NICE National Institute for Health and Care Excellence

# Appendix B: Stakeholder consultation comments table

## 2020 surveillance of Cirrhosis in over 16s: assessment and management (2016)

Consultation dates: 27 July 2020 to 7 August 2020

| 1. Do you agree with the proposal to a partial update of the guideline? | | | |
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| **Stakeholder** | **Overall response** | **Comments** | **NICE response** |
| W.L. Gore and Associates UK Ltd. | No | We would like to acknowledge the work of the original guideline committee and the proposal from the surveillance team to update the areas:<br>● Primary prophylaxis of variceal haemorrhage<br>● Primary prevention of spontaneous bacterial peritonitis (SBP) in people with cirrhosis and ascites<br>However, we wish to highlight the additional and emerging clinical and cost-effectiveness evidence (see below) in the Transjugular intrahepatic portosystemic shunt (TIPS) versus large-volume paracentesis (LVP) for ascites - Question 12 from the original guidance document. | Thank you for your response and comments.<br>We have responded below to your comments on evidence for transjugular intrahepatic portosystemic shunt (TIPS) for people with cirrhosis who have refractory ascites. |

*Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees*

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| Intercept Pharmaceuticals UK & Ireland | Yes | Appropriate screening for advanced fibrosis in the NAFLD population may limit the number of people progressing to cirrhosis by enabling more timely intervention both with lifestyle modification and potentially new pharmacotherapies in the future.<br><br>The presence of non-alcoholic steatohepatitis (NASH) is a risk factor for liver fibrosis which may progress to cirrhosis if not detected. The NICE NAFLD guideline covers the monitoring of advanced fibrosis in the NAFLD/NASH populations, as NG50 duly notes. A better link to the existing NAFLD guideline may be drawn if the current list of risk factors for cirrhosis (as set out in NG50 section 1.1.1 - viral hepatitis, excessive alcohol consumption, obesity and type 2 diabetes) were expanded to consistently also include NAFLD and NASH. | Thank you for your response and comments.<br><br>The assessment for advanced liver fibrosis in people with NAFLD is covered by non-alcoholic fatty liver disease (NAFLD): assessment and management NICE guideline NG49. There is a link from the diagnosis section of Cirrhosis in over 16s (NG50) to NG49 which cross-refers the audience of NG50 to the guideline on NAFLD (NG49). In addition, NG49 recommendation 1.2.9 states: Monitor adults and young people over 16 with NAFLD and advanced liver fibrosis for cirrhosis in line with NICE's cirrhosis guideline. Therefore, links already exist between the 2 guidelines which should support timely intervention and awareness of the 2 related guidelines. Links are also available between the NICE cirrhosis pathway and the NICE Non-alcoholic fatty liver disease pathway.<br><br>Regarding lifestyle modification for NAFLD, this topic is covered in detail in recommendations 1.2.12 to 1.2.16 of NG49.<br><br>We did not identify evidence on the relative risk of cirrhosis in the NAFLD/NASH population that would support an update of the guideline recommendation 1.1.1. We will consider evidence in this area at the next surveillance review of this guideline. |
| Sheffield Teaching Hospital NHSFT | Yes | Additional comments:<br><br>1.1.4. - in our catchment GPs do not use ELF testing – likely due to cost implications – they use Fib-4 or NFS to assess risk for cirrhosis and refer accordingly for clinic and/or Fibroscan (transient Elastography) – I think this is widespread and should be reflected in the guideline<br><br>1.2.1. - patients with cirrhosis should be referred a specialist at diagnosis – if low risk for complications they could be discharged with advise to GP or a shared care | Thank you for your response and comments.<br><br>Recommendation 1.1.4: Regarding the availability of ELF tests locally, this recommendation mirrors the advice provided in non-alcoholic fatty liver disease (NAFLD): assessment and management (NICE guideline NG49). 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 will consider this issue at the next surveillance |

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| | | approached used. I do not think GPs will feel happy to diagnose which cirrhotics are at high risk of complications (and rightly so)<br><br>1.3.5. - primary prophylaxis for SBP is controversial – locally only in very selected cases after consultant | review of that guideline (likely to be in 2021). We have also noted that FIB-4 blood fibrosis tests, which can be calculated by GP-accessible tests without recourse to specialised tests, may be more readily available.<br><br>Recommendation 1.2.1: The recommendation refers to practice after a diagnosis of cirrhosis, with complications likely to arise at a future point after diagnosis. The committee felt that MELD is easy to calculate using the results of blood tests undertaken as part of standard practice, but noted that it would be useful if laboratories were encouraged to generate a MELD score automatically on liver blood tests, which could be used easily by clinicians. The committee agreed that this recommendation is largely aimed at secondary care clinicians, as people with a diagnosis of cirrhosis are routinely seen in secondary care.<br><br>Recommendation 1.3.5: This recommendation will be part of the proposed update. This will provide an opportunity to re-evaluate the available evidence; also noting that norfloxacin is no longer available in the UK. |
| British Association for the Study of the Liver (BASL) | Yes | We agree on the need to update the guidance with regards to primary prevention of variceal bleeding.<br><br>We believe there appears to be equipoise with regards to carvedilol and banding. We believe further study is required in primary prevention comparing carvedilol with banding in primary prevention of variceal bleeding in patients with medium to large varices. In addition to clinical outcomes, heath economic and quality of life should be studied. This is being done already (CALIBRE trial, ISRCTN73887615). | Thank you for your response and comments.<br><br>We checked for relevant ongoing research; of the ongoing studies identified, 8 were assessed as having the potential to change recommendations. These studies include:<br><br>• CALIBRE trial, ISRCTN73887615 - Carvedilol versus variceal band ligation in primary prevention of variceal bleeding in liver cirrhosis<br><br>• BOPPP trial, ISRCTN10324656 - Beta-blockers or placebo for primary prophylaxis of oesophageal varices trial |

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| | | We also agree that further study is necessary in patients with small varices and would recommend carvedilol as the beta-blocker of choice. This is already being done (BOPPP trial, ISRCTN10324656).<br><br>We agree on the need to reconsider quinolones in light of MHRA guidance. | We will consider the impact of the research findings when they are available.<br><br>The recommendation 1.3.5 which includes reference to fluoroquinolone antibiotics (ciprofloxacin and norfloxacin) will be updated in the future. New evidence will be considered which may change the recommendation. In the interim, the guideline acknowledges that 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 Drug Safety Update for details). |
| British Society of Gastroenterology (BSG | Yes | We agree on the need to update the guidance with regards to primary prevention of variceal bleeding.<br><br>We believe there appears to be equipoise with regards to carvedilol and banding. We believe further study is required in primary prevention comparing carvedilol with banding in primary prevention of variceal bleeding in patients with medium to large varices. In addition to clinical outcomes, heath economic and quality of life should be studied. This is being done already (CALIBRE trial, ISRCTN73887615 ).<br><br>We also agree that further study is necessary in patients with small varices and would recommend carvedilol as the beta-blocker of choice. This is already being done (BOPPP trial, ISRCTN10324656).<br><br>We agree on the need to reconsider quinolones in light of MHRA guidance.<br><br>Research in surveillance strategies (imaging and biomarkers) for hepatocellular carcinoma is a priority for | Thank you for your response and comments.<br><br>We checked for relevant ongoing research; of the ongoing studies identified, 8 were assessed as having the potential to change recommendations. These studies include:<br><br>• CALIBRE trial, ISRCTN73887615 - Carvedilol versus variceal band ligation in primary prevention of variceal bleeding in liver cirrhosis<br><br>• BOPPP trial, ISRCTN10324656 - Beta-blockers or placebo for primary prophylaxis of oesophageal varices trial<br><br>We will consider the impact of the research findings when they are available.<br><br>The recommendation 1.3.5 which includes reference to fluoroquinolone antibiotics (ciprofloxacin and norfloxacin) will be updated in the future. New evidence will be considered which may change the recommendation. In the interim, the guideline acknowledges that MHRA issued restrictions and precautions for the use of fluoroquinolone antibiotics because of rare reports of |

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| | | the following reasons: 1) the epidemiology for HCC is changing remarkably due to treatments for HCV and HBV as well as rising proportion of obesity and alcohol related cirrhosis. So, ultrasound is not a tool which will be suitable for surveillance. 2) new algorithms and techniques (both molecular and imaging) are emerging which make it essential that we will need to generate evidence to inform surveillance strategies.<br><br>We would suggest that rifaximin is considered as a recommendation in hepatic encephalopathy. There is high level evidence to recommend rifaximin in prevention of recurrent overt hepatic encephalopathy (NICE TA337). Indeed, rifaximin is a widely prescribed and licenced therapy for hepatic encephalopathy in the UK.<br><br>In the section relating to TIPS for ascites, it is important to emphasise that in all patients with refractory ascites eligibility for liver transplantation should be considered which is consistent with published guidance: https://www.bsg.org.uk/clinical-resource/transjugular-intrahepatic-portosystemic-stent-shunt-tipss-in-the-management-of-portal-hypertension/ | disabling and potentially long-lasting or irreversible side effects (see Drug Safety Update for details).<br><br>Further, the guideline review protocol assumes that the surveillance system uses liver ultrasound (with or without serum alpha-fetoprotein testing) for hepatocellular carcinoma; the review question is concerned with the frequency of surveillance testing only. Therefore, the purpose of the current surveillance review was not to assess diagnostic accuracy of ultrasound and AFP, or other approaches, for the diagnosis of hepatocellular carcinoma (HCC). Currently the guideline only covers regular surveillance of hepatocellular carcinoma interventions using ultrasound (with or without serum alpha-fetoprotein testing).<br><br>At the time of developing the guideline the committee agreed that ultrasound is still the favoured option for surveillance. They acknowledged that biomarkers such as AFP can aid diagnosis of HCC, but it is thought that only around 60% of HCCs are AFP-secreting. The accuracy of AFP would also be reduced in certain aetiologies such as alcohol-related cirrhosis. The committee also felt that an important clinical aspect of ultrasound surveillance was not only the detection of HCC, but also the assessment for other complication of cirrhosis, such as portal hypertension, portal vein thrombus and ascites. It was discussed that surveillance for HCC could have further benefit if used as part of an integrated package of surveillance for other complications of cirrhosis.<br><br>We will make a note of potential emerging evidence in the area of diagnostic tests for HCC, such as new algorithms and molecular and imaging techniques, and check this area at the next surveillance review.<br><br>Regarding research and surveillance strategies for imaging and biomarkers for hepatocellular carcinoma, the guideline does not |

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| | | | include a research recommendation in this area. However, we are tracking the following Cochrane review and will consider the impact of the evidence when it is available: Abdominal ultrasound and alpha-fetoprotein for the diagnosis of hepatocellular carcinoma.<br><br>Rifaximin is currently recommended in the UK by NICE TA337 for the treatment of recurrent episodic hepatic encephalopathy (HE) in conjunction with a non-absorbable disaccharide. Further, TA337 is included in the NICE cirrhosis pathway under managing complications: Rifaximin is recommended, within its marketing authorisation, as an option for reducing the recurrence of episodes of overt HE in people aged 18 years or older. The pathway brings together all the relevant guidance on the topic of cirrhosis.<br><br>The TA337 concerned recurrent, whereas the NG50 guideline looked at one-off, first episode HE. The licence is for the reduction in recurrence of episodes of overt hepatic encephalopathy, and the main trial in the TA was in people with a Conn score of 0 or 1 and were in remission after documented recurrent episodes of overt hepatic encephalopathy (2 or more episodes, equivalent to a Conn score of 2 or more, in the 6 months before screening) associated with chronic liver disease or portal hypertension. At the time of developing NG50 the committee did not think there was enough evidence of clinical effectiveness in an episode of acute hepatic encephalopathy to warrant an off-label recommendation; there is no new evidence to change this assessment.<br><br>Regarding TIPS for ascites, the guideline committee emphasised that all patients with cirrhosis and refractory ascites should be reviewed by a hepatologist and considered for transplantation (this can be found in the NG50 full guideline on page 220). They go on to say, those who are suitable for transplantation may undergo TIPS as a 'holding procedure' while on the transplant waiting list. Those who |

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| | | | are not suitable for transplantation would undergo TIPS as a definitive procedure. The committee was in agreement that there is currently wide variation in UK practice and were concerned that there are patients who may benefit from TIPS but who are not being offered this service. Whilst this is not covered in the recommendations, as it was not a topic that was formally assessed, it is acknowledged in the NG50 full guideline. |
| Royal College of Physicians - Endorses comments made by the British Society of Gastroenterology | Yes | We agree on the need to update the guidance with regards to primary prevention of variceal bleeding. We believe there appears to be equipoise with regards to carvedilol and banding. We believe further study is required in primary prevention comparing carvedilol with banding in primary prevention of variceal bleeding in patients with medium to large varices. In addition to clinical outcomes, heath economic and quality of life should be studied. This is being done already (CALIBRE trial, ISRCTN73887615 ).<br><br>We also agree that further study is necessary in patients with small varices and would recommend carvedilol as the beta-blocker of choice. This is already being done (BOPPP trial, ISRCTN10324656).<br><br>We agree on the need to reconsider quinolones in light of MHRA guidance.<br><br>Research in surveillance strategies (imaging and biomarkers) for hepatocellular carcinoma is a priority for the following reasons: 1) the epidemiology for HCC is changing remarkably due to treatments for HCV and HBV as well as rising proportion of obesity and alcohol related cirrhosis. So, ultrasound is not a tool which will be suitable for surveillance. 2) new algorithms and techniques (both | Thank you for your response and comments.<br><br>We checked for relevant ongoing research; of the ongoing studies identified, 8 were assessed as having the potential to change recommendations. These studies include:<br><br>• CALIBRE trial, ISRCTN73887615 - Carvedilol versus variceal band ligation in primary prevention of variceal bleeding in liver cirrhosis<br><br>• BOPPP trial, ISRCTN10324656 - Beta-blockers or placebo for primary prophylaxis of oesophageal varices trial<br><br>We will consider the impact of the research findings when they are available.<br><br>The recommendation 1.3.5 which includes reference to fluoroquinolone antibiotics (ciprofloxacin and norfloxacin) will be updated in the future. New evidence will be considered which may change the recommendation. In the interim, the guideline acknowledges that 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 Drug Safety Update for details). |

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| | | | of the evidence when it is available: Abdominal ultrasound and alpha-fetoprotein for the diagnosis of hepatocellular carcinoma.<br><br>Rifaximin is currently recommended in the UK by NICE TA337 for the treatment of recurrent episodic hepatic encephalopathy (HE) in conjunction with a non-absorbable disaccharide. Further, TA337 is included in the NICE cirrhosis pathway under managing complications: Rifaximin is recommended, within its marketing authorisation, as an option for reducing the recurrence of episodes of overt HE in people aged 18 years or older. The pathway brings together all the relevant guidance on the topic of cirrhosis.<br><br>The TA337 concerned recurrent, whereas the NG50 guideline looked at one-off, first episode HE. The licence is for the reduction in recurrence of episodes of overt hepatic encephalopathy, and the main trial in the TA was in people with a Conn score of 0 or 1 and were in remission after documented recurrent episodes of overt hepatic encephalopathy (2 or more episodes, equivalent to a Conn score of 2 or more, in the 6 months before screening) associated with chronic liver disease or portal hypertension. At the time of developing NG50 the committee did not think there was enough evidence of clinical effectiveness in an episode of acute hepatic encephalopathy to warrant an off-label recommendation; there is no new evidence to change this assessment.<br><br>Regarding TIPS for ascites, the guideline committee emphasised that all patients with cirrhosis and refractory ascites should be reviewed by a hepatologist and considered for transplantation (this can be found in the NG50 full guideline on page 220). They go on to say, those who are suitable for transplantation may undergo TIPS as a 'holding procedure' while on the transplant waiting list. Those who are not suitable for transplantation would undergo TIPS as a definitive procedure. The committee was in agreement that there is |

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| | | | currently wide variation in UK practice and were concerned that there are patients who may benefit from TIPS but who are not being offered this service. Whilst this is not covered in the recommendations, as it was not a topic that was formally assessed, it is acknowledged in the NG50 full guideline. |
| British Liver Trust | Yes | | Thank you for your response. |

**2. Do you have any comments on areas excluded from the scope of the guideline?**

| Stakeholder | Overall response | Comments | NICE response |
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| W.L. Gore and Associates UK Ltd. | Yes | We feel that evidence regarding question 12 considering TIPS versus LVP for ascites has significantly changed since the original guidance document and requires a re-evaluation.<br><br>In particular, we feel that the current guidance does not consider the most contemporary and appropriate clinical evidence for this indication (Bureau C, Thabut D, Oberti F. et al. Transjugular intrahepatic portosystemic shunts with covered stents increase transplant-free survival of patients with cirrhosis and recurrent ascites. Gastroenterology 2017;152:157–63.).<br><br>This RCT comparing Polytetrafluoroethylene (PTFE)-covered TIPS vs. LVP in patients with recurrent ascites, a better one-year transplant-free survival, without any significant increase in occurrence of hepatic encephalopathy. Specifically, the study supports the use of | Thank you for your response and comments. We have considered the evidence you identified in relation to the review question: What is the clinical and cost-effectiveness of transjugular intrahepatic portosystemic shunt (TIPS) compared with large-volume paracentesis (LVP) with albumin in the management of diuretic-resistant ascites due to cirrhosis? Our responses are outlined below.<br><br>Through our searches for systematic reviews and randomised control trials we did not identify any evidence that was eligible for inclusion and compared non-covered versus covered stents.<br><br>The Bureau et al (2017) study you identify was eligible for inclusion in our surveillance review and was included in Appendix A. This study supports the use of covered stents for TIPS over the use of large-volume paracenteses and albumin. This evidence does not support the use of PTFE-covered stents over bare metal stents as bare metal stents did not feature in the trial. |

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| | | PTFE-covered stents over bare metal stents for the TIPS procedure and reflects the current UK clinical practice for the management of ascites in this patient group.<br><br>Evidence to support the efficacy of covered stents has also been robustly demonstrated in retrospective studies (Tan HK, James PD, Sniderman KW, Wong F. Long-term clinical outcome of patients with cirrhosis and refractory ascites treated with transjugular intrahepatic portosystemic shunt insertion Journal of Gastroenterology and Hepatology 30 (2015) 389–395).<br><br>Importantly, the preference for PTFE-covered stents for TIPS is strongly supported by very recent guidance from the British Society for Gastroenterology (BSG) (Tripathi D, Stanley AJ, Hayes PC, Travis S, Armstrong MJ, Tsochatzis EA, Rowe IA, Roslund N, Ireland H, Lomax M, Leithead J, Homoyon M, Aspinall RJ, McDonagh J, Patch D. Transjugular intrahepatic portosystemic stent-shunt in The management of portal hypertension Gut Epub ahead of print:doi:10.1136/gutjnl-2019-320221.)<br><br>• All TIPSS should be performed using PTFE-covered stents as they are associated with better patency rates than bare stents.<br><br>Moreover, international guidance from the European Association from the Study of the Liver (EASL) reiterate a preference for TIPS with a PTFE-covered stent *(The European Association for the Study of the Liver. EASL Clinical Practice Guidelines for the management of patients with decompensated cirrhosis. J Hepatol (2018)).*<br><br>The guideline developers at EASL use the level 1 (RCT) evidence to make a strong recommendation for the use of | The Tan et al (2015) study is not eligible for inclusion in our review of evidence as this fell outside of the search date (our searches start from August 2015) and would have been excluded by study type.<br><br>The Trebicka et al (2019) study does not meet our inclusion criteria based on study type and included populations.<br><br>The cost effectiveness studies from Shen et al (2018) and Kwan et al (2018) do not meet our inclusion criteria, as the economic analysis applies to a US healthcare system. In addition, these studies do not consider bare metal stents in the analysis, as a comparison.<br><br>The BSG guidance that you cite (Tripathi et al 2020) does recommend that TIPSS should be performed using PTFE-covered stents, although evidence to support the recommendation is extrapolated from broader evidence which does not apply directly to this indication.<br><br>The NICE guideline recommendation 1.3.4 does not specify the type of stent that should be used.<br><br>As the technology develops new versions of stents may show better performance, although further controlled studies with covered stents are required. The currently available evidence does not suggest that the NG50 recommendation 1.3.4 should be updated or changed to specify that only covered stents should be used in patients with refractory ascites. However, we will consider developments in the evidence base at the next surveillance review for this guideline. |

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| | | PTFE-covered stents for the management of Ascites in these patients (see below).<br><br>• TIPS insertion is recommended in patients with recurrent ascites (I;1) as it improves survival (I;1) and in patients with refractory ascites as it improve the control of ascites (I;1).<br><br>• The use of small-diameter PTFE-covered stents inpatients is recommended to reduce the risk of TIPS dysfunction and hepatic encephalopathy with a high risk of hepatic encephalopathy is recommended (I;1).<br><br>Based on this evidence, we strongly feel that the guideline update should review this clinical evidence and align with recent national and international guidance.<br><br>Furthermore, in reviewing the guidance it may also be worth noting real-world evidence from current generations of PTFE-covered stents which have demonstrated improved outcomes for overall survival and control hepatic encephalopathy (*Trebicka J, Bastgen D,Byrtus J, Praktiknjo M, Terstiegen S, Meyer C, Thomas D, Fimmers D, Treitl M,Wulf Euringer W, Sauerbruch T,* and Rössle M. Smaller-Diameter Covered Transjugular Intrahepatic Portosystemic Shunt Stents Are Associated With Increased Survival. Clinical Gastroenterology and Hepatology 2019;17:2793–2799).*<br><br>Regarding economic data, a single cost consequence analysis (Gines et al. 2002) was identified in the original guidance (Table 88); which was driven by clinical data using bare metal stents and from the perspective of the United States (US) and Spain.<br><br>For the indication of ascites, at least 2 cost-utility analysis have been published in the interim. | |

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| | | *(Shen NT, Schneider Y, Congly SE, Rosenblatt RE, Namn Y, Fortune BE, Jesudian A, Brown RS. Cost Effectiveness of Early Insertion of Transjugular Intrahepatic Portosystemic Shunts for Recurrent Ascites. Clinical Gastroenterology and Hepatology 2018;16:1503–1510.;*<br>*Kwan SW, Allison SK, Gold LS, Shin DS. Cost-Effectiveness of Transjugular Intrahepatic Portosystemic Shunt versus Large-Volume Paracentesis in Refractory Ascites: Results of a Markov Model Incorporating Individual Patient-Level Meta-Analysis and Nationally Representative Cost Data. Journal of Vascular and Interventional Radiology Volume 29, Issue 12, December 2018, Pages 1705-1712.)*<br><br>While both studies are from the US perspective, both analysis employ the use of a Markov Model and systematic review of the clinical and economic evidence and suggest that the use of PTFE-covered TIPS is cost effective compared to LVP.<br>Finally, W.L. Gore and Associates have developed a cost-consequence and cost-utility analysis, using the NICE reference case, to evaluate the cost-effectiveness of PTFE-covered TIPS vs. LVP. The model was developed with UK Key Opinion Leaders and will be presented at the British Association for the Study of the Liver conference in September 2020.<br>The results are anticipated to be highly relevant and could be considered as part of any update to the guidance. | |
| Intercept Pharmaceuticals UK & Ireland | No | | Thank you for your response. |
| Sheffield Teaching Hospital NHSFT | Yes | Hepatic encephalopathy – common – difficult to manage and high associated morbidity | Thank you for your response and comment.<br>Evidence available on hepatic encephalopathy (HE) at the time of development and that informed the current guideline was |

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| | | | inconclusive; thus, the guideline did not include any recommendation on managing an episode of acute HE.<br><br>The current surveillance review identified new evidence, including Cochrane reviews and other evidence highlighted by topic experts, which improves the evidence base for management of acute HE, both for non-absorbable disaccharides (NAD) (i.e. lactulose in the UK) and alternative treatments. Evidence from current surveillance may indicate that NAD is effective in managing overt HE compared with placebo/no intervention. Limited evidence may also indicate increased effectiveness for polyethylene glycol (PEG), and/or branched-chain amino acids (BCAA) compared with NAD.<br><br>Whilst new evidence to support lactulose treatment of overt HE episodes was included in this surveillance review, it was noted that lactulose is standard NHS practice (see, e.g. McPherson and Thomson, 2019: Management of hepatic encephalopathy: beyond the acute episode [British Society of Gastroenterology]), Other products in the studies are not available in the UK. There would be little benefit of undertaking a formal evidence review in this area and there is no impact on the guideline. |
| British Association for the Study of the Liver (BASL) | Yes | There is recent evidence on the role of beta-blockers in early cirrhosis suggesting they can reduce the risk of hepatic decompensation and improve survival: https://doi.org/10.1016/S0140-6736(18)31875-0. We believe prevention of decompensation to be a research priority, focusing on surrogate markers of portal hypertension as selection criteria for beta-blockers. As mentioned in the document BOPPP and CALIBRE trials can both provide some evidence on the role of beta-blockers in prevention of decompensation, although this is not the primary outcome. | Thank you for your response and comment.<br><br>The NICE guideline NG50 was intended to focus on areas of uncertainty or variability in practice. The NG50 guideline did not cover all approaches that focus on prevention of decompensation, but did cover prophylaxis of variceal haemorrhage. We plan to update that section of the guideline: prophylaxis of variceal haemorrhage (currently recommendation 1.3.1). The study that you identify by Villanueva et al (2019) may inform that update if it meets the inclusion criteria. We |

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| | | Another area of topical interest is the safety of beta-blockers in advanced cirrhosis, in particular refractory ascites. CALIBRE in particular may provide some data in relation to this question.<br><br>An area of particular interest at this time is the role of early TIPSS in acute variceal bleeding. We believe further study is important. May we suggest that early TIPSS review is considered as part of the review of the NICE guidelines on GI bleeding (CG141).<br><br>We believe cirrhosis should be further classified/staged for example decompensated versus compensated cirrhosis. This can determine management strategies. Examples where this is relevant include the following:<br><br>1. Screening for varices in decompensated cirrhosis should always be with endoscopy and non-invasive markers do not have a role. On the other hand, in compensated cirrhosis, non-invasive methods for varices surveillance as discussed in the NICE guidance have a role.<br>2. Staging cirrhosis in terms of determining severity, progression and impact on mortality in the decompensated group requires further study. The current scoring systems such as MELD and Child-Pugh score do not have sufficient precision. We believe there is clearly an unmet need here. | The guideline did not cover the primary prevention of decompensation and ascites in people with compensated cirrhosis, and as such the study by Villanueva et al (2019) did not meet the inclusion criteria for the current surveillance review. We will, however, consider this topic in the next surveillance review when there may be more evidence available.<br><br>As mentioned above, we had identified the BOPP and CALIBRE trials as relevant to the guideline recommendations, so we will track these studies and assess an impact on the guideline when the findings are available.<br><br>Regarding 'early TIPSS review' comment, we will make a note of your comment and ensure it is considered in the next review of Acute upper gastrointestinal bleeding in over 16s: management (CG141).<br><br>Regarding the comment about staging and screening for varices, we have considered feedback from stakeholders (details below) in respect of varices in compensated cirrhosis and do not plan to change the recommendations 1.2.7 and 1.2.8 which cover detection of oesophageal varices.<br><br>Regarding classified/staged cirrhosis, the current review has considered evidence on the use of risk assessment tools (such as MELD and Child-Pugh) in people with compensated cirrhosis only. We have not looked at similar tools for people with decompensated cirrhosis as this was not covered by the guideline and was not within the scope of the current review. |
| British Society of Gastroenterology (BSG) | Yes | There is recent evidence on the role of beta-blockers in early cirrhosis suggesting they can reduce the risk of hepatic decompensation and improve survival: https://doi.org/10.1016/S0140-6736(18)31875-0. We believe prevention of decompensation to be a research | Thank you for your response and comment.<br><br>The NICE guideline NG50 was intended to focus on areas of uncertainty or variability in practice. The NG50 guideline did not |

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| | | priority, focusing on surrogate markers of portal hypertension as selection criteria for beta-blockers. As mentioned in the document BOPPP and CALIBRE trials can both provide some evidence on the role of beta-blockers in prevention of decompensation, although this is not the primary outcome.<br><br>Another area of topical interest is the safety of beta-blockers in advanced cirrhosis, in particular refractory ascites. CALIBRE in particular may provide some data in relation to this question.<br><br>An area of particular interest at this time is the role of early TIPSS in acute variceal bleeding. We believe further study is important. May we suggest that early TIPSS review is considered as part of the review of the NICE guidelines on GI bleeding (CG141).<br><br>We believe cirrhosis should be further classified/staged for example decompensated versus compensated cirrhosis. This can determine management strategies. Examples where this is relevant include the following:<br><br>1. Screening for varices in decompensated cirrhosis should always be with endoscopy and non-invasive markers do not have a role. On the other hand, in compensated cirrhosis, non-invasive methods for varices surveillance as discussed in the NICE guidance have a role.<br>2. Staging cirrhosis in terms of determining severity, progression and impact on mortality in the decompensated group requires further study. The current scoring systems such as MELD and Child-Pugh score do not have sufficient precision. We believe there is clearly an unmet need here. | cover all approaches that focus on prevention of decompensation, but did cover prophylaxis of variceal haemorrhage. We plan to update that section of the guideline: prophylaxis of variceal haemorrhage (currently recommendation 1.3.1). The study that you identify by Villanueva et al (2019) may inform that update if it meets the inclusion criteria. We<br><br>The guideline did not cover the primary prevention of decompensation and ascites in people with compensated cirrhosis, and as such the study by Villanueva et al (2019) did not meet the inclusion criteria for the current surveillance review. We will, however, consider this topic in the next surveillance review when there may be more evidence available.<br><br>As mentioned above, we had identified the BOPP and CALIBRE trials as relevant to the guideline recommendations, so we will track these studies and assess an impact on the guideline when the findings are available.<br><br>Regarding 'early TIPSS review' comment, we will make a note of your comment and ensure it is considered in the next review of Acute upper gastrointestinal bleeding in over 16s: management (CG141).<br><br>Regarding the comment about staging and screening for varices, we have considered feedback from stakeholders (details below) in respect of varices in compensated cirrhosis and do not plan to change the recommendations 1.2.7 and 1.2.8 which cover detection of oesophageal varices.<br><br>Regarding classified/staged cirrhosis, the current review has considered evidence on the use of risk assessment tools (such as MELD and Child-Pugh) in people with compensated cirrhosis only. We have not looked at similar tools for people with decompensated |

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| | | | cirrhosis as this was not covered by the guideline and was not within the scope of the current review. |
| Royal College of Physicians - Endorses comments made by the British Society of Gastroenterology | Yes | There is recent evidence on the role of beta-blockers in early cirrhosis suggesting they can reduce the risk of hepatic decompensation and improve survival: https://doi.org/10.1016/S0140-6736(18)31875-0. We believe prevention of decompensation to be a research priority, focusing on surrogate markers of portal hypertension as selection criteria for beta-blockers. As mentioned in the document BOPPP and CALIBRE trials can both provide some evidence on the role of beta-blockers in prevention of decompensation, although this is not the primary outcome.<br><br>Another area of topical interest is the safety of beta-blockers in advanced cirrhosis, in particular refractory ascites. CALIBRE in particular may provide some data in relation to this question.<br><br>An area of particular interest at this time is the role of early TIPSS in acute variceal bleeding. We believe further study is important. May we suggest that early TIPSS review is considered as part of the review of the NICE guidelines on GI bleeding (CG141).<br><br>We believe cirrhosis should be further classified/staged for example decompensated versus compensated cirrhosis. This can determine management strategies. Examples where this is relevant include the following:<br><br>1. Screening for varices in decompensated cirrhosis should always be with endoscopy and non-invasive markers do not have a role. On the other hand, in compensated cirrhosis, non-invasive methods for varices surveillance as discussed in the NICE guidance have a role. | Thank you for your response and comment.<br><br>The NICE guideline NG50 was intended to focus on areas of uncertainty or variability in practice. The NG50 guideline did not cover all approaches that focus on prevention of decompensation, but did cover prophylaxis of variceal haemorrhage. We plan to update that section of the guideline: prophylaxis of variceal haemorrhage (currently recommendation 1.3.1). The study that you identify by Villanueva et al (2019) may inform that update if it meets the inclusion criteria. We<br><br>The guideline did not cover the primary prevention of decompensation and ascites in people with compensated cirrhosis, and as such the study by Villanueva et al (2019) did not meet the inclusion criteria for the current surveillance review. We will, however, consider this topic in the next surveillance review when there may be more evidence available.<br><br>As mentioned above, we had identified the BOPP and CALIBRE trials as relevant to the guideline recommendations, so we will track these studies and assess an impact on the guideline when the findings are available.<br><br>Regarding 'early TIPSS review' comment, we will make a note of your comment and ensure it is considered in the next review of Acute upper gastrointestinal bleeding in over 16s: management (CG141).<br><br>Regarding the comment about staging and screening for varices, we have considered feedback from stakeholders (details below) in respect of varices in compensated cirrhosis and do not plan to |

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| | | 2. Staging cirrhosis in terms of determining severity, progression and impact on mortality in the decompensated group requires further study. The current scoring systems such as MELD and Child-Pugh score do not have sufficient precision. We believe there is clearly an unmet need here. | change the recommendations 1.2.7 and 1.2.8 which cover detection of oesophageal varices.<br><br>Regarding classified/staged cirrhosis, the current review has considered evidence on the use of risk assessment tools (such as MELD and Child-Pugh) in people with compensated cirrhosis only. We have not looked at similar tools for people with decompensated cirrhosis as this was not covered by the guideline and was not within the scope of the current review. |
| British Liver Trust | Yes | Is it possible that surveillance of NAFLD/NASH can also be considered? We have many reports from patients regarding variation in care and accessibility to tests locally. Can other mechanisms be considered apart from the enhanced liver fibrosis (ELF) test and transient elastography and can the new guideline make clear the benefits/limitations of different tests.<br><br>Research in surveillance strategies (imaging and biomarkers) for hepatocellular carcinoma should be considered.<br>Currently, surveillance for HCC is centre-based rather than there being a national strategy. This has resulted in wide variation of practice across the UK. Patients report practice as being more or less consistent in liver units, but many patients who are treated outside of liver units in district general hospitals are missed. As a result, only 20-25% of patients with HCC are diagnosed at BCLC Stage 0 or BCLC Stage A; when curative or radical treatments can be provided.<br><br>A robust system is needed so that all those defined to require surveillance undergo a six-monthly USS scan. This must be coupled with robust mechanisms for recall and further investigation if an abnormality is found on USS. | Thank you for your response and comments.<br><br>When identifying the most appropriate non-invasive cirrhosis test, the committee that developed the guideline noted the practicality of recommending a common test for all. Taking this factor into account, the committee recognised that there was adequate evidence across all aetiologies to conclude that transient elastography (at the appropriate threshold for each aetiology) is a cost-effective option for the diagnosis of cirrhosis.<br><br>The guideline, therefore, makes recommendations about the most effective and cost effective test approach or approaches; it does not aim to clarify the benefits or limitations of approaches that are not recommended, although detailed assessments of available approaches can be found in the NG50 full guideline.<br><br>Non-alcoholic fatty liver disease (NAFLD): assessment and management (NG49) recommends testing those diagnosed with NAFLD for advanced fibrosis. The guideline recommends using the ELF test, with a threshold of 10.51 to test for advanced fibrosis, as it was found to be the most diagnostically accurate test, and to be cost-effective compared to all other testing and non-testing strategies. As all those who will go on to develop cirrhosis will first develop advanced fibrosis it is sufficient to test those with both |

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| | | An issue of increasing importance is that HCC occurs in patients with non-alcohol related liver disease who do not have cirrhosis. The numbers who would require surveillance are potentially extremely large. This underlines the absolute importance in the development of biomarkers for the early detection of HCC. This is an important goal if we are to attain the 75% rate of early stage diagnosis for liver cancer. | NAFLD and advanced fibrosis for cirrhosis; people with NAFLD but without advanced fibrosis do not need to be tested for cirrhosis. The committee therefore adopted the subgroup of people with NAFLD and advanced fibrosis (as determined by testing using ELF) as the population of interest in testing people with NAFLD for cirrhosis.<br><br>Assessment for NAFLD and testing for advanced liver in that population disease is covered by NG49. We will note your comments and ensure they are considered during the next review of that guideline.<br><br>Regarding research and surveillance strategies for imaging and biomarkers for hepatocellular carcinoma, the guideline does not include a research recommendation in this area.<br><br>At the time of developing the guideline the committee agreed that ultrasound is still the favoured option for surveillance. They acknowledged that biomarkers such as AFP can aid diagnosis of HCC, but it is thought that only around 60% of HCCs are AFP-secreting. The accuracy of AFP would also be reduced in certain aetiologies such as alcohol-related cirrhosis. However, we are tracking the following Cochrane review and will consider the impact of the review when it is available: Abdominal ultrasound and alpha-fetoprotein for the diagnosis of hepatocellular carcinoma.<br><br>Currently the guideline recommends 6 month surveillance of hepatocellular carcinoma using ultrasound (with or without serum alpha-fetoprotein testing) for people with cirrhosis. The local implementation issues that you identify, indicating a lack of robust systems to ensure consistent practice, is outside the scope of the guideline. The surveillance of HCC in patients with non-alcohol related liver disease who do not have cirrhosis is also outside of the scope of the guideline. |

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| | | | Regarding the comment that surveillance for HCC is on a centre-based rather than a national strategy: this issue is beyond the remit of the guideline. We acknowledge, however, that this is a broader issue that may affect implementation of the recommendations. |

| 3. Do you have any comments on equalities issues? | | | |
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| **Stakeholder** | **Overall response** | **Comments** | **NICE response** |
| W.L. Gore and Associates UK Ltd. | No | | Thank you for your response. |
| Intercept Pharmaceuticals UK & Ireland | No | | Thank you for your response. |
| Sheffield Teaching Hospital NHSFT | No | | Thank you for your response. |
| British Association for the Study of the Liver (BASL) | No | | Thank you for your response. |
| British Society of Gastroenterology (BSG) | No | | Thank you for your response. |
| Royal College of Physicians - Endorses comments made | No | | Thank you for your response. |

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| by the British Society of Gastroenterology | | | |
| British Liver Trust | No | | |

**4. Monitoring (oesophageal varices): How often (and why) are non-invasive (platelet count, spleen length, and platelet count-to-spleen length ratio) tests used in the detection varices in people with cirrhosis in the UK as an alternative to endoscopy?**

| Stakeholder | Overall response | Comments | NICE response |
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| W.L. Gore and Associates UK Ltd. | No | | Thank you for your response. |
| Intercept Pharmaceuticals UK & Ireland | No comment | | Thank you for your response. |
| Sheffield Teaching Hospital NHSFT | No comment | | Thank you for your response. |
| British Association for the Study of the Liver (BASL) | Yes | These non-invasive surrogate markers of varices ((platelet count, spleen length, and platelet count-to-spleen length ratio) are not widely used as an alternative to endoscopy. They are not useful in detecting varices needing treatment.<br><br>Baveno VI criteria (liver stiffness and platelet count) have greater sensitivity in detecting varices needing treatment. However, the specificity is poor. Thus they are useful for deciding on patients that do not need endoscopy. Expanded Baveno VI criteria has greater sensitivity (DOI: 10.1002/hep.29363), sparing more endoscopies | Thank you for your comment. Based on the consultation comments we have received we will not be updating the NG50 recommendations 1.2.7 and 1.2.8 that concern monitoring oesophageal varices. A no endoscopy approach would potentially lead to adults with varices of any size being missed. Based on comments received, current practice appears to be in-line with the recommendations and is similar to existing guidance from the British Society of Gastroenterology (BSG) UK Guidelines for the Management of Variceal Haemorrhage in Cirrhotic Patients). |

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| | | (platelet count >110 × $10^9$ cells/L and LSM <25 kPa). We believe Baveno VI criteria is more widely used than platelet count-to-spleen ratio) and could have a role in reducing the endoscopy burden, although further study is necessary. The availability of liver stiffness measurement is also limited in smaller hospitals. Adopting Baveno VI criteria should be balanced against the impact on current clinical trials in the primary prevention of variceal bleeding (CALIBRE and BOPPP). | |
| British Society of Gastroenterology (BSG) | Yes | These non-invasive surrogate markers of varices ((platelet count, spleen length, and platelet count-to-spleen length ratio) are not widely used as an alternative to endoscopy. They are not useful in detecting varices needing treatment.<br><br>Baveno VI criteria (liver stiffness and platelet count) have greater sensitivity in detecting varices needing treatment. However, the specificity is poor. Thus they are useful for deciding on patients that do not need endoscopy. Expanded Baveno VI criteria has greater sensitivity (DOI: 10.1002/hep.29363), sparing more endoscopies (platelet count >110 × $10^9$ cells/L and LSM <25 kPa). We believe Baveno VI criteria is more widely used than platelet count-to-spleen ratio) and could have a role in reducing the endoscopy burden, although further study is necessary. The availability of liver stiffness measurement is also limited in smaller hospitals. Adopting Baveno VI criteria should be balanced against the impact on current clinical trials in the primary prevention of variceal bleeding (CALIBRE and BOPPP). | Thank you for your comment. Based on the consultation comments we have received we will not be updating the NG50 recommendations 1.2.7 and 1.2.8 that concern monitoring oesophageal varices. A no endoscopy approach would potentially lead to adults with varices of any size being missed. Based on comments received, current practice appears to be in-line with the recommendations and is similar to existing guidance from the British Society of Gastroenterology (BSG) UK Guidelines for the Management of Variceal Haemorrhage in Cirrhotic Patients). |

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| Royal College of Physicians - *Endorses comments made by the British Society of Gastroenterology* | Yes | These non-invasive surrogate markers of varices ((platelet count, spleen length, and platelet count-to-spleen length ratio) are not widely used as an alternative to endoscopy. They are not useful in detecting varices needing treatment.<br><br>Baveno VI criteria (liver stiffness and platelet count) have greater sensitivity in detecting varices needing treatment. However, the specificity is poor. Thus they are useful for deciding on patients that do not need endoscopy. Expanded Baveno VI criteria has greater sensitivity (DOI: 10.1002/hep.29363), sparing more endoscopies (platelet count >110 × $10^9$ cells/L and LSM <25 kPa). We believe Baveno VI criteria is more widely used than platelet count-to-spleen ratio) and could have a role in reducing the endoscopy burden, although further study is necessary. The availability of liver stiffness measurement is also limited in smaller hospitals. Adopting Baveno VI criteria should be balanced against the impact on current clinical trials in the primary prevention of variceal bleeding (CALIBRE and BOPPP). | Thank you for your comment. Based on the consultation comments we have received we will not be updating the NG50 recommendations 1.2.7 and 1.2.8 that concern monitoring oesophageal varices. A no endoscopy approach would potentially lead to adults with varices of any size being missed. Based on comments received, current practice appears to be in-line with the recommendations and is similar to existing guidance from the British Society of Gastroenterology (BSG) UK Guidelines for the Management of Variceal Haemorrhage in Cirrhotic Patients). |
| British Liver Trust | No comment | | Thank you for your response. |

**5. Monitoring (oesophageal varices): Is evidence available on the long-term outcomes (mortality and bleeding events) of non-invasive (platelet count, spleen length, and platelet count-to-spleen length ratio) tests versus endoscopy in the detection of varices in people with cirrhosis?**

| Stakeholder | Overall response | Comments | NICE response |
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| W.L. Gore and Associates UK Ltd. | No | | Thank you for your response. |
| Intercept Pharmaceuticals UK & Ireland | No comment | | Thank you for your response. |

*Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees*

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| Sheffield Teaching Hospital NHSFT | No comment | | Thank you for your response. |
| British Association for the Study of the Liver (BASL) | Yes | Studies which have performed serial measurements of liver stiffness show a wide variation in the long-term without any changes in the clinical outcome. Therefore, we would advise caution in particular on repeated measurements of liver stiffness due to significant confounders.<br><br>Research is needed in particular with regards to the use of non-invasive methods such as multi-organ MRI in the long-term monitoring of cirrhosis. | Thank you for your response and comment. |
| British Society of Gastroenterology (BSG) | Yes | Studies which have performed serial measurements of liver stiffness show a wide variation in the long-term without any changes in the clinical outcome. Therefore, we would advise caution in particular on repeated measurements of liver stiffness due to significant confounders.<br><br>Research is needed in particular with regards to the use of non-invasive methods such as multi-organ MRI in the long-term monitoring of cirrhosis. | Thank you for your response and comment. |
| Royal College of Physicians - Endorses comments made by the British Society of Gastroenterology | Yes | Studies which have performed serial measurements of liver stiffness show a wide variation in the long-term without any changes in the clinical outcome. Therefore, we would advise caution in particular on repeated measurements of liver stiffness due to significant confounders.<br><br>Research is needed in particular with regards to the use of non-invasive methods such as multi-organ MRI in the long-term monitoring of cirrhosis. | Thank you for your response and comment. |
| British Liver Trust | Yes | Does the updated guidance need to acknowledge Avatrombopag for treating thrombocytopenia in people | Thank you for your comment and response. |

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| | | with chronic liver disease needing a planned invasive procedure? Technology appraisal guidance [TA626] | The NICE TA626 is included in the NICE cirrhosis pathway management section. The pathway brings together all the relevant guidance on the topic of cirrhosis. |
| **6. NICE acknowledges that services and treatment may be affected by the current COVID-19 situation, however most of the content of the guideline was developed before this arose. Please tell us if there are any particular issues we should be considering?** | | | |
| Stakeholder | Overall response | Comments | NICE response |
| W.L. Gore and Associates UK Ltd. | Yes | For the management of ascites, Patients undergoing LVP require regular outpatient procedures to manage their condition (up to 2 times a month). A key benefit of TIPS is the reduction in procedure which may mitigate risks associated with spread of COVID-19 and reduce overall resource use and pressure on the healthcare system. Indeed, this is reflected in the economic analysis in which increased LVP episodes are a key driver of increased cost in the LVP arm.<br>Finally, while the management of oesophageal varices using TIPS was not reviewed in the original guidance (only endoscopic band ligation (EBL), non-selective Beta-Blockers and no intervention considered). TIPS with PTFE-covered stents has been robustly demonstrated to reduce incidence of bleeding, and therefore likely re-admission and resource use compared to EBL.<br>While we accept it may be out of the scope of the original update – can this be reviewed considering the aforementioned BGS guidance by Tripathi et al. states:<br>In patients who have gastro-oesophageal variceal bleeding refractory to endoscopic and drug therapy as defined by | Thank you for your response and comment.<br>The NG50 guideline does not currently recommend the use of large-volume paracentesis (LVP) for ascites nor in relation to management approaches covered by other areas of the guideline.<br>Regarding the management of oesophageal varices using TIPS, you correctly indicate that NG50 did not consider primary prophylaxis of variceal bleeding using TIPS.<br>The section of the guideline that covers primary prophylaxis of variceal bleeding is scheduled to be updated, although this will not consider the use of TIPS (see also the BSG guidance: UK guidelines on the management of variceal haemorrhage in cirrhotic patients). It will consider the following review questions:<br>Review question 1: What is the clinical and cost-effectiveness of non-selective beta-blockers for the primary prevention of bleeding in people with oesophageal varices due to cirrhosis?<br>Review question 2: What is the clinical and cost-effectiveness of endoscopic band ligation for the primary prevention of bleeding in people with oesophageal varices due to cirrhosis?<br>The recommendation you cite in BSG's guidance Transjugular intrahepatic portosystemic stent-shunt in the management of |

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| | | Baveno 6 critera. Transjugular intrahepatic portosystemic stent shunt (TIPSS) is recommended. (strong recommendation, moderate-quality evidence)<br>Considering the COVID-19 situation we feel the use of early TIPS (within 72 hours of Early TIPS) within a well-managed TIPS service may reduce overall burden on the healthcare system. | portal hypertension doesn't appear to relate to relate to primary prophylaxis of variceal bleeding; it refers to management of gastro-oesophageal variceal bleeding refractory to endoscopic and drug therapy, and would therefore be a different patient population and informed by a different evidence base than the proposed area for update (ie NG50 recommendation 1.3.1). The BSG's UK Guidelines for the Management of Variceal Haemorrhage in Cirrhotic Patients may be more relevant for comparison.<br>We note your comment on the COVID-19 situation and the use of TIPS. Other stakeholders have also highlighted the BSG-BASL advice on use of TIPPS as salvage therapy and the Prevention of Variceal Bleeding during COVID-19. |
| Intercept Pharmaceuticals UK & Ireland | No | | Thank you for your response. |
| Sheffield Teaching Hospital NHSFT | Yes | 1.2.4. - should the implication of COVID on ultrasound be taken into account here (a specialist appointment could help to determine who needs/will benefit from surveillance and who does not – and when to stop?<br>1.2.7. - implications from COVID on endoscopy likely will also need to be taken in to account – role for VCE? | Thank you for your response. We will make a note of your comments and continue to monitor intelligence on the impact of COVID-19 on the guideline and recommendations, as well as likely impact on the portfolio of NICE guidance in general.<br>Recommendation 1.2.4: We acknowledge that capacity and appointments for ultrasound have been affected during the COVID-19 pandemic.<br>Recommendation 1.2.7: regarding endoscopy, stakeholders during this consultation have identified that the British Society of Gastroenterology have provided relevant guidance on endoscopy. In addition, the BSG Guidance on recommencing GI Endoscopy in the deceleration & early recovery phases of the COVID-19 pandemic which is linked from the COVID-19 rapid guideline: gastrointestinal |

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| | | | and liver conditions treated with drugs affecting the immune response (NG172).<br>Please also note: NICE is providing guidance about COVID-19, which includes COVID-19 rapid guideline: arranging planned care in hospitals and diagnostic services (NG179). |
| British Association for the Study of the Liver (BASL) | No comment | The main issue is the availability of gastroscopy. As this is an aerosol generating procedure there is potential additional risk of transmission of COVID19. However, as discussed earlier non-invasive markers of varices have significant limitations and further long term study is necessary. It is important to stress that the availability of endoscopy varies considerably throughout the UK. Where endoscopy is not available, BSG and BASL have taken a pragmatic view and published interim guidance where patients are selected for beta-blockers depending on stage of liver disease and expanded Baveno VI criteria: https://www.bsg.org.uk/covid-19-advice/bsg-basl-advice-on-use-of-tipps-as-salvage-therapy-and-the-prevention-of-variceal-bleeding-during-covid-19/ . These should be reviewed regularly based on primarily local circumstances. | Thank you for your response and comment.<br>We will make a note of your comments and continue to monitor intelligence on the impact of COVID-19 on the guideline and recommendations, as well as likely impact on the portfolio of NICE guidance in general.<br>Thank you for bringing to our attention the variable availability of local endoscopy services during the COVID-19 pandemic and the related BSG guidance which is a response to changes in practice.<br>Please note: NICE is providing guidance about COVID-19, which includes COVID-19 rapid guideline: arranging planned care in hospitals and diagnostic services (NG179). |
| British Society of Gastroenterology (BSG) | No comment | The main issue is the availability of gastroscopy. As this is an aerosol generating procedure there is potential additional risk of transmission of COVID19. However, as discussed earlier non-invasive markers of varices have significant limitations and further long term study is necessary. It is important to stress that the availability of endoscopy varies considerably throughout the UK. Where endoscopy is not available, BSG and BASL have taken a pragmatic view and published interim guidance where patients are selected for beta-blockers depending on stage of liver disease and expanded Baveno VI criteria: https://www.bsg.org.uk/covid-19-advice/bsg-basl-advice-on-use-of-tipps-as-salvage-therapy-and-the-prevention-of- | Thank you for your response and comment.<br>We will make a note of your comments and continue to monitor intelligence on the impact of COVID-19 on the guideline and recommendations, as well as likely impact on the portfolio of NICE guidance in general.<br>Thank you for bringing to our attention the variable availability of local endoscopy services during the COVID-19 pandemic and the related BSG guidance which is a response to changes in practice. |

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| | | variceal-bleeding-during-covid-19/ . These should be reviewed regularly based on primarily local circumstances. | Please note: NICE is providing guidance about COVID-19, which includes COVID-19 rapid guideline: arranging planned care in hospitals and diagnostic services (NG179). |
| Royal College of Physicians - *Endorses comments made by the British Society of Gastroenterology* | No comment | The main issue is the availability of gastroscopy. As this is an aerosol generating procedure there is potential additional risk of transmission of COVID19. However, as discussed earlier non-invasive markers of varices have significant limitations and further long term study is necessary. It is important to stress that the availability of endoscopy varies considerably throughout the UK. Where endoscopy is not available, BSG and BASL have taken a pragmatic view and published interim guidance where patients are selected for beta-blockers depending on stage of liver disease and expanded Baveno VI criteria: https://www.bsg.org.uk/covid-19-advice/bsg-basl-advice-on-use-of-tipps-as-salvage-therapy-and-the-prevention-of-variceal-bleeding-during-covid-19/ . These should be reviewed regularly based on primarily local circumstances. | Thank you for your response and comment.<br>We will make a note of your comments and continue to monitor intelligence on the impact of COVID-19 on the guideline and recommendations, as well as likely impact on the portfolio of NICE guidance in general.<br>Thank you for bringing to our attention the variable availability of local endoscopy services during the COVID-19 pandemic and the related BSG guidance which is a response to changes in practice.<br>Please note: NICE is providing guidance about COVID-19, which includes COVID-19 rapid guideline: arranging planned care in hospitals and diagnostic services (NG179). |
| British Liver Trust | Yes | Could the updated guidance make reference to telephone/video consultations and where these might (and might not) be appropriate and what might be considered best practice? | Thank you for your response and comments.<br>In the context of COVID-19 and related restrictions on practice, we acknowledge that replacing face-to-face appointments with virtual appointments has been widely adopted to help prevent the spread of COVID-19. This is not likely to impact NG50 guideline as there are no recommendations for remote or virtual appointments and we have not identified evidence that is directly relevant. However, we will make a note of your comment and continue to monitor intelligence on the impact of COVID-19 on the guideline and recommendations, as well as likely impact on the portfolio of NICE guidance in general. |

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| | | | We will also pass your comment to the team who are managing NICE's guidelines about COVID-19. |