

Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD)

What is MASLD?

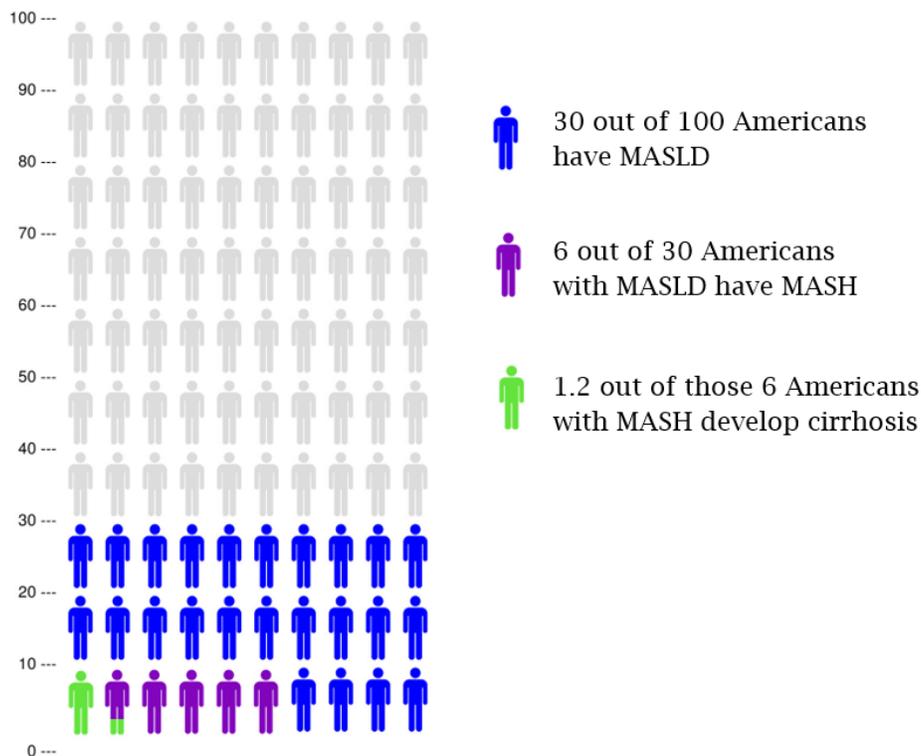
Metabolic dysfunction-associated steatotic liver disease (MASLD) is caused by a buildup of fat in the liver in people with **metabolic diseases** (like diabetes, obesity, high blood pressure, or high cholesterol) who don't drink too much alcohol. MASLD used to be called **non-alcoholic fatty liver disease, or NAFLD**, and you may still hear people call it NAFLD.

- People with MASLD generally have high levels of the hormone insulin but they are resistant to some of the actions of insulin (**insulin resistance**). This imbalance is likely to cause fat buildup in the liver.
- Fat buildup in the liver can also come from diet, increased fat production in the liver, or decreased ability of the liver to clear the fat out. **Genetics** (the health traits passed on to you from your parents) can affect all of these things as well.
- Diets that contain high amounts of carbohydrates and sugars (including fructose and high fructose corn syrup) can also cause fat production in the liver cells.

Some people with MASLD have not just fat in the liver (called **steatosis**) but also both fat and inflammation (swelling) in the liver (called **steatohepatitis**). This condition is called **metabolic dysfunction-associated steatohepatitis (MASH)**, and it is the more severe form of MASLD.

How common is MASLD and MASH?

- Up to 30 out of 100 people, or 30% of the US population, are estimated to have MASLD!
- MASLD is the most common liver disorder in the United States and most of the rest of the world. As conditions like obesity and diabetes are increasing, so is MASLD.
- MASLD is usually found on imaging tests like an ultrasound or a CAT scan. Under the microscope, the liver structures are normal, but the liver cells have accumulations of fat in them.
- About 20 out of 100 (20%) of people with MASLD are estimated to have MASH. MASH is a worsening (progressive) form of MASLD where the inflammation causes liver damage. This damage consists of cell death and scar tissue (also called **fibrosis**). Fibrosis can get worse over time, and about 20 out of 100 (20%) of people with MASH may develop severe scar tissue called **cirrhosis**.



Who is at risk for MASLD and MASH?

People with 1 or more features of metabolic syndrome are more at risk for MASLD. Also, because of similar lifestyles and genetics, people with a family history of MASLD may also be at higher risk of developing the disease.

Metabolic syndrome is defined as having 3 or more of the following features:

- Obesity (having a body mass index (BMI) greater than or equal to 30), particularly those with a large waistline or abdominal (belly) obesity
- Pre-diabetes or diabetes (People with MASLD and diabetes have a greater risk for MASH)
- Low HDL cholesterol (low levels of good cholesterol)
- High lipids (fat) called triglycerides
- High blood pressure

What are signs and symptoms of MASLD and MASH?

People with MASLD and MASH may have no symptoms or findings on a physical exam. Often, people will say they feel some discomfort in their right upper abdomen, or fatigue (tiredness). We often find MASLD when a person is having abdominal imaging tests done for other reasons.

How is MASLD diagnosed?

- Diagnosis (confirming that you have MASLD) is not always easy, because people usually have no symptoms and liver blood tests can be completely normal. Even if liver tests (such as ALT and AST) are elevated, liver tests alone cannot tell us how severe MASLD is.
- We usually diagnose MASLD when the testing for other causes of liver disease is negative and there is a certain type of fat deposit on your liver imaging tests (ultrasound, CAT scan, or MRI).

- In the past, taking a sample of the liver (called a **biopsy**) was the only way to figure out if a patient had MASLD or MASH. Doing a biopsy can also help us see how much liver damage and fibrosis (scar tissue) there is. However, there are now newer, **noninvasive** (not requiring surgery or cutting tissue) ways to find if someone has MASH.
 - Noninvasive tests, like FibroScan® (a special ultrasound for the liver), can also estimate (make a good guess about) the amount of fat and scar tissue in the liver. FibroScan® is less accurate for people with obesity, but it is a safe and simple test that can be repeated to track liver damage over time.

What are the health risks related to MASLD and MASH?

Health risks from MASLD

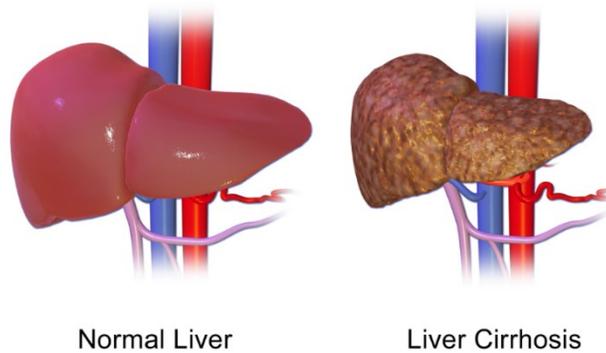
The risk of developing advanced liver disease, like cirrhosis, is low. However, patients with MASLD are at increased risk of having or developing serious medical conditions like heart disease (including heart attacks and high blood pressure) and diabetes. In fact, heart disease is the number one cause of death in patients with MASLD.

Health risks from MASH

People with MASH also have an increased risk of having or developing heart disease, including heart attacks and high blood pressure. About 20% of people with MASH may develop severe scarring of the liver (cirrhosis).

What are health issues related to cirrhosis?

- When something causes injury to the liver, liver cells are killed and scar tissue forms (fibrosis). When the entire liver is scarred, the liver becomes stiff and shrunken. This is called **cirrhosis**.



- Cirrhosis changes the way blood can flow through the vessels in the liver, and it can cause high pressure in those blood vessels (called **portal hypertension**). As normal liver cells are replaced with scar tissue, the liver stops performing some of its important functions like making proteins.
- Over time, patients with cirrhosis have increased risk for developing complications (health problems) related to their liver disease. Some of these complications are listed below.

Large blood vessels (varices) with possible internal bleeding

Because livers with cirrhosis are very stiff, pressure can build up in the blood vessels that feed the liver. This pressure makes the blood vessels around the liver grow larger than normal. These large vessels are called **varices**. Large varices that form around the **esophagus** (food tube) and stomach can burst and bleed into the gastrointestinal tract.

Fluid accumulation in the abdomen (ascites) and legs

High pressure in the veins of the liver also causes fluid to leak into the abdomen, which is called **ascites**. The feet and legs can get swollen too. This can become very uncomfortable and make eating and breathing difficult. The most dangerous problem related to ascites is infection, which can be life threatening.

Confusion (hepatic encephalopathy)

When the liver is unable to clear away toxic substances, they can build up in the bloodstream and go into the brain. This can cause changes in your behavior and sleep, as well as confusion and sleepiness. These changes are called **hepatic encephalopathy**.

Liver cancer

Livers with large amounts of scar tissue or cirrhosis have an increased risk of developing liver cancer, called **hepatocellular carcinoma**.

How is MASLD and MASH treated?

Medical experts continue to actively research MASLD, but for now, there are no specific medications that can cure MASLD. However, studies have shown that both fat, inflammation, and scar tissue can leave your liver. This means that MASLD and MASH can be **reversible**. Some ways to reverse the effects of MASLD and MASH are below.

Making lifestyle changes, including diet and exercise

Reducing liver fat and inflammation is possible when people lose weight and change their lifestyle. This is the first recommended treatment for MASLD and MASH.

- Lifestyle changes include eating a healthy diet as well as increasing physical activity. The goal is that these changes will become a regular part of your daily routine for the rest of your life.
- Losing 10% of your total current body weight makes it more likely that you will reduce the amount of fat and inflammation in your liver. Weight loss must be slow (not losing more than 1-3 pounds per week), since fast weight loss can actually make your liver disease worse.

Taking medications

Sometimes we may ask people diagnosed with MASH to start taking vitamin E (in a particular type called alpha-tocopherol).

- Vitamin E is an antioxidant that experts think helps reduce liver inflammation.
- This medicine may be less helpful or less safe for people with diabetes or significant heart disease, so **do not start this medication without talking with your liver doctor first.**

Managing any other diseases

Improving your control of any other metabolic diseases you have, such as diabetes, high blood pressure and high cholesterol or lipids, can also help your MASLD.

Avoiding alcohol

Heavy alcohol use can cause extra damage and fat buildup in the liver.

- Heavy alcohol use in women means having 7 or more drinks per week, or 4 or more drinks on the same day. In men, heavy alcohol use means having 14 or more drinks per week, or 5 or more drinks on the same day.
- People with MASLD should stop drinking alcohol entirely if possible. If you do not think you can completely stop drinking alcohol, it is important to reduce the amount of alcohol you drink to less than 7 drinks per week for women and less than 14 drinks per week for men.

What medications can I take safely with MASLD or MASH?

- People with cirrhosis must avoid pain medications called **non-steroidal anti-inflammatory drugs (NSAIDs)**. These include over-the-counter medications such as ibuprofen (Motrin® or Advil®) and naproxen (Aleve® or Naprosyn®), as well as some prescription medications. Ask your doctor if any of your medications are NSAIDs.

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- It is safe to take acetaminophen (Tylenol®), at doses of 2000 milligrams or less a day.
 - This means that you should take no more than 6 regular strength pills, or no more than 4 extra strength pills, each day. You should not take more than 20 regular strength pills, or more than 15 extra strength pills, each week.
 - Some cold medications and prescription pain medications contain acetaminophen, so read the labels and make sure you don't take too much by mistake.
- Unless your doctor says otherwise, statin medications (such as Lipitor®, Crestor®, or Zocor®) are completely safe for people with early cirrhosis.

What vaccinations should I get?

- Those who are not immune to hepatitis A and B should get those vaccines. This will prevent significant liver damage if you are exposed to either of these viruses.
- We also recommend that you get the influenza vaccination (flu shot) every year.

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