METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE (MASLD) IN PEOPLE WITH DIABETES

AN OVERVIEW OF THE CONSENSUS REPORT OF THE AMERICAN DIABETES ASSOCIATION

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NO CONFLICTS OF INTEREST

WHY THE NEED FOR SCREENING AND EARLY INTERVENTION

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- **MASLD** is a **growing but often unrecognized** medical problem for people with **diabetes -particularly type 2 and when associated with obesity**
- **Liver steatosis** affects approximately **2 out of 3 people with type 2 DM** placing them at risk for MASH, cirrhosis, hepatocellular carcinoma, and liver-related mortality.
- **Prevalence of MASLD** among **pre-diabetics is between 37% and 50%**
- **MASLD is associated with extrahepatic cancers, ASCVD, and progression from pre-diabetes to diabetes.**

WHY THE NEED FOR SCREENING AND EARLY INTERVENTION

- Half of diabetics with MASLD have MASH and about 1in 5 have advanced liver fibrosis.
- MASLD is one of the most common indications for liver transplantation.
- Liver health has not been at the forefront of complications tracked for disease prevention as traditionally done for diabetic retinopathy, nephropathy, and neuropathy.

AND

Most individuals and their health care professionals remain unaware of the severe hepatic and extrahepatic health risks associated with MASLD and the need for early identification.

PURPOSE FOR THE CONSENSUS STATEMENT

- **A call to action** to screen for liver fibrosis and risk stratify people with prediabetes and type 2 diabetes, in particular if obesity is present.

A LITTLE MORE MASLD EPIDEMIOLOGY

- **In the US, MASLD prevalence** differs by ethnicity and is **highest for Hispanic,** especially **Mexican** Americans, and **lowest for Black individuals**. This is believed to be related to a combination of acquired risk factors and genetics.
- **MASH is the number one cause of liver transplantation among women.**

NOMENCLATURE

- _ _ _ _ _ changed to MASLD
  - MASLD defined at steatotic liver disease (SLD) in the presence of at least on cardiometabolic risk factor such as prediabetes or type 2 diabetes without other identifiable causes of steatosis
- _ _ _ _ changed to MASH

The aim of the new names is to highlight the pathogenic role of insulin resistance and metabolic dysfunction.

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- **NASH changed to MASH**

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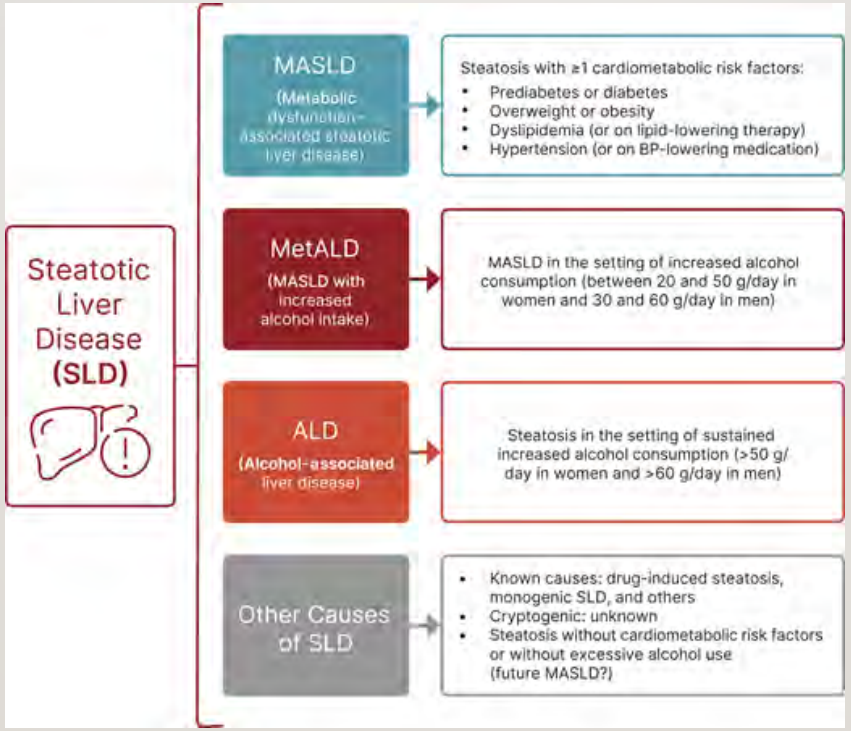
CLASSIFICATIONS OF STEATOTIC LIVER DISEASE



NOMENCLATURE

Nomenclature	Definition
Steatotic liver disease (SLD)	• An "umbrella" term encompassing different disease subcategories, characterized by predominantly hepatic macrovesicular steatosis
Metabolic dysfunction–associated steatotic liver disease (MASLD)*	• Presence of SLD with at least one metabolic risk factor (overweight or obesity or waist circumference >95th percentile, hypertension, prediabetes or type 2 diabetes, elevated triglycerides, or low HDL cholesterol) and either no alcohol consumption or consumption in amounts not likely to directly lead to liver outcomes (<20 g/day for women, <30 g/day for men)
Metabolic dysfunction–associated steatotic liver (MASL)	• Steatosis with either no or minimal lobular inflammation and without ballooning and alcohol consumption below thresholds noted above
Metabolic dysfunction–associated steatohepatitis (MASH)	• Presence of steatohepatitis and at least one metabolic risk factor for SLD and no alcohol consumption or consumption in amounts not considered likely to cause liver outcomes by itself as noted above
At-risk MASH	• Steatohepatitis (with histological MASLD activity score [MAS] ≥4) and fibrosis stage ≥F2 (i.e., people who are at a higher risk of developing future cirrhosis) (see below)
MASLD activity score (MAS)**	• Sum of scores for steatosis (0–3) plus hepatocellular ballooning (0–2) plus lobular inflammation (0–3)
Fibrosis stages	• Based on severity and distribution of scar tissue
	• Mild fibrosis: stage F1 (i.e., fibrosis in hepatic sinusoids in pericellular location)
	• Moderate fibrosis: stage F2 (i.e., sinusoidal and portal fibrosis)
	• Advanced fibrosis: stage F3 (i.e., bridging fibrosis, usually central-to-portal or central-to-central bridges) or stage F4 (cirrhosis)**
Clinically significant fibrosis	• Fibrosis stage ≥F2

SCREENING

What is the target for screening?

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- Screening for hepatic fibrosis in prediabetes and diabetes meets screening criteria …… we are applying adequate diagnostic tools to eventually treat a condition that may lead to serious morbidity and mortality.
- Several professional societies recommend screening high risk individuals for at-risk MASH to prevent fibrosis progression and cirrhosis.

SCREENING

In Prediabetes and Diabetes

- Start screening with……?

SCREENING

In Prediabetes and Diabetes

- Start with screening for hepatic steatosis by taking a medical history and checking lab work.

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- **Liver ultrasound with the presence of echogenicity is not highly specific**

SCREENING

In Prediabetes and Diabetes

- Start with screening for hepatic steatosis by taking a medical history and checking lab work.
- **Liver ultrasound with the presence of echogenicity is not highly specific**
- **Because having obesity with prediabetes and diabetes is associated with a high pretest probability of steatosis, one may proceed directly to fibrosis risk assessment.**
- In individuals with MASLD having an elevated ALT is suggestive of steatohepatitis but not necessarily of more severe fibrosis or cirrhosis.

SCREENING

- **Finding elevated liver enzymes should prompt a review of history** relative to other causes including……?

SCREENING

- **Finding elevated liver enzymes should prompt a review of history** relative to other causes including alcohol and testing for infectious causes.

SCREENING

- **Finding elevated liver enzymes should prompt a review of history** relative to other causes including alcohol and testing for infectious causes.
- **Adults with type 2 diabetes should undergo a two-tier process** for assessment for diagnosing at-risk MASH because fibrosis stage reflects proximity to development of cirrhosis.
- The first step in the two-tier process begins with lab testing to determine the Fibrosis 4 Index or **FIB-4.**

SCREENING
1ST STEP IN TWO TIER PROCESS

- The first step in the two-tier process begins with lab testing to determine the Fibrosis 4 Index or FIB-4.
  - **Check CMP, CBC, ALT, AST**
  - **Age**
- **FIB-4 score of <1.3** can reliably be used to exclude advanced fibrosis with a negative predictive value of >90%
- **FIB-4 score of > 1.3** should undergo a second test for further risk stratification.
- **FIB-4 score of > 2.67** should be referred to a gastroenterologist or hepatologist.

SCREENING
2ND STEP IN TWO -TIER PROCESS

- The second step in the two-tier process recommended by most clinical pathways is a liver stiffness measurement (LSM).
  - Most commonly measured with transient elastography (VCTE)
- A VCTE-derived LSM of <8.0 kPa rules out advanced fibrosis
  - **Can be followed in primary care with repeat surveillance every 1-2 years.**
- LSM of >8.0 should be referred to a gastroenterologist or hepatologist.

SCREENING
ALTERNATE 2ND STEP IN TWO TIER PROCESS

- **The Enhanced Liver Fibrosis (ELF) test can be used as a second-tier test** when the VCTE is not available or has limited availability.
  - Includes a panel of 3 biomarkers.
  - **ELF score < 9.8** suggests low risk for advanced fibrosis
    - May be followed by primary care with surveillance every 2 years or greater
  - **ELF score > 9.8** should be referred to gastroenterology or hepatology

From: **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. doi:10.2337/dci24-0094

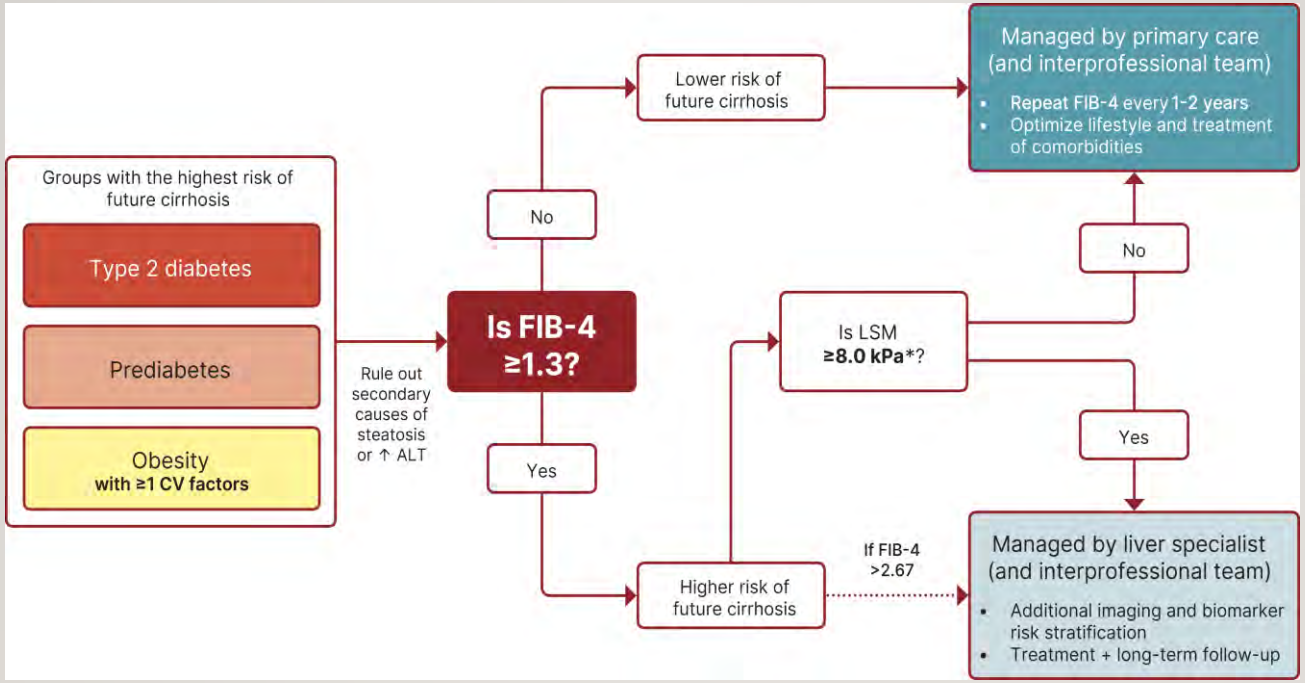

Figure Legend:

Diagnostic algorithm for risk stratification and the prevention of cirrhosis in individuals with MASLD. *In the absence of LSM, consider the blood-based ELF test as a diagnostic alternative. If ELF score is ≥9.8, a referral to a liver specialist is recommended, as there is a high risk of MASH with advanced liver fibrosis. Adapted from “Standards of Care of Diabetes—2025” (59).

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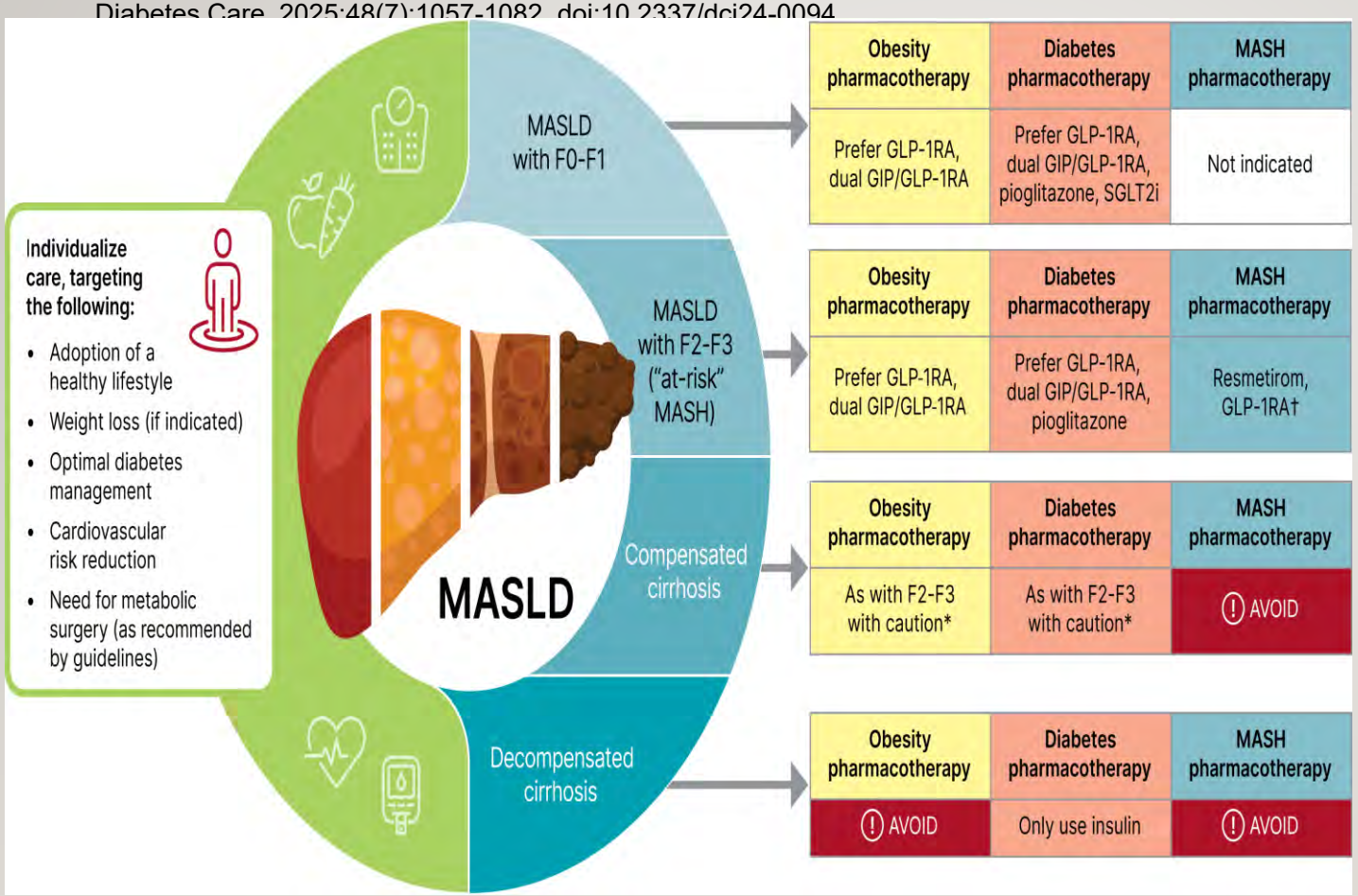

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