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

NICE guideline: short version

Draft for consultation, December 2015

This guideline covers assessing and managing non-alcoholic fatty liver disease (NAFLD) in adults, young people and children. It aims to improve how NAFLD is identified, diagnosed and managed with pharmacological and non-pharmacological treatment. It recommends tools to assess the severity of NAFLD and gives advice on monitoring people with NAFLD for advanced liver fibrosis.

The guideline does not cover the investigation of people with incidentally-found abnormal liver blood tests, of which NAFLD is but 1 of the common causes, and does not cover the complications of NAFLD cirrhosis.

Who is it for?

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

This version of the guideline contains the recommendations, context and recommendations for research. The Guideline Committee’s discussion and the evidence reviews are in the full guideline.

Other information about how the guideline was developed is on the project page. This includes the scope, and details of the Guideline Committee and any declarations of interest.
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1 **Recommendations**

People have the right to be involved in discussions and make informed decisions about their care, as described in [Your care](#).

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

At the time of consultation (December 2015), 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.

2 **1.1 Assessment**

3 **When to suspect NAFLD**

4 1.1.1 Suspect non-alcoholic fatty liver disease (NAFLD) in people who have:

5  - type 2 diabetes or
6  - metabolic syndrome.

8 **Diagnosing NAFLD**

9 1.1.2 Take an alcohol history to rule out alcohol-related liver disease.

10 See also NICE’s [cirrhosis](#) guideline¹.

11 1.1.3 Do not use routine liver blood tests to rule out NAFLD.

12 **Diagnosing NAFLD in adults**

13 1.1.4 Consider testing adults for NAFLD if:

14  - they have type 2 diabetes or metabolic syndrome and

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¹ The NICE [cirrhosis](#) guideline is currently out for consultation.
• alcohol-related liver disease has been ruled out.

1.1.5 Use the fatty liver index (FLI) test if testing adults for NAFLD.

1.1.6 Diagnose adults with NAFLD if:

• they have an FLI score of 60 or above and
• other suspected causes of fatty liver have been ruled out.

1.1.7 Consider retesting adults for NAFLD using FLI every 5 years if they have:

• an FLI score of less than 60 and
• type 2 diabetes or metabolic syndrome.

**Diagnosing NAFLD in children and young people**

1.1.8 Test children and young people for NAFLD using ultrasound if:

• they have type 2 diabetes or metabolic syndrome and
• do not misuse alcohol.

1.1.9 Diagnose children and young people with NAFLD if:

• they have fatty liver on ultrasound and
• other suspected causes of fatty liver have been ruled out.

1.1.10 Retest children and young people for NAFLD using ultrasound every 3 years if:

• they have a normal ultrasound and
• type 2 diabetes or metabolic syndrome.

**Diagnosing advanced liver fibrosis**

1.1.11 Use the enhanced liver fibrosis (ELF) test to test people for advanced liver fibrosis if NAFLD has been diagnosed (either by targeted case-finding as in recommendations 1.1.4 and 1.1.8 or by incidental findings).
1.1.12 Diagnose people with advanced liver fibrosis and refer them to a relevant specialist in hepatology, if they have:

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

1.2 Monitoring

Advanced liver fibrosis

1.2.1 Retest adults with NAFLD and an ELF score of less than 10.51 for advanced liver fibrosis using ELF every 3 years.

1.2.2 Retest children and young people with NAFLD and an ELF score of less than 10.51 for advanced liver fibrosis using ELF every 2 years.

1.2.3 Monitor adults and young people over 16 with NAFLD and advanced liver fibrosis for cirrhosis in line with NICE’s cirrhosis guideline.

Extra-hepatic conditions

1.2.4 Be aware that NAFLD is a risk factor for type 2 diabetes, hypertension and chronic kidney disease.

1.2.5 Be aware that in people with type 2 diabetes, NAFLD is a risk factor for atrial fibrillation, myocardial infarction, ischaemic stroke and cardiovascular death.

1.3 Managing NAFLD

Lifestyle modifications

Weight reduction

1.3.1 Manage overweight and obesity in people with NAFLD in line with the recommendations on physical activity and diet in NICE's obesity guideline.

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The NICE cirrhosis guideline is currently out for consultation.
1.3.2 Explain to people with NAFLD that there is some evidence that
exercise reduces liver fat content.

1.3.3 Consider the lifestyle interventions in NICE’s obesity guideline for
people with NAFLD regardless of their BMI.

1.3.4 Explain to adults with NAFLD that there is some evidence that the
following probiotics could be effective for reducing liver fat content
and liver fibrosis:

- *Bifidobacterium bifidum*
- *Bifidobacterium breve*
- *Bifidobacterium infantis*
- *Bifidobacterium longum*
- *Lactobacillus acidophilus*
- *Lactobacillus casei*
- *Lactobacillus delbrueckii bulgaricus*
- *Lactobacillus paracasei*
- *Lactobacillus plantarum*
- *Lactobacillus rhamnosus*
- *Streptococcus thermophilus.*

1.3.5 Explain to children and young people with NAFLD, and their
parents or carers, that there is no evidence that probiotics reduce
liver fat content and liver fibrosis.

1.3.6 Do not offer omega-3 fatty acids to adults with NAFLD because
there is not enough evidence to recommend their use.

1.3.7 Explain to children and young people with NAFLD, and their
parents or carers, that there is some evidence that the omega-3
fatty acid docosahexaenoic acid reduces liver fat content and
alanine aminotransferase levels but the clinical significance of these is uncertain.

**Alcohol advice**

1.3.8 Explain to people with NAFLD who drink alcohol of the importance of staying within the national recommended limits for alcohol consumption.

**Pharmacological treatment**

1.3.9 In secondary care settings only, consider pioglitazone\(^3\) or vitamin E\(^4\) for adults with advanced liver fibrosis, whether they have diabetes or not.

1.3.10 Before prescribing pioglitazone or vitamin E, take into account any comorbidities that the person has and the risk of adverse events associated with these conditions.

1.3.11 In secondary or tertiary care settings only, consider vitamin E for children and young people with advanced liver fibrosis, whether they have diabetes or not.

1.3.12 Offer the ELF test to people with advanced liver fibrosis 2 years after they start new pharmacological therapy to assess if treatment is effective.

1.3.13 If an adult’s ELF test score has risen, stop either vitamin E or pioglitazone and consider switching to the other pharmacological therapy.

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\(^3\) When prescribing pioglitazone, exercise particular caution if the person is at high risk of the adverse effects of the drug. 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.

\(^4\) At the time of consultation (December 2015), neither pioglitazone nor vitamin E had a UK marketing authorisation for this indication. 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 [Good practice in prescribing medicines — guidance for doctors](https://www.gmc-uk.org/-/media/documents/good-practice-in-prescribing-medicines-guidance-for-doctors.pdf) for further information.
1.3.14 If a child or young person’s ELF test score has risen, stop vitamin E.

**People with NAFLD who are taking statins**

1.3.15 Be aware that people with NAFLD who are taking statins should keep taking statins.

1.3.16 Only consider stopping statins if liver blood tests double within 3 months of starting statins, including in people with abnormal baseline liver blood tests.

To find out what NICE has said on topics related to this guideline, see our web page on liver conditions.

**Terms used in this guideline**

**Advanced liver fibrosis**

A grade of F3 or above using the Kleiner (NASH-CRN) or the SAF score. This is referred to as bridging fibrosis (the presence of fibrosis that reaches from one portal area to another).

**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 for example, side effects of certain medications, hepatitis C virus infection and particular endocrine conditions. NAFLD ranges from hepatic steatosis, through to inflammatory non-alcoholic steatohepatitis (NASH), to fibrosis or cirrhosis.

The prevalence of NAFLD in the general population is estimated at 20–30%.

Around 2–3% of the population have NASH. NAFLD is more common in people who have central obesity (excessive abdominal fat), insulin resistance or type 2 diabetes, hypertension and dyslipidaemia. This group of chronic
conditions is indicative of increased cardiovascular risk and together comprise ‘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 40–50 years and for NASH-cirrhosis 50–60 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 issues 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 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 who would be suitable for treatments is by
performing an invasive liver biopsy and assessing the risk 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 of these people have NASH. Then they can start the treatment to prevent them from developing fibrosis and end-stage complications of liver disease.

2 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 increasing obesity rates. The presence of NAFLD in children and young people is often suspected in those presenting with abnormal liver tests or evidence of fatty changes on ultrasound. However, the full spectrum of NAFLD (from simple steatosis to steatohepatitis, fibrosis, cirrhosis and liver-related morbidity) can also be present in the absence of abnormal liver tests.

Early detection and assessment of severity of NAFLD would be beneficial to identify children and young people with potential silent progressive fatty liver disease. Diagnostic practice varies widely and includes clinical, biochemical and radiographic tests. The review of evidence in this guideline showed that very few diagnostic techniques have been assessed in children and young people and although there is some evidence for ELF in diagnosing advanced liver fibrosis in children and young people with NAFLD, this was only from 1 study. Further research is therefore warranted to confirm the most accurate tests in this group of people.
3 Probiotic and prebiotic supplements

What is the clinical and cost effectiveness of using 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 the results of 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.

4 Alcohol advice

Should people with NAFLD restrict their consumption of alcohol to below national limits?

Why this is important

In people with NAFLD, but without advanced liver fibrosis, there is uncertainty about the effect of drinking alcohol below national limits on progression of NAFLD. Some studies have suggested that modest consumption of alcohol (1 unit/day) may confer cardiovascular benefits and reduce likelihood of NAFLD. However there is concern that these studies have not accounted for other factors and that even modest alcohol consumption may accelerate progression of liver fibrosis in the setting of NAFLD. Ensuring people with NAFLD are given the correct advice on alcohol consumption will reduce progression of liver disease and therefore reduce morbidity and cost to the NHS.
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 will be 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.