB4 Score	0.95

EPIC FIB-4 Dot Phrase

Fibrosis 4 (FIB-4) Score: Evaluates liver fibrosis based on age, platelet count, AST and ALT to help with cirrhosis diagnosis[1]

FIB4 Score: 0.95 (2/16/2026 12:01 AM)

Values used to calculate this score (if multiple, calculator uses most recent):

Age: 63 y.o.

Lab Results

Component	Value	Date
AST	21	02/16/2026
AST	25	08/25/2025

Lab Results

Component	Value	Date
ALT	21	02/16/2026
ALT	21	08/25/2025

Lab Results

Component	Value	Date
PLATELETS	303	02/16/2026
PLATELET	311	08/25/2025

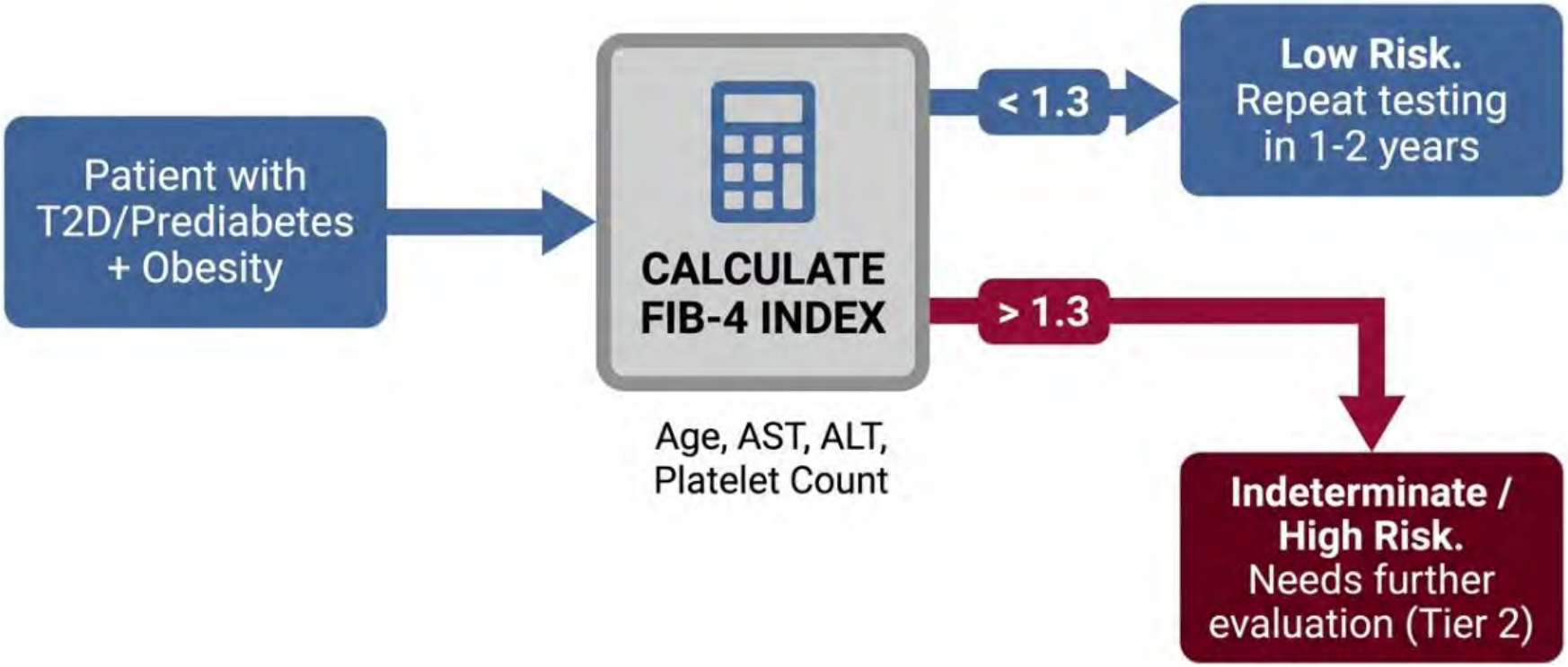
Score interpretation for adults between 35 - 65yo

- FIB 4 scores <1.3 absence of cirrhosis more likely (with a negative predictive value of 90% for advanced fibrosis).
- FIB 4 scores 1.3 - 2.67 indicates intermediate risk; advanced fibrosis possible, more investigation recommended.
- FIB 4 scores >2.67 indicate cirrhosis more likely (with a positive predictive value of 65% for advanced fibrosis).

For >65yo, <2 is considered low risk.

Screening for LIVER FIBROSIS

Step 1: The FIB-4 First Strategy



Post Fib 4 action

Low Risk < 1.3

- Focus on Prevention
- Diet – Mediterranean
- Exercise – Daily 30 min
- Aggressive treatment of metabolic disease, weight loss, Type 2 diabetes.
- Attention to other common causes of liver disease
- Recheck Fib-4 in 2 years

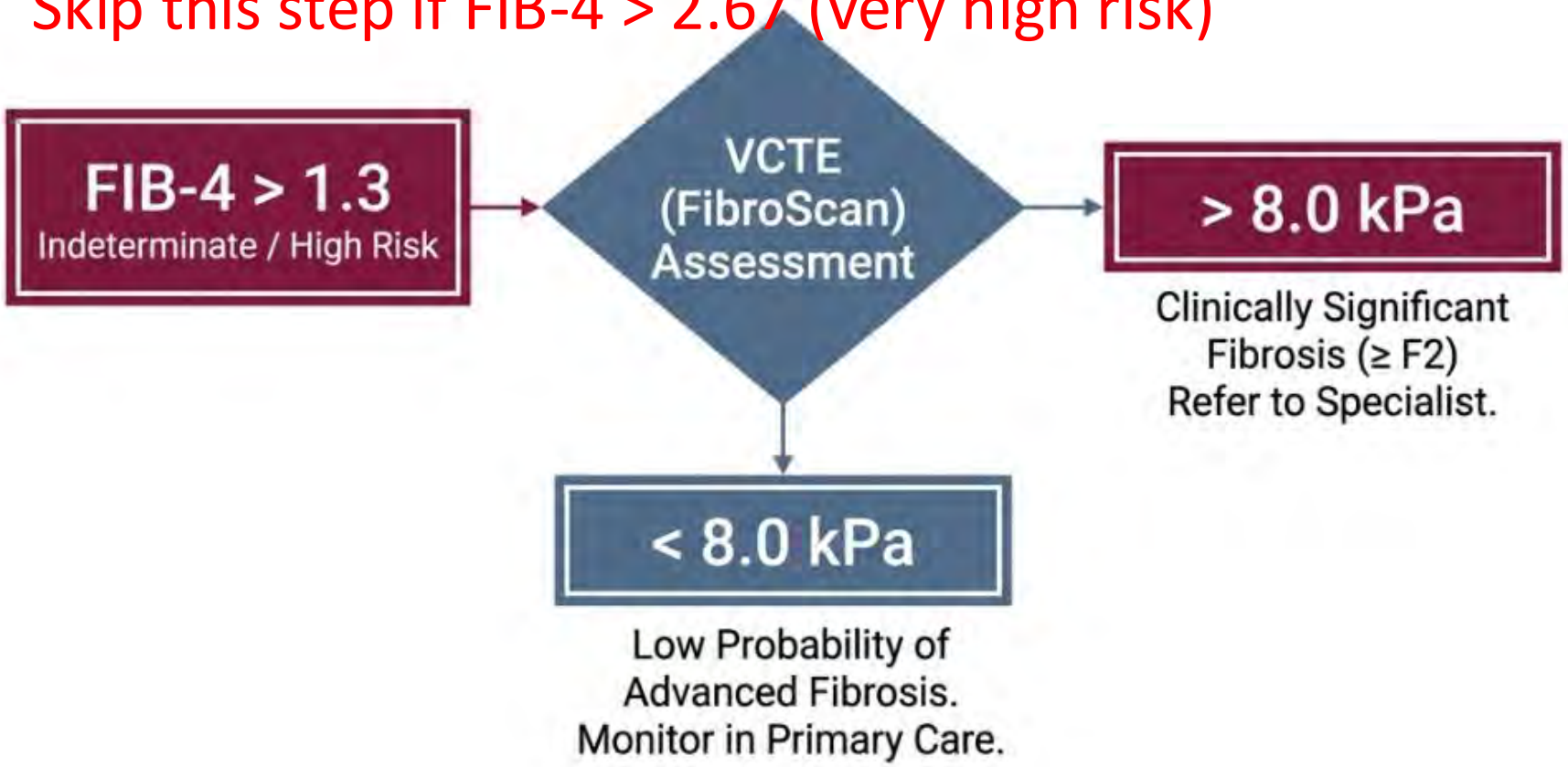
High Risk > 1.3

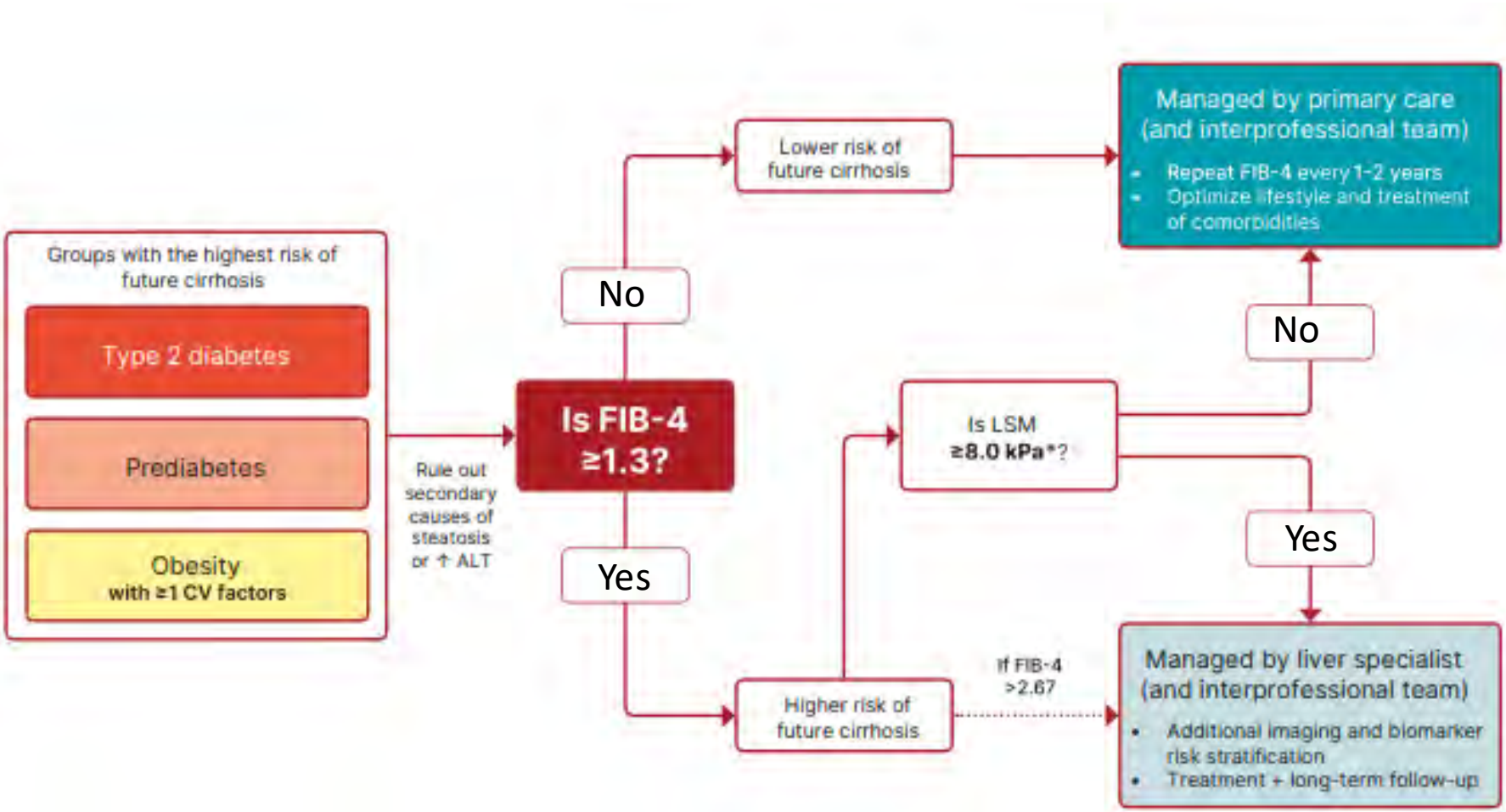
Further Risk Stratification

Step 2: Refining Risk with Second-Tier

ORDER FIBROSCAN , Liver Elastography

Skip this step if FIB-4 > 2.67 (very high risk)




Groups with the highest risk of future cirrhosis
Type 2 diabetes
Prediabetes
Obesity
with ≥1 CV factors
Rule out secondary causes of steatosis or ↑ ALT
Is FIB-4 ≥1.3?
No
Yes
Lower risk of future cirrhosis
Managed by primary care (and interprofessional team)
Repeat FIB-4 every 1-2 years
Optimize lifestyle and treatment of comorbidities
Is LSM ≥8.0 kPa*?
No
Yes
Higher risk of future cirrhosis
If FIB-4 >2.67
Managed by liver specialist (and interprofessional team)
Additional imaging and biomarker risk stratification
Treatment + long-term follow-up

Pillar 1: Lifestyle as Medicine

Nutritional Therapy

- Mediterranean Diet (Gold Standard).
- Minimize Ultra-Processed Foods.
- Restrict High-Fructose Corn Syrup & Added Sugars.

Physical Activity

- Aerobic: 150 min/week moderate intensity.
- Resistance Training: 2-3 times/week to prevent Sarcopenia.

Even without weight loss, exercise improves liver fat and insulin sensitivity.

Pillar 2: The "Double Duty" Agents

Pharmacotherapy for T2D/Obesity with Liver Benefits

PREFERRED (Evidence of MASH Efficacy)	
✓ GLP-1 RAs (Semaglutide)	Potent weight loss, reduction in liver fat, and MASH resolution
✓ Dual GIP/GLP-1 RAs (Tirzepatide)	
✓ Pioglitazone	

NEUTRAL / MODEST LIVER DATA	
• SGLT2 Inhibitors	Excellent cardiorenal protection, but modest liver steatosis reduction
• Metformin / DPP-4i	Neutral for liver histology

Pillar 3: The New Era of MASH-Targeted Therapy

RESMETIROM

- **Class:** THR-β Agonist (Thyroid Hormone Receptor Beta).
- **Indication:** Adults with MASH and moderate/advanced fibrosis (F2-F3).
- **Mechanism:** Improves mitochondrial function and fat metabolism.
- **Key Requirement:** No liver biopsy required for initiation (NIT diagnosis sufficient).

Caution: Monitoring: Check thyroid function and watch for interactions.

Ketogenic Diets & MASLD / MASH

Mechanism

Carbohydrate restriction reduces hepatic de novo lipogenesis and insulin levels, shifting metabolism toward fatty acid oxidation and ketone production — directly targeting the pathophysiology of MASLD.

Evidence of Benefit

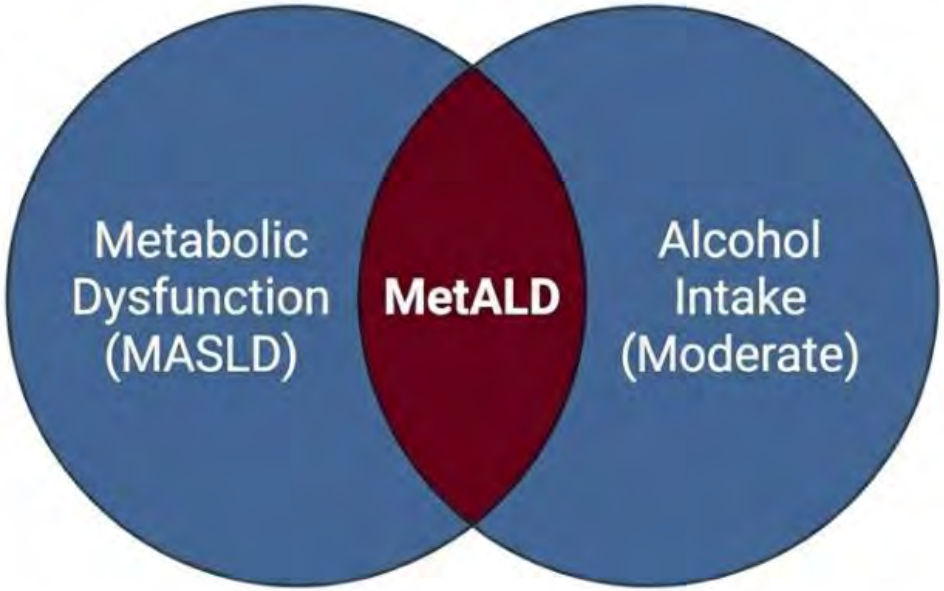
- ↓ Intrahepatic triglyceride (up to 40–50% reduction in trials)
- Improvements in ALT, insulin resistance, and histologic steatosis
- Weight loss of 5–10% — threshold for MASH improvement

Practical Concerns

- Long-term adherence is challenging — consider low-carb as alternative
- Monitor lipids: LDL may rise, especially with saturated fat excess
- Limited long-term RCT data on fibrosis regression and hard outcomes

DON’T FORGET OTHER CAUSES OF LIVER DISEASE

The Toxicity Synergy: Alcohol and MetALD



Definition

- Women: 20–50g alcohol/day.
- Men: 30–60g alcohol/day.

CLINICAL ACTION: For patients with significant fibrosis (≥ F2), recommend **COMPLETE ABSTINENCE.**

1 to 3 drinks a day for women, 2 to 4 drinks a day for men

Alcohol Use Disorder is Common and Treatable

- Ask every patient about ETOH
- Blood tests for ETOH (
- Consider Behavioral Therapy
- Naltrexone 50 mg PO tab daily
- Long-Acting Injectable Monthly Naltrexone (Vivitrol)
- Campral (Acamprosate) - 2 tabs 3 x / day, ok with opiates, suboxone, fentanyl patches.

- Stopping ETOH does not treat underlying mental health problems (if self-medicating, you are taking away the medication, replace with something safer).

Hepatitis B & C in Patients with MASLD

Screening

- Universal HBV & HCV screening recommended for all adults (USPSTF)
- All MASLD patients: HBsAg, anti-HBs, anti-HBc, anti-HCV
- HCV RNA confirmation if anti-HCV positive
- Co-existing viral hepatitis accelerates fibrosis progression in MASLD
- Re-screen if ongoing risk factors (IVDU, high-prevalence birth cohort)

HBV Vaccination

- Vaccinate all non-immune MASLD patients (anti-HBs <10 mIU/mL)
- Heplisav-B (2-dose): preferred for adults ≥18 — stronger immune response
- Standard series: Engerix-B or Recombivax (3-dose, 0-1-6 months)
- Check anti-HBs titer 1–2 months post-series to confirm immunity
- Revaccinate non-responders; consider double-dose for immunocompromised

Treatment

- HCV: DAAs (e.g., sofosbuvir/velpatasvir) cure >95% – treat ALL patients
- HCV cure reduces fibrosis progression and hepatic decompensation risk
- HBV: Tenofovir or entecavir for active disease (elevated ALT + high viral load)
- HBV reactivation risk: screen before immunosuppressants/biologics
- Coordinate with hepatology for cirrhotic patients or complex co-infections

Analgesic Use in MASLD / Liver Disease

Acetaminophen (Tylenol)

- Generally SAFE in compensated liver disease
- Preferred analgesic over NSAIDs in cirrhosis
- Limit to ≤2 g/day (reduced from standard 4 g/day)
- Avoid in acute liver failure or active heavy alcohol use
- Short-term use at low doses is well-tolerated

NSAIDs (Ibuprofen, Naproxen, etc.)

- AVOID in cirrhosis — risk of GI bleeding, renal injury, fluid retention
- Inhibit prostaglandins → ↓ renal blood flow in portal hypertension
- May use cautiously in early MASLD (F0–F2) without cirrhosis
- ↑ Risk of variceal bleeding and hepatorenal syndrome
- If needed short-term, use lowest dose for shortest duration

HCC Screening in Patients with Cirrhosis

Surveillance Protocol

Ultrasound ± AFP
every 6 months

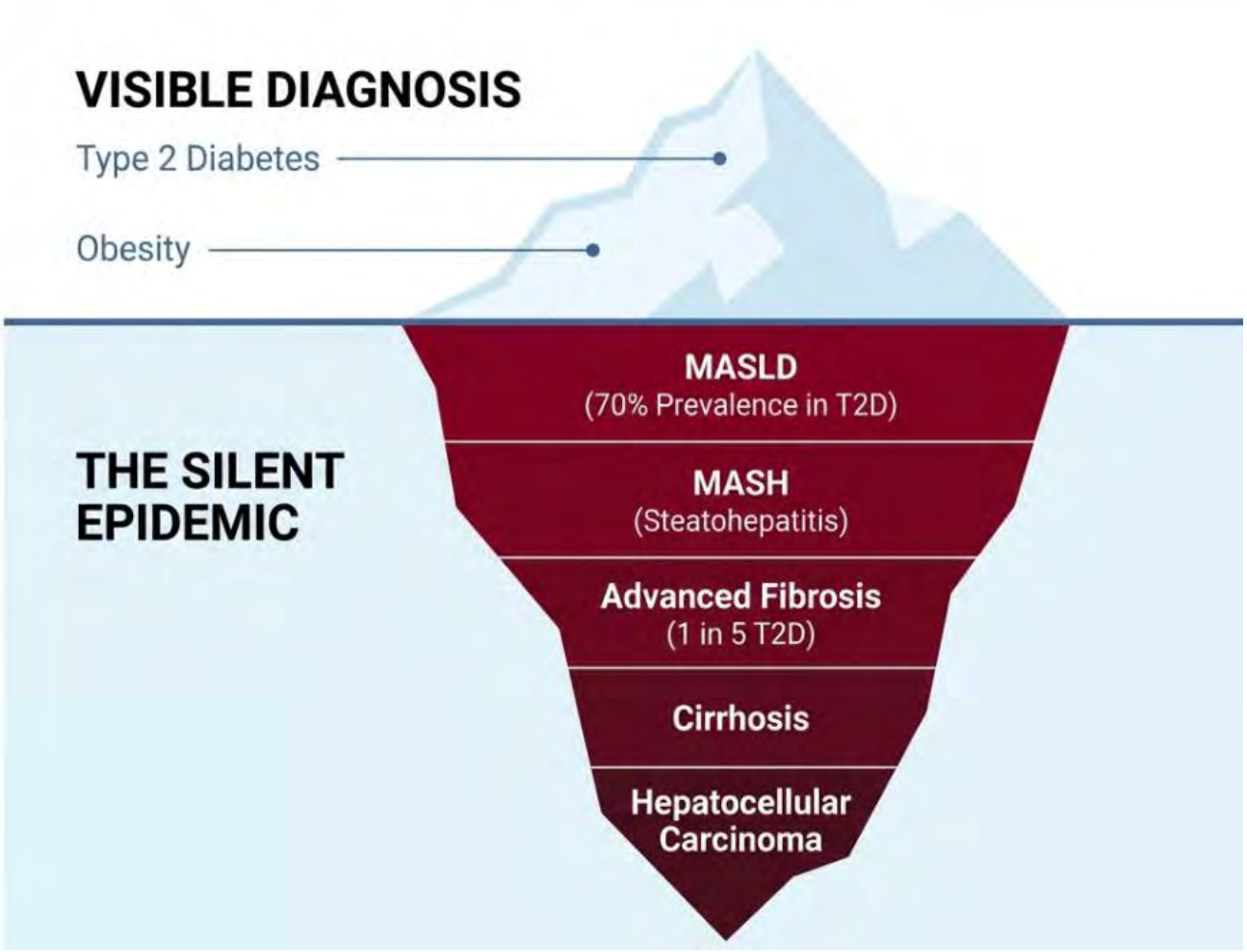
All patients with cirrhosis regardless of etiology, including MASLD-related cirrhosis

Who to Screen

- All patients with cirrhosis (Child-Pugh A, B, or C)
- HBV carriers — even without cirrhosis (higher baseline HCC risk)
- Consider screening in advanced fibrosis (F3) with MASLD or HCV

Practical Pearls

- US sensitivity is lower in obesity — consider CT/MRI if inadequate views
- AFP alone is insufficient — use in combination with ultrasound
- Abnormal screening → multiphase CT or MRI with contrast (LI-RADS)



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Annual rates

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TOP 10 Actions for MASLD in T2D

Medications:

1. Semaglutide, Tirzepatide
2. Pioglitazone
3. Oral Naltrexone or IM Vivitrol

Vaccinations

4. Heplisav-B x2

- **Labs:**
  5. CBC
  6. HBsAg, Anti-HBs, Anti-HBc
  7. Anti-HCV antibody
  8. AFP
- **Imaging:**
  9. Fibroscan
  10. Liver ultrasound