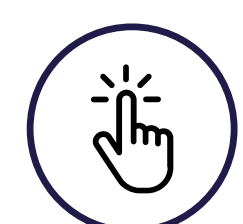


Disease Progression Overview of Metabolic Dysfunction–Associated Steatohepatitis (MASH)

The purpose of this resource is to educate the user on the progression of MASH and highlight the importance of early recognition and intervention

Use the links below to explore each stage of the disease

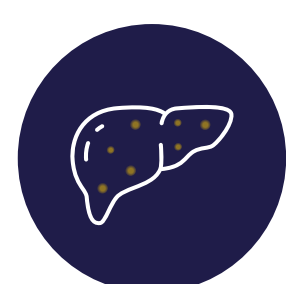


Overview



Healthy Liver

Normal amount of fat



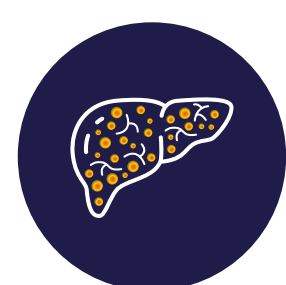
Steatotic Liver

Fat buildup



MASH

Toxic fat buildup and inflammation



MASH With Fibrosis

Toxic fat buildup, inflammation, and scarring or fibrosis



Cirrhosis

Severe scarring or fibrosis and possible permanent damage

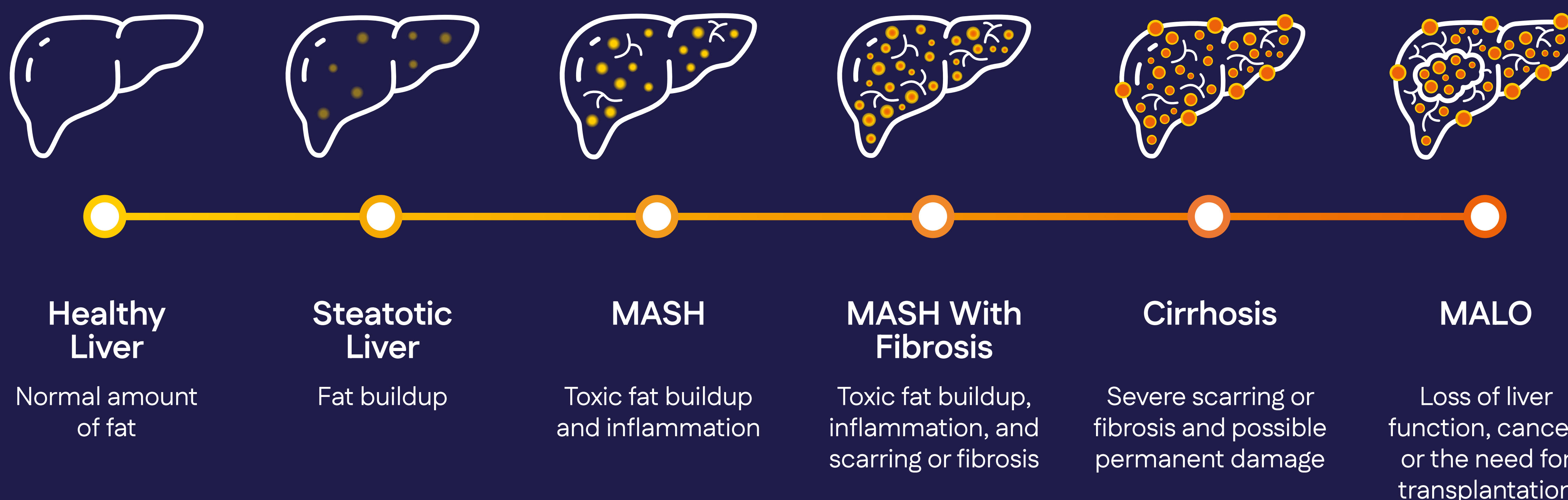


MALO

Loss of liver function, cancer, or the need for transplantation

Progression of MASH from steatosis to cirrhosis and MALO

The natural history of MASLD is **complex and variable**. Some patients develop **inflammation** and risk **progressive fibrosis** that can result in **cirrhosis**^{1,2}



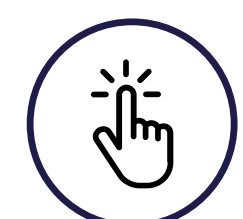
Fibrosis progression in MASLD/MASH is unpredictable and may occur rapidly, even in early disease stages.^{1,2} In a **subset of patients**, MASLD/MASH can **progress to cirrhosis** in as little as **3 years** from the date of diagnosis³



Optimise patient outcomes

Early risk stratification for advanced fibrosis in patients with MASLD/MASH is critical for optimisation of patient outcomes⁴

Use the links below to explore each stage of the disease



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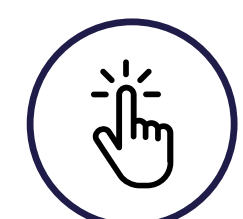
The liver is located in the upper right of the abdominal cavity, is a dark reddish-brown colour, and weighs approximately 1400 grams



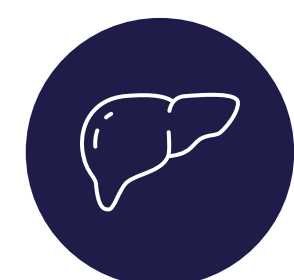
The liver regulates many metabolite levels in the blood

Functions include production of bile, production of cholesterol, glucose homeostasis, and production of certain proteins for blood plasma

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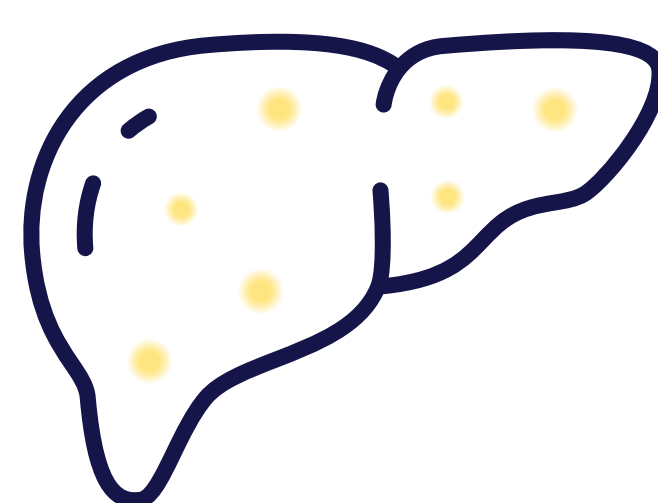
Fat buildup

< Healthy Liver

MASH >

The presence of **excess triglycerides** in the liver is called **hepatic steatosis**¹⁻³

MASLD



MASLD is defined as the **presence of hepatic steatosis** in conjunction with **at least one cardiometabolic risk factor** and **no other discernible cause**^{1-3,a}



38% of all adults^{4,b} and 13% of children and adolescents^{5,c} have MASLD worldwide

^aMASLD can coexist with other causes of chronic liver injury.¹

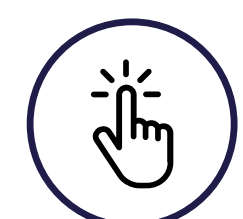
^bBased on a meta-analysis of 23 studies involving 48,044 individuals. Study period: 2016-2019.⁴

^cBased on a meta-analysis of 27 studies involving 34,112 individuals published between 2005 and 2022.⁵

EASD, European Association for the Study of Diabetes; **EASL**, European Association for the Study of the Liver; **EASO**, European Association for the Study of Obesity; **MALO**, major adverse liver outcomes; **MASH**, metabolic dysfunction–associated steatohepatitis; **MASLD**, metabolic dysfunction–associated steatotic liver disease.

1. Rinella ME et al. *J Hepatol.* 2023;79(6):1542-1556. 2. EASL, EASD, EASO. *J Hepatol.* 2024;81(3):492-542. 3. Qadri S, Yki-Järvinen H. *Diabetologia.* 2024;67(6):961-973. 4. Younossi ZM et al. *Hepatology.* 2023;77(4):1335-1347. 5. Lee EJ et al. *World J Pediatr.* 2024;20(6):569-580.

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MASH With Fibrosis >



Some patients progress from simple steatosis to **MASH**, a condition characterised by **histological features of liver injury, hepatocellular ballooning, and lobular inflammation** in the presence of hepatic steatosis, which can lead to liver fibrosis^{1,2}

Why some patients progress from simple steatosis to MASH with inflammation and increased fibrogenesis is **complex and not fully understood**²



The **global prevalence of MASH** among the general population is estimated at **5.3%**^{3,a}

Prevalent MASH cases are forecasted to increase by 45%, from 12.7 million (2016) to 18.3 million (2030) in **France, Germany, Italy, Spain, and the United Kingdom**⁴

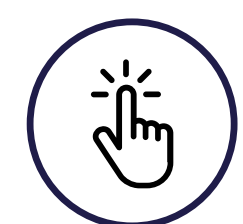
Similar trends are seen in the **United States**, where **MASH cases** are projected to **rise by 63%**, from 16.5 million (2015) to 27.0 million (2030)⁵

^aBased on a meta-analysis of 92 studies involving 9,361,716 individuals. Study period: 1990–2019.³

EASD, European Association for the Study of Diabetes; EASL, European Association for the Study of the Liver; EASO, European Association for the Study of Obesity; MALO, major adverse liver outcomes; MASH, metabolic dysfunction–associated steatohepatitis.

1. EASL, EASD, EASO. *J Hepatol.* 2024;81(3):492–542. 2. Hagström H et al. *Lancet Gastroenterol Hepatol.* 2024;9(10):944–956. 3. Younossi ZM, et al. *Hepatology.* 2023;77(4):1335–1347. 4. Estes C et al. *J Hepatol.* 2018;69(4):896–904. 5. Estes C et al. *Hepatology.* 2018;67(1):123–133.

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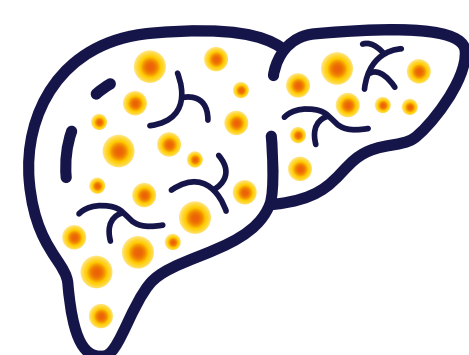


MASH With Fibrosis

Toxic fat buildup, inflammation, and scarring or fibrosis

< MASH

Cirrhosis >



As fibrosis accumulates, the risk of all-cause and liver-related mortality increases substantially¹



A retrospective cohort study of 646 patients with MASLD with a mean follow-up period of 20 years found that decompensated liver disease occurred in^{2,a}

3.7% of patients with F0

4.3% of patients with F1

8.7% of patients with F2

12.1% of patients with F3

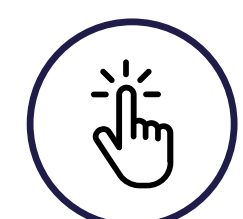
45% of patients with cirrhosis (compared with 1.8% in controls)

^aBased on a retrospective cohort study which included 646 patients with MASLD and 6,345 controls in 2 hospitals in Sweden. Study period: 1971-2009.² At baseline, patients with MASLD had F0 (n = 163), F1, (n = 255), F2 (n = 149), F3 (n = 58) and F4 (n = 20) fibrosis.

F0-F4, fibrosis stage (F0: no fibrosis, F1: mild fibrosis, F2: moderate fibrosis, F3: advanced fibrosis, F4: cirrhosis); MALO, major adverse liver outcomes; MASH, metabolic dysfunction–associated steatohepatitis; MASLD, metabolic dysfunction–associated steatotic liver disease.

1. Ng CH et al. *Clin Gastro Hep.* 2024;21(4):931-939. 2. Hagström H et al. *J Hepatol.* 2017;67(6):1265-1273.

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< MASH With Fibrosis

MALO >



Cirrhosis is the most important **risk factor** for progression to **liver transplant, development of HCC, and death**¹

Transition to cirrhosis involves **inflammatory, hormonal, and structural changes** that lead to **portal hypertension**¹

A meta-analysis of **13 multinational studies** in **4428 patients with MASLD** found that **cirrhosis was associated with an approximately**^{2,a}

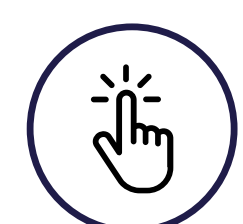
- 13x** higher rate of liver-related events
- 11x** higher rate of liver-related mortality
- 3x** higher rate of all-cause mortality (compared with patients without fibrosis)

^aMeta-analysis of 13 multinational studies in 4428 patients with MASLD (study period: 1971–2017). Of the 4428 patients, 2875 were reported to have MASH.²

HCC, hepatocellular carcinoma; MALO, major adverse liver outcomes; MASH, metabolic dysfunction–associated steatohepatitis; MASLD, metabolic dysfunction–associated steatotic liver disease.

1. Hagström H et al. *Lancet Gastroenterol Hepatol*. 2024;9(10):944–956. 2. Taylor RS. *Gastroenterology*. 2020;158(6):1611–1625.

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Major Adverse Liver Outcomes

Loss of liver function, cancer, or the need for transplantation

< Cirrhosis



MASH can progress to MASH with fibrosis, cirrhosis, or liver cancer and may ultimately lead to liver transplantation or death¹

Liver cancer remains a global health challenge, with an estimated incidence of >1 million cases by 2025²
MASLD is becoming the second leading cause of HCC behind alcohol-related liver disease³



Progression from compensated cirrhosis to decompensation events, liver transplant, or death may be rapid compared with progression at earlier stages of MASH⁴