NICE National Institute for Health and Care Excellence

2020 surveillance of cirrhosis in over 16s: assessment and management (NICE guideline NG50)

Surveillance report

Published: 21 October 2020

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Surveillance decision

We will update the NICE guideline on cirrhosis in over 16s: assessment and management. The update will focus on primary prophylaxis of variceal haemorrhage and primary prevention of spontaneous bacterial peritonitis (SBP) in people with cirrhosis and ascites.

Reasons for the decision

This section provides a summary of the areas that will be updated and the reasons for the decision to update.

Primary prophylaxis of variceal haemorrhage

The guideline recommends oesophageal variceal ligation (EVL) as primary prophylaxis for preventing bleeding from medium/large varices. Evidence identified through the current review shows that non-specific beta-blockers may be as effective as EVL for reducing bleeding or mortality and offer an alternative approach. New published evidence may also change the guideline cost-effectiveness estimates for EVL and this may impact on the recommendations.

Primary prevention of SBP in people with cirrhosis and ascites

Evidence indicates fluoroquinolones may no longer be the antibiotics of first choice for primary prevention of SBP in people with cirrhosis and ascites. New published evidence suggests that rifaximin or co-trimoxazole, when compared with the fluoroquinolone antibiotics, may be at least equivalent for reducing both SBP and mortality. Taken together with a recent MHRA drug safety update on fluoroquinolones and withdrawal of norfloxacin from the UK, there is a potential impact on recommendations.

Other areas of the guideline

No update is suggested for other areas of the guideline relating to: diagnosis; monitoring; primary prevention of bacterial infections in cirrhosis and upper gastrointestinal bleeding; and management of ascites. For these areas of the guideline there was limited new evidence, or new evidence generally supported existing recommendations.

We also re-examined areas that were considered during development of the guideline but where recommendations could not be made. We identified no new evidence for volume replacers in hepatorenal syndrome. New evidence was available on the management of hepatic encephalopathy (HE). While new evidence to support lactulose treatment of overt HE episodes was identified, it was noted that lactulose is standard NHS practice and therefore should not need to be addressed by the guideline.

For further details and a summary of all evidence identified in surveillance, see appendix A.

Overview of 2020 surveillance methods

NICE's surveillance team checked whether recommendations in NICE's guideline on cirrhosis in over 16s: assessment and management remain up to date.

The surveillance process consisted of:

- Feedback from topic experts via a questionnaire.
- Examining related NICE guidance and quality standards and NIHR signals.
- A search for ongoing research.
- Examining the NICE event tracker for relevant ongoing and published events.
- Literature searches to identify relevant evidence.
- Assessing the new evidence against current recommendations to determine whether or not to update sections of the guideline, or the whole guideline.
- Consulting on the proposal with stakeholders.
- Considering comments received during consultation and making any necessary changes to the proposal.

For further details about the process and the possible update decisions that are available, see ensuring that published guidelines are current and accurate in developing NICE guidelines: the manual.

Evidence considered in surveillance

Search and selection strategy

We searched for new evidence related to the whole guideline based on 2 searches: the first search for the diagnosis and monitoring sections of the guideline included observational and experimental studies and systematic reviews; the second search for the management section of the guideline included randomised controlled trials and systematic reviews.

We found 38 studies in a search for diagnosis and monitoring studies published between 24 August 2015 and 30 November 2019.

We found 27 studies in a search for management studies published between 24 August 2015 and 30 November 2019.

We also included 17 relevant studies and 3 guidelines from a total of 46 references identified by topic experts; 16 of the relevant studies were identified by searches.

One recent Cochrane systematic review (Komolafe et al.) recommended by a topic expert published in January 2020 was outside of the search period, but as it provides important evidence in a key area for the guideline it was included in the evidence summary below.

From all sources, we considered 67 studies to be relevant to the guideline.

See appendix A for details of all evidence considered, and references.

Selecting relevant studies

Studies were selected in accordance with criteria used for the guideline.

Ongoing research

We checked for relevant ongoing research; of the ongoing studies identified, 8 were assessed as having the potential to change recommendations. Therefore, we plan to check regularly whether these studies have published results and evaluate the impact of them on current recommendations as quickly as possible. These studies are:

- Prevention of infection in patients with cirrhosis with probiotic Lactobacillus casei Shirota
- Macrophage therapy for liver cirrhosis
- Beta-blockers or placebo for primary prophylaxis of oesophageal varices trial
- Carvedilol versus variceal band ligation in primary prevention of variceal bleeding in liver cirrhosis

- A trial to investigate whether giving albumin to patients with advanced liver cirrhosis will reverse immune suppression and improve outcome for infection
- Rifaximin to reduce infection in decompensated cirrhosis
- Primary antibiotic prophylaxis using cotrimoxazole to prevent spontaneous bacterial peritonitis in cirrhosis.

We also identified 3 Cochrane review protocols with potential to change recommendations:

- Antibiotic prophylaxis for people with cirrhosis and variceal bleeding
- Medical interventions for prevention and treatment of hepatic encephalopathy in adults with cirrhosis: a network meta-analysis
- Abdominal ultrasound and alpha-fetoprotein for the diagnosis of hepatocellular carcinoma.

Intelligence gathered during surveillance

Views of topic experts

We considered the views of topic experts who were recruited to the NICE Centre for Guidelines Expert Advisers Panel to represent their specialty. For this surveillance review, topic experts completed a questionnaire about developments in evidence, policy and services related to the guideline.

We received 6 questionnaire responses from experts which included 2 consultant readers in hepatology, a general practitioner with special interest in liver disease, a specialist nurse and 2 professors (clinical) of hepatology.

Five topic experts thought the guideline should be updated and 1 expert identified that it should not be updated.

Reasons to consider updating included the following points:

- One expert raised 2 points concerning the enhanced liver fibrosis (ELF) test which is mentioned in the diagnosis section of the guideline: applicability of the ELF test in people with NAFLD for identifying advanced liver fibrosis; and the availability of such tests locally.
- With regard to recommendation 1.2.4, 'offer ultrasound (with or without measurement of serum alpha-fetoprotein) every 6 months as surveillance for hepatocellular carcinoma (HCC) for people with cirrhosis who do not have hepatitis B virus infection', 1 expert queried the need for measurement of serum alpha-fetoprotein (AFP).
- One expert queried the application of recommendation 1.2.7, 'after a diagnosis of cirrhosis, offer upper gastrointestinal endoscopy to detect oesophageal varices'. It was noted that invasive endoscopy is increasingly reserved for those with high liver stiffness and low platelet count rather than all patients with newly diagnosed cirrhosis.
- One expert highlighted that recommendation 1.3.1, 'offer endoscopic variceal band ligation for the primary prevention of bleeding for people with cirrhosis who have medium to large oesophageal varices', is contentious, with health professionals deferring to other guidelines in this area.

Other sources of information

We considered all other correspondence received since the guideline was published.

In March 2019, the MHRA issued restrictions and precautions for the use of fluoroquinolone antibiotics because of rare reports of disabling and potentially long-lasting or irreversible side effects (see the MHRA's drug safety update for details). The current 2019/20 surveillance review was conducted early to enable a check of the use of fluoroquinolones in the guideline.

Views of stakeholders

Stakeholders are consulted on all surveillance reviews except if the whole guideline will be updated and replaced. Because this surveillance proposal was to update part of the guideline, we consulted with stakeholders.

Seven stakeholders commented and 6 agreed to a partial update of the guideline. Responses were received from 2 commercial companies, 1 hospital trust, 3 professional bodies and 1 charity; the 3 professional bodies provided joint responses.

Stakeholders highlighted 3 main areas, beyond the area for proposed update, where they felt an update was necessary. First, joint comments from 2 stakeholders queried whether liver ultrasound (with or without serum alpha-fetoprotein) is an appropriate tool for surveillance of hepatocellular carcinoma (HCC) in all patient groups. The current review only concerned the appropriate surveillance interval, and method of surveillance was beyond the scope. The stakeholders identified that tools for detecting HCC is an area where new research may emerge in the future. We will consider this area at the next surveillance review.

Joint comments from 3 stakeholders identified a new study on the primary prevention of ascites in people with compensated cirrhosis. However, this topic was not covered by the original guideline as its objective was to cover areas of uncertainty or variability in practice and to aid non-specialists, and thus was not in the scope of the surveillance review.

A stakeholder queried whether the guideline should specify that covered transjugular intrahepatic portosystemic shunt (that is, PTFE-covered stents) should be used for people with cirrhosis who have refractory ascites, in preference to bare metal stents. There was, however, no direct evidence to support such a change, although we will revisit this issue at future review timepoints.

Two stakeholders identified that the ELF test, which is mentioned in the diagnosis section of the guideline is not available in all localities. This issue was also raised by 1 topic expert. The recommendations concerning ELF tests are adapted from NICE's guideline on non-alcoholic fatty liver disease (NAFLD): assessment and management. The recommendation to consider the ELF test, with a threshold of 10.51 to test for advanced fibrosis, is based on evidence that it was the most diagnostically accurate and also the most cost-effective test compared with all other testing and non-testing strategies. We have noted this implementation issue for the forthcoming review of the NAFLD guideline.

At the time of consultation we asked stakeholders for views on the use of non-invasive tests, in place of endoscopy, as a method to identify oesophageal varices. There was general consensus that non-invasive approaches have significant limitations, that further long-term study is necessary and that the guideline position that endoscopy should be used remains sound.

No changes to the surveillance proposal were made in response to stakeholders' comments.

See appendix B for full details of stakeholders' comments and our responses.

See ensuring that published guidelines are current and accurate in developing NICE guidelines: the manual for more details on our consultation processes.

Equalities

No equalities issues were identified during the surveillance process.

Overall decision

After considering all evidence and other intelligence and the impact on current recommendations, we decided that an update is necessary.

ISBN: 978-1-4731-3899-5