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DIAGNOSTICS ASSESSMENT PROGRAMME

SeHCAT (tauroselcholic [75 selenium] acid) for diagnosing bile acid diarrhoea
Diagnostics Consultation Document – Comments

Diagnostics Advisory Committee date: 19 August 2021
Theme: Evidence on the effects of SeHCAT testing in people with primary bile acid diarrhoea

Comment number	Name and organisation	Section number	Comment	NICE response
1	UK Bile acid related diarrhoea network (UK-BARDN)	3	Has all of the relevant evidence been taken into account? No. Many studies have not been identified, or have been excluded for ill-defined reasons. The clinical effectiveness of SeHCAT was clearly established in the 1980's with small but convincing studies by Merrick and Sciarretta (sic) that met the standards of that time (see Table 1). However, these studies have been assessed by 2020 standards as limited in quality. SeHCAT was established as the gold-standard measurement for faecal loss of bile acids. Later studies have tried to expand on this, looking at other markers, clinical characteristics or treatments, which were now considered novel and not repetitive. By 1990, studies with bile acid sequestrants had already shown they benefitted many patients with low SeHCAT and they were unlikely to produce a sustained response in patients with a normal SeHCAT, so it was hard ethically to justify further treatment trials. Studies relating to other potential biomarkers of BAD are not discussed. These have helped establish SeHCAT as the diagnostic gold-standard, but their clinical performance is not so good. Consequently they are unavailable in the UK, and so were outside the scope for diagnostic comparison. They are relevant though for understanding the pathophysiology underlying the diagnosis of BAD. Measurements of faecal bile acids, 7α-OH-cholestenone and FGF19 help validate the use of SeHCAT as the best biomarker for bile acid diarrhoea (see Valentin 2016, ref.73, Borup 2020, PMID: 32740083). In the studies excluded (Table 56), Bajor 2015, Darmsgaard 2018, Orekoya 2015 (among others) are all large studies, where close reading should be able to provide the information said to be missing. Precise definitions of chronic diarrhoea into Rome criteria for IBS-D or functional diarrhoea are not relevant here in establishing the nature of the populations. Papers highlighted in the introduction to the report (Fernandes 2019, Turner 2017, Bannaga 2017) seem	Thank you for your comment which the committee considered. The external assessment group confirmed that all of the studies listed were identified by their searches and provided the committee with the following details on their study quality assessment and the reasons why the studies had been excluded: • The studies by Merrick et al. and Sciarretta et al. were included in the diagnostics assessment report and were described in full. In order for the assessment to provide information on how the evidence may apply to current care in the NHS, the assessment of the methodological quality of these (and other included) studies was done using the currently recommended assessment tools. This meant and is likely to mean that, in many instances, older studies are considered to be less informative. The quality assessment section of the diagnostics assessment report also acknowledges that the 'high risk' components of the assessment are, in large part, a consequence of the age of the studies. • Based on the quality assessment, the studies by Merrick et al. and Sciarretta et al. had also other issues with applicability that were not just because of the age of the studies. In the study by Merrick et. al., the issue was with treatment of SeHCAT negative patients. This is described in the diagnostics assessment report as follows: 'Merrick et al. (1985) was also rated as having 'high' concerns regarding

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			not to have been considered further. Other missing papers include Shiha 2020 PMID: 32954237, Pattni 2013, PMID: 23981126	the applicability of the reference standard, because the management of patients with a negative SeHCAT test was not considered likely to provide a reliable indication of whether or not these patients would have responded to treatment with BAS.' and 'it should be noted that, although all 31 patients with a negative SeHCAT test result were classified as true negatives, this assessment was based on long term follow-up: none of the 31 patients with irritable bowel disease who retained more than 15% at seven days showed any evidence of small bowel disease, and none appeared during a follow up of at least 12, and in some up to 24 months. Simple conservative treatment resolved or eased most symptoms. None of these 31 patients received treatment with colestyramine and it therefore remains uncertain whether any of these patients could have benefited from treatment with BAS.' • In Sciarretta et al., although this study does report sufficient data to allow the calculation of the performance of SeHCAT for predicting treatment response, the decision threshold is <5%, which is lower than that commonly used in UK clinical practice and likely to define a more severely affected population. This study also includes only 13 patients in the analysis. • Studies of other potential biomarkers of BAD do not, as suggested, 'establish SeHCAT as the diagnostic gold-standard'. Studies of this type, e.g. Valentin et al.

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				(2016), provide estimates of the proportion of people with abnormal results based on various biomarkers and based on SeHCAT. Most of the studies included in Valentin et al. (2016) only provided data for SeHCAT (i.e. no comparative data), and the article explicitly states that 'performance characteristics relative to a gold standard test could not be estimated.' Borup et al. (2020) reports a diagnostic accuracy study of the biomarkers 7α-hydroxy-4-cholesten-3-one (C4) and fibroblast growth factor 19 (FGF19); this study takes SeHCAT testing as the reference standard, but is not evidence of the validity of SeHCAT as a reference standard. • The studies by Bajor et al. (2015), Damsgaard et al. (2018) and Orekoya et al. (2015) were excluded at the full paper screening stage. This was because Bajor et al. (2015) and Orekoya et al. (2015) included a mixed population and no data was reported separately for either of the populations included in the assessment. Damsgaard et al. (2018) was excluded because it was unclear whether response to treatment with bile acid sequestrants was used as the reference standard for the SeHCAT test results. It was unclear whether Bajor et al. (2015) or Damsgaard et al. (2018) reported on any of the eligible outcomes. In all three cases, attempts were made to contact the study authors, with a view to obtaining relevant data if available, but either no response was received or data were not available. All

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				three studies lack sufficient data to link SeHCAT test results to treatment response, in the specified populations. The reasons for exclusion for all the studies excluded at this stage of the review are described in Table 56, Appendix 4 of the diagnostics assessment report. • Fernandes et al. (2019), Turner et al. (2017) and Bannaga et al. (2017) were excluded at the title and abstract screening stage and so do not appear in Table 56, Appendix 4 of the diagnostics assessment report which details the reason for excluding full text articles. Fernandes et al. (2019) compares the median diagnostic cost between patients in whom SeHCAT testing was ordered at first consultation and those in whom SeHCAT was ordered later; this study is a retrospective analysis of all patients for whom SeHCAT testing was ordered and does not provide separate costs data for the populations of interest, or any data linking SeHCAT result to treatment response. Turner et al. (2017) reports a comparison of the number of investigations (both before and after SeHCAT) in SeHCAT positive (<15%) and SeHCAT negative (>15%) patients but provides no information about treatment or response to treatment. Bannaga et al. (2017) reports the results of a patient survey, conducted by BAM Support UK and the Bile Salt Malabsorption Facebook group and describes method of diagnosis, and patient experience with respect to symptoms and treatment; this study does not provide

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				any data linking SeHCAT test results to treatment or treatment response. • Shiha et al. (2020), reports the prevalence of abnormal SeHCAT results in patients with IBS-D and functional diarrhoea, but, again, provides no information linking test results to treatment or treatment response. Pattni et al. (2013) assessed the correlation between FGF19 and SeHCAT in normal controls and patients with primary and secondary bile acid diarrhoea; this study also reported accuracy data for FGF19, where SeHCAT was the reference standard, however, there were no data linking SeHCAT test result to treatment or response to treatment. The clinical effectiveness evidence is summarised in sections 3.2 to 3.9 and the committee's considerations of the evidence are described in sections 4.3 to 4.7 of the diagnostics guidance document. The committee decided not to change these sections of the diagnostics guidance document.
2	UK Bile acid related diarrhoea network (UK-BARDN)	3.4	Response rates to treatment at different SeHCAT cut-offs have been previously reported in a systematic review (Wedlake 2009, ref.23)	Thank you for your comment which the committee considered. The external assessment group clarified that Wedlake et al. (2009) was identified by their searches. This study is a relevant systematic review and was treated as a potential source of relevant primary studies. All studies included in this review were independently identified by their searches and evaluated for inclusion in their assessment report.

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				The clinical effectiveness evidence is summarised in sections 3.2 to 3.9 and the committee's considerations of the evidence are described in sections 4.3 to 4.7 of the diagnostics guidance document. The committee decided not to change these sections of the diagnostics guidance document.
3	UK Bile acid related diarrhoea network (UK-BARDN)	4.15	There are data which do inform the clinical utility of SeHCAT testing in terms of the response to treatment, how it informs clinical decision making, and the longer term clinical outcomes (Lin 2016, ref.26; Orekoya 2015, ref.102 etc). As stated repeatedly above, many studies have been ignored or assessed against unrealistic criteria.	Thank you for your comment which the committee considered. The study by Orekoya et al. (2015) was excluded at the full paper screening stage. This was because it included a mixed population and no data was reported separately for either of the populations included in the assessment. Attempts were made to contact the study authors, with a view to obtaining relevant data if available, but either no response was received or data were not available. The study lacks sufficient data to link SeHCAT test results to treatment response, in the specified populations. The external assessment group further noted that Lin et al. (2016, reference 29 in the diagnostics assessment report) was included in the diagnostics assessment report (see Table 5). This article reports limited information (number taking bile acid sequestrants at follow-up and number receiving other treatments at follow-up) about 29 patients with SeHCAT retention values <10%. The clinical effectiveness evidence is summarised in sections 3.2 to 3.9 and the committee's considerations of the evidence are described in sections 4.3 to 4.7 of the diagnostics guidance document. The committee decided not to change these sections of the diagnostics guidance document.

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4	UK Bile acid related diarrhoea network (UK-BARDN)	4.4 and 4.5	This is unclear and probably wrong -- as the studies do report a large segment of NHS clinical out-patient practice. For further review, please see the BSG Guidelines on chronic diarrhoea from 2018 (ref.2) and Frontline Gastroenterol 2019;11:358-363.	Thank you for your comment which the committee considered. The committee noted the differences between the results of the evidence review in the assessment report and in the British Society of Gastroenterology guidelines for the investigation of chronic diarrhoea in adults. It considered that this NICE assessment aimed to evaluate the test as well as its link to longer-term clinical outcomes to show whether it was cost effective and concluded that there is no robust data on the link between the test and longer-term outcomes. The external assessment group reiterated their acknowledgement of an oversight in not including the article on the UK survey of expert opinion and practice, by Walters et al. (Frontline Gastroenterology), in the background section of their report. This article was identified by their searches but did not meet the inclusion criteria for their review. Whilst they endeavoured to include as much relevant information as possible in the background sections of their reports, they advised that the selection of studies for citation in the background is not a systematic process and acknowledge that readers may sometimes find that studies that they are aware of have not been cited. However, they noted that the results in this paper were, in general, aligned with the estimates provided by the experts consulted. The committee decided not to change sections 4.4 and 4.5 of the diagnostics guidance document. Additional paragraphs have been added to section 4.14 of the guidance document to

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				describe the committee's consideration of the British Society of Gastroenterology guideline recommendations.
5	UK Bile acid related diarrhoea network (UK-BARDN)	4.7	This diagnostic assessment should not be about the benefits and complications of current therapies. However, colestyramine has been used for more than 50 years with a large amount of accumulated clinical and published experience included in many of the studies referred to. Patient experts appreciate there are large residual symptoms and unmet needs with these therapies which make them less than perfect. Colestipol has been studied in Bajor 2015. This paper was excluded by the assessors, despite being a relevant and highly cited paper (160 citations).	Thank you for your comment which the committee considered. The external assessment group and the committee noted that the benefits and complications of current therapies are key parameters for the cost effectiveness model, which models the costs and consequences of using SeHCAT testing. These consequences extend to treatment given as a result of using the test. The study by Bajor et al. (2015) was excluded at the full paper screening stage. This was because it included a mixed population and no data was reported separately for either of the populations included in the assessment. It was unclear whether Bajor et al. reported on any of the eligible outcomes Attempts were made to contact the study authors, with a view to obtaining relevant data if available, but either no response was received or data were not available. The study lacks sufficient data to link SeHCAT test results to treatment response, in the specified populations. The committee decided not to change section 4.7 of the diagnostics guidance document.
6	UK Bile acid related diarrhoea network (UK-BARDN)	1.2	Much of the existing research has been overlooked or downgraded. The effectiveness and tolerability of treatment, although clearly a problem, should not be part of this diagnostic assessment.	Thank you for your comment which the committee considered. Please see response to comment 1 above.

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				The external assessment group and the committee noted that the ability to establish a link between testing and effective treatments is a critical component of any cost effectiveness analysis which seeks to assess a test within a treatment pathway. The committee decided not to change section 1.2 of the diagnostics guidance document.
7	UK Bile acid related diarrhoea network (UK-BARDN)	4.8	Evidence is limited on quality of life changes, but patient reported symptoms before and after treatment have been published (Bannaga 2015). Like other intestinal disorder (including inflammatory bowel disease and coeliac disease) there is a cross-over with symptoms for visceral hypersensitivity (IBS) which may need additional treatments.	Thank you for your comment which the committee considered. The external assessment group noted that despite the potential relevance of the findings in Bannaga et al. (2016), it is unclear how those findings could be translated into utility (EQ-5D) values that could have been used in the cost-effectiveness analyses. The committee decided not to change section 4.8 of the diagnostics guidance document.
8	UK Bile acid related diarrhoea network (UK-BARDN)	1.1	See comments above on the assessment of the amount of evidence.	Thank you for your comment which the committee considered. Please see response to comment 1 above. The committee decided not to change section 1.1 of the diagnostics guidance document.

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9	UK Bile acid related diarrhoea network (UK-BARDN)	4.6	The radiation dose of 75Se in test-negative patients is known to be small. This was studied in normal individuals in 1982 (Soudry. J Nucl Med 1982; 23: 157-161) with the conclusion that the absorbed dose is small compared with other techniques. These calculations are still relevant. In a normal subject, wi13.ith 30% SeHCAT retention after 7d, less than 1% of the dose will be retained at 4 weeks. The radioactive decay is slow and the radiation exposure is far less than many other tests that are now in use.	Thank you for your comment which the committee considered. The committee discussed the uncertainty around outcomes for people with negative test results. While the committee was concerned about not having evidence of the potential benefits and harms for people with negative test result, it concluded that this was not primarily because of the radiation exposure. The committee decided to remove comments relating to the radiation exposure from the diagnostics guidance document and revise section 4.6.

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Theme: Model inputs and assumptions

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10	UK Bile acid related diarrhoea network (UK-BARDN)	3.13	The expert opinion used to inform the EAG could have included the published views of a large group (>20 experts) rather than 3-4. (Frontline Gastroenterol 2019;11:358-363) There is no stated reason why this paper did not meet the inclusion criteria for review. The model does not cost in investigations for many other causes of chronic diarrhoea which may be considered necessary before IBS-D/FD is diagnosed. Many of the assumptions could have been better justified with a larger survey of expert group opinion.	Thank you for your comment which the committee considered. The external assessment group noted that this point had been raised in comments received on the diagnostics assessment report prior to the first committee meeting for this topic. They reiterated their acknowledgement of an oversight in not including the article on the UK survey of expert opinion and practice, by Walters et al. (Frontline Gastroenterology), in the background section of their report. This article was identified by their searches but did not meet the inclusion criteria for their review. Whilst they endeavoured to include as much relevant information as possible in the background sections of their reports, they advised that the selection of studies for citation in the background is not a systematic process and acknowledge that readers may sometimes find that studies that they are aware of have not been cited. However, they noted that the results in this paper were, in general, aligned with the estimates provided by the experts consulted. Regarding “The model does not cost in investigations for many other causes of chronic diarrhoea which may be considered necessary before IBS-D/functional diarrhoea is diagnosed”, the external assessment group acknowledged this as a limitation of the model. Including many other causes of chronic diarrhoea would require more evidence, that are unlikely to be available. They explained that all models include simplifications. To the best of their knowledge, the external assessment group included in the model the most important/common causes of chronic diarrhoea.

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				The committee's considerations on the source of model inputs are described in section 4.13 of the diagnostics guidance document. The committee decided that no changes were needed to the diagnostics guidance document.
11	UK Bile acid related diarrhoea network (UK-BARDN)	4.10	Regarding use of a 15% threshold, it must be remembered that SeHCAT retention is a continuous variable with an incomplete association with bowel frequency, stool form, urgency and other symptoms. As with blood pressure, cholesterol, BMI and most other clinical measurements, there is a gradation of risk so that bile acid-related symptoms are greater at, for instance, 10%, than at 15% retention.	Thank you for your comment which the committee considered. The external assessment group noted that, with the current evidence, it was deemed unfeasible to include a continuous threshold in the cost effectiveness analyses. The committee's considerations on the modelling the use of SeHCAT at a 15% threshold for a positive test result are described in section 4.8 of the diagnostics guidance document. The committee decided that no changes to this section were needed.
12	UK Bile acid related diarrhoea network (UK-BARDN)	4.11	The place of colonoscopy is governed by many factors, but the need to exclude microscopic colitis is also a consideration in chronic diarrhoea.(see ref.2)	Thank you for your comment which the committee considered. The external assessment group acknowledged that not all the investigations for different causes of diarrhoea were included in the model and that this as a limitation of the model. However, including many other causes of chronic diarrhoea would require more evidence, that are unlikely to be available. They explained that all models include simplifications. To the best of their knowledge, the external assessment group included in the model the most important/common causes of chronic diarrhoea. The committee's considerations on whether the model captured the resource impact of preventing colonoscopies

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				when SeHCAT is used is described in section 4.9 of the diagnostics guidance document. The committee decided that no changes to this section were needed.
13	UK Bile acid related diarrhoea network (UK-BARDN)	4.12	The need for different imaging room usage is but one of the many costs which are hard to estimate.	Thank you for your comment which the committee considered. The committee's considerations of costs of providing SeHCAT testing and whether these were captured in the model are described in section 4.10 of the diagnostics assessment report. The committee decided that no changes to this section were needed.
14	UK Bile acid related diarrhoea network (UK-BARDN)	4.13 and 4.14	These factors could have been more accurately estimated if expert opinion had been used (see above)	Thank you for your comment which the committee considered. Please see response to comment 10. The committee's considerations on the source of model inputs are described in section 4.13 of the diagnostics guidance document. The committee decided not to change this section or the referred sections describing its considerations on whether the model reflected the variable severity of bile acid diarrhoea in section 4.11 and on the validity of the model assumptions in section 4.12.

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Theme: Recommendations

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15	UK Bile acid related diarrhoea network (UK-BARDN)	1	Are the recommendations sound, and a suitable basis for guidance to the NHS? No. Clinical guidelines, including real world evidence and patient experience have established the value of diagnosing BAD, without the delay which is common (please read the patient reported survey by Bannaga 2017, ref. 9). Also relevant are Fernandes 2019, ref. 7 and Vijayvargiya 2020, PMID: 32618660. This is a large group of patients (5% of outpatients, 1% of the population) who are poorly served by lack of awareness, mixed messaging and poor therapeutic options. Following an idealistic approach to confirm this test as recommended will require significant research funding and an informed, realistic and appropriate design. We would welcome the commitment of research funding before these recommendations can be accepted.	Thank you for your comment which the committee considered. The external assessment group noted that Fernandes et al. (2019), Bannaga et al. (2017) and Vijayvargiya et al. (2020) were identified by their searches and excluded at the title and abstract screening stage. Bannaga et al. (2017) reports the results of a patient survey, conducted by BAM Support UK and the Bile Salt Malabsorption Facebook group and describes method of diagnosis, and patient experience with respect to symptoms and treatment; this study does not provide any data linking SeHCAT test results to treatment or treatment response. Fernandes et al. (2019) compares the median diagnostic cost between patients in whom SeHCAT testing was ordered at first consultation and those in whom SeHCAT was ordered later; this study is a retrospective analysis of all patients for whom SeHCAT testing was ordered and does not provide separate costs data for the populations of interest, or any data linking SeHCAT result to treatment response. Vijayvargiya et al. (2020) is primarily an evaluation of faecal bile acid testing. It does not provide relevant data about SeHCAT testing in the specified populations. The committee discussed the current evidence gaps that prevent the test from being recommended for widespread use in the NHS. Given the unmet clinical need for a test to diagnose bile acid diarrhoea, the committee concluded that there is an urgent need for further data collection and research to support future evaluations of the test and to improve outcomes for people with bile acid diarrhoea.

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				The committee decided to amend the last sentence of section 4.14 of the diagnostics guidance document and add an additional section, 4.15, to the diagnostics guidance document to highlight the importance and urgency of the recommended data collection and research.
16	UK Bile acid related diarrhoea network (UK-BARDN)	3.40	We note the statement that "the SeHCAT strategy was more effective and less expensive (dominant) than the strategy of offering a trial of bile acid sequestrants. It was also more effective but more expensive than the strategy in which bile acid diarrhoea was not investigated or treated. The incremental cost-effectiveness ratio (ICER) for the SeHCAT strategy compared with this strategy was £9,661 per QALY gained (probabilistic base-case analysis)." This would usually be considered to be cost-effective and should inform the overall recommendation in section 1.	Thank you for your comment which the committee considered. The committee discussed whether the analyses presented had fully quantified the uncertainty caused by the lack of clinical outcome data which link the results of testing to treatment outcomes. It concluded that, in the absence of key clinical outcome data, the results of the economic model cannot be used to inform adoption recommendations. The committee decided to update Section 4.13 of the diagnostics guidance document to more accurately describe its considerations and conclusion.
17	The IBS Network	General	My comments relate to the entire document from the perspective of patients living with chronic diarrhoea or presumed irritable bowel syndrome (IBS) with diarrhoea, and as a physician treating them, but exclude individuals with Crohn's disease. I find it surprising that it is being proposed that a test that is useful for the investigation and management of patients with chronic diarrhoea have its use restricted to research or further data collection, and this recommendation is at odds with current national guidelines from the British Society of Gastroenterology for both the management of chronic diarrhoea and the management of irritable bowel syndrome.	Thank you for your comment which the committee considered. The external assessment group noted that the prevalence of abnormal SeHCAT test results in the specified populations had been acknowledged in describing the strengths and limitations of the assessment in the diagnostics assessment report. The key issue, with respect to recommendation for use in research or further data collection, is the lack of evidence linking SeHCAT test results to clinical outcome. In describing the strengths and limitations of the assessment, the external

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			We have audited our own use of SeHCAT among patients with chronic diarrhoea on two separate occasions over the last 16 years. On both occasions we have demonstrated (in almost 1500 patients with chronic diarrhoea) that SeHCAT testing is abnormal in up to 50% of individuals, a substantial proportion of whom would have undergone exhaustive testing to exclude other cause of their diarrhoea prior to SeHCAT. Many of these patients were found to have idiopathic (primary) bile acid diarrhoea i.e., there was no underlying explanation or risk factor for the condition. In fact, in our audits, among individuals with no risk factors whatsoever for bile acid diarrhoea, 35% to 45% were found to have an abnormal SeHCAT retention, and in one-in-four of these individuals this would be compatible with severe bile acid diarrhoea, which responds well to bile acid sequestrants. Similarly, we have shown that among a well-characterised group of over 100 patients with presumed IBS with diarrhoea, who had no risk factors for bile acid diarrhoea (e.g. prior cholecystectomy) and in whom investigations to exclude other potential causes of their diarrhoea (including coeliac disease and microscopic colitis) had been performed and were negative, SeHCAT scanning detected a retention of <10% in one-in-six patients. A diagnosis of bile acid diarrhoea with institution of appropriate treatment can, therefore, be life-changing for some patients with chronic diarrhoea and/or presumed IBS with diarrhoea and, in the latter instance, the treatments used are quite different. I believe, strongly, that the level of evidence the advisory committee were searching for would be highly unlikely to be available for a diagnostic test such as SeHCAT. If one were to apply this across other aspects of gastroenterology, nuclear medicine, or radiology, I suspect many investigations that are an accepted part of current best clinical practice would also have their use restricted.	assessment group stated that despite the apparent significance of bile acid diarrhoea in the adult IBS-D/functional diarrhoea population, and the expansion of provision of SeHCAT testing in the UK, there remains a surprising lack of evidence linking the use of SeHCAT testing to patient-perceived outcomes. The committee discussed and recognised the importance of recognising bile acid diarrhoea as a condition, being able to give a diagnosis and offering treatment for it. It agreed that it was important to highlight this early in the diagnostics guidance document. The committee further noted the differences between its recommendations and the recommendations of the British Society of Gastroenterology guidelines for the investigation of chronic diarrhoea in adults. It considered that this NICE assessment aimed to evaluate the test as well as its link to longer-term clinical outcomes to show whether it was cost effective and concluded that there is no robust data on the link between the test and longer-term outcomes. The committee also discussed and agreed that it was important that the centres currently using SeHCAT for diagnosing bile acid diarrhoea would continue to do so but that it was also important that these centres would collect data to help address the gaps in the evidence. The committee discussed the evidence gaps that prevent the test from being recommended for widespread use in the NHS. Given the unmet clinical need for a test to diagnose bile acid diarrhoea, the committee concluded that there is an urgent need for further data collection and research to support future evaluations of the test and to improve outcomes for people with bile acid diarrhoea.

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Diagnostics Consultation Document – Comments

Diagnostics Advisory Committee date: 19 August 2021
Theme: Recommendations

Comment number	Name and organisation	Section number	Comment	NICE response
				The committee's considerations of the importance of recognising bile acid diarrhoea as a condition and getting a diagnosis and offering treatment for it are described in sections 4.1 and 4.2 of the diagnostics guidance document. Additional paragraphs have been added in the section 'Why the committee made these recommendations' (below section 1.3) of the diagnostics guidance document to emphasise the importance of the condition, getting a diagnosis and offering treatment for it. Additional paragraphs have been added to section 4.14 of the guidance document to describe the committee's consideration of the British Society of Gastroenterology guideline recommendations. The committee decided to amend the wording of section 1.2 of the diagnostics guidance document to make it clearer that the centres currently using SeHCAT for diagnosing bile acid diarrhoea should continue to do so while collecting further data. The committee's recommendations for further data collection and research are described in section 5 of the diagnostics guidance document. The last sentence of section 4.14 of the diagnostics guidance document has been amended slightly and an additional section, 4.15, has been added to the diagnostics guidance document to highlight the importance and urgency of the recommended data collection and research.

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18	British Society of Gastroenterology (BSG)	1.1	The main concerns here is the impression there is no priority given to the pursuit of a diagnosis of those with bile acid diarrhoea. This reflects a different view by an expert panel who authors the British Society of Gastroenterology 2018 guidelines. If the committee felt that the lack of evidence pertaining to Se^{75}HCAT then, alternatives should be suggested and considered for example either a spot or 24hr faecal bile acid sampling. The current recommendations almost dismiss the importance of the clinical condition.	Thank you for your comment which the committee considered. The committee discussed and recognised the importance of recognising bile acid diarrhoea as a condition, being able to give a diagnosis and offer treatment for it. They agreed that it was important to highlight this early in the diagnostics guidance document. The committee further noted the differences between its recommendations and the recommendations of the British Society of Gastroenterology guidelines for the investigation of chronic diarrhoea in adults. It considered that this NICE assessment aimed to evaluate the test as well as its link to longer-term clinical outcomes to show whether it was cost effective and concluded that there is no robust data on the link between the test and longer-term outcomes. The committee's considerations of the importance of recognising bile acid diarrhoea as a condition and getting a diagnosis and offering treatment for it are described in sections 4.1 and 4.2 of the diagnostics guidance document. Additional paragraphs have been added in the section 'Why the committee made these recommendations' (below section 1.3) of the diagnostics guidance document to also highlight early in the guidance document that the committee recognised the importance of the condition, giving a diagnosis and offering treatment. Additional paragraphs have been added to section 4.14 of the guidance document to describe the committee's

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				considerations of the British Society of Gastroenterology guideline recommendations.
19	British Society of Gastroenterology (BSG)	1.3	This remains rather vague for many centres that offer this test as part of standard clinical care. It would be helpful if NICE would define what 'standard data collection' entails to ensure that all centres undertaking Se^{75}HCAT testing can have uniform data collection.	Thank you for your comment which the committee considered. The committee discussed the recommended data collection by the centres currently using SeHCAT and agreed that it was important to provide clear indications for this. The committee further discussed the current evidence gaps that prevent the test from being recommended for widespread use in the NHS. Given the unmet clinical need for a test to diagnose bile acid diarrhoea, the committee concluded that there is an urgent need for further data collection and research to support future evaluations of the test and to improve outcomes for people with bile acid diarrhoea. The committee decided to amend section 1.2 and section 5 to make it clearer that the committee's recommendations for research also apply to the data the centres currently using SeHCAT should collect. The last sentence of section 4.14 of the diagnostics guidance document has been amended slightly and an additional section, 4.15, has been added to the diagnostics guidance document to highlight the importance and urgency of the recommended data collection and research.
20	British Society of Gastroenterology (BSG)	5.1	We disagree with this point as there is good systematic review and meta-analysis for example Wedlake et al. and subsequently other studies demonstrating that the severity of BAD as defined by the 7 day retention value of Se^{75}HCAT study proffers a guide on treatment and dosing regimes.	Thank you for your comment which the committee considered.

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				The external assessment group clarified that Wedlake et al. (2009) was identified by their searches. This study is a relevant systematic review and was treated as a potential source of relevant primary studies. All studies included in this review were independently identified by their searches and evaluated for inclusion in their assessment report. No changes to section 5.1 of the diagnostics guidance document were needed.
21	UK Bile acid related diarrhoea network (UK-BARDN)	5	The ability to do further research is welcomed. However, duplication of established knowledge will not be fundable. It must be focussed on answering aspects which are unclear, with careful choice of measurable outcomes, particularly in view of the current therapeutic difficulties. It will need a realistic budget so that the current situation can be effectively resolved.	Thank you for your comment which the committee considered. The committee discussed the current evidence gaps that prevent the test from being recommended for widespread use in the NHS. Given the unmet clinical need for a test to diagnose bile acid diarrhoea, the committee concluded that there is an urgent need for further data collection and research to support future evaluations of the test and to improve outcomes for people with bile acid diarrhoea. The committee's recommendations for further data collection and research are described in section 5 of the diagnostics guidance document. In addition, the last sentence of section 4.14 of the diagnostics guidance document has been amended slightly and an additional section, 4.15, has been added to the diagnostics guidance document to highlight the importance and urgency of the recommended data collection and research.

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Theme: General comments

Comment number	Name and organisation	Section number	Comment	NICE response
22	UK Bile acid related diarrhoea network (UK-BARDN)	General	The Diagnostics Consultation Document, reflecting the Diagnostics Assessment Report prepared by Kleijnen Systematic Reviews, has multiple defects, showing a selective and poor basis of understanding of the role of SeHCAT, the condition of bile acid diarrhoea, and the impact on patients. Although the views of some experts on the committee are noted, much other information and consensus guidelines have been ignored. The focus on response to bile acid sequestrants as the reason for using SeHCAT to too narrow and ignores other approaches (drugs, diet) to reverse the pathophysiology of the disorder. The data relating to SeHCAT use in Crohn's disease without ileal resection who have chronic diarrhoea are undoubtedly limited. These comments are restricted to chronic diarrhoea with an unknown cause, suspected or diagnosed diarrhoea-predominant irritable bowel syndrome (IBS-D) or functional diarrhoea.	Thank you for your comment which the committee considered. The external assessment group noted that the systematic review and cost-effectiveness modelling were conducted in line with the agreed scope for this assessment. The committee discussed and recognised the importance of recognising bile acid diarrhoea as a condition, being able to give a diagnosis and offering treatment for it. They agreed that it was important to highlight this early in the diagnostics guidance document. The committee further noted the differences between its recommendations and the recommendations of the British Society for Gastroenterology guidelines for the investigation of chronic diarrhoea in adults. It considered that this NICE assessment aimed to evaluate the test as well as its link to longer-term clinical outcomes to show whether it was cost effective and concluded that there is no robust data on the link between the test and longer-term outcomes. The committee's considerations of the importance of recognising bile acid diarrhoea as a condition and getting a diagnosis and offering treatment for it are described in sections 4.1 and 4.2 of the diagnostics guidance document. Additional paragraphs have been added in the section 'Why the committee made these recommendations' (below section 1.3) of the diagnostics guidance document to also make it clearer early in the guidance document that the committee recognised the importance of the condition, giving a diagnosis and offering treatment for it.

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				Additional paragraphs have been added to section 4.14 of the guidance document to describe the committee's considerations of the British Society for Gastroenterology guideline recommendations.
23	UK Bile acid related diarrhoea network (UK-BARDN)	3	Are the summaries of clinical and cost effectiveness reasonable? We recommend that these are revised significantly.	Thank you for your comment which the committee considered. The committee considered that these sections were an accurate description of the available evidence and the external assessment group's economic analyses. No changes to these sections were needed.
24	UK Bile acid related diarrhoea network (UK-BARDN)	4.1 and 4.2	The recorded experience of the clinical experts and patients is in line with the experience of UK-BARDN and should weigh heavily in the conclusions of the committee report.	Thank you for your comment which the committee considered.
25	GE Healthcare	General	Thank you for the below email. At the present time we don't have comments from our side.	Thank you for your comment which the committee considered.