

# The Language of NASH

A narrative to guide communication on NASH

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## Background

Nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH) are serious, chronic, and progressive liver conditions affecting millions of people worldwide<sup>1</sup> and the prevalence of NASH could increase by over 50% by 2030.<sup>2</sup> NAFLD occurs when too much fat accumulates in the liver. NASH is caused when that extra fat leads to inflammation and injury of the liver.<sup>3,4</sup>

There are several reasons people may develop NASH including genetic predisposition and the presence of metabolic disorders<sup>5,6</sup> such as obesity, Type 2 diabetes, high cholesterol, hypertension<sup>1,3,7</sup> or other cardiovascular disease (CVD).<sup>1,8</sup>

NASH is currently underdiagnosed due to a lack of disease awareness, symptoms which are difficult to identify, current screening procedures, and limited treatment options.<sup>3,5,9</sup> Screening guidelines are necessary to respond to the growing incidence.

Following a healthy lifestyle can help reduce the risk of NASH.<sup>10–13</sup> Left untreated, NASH can progress into cirrhosis, liver cancer, the need for a liver transplant, or result in death.<sup>2,3,14</sup>

However, the NASH story is changing. With new treatments in the pipeline, more ways to identify the disease beyond biopsy, and more scientific research, there is hope for the future of this pervasive and life-threatening disease.

## The challenge

**The field of NASH is evolving rapidly. This rapid pace has contributed to a complex NASH story and an inconsistent lexicon that can result in messages becoming unclear and confusing for key audiences.**

There is a lack of consensus on the appropriate terminology relating to NASH – including the ongoing dialogue around NAFLD vs MAFLD – as well as disparity in agreed prevalence rates and the scale of the impact in NASH.<sup>3,5</sup>

Each of these are attributing to a lack of awareness of the condition and/or under diagnosis<sup>5</sup> and has the potential to negatively impact patient outcomes.

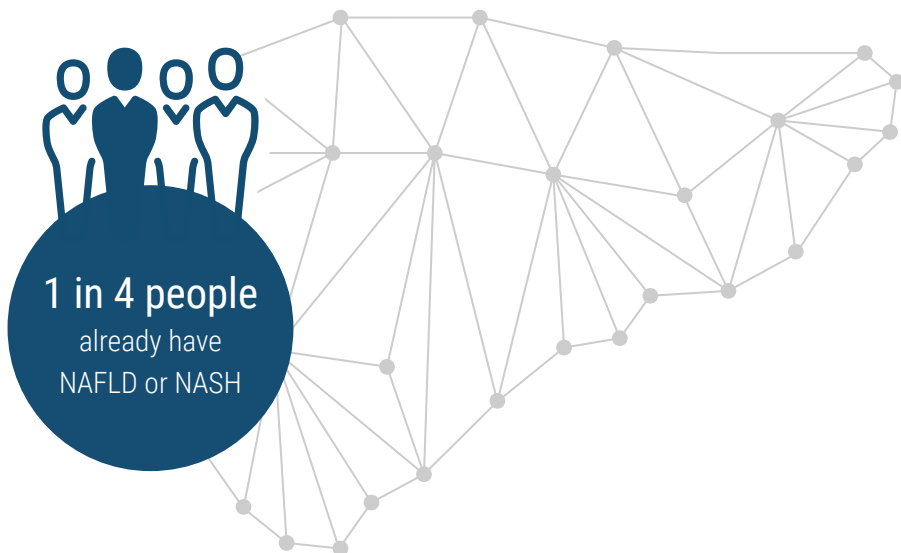
In light of this, the Global Liver Institute, along with our NASH Council, has developed this core NASH message framework that should be used as a foundation for communication.



## Key messages

### 1. What is NASH?

- NASH is a chronic, progressive, and life-threatening liver disease that affects millions of people globally<sup>1</sup>
- Current estimates show that as many as 1 in 4 people already have NAFLD or NASH<sup>2,3</sup> yet these conditions are under recognized, under diagnosed, and undertreated<sup>3,5</sup>
- NASH is the most severe form of NAFLD, which includes accumulation of fat in the liver, inflammation, and injury (ballooning) with or without scarring (fibrosis).<sup>4</sup> 1 in 4 people have NAFLD (25–30%), and 2–6% have NASH<sup>3</sup>
- NAFLD and NASH can be reversed, but left untreated it can progress into other conditions such as cirrhosis, liver cancer, or result in death<sup>2,3,14</sup>

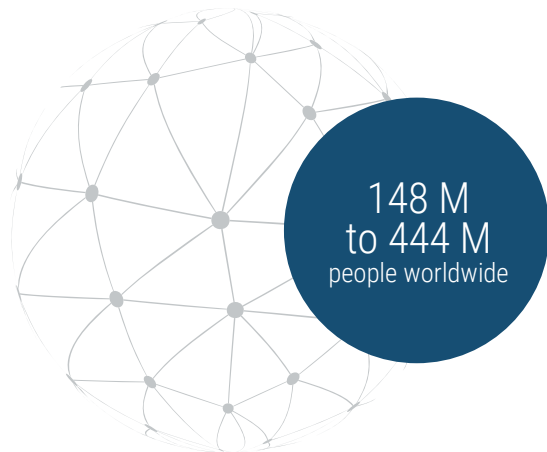


### 2. Why is NASH important?

- NASH is an epidemic, affecting more than 148 million people worldwide<sup>15</sup>
- NASH impacts individuals, families, and communities.
- Having NASH can increase the risk of liver failure, requiring liver transplant<sup>2,3,14</sup>
- Untreated, NASH can progress into cirrhosis, liver cancer, or result in death.<sup>2,3,14</sup> NASH is the second leading cause of liver transplant in the US and is predicted to become the leading cause<sup>16</sup>
- NASH is closely associated with metabolic disorders<sup>1,3,5–7</sup> and people with NASH are at a higher risk of developing cardiovascular disease.<sup>1,8</sup> Cardiac-related deaths are one of the leading causes of death for people living with NASH or nonalcoholic fatty liver disease<sup>8</sup>
- NASH is under diagnosed due to a lack of disease awareness, symptoms which are difficult to identify, lack of consensus on current screening procedures, and limited treatment and management options<sup>3,5</sup>
- People with NASH can remain unaware of their liver condition until the disease progresses to where it is often too late to reverse<sup>17</sup>
- NASH impacts individuals, families, and communities, and is predicted to increase.<sup>2</sup> This will present a huge future burden on healthcare budgets and reinforce the need for inexpensive screening methods<sup>5</sup>

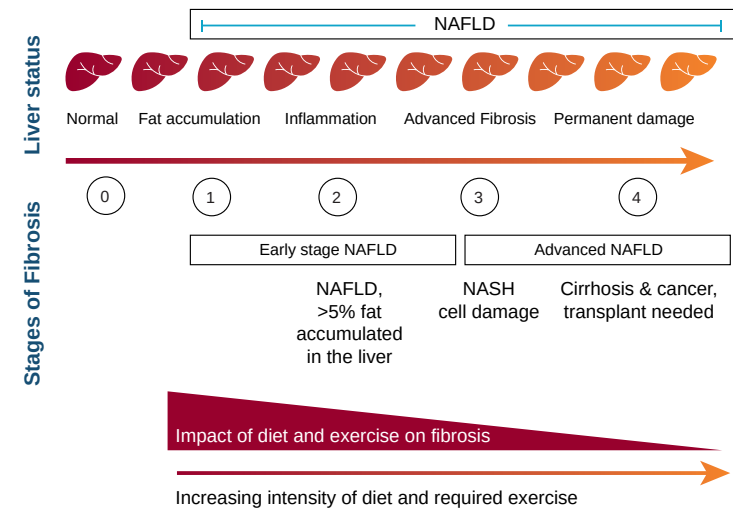
### 3. How prevalent is NASH?

- Nonalcoholic fatty liver disease is becoming the most common chronic liver condition globally and it is estimated that 1 in 4 people have NAFLD (25–30%).<sup>2,4</sup> Of those, 1 in 5 people (20–25%) living with NAFLD will develop NASH<sup>2</sup>
- The most recent estimates for NASH prevalence are between 2% and 6%.<sup>3</sup> Based on global population figures, this equates to an estimated 148 million to 444 million people worldwide<sup>15</sup>
- Whilst prevalence of NASH is increasing, there can be many aspects to treating NASH. Lifestyle modifications can have an impact on NASH progression and can even reverse the disease in early stages<sup>10,11</sup>



### 4. NAFLD and NASH

- NAFLD describes a spectrum of liver disease including NASH through to cirrhosis<sup>3,4</sup>
- Early stage NAFLD is when fat accumulates in the liver with little or no inflammation or liver cell damage<sup>3,4</sup>
- Left untreated, NAFLD can progress to NASH, which is characterized by the accumulation of fat in the liver, inflammation and injury to the liver cells with or without scarring<sup>3,4</sup>
- NASH is considered the most severe form of NAFLD<sup>3,4</sup>
- NAFLD has commonly been described as fibrosis 0–4<sup>3,4</sup>



## 5. What are the causes of NASH?

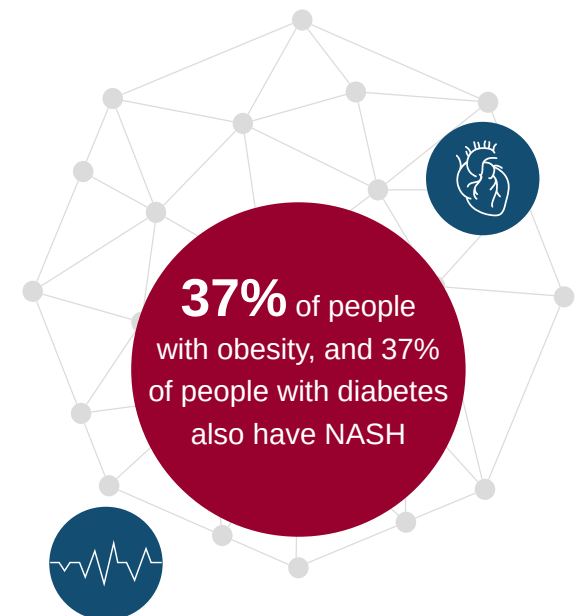
- NASH occurs when fat continues to accumulate in the liver cells leading to inflammation and injury of the cells<sup>4</sup>
- There are several reasons people may develop NASH including genetic predisposition and the presence of metabolic disorders<sup>5,6</sup> such as obesity, type 2 diabetes, high cholesterol, high blood pressure,<sup>1,3,7</sup> or other cardiovascular disease increase the risk of developing NASH<sup>1,8</sup>

## 6. What are the symptoms of NASH?

- The symptoms of NASH are hard to recognize, as such, it remains under diagnosed.<sup>5</sup> The most common are fatigue and pain in the upper right abdomen<sup>18</sup>
- People with NASH can remain unaware of their liver condition until the disease progresses to more advanced stages and it is often then too late to reverse<sup>17</sup>

## 7. What other conditions are associated with NASH?

- NASH is closely associated with many other health conditions,<sup>5,6</sup> specifically metabolic disorders, and people with NASH are at a higher risk of developing cardiovascular disease<sup>1,8</sup>
- People living with NASH usually have one or more metabolic disorders<sup>5,6</sup> (such as obesity, type 2 diabetes, high cholesterol levels, and high blood pressure)<sup>1,3,7</sup> and/or cardiovascular disease<sup>1,8</sup>
- These conditions drive NASH (especially type 2 diabetes) and NASH drives these conditions<sup>1,3,7</sup>
- 37% of people with obesity also have NASH.<sup>19</sup> 37% of people with type 2 diabetes also have NASH<sup>20</sup>



## 8. How is NASH managed?



Following a healthy lifestyle can help reduce the risk of NASH and prevent NASH from becoming more serious.<sup>10,11</sup> For some individuals, a weight loss of up to 7–10% is needed to impact NASH.<sup>11–13</sup>



People with NAFLD or NASH should follow recommended dietary guidelines, lose weight (if overweight or living with obesity), avoid excess alcohol, and take regular physical exercise.<sup>10,21</sup>



Diet should include foods high in fiber such as fruits, vegetables, whole grains and healthy fats. Foods high in fats, processed foods, fast food or fried food, and sugar beverages (especially those high in fructose) should be limited.<sup>10,21</sup>



Early identification, diagnosis, and intervention are imperative. At-risk populations should be strongly encouraged to talk to their doctor about their individual risk.



An improved understanding of NASH – the causes, the increased risk of CVD, and associated risk to develop cirrhosis and liver cancer – will reduce the burden of liver disease by improving diagnosis, management, and treatment.

## 9. How is NASH identified?

- NASH is often a diagnosis of exclusion and is mainly identified through clinical history, physical examination, blood tests, and/or imaging tests
- Liver biopsy has historically been associated with diagnosing liver disease and is still frequently used in clinical trials. Liver biopsy may be valuable but, increasingly in clinical practice, noninvasive diagnostics can be used. Liver biopsies are invasive, carry risk to patients, and subject to performance and interpretation inaccuracies<sup>9,22</sup>
- In the majority of circumstances, noninvasive diagnostics (such as blood tests and imaging tests) can be used to avoid liver biopsy and provide more information than a biopsy through their ability to assess broader changes in the liver rather than only in the relatively small amount of liver tissue typically obtained from a liver biopsy<sup>22</sup>
- Noninvasive alternatives and screening guidelines are necessary to respond to the growing incidence of NAFLD, NASH, and other liver diseases<sup>9</sup>
- Newer noninvasive screening and diagnostic tools are now being used, offering a safer and more thorough examination of the liver



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