NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

HEALTH AND SOCIAL CARE DIRECTORATE

QUALITY STANDARD CONSULTATION

SUMMARY REPORT

1 Quality standard title

Liver disease

Date of quality standards advisory committee post-consultation meeting:
9 March 2017.

2 Introduction

The draft quality standard for liver disease was made available on the NICE website for a public consultation period between 19 December 2016 and 2 February 2017. Registered stakeholders were notified by email and invited to submit consultation comments on the draft quality standard. General feedback on the quality standard and comments on individual quality statements were accepted.

Comments were received from 23 organisations, which included service providers, national organisations, professional bodies and others.

This report provides the quality standards advisory committee with a high-level summary of the consultation comments, prepared by the NICE quality standards team. It provides a basis for discussion by the committee as part of the final meeting where the committee will consider consultation comments. Where appropriate the quality standard will be refined with input from the committee.

Consultation comments that may result in changes to the quality standard have been highlighted within this report. Comments suggesting changes that are outside of the process have not been included in this summary. The types of comments typically not included are those relating to source guidance recommendations and suggestions for non-accredited source guidance, requests to broaden statements out of scope, requests to include thresholds, targets, large volumes of supporting information, general comments on the role and purpose of quality standards and requests to change NICE templates. However, the committee should read this summary alongside the full set of consultation comments, which are provided in appendices 1 and 2.

3 Questions for consultation

Stakeholders were invited to respond to the following general questions:

1. Does this draft quality standard accurately reflect the key areas for quality improvement?

2. Are local systems and structures in place to collect data for the proposed quality measures? If not, how feasible would it be to be for these to be put in place?

3. Do you have an example from practice of implementing the NICE guideline(s) that underpins this quality standard? If so, please submit your example to the NICE local practice collection on the NICE website. Examples of using NICE quality standards can also be submitted.

4. Do you think each of the statements in this draft quality standard would be achievable by local services given the net resources needed to deliver them? Please describe any resource requirements that you think would be necessary for any statement. Please describe any potential cost savings or opportunities for disinvestment.

Stakeholders were also invited to respond to the following statement specific questions:

5. For draft quality statement 1: Lifestyle interventions for people who are overweight or obese are included in the NICE quality standards on obesity in children and young people and obesity in adults. In this context, is it helpful for this quality standard to include this statement on healthy lifestyle advice for people of all ages who are diagnosed with non-alcoholic fatty liver disease?

6. For draft quality statement 2: This statement currently includes adults, young people and children. Does the priority for quality improvement apply to adults and young people only?

4 General comments

The following is a summary of general (non-statement-specific) comments on the quality standard.

- There was some support for the quality standard although stakeholders felt it does not reflect all priority areas.
- There was a concern that the quality standard does not emphasise the importance of alcohol misuse as a cause of liver disease, including co-existing alcohol misuse and obesity.
- The quality standard is currently focussed on adults. It was suggested that it may be difficult to include adult and paediatric liver disease in the same quality standard because they are very different.
- Stakeholders suggested that the quality standard should include other causes of liver disease such as autoimmune, metabolic and genetic liver disease.

Consultation comments on data collection

- Data collection in secondary care is likely to require some investment and co-ordination as it is not currently uniformly in place.
- It was suggested that the quality standard will require the development of a patient management system for people with liver disease in order to monitor disease staging and surveillance.

- Data collection in primary care will need further development as there is currently a lack of systems and structures to collect the data. This includes a lack of standardisation for the diagnosis of NAFLD.
- Public Health England identified a current project to develop a comprehensive set of Read codes relevant to both the prevention and management of liver disease which is likely to be relevant to the quality standard.

Consultation comments on resource impact

- Stakeholders were concerned that the quality standard will have a significant resource impact for the following reasons:
  - although it may result in fewer referrals to secondary care, more people will be identified with advanced liver disease at an earlier stage
  - increased demand on already stretched diagnostic services
  - considerable variation in the burden of liver disease in different localities
  - non-invasive testing in primary care will require additional training and resources for GPs and nurse specialists

5 Summary of consultation feedback by draft statement

5.1 Draft statement 1

Adults, young people and children newly diagnosed with non-alcoholic fatty liver disease are given healthy lifestyle advice.

Consultation comments

Stakeholders made the following comments in relation to draft statement 1:

- The statement needs to go beyond simple one-off advice to be effective, such as:
  - focussing on ongoing support including referral to a dietician or a physical trainer
  - identifying NAFLD as a co-morbidity for people with BMI > 35kg/m^2 and ensuring rapid referral and access to comprehensive weight management services

  - addressing lifestyle within family and social settings for children who are overweight or obese and ensuring parents are responsible for lifestyle changes.
- The population should be extended to people with other types of liver disease.
- The rationale overstates the benefits of healthy lifestyle advice for people with NAFLD given the evidence base considered by the guideline.
- The definition of healthy lifestyle advice should:
  - include weight loss and dietary composition
  - replace the term 'exercise' with 'activity'
  - be consistent with the Chief Medical Officer's low risk guidelines which states that there is 'no safe level of alcohol consumption'.
- An additional measure on the success of healthy lifestyle advice is needed.

Consultation question 5

Lifestyle interventions for people who are overweight or obese are included in the NICE quality standards on obesity in children and young people and obesity in adults. In this context, is it helpful for this quality standard to include this statement on healthy lifestyle advice for people of all ages who are diagnosed with non-alcoholic fatty liver disease?

Stakeholders made the following comments in relation to consultation question 5:

- It was suggested that this statement does not add to current clinical practice as people with NAFLD, including children and young people, should already receive healthy lifestyle advice because they have metabolic risk factors.
- Other stakeholders felt it is helpful as there is a lack of awareness of the impact of poor diet and lack of exercise on the liver and issues regarding obesity are often avoided by clinicians.

5.2 Draft statement 2

Adults, young people and children with non-alcoholic fatty liver disease are offered regular testing for advanced liver fibrosis.

Consultation comments

Stakeholders made the following comments in relation to draft statement 2:

- There was concern about the potential resource impact of including a large number of people in a surveillance programme that will require significant investment in testing services but may not improve outcomes.
- The definition of regular testing for advanced liver fibrosis:
  - implies that the ELF test should be offered whereas the guideline recommendation is only 'consider'.
  - should recognise variability in local access to different types of test. It would be helpful to list other available options including transient elastography, acoustic radiation force impulse imaging, ultrasound scan, Fib4, and NAFLD fibrosis score.
  - should acknowledge different approaches to testing for advanced liver fibrosis in paediatric hepatology.
- The definition of advanced liver fibrosis should make clear that the measure is derived from a liver biopsy.
- The process measures should include transient elastography scores as well as the ELF score to define a low risk of liver fibrosis.

Consultation question 6

This statement currently includes adults, young people and children. Does the priority for quality improvement apply to adults and young people only?

Stakeholders made the following comments in relation to consultation question 6:

- It is important to identify the rate of progression of NAFLD in all age groups and therefore it is reasonable to include all ages in the statement.
- The statement should be limited to adults and young people because the focus is on fibrosis testing in primary care and a referral pathway to secondary care.

5.3 Draft statement 3

Adults and young people with risk factors for cirrhosis are offered non-invasive testing for cirrhosis.

Consultation comments

Stakeholders made the following comments in relation to draft statement 3:

- There were concerns about potential resource impact and it was suggested that it should be identified as a developmental statement to reflect that:
  - potential demand is large due to the high prevalence of harmful drinking and obesity
  - it will require considerable investment in scanners which are not currently available in primary care
  - without the required investment it could lead to increased referrals to secondary care.
- There were concerns about including harmful drinkers in the statement:
  - it is not clear how the test for cirrhosis fits into the wider pathway for harmful drinkers, including treatment for alcohol misuse
  - a negative test for cirrhosis could lead to false reassurance that may reinforce problem behaviour
  - is the test reliable when a person is continuing to drink at a harmful level?
- The definition of risk factors for cirrhosis:
  - is vague/poorly defined
  - should include rarer causes of liver disease e.g. auto-immune conditions and genetic disorders.
- The definition of non-invasive testing for cirrhosis should:
  - allow for the future development of other blood-based or MR-based non-invasive tests
  - acknowledge the circumstances when a liver biopsy may still be required.
- The availability of non-invasive testing for cirrhosis should be included in the measures and audience descriptors as they are a minimum requirement of regional Hepatitis C Operational Delivery Networks.

- The equality consideration should:
  - refer to all homeless people, with alcohol use removed
  - include outreach to people who inject drugs and prisoners.

5.4 Draft statement 4

Adults and young people with cirrhosis who do not have hepatitis B are offered 6-monthly ultrasound surveillance for hepatocellular carcinoma.

Consultation comments

Stakeholders made the following comments in relation to draft statement 4:

- Although surveillance for hepatocellular carcinoma is generally accepted by clinicians there are concerns that it is not associated with improved mortality and may not be cost-effective.
- This will require significant investment in radiology and recall systems but hopefully this will be balanced by savings from earlier diagnosis.
- The statement should include all people with cirrhosis and not exclude people with hepatitis B.
- There should be more flexibility in the type of surveillance to allow MR-based screening, pending further research.

5.5 Draft statement 5

Adults and young people with cirrhosis who have medium to large oesophageal varices are offered endoscopic variceal band ligation for the primary prevention of bleeding.

Consultation comments

Stakeholders made the following comments in relation to draft statement 5:

- Stakeholders were concerned that this intervention is not widely accepted by clinicians and is contrary to other guidelines and recommendations.
- There was concern that primary prevention of oesophageal variceal bleeding is not associated with improved mortality.
- This will put additional pressure on already stretched endoscopy departments.

- Patient choice and shared decision making should be emphasised as variceal band ligation has significant adverse effects.

6 Suggestions for additional statements

The following is a summary of stakeholder suggestions for additional statements.

Suggested additional areas with NICE guidance (in scope)

- Interventions to lower risk of liver disease in people at risk
- Early identification of alcohol related liver disease
- Retesting for cirrhosis for people with alcohol-related liver disease, non-alcoholic fatty liver disease and people with hepatitis C
- Surveillance for oesophageal varices in people with cirrhosis
- Referral to tertiary care for people with cirrhosis at risk of complications
- 6 monthly assessment of risk of complications for people with cirrhosis
- Prophylactic antibiotics for people with cirrhosis who have acute upper gastrointestinal bleeding
- Albumin and antibiotic prescription within 12 hours for people with cirrhosis and ascites diagnosed with spontaneous bacterial peritonitis

Other suggested areas

- People diagnosed with NAFLD are assessed and treated for other features of the metabolic syndrome including hypertension, diabetes and hyperlipidaemia
- Full hepatitis screen (including viruses, autoimmune disease, metabolic diseases, cholestatic diseases and metabolic syndrome) for all people with persistently raised liver function tests
- Testing and treatment for people with hepatitis B and C and testing and vaccination for their family and contacts
- Monitoring hepatitis C sustained virologic response rates for people with cirrhosis
- Diagnostic paracentesis for people admitted to hospital with ascites due to cirrhosis
- People admitted with decompensated liver disease are seen by a specialist within 24 hours

Appendix 1: Quality standard consultation comments table – registered stakeholders

ID	Stakeholder	Statement number	Comments[1]
1	Alcohol Health Alliance UK	General	The Alcohol Health Alliance UK would like to formally endorse the response from British Association for BASL (British Association for the study of the liver) and their supporting this process
2	Children's Liver Disease Foundation	General	The quality standards are heavily adult focussed and don't address the same areas faced by paediatric liver disease. It is difficult to address both adult and paediatric liver disease with the same standards as they are so different in nature.
3	Department of Health	General	Thank you for the opportunity to comment on the draft for the above quality standard. I wish to confirm that the Department of Health has no substantive comments to make, regarding this consultation.
4	Merck Sharp & Dohm	General	Thank you for giving MSD the opportunity to comment on this quality standard. Please find attached our comments form- we have no specific comments at present but we fully support this process and welcome initiatives aimed at improving the identification, assessment and management of liver disease.
5	Perspectum Diagnostics	General	This quality standard lacks any statement to direct improvement in identification of liver disease in primary care, despite this being highlighted as one of five key areas for improvement, identified by stakeholders during consultation (Briefing Paper, Table 3, p9). This (at least in part) reflects the shortcomings of the recently published NAFLD guidelines, which fail to provide any guidance on how to diagnose NAFLD (due to the lack of sufficient quality evidence). In the absence of any clear statements on potential strategies for risk stratification, there is a risk that awareness and access to liver tests will remain low. Due to the lack of guidance the impact of this standard on Public Health Outcomes will be limited and uncertainty among GPs will remain.
6	Royal College of Nursing	General	This is to inform you that the Royal College of Nursing have no comments to submit to inform on this QS consultation at this time. Thank you for the opportunity to participate.
7	Royal College of Paediatrics and Child Health	General	Our commentator advised that he was happy with form and content of this quality standard document.
8	Royal College of Physicians	General	The RCP is grateful for the opportunity to respond to the above consultation. We would like to endorse the response submitted by British Society of Gastroenterology.
9	Royal College of Physicians of Edinburgh	General	The College welcomes the publication of this draft Quality Standard and considers that the statements are comprehensive and appropriate.

[1]PLEASE NOTE: 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 quality standards are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its staff or its advisory committees.

ID	Stakeholder	Statement number	Comments[1]
10	The Hepatitis C Coalition	General	There are several potential Quality Statements missing. a) All patients who have a history of intravenous drug use (past or present), transfusion prior to 1991 or who have moved to the UK from high prevalence country should be offered testing for hepatitis B and hepatitis C virus infection b) All patients with persistently raised liver function tests should be offered a full hepatitis screen. This should include tests for viruses, autoimmune disease, metabolic diseases, cholestatic diseases and metabolic syndrome c) All patients diagnosed with NAFLD should have assessment and treatment for other features of the metabolic syndrome, including hypertension, diabetes and hyperlipidaemia. d) Family and contacts of patients with HBV or HCV infection should be offered testing and treatment, where necessary. HBV vaccination should be offered to susceptible (anti-HBs negative) family or contacts
11	The Hepatitis C Trust	General	With reference to page 2 of the draft quality standard, The Hepatitis C Trust would request that an additional NICE guideline – Hepatitis B & C testing: people at risk of infection (PH43) - should be included within the list of those quality standards that should be considered when commissioning liver disease services.
12	The Hepatitis C Trust	General	The Hepatitis C Trust recognises that the accompanying briefing paper (p.30) states that: “A number of stakeholder suggestions were received in relation to hepatitis B and C. These are either addressed in the separate quality standard on hepatitis B (QS65) or are likely to be within the scope of a future quality standard on hepatitis C.” However, regardless of the upcoming quality standard on hepatitis C, we would like to emphasise the need to include within the liver disease quality standard three additional hepatitis C-related areas for improvement. Firstly, we stress the importance of ensuring the availability of NICE-approved, curative treatments for hepatitis C as a means of preventing new cases of hepatitis C-related liver disease, as well as hepatitis C-related hepatocellular carcinoma. Currently, only 4.2% of those chronically infected with hepatitis C receive treatment each year. We believe that the need to increase the numbers of people treated and cured for hepatitis C should be reflected in the quality standard, such is its importance in preventing liver disease. Secondly, given the quality standard’s remit around the identification and assessment of chronic liver disease, we would also emphasise the need for the quality standard to include a focus on improving hepatitis C treatment referral pathways. Currently, individuals testing positive for hepatitis C often receive a diagnosis but fail to subsequently engage with specialist services due to inadequate referral pathways. The likely effect on liver disease incidence is

ID	Stakeholder	Statement number	Comments[1]
			significant, with individuals not being monitored for possible fibrosis or cirrhosis, and with the likelihood of liver disease increasing the longer they are not engaged with specialist care. Finally, we would stress the importance of a focus within the quality standard on testing for hepatitis B and C. Diagnosing hepatitis C at an early stage is one of the key preventative actions which can be taken to enable and support early identification and management of chronic liver disease. With levels of testing among at-risk groups still low, this is a clear area for quality improvement that should be addressed by service providers, healthcare professionals and commissioners.
13	The Royal College of Pathologists	General	The focus appears to be entirely on the 3 main (preventable) causes of liver disease – alcohol, NAFLD and viral hepatitis. No mention is made of how other causes of chronic liver disease (e.g. autoimmune, metabolic) may be identified in primary care or how these should be referred to a specialist (a similar comment has been made by Norgine – Appendix 5, page 37)
14	The Royal College of Pathologists	General	Little information is provided concerning how the management of autoimmune and genetic liver disease should be improved (similar comments have been made by British Liver Trust and Perspectum Diagnostics – Appendix 5, page 57)
15	The Royal College of Pathologists	General	The focus appears to be entirely on non-invasive methods for diagnosing advanced fibrosis/cirrhosis. Although these have large replaced the need for liver biopsy in many settings, there are still a number of situations in which liver biopsy is required to assess the severity of liver disease. A brief consideration of these would be appropriate.
16	British Society of Gastroenterology	Question 1	Question 1 Does this draft quality standard accurately reflect the key areas for quality improvement? Response: The quality standard identifies a number of areas for quality improvement but we feel some additional areas need to be added. In particular, given the concerns regarding inpatient management of decompensated cirrhosis identified in the 2013 NCEPOD report “Measuring the Units”, we would suggest adding the following KPIs (in line with NICE guidance, the BSG/BASL “care bundle” and the Liver QuEST project): 1] Administration of prophylactic antibiotics to patients with cirrhosis who have acute upper gastrointestinal bleeding. 2] Performance of a diagnostic paracentesis in all patients admitted to hospital with ascites due to cirrhosis. 3] Albumin and Antibiotic prescription in patients diagnosed with SBP within 12 hours of diagnosis 4]. Percentage of acute admissions with decompensated liver disease who are seen by a gastroenterologist/Hepatologist within 24 hours of admission 5] HCV SVR rates per genotype/cirrhosis status Additional KPIs from NICE Cirrhosis guidance could also be included:

ID	Stakeholder	Statement number	Comments[1]
			1] Proportion of patients retested for cirrhosis with ALD/NAFLD/HCV 2] Proportion of patients with cirrhosis who are screened for oesophageal varices 3] Proportion of cirrhotic patients undergoing primary band ligation of medium to large varices 4] Proportion of cirrhotic patients undergoing 6 mo ultrasound/afp HCC screening 5] Proportion of cirrhotic patients with ascites with albumin content < 15g/l on quinolone primary prophylactic antibiotics. 6] Proportion of cirrhotic patients under follow up with 6 monthly MELD and/or UKELD calculation
17	Public Health England	Question 1	This QS is entitled "Liver disease NICE quality standard" and the topic overview indicates that this standard will include: • alcohol-related liver disease • the identification of people with non-alcoholic fatty liver disease who have advanced liver fibrosis and are most at risk of further complications • liver disease associated with hepatitis B or C • cirrhosis in people over 16 We understand that the statements in the draft liver disease quality standard are mainly based on the non-alcoholic fatty liver disease guideline (NG49) and the cirrhosis guideline (NG50). We believe that the focus on NAFLD in the draft standard and the very limited coverage of alcohol misuse as a causal factor is a cause for serious concern, as is the absence of any acknowledgement of increased risk from co-morbid obesity and alcohol misuse, given that the main risk factors for liver disease are obesity and alcohol and these are often co-existing. There probably needs to be a quality statement dealing with the early identification of ARLD among patients who are heavy drinkers or who have been diagnosed with other alcohol-related conditions. Some of the quality statements that apply to NAFLD, such as "Adults, young people and children newly diagnosed with non-alcoholic fatty liver disease are given healthy lifestyle advice." And "Adults, young people and children with non-alcoholic fatty liver disease are offered regular testing for advanced liver fibrosis" should be amended to cover ARLD also. The QS recognises the importance of detecting liver disease early, which is essential to reverse the increasing trend in liver disease mortality in the UK however its focus on alcohol is limited. This is noteworthy, given that alcohol-related liver disease is the most common cause of liver disease in England and accounts for up to 85% of liver disease mortality. This is based on 7,655 liver deaths in 2014, of which 4,637 (61%) are ICD coded K70 Alcoholic Liver Disease and a further 1,775 (23%) K74 are due to fibrosis and cirrhosis of undetermined aetiology, the latter is now counted as alcohol related by ONS (1). Obesity induced fatty liver can progress to cirrhosis and liver failure, but obesity can also amplify the impact of alcohol consumption on the liver. The excess risk of liver disease due to body mass index (BMI) is small compared with that due to alcohol, but the relative excess risk due to being both overweight and consuming alcohol is large (2). Simply,

ID	Stakeholder	Statement number	Comments[1]
			for a person with a BMI >35, the liver risk doubles at any given alcohol intake. The QS, as is, do not take into account this important synergy. The operational definition of alcohol as a 'risk factor' in the present QS is "more than 50 units of alcohol per week for men and more than 35 units per week for women". The QS may benefit from including a lower risk threshold for individuals who are classified as overweight or obese. Similar synergies exist among those who have autoimmune (3) or viral (4) liver disease and consume alcohol, and the QS may benefit from recognising these synergies with differential definitions of alcohol as a risk factor among these groups. References: (1) Office of National Statistics 2016. Alcohol Related Deaths in the United Kingdom: Registered in 2014 Available from: www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/causesofdeath/bulletins/alcoholrelateddeathsintheunitedkingdom/registeredin2014 (2) Hart CL, Morrison DS, Batty GD, Mitchell RJ, Davey Smith G. Effect of body mass index and alcohol consumption on liver disease: analysis of data from two prospective cohort studies. BMJ. 2010;340:c1240–c1240. (3) Hsu CC, Kowdley KV. The Effects of Alcohol on Other Chronic Liver Diseases. Clin Liver Dis. 2016 Aug 1;20(3):581–94. (4) Mueller S, Millonig G, Seitz HK. Alcoholic liver disease and hepatitis C: A frequently underestimated combination. World J Gastroenterol WJG. 2009 Jul 28;15(28):3462–71.
18	Royal College of Physicians and Surgeons of Glasgow	Question 1	Yes in general. Although the objectives are restricted in ambition, targeting only specific disease groups for lifestyle advice and non-invasive testing. They reflect some but not all of the key areas in this area.
19	British Society of Gastroenterology	Question 2	Question 2 Are local systems and structures in place to collect data for the proposed quality measures? If not, how feasible would it be for these to be put in place? Response: We feel that, currently, a robust mechanism for recording this data is not uniformly in place across acute trusts. For example, very few providers have computerised recall systems to ensure ultrasound screening for hepatocellular carcinoma is carried out at the appropriate interval. This would require some investment and co-ordination of clinical hepatology and radiology services. There are major data gaps in primary care – for example the numbers of patients identified as having risk factors for cirrhosis who could be screened for the condition. Again, this would require some investment in primary care to identify and process these cases.
20	Public Health England	Question 2	National population surveys reveal that the prevalence of increasing and higher-risk alcohol consumption is common, with over 10 million adults reporting regularly drinking more than 14 units of alcohol each week in 2014 (5), however the full range of practice-based data on alcohol consumption recorded in consultations is not easily available. Data on

ID	Stakeholder	Statement number	Comments[1]
			direct engagement with alcohol issues in a GP consultation have to be sourced indirectly. The success of the proposed QS is contingent on the ability of commissioners to have access to this data. To note, as reported in the most recent Lancet Liver Commission, there is a need to "draft and adopt a suite of Read codes [the standard clinical terminology system used in general practice in the UK] to cover liver disease risk factors, diagnoses, and interventions to facilitate excellence of clinical care and practice audit and performance monitoring" (6). A review by the commission team has "identified an opportunity to develop a comprehensive set of Read codes relevant to both prevention and management of liver disease and associated risk factors". This project will be taken forward by the Commission team over the next year and it is anticipated that this will be of central importance to the current QS. References: (5) Health Survey for England 2014. Chapter 8: Adult alcohol consumption [Internet]. 2015. Available from: http://www.hscic.gov.uk/catalogue/PUB19295/HSE2014-ch8-adult-alc-con.pdf (6) Williams R, Alexander G, Aspinall R, Bosanquet J, Camps-Walsh G, Cramp M, et al. New metrics for the Lancet Standing Commission on Liver Disease in the UK. The Lancet [Internet]. 2016 Dec 15 [cited 2017 Jan 18];0(0). Available from: /journals/lancet/article/PIIS0140-6736(16)32234-6/abstract
21	Royal College of Physicians and Surgeons of Glasgow	Question 2	It is unlikely that structures are in place to capture much of the necessary data for these quality measures. In primary care, there is a lack of systems and structures to collect all the relevant data (eg documenting GPs giving lifestyle advice; measuring and assessment of markers of advanced liver fibrosis in primary care. In many places this activity takes place in secondary care and here too there is a lack of structured data capture on patients with liver disease. It is likely that in most centres this will be quite labour intensive, particularly with the plan for continuous monitoring.
22	British Society of Gastroenterology	Question 3	Question 3 Do you have an example from practice of implementing the NICE guidelines that underpin this quality standard? If so, please submit your example to the NICE local practice collection on the NICE website. Examples of using NICE quality standards can also be submitted. Response: The NICE clinical guidelines on cirrhosis and NAFLD were released less than a year ago and we do not believe this has allowed adequate time for the guidance to be widely implemented and formally evaluated. We are aware that the quality standards proposing variceal band ligation as primary prophylaxis and the use of 6-monthly ultrasound screening for HCC have not been uniformly accepted and remain controversial amongst some colleagues. As mentioned above, relatively few institutions currently have systematic recall mechanisms for co-ordinating ultrasound screening programmes for HCC. One example where this has been piloted is at the Royal Liverpool

ID	Stakeholder	Statement number	Comments[1]
			Hospital. However, the recently published data (Farrell C et al, Clin Radiol 2016) revealed that screening uptake rates remained low and the effective implementation of a universal screening programme is likely to be challenging.
23	British Society of Gastroenterology	Question 4	Question 4 Do you think each of the statements in this draft quality standard would be achievable by local services given the net resources needed to deliver them? Please describe any resource requirements that you think would be necessary for any statement. Please describe any potential cost savings or opportunities for disinvestment. The proposal that individuals who have risk factors for cirrhosis should be screened for cirrhosis using transient elastography (Fibroscan) or ARFI would require an enormous investment in the scanners required. Currently, there are very few of these scanners in the community and even large acute hospitals would typically have only 1-2 scanners, which are currently occupied monitoring patients with diagnosed liver conditions. The proposal to repeat screening after an interval of a few years in patients who remain at risk will lead to considerable snowballing of the numbers of people needed to be scanned. Given the prevalence of obesity/NAFLD and harmful drinking in the general population, this has the potential to swamp clinical services without considerable prior investment or, at the very least, detailed modelling of the numbers of screening scans required. In addition, there are two major concerns with regard to using Fibroscan/ARFI to diagnose cirrhosis in people actively drinking alcohol at harmful levels: 1. Transient elastography values are often falsely raised (due to inflammation and alcoholic steatosis) during harmful drinking, regardless of fibrosis stage, and typically fall to more realistic values after 3-4 weeks of abstinence. If introduced at a population level, there is the risk of triggering many false positives, requiring unnecessary investigations. 2. Liver “Fibroscans” only detect liver disease and will not pick up other organ damage from alcohol misuse. The finding of a low transient elastography value in a patient who is drinking at harmful levels can therefore lead to false reassurance and may reinforce problem behaviours if it appears there is no damage. Given the low proportion of people with alcohol misuse who access treatment for dependency, it may be more appropriate to advise that all patients drinking at harmful levels should be offered treatment for their alcohol misuse rather than simply screening them for cirrhosis.
24	British Society of Gastroenterology	Question 4	Question 4 Do you think each of the statements in this draft quality standard would be achievable by local services given the net resources needed to deliver them? Please describe any resource requirements that you think would be necessary for any statement. Please describe any potential cost savings or opportunities for disinvestment.

ID	Stakeholder	Statement number	Comments[1]
			Many of these will require new funds and co-ordination to implement. Whilst they may reduce secondary care referrals in many cases they will identify more patients with advanced liver disease raising the overall cost to the health service. General points – 1. Why is ELF recommended for NAFLD yet Fibroscan recommended for cirrhosis – these are not different entities but part of a spectrum. The recommendations on modalities looking at liver fibrosis are unnecessarily prescriptive and should factor in local expertise/availability. What about algorithms such as Fib4/NAFLD Fibrosis Score?. Transient elastography (FibroScan) has also got a good negative predictive value to rule out advanced fibrosis (F3+) and is commonly used in UK clinical practice. The recent EASL/EASD/EASO NAFLD guidelines 2016 also recommend the use of transient elastography in this setting and is under-pinned by an adult/paediatric literature. 2. Banding for primary prophylaxis is contentious and not in concert with BAVENO recommendations.
25	NHS England	Question 4	I think there are significant resource implications for localities in implementing these quality standards. They don't say explicitly which diagnostic tests are involved in the standards (there is some info in the appendix) and this is unhelpful especially since new diagnostic tests are available in some centres. The demand on already stretched diagnostic services such as USS for cirrhosis surveillance is likely to be significant.
26	Public Health England	Question 4	In 1998, a survey revealed that GPs did not routinely enquire about their patients' alcohol consumption (7), and while a more recent survey suggests this has improved (8), lack of time and the need to manage competing multiple problems within a single consultation were cited as key inhibitors to managing a greater number of risky drinkers. These are important considerations when understanding the feasibility of implementing this QS. The National Confidential Enquiry into Patient Outcome and Death (NCEPOD) found, in its 2013 review of patients who died with ARLD that in more than half of the cases reviewed, the care of patients who died with a diagnosis of ARLD was rated as less than good. The majority of patients had been to hospital at least once in the two years before the admission when they died, but not enough was done about their harmful drinking at that time. There was a failure to screen adequately for harmful use of alcohol and even when this was identified, patients were not referred for support. The report recommended that: • All patients presenting to hospital services should be screened for alcohol misuse. An alcohol history indicating the number of units drunk weekly, drinking patterns, recent drinking behaviour, time of last drink, indicators of dependence and risk of withdrawal should be documented. (All Doctors)

ID	Stakeholder	Statement number	Comments[1]
			• All patients presenting to acute services with a history of potentially harmful drinking, should be referred to alcohol support services for a comprehensive physical and mental assessment. The referral and outcomes should be documented in the notes and communicated to the patient's general practitioner. (All Doctors). There are published evaluations of where routine identification of alcohol misuse and subsequent referral to specialist treatment for alcohol dependence has been significantly improved in secondary care. These indicate reductions in re-admission for alcohol-related liver disease. Specialist alcohol care is available in around 80% of district general hospitals and in the community, to which patients can be referred for treatment of alcohol dependence as long as pathways are in place for timely referral (PHE in press). Furthermore, recent analysis of liver disease data from the Foundation for Liver Disease Research reveals a 17-fold difference between the burden of liver disease in the North West of England and rates in the Home Counties (9). It is clear that liver disease is not evenly distributed across populations and this is an important consideration to inform not only the commissioning and delivery of preventative services, but clinical audits of health promotion practices. The QS as stands, does not appear to emphasise these important differences across local populations and their implications for resources and clinical practice. For example, the QS states "commissioners [should] commission services that provide healthy lifestyle advice to adults, young people and children who are newly diagnosed with NAFLD". In order to commission services to meet demand, it is essential that there is readily accessible local data. As stated earlier, the development of Read codes by the Lancet Commission are likely to be important for this proposed QS (10). References: (7) Kaner EF, Heather N, McAvoy BR, Lock CA, Gilvarry E. Intervention for excessive alcohol consumption in primary health care: attitudes and practices of English general practitioners. Alcohol Alcohol Oxf Oxfs. 1999 Aug;34(4):559–66. (8) Rapley T, May C, Frances Kaner E. Still a difficult business? Negotiating alcohol-related problems in general practice consultations. Soc Sci Med 1982. 2006 Nov;63(9):2418–28 (9) Constituency liver disease profiles [Internet]. Foundation for Liver Disease Research; 2016. Available from: http://www.liver-research.org.uk/liver-profiles/constituency-liver-profiles.html

ID	Stakeholder	Statement number	Comments[1]
			(10) Williams R, Alexander G, Aspinall R, Bosanquet J, Camps-Walsh G, Cramp M, et al. New metrics for the Lancet Standing Commission on Liver Disease in the UK. The Lancet [Internet]. 2016 Dec 15 [cited 2017 Jan 18];0(0). Available from: /journals/lancet/article/PIIS0140-6736(16)32234-6/abstract
27	Royal College of Physicians and Surgeons of Glasgow	Question 4	Current resources are not sufficient to deliver the changes suggested by these quality statements. The standards would be achievable, in that most of this is conducted within routine clinical care. However it is likely to require a means of prospective data capture on patients in terms of disease staging, offer of lifestyle advice and surveillance strategies for varices by endoscopy and liver lesions by ultrasound. This will likely require time consuming prospective data recording or patient management systems for patients with liver disease (as currently used in renal units) which are not currently in existence. If for example, testing for advanced fibrosis (and possibly non-invasive testing for cirrhosis) is done in primary care then training and resources for GPs and/or nurse specialists will be required.
28	BASL (British Association for the study of the liver)	Statement 1	We welcome interventions aimed at reducing the morbidity and mortality associated with liver disease. This statement however does not add to current clinical practice. Patients with NAFLD will have metabolic risk factors and should already receive lifestyle advice. For instance, the vast majority will be classified as overweight or obese and lifestyle interventions for the management of these individuals is covered the NICE Clinical Guideline 189. There are no specific data that suggest individuals with NAFLD are denied these interventions, nor are there data to support increased efficacy of these interventions in this population
29	NHS England	Statement 1	In addition to lifestyle advise, as NAFLD is associated with increased risk of diabetes and cardiovascular disease, these should also be addressed and will need targeted screening for diabetes and management of risk factors for cardiovascular disease
30	Obesity Group of the British Dietetic Association	Statement 1	We strongly agree that those diagnosed with non-alcoholic fatty liver disease should be given advice about healthy lifestyles. However we have concerns that NAFLD may not be diagnosed in all those who have it; since overweight and obesity and particularly visceral obesity are strongly related to risk of NAFLD we suggest that this QS should be amended to reflect this (e.g. Healthy lifestyle advice should be given to all adults, young people and children newly diagnosed with NAFLD and those who are overweight or obese, particularly those with abdominal (visceral) obesity).
31	Obesity Group of the British Dietetic Association	Statement 1	In our view NAFLD should be a recognised co-morbidity for those with BMI ≥35kg/m2, to ensure rapid referral and access to comprehensive weight management services for this high-risk group.

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32	Obesity Group of the British Dietetic Association	Statement 1	As NAFLD is more common in those with diabetes, in our view this should be highlighted and linked to the need to provide advice and support to this high-risk population as well.
33	Obesity Group of the British Dietetic Association	Statement 1	What the quality statement means for different audiences - Healthy lifestyle advice should include weight loss (which is more likely to be needed than not), activity and safe alcohol consumption. It should also include specific advice related to dietary composition particularly fat and carbohydrate intakes. For this reason in our view, the advice should be given by a registered dietitian.
34	Obesity Group of the British Dietetic Association	Statement 1	Definitions of terms used in this quality statement - Advice on physical activity and diet by itself may not facilitate changed behaviours in many individuals; in our view this definition should also include ongoing support.
35	Obesity Group of the British Dietetic Association	Statement 1	Definitions of terms used in this quality statement - We also suggest that the term 'exercise' should be replaced by the term 'activity' to include all movement and aid understanding that all activity is beneficial
36	Perspectum Diagnostics	Statement 1	It is helpful to include a statement on healthy lifestyle advice for people diagnosed with fatty liver disease, in the absence of clear guidance on the diagnosis of NAFLD itself. Awareness among the public of the impact of poor diet and lack of exercise on the liver remains low. Measures to increase awareness are likely to improve wider public health outcomes. Moreover, NICE NG49 recommendation 1.2.13 states that lifestyle interventions in NICE's obesity guideline should be considered for people with NAFLD, regardless of their BMI.
37	Perspectum Diagnostics	Statement 1	The measure is quite static as it only requires the Primary Care Physician to offer advice – there is no measure of success. It is also likely to be hard to measure due to the lack of any standardization for diagnosis of NAFLD.
38	RCGP	Statement 1	I'm not going to argue that patients should not have healthy lifestyle advice (this is standard advice for all patients, with and without NAFLD). But the uncertainties make it difficult. In the full guideline the evidence for the risks & benefits of lifestyle advice (pages 190-198, tables 61-68) presents a rather mixed picture. The evidence is graded mostly low or very low quality, and many of the studies give estimates of effect that include no effect; they also used a variety of mostly surrogate markers to assess disease progression. The group summarised the evidence in a balanced way, concluding on balance that lifestyle advice was probably beneficial, and see no risks. In the quality statement, this becomes something altogether more certain: 'Adopting a healthy lifestyle can reduce the rate of progression of non-alcoholic fatty liver disease (NAFLD). Providing healthy lifestyle advice to people when they are diagnosed with NAFLD can encourage them to consider changes they can make to help them avoid more serious liver disease.' The difficulty is that we are apparently expected to give 'healthy lifestyle advice' without discussing the uncertainties around the nature and the prognosis of the 'diagnosis' of NAFLD. In my view this simply amounts to bad medicine. In addition it fails to take into account the potential harm of this advice. Such harms include: • Making patients worry about their livers for no good reason

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			• Succeeding in getting patients to change diet & exercise without it improving the progression of NAFLD (Here no doubt NICE would reply that the changes would benefit them in other ways) • Giving patients the advice; they find themselves unable to follow it, and then both they & their doctors blame them for the progression of the problem. • There is the additional risk of including large numbers of patients in a surveillance programme and creating more work with little benefit to anyone (just as we have done with CKD). I should add that as a patient, if I would found to have the appearance of NAFLD I should probably not want to know. (DJ) All the statements are reasonable and evidenced. However although the possibility of collecting evidence exists, the collection of data to measure would be difficult and bureaucratic. I'm not sure of point of measuring these. (KS) There are often insufficient lifestyle advice services. Would investing in obesity services for those at risk be more cost effective than scanning asymptomatic patients? (CH) Addressing lifestyle issues is often difficult and particularly issues regarding obesity are avoided by clinicians. The additional emphasis here in this QS is definitely required. (JD)
39	Royal College of Physicians and Surgeons of Glasgow	Statement 1	This seems reasonable, logical and relatively easy to implement. Patients could be given simple advice on diet and exercise by GP, and if needed referred to local dietician (if resources allow). However robust outcome data may be slightly hard to measure, dependent on accuracy of documentation of advice being given by GPs. We wonder why the standard is only for patients with established NAFLD. Why not give healthy lifestyle advice for all patients with liver disease? NAFLD is common (circa 30% of the population) and a cofactor for the progression of other liver diseases. Hence this advice is warranted for all patients with suspected liver disease, particularly for patients with NAFLD but equally relevant for patients with other liver disease.
40	The Hepatitis C Coalition	Statement 1	Whilst there is good evidence that weight loss and increasing exercise improve non-alcoholic fatty liver disease there is very little evidence that providing lifestyle advice achieves this aim. The intervention requires a dietician and physical trainers with expertise in obesity in order to be successful. Providing advice on its own cannot be considered as a quality standard.
41	The Hepatitis C Trust	Statement 1	This statement would benefit from a focus on people diagnosed with hepatitis B and C, in addition to people diagnosed with non-alcoholic fatty liver disease. From a hepatitis C perspective, a healthy lifestyle is essential if people living with the virus are to reduce their risk of developing liver disease, however often advice related to lifestyle is not provided at the point of diagnosis. Given the high prevalence of comorbidities among people living with hepatitis C, and in particular people who acquired hepatitis C through injecting drug use (e.g. substance misuse and alcohol

ID	Stakeholder	Statement number	Comments[1]
			issues), the provision of tailored lifestyle advice and support (particularly around alcohol consumption and diet) is required to prevent or decelerate damage to the liver. In addition to healthy lifestyle advice, The Hepatitis C Trust also recommends the inclusion of more general information provision within the quality statement, for example the provision of information related to treatment options, in order to support shared decision-making and patient activation.
42	British Society of Gastroenterology	Statement 1 – Question 5	Question 5 For draft quality statement 1: Lifestyle interventions for people who are overweight or obese are included in the NICE quality standards on obesity in children and young people and obesity in adults. In this context, is it helpful for this quality standard to include this statement on healthy lifestyle advice for people of all ages who are diagnosed with non-alcoholic fatty liver disease? Not really – provision of lifestyle advice outside a structured programme and government intervention is unlikely to be effective. Moreover, it will be difficult to implement as there is no record/database of NAFLD diagnoses. Moreover, there are multiple different fatty liver codes in primary care so these would need to be rationalised first. How would giving of advice be recorded? There are no accepted methods of establishing disease progression in NAFLD without recourse to a liver biopsy – what method would therefore be used? Moreover, many patients will be enrolled in clinical trials making it difficult to evaluate the effect of lifestyle intervention.
43	Obesity Group of the British Dietetic Association	Statement 1 – Question 5	Yes. In our opinion it is vital that this statement on healthy lifestyle advice for people of all ages is included, with the provisos already mentioned.
44	Public Health England	Statement 1 – Question 5	Yes it is helpful to repeat this across QS. However, the QS is inconsistent in its reference to the low risk guidelines and states advice should be given regarding how to “stay within the government’s guidelines on how much alcohol is safe to drink”. In light of the recent Chief Medical Officer’s (CMO) guidelines which clearly states “there is no safe level of alcohol consumption” (11), we suggest the wording be replaced with “drink within the UK Chief Medical Officers’ low-risk guidelines” or similar. However, the CMO guidelines are for otherwise healthy people and need to be revised down for people with diagnosed conditions. The QS may benefit from including a low-risk threshold of zero consumption for individuals with diagnosed liver disease. The 2016 guideline from the UK CMOs is for adults. The guideline that still stands for people under 18 is “Guidance on the consumption of alcohol by children and young people” (2009), which recommends that: • an alcohol-free childhood is the healthiest and best option. However if children drink alcohol it should not be at least until the age of 15 years

ID	Stakeholder	Statement number	Comments[1]
			• Parents and young people should be aware that drinking, even at age 15 or older, can be hazardous to health and that not drinking is the healthiest option for young people • If 15 to 17 year olds do consume alcohol, they should do so infrequently and certainly on no more than one day a week. Young people aged 15 to 17 years should never exceed recommended adult daily limits and, on days when they drink, consumption should usually be below such levels. The guidance also states that "Adolescents who drink heavily may experience adverse effects on liver, bone, growth and endocrine development." And "Levels of enzymes that are used as indicators of liver damage are higher in adolescents with alcohol use disorders (Clark et al, 2001). Levels are also higher in obese adolescents who drink more moderate amounts (Strauss et al, 2000)" Similarly to the point on drinking alcohol for adults diagnosed with liver disease, advice should be to revise these consumption guidelines for young people downwards to zero. References: (11) Alcohol Guidelines Review – Report from the Guidelines development group to the UK Chief Medical Officers. [Internet]. Department of Health; 2016. Available from: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/489797/CMO_Alcohol_Report.pdf Footnote: i) Guidance on the consumption of alcohol by children and young people. [internet]. Department of Health; 2009. Available from: http://www.cph.org.uk/wp-content/uploads/2013/09/Guidance-on-the-consumption-of-alcohol-by-children-and-young-people.pdf
45	Royal College of Physicians and Surgeons of Glasgow	Statement 1 – Question 5	Yes it is advisable to include this healthy lifestyle advice for people who are overweight or obese, but likewise this advice should be offered to other patient populations with risk factors for liver disease (eg excess alcohol consumption) and in particular diagnosed with liver disease regardless of the aetiology. It is important to emphasis this simple and cheap intervention when discussing non-alcoholic liver disease.
46	Children's Liver Disease Foundation	Statement 1 – Question 5	In our experience young people with NAFLD are given healthy lifestyle advice as a matter of course and therefore its inclusion will have limited effect. It is also covered within other NICE guidelines. It would be more impactful to use the following recommendations from NICE's obesity guideline: For children and young people with NAFLD to: Ensure that interventions for children who are overweight or have obesity address lifestyle within the family and in social settings.

ID	Stakeholder	Statement number	Comments[1]
			Encourage parents (or carers) to take main responsibility for lifestyle changes in children who are overweight or obese, especially if they are younger than 12 years. Take into account the age and maturity of the child, and the preferences of the child and the parents.
47	BASL (British Association for the study of the liver)	Statement 2	We welcome interventions aimed at reducing the morbidity and mortality associated with liver disease. However, there are no prospective data to suggest that screening for advanced liver fibrosis in patients with NAFLD improves outcomes. This recommendation is based on cost-effectiveness modelling done for the recent NICE guideline. Since there is no specific treatment licensed for NAFLD above lifestyle intervention the benefits of early diagnosis of advanced fibrosis or cirrhosis must be accrued through improved management of cirrhosis. The interventions here, i.e. surveillance for and primary prevention of oesophageal variceal bleeding, and surveillance for the development of HCC have not been shown to be associated with improved mortality in randomised controlled clinical trials. Basing quality standards on low quality evidence has the risk of diverting resource from effective strategies, such as lifestyle intervention, to those where efficacy is unclear.
48	BSPGHAN	Statement 2	The term “regular testing for advanced liver fibrosis” is used throughout. The scores referred to (ELF, Kleiner, SAF) are not well validated and therefore not in routine use in paediatrics. Other parameters that are used however include US scan and biopsy, and also ARFI / fibroscan elastography. It is helpful that the statements are kept vague, so that all modalities could be used depending on local practice, until it is clear what evidence there is to support a particular test in children. This is consistent with the NICE NAFLD guideline, which states that further research is needed in children.
49	ECHOSENS	Statement 2	Quality measures - In this section, we find it surprising that only the ELF Score (with a cut-off of 10.51) is mentioned as a marker to rule out the risk of NAFLD in adult patients. Indeed Transient Elastography (FibroScan) has also strong negative predictive value to rule out advanced fibrosis F3. The EASL NAFLD guidelines 2016 actually mention the use of transient elastography in this setting: “Biomarkers and scores of fibrosis, as well as transient elastography, are acceptable non-invasive procedures for the identification of cases at low risk of advanced fibrosis/cirrhosis” (A2). This is also supported by several papers including: Wong et al. (Hepatology 2010) in which TE is mentioned as a useful tool to exclude advanced fibrosis in NAFLD patients, with a high negative predictive value (TE cut-off of 7.9 kPa is associated with 90.5% NPV to rule out F3) Tapper et al. (American Journal of Gastroenterology 2016) also reported that the 7.9 kPa TE cut off was associated with a 100 NPV to exclude the risk of advanced fibrosis. Reference papers provided.
50	ECHOSENS	Statement 2	Quality measures - In this section, we find it surprising that only the ELF Score (with a cut-off of 10.51) is mentioned as a marker to rule out the risk of NAFLD in children.

ID	Stakeholder	Statement number	Comments[1]
			Nobili et al. (Hepatology 2008) report a TE cut off of 10.2 kPa associated with a NPV of 100% to rule out advanced fibrosis in NAFLD children, and a cut off of 9 kPa Is associated with a likelihood ratio (LR) of 22.5 (6.825-62.255) to diagnose presence of advanced fibrosis. We believe that Transient Elastography should be mentioned as well Reference paper provided.
51	ECHOSENS	Statement 2	What the quality statement means for different audiences - We find it surprising that again only ELF score is mentioned as a non-invasive tool for tertiary care to test patients for advanced fibrosis in NAFLD, for the same reasons as mentioned above.
52	NHS England	Statement 2	Use of ELF test for monitoring for liver fibrosis is not uniformly accepted amongst Hepatologist and other methods such as Fibroscan, NAFLD fibrosis score, and FIB4 needs to be taken into account according to local guidelines and expertise.'
53	Perspectum Diagnostics	Statement 2	As for Statement 1, this statement may be difficult to measure due to the lack of any standardization for diagnosis of NAFLD. NICE NG49 recommendation 1.2.2 states only that ELF should be 'considered' in people who have been diagnosed with NAFLD to test for advanced liver fibrosis – this should be made more explicit in the definition of terms in this quality statement i.e. on page 11, the wording in the definition implies that ELF should be offered. It should also be made clearer in the definition of advanced liver fibrosis that the measures (F3 fibrosis using the Kleiner (NASH-CRN or SAF score) are derived from a liver biopsy.
54	Perspectum Diagnostics	Statement 2	Definitions - This quality improvement should be applied to adults, young people and children alike. However, it may be useful to include a statement in the definition regarding methods for testing advanced fibrosis that may differ for children vs. adults.
55	RCGP	Statement 2	There are often no local facilities in our area for primary care to order any tests except a routine liver ultrasound. This would require significant investment in screening services. (CH) Is the evidence that fibroscan is superior to US. If there is evidence that fibroscans is superior to ultrasound then fibroscan will need require commissioning in every area, as this is a potentially large group of patients. (KS) How accurate are the available tests? What is the risk that patients are falsely classified either as having or as not having fibrosis? What are the consequences of such misclassification? Again, it is important to remember that there is no clear prevention strategy for cirrhosis. It's a minor objection that as far as I know ELF is not available here in Bristol. (DJ)
56	Royal College of Physicians and Surgeons of Glasgow	Statement 2	This may be hard to implement as there is uncertainty which is the optimum (and cost effective) test for advanced fibrosis. It is probable that most GPs do not offer this routinely at present. Therefore there would be resource/cost implications.

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57	The Hepatitis C Coalition	Statement 2	The progress of NAFLD is extremely slow. The rationale for a 3 year interval for non-invasive testing is not clear. Potentially an interval of 5 years should be considered.
58	The Hepatitis C Coalition	Statement 2	Encouraging and increasing the use of fibroscanners could aid community provision of testing. NHS England's service specification for hepatitis C Operational Delivery Networks policy requires services to accept referrals from 'primary care, substance misuse services, genito-urinary medicine services and all other services undertaking HCV testing or subsequent care'; the service specifications also require 'as a mimumum…access to validated non-invasive methods of estimation of liver fibrosis (e.g.Fibroscan, ARFI elastography, Fibrotest)'. NHS England's service specification for hepatitis C Operational Delivery Networks is available at: https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2015/10/hep-c-netwrks-spec.pdf
59	University College London Institute for Liver and Digestive Health	Statement 2	Quality measures - The ELF score is proposed as the only non-invasive method to rule out the risk of NAFLD-related liver fibrosis in the paediatric sector. This is not correct since the work by Nobili et al (Hepatology 2008) report a transient elastography cut off of 10.2 kPa associated with a NPV of 100% to rule out advanced fibrosis in NAFLD children, and a cut off of 9 kPa Is associated with a likelihood ratio (LR) of 22.5 (6.825-62.255) to diagnose presence of advanced fibrosis. Therefore, both methodologies should be mentioned.
60	University College London Institute for Liver and Digestive Health	Statement 2	Quality measures - Once again the ELF score is mentioned as the only marker to rule out the presence of NAFLD-induced liver fibrosis in adults. This is not correct since transient elastography has also a strong negative predictive value to rule out advanced fibrosis and its use is recommended by the EASL NAFLD guidelines published in 2016 and is confirmed by several papers (Wong et al Hepatology 2010; Tapper Et al. Am J Gastroenterology 2016).
61	Royal College of Physicians and Surgeons of Glasgow	Statement 2 – Question 6	It is reasonable to include all ages in this statement. Staging of liver disease in children seems advisable to characterise the rate of progression of NAFLD in all age groups within the UK.
62	British Society of Gastroenterology	Statement 2 – Question 6	Question 6 For draft quality statement 2: This statement currently includes adults, young people and children. Does the priority for quality improvement apply to adults and young people only? Yes it should be limited to adults/young people. The provision of fibrosis testing should be develop din primary care but in concert with a pathway with secondary care. There remains an issue with collecting data however as indicated earlier.
63	BASL (British Association for the study of the liver)	Statement 3	There are no prospective data to suggest that screening for advanced liver fibrosis in patients with risk factors for highly prevalent liver diseases improves outcomes. To make a significant impact on improving outcomes for individuals with liver disease it is critical that those with highly prevalent liver diseases are targeted, specifically those with alcohol related liver disease (ArLD). The greatest determinant of outcome for these individuals is reducing alcohol consumption with the aim of achieving abstinence. There is existing guidance that covers identification of individuals who are drinking hazardously and an evidence base

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			that supports brief interventions (NICE Clinical Guideline 115 and Quality Statement 11). There are no data that diagnosing advanced liver fibrosis or cirrhosis in that patient group improves the efficacy of such interventions. The impact of this recommendation would therefore be in the standardised delivery of surveillance strategies for cirrhosis. The interventions here, i.e. surveillance for and primary prevention of oesophageal variceal bleeding, and surveillance for the development of HCC have not been shown to be associated with improved mortality in randomised controlled clinical trials. Basing quality standards on low quality evidence has the risk of diverting resource from effective strategies, such as brief intervention, to those where efficacy is unclear.
64	Liver4life	Statement 3	Risk Factors for Cirrhosis -No mention of any Auto-immune conditions for the risk factors of Cirrhosis – page 14
65	Liver4life	Statement 3	Equality - Remove the word alcohol, any homeless person should be supported – should match statement 4 equality statement
66	Norgine Pharmaceuticals Limited	Statement 3	Data source -There is no mention of monitoring, managing complications early or referral into tertiary care. The suggested wording would be “Adult and young people with risk factors for cirrhosis are offered advice on monitoring, managing complications early and referral into tertiary care (ref NG50)” There is no mention of a cirrhosis registry which would help quantify these patients at risk and aim to ensure the consistent data collection required to measure the implementation of this quality standard nationally. The suggested wording would be” Adult and young people with risk factors for cirrhosis are recorded on a cirrhosis registry”
67	Perspectum Diagnostics	Statement 3	This statement reflects a key area for quality improvement. To ensure this quality statement can be met, it should be made explicit that this is a development quality improvement with resource implications.
68	Perspectum Diagnostics	Statement 3	The definitions are limited to only two non-invasive tests for cirrhosis and do not include any reference to other blood-based or MR-based non-invasive tests. A statement on the need for further research into the utility of different non-invasive method for cirrhosis is also warranted, and should be included in the description.
69	RCGP	Statement 3	This quality standard misses what are the really crucial issues in this clinical area. The focus of each quality standard is on those WITH established, albeit early, liver disease, whether NAFLD or cirrhosis. Because the major risk factors are modifiable, I would like to see a standard for the identification of those with risk factors, such as at-risk drinking and obesity/metabolic syndrome, and the delivery of interventions to lower risk before liver disease develops. (JT) This is large group of patients and many areas don’t have GP access to fibroscans. Is there evidence that doing imaging is more effective than spending the time/ money on lifestyle advice? The evidence will need to be compelling to get this service commissioned across England (KS)

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			In view of the increasing prevalence of childhood obesity this guidance should apply to children as well (JD)
70	Royal College of Physicians and Surgeons of Glasgow	Statement 3	Identification of those "at risk of cirrhosis" is rather vague (eg which patients with alcohol excess are defined as having "alcohol related liver disease"). The list of diagnoses/risk factor for cirrhosis does not include many rarer causes of liver disease – patients with these conditions eg autoimmune liver disease, inherited genetic disorders eg alpha 1 antitrypsin deficiency and haemochromatosis should also undergo staging of their disease to establish if they have cirrhosis. While these conditions are rarer they are associated with significant morbidity and mortality in those affected. What is the justification for excluding them if we aim to improve the standard of care for patients with all liver disease? In addition, the availability of Fibroscan etc in primary care is very limited. Therefore these patients should be referred to secondary care where these tests can be undertaken. It seems reasonable to suggest those who may be at risk of cirrhosis are all referred to secondary care, but identifying these patients easily is not always straightforward.
71	The Hepatitis C Coalition	Statement 3	The risk factors for cirrhosis are very poorly defined. They appear to ignore PBC, PSC, AIH, Haemochromatosis … Testing for stage of fibrosis (of which cirrhosis is the final stage) should be performed in all patients with persistently raised LFTs
72	The Hepatitis C Coalition	Statement 3	The call for non-invasive testing for cirrhosis for adults and young people at risk is welcome, but this should include a call for expanding testing for hepatitis C. In its annual report on hepatitis C in the UK, Public Health England highlights testing as critical to tackling HCV infection in the UK and working towards elimination of the virus as a major public health threat by 2030. The report also notes that, "testing in alternative/community settings, using alternative technologies like dried blood spot (DBS) testing, will be key in reducing the levels of undiagnosed infection". Public Health England's Annual report on hepatitis C in the UK is available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/541317/Hepatitis_C_in_the_UK_2016_report.pdf. Existing NICE guidance on this topic is set out in PH43: https://www.nice.org.uk/guidance/ph43. There has been underperformance in hepatitis C services in England which has led to low rates of diagnosis and treatment, increasing the number of people with hepatitis C with preventable cirrhosis and liver cancer. Improving testing rates for hepatitis C would therefore be an important step. The British Society of Gastroenterology clinical guidance on hepatitis C is available at: http://www.bsg.org.uk/pdf_word_docs/clinguidehepc.pdf.
73	The Hepatitis C Coalition	Statement 3	Equality and diversity considerations - The statement that 'community outreach services should support people who are homeless and known to be drinking alcohol in a harmful way to enable them to have access to non-invasive testing for cirrhosis' is welcome, but this should be extended to include outreach to people who inject drugs (PWIDs) and prisoners. According to Public Health England's report, 'In the UK, more than 200,000 people have chronic (long-

ID	Stakeholder	Statement number	Comments[1]
			term) infection with hepatitis C (HCV), the majority of whom are from marginalised and under-served groups in society, such as people who inject drugs (PWID).'
74	The Hepatitis C Trust	Statement 3	Measure - This statement is fully supported by The Hepatitis C Trust, and we welcome the inclusion of hepatitis C as one of the key risk factors for cirrhosis. We would additionally note that the availability of non-invasive methods of estimation of liver fibrosis (e.g. Fibroscan, ARFI elastography, Fibrotest) are a minimum requirement of regional Hepatitis C Operational Delivery Networks, which could be reflected in the quality measures section of quality statement 3, as well as the 'What the quality statement means for different audiences' section.
75	BASL (British Association for the study of the liver)	Statement 4	The evidence supporting surveillance for HCC in patients with cirrhosis is of low quality. There are no prospective studies of individuals with cirrhosis that show a survival benefit with surveillance. The cirrhosis Guideline Development Group recognised this but felt that since surveillance was done (albeit infrequently, and often poorly) that a recommendation not to do surveillance could not be considered. As a consequence, a cost-effectiveness analysis comparing no surveillance vs. 6 monthly surveillance was not done. There are however UK based studies that were included in the initial evidence review that indicate that surveillance is not cost-effective at the £20,000/QALY threshold (e.g. Thompson-Coon et al) Using low quality evidence to support a recommendation that is likely to not meet established cost-effectiveness thresholds carries significant risk. In particular, there is a risk of diverting resource from established, cost-effective interventions and as a consequence it is difficult to support that recommendation.
76	Perspectum Diagnostics	Statement 4	This statement, should include some discussion of the fact that some centres may choose to use MR-based screening for HCC in cirrhotic patients. A statement on the need for further research into the utility of MRI for HCC screening is also warranted, and should be included in the description.
77	RCGP	Statement 4	There will need to be a significant investment in radiology and recall systems to meet the standards regarding scanning and identified. This hopefully will be funded by savings from earlier diagnosis and better management (JD
78	Royal College of Physicians and Surgeons of Glasgow	Statement 4	Most clinicians would agree that all patents with cirrhosis are offered 6 monthly US scans (although the data to prove mortality benefit are weak). Rather than include the words "do not have Hep B" which implies those patients have a different pathway, I think it should be simply stated that "cirrhosis from any cause are offered 6-monthly US"
79	The Hepatitis C Coalition	Statement 4	It is potentially misleading to say 'Adults and young people with cirrhosis who do not have hepatitis B….' Given that we should also include patients with hepatitis B cirrhosis in surveillance programmes there is no need to leave them out in the initial statement.
80	BASL (British Association for the study of the liver)	Statement 5	This statement is at odds with much of clinical practice within the UK with the majority of practitioners using Beta Blockade. The recommendation for variceal band ligation from the GDG was made as a consequence of cost-effectiveness modelling but there is sufficient equipoise over the decision between treatment with beta-blockers and variceal band ligation that NIHR has commissioned a randomised controlled trial to define the most effective strategy.

ID	Stakeholder	Statement number	Comments[1]
			Indeed whilst the evidence review indicated that there was a reduction in the number of individuals experiencing variceal haemorrhage with banding ligation there was no effect on mortality. There are substantial service implications for already stretched endoscopy departments if variceal band ligation were to be recommended for all patients requiring primary prevention of variceal haemorrhage. There are also significant adverse effects with band ligation and a need for repeated endoscopy through follow up. In comparison for those individuals treated with beta blockade there is no requirement for further endoscopy but there are the adverse effects of treatment. Some or perhaps many patients would prefer not to have repeated endoscopy and a more appropriate recommendation given the absence of an effect on mortality would be to use shared decision making with the patient offering both alternative treatments.
81	Royal College of Physicians and Surgeons of Glasgow	Statement 5	Many (possibly most) UK consultants in this area do not agree with this, but use non-selective betablockers rather than variceal band ligation as primary prophylaxis for bleeding. The advice for band ligation as preferred primary prophylaxis conflicts with the recent BSG (British Society of Gastroenterology) guidelines on variceal haemorrhage where non-selective B blockers are recommended with band ligation reserved for those intolerant to B blockers. Other international guidelines (eg Baveno VI European guidelines in 2015) suggest either therapy could be considered. In addition this measure identifies only those patient diagnosed with medium or large varices as a denominator. No mention is made of the number of patients with confirmed cirrhosis (established elsewhere in the quality standards) who have undergone endoscopy to survey for oesophageal varices in the past 2-3 years (in compensated cirrhosis) and in the last 1 year for decompensated cirrhosis. These are process measures but it is important to know what % of patients with cirrhosis are being surveyed appropriately for varices (as recommended by the 2016 BSG guidance) rather than just the proportion of patients who have confirmed varices undergoing treatment.
82	The Hepatitis C Coalition	Statement 5	This is wrong and not compliant with International Guidelines! This is also not in keeping with current clinical practice. Primary prevention of bleeding (i.e. in patients who have not bled before) is normally via starting beta blockers and not routinely banded unless there is a contraindiction to beta-blockers or intolerant to them. Secondary prevention (i.e. patients who have bled before) are offered banding.

Registered stakeholders who submitted comments at consultation

- Alcohol Health Alliance UK

- British Association for the Study of the Liver (BASL)
- British Dietetic Association – Obesity Group
- British Society of Gastroenterology
- British Society of Paediatric Gastroenterology, Hepatology and Nutrition (BSPHGAN)
- Children’s Liver Disease Foundation
- Department of Health
- Echosens
- Liver4life
- Merck, Sharp & Dohm
- NHS England
- Norgine Pharmaceuticals Ltd
- Perspectum Diagnostics
- Public Health England
- Royal College of General Practitioners (RCGP)
- Royal College of Nursing
- Royal College of Paediatrics and Child Health
- Royal College of Physicians of Edinburgh
- Royal College of Physicians and Surgeons of Glasgow
- The Hepatitis C Coalition

- The Hepatitis C Trust
- The Royal College of Pathologists
- University College London Institute for Liver and Digestive Health