

Non-alcoholic fatty liver disease (NAFLD): assessment and management

NICE guideline

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Your responsibility

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals and practitioners are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or the people using their service. It is not mandatory to apply the recommendations, and the guideline does not override the responsibility to make decisions appropriate to the circumstances of the individual, in consultation with them and their families and carers or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the [Yellow Card Scheme](#).

Local commissioners and providers of healthcare have a responsibility to enable the guideline to be applied when individual professionals and people using services wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with complying with those duties.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should [assess and reduce the environmental impact of implementing NICE recommendations](#) wherever possible.

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This guideline is the basis of QS152.

Overview

This guideline covers how to identify the adults, young people and children with non-alcoholic fatty liver disease (NAFLD) who have advanced liver fibrosis and are most at risk of further complications. It outlines the lifestyle changes and pharmacological treatments that can manage NAFLD and advanced liver fibrosis.

Who is it for?

- Healthcare professionals caring for people with NAFLD
- Commissioners and providers of healthcare services
- People with NAFLD, their families and carers

Recommendations

People have the right to be involved in discussions and make informed decisions about their care, as described in [NICE's information on making decisions about your care](#).

[Making decisions using NICE guidelines](#) explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

At the time of publication (July 2016), neither pioglitazone nor vitamin E had a UK marketing authorisation for the treatment of non-alcoholic fatty liver disease (NAFLD). The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the [General Medical Council's Prescribing guidance: prescribing unlicensed medicines](#) for further information.

1.1 Assessment for NAFLD

Identifying NAFLD in higher-risk groups

- 1.1.1 Be aware that non-alcoholic fatty liver disease (NAFLD) is more common in people who have:
- type 2 diabetes **or**
 - metabolic syndrome.
- 1.1.2 Take an alcohol history to rule out alcohol-related liver disease. See also [NICE's guideline on cirrhosis](#).
- 1.1.3 Do not use routine liver blood tests to rule out NAFLD.

Diagnosing NAFLD in children and young people

- 1.1.4 Offer a liver ultrasound to test children and young people for NAFLD if they:
- have type 2 diabetes or metabolic syndrome **and**
 - do not misuse alcohol.
- 1.1.5 Refer children with suspected NAFLD to a relevant paediatric specialist in hepatology in tertiary care.
- 1.1.6 Diagnose children and young people with NAFLD if:
- ultrasound shows they have fatty liver **and**
 - other suspected causes of fatty liver have been ruled out.
- 1.1.7 Offer liver ultrasound to retest children and young people for NAFLD every 3 years if they:
- have a normal ultrasound and
 - have type 2 diabetes or metabolic syndrome **and**
 - do not misuse alcohol.

1.2 Assessment for advanced liver fibrosis in people with NAFLD

Identifying people with advanced liver fibrosis

- 1.2.1 Offer testing for advanced liver fibrosis to people with NAFLD.
- 1.2.2 Consider using the enhanced liver fibrosis (ELF) test in people who have been diagnosed with NAFLD to test for advanced liver fibrosis.
- 1.2.3 Do not use routine liver blood tests to assess for advanced liver fibrosis in people

with NAFLD.

1.2.4 Diagnose people with advanced liver fibrosis if they have:

- an ELF score of 10.51 or above **and**
- NAFLD.

1.2.5 Refer adults and young people diagnosed with advanced liver fibrosis to a relevant specialist in hepatology.

1.2.6 Explain to people with an ELF score below 10.51 that:

- they are unlikely to have advanced liver fibrosis **and**
- reassessment for advanced liver fibrosis every 3 years for adults and every 2 years for children and young people is sufficient for regular monitoring **and**
- no interim tests are needed.

Give the person advice about lifestyle modifications they may be able to make (see section 1.2).

1.2.7 Offer retesting for advanced liver fibrosis for people with an ELF score below 10.51:

- every 3 years to adults
- every 2 years to children and young people.

1.2.8 Consider using ELF for retesting people with advanced liver fibrosis.

Monitoring adults and young people over 16 for cirrhosis

1.2.9 Monitor adults and young people over 16 with NAFLD and advanced liver fibrosis for cirrhosis in line with [NICE's guideline on cirrhosis](#).

Extra-hepatic conditions

- 1.2.10 Be aware that NAFLD is a risk factor for type 2 diabetes, hypertension and chronic kidney disease.
- 1.2.11 Be aware that in people with type 2 diabetes, NAFLD is a risk factor for atrial fibrillation, myocardial infarction, ischaemic stroke and death from cardiovascular causes.

Lifestyle modifications for NAFLD

- 1.2.12 Offer advice on physical activity and diet to people with NAFLD who are overweight or obese in line with [NICE's guideline on overweight and obesity management](#).
- 1.2.13 Explain to people with NAFLD that there is some evidence that exercise reduces liver fat content.
- 1.2.14 Consider the lifestyle interventions in [NICE's guideline on overweight and obesity management](#) for people with NAFLD regardless of their BMI.
- 1.2.15 Do not offer omega-3 fatty acids to adults with NAFLD because there is not enough evidence to recommend their use.
- 1.2.16 Explain to people with NAFLD who drink alcohol the importance of staying within the national recommended limits for alcohol consumption.

1.3 People with NAFLD who are taking statins

- 1.3.1 Be aware that people with NAFLD who are taking statins should keep taking them.
- 1.3.2 Only consider stopping statins if liver enzyme levels double within 3 months of starting statins, including in people with abnormal baseline liver blood results.

1.4 Pharmacological treatment

In July 2016, the use of pioglitazone and vitamin E in recommendations 1.4.1 to 1.4.5 was off label.

See [NICE's information on prescribing medicines](#).

- 1.4.1 In secondary or tertiary care settings only, consider pioglitazone or vitamin E for adults with advanced liver fibrosis, whether they have diabetes or not.
- 1.4.2 Before prescribing pioglitazone or vitamin E to adults, take into account any comorbidities that they have and the risk of adverse events associated with these conditions.
- 1.4.3 When prescribing pioglitazone, exercise particular caution if the person is at high risk of the adverse effects of the drug. Be aware that:
 - pioglitazone is contraindicated in people with a history of heart failure, previous or active bladder cancer and uninvestigated macroscopic haematuria (visible red blood cells in the urine)
 - known risk factors for these conditions, including increased age, should be carefully evaluated before treatment: see the manufacturers' summaries of product characteristics for details.
- 1.4.4 In tertiary care settings only, consider vitamin E for children with advanced liver fibrosis, whether they have diabetes or not.
- 1.4.5 In secondary or tertiary care settings only, consider vitamin E for young people with advanced liver fibrosis, whether they have diabetes or not.
- 1.4.6 Offer to retest people with advanced liver fibrosis 2 years after they start a new pharmacological therapy to assess whether treatment is effective.
- 1.4.7 Consider using the ELF test to assess whether pharmacological therapy is effective.

- 1.4.8 If an adult's ELF test score has risen, stop either vitamin E or pioglitazone and consider switching to the other pharmacological therapy.
- 1.4.9 If a child or young person's ELF test score has risen, stop vitamin E.

Terms used in this guideline

Advanced liver fibrosis

A grade of F3 or above using the Kleiner (NASH-CRN) or the steatosis, activity and fibrosis (SAF) score. This is referred to as bridging fibrosis (the presence of fibrosis linking hepatic veins to portal tracts).

Adults, children and young people

These are defined as:

- Children: over 1 year to under 16 years.
- Young people: 16 to under 18.
- Adults: 18 or older.

Metabolic syndrome

A group of chronic conditions that indicates increased cardiovascular risk. It includes central obesity (excessive abdominal fat), insulin resistance or type 2 diabetes, hypertension and dyslipidaemia.

Putting this guideline into practice

NICE has produced [tools and resources](#) to help you put this guideline into practice.

Putting recommendations into practice can take time. How long may vary from guideline to guideline, and depends on how much change in practice or services is needed. Implementing change is most effective when aligned with local priorities.

Changes recommended for clinical practice that can be done quickly – like changes in prescribing practice – should be shared quickly. This is because healthcare professionals should use guidelines to guide their work – as is required by professional regulating bodies such as the General Medical and Nursing and Midwifery Councils.

Changes should be implemented as soon as possible, unless there is a good reason for not doing so (for example, if it would be better value for money if a package of recommendations were all implemented at once).

Different organisations may need different approaches to implementation, depending on their size and function. Sometimes individual practitioners may be able to respond to recommendations to improve their practice more quickly than large organisations.

Here are some pointers to help organisations put NICE guidelines into practice:

1. Raise awareness through routine communication channels, such as email or newsletters, regular meetings, internal staff briefings and other communications with all relevant partner organisations. Identify things staff can include in their own practice straight away.
2. Identify a lead with an interest in the topic to champion the guideline and motivate others to support its use and make service changes, and to find out any significant issues locally.
3. Carry out a baseline assessment against the recommendations to find out whether there are gaps in current service provision.
4. Think about what data you need to measure improvement and plan how you will collect it. You may want to work with other health and social care organisations and specialist groups to compare current practice with the recommendations. This may also help identify

local issues that will slow or prevent implementation.

5. Develop an action plan, with the steps needed to put the guideline into practice, and make sure it is ready as soon as possible. Big, complex changes may take longer to implement, but some may be quick and easy to do. An action plan will help in both cases.

6. For very big changes include milestones and a business case, which will set out additional costs, savings and possible areas for disinvestment. A small project group could develop the action plan. The group might include the guideline champion, a senior organisational sponsor, staff involved in the associated services, finance and information professionals.

7. Implement the action plan with oversight from the lead and the project group. Big projects may also need project management support.

8. Review and monitor how well the guideline is being implemented through the project group. Share progress with those involved in making improvements, as well as relevant boards and local partners.

NICE provides a comprehensive programme of support and resources to maximise uptake and use of evidence and guidance. See our [into practice](#) pages for more information.

Also see Leng G, Moore V, Abraham S, editors (2014) Achieving high quality care – practical experience from NICE. Chichester: Wiley.

Context

Primary non-alcoholic fatty liver disease (NAFLD) is an excess of fat in the liver (steatosis) that is not a result of excessive alcohol consumption or other secondary causes. These secondary causes include side effects of certain medications, hepatitis C virus infection and particular endocrine conditions. NAFLD ranges from hepatic steatosis, through inflammatory non-alcoholic steatohepatitis (NASH), to fibrosis or cirrhosis.

The prevalence of NAFLD in the general population is estimated at 20% to 30%. Around 2% to 3% of the population have NASH. NAFLD is more common in people who have type 2 diabetes or metabolic syndrome.

The prevalence of NAFLD is increasing, placing a greater burden on healthcare resources. The rate of progression of NAFLD is variable; being overweight and having diabetes are associated with an increased risk of progressive disease. The average age of people with NASH is 40 years to 50 years and for NASH-cirrhosis 50 years to 60 years. However the emerging epidemic of childhood obesity means that increasing numbers of younger people have NAFLD, with some prevalence studies showing that up to 38% of obese children have evidence of NAFLD. With NAFLD progressing through its spectrum even in childhood, the age that people develop significant liver disease is likely to fall and early diagnosis and management are therefore important at all ages. There is currently no licensed treatment for NAFLD. Guidance is needed for use in both primary and secondary care settings.

Recommendations for research

The guideline committee has made the following recommendations for research. The guideline committee's full set of research recommendations is detailed in the [full guideline](#).

1 Non-invasive tests for diagnosing NAFLD in adults

Which non-invasive tests are most accurate and cost-effective in identifying non-alcoholic fatty liver disease (NAFLD) in adults with risk factors, type 2 diabetes and metabolic syndrome?

Why this is important

Non-alcoholic fatty liver disease (NAFLD) is present in over 50% of adults with type 2 diabetes mellitus or metabolic syndrome. Untreated it can progress to fibrosis, cirrhosis and hepatocellular cancer. In most patients NAFLD is asymptomatic and is only detected incidentally when liver blood tests or abdominal ultrasound are performed for some other reason. Even then, more than 80% of patients with NAFLD have normal routine liver blood tests. There is an urgent need for a simple, accessible, cost-effective, non-invasive test capable of case-finding NAFLD in the huge numbers of people at risk.

The 'gold standard' for diagnosis is liver biopsy. It is not feasible to perform liver biopsy in large numbers of at risk patients, so magnetic resonance based techniques are increasingly used as the comparison in studies assessing non-invasive tests for NAFLD. These demonstrate high diagnostic accuracy but are impractical or too expensive for large scale case finding.

2 Non-invasive tests for diagnosing NASH

Which non-invasive tests most accurately identify non-alcoholic steatohepatitis (NASH) in people with non-alcoholic fatty liver disease (NAFLD)?

Why this is important

NASH develops in only a minority of people with NAFLD. It is thought to be the precursor

of liver fibrosis, which is associated with morbidity and mortality. As a result, NASH has been the main target for treatment in NAFLD. This is because reducing the severity of NASH would reduce the risk of a person progressing to fibrosis and advanced liver disease. However, the only way to identify people with NASH is by performing an invasive liver biopsy which is impractical in view of its risks to health and cost. Given that between 20 and 30% of the population have NAFLD, it is important that we have a simple non-invasive method for determining which people have NASH. Then they can start treatment to reduce the risk of developing fibrosis and complications of end-stage liver disease.

3 Non-invasive tests for diagnosing NAFLD and advanced liver fibrosis in children and young people

Which non-invasive tests most accurately diagnose NAFLD and advanced liver fibrosis in children and young people?

Why this is important

NAFLD has become the most common chronic liver disease in children and young people in industrialised countries, mainly as a result of obesity.

NAFLD is often suspected in children and young people with abnormal liver tests or evidence of fatty changes on ultrasound. However, the spectrum of NAFLD (from simple steatosis to steatohepatitis, fibrosis, cirrhosis and liver-related morbidity) can be present in the absence of abnormal liver tests. Early detection and assessment of severity of NAFLD would help identify potential silent progressive fatty liver disease.

Diagnostic practice varies and includes clinical, biochemical and radiographic tests. The evidence review showed that few diagnostic techniques have been assessed in children and young people. There is some evidence for ELF in diagnosing advanced liver fibrosis in children and young people with NAFLD, but only from 1 study. Further research is needed to confirm the most accurate tests in this group.

4 Probiotic and prebiotic supplements

What is the clinical and cost effectiveness of probiotics or prebiotics to treat NAFLD in

adults, young people and children?

Why this is important

NAFLD is the most common metabolic liver disease, occurring in approximately 30% of all adults, around 46% of obese people and around 53% of people with type 2 diabetes. Liver fat accumulation is the first stage of more serious chronic liver disease in NAFLD. A small body of evidence supports the use of probiotics in NAFLD but the data are inconclusive and high-quality double-blind randomised placebo-controlled trials are needed. The evidence from cross-sectional studies suggests associations between unfavourable disturbance in gut microbiota and obesity or type 2 diabetes, but there is very limited evidence on whether modifying the gut microbiota influences NAFLD.

5 Pharmacological therapy for advanced liver fibrosis in children and young people

What is the clinical and cost effectiveness of pharmacological therapy in children and young people with advanced liver fibrosis?

Why this is important

Observational studies reported that up to 10% of children and young people diagnosed with NAFLD progress to advanced liver fibrosis and are at risk of developing advanced stages of liver disease. Pharmacological treatment (for example, pioglitazone or vitamin E) could prevent progression to advanced liver fibrosis or end-stage liver disease, as has been reported in a number of high quality studies in adults with confirmed NAFLD. There are insufficient data on the efficacy of similar pharmacological treatment in children and young people with NAFLD to make clear treatment recommendations.

Finding more information and committee details

To find NICE guidance on related topics, including guidance in development, see the [NICE topic page on liver conditions](#).

For full details of the evidence and the guideline committee's discussions, see the [full guideline](#). You can also find information about [how the guideline was developed](#), including [details of the committee](#).

NICE has produced [tools and resources to help you put this guideline into practice](#). For general help and advice on putting our guidelines into practice, see [resources to help you put NICE guidance into practice](#).

Update information

Minor changes since publication

March 2025: We updated links following publication of NICE's guideline on overweight and obesity management.

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