NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE Guideline Cirrhosis in over 16s: assessment and management

This guideline covers assessing and managing suspected or confirmed cirrhosis in people who are 16 years or older. It aims to improve how cirrhosis is identified and diagnosed. It recommends tools to assess the severity of cirrhosis and gives advice on monitoring people with cirrhosis to detect and manage complications early, and referral criteria for tertiary care.

Draft for consultation, May 2023

This guideline will update <u>NICE guideline NG50</u> (published July 2016).

Who is it for?

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

What does it include?

- the recommendations that have been updated
- related recommendations that have not been updated (shaded in grey and marked [2016]), included here for context
- recommendations for research
- rationale and impact sections that explain why the committee made the
 2023 recommendations and how they might affect practice
- the guideline context.

Information about how the guideline was developed is on the <u>guideline's</u> <u>webpage</u>. This includes the evidence reviews, the scope, details of the committee and any declarations of interest.

New and updated recommendations

We have reviewed the evidence on monitoring for, and managing, oesophageal variceal bleeding, preventing spontaneous bacterial peritonitis in people with cirrhosis and ascites, and preventing decompensation in people with compensated cirrhosis. You are invited to comment on the new and updated recommendations. These are marked as [2023].

You are also invited to comment on recommendations that we propose to delete from the 2016 guideline.

We have not reviewed the evidence for the recommendations marked [2016] (shaded in grey) and cannot accept comments on them.

Sections of the guideline that have had no changes at all have been temporarily removed for this consultation and will be reinstated when the final guideline is published. See the current version of the guideline.

See <u>update information</u> for a full explanation of what is being updated.

Full details of the evidence and the committee's discussion on the 2023 recommendations are in the <u>evidence reviews</u>. Evidence for the 2016 recommendations is in the full version of the 2016 guideline.

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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 NICE's information about 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.

1.2 Monitoring

years. [2016]

3 Oesophageal varices

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- After a diagnosis of cirrhosis, offer upper gastrointestinal endoscopy to detect oesophageal varices. [2016]
 1.2.8 For people in whom no oesophageal varices have been detected, offer surveillance using upper gastrointestinal endoscopy every 3
- 9 1.2.9 If medium to large varices are detected during upper
 10 gastrointestinal endoscopy, consider simultaneous endoscopic
 11 variceal band ligation. [2023]

For a short explanation of why the committee made the 2023 recommendation and how it might affect practice, see the <u>rationale and impact section on oesophageal varices</u>.

Full details of the evidence and the committee's discussion are in <u>evidence</u> review A: clinical and cost effectiveness of non-selective beta-blockers and

endoscopic variceal band ligation for the primary prevention of bleeding in people with oesophageal varices due to cirrhosis.

1.3 Managing complications

2 Preventing oesophageal variceal bleeding

In May 2023, the use of carvedilol for preventing oesophageal variceal bleeding was off-label. See <u>NICE's information on prescribing medicines</u>.

Carvedilol is contraindicated in people with clinically significant hepatic impairment.

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- 1.3.1 If the person with cirrhosis has medium to large varices:
- discuss the benefits and harms of all treatment options in line with <u>NICE's guidelines on shared decision making</u> and <u>patient</u> experience in adult NHS services
 - explain what treatment involves and ask about any potential barriers that could prevent them from accessing treatment (for example, they may find it difficult to take tablets regularly because they are dependent on alcohol or are experiencing homelessness). [2023]
- 1.3.2 Offer carvedilol or propranolol for preventing variceal bleeding, unless the person is unable to:
 - tolerate either carvedilol or propranolol, or take either for medical reasons. or
 - take tablets regularly because of their circumstances. [2023]
- 18 1.3.3 Be aware that carvedilol and propranolol should be used with

 19 caution in people with cirrhosis because it can have a greater effect

2		on their heart rate and blood pressure than in people who are taking these medicines for other conditions. [2023]
3 4	1.3.4	Titrate the dose of carvedilol or propranolol based on the person's heart rate and blood pressure. [2023]
5 6 7	1.3.5	When starting treatment with carvedilol, begin with a low dosage (for example, 6.25 mg a day) and increase the dose depending on the results of heart and blood pressure monitoring. [2023]
8	1.3.6	Offer endoscopic variceal band ligation if the person is unable to:
9 10		 tolerate carvedilol or propranolol, or take either for medical reasons, or
11		take tablets regularly because of their circumstances. [2023]

For a short explanation of why the committee made the 2023 recommendations and how they might affect practice, see the <u>rationale and</u> impact section on preventing oesophageal variceal bleeding.

Full details of the evidence and the committee's discussion are in <u>evidence</u> review A: clinical and cost effectiveness of non-selective beta-blockers and <u>endoscopic variceal band ligation for the primary prevention of bleeding in people with oesophageal varices due to cirrhosis.</u>

Preventing spontaneous bacterial peritonitis

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- 13 1.3.7 Do not routinely offer antibiotics to prevent spontaneous bacterial peritonitis (SBP) in people with cirrhosis and ascites unless:
 - they are at high risk of developing SBP because they have severe liver disease (for example, they have an ascitic protein of 15 g per litre or less, a Child–Pugh score of more than 9 or a MELD score of more than 16) or
 - the consequences of an infection could seriously impact their care, for example, if it could affect their wait for a transplant or a

1 2		transjugular intrahepatic portosystemic shunt (TIPS) procedure. [2023]
3	1.3.8	When offering antibiotics to prevent SBP:
4		 follow local microbiological advice (in line with the <u>NICE</u>
5		guideline on antimicrobial stewardship: systems and processes
6		for effective antimicrobial medicine use)
7		 continue with treatment until the ascites is resolved. [2023]
	For a s	hort explanation of why the committee made the 2023
	recomn	nendations and how they might affect practice, see the <u>rationale and</u>
	impact	section on preventing spontaneous bacterial peritonitis.
	Full det	ails of the evidence and the committee's discussion are in evidence
	review	B: use of antibiotics to prevent spontaneous bacterial peritonitis.
8	Primary	prevention of decompensation
	In May	2023, the use of carvedilol and propranolol for the primary
	preven	tion of decompensation was off-label. See NICE's information on
	prescri	bing medicines.
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11	1.3.9	Consider carvedilol or propranolol for the primary prevention of
12		decompensation in people who have cirrhosis and confirmed, or
13		suspected, clinically significant portal hypertension. [2023]
14	1.3.10	Titrate the dose of carvedilol or propranolol based on the person's
15		heart rate and blood pressure. See recommendation 1.3.3 in the
16		section on preventing oesophageal variceal bleeding for further
17		advice on starting treatment with carvedilol or propranolol. [2023]

1 1.3.11 When starting treatment with either carvedilol or propranolol, use a low dosage (for example, 6.25 mg a day for carvedilol or 40 mg twice a day for propranolol) and increase the dose depending on the results of heart and blood pressure monitoring. [2023]

For a short explanation of why the committee made the 2023 recommendations and how they might affect practice, see the <u>rationale and impact section on preventing primary decompensation</u>.

Full details of the evidence and the committee's discussion are in <u>evidence</u> review C: clinical and cost effectiveness of non-selective beta-blockers for the primary prevention of decompensation in people with compensated <u>cirrhosis</u>.

Other complications

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6 1.3.12 Offer prophylactic intravenous antibiotics for people with cirrhosis 7 who have upper gastrointestinal bleeding. [2016] 1.3.13 Review intravenous antibiotics prescriptions in line with the section 8 9 on prescribing intravenous antimicrobials in the NICE guideline on antimicrobial stewardship: systems and processes for effective 10 antimicrobial medicine use. [2016] 11 Consider a TIPS procedure for people with cirrhosis who have 12 1.3.14

14 Recommendations for research

refractory ascites. [2016]

- 15 The guideline committee has made the following recommendations for
- 16 research.

1 Key recommendations for research

- 1 Effectiveness of endoscopic variceal band ligation plus a non-
- 3 selective beta-blocker for preventing variceal bleeding in people with
- 4 medium to large oesophageal varices
- 5 What is the clinical and cost effectiveness of endoscopic variceal band ligation
- 6 plus a non-selective beta-blocker compared with either of these interventions
- 7 alone for preventing variceal bleeding in adults with cirrhosis and medium to
- 8 large oesophageal varices? [2023]

For a short explanation of why the committee made this recommendation for research, see the <u>rationale and impact section on preventing</u> oesophageal variceal bleeding.

Full details of the evidence and the committee's discussion are in <u>evidence</u> review A: clinical and cost effectiveness of non-selective beta-blockers and <u>endoscopic variceal band ligation for the primary prevention of bleeding in people with oesophageal varices due to cirrhosis.</u>

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2 Antibiotic prophylaxis to prevent spontaneous bacterial peritonitis

- What is the clinical and cost effectiveness of antibiotic prophylaxis to prevent
- spontaneous bacterial peritonitis (SBP) in people with cirrhosis and ascites?
- 13 **[2023]**

For a short explanation of why the committee made this recommendation for research, see the <u>rationale and impact section on preventing</u> spontaneous bacterial peritonitis.

Full details of the evidence and the committee's discussion are in <u>evidence</u> review B: use of antibiotics to prevent spontaneous bacterial peritonitis.

- 1 3 Primary prevention of decompensation using non-selective beta-
- 2 blockers
- 3 What is the clinical and cost effectiveness of non-selective beta-blockers for
- 4 the primary prevention of decompensation in people with compensated
- 5 cirrhosis and signs of clinically significant portal hypertension? [2023]

For a short explanation of why the committee made this recommendation for research see the <u>rationale and impact section on primary prevention of decompensation</u>.

Full details of the evidence and the committee's discussion are in <u>evidence review</u>

C: clinical and cost effectiveness of non-selective beta-blockers for the primary

prevention of decompensation in people with compensated cirrhosis.

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7 Other recommendations for research

- 8 Treating small oesophageal varices
- 9 Do non-selective beta-blockers improve survival and prevent first variceal
- bleeds in people with cirrhosis that is associated with small oesophageal
- 11 varices? **[2016]**
- 12 Antibiotic resistance in treating spontaneous bacterial peritonitis
- How frequently does antibiotic resistance occur, and how significant are
- 14 antibiotic treatment-related complications when antibiotics are used for the
- primary prevention of spontaneous bacterial peritonitis in people at high risk of
- having, or developing, cirrhosis? [2016]

17 Rationale and impact

- 18 These sections briefly explain why the committee made the recommendations
- 19 and how they might affect practice.

20 Oesophageal varices

21 Recommendation 1.2.9

1 Why the committee made the recommendation

- 2 Everyone diagnosed with cirrhosis should be offered an upper gastrointestinal
- 3 endoscopy to detect oesophageal varices. Based on their knowledge and
- 4 experience, the committee agreed that this also presents an opportunity to
- 5 carry out one-off endoscopic variceal band ligation on medium to large varices
- 6 at the same time because the equipment and preparation is the same for both
- 7 procedures. However, it may not always be possible to offer the treatment
- 8 during endoscopy because some healthcare professionals will not be trained
- 9 or have experience in carrying out endoscopic variceal band ligation.

10 How the recommendation might affect practice

- All people undergo an exploratory endoscopy when diagnosed with cirrhosis,
- so the additional resource impact of carrying out endoscopic variceal band
- ligation at the same time, where possible, is expected to be small.
- 14 Return to recommendation

15 Preventing oesophageal variceal bleeding

16 Recommendations 1.3.1 to 1.3.6

17 Why the committee made the recommendations

- Following initial endoscopic variceal band ligation, non-selective beta-blockers
- or further endoscopic variceal band ligation can be used to prevent
- 20 oesophageal variceal bleeding. The committee agreed that most people would
- 21 prefer to take non-selective beta-blockers over endoscopic variceal band
- 22 ligation because they are less invasive and would prevent further hospital
- visits. However, some people will need further endoscopic variceal band
- 24 ligation instead because they have had adverse reactions to non-selective
- 25 beta-blockers, the medicines do not work as expected, or they find it difficult to
- take tablets every day. The committee therefore agreed it was important to
- 27 discuss all these treatment options and talk to the person about their
- 28 preferences and personal circumstances to identify the right treatment for
- 29 them.

- 1 The evidence did not distinguish between the clinical effectiveness of non-
- 2 selective beta-blockers and endoscopic variceal band ligation. However, non-
- 3 selective beta-blockers were found to be more cost effective when people
- 4 were able to take these medicines regularly.
- 5 Carvedilol and propranolol are commonly used in practice to prevent variceal
- 6 bleeding, although the committee noted that clinicians often prefer to
- 7 prescribe carvedilol because it has fewer side effects. Both medicines need to
- 8 be used with caution because they have a much larger effect on the heart rate
- 9 and blood pressure of people with liver disease than in people who do not
- 10 have liver disease (carvedilol is contraindicated in people with clinically
- significant hepatic impairment for this reason). The committee noted that the
- 12 BNF already recommends a lower starting dose for propranolol because of
- this, but was concerned that healthcare professionals may not be aware of
- 14 this important consideration for carvedilol because this is an off-label use of
- 15 the medicine. Therefore, they agreed that carvedilol should be started at a
- much lower dose than in people without liver disease. The studies did not look
- at the use of endoscopic variceal band ligation with a non-selective beta-
- 18 blocker to prevent variceal bleeding, which the committee agreed could have
- 19 an additional benefit. They therefore made a research recommendation to
- 20 look at its effectiveness.

21 How the recommendations might affect practice

- In the committee's experience, both non-selective beta-blockers and
- 23 endoscopic variceal band ligation are in common use for preventing
- 24 oesophageal variceal bleeding. These recommendations will increase the use
- 25 of non-selective beta-blockers and should reduce the use of endoscopic
- variceal band ligation, and therefore reduce the costs associated with
- 27 preventing variceal bleeding.
- 28 Return to recommendations

29 Preventing spontaneous bacterial peritonitis

30 Recommendations 1.3.7 and 1.3.8

Why the	committee	made the	recomme	ndations
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- 2 The committee considered evidence from a network meta-analysis (NMA)
- 3 comparing different types of antibiotics for preventing spontaneous bacterial
- 4 peritonitis (SBP) in people with cirrhosis and ascites. They noted that 1 of the
- 5 antibiotics in the analysis (norfloxacin) was not available in the UK, and that
- 6 the fluoroquinolone class of antibiotics (which includes ciprofloxacin) was the
- 7 subject of a 2019 Medicines and Healthcare products Regulatory Agency
- 8 (MHRA) drug safety update that includes restrictions and precautions for their
- 9 use.

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- 10 The NMA did not demonstrate any overall benefit of antibiotic prophylaxis
- when compared with no prophylactic treatment. Therefore, the committee
- agreed that antibiotics should not be routinely offered to prevent SBP in
- people with cirrhosis and ascites, unless they were either at high risk of
- developing the infection or its impact could be severe. Most of the evidence
- 15 focused on people who had low ascites protein count, so this was included as
- an example of a measure that could be used to identify risk factors. However,
- 17 the committee also included other measures for assessing the severity of liver
- 18 disease.
- 19 The committee agreed that, because the NMA showed no overall benefit of
- using 1 antibiotic over another, prescribers should follow local microbiological
- 21 advice. This would mean local pathogen distribution would be taken into
- 22 account and would lead to better antimicrobial stewardship.
- 23 The committee also noted that the evidence was not methodologically robust,
- the sample sizes were small, and none of the studies looked at quality-of-life
- 25 data. Therefore, they made a research recommendation to encourage studies
- that are more rigorous and which look at clinically important outcomes such as
- 27 mortality, health-related quality of life and serious adverse events.

28 How the recommendations might affect practice

- 29 In the committee's experience, there is wide variation in practice in the
- prescribing of antibiotics for preventing SBP. The 2023 recommendations

- suggest using antibiotics for people at high risk, but do not specify which
- 2 antibiotics. This means that antibiotic choice can be based on local
- 3 microbiological advice and funding agreements, which may reduce the costs
- 4 of prescribing antibiotics where necessary. The 2023 recommendations also
- 5 emphasise that antibiotics are not necessary for everyone with cirrhosis and
- 6 ascites.
- 7 Return to recommendations
- 8 Primary prevention of decompensation
- 9 Recommendations 1.3.9 to 1.3.11
- 10 Why the committee made the recommendations
- 11 Emerging evidence on the effectiveness of carvedilol and propranolol in
- 12 preventing primary decompensation in people with clinically significant portal
- 13 hypertension is unclear but looks promising. Therefore, the committee agreed
- that either medicine could be a potential treatment option.
- 15 The committee made a research recommendation on the effectiveness of
- non-selective beta-blockers. They also noted that a large, National Institute for
- Health and Care Research-funded trial underway in the UK is looking at the
- use of carvedilol for this indication. They agreed this evidence could help
- inform future updates of this guideline.
- 20 How the recommendations might affect practice
- 21 The committee noted that prescribing non-selective beta-blockers for this
- indication was a new practice, and that they are not widely used in this way
- 23 across the NHS. Health economic analysis shows that the additional cost of
- 24 prescribing these medicines is outweighed by savings in terms of preventing
- 25 decompensation.
- 26 Return to recommendations

1 Finding more information and committee details

- 2 To find NICE guidance on related topics, including guidance in development,
- 3 see the NICE topic page on liver conditions.
- 4 For full details of the evidence and the guideline committee's discussions, see
- 5 the <u>full guideline</u>. You can also find information about <u>how the guideline was</u>
- 6 <u>developed</u>, including <u>details of the committee</u>.
- 7 NICE has produced tools and resources to help you put this guideline into
- 8 practice. For general help and advice on putting our guidelines into practice,
- 9 see resources to help you put NICE guidance into practice.

10 Update information

11 **September 2023**

- We have reviewed the evidence on preventing oesophageal variceal bleeding
- and spontaneous bacterial peritonitis in people with cirrhosis. We have added
- 14 a new section on using non-selective beta-blockers to prevent
- decompensation in people with compensated cirrhosis.
- Recommendations are marked [2023] if the evidence has been reviewed.

17 Recommendations that have been deleted, or changed

18 without an evidence review

- We propose to delete some recommendations from the 2016 guideline. <u>Table</u>
- 1 sets out these recommendations and includes details of replacement
- 21 recommendations. If there is no replacement recommendation, an explanation
- for the proposed deletion is given.
- 23 For recommendations shaded in grey and ending [2016], we have not
- 24 reviewed the evidence.
- 25 See also the current NICE guideline and supporting documents.

1 Table 1 Recommendations that have been deleted

Comment		
Replaced by: 1.3.1 If the person with cirrhosis has medium to large varices: • discuss the benefits and harms of all treatment options in line with NICE's guidelines on shared decision making and patient experience in adult NHS services • explain what treatment involves and ask about any potential barriers that could prevent them from accessing treatment (for example, they may find it difficult to take tablets regularly because they are dependent on alcohol or are experiencing homelessness). [2023] 1.3.2 Offer carvedilol or propranolol for preventing variceal bleeding, unless the person is unable to: • tolerate either carvedilol or propranolol, or take either for medical reasons, or • take tablets regularly because of their circumstances. [2023] 1.3.3 Be aware that carvedilol and propranolol should be used with caution in people with cirrhosis because it can have a greater effect on their heart rate and blood pressure than in people who are taking these medicines for other conditions. [2023] 1.3.4 Titrate the dose of carvedilol or propranolol based on the person's heart rate and blood pressure. [2023] 1.3.5 When starting treatment with carvedilol, begin with a low dosage (for		
have a greater effect on their heart rate and blood pressure than in people who are taking these medicines for other conditions. [2023] 1.3.4 Titrate the dose of carvedilol or propranolol based on the person's heart rate and blood pressure. [2023] 1.3.5 When starting treatment with		
 [2023] 1.3.6 Offer endoscopic variceal band ligation if the person is unable to: tolerate carvedilol or propranolol, or take either for medical reasons, or take tablets regularly because of their circumstances. [2023] 		

Offer prophylactic oral ciprofloxacin or norfloxacin for people with cirrhosis and ascites with an ascitic protein of 15 g/litre or less, until the ascites has resolved.

At the time of publication (July 2016), neither ciprofloxacin nor norfloxacin 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 for further information. (1.3.5)

Replaced by:

- 1.3.7 Do not routinely offer antibiotics to prevent spontaneous bacterial peritonitis (SBP) in people with cirrhosis and ascites unless:
- they are at high risk of developing SBP because they have severe liver disease (for example, they have an ascitic protein of 15 g per litre or less, a Child–Pugh score of more than 9, or a MELD score of more than 16) **or**
- the consequences of an infection could seriously impact their care, for example, if it could affect their wait for a transplant or a transjugular intrahepatic portosystemic shunt (TIPS) procedure. [2023]
- 1.3.8 When offering antibiotics to prevent SBP:
- follow local microbiological advice (in line with the <u>NICE guideline on</u> <u>antimicrobial stewardship: systems</u> <u>and processes for effective</u> <u>antimicrobial medicine use</u>)
- continue with treatment until the ascites is resolved. [2023]

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