

Non-alcoholic Fatty liver disease (NAFLD):

How you can reduce the risk for your liver and for other health issues?

14 important Points for People at risk for or living with NAFLD



This short version has been developed by Diane Langenbacher (Kautz⁵ gUG) in cooperation with EASL based on the full paper ["Non-alcoholic fatty liver disease: A patient guideline"](#) published in JHEP Reports 2021.

Purpose of this short version patient guideline

This short version of the **non-alcoholic fatty liver disease (NAFLD) patient guideline** is intended to give you an overview on the most important topics for people at risk for or living with non-alcoholic fatty liver disease (NAFLD). Please refer back to the full guideline for additional scientific background and clinical context (<https://easl.eu/publication/non-alcoholic-fatty-liver-disease-a-patient-guideline/>) for those topics most relevant for you.

Fatty liver disease should not be ignored. It may be mild in some patients but when it gets worse, it can seriously harm your liver. It also increases the risk of other health issues, such as heart disease, stroke, diabetes and some types of cancer. If you have NAFLD, talk to your doctor about taking steps to reduce these risks.

It is important that you develop a full understanding of it. This has several **advantages**:

It enables you to take an active role in your own healthcare.

You develop a better understanding of what the doctor or other healthcare providers are discussing with you.

You can monitor your condition and assess the success of various measures yourself.

This guide will help you do that. It has been developed by patients, patient representatives, physicians and scientists and is based on current scientific knowledge and recommendations. It cannot and should not replace the individual consultation with your personal physician and health care team but should support you in making informed decisions.

What does the liver do?

The liver is a large **organ** on the right-hand side of the body, located in the upper-right quadrant of your abdomen.

As the chemical factory of your body, the liver performs an **extraordinarily complex set of functions to keep the body in a healthy condition**. It receives blood from the gut via the portal vein, which carries most of the nutrients absorbed after eating. Thus, the liver plays a key role in processing nutrients. For example, the liver has a central role in handling sugars, proteins and fats.

After transformation of these substances, the liver **releases these building blocks for energy and growth** required by organs. So, the liver is in close interaction with many organs. Energy substrates that are not immediately needed as fuel are stored in the fat tissue, until your body needs them. The liver also plays an **important role in detoxification of drugs and other substances**, in the synthesis of many important substances for blood clotting and for transport in the blood, and in the production of bile.

This shows how **important the liver is for human health** and all these processes your liver carries out in silence. There are not many pain sensors in the liver, except in the liver capsule, and therefore liver diseases are often not painful, which is one reason why chronic liver disease can remain undiagnosed for a long period of time.

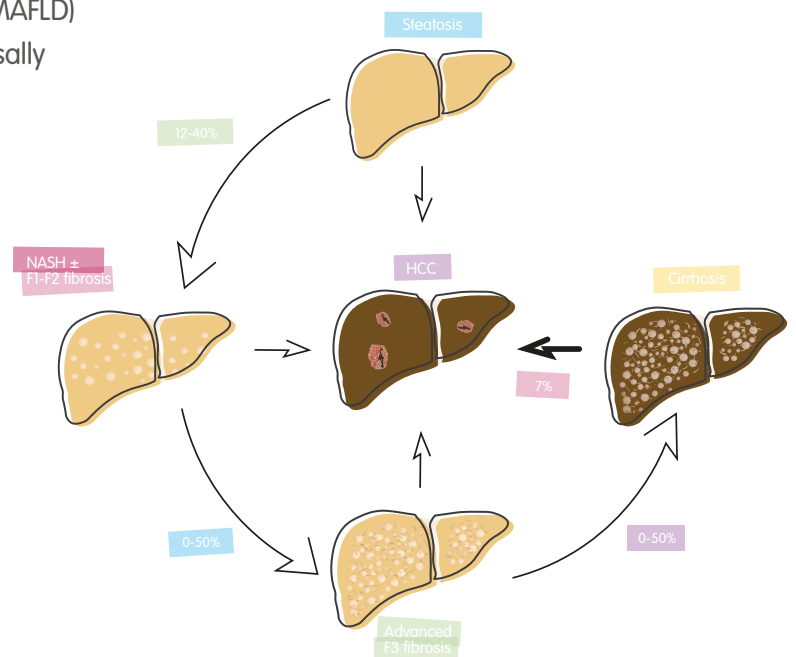
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What is NAFLD and how does it occur?

NAFLD stands for non-alcoholic fatty liver disease. The liver is a key organ involved in energy regulation. However, your liver is normally not supposed to store excess energy in the form of fat. **NAFLD is defined as an increase (> 5%) of fat in the liver** not due to medication or increased alcohol consumption.

The accumulation of fat in the liver in the context of the disease called NAFLD is in most cases due to a **combination of eating more calories than the body needs and leading a more sedentary (inactive) lifestyle**. Therefore, it occurs most commonly, but not always, in association with being overweight. Another group of people at risk are people living with diabetes, more often **type 2 diabetes (T2D)**, or earlier stages of altered glucose handling in the body. Some have therefore advocated to rename the disease to metabolic associated fatty liver disease (MAFLD) but this proposal has not yet been universally accepted (reason why the full guideline as well as this short version stick to the name of NAFLD).

A fatty liver can have many causes, so before a diagnosis of NAFLD can be made, **other causes should be evaluated**. The most frequent of these alternative causes are related to the consumption of alcohol (the terms ALD, for alcohol-related liver disease, and ASH, alcoholic steatohepatitis, are used).



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How does the extra fat in my liver affect its function?

Per se, the extra fat in the liver cells does not seem to be harmful or affect how well the liver works. This is therefore called simple or isolated fatty liver, or non-alcoholic fatty liver (NAFL, without the “D” for disease). When the liver cells containing the fat-droplets become damaged and die, the immune system is activated, and this is then referred to as non-alcoholic steatohepatitis or NASH. **The term hepatitis refers to inflammation of the liver,** whatever the cause. NASH is the subtype of NAFLD that carries more long-term risks.

When your liver is damaged, it tries to repair itself by creating new, healthy tissue. If the damaging process continues, the liver’s ability to create enough healthy tissue and clean-up the damage may be exhausted. As a consequence, scar tissue will develop and can accumulate. **This scarring is called fibrosis.** Some (but not all) people with NASH will develop fibrosis over time called progressive fibrosis. **Fibrosis can lead to cirrhosis,** which means that large strands of scar tissue alter the liver structure, with regenerating liver tissue in between. This is called NASH-cirrhosis. **This does not necessarily imply that the liver is not functioning well.** The liver will, however, struggle more and more to function properly as the disease progresses. Eventually, liver function can be so poor that problems occur (decompensated cirrhosis) to the point where liver function becomes insufficient to support life (liver failure).

Liver cancer (hepatocellular carcinoma, HCC) is another potential consequence of NAFLD.

This risk of developing HCC is well known in patients with cirrhosis from other causes and is now also well documented in NASH-cirrhosis. Importantly, **HCC has also been reported in patients with NASH who do not have cirrhosis,** and even in some patients with NAFL. It is not clear how big this risk is exactly, but in general, the more severe the disease is, the higher the risk is. The highest risk is when you have cirrhosis. If there are other conditions such as obesity or more liver-damaging factors such as alcohol, they also contribute to the risk of developing HCC.

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What is the impact on my general health and health-related quality of life?

NAFLD increases the risk of developing T2D due to the less effectiveness of the action of insulin on the fatty and diseased liver. If you already have T2D, it makes controlling your T2D and blood sugar more difficult.

NAFLD also increases the risk of cardiovascular (heart) disease because of changes in blood lipids towards a more damaging composition and because of a chronic low-grade inflammation, both playing a role by damaging the walls of blood vessels and by an effect on the heart muscle and the system that regulates heart rhythm. Blood vessel wall damage mainly refers to the build-up of mineral deposits or calcifications on the vessel walls, which is called atherosclerosis.

NAFLD may also increase the risk of other types of cancer (including bowel cancer) and the development of kidney problems. This shows how crucial the liver is in maintaining health!

The burden of NAFLD on health-related quality of life becomes progressively more important with advancing disease. When fatigue and impaired physical conditions related to NASH accumulate, this has a significant impact on daily life. In the more severe stages of the disease, the physical and psychological consequences of liver disease add to those of the metabolic comorbidities (obesity, T2D, changes in blood lipids such as cholesterol (dyslipidaemia), cardio-vascular disease/CVD). Clearly, **health-related quality of life deteriorates if NAFL progresses to early NASH, NASH-cirrhosis and liver failure, or liver cancer.**

The impact of NAFLD may be made even worse by the stigma associated with obesity and/or T2D, problems of shame/guilt linked to presumed alcoholism and unhealthy lifestyle, and difficulties accepting the diagnosis and even accessing healthcare.

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Who is at risk for NAFLD, who should be tested and how?

NAFLD affects people of all ages, including children and is in most cases directly linked to chronic excess calorie consumption of unhealthy food (high sugar rate), inadequate physical activity and living with overweight/ obesity.

Thus, you are **more likely to have NAFLD if you are living with obesity and/or T2D** (which is also related with a greater chance of having more severe liver disease) or if you have high lipid levels (such as LDL cholesterol and/or triglycerides) in the blood. The number of people with NAFLD increases progressively with age. Genetic factors are also important.

Some people with NAFLD have a normal body weight within the normal range (lean NAFLD, or better: NAFLD in lean people) or are living with overweight but do not have obesity.

Although there is no global consensus, there is a growing understanding that **physicians should at least consider screening people who are at risk of having NAFLD**. This is probably even more important for those at risk of developing NASH and/or fibrosis. These risk categories also include people with chronically elevated liver blood tests (for more than 6 months, so at least 2 blood samples 6 months apart are needed). It may include people living with T2D, cardiovascular diseases or obesity (in particular abdominal obesity (having a belly)), hypertension, high serum lipids and fasting glucose levels above normal known, all together known as metabolic syndrome.

Most screening strategies rely on **non-invasive tests**, i.e. a blood test score, a liver ultrasound or a liver stiffness assessment, or a combination of these. All these tests could be performed during a single visit or in a sequential way, which means that the second test is only performed if the first one is positive or gives an unclear result. **In some situations, a biopsy may be required, especially to confirm the diagnosis.** To date, there is no universal strategy.

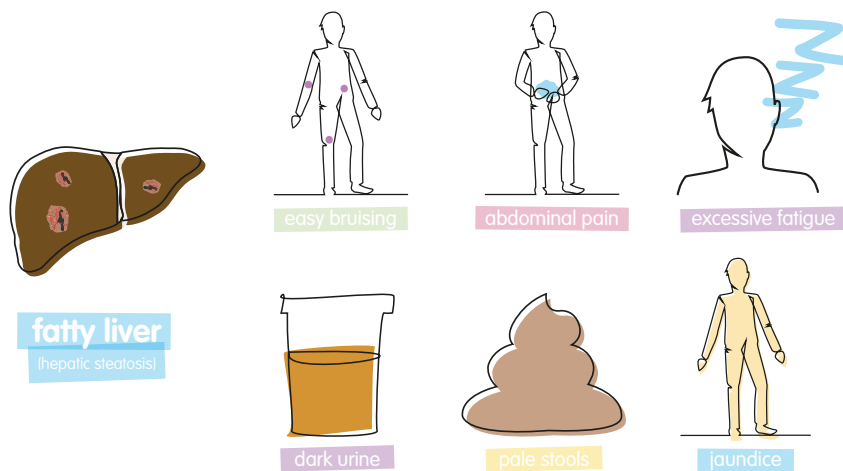
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What do symptoms look like?

Some patients experience **fatigue** or tiredness, **general lethargy**, and right-sided abdominal discomfort or an ache on the right side of your body just under the ribs without linking these to NAFLD but to other simultaneously present diseases. These symptoms are sometimes reported and might worsen over time as NAFLD progresses. However, other causes of these symptoms need to be ruled out.

You may experience **more severe symptoms when your liver becomes increasingly scarred** (i. e. if you have cirrhosis), such as unexplained weight loss, yellowing of the skin and the whites of the eyes (jaundice), itchy skin, and swelling in the legs or tummy.

Symptoms of fatty liver



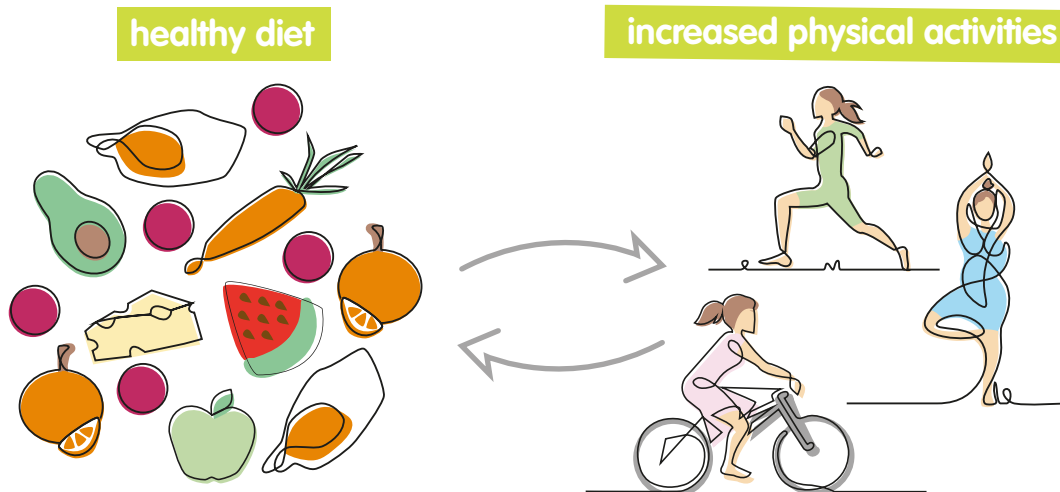
Because NAFLD starts off without noticeable symptoms (i.e. is asymptomatic), your doctor may **perform tests if you have risk factors** associated with getting NAFLD (like T2D, metabolic syndrome or cardiovascular disease) to see if you have NAFLD with or without fibrosis.

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What happens after diagnosis?

If you are diagnosed with NAFLD, your doctor should discuss choices of **changing lifestyle including healthy dietary measurements and increase of physical activity**. This is the cornerstone of NAFLD care and should always be the first treatment option. **There are currently no medicines to specifically treat NAFLD**, although research is well underway to develop them. Some drugs approved to treat T2D and obesity might also have a positive effect on your NAFLD. Without specific drugs for treatment, **weight loss is key**, and this can be achieved by dietary changes, primarily. In combination with increasing physical activity levels the impact of weight loss can be higher and can help to:

- **Reduce the amount of fat and inflammation in your liver.** Even if your liver is scarred, improvement can be achieved if you make and sustain lifestyle changes, given that the liver can regenerate.
- **Improve your metabolic profile** and thereby lower your risk of CVD, T2D and liver cancer.

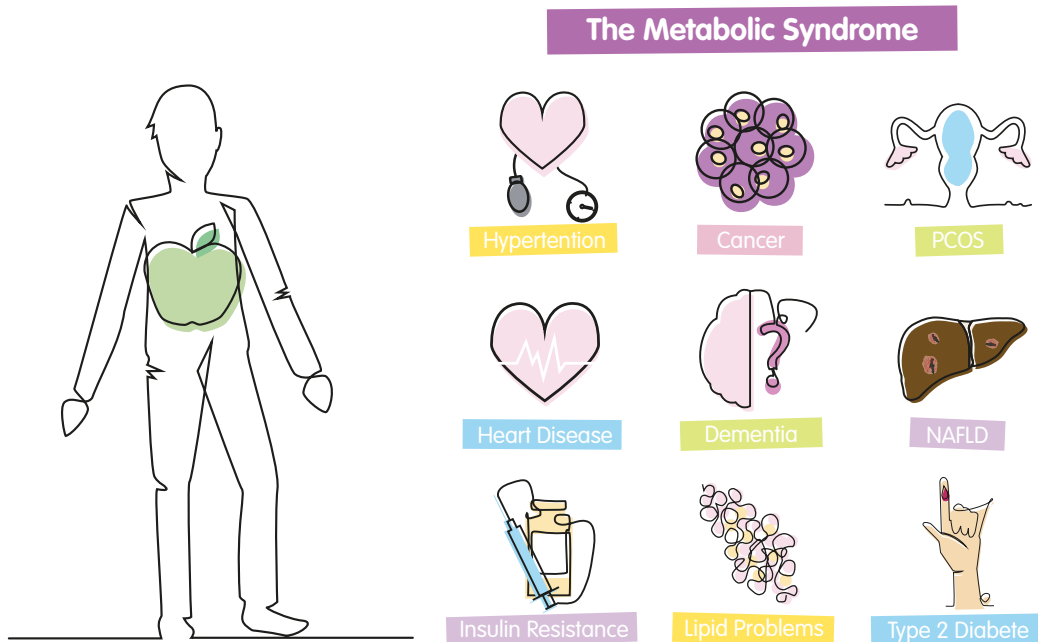


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What additional checks for comorbidities will be performed?

As part of the diagnostic work-up, your physicians should check for other liver diseases that can exist alongside NAFLD like **viral hepatitis** or **iron accumulation** (haemochromatosis).

In addition, **all cardiometabolic risk factors should be checked** and treated according to their proper care guidelines and other chronic diseases should be checked, including psychological conditions.



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Lifestyle Modification – what does this mean?

Maximum effort should be made to improve the factors that drive the disease: this is what is meant by **“lifestyle modification”**.

Weight reduction and healthy dietary pattern lead to improvements in your liver blood tests (liver enzymes), the amount of liver fat and liver inflammation, as well as the amount of scar tissue or fibrosis. The impact of weight loss on liver improvement depends on the degree of weight reduction. Weight loss can be achieved by any healthy dietary pattern (like Mediterranean, low-carb, low-fat diets) that reduces calories, highly processed food and meats, sugar and saturated fat intake. **Some drastic diets may not be healthy for you and can cause other problems.**

Please refer to the full paper for more detailed information.

Physical activity is effective in reducing liver fat. It can also help reducing the risk of other comorbid metabolic diseases such as T2D, CVD and obesity. Guidelines recommend over **150 minutes a week of moderate intensity physical activity** over 3–5 sessions including a combination of aerobic and resistance training (activity that strengthen the muscles).

Dietary changes and physical activity are key components of any lifestyle change package for people with NAFLD, not just to improve liver health but also to support weight loss and reduce the risk of other chronic diseases. Tailoring this to your personal preferences, daily routine and baseline fitness is essential for long-term success. Find something you enjoy and, if possible, find someone who will support you in making these changes – **having a “buddy” is known to increase motivation and long-term adherence.**

Setting SMART (**s**pecific, **m**easurable, **a**chievable, **r**elevant, **t**imely) weight loss and/or physical activity goals can help you to initiate and maintain changes.

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What else could be done to improve my liver?

A broad range of drugs are under investigation, but **there are currently no drugs approved** by regulatory agencies for the treatment of NAFLD. This is a field of very active research. As an increasing number of clinical studies are running and results are reported, recommendations may rapidly change. Information on which clinical trials are ongoing can be found on www.clinicaltrials.gov and you should ask your physician for newest updates. Some drugs that are used to treat other conditions have also been tested for NASH. Based on their effects demonstrated by liver biopsy, the following drugs seem to have some efficacy.

- Vitamin E showed promise, but only in patients without cirrhosis and without T2D. Given long-term and at high doses, however, vitamin E potentially had negative effects and some data indicate that it could increase the risk of early death and certain cancers.
- Pioglitazone, which is approved for the treatment of diabetes, showed promise for NASH in patients with diabetes and pre-diabetes. Side effects such as weight gain and bone fractures should be considered.
- Liraglutide and semaglutide are approved for the treatment of obesity and for diabetes. They have also shown promise in reducing liver fat and inflammation in NASH and will be evaluated further.

Important: all these drugs must be discussed with your doctor and can harm when self-administered.

Future available drugs will be an add-on therapy because **lifestyle changes are essential** as NAFLD is mainly a lifestyle-related disease.

Bariatric surgery very effectively achieves weight loss and weight loss maintenance in patients

with obesity. The agreed criteria for the surgical management of obesity and metabolic disorders (BMI ≥ 40 kg/m² or BMI ≥ 35 kg/m² with complicating disorders, no resolution after medical treatment) are also applicable for NAFLD. Patients with a BMI of 30–35 kg/m² who also have T2D that is not adequately controlled by medical therapy may also be candidates for surgery.

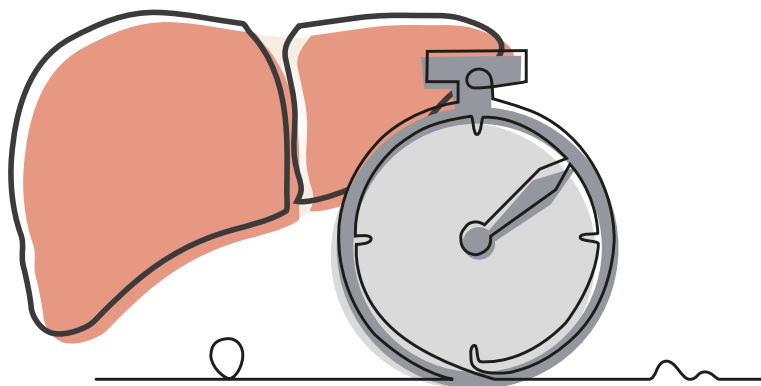
It is important to know that the change in the anatomy by bariatric surgery can lead to the need of lifelong follow up and this should be considered in discussing this option for patients.

If you wonder whether vitamin E, the above-mentioned drugs or bariatric surgery could be helpful for you, please consult your doctor and discuss the potential risks and benefits. Any treatment decision should be based on your individual situation and medical history.

How should a patient be managed?

The recommended care pathway is based on the severity of the disease. Control examinations can include physical examination and blood test, as well as ultrasound and liver stiffness measurement, depending on your personal situation. Sometimes follow-up may require specialised care, but this also depends on your personal situation and is not always needed. The following recommendations are just indicative of a general policy that could be followed, as there are no universally accepted rules on this issue:

- **NAFL (isolated or simple fatty liver [steatosis]): ~every 2–5 years**
- **NASH with no or minimal fibrosis (fibrosis below F2): once a year or every 2 years**
- **NASH with significant fibrosis (fibrosis equal or higher than F2): at least once a year (probably better every 6 months)**
- **NASH (Cirrhosis): every 3–6 months**



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How can I monitor whether my treatment is working?

There are **2 ways** of monitoring the success of a treatment (including lifestyle modifications).

1. your doctor will be **checking regularly via blood tests, ultrasound and/or elastometry** (i. e., the measurement of the stiffness of the liver tissue) to monitor the success of treatment. In this case, you obtain an idea of a change of the liver enzymes and the fibrosis level. The exact meaning of a change in these tests in relation to the true severity of the disease is not fully established. Therefore, even though you could logically think that improved test results mean that the liver has improved, this has not been scientifically proven and hence needs to be discussed with your doctor. In this regard, **it is important to look at different tests and not to rely on a single test to conclude.**
2. To some extent, **you can also monitor the success of treatment by yourself.** Of course, you cannot do blood tests at home but there are many ways to observe the effect of the treatment including lifestyle modifications. The simplest way is to **regularly monitor your weight and your waist circumference.** You can track both and observe changes. Based on these data you can also use the body mass calculator to work out your BMI. Another way is to **observe your symptoms.** If you have symptoms like fatigue or general discomfort you can write them down and talk with your healthcare provider. Additionally, you can **monitor the improvements in your fitness level.** For example, you can keep track of how easy it is for you to go upstairs or to walk a specific distance. If you choose to go swimming regularly, write down how many lengths you manage and how you feel felt afterward. Once you have initiated treatment and have good adherence, **the effect on your quality of life can be substantial.** The impact is, for example, significantly noticeable whenever weight loss is achieved.

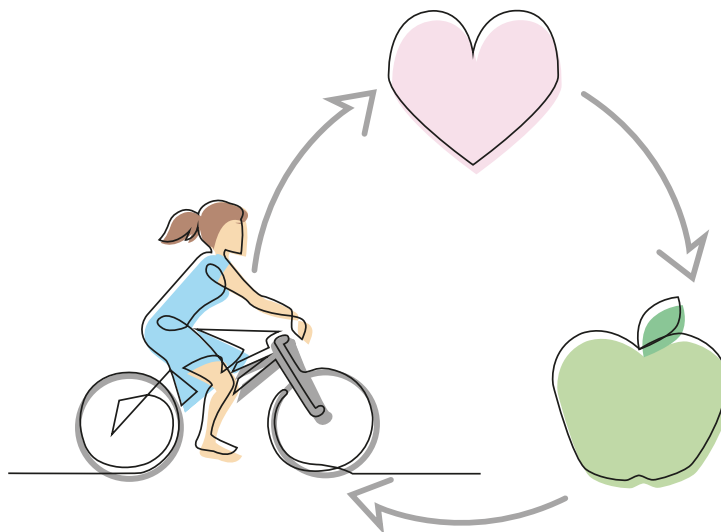
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Self-management: Looking after yourself when you have NAFLD

When you have NAFLD, the goal is to **manage your risk factors** for liver disease and general health worsening. Although NAFLD progresses very slowly, it is important to **eat a healthy diet and increase your physical activity** (less sitting time and more daily activities) and exercise (like walking, swimming, riding bicycle and/or activity that strengthens the muscles for at least 3 times per week) levels.

This will help to improve the health of your liver and lower your risk of worsening health.

As a person with NAFLD, you are at risk of several serious conditions including, T2D and heart disease (CVD). It is important to work with your family doctor and other healthcare providers to check and **manage your weight, blood glucose, blood pressure and blood lipids to reduce your risk of heart disease and T2D.** Physical activity and a healthy diet will help both in the prevention of NAFLD progression and in the prevention and treatment of T2D and heart disease.



Where can I find additional information?

For additional background and scientific context, you should refer to the full version of this patient guideline. [<https://easl.eu/publication/non-alcoholic-fatty-liver-disease-a-patient-guideline/>]

If you may need support with some of the medical/clinical language used please refer to the glossary in the following.

Your Family Doctor/GP and Primary Care team are at the front line and will be supporting you as to reach correct information, preventing misleading information, and contributing your empowerment and health literacy.

Patient advocacy groups and patient self-help groups are also excellent contact points.

They often have very well-informed consultants and are available in many European countries.

List of PAGs

The following umbrella organizations represents a lot of local and national Patient Advocacy Groups. You can find details of the members on their respective webpages.

ELPA – European Liver Patient Association

www.elpa.eu

Mail: contact@elpa.eu

Rue de la Loi 235/27, 1040 Brussels, Belgium

ECPO – European Coalition for People living with Obesity

www.eurobesity.org

Mail: contactus@eurobesity.org

101 Furry Park Road, Howth Road, Dublin, Ireland D05 KD52

LPI – Liver Patients International

www.liverpatientsinternational.org

Mail: info@liverpatients.international

Dreuve du Pressoir 38, 1190 Brussels, Belgium

GLI – Global Liver Institute

www.globalliver.org

Mail: info@globalliver.org

Washington DC, USA

List of acronyms

ALD: alcoholic liver disease

CVD: cardio-vascular disease

HCC: hepato-cellular carcinoma, liver cancer

LDL (cholesterol) low-density lipoprotein

NAFL: non-alcoholic fatty liver

NAFLD: non-alcoholic fatty liver disease

NASH: non-alcoholic steatohepatitis

T2D: type II diabetes mellitus

For references please refer to

<https://easl.eu/publication/non-alcoholic-fatty-liver-disease-a-patient-guideline/>

Glossary

ASH: Alcoholic fatty liver disease (ASH) – also called alcoholic steatohepatitis. Severe liver disease caused by alcohol consumption.

Bariatric surgery: is a branch of surgery that deals with surgical interventions that are intended to lead to a reduction in body weight.

Biopsy: removal of tissues or cells from the body organs (e.g. liver) for microscopic examination

Blood pressure: blood pressure is the force of the blood that it exerts when it passes through to the vessels.

Capsule: is the outer shell of the liver. It encloses them and thus distinguishes them from other institutions.

Carcinoma: malignant tissue degeneration, tumour

Cirrhosis: advanced scarring of the liver that happens when the liver is damaged

Cholesterol: It is made up of LDL and HDL cholesterol. The aim should be to reduce the LDL (bad cholesterol) in the blood. This is supported by a healthy and balanced diet and exercise

Clinical trials: medical study. It is carried out with patients or healthy volunteers and is a prerequisite for drug approval by the authorities.

Comorbidities: additional diseases to the underlying disease. It does not have to be related to the underlying disease, but this is often the case in practice.

Elastometry: Determination of the degree of liver fibrosis in patients

Fibrosis: fibrosis in the liver fibrosis is the scarring laid down following damage to the liver cells

Fatigue: extreme tiredness and fatigue that cannot be remedied by getting enough sleep. Feeling of exhaustion even with everyday tasks

Inflammation: this is a body's own reaction to stimuli. Signs of inflammation include redness, swelling, overheating, pain and functional limitations

Metabolic disorder: the complex metabolic system of the body is out of balance due to a disorder, illness or malfunction

Metabolic syndrome: metabolic syndrome is the medical term for a combination of conditions including diabetes, high blood pressure (hypertension) and obesity.

Obesity: morbid overweight or obesity. Obesity can be the cause of fatty liver.

Prevention: preventive measures, e.g. to prevent a disease or to prevent damage to health.

Progressive: Translated: progressive – Increase in scope and severity

Proteins: universal building material of the body. Proteins from the diet are broken down in the body and converted into the body's own protein.

Steatosis: steatosis refers to the presence of fat in liver cells

Symptom: side effect in case of a disease, for example the possible itching in a liver disease

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Summary of lifestyle recommendations for who is living with NAFLD

Weight reduction

- The more severe the liver disease is, the higher the goals are in terms of weight loss
- Healthy diet with caloric restriction tailored for your preferences

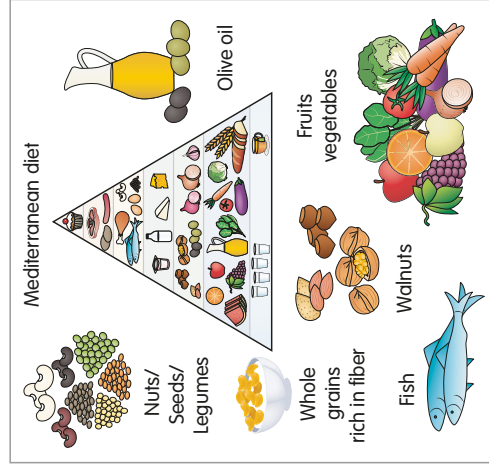
Overweight/obesity NAFLD

- 3–5% reduction of weight even within the normal BMI range (especially if recent weight gain occurred or if abdominal obesity is present)

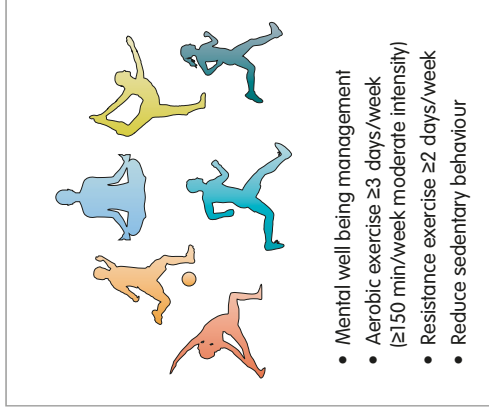
Non-obesity NAFLD

Lifestyle advice for ALL patients with NAFLD

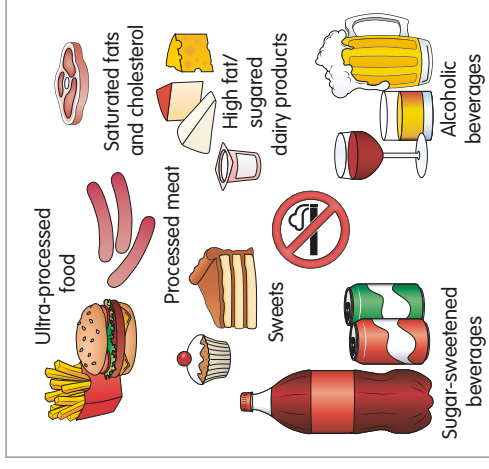
Recommended foods



Recommended activity



Non-recommended foods/ Minimize consumption



- Reduce added sugar (e.g. by reducing sweets, processed foods, sugared dairy products, etc.)
- Avoid sugar-sweetened beverages
- Reduce saturated fat and cholesterol (e.g. by eating low fat meat and low fat dairy products)

- Increase n-3 fatty acids found in fish, and walnuts; utilize olive oil over other oils more often
- Minimize “fast food” and ultra-processed food
- Home-cooked meals are preferable
- Try to follow the Mediterranean dietary pattern