

What is NASH?



NASH is the most severe form of non-alcoholic fatty liver disease (NAFLD), and it can lead to end-stage liver disease and death if not managed properly

NAFLD encompasses:¹

1. **Non-alcoholic fatty liver (NAFL)** – build up of fat in the liver (steatosis).
2. **Non-alcoholic steatohepatitis (NASH)** – in addition to fat in the liver, there is also inflammation of the liver tissue leading to liver damage and cell death. NASH is the most severe form of NAFLD.



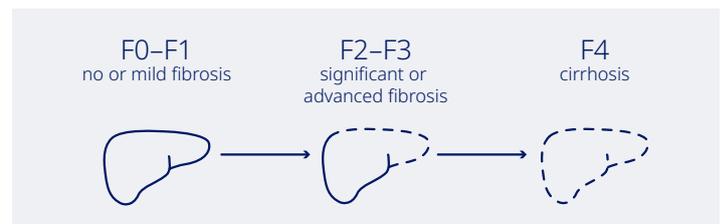
NASH is more common in people living with obesity

82% of people with NASH are living with obesity³

and conditions related to obesity, such as type 2 diabetes

44% of people with NASH are living with type 2 diabetes.⁶

NASH severity is often assessed using a scale that ranges from F0 to F4:^{4,5}



- **Fibrosis** – scarring of the liver
- **Cirrhosis** – severe scarring of the liver that can lead to loss of liver function, liver failure and liver cancer

NASH can have serious consequences

- Cardiovascular disease is the most common cause of death in people living with NAFLD^{7,8}
- People living with NASH may progress and develop end-stage liver disease and/or liver cancer,⁹ where a liver transplant may be the only treatment option²

The burden of NASH

- Lower overall health-related quality of life¹⁰
- Impact on mental health and wellbeing,¹¹ including tiredness, low energy and limitations in social and work activities
- NASH is predicted to be the leading cause of liver transplantation by 2030⁷
- In the US, NASH-related direct medical costs estimated to be \$104 billion (€89) billion per year¹²



Challenges in diagnosing NASH

NASH is known as a 'silent disease'

- Few or no symptoms seen in its initial stage, leading to lower patient diagnosis and referral
- When symptoms do occur, they are often non-specific for example abdominal pain, fatigue or weakness^{13,14}



Use of liver biopsy

- An invasive liver biopsy is still considered the gold standard, which is expensive and not without risk
- Diagnosis of NASH is defined by histological features (joint presence of steatosis, ballooning and inflammation)



Because of these challenges, people with NASH are often unaware they have the condition until the disease is in its later stages, at which point liver damage may be irreversible.^{15,16}

Limited treatment options

No globally approved treatment that addresses the underlying cause of the disease.^{17,18}



Weight loss sustained at around 7–10%¹⁹ can sometimes pause the progression of NASH.²⁰

References: 1. Chalasani N, Younossi Z, Lavine JE, et al. The diagnosis and management of nonalcoholic fatty liver disease: Practice guidance from the American Association for the Study of Liver Diseases. *Hepatology*. 2018; 67:328–357. 2. Estes C, Razavi H, Loomba R, et al. Modeling the epidemic of nonalcoholic fatty liver disease demonstrates an exponential increase in burden of disease. *Hepatology*. 2018; 67:123–133. 3. Younossi ZM, Koenig AB, Abdelatif D, et al. Global epidemiology of nonalcoholic fatty liver disease-Meta-analytic assessment of prevalence, incidence, and outcomes. *Hepatology*. 2016; 64:73–84. 4. Dulai PS, Singh S, Patel J, et al. Increased risk of mortality by fibrosis stage in nonalcoholic fatty liver disease: Systematic review and meta-analysis. *Hepatology*. 2017; 65:1557–1565. 5. EASO. EASL-EASD-EASO Clinical Practice Guidelines for the management of non-alcoholic fatty liver disease. *J Hepatol*. 2016; 64:1388–1402. 6. Younossi ZM, Golabi P, de Avila L, et al. The global epidemiology of NAFLD and NASH in patients with type 2 diabetes: A systematic review and meta-analysis. *J Hepatol*. 2019; 71:793–801. 7. Tana C, Ballestri S, Ricci F, et al. Cardiovascular Risk in Non-Alcoholic Fatty Liver Disease: Mechanisms and Therapeutic Implications. *Int J Environ Res Public Health*. 2019; 16. 8. Targher G, Day CP and Bonora E. Risk of cardiovascular disease in patients with nonalcoholic fatty liver disease. *N Engl J Med*. 2010; 363:1341–1350. 9. Tesfay M, Goldkamp WJ, Neuschwander-Tetri BA. NASH: The Emerging Most Common Form of Chronic Liver Disease. *Mo Med*. 2018; 115(3):225–229. 10. Kennedy-Martin T, Bae J, Paczkowski R, et al. Health-related quality of life burden of nonalcoholic steatohepatitis: a robust pragmatic literature review. *J Patient Rep Outcomes*. 2018; 2:28. 11. Balp MM, Krieger N, Przybysz R, et al. The burden of non-alcoholic steatohepatitis (NASH) among patients from Europe: A real-world patient-reported outcomes study. *JHEP Rep*. 2019; 1:154–161. 12. Younossi ZM, Blissett D, Blissett R, et al. The economic and clinical burden of nonalcoholic fatty liver disease in the United States and Europe. *Hepatology*. 2016; 64:1577–1586. 13. Rinella ME. Nonalcoholic fatty liver disease: a systematic review. *JAMA*. 2015; 313:2263–2273. 14. Nascimbeni F, Pais R, Bellentani S, et al. From NAFLD in clinical practice to answers from guidelines. *J Hepatol*. 2013; 59:859–871. 15. Mayo Clinic. Nonalcoholic fatty liver disease. Available at: <https://www.mayoclinic.org/diseasesconditions/nonalcoholic-fatty-liver-disease/symptoms-causes/syc-20354567?p=1>. Last accessed: December 2021. 16. Araujo AR, Rosso N, Bedogni G, et al. Global epidemiology of non-alcoholic fatty liver disease/nonalcoholic steatohepatitis: What we need in the future. *Liver Int*. 2018; 38:47–51. 17. Banini B and Sanyal A. Nonalcoholic Fatty Liver Disease: Epidemiology, Pathogenesis, Natural History, Diagnosis, and Current Treatment Options. *Clin Med Insights Ther*. 2016; 8:75–83. 18. Stengel J and Harrison S. Nonalcoholic Steatohepatitis: Clinical Presentation, Diagnosis, and Treatment. *Gastroenterol Hepatol*. 2006; 2:10. 19. European Association for the Study of the L, European Association for the Study of O. EASL-EASD-EASO Clinical Practice Guidelines for the management of non-alcoholic fatty liver disease. *J Hepatol*. 2016; 64:1388–1402. 20. Hallsworth K and Adams LA. Lifestyle modification in NAFLD/NASH: Facts and figures. *JHEP Rep*. 2019; 1:468–479.