

FIGHTING THE FATTY LIVER

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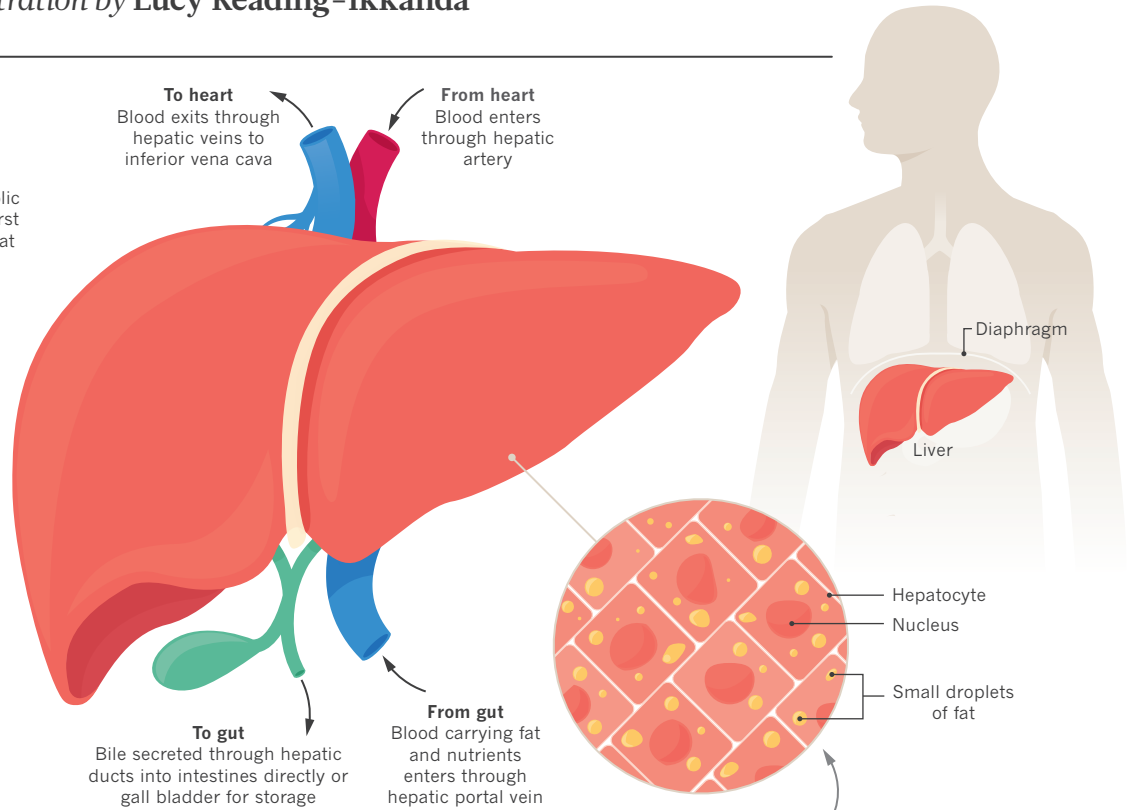
Increased levels of obesity are driving an epidemic of non-alcoholic fatty liver disease. Understanding, diagnosing and treating this progressive condition are now priorities.
 By Liam Drew; illustration by Lucy Reading-Ikkanda

CALORIES NOT ALCOHOL

An advanced stage of non-alcoholic fatty liver disease (NAFLD) was first described in 1980, confirming that liver disease characterized by an accumulation of fat can develop in people who do not consume excess alcohol¹. Associated with obesity and type 2 diabetes, NAFLD is set to become the most common cause of serious liver disease in many nations.

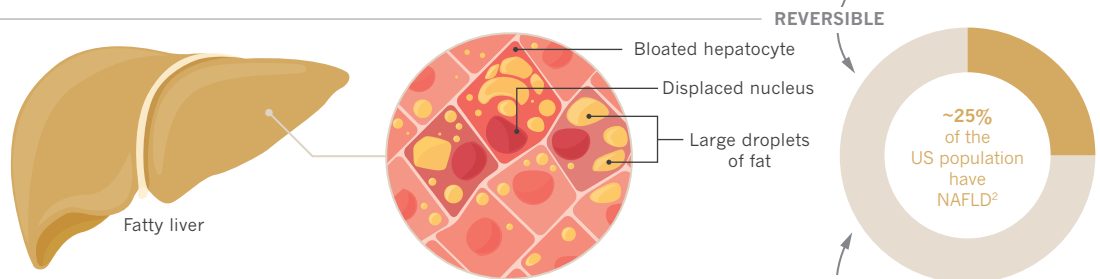
1 HEALTHY LIVER

The liver carries out many tasks, including processing nutrients absorbed from the gut, and controlling the levels of glucose, fat and protein in the blood. It stores carbohydrates and a limited amount of fat. Most liver cells are hepatocytes, which can metabolize almost all types of nutrient. A healthy hepatocyte contains a nucleus at its centre and evenly distributed droplets of fat.



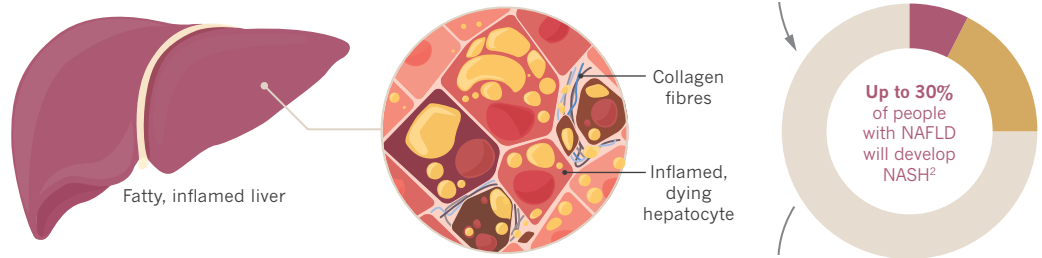
2 NAFLD

In NAFLD, hepatocytes accumulate excess fat, a process known as steatosis. Such fat can come from the diet, be made in the liver or be released by insulin-resistant fatty (adipose) tissue.



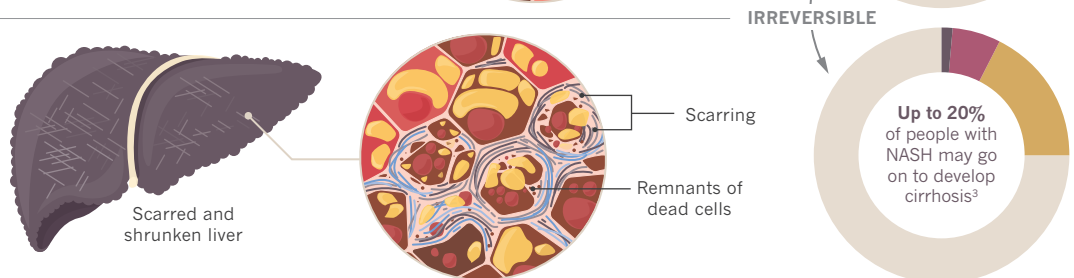
3 NASH

If accumulated fat causes stress and injury to hepatocytes, non-alcoholic steatohepatitis (NASH) develops. Already-bloated hepatocytes swell further and start to die, causing inflammation. Scarring (fibrosis) occurs as collagen fibres replace dead cells.



4 CIRRHOSIS

Over the years or decades, dead hepatocytes are broken down and scar tissue accumulates, which stiffens the liver and impairs its function. Known as cirrhosis, this can lead to liver failure and an increased risk of liver cancer.



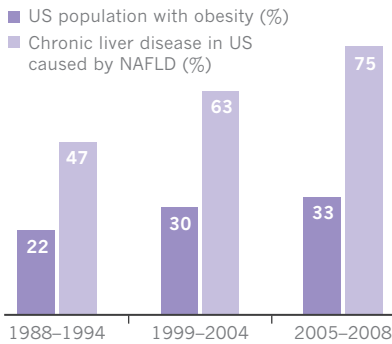
RISK FACTORS

Age, gender and genetics all contribute to a person's risk of developing NAFLD and NASH. But the main risk factors are obesity and diabetes, as well as other features of metabolic syndrome, including high blood pressure and insulin resistance.

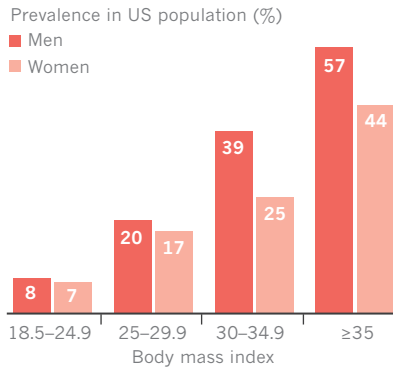
OBESITY

The link between obesity, its complications and NAFLD is strong.

As levels of obesity have increased, so too has the prevalence of NAFLD⁴.

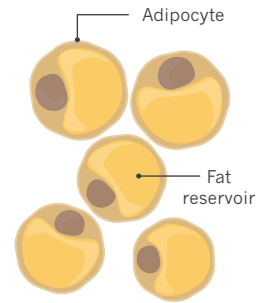


NAFLD increases in prevalence with body mass index, and is more common in men⁵.

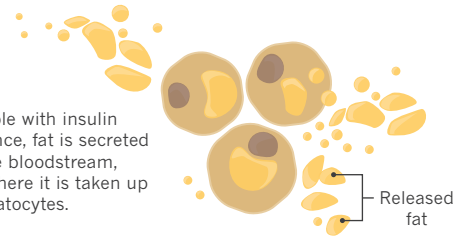


DIABETES AND INSULIN RESISTANCE

In healthy people, insulin inhibits the breakdown and release of fat by fat cells (adipocytes).

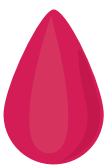


In people with insulin resistance, fat is secreted into the bloodstream, from where it is taken up by hepatocytes.



DIAGNOSIS

To determine the extent of NAFLD and associated fibrosis, and to monitor patients' responses to treatment — without using an invasive liver biopsy — biomarker discovery and advances in imaging technology are needed.

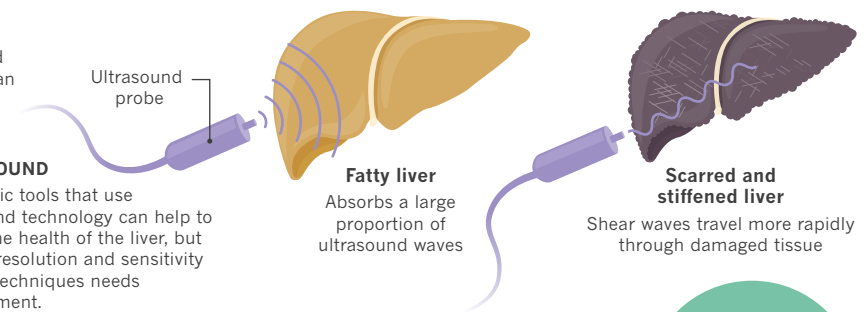


IN THE BLOOD

Although current blood tests for liver disease can help to assess the severity of NAFLD, researchers are seeking new biomarkers with concentrations that reliably correlate with disease activity.

ULTRASOUND

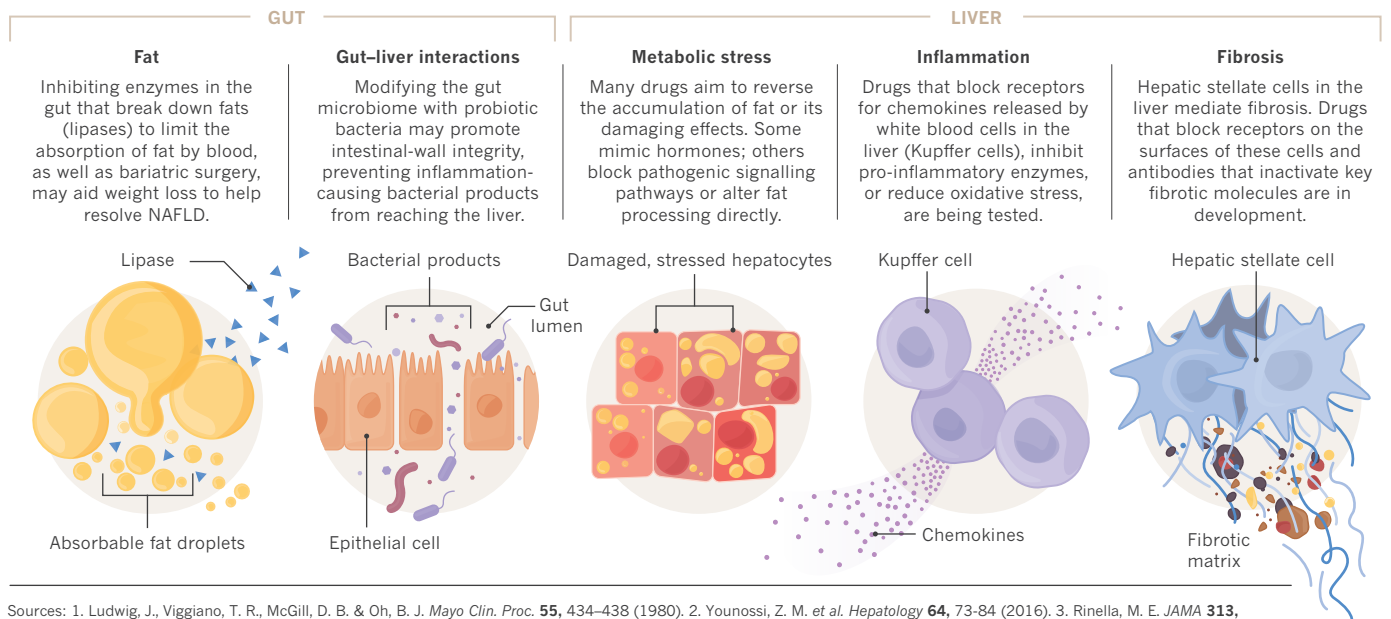
Diagnostic tools that use ultrasound technology can help to assess the health of the liver, but the fine resolution and sensitivity of such techniques needs improvement.



HALTING NAFLD

The cornerstones of NAFLD treatment are weight loss and increased amounts of exercise, but maintaining these lifestyle changes can be hard. NASH is now considered to be a serious condition that requires the development of targeted drugs. As a result, hundreds of trials of potential treatment strategies are under way.

MORE THAN 75 MILLION
people in the United States may have NAFLD²



Sources: 1. Ludwig, J., Viggiano, T. R., McGill, D. B. & Oh, B. J. *Mayo Clin. Proc.* **55**, 434-438 (1980). 2. Younossi, Z. M. *et al. Hepatology* **64**, 73-84 (2016). 3. Rinella, M. E. *JAMA* **313**, 2263-2273 (2015). 4. Younossi, Z. M. *et al. Clin. Gastroenterol. Hepatol.* **9**, 524-530 (2011). 5. Lazo, M. *et al. Am. J. Epidemiol.* **178**, 38-45 (2013).