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Metabolic dysfunction–associated steatohepatitis (MASH)

# A hidden risk in cardiometabolic health[1]

## MASH is a chronic, progressive, and potentially life-threatening liver disease[2]

**Characterized by hepatic steatosis (excess fat accumulation in the liver) that leads to inflammation and hepatocyte ballooning (cellular injury), with or without fibrosis (scarring)[1,3]**

Previously known as nonalcoholic steatohepatitis (NASH), the term MASH now reflects its metabolic etiology[4]

## MASH is a growing epidemic in the US, yet the majority of cases remain undiagnosed[5]

According to one estimate, MASH is **projected to affect ~27 million people by 2030[5]***

Predicted to be the **#1 cause of liver transplants** among adults by 2030[6]

Recent estimates suggest approximately **5% of adults** are living with MASH[7]

**People with MASH tend to have a high burden of cardiometabolic comorbidities[3,8]**

~82% are living with obesity†

~44% are living with T2D†

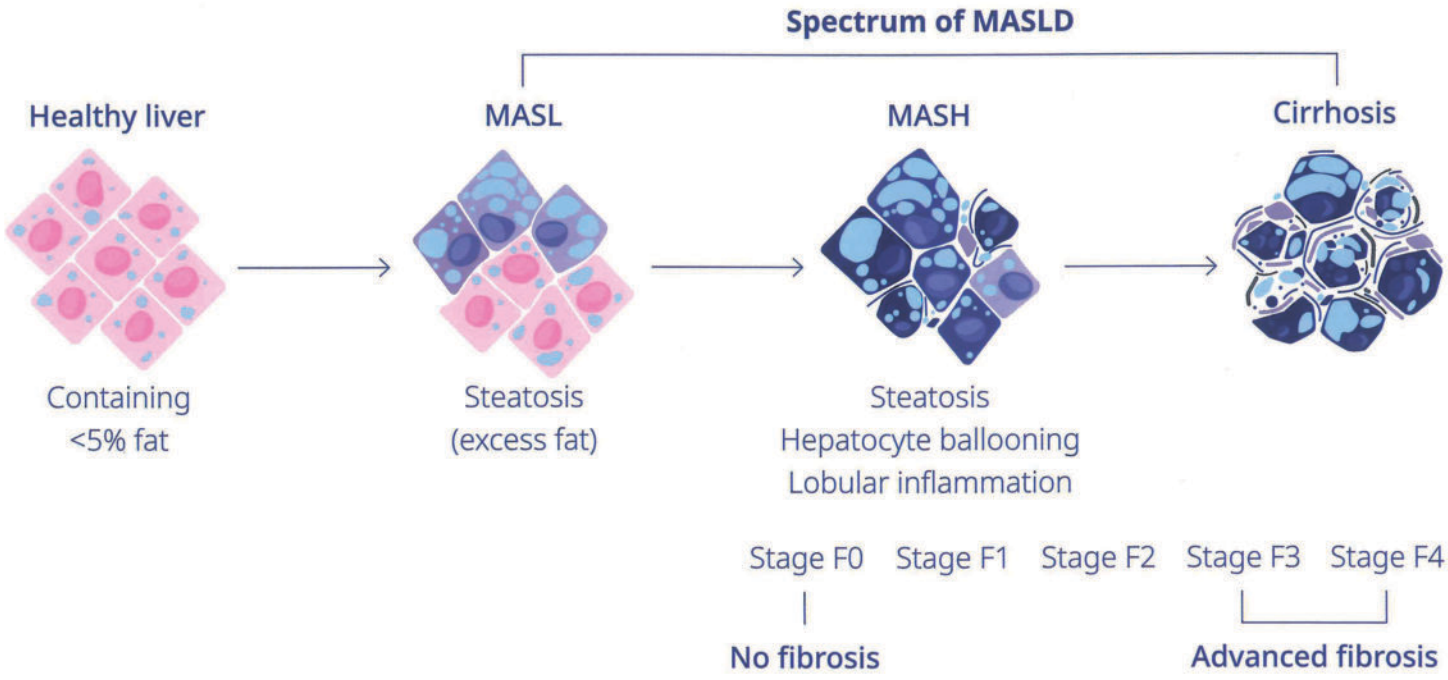
*According to estimates from a Markov model based on the assumption that approximately 20% of MASLD cases would be classified as MASH in 2015, corresponding to 3% of the adult US population.[5]

†The study utilized a systematic review and meta-analytic approach to examine global data spanning from 1989 to 2015 on the incidence, prevalence, disease progression, and burden of MASLD. The meta-analysis comprised a total of 8,515,431 patients, with North America contributing to 94% of the patient population.[8]

MASLD, metabolic dysfunction–associated steatotic liver disease; T2D, type 2 diabetes.

# MASH is a more severe form of metabolic dysfunction–associated steatotic liver disease (MASLD)[9]

**How liver damage progresses in MASLD[10,11]:**




## MASH is associated with both cardiovascular as well as liver-related outcomes[3,12,13]

**Cardiovascular disease mortality was found to be ~3X higher in patients with advanced fibrosis (F3-F4)[14]***

**~20% of patients with Stage F3 fibrosis will progress to cirrhosis over 2 years[15†]**

**HCC incidence rate was ~21X higher in MASLD cirrhosis vs non-cirrhosis[16‡]**

## Undiagnosed MASH can leave people at risk for undetected fibrosis progression[17]

*Compared to patients with F0-F2. Based on a cohort study of 229 biopsy-proven MASLD patients (n=16 in F3-F4) followed for a mean of 26.4 years. Data from the Registry of Causes of Death and the Swedish National Registry of Population were used to calculate hazard ratios and 95% confidence intervals for causes of death in the entire cohort and in histopathological subgroups against a reference population.[14]

†This study followed 475 patients with MASH and bridging fibrosis or compensated cirrhosis over 96 weeks to assess disease progression, predictors of fibrosis progression, and monitoring strategies.[15]

‡In stratified analyses, MASLD cirrhosis (n=16,291) carried a higher HCC incidence rate than non-cirrhosis (n=1,795,170). This prognostic study included 1,811,461 Kaiser Permanente Northern California adult patients, enrolled from 2009-2018 and followed retrospectively until HCC development, death, disenrollment, or study termination up to 2021.[16]

HCC, hepatocellular carcinoma; MASH, metabolic dysfunction–associated steatohepatitis; MASL, metabolic dysfunction–associated steatotic liver.

# Consider primary risk assessment with the FIB-4 test to evaluate the risk of advanced fibrosis in patients with metabolic risk factors such as obesity and T2D[17]

## Noninvasive tests (NITs) provide an accessible approach to early detection of advanced fibrosis and can be integrated into primary care[1,10]

- **Suspect:** Review the guidelines and use NITs to screen your appropriate patients
- **Detect:** Use NITs to screen for and detect MASH in people who are at risk (**utilize lab values** that may already be evaluated as part of routine blood work)
- **Review:** After reviewing guidelines and using NITs, speak to your patient about how you both can act against MASH

**The Fibrosis-4 (FIB-4) score is calculated based on 4 parameters[1]:**
age (years), AST (U/L), ALT (U/L), and platelet count ($10^9$/L)

$$\frac{\text{Age x AST}}{\text{Platelet count x } \sqrt{\text{ALT}}}$$

If you do not have these values available, FIB-4 tests can be ordered from major lab companies such as Labcorp and Quest Diagnostics.[18,19]

## Select AACE- and AASLD-recommended NITs to screen for MASH with advanced fibrosis[10,17]

**Primary fibrosis risk stratification: FIB-4**

A screening tool for advanced fibrosis

| Low risk | Intermediate/indeterminate risk | High risk |
|---|---|---|
| FIB-4 <1.3 | FIB-4 1.3-2.67 | FIB-4 >2.67 |

↓

**Secondary fibrosis risk stratification: vibration-controlled elastography (VCTE) or Enhanced Liver Fibrosis (ELF™)**

**VCTE (eg, FibroScan):** Ultrasound-based method to assess liver stiffness and to exclude significant fibrosis
**ELF™:** Blood-based biomarker to assess the risk of progression to cirrhosis and liver-related clinical events

| Low risk | Intermediate/indeterminate risk | High risk |
|---|---|---|
| VCTE <8 kPa **or** ELF™ <7.7 | VCTE 8-12 kPa **or** ELF™ 7.7-9.8 | VCTE >12 kPa **or** ELF™ >9.8 |

↓

| | |
|---|---|
| Refer to primary care, endocrinology, or other specialties for cardiometabolic risk reduction | Refer to gastroenterology or hepatology |

## Start with FIB-4 first so you can determine next steps in MASH management[1]

AACE, American Association of Clinical Endocrinology; AASLD, American Association for the Study of Liver Diseases; ALT, alanine aminotransferase; AST, aspartate aminotransferase; MASH, metabolic dysfunction–associated steatohepatitis; T2D, type 2 diabetes.

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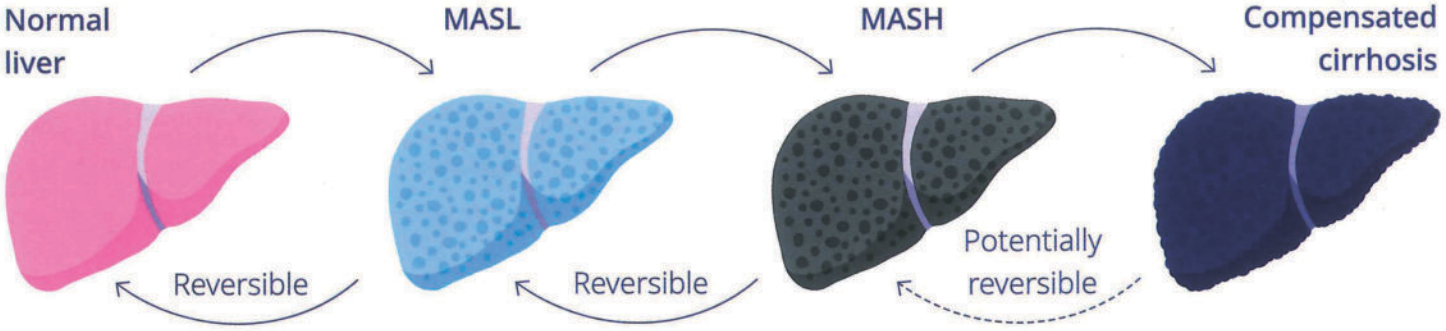
# Steatosis and fibrosis may be reversible[10,11,17,20,21]




## Early and routine screening by all health care professionals can be a critical component to identify patients at risk of disease progression and fibrosis[17,22]

## To learn more about MASH, visit **MASHawareness.com**

MASH, metabolic dysfunction–associated steatohepatitis; MASL, metabolic dysfunction–associated steatotic liver; MASLD, metabolic dysfunction–associated steatotic liver disease.

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