A Primary Care MD Talks About Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD)

The more definitive, less stigmatizing, new term for Non-Alcoholic Fatty Liver Disease (NAFLD)

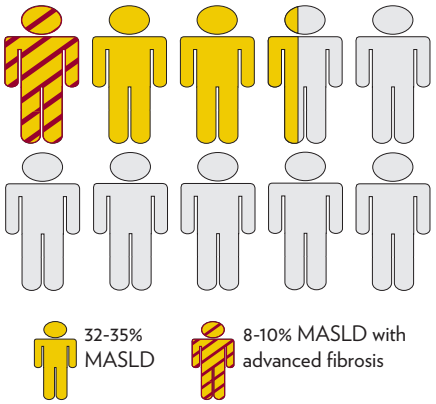
Primary Care provides the opportunity to prevent development of hepatic and extrahepatic complications.

HELPING YOUR PATIENTS IMPROVE LIVER HEALTH IS DOABLE

Discuss with your patient the importance of addressing a MASLD diagnosis to prevent, reverse, or minimize disease progression.

- MASLD is the presence of fat in the liver (often an incidental finding on imaging) PLUS at least one of five cardiometabolic risk factors (CMRFs - *See reverse page*) in the absence of significant alcohol consumption or other discernible causes.[1]
- MASLD may be asymptomatic initially and can progress to advanced fibrosis, cirrhosis, complications of cirrhosis, and death.
  - Fibrosis is the **primary cause** of liver-related complications and mortality.[2]
- Opinions differ on MASLD screening with non-invasive tests when there is no evidence of fat in the liver.

Predicted Prevalence of MASLD and MASLD with Advanced Fibrosis in U.S. Adults



Assess severity of liver disease with non-invasive tests and take action based on severity.

- MASLD guidelines and guidances recommend calculating a Fibrosis-4 Index (FIB-4) as the initial screen for advanced liver fibrosis (F2 or higher)[3] to help estimate the amount of scarring.
- A FIB-4 score uses patient age and **readily available** lab values.
- This single screen has good negative predictive value to rule out advanced liver fibrosis; higher scores necessitate additional testing.

FIB-4 Calculator

$$\text{FIB-4} = \frac{\text{Age } (\textit{years}) \times \text{AST Level } (\textit{U/L})}{\text{Platelet Count } (\textit{10}^9\textit{/L}) \times \sqrt{\text{ALT } (\textit{U/L})}}$$

LIVER FIBROSIS RISK STRATIFICATION IN ADULTS

Useful initially and ongoing to predict disease risk/progression and assess response to treatment

FIB-4 SCORE[4]	RISK	NEXT STEPS AND ONGOING MONITORING		
< 1.3 (age < 65)	Low	*Calculate* every 1 – 2 years if T2DM/prediabetes or ≥ 2 CMRFs		
< 2.0 (age ≥ 65)		*Calculate* every 2 – 3 years if no T2DM and < 2 CMRFs		
1.3 – 2.67 (age < 65)	Indeterminate	*Confirm risk assessment:* Liver Stiffness Measurement (LSM) by VCTE or ELF blood test	LSM < 8 kPa or ELF < 7.7	Manage as low risk
2.0 – 2.67 (age ≥ 65)			LSM ≥ 8 kPa[6,7] or ELF ≥ 7.7[6,7]	Refer to a specialist
> 2.67	High[5]			

Any patient plan at any disease stage requires good nutrition, active lifestyle, good sleep, and stress management.

KEY: CMRFs Cardiometabolic Risk Factors; **ELF** Enhanced Liver Fibrosis blood test; **T2DM** Type 2 Diabetes Mellitus; **VCTE** Vibration-controlled Transient Elastography (ultrasound-like test)

1. Metabolic dysfunction-associated steatohepatitis (MASH) is the more severe form of MASLD with evidence by biopsy of inflammation and hepatocellular injury with or without fibrosis. **2.** Non-hepatic cancers occur in the absence of fibrosis. **3.** Stages of fibrosis (amount of scarring): F0 – none; F1 – mild; F2 – moderate; F3 – severe; F4 – cirrhosis. **4.** Lower accuracy in patients < 35 years old. **5. Consider referral to specialist for FIB-4 > 2.67 without a confirmatory risk assessment. 6.** LSM 8 - 12 kPa or ELF 7.7 - 9.8 indeterminate risk; LSM > 12 kPa or ELF > 9.8 high risk. **7.** FIB-4 and VCTE may be the better multi-test combination.

Engage all patients in ways to eat healthy, get moving, and drink less or stop drinking alcohol to prevent progression and possibly reverse MASLD.

- Lifestyle changes are at the core of MASLD management. Frequent visits and continued support to monitor progress and reinforce individualized goals are worth it.
- Weight reduction of just 5% or more may **reduce** liver fat; 10% or more may **reverse** liver fibrosis.
  - Guidelines commonly recommend the Mediterranean diet to focus on "good calories" and instill healthier eating habits.
  - *REMEMBER*: the best diet to lose weight is the one the patient is likely to follow and maintain.
- Regular exercise has hepatic and cardiometabolic benefit **independent of weight loss**.
  - Both aerobic and resistance exercise are beneficial and can improve muscle mass; regularity in exercise is key.
- Smoking cessation is an important addition to ongoing conversations about lifestyle changes.

TALK ABOUT HEALTHY EATING TIPS

LESS	MORE
• Soda, sugary drinks	• Water, coffee, unsweet tea
• Fruit juice	• Fruits and vegetables
• Fast food	• Home-cooked meals
• Red meat, deli meats	• Fish, chicken
• White bread, rice, pasta	• Whole grains, fiber
• Saturated fat	• Healthy fats

Watch your sodium, check labels for "Added Sugars," limit alcohol, enjoy 1 - 3 cups of coffee, consider probiotics

TALK ABOUT PHYSICAL ACTIVITY GOALS

- MOVE every day
- Increase weekly activity by 60 minutes or more
- Aim for at least 150 minutes each week
- Aim for regular exercise 5 times each week

Manage cardiometabolic medical conditions using best practices, including evidence-supported pharmacotherapy.

MASLD CARDIOMETABOLIC RISK FACTORS

(1) BMI ≥ 25 kg/m^2 (≥ 23 kg/m^2 in Asians) OR waist circumference > 94 cm in men, > 80 cm in women, OR ethnicity adjusted

(2) Fasting serum glucose ≥ 100 mg/dL OR 2-hour post-load glucose level ≥ 140 mg/dL OR HbA1c ≥ 5.7%*

(3) Blood pressure ≥ 130/85 mmHg*

(4) Plasma triglycerides ≥ 150 mg/dL*

(5) Plasma HDL cholesterol ≤ 40 mg/dL for men and ≤ 50 mg/dL for women*

*OR on medication to manage the condition

- Offer pharmacotherapy when appropriate that treats both the cardiometabolic condition and reduces hepatocellular changes.[1]
  - **Offer moderate- to high-intensity statins to patients with dysplipidemia** to lower the risk of cardiovascular disease, the number one cause of death in MASLD patients.
    - Studies support statins are safe in MASLD, even with advanced liver disease.
- Consider pharmacotherapy for obesity if significant weight loss is not achieved with non-pharmacologic strategies alone; bariatric surgery may be a consideration.

Recognize FDA's conditional approval of the first medication to treat steatohepatitis with moderate to advanced liver fibrosis (F2 – F3) when combined with diet and exercise.[2,3]

- Patients showed significant reduction in liver steatosis.
- A halt in progression of fibrosis and improvement in fibrosis by at least one stage were significant findings in pre-approval trials.

Medication (Brand) Strengths and Dosage Form	Typical Dosing	Select Safety Concerns[4] *Reported as generally safe; effects of long-term treatment unknown (safety in thyroid dysregulation unknown)*
Resmetirom (Rezdiffra™) 60, 80, 100 mg tablets	80 mg daily (< 100 kg) 100 mg daily (≥ 100 kg)	Limitations of use: Avoid in decompensated cirrhosis Common side effects: gastrointestinal, pruritis Increased plasma level of some statins – reduce dose of atorvastatin, pravastatin, rosuvastatin, simvastatin

1. Consider GLP-1 RAs (e.g., liraglutide, semaglutide) and pioglitazone for patients with MASLD and T2DM; weigh benefits and risks. **2.** FDA-approval is technically for noncirrhotic nonalcoholic steatohepatitis (NASH), not MASH. **3.** Continued approval is contingent upon ongoing clinical trials studying its long-term benefits. **4.** Refer to https://dailymed.nlm.nih.gov/dailymed/lookup for more detail on drug interactions, adverse effects, and medication monitoring.