NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Centre for Health Technology Evaluation

Review decision

Review of DG7: SeHCAT (tauroselcholic [75 selenium] acid) for the investigation of diarrhoea due to bile acid malabsorption in people with diarrhoea-predominant irritable bowel syndrome (IBS-D) or Crohn's disease without ileal resection

This guidance was issued November 2012.

The review date for this guidance was November 2015. A decision to defer the 2015 review was made in March 2016 because the British Society of Gastroenterology (BSG) was updating its guidelines on chronic diarrhoea in adults, which could impact upon the position of the SeHCAT test in the diagnostic pathway. The BSG guideline published in April 2018.

NICE proposes an update of published guidance if the evidence base or clinical environment has changed to an extent that is likely to have a material effect on the recommendations in the existing guidance. Other factors such as the introduction of new technologies relevant to the guidance topic, or newer versions of technologies included in the guidance, will be considered relevant in the review process, but will not in individual cases always be sufficient cause to update existing guidance.

1. Review decision

A standard update of the guidance.

At the Guidance Executive meeting of 14 January 2020 the proposal to update the guidance was agreed without consultation. A list of the options that were considered, and the consequences of each option is provided in Appendix 2 at the end of this paper.

2. Rationale

The guidance will be updated because a substantial amount of new evidence is available which could potentially have a material effect on recommendations. A standard update of the guidance will be done rather than an accelerated update of the guidance because adjustments may need to be made to the structure of the model; SeHCAT may now be used earlier in the care pathway, as recommended in the British Society of Gastroenterology (BSG) guidelines on chronic diarrhoea, and

there is new evidence that dietary changes may be used to manage bile acid malabsorption and this management option was not included in the original model.

Clinical experts have noted that the SeHCAT test is now in routine use in the NHS, which would normally make a test a candidate for inclusion in a clinical guideline, rather than diagnostics guidance. However, the SeHCAT test would fit into 2 separate guidelines: Crohn's disease: management (2012 – last updated May 2019) and irritable bowel syndrome in adults: diagnosis and management (2008 - last updated April 2017). If used earlier in the pathway as part of investigations for chronic diarrhoea, there isn't a NICE guideline that covers this specific part of the care pathway. Additionally, the BSG guideline didn't include a cost effectiveness evaluation of using SeHCAT for investigating chronic diarrhoea so there is still a need to consider the clinical and cost effectiveness of the SeHCAT technology.

3. Implications for other guidance producing programmes

No overlaps were identified.

4. Original objective of guidance

To assess the clinical and cost effectiveness of SeHCAT for the investigation of diarrhoea related to bile acid malabsorption.

5. Current guidance

Adoption recommendations

1.1 SeHCAT (tauroselcholic [75 selenium] acid) is a potentially clinically important test for diagnosing bile acid malabsorption, which may be currently underdiagnosed. There is insufficient evidence to determine whether SeHCAT is a cost-effective option for diagnosing bile acid malabsorption in people with diarrhoea-predominant irritable bowel syndrome (IBS-D) and people with Crohn's disease without ileal resection. Therefore, for people with these conditions, SeHCAT is recommended for use in research to collect evidence about its clinical benefits and risks and the acceptability associated with diagnosing and treating bile acid malabsorption.

Research recommendations

7.1 Research is needed to establish the validity and accuracy of the SeHCAT test and of any potential alternative technologies for measuring bile acid malabsorption in people with chronic diarrhoea diagnosed with IBS-D or Crohn's disease without ileal resection.

7.2 Research is needed to establish the nature of bile acid malabsorption and whether bile acid malabsorption is a primary or secondary condition in people diagnosed with IBS-D or Crohn's disease without ileal resection.

7.3 Research is needed to establish the efficacy and tolerability of bile acid sequestrants among people with IBS-D or Crohn's disease without ileal resection.

6. New evidence

The search strategies from the original diagnostics assessment report were re-run on Medline, Embase, Cochrane Library and the Web of Science. References from January 2012 onwards were considered in the original review (November 2015) and references from January 2015 onwards were considered in the most recent review. Additional searches of clinical trials registries were also carried out and relevant guidance from NICE and other professional bodies was reviewed to determine whether there have been any changes to the diagnostic and care pathways. Companies were asked to submit all new literature references relevant to their technology along with updated costs and details of any changes to the technology itself or the CE marked indication for use for their technology. Specialist committee members for this guidance topic were also consulted and asked to submit any information regarding changes to the technology, the evidence base and clinical practice. The results of the literature search are discussed in the 'Summary of evidence and implications for review' section below. See Appendix 2 for further details of ongoing and unpublished studies.

6.1 Technologies

6.1.1 SeHCAT

Since the publication of DG7 there have not been any changes to SeHCAT. The acquisition cost provided by the manufacturer for each SeHCAT capsule is £195 (excluding VAT). This cost is unchanged since the original assessment.

6.1.2 Alternative technologies

No alternative technologies were included in DG7. Since its publication the following technologies have been proposed for the investigation of bile acid malabsorption:

- 14C glycocholate breath and stool test
- Serum C4
- Faecal bile acid
- Fibroblast growth factor 19
- Urine 2-propanol and acetamide

The 2018 British Society of Gastroenterology (BSG) guidelines for the investigation of chronic diarrhoea in adults discusses the following diagnostic tests for diarrhoea due to BAM: SeHCAT, serum C4, serum FGF19 and faecal bile acid measurement. According to clinical experts, none of these alternatives to SeHCAT scanning are currently in routine clinical use for the assessment and management of BAM.

6.2 Clinical practice

Since the original guidance was published, the BSG updated the guidelines for the investigation of chronic diarrhoea in adults, repositioning SeHCAT earlier in the diagnostic protocol, which may avoid additional tests such as colonoscopy or flexible sigmoidoscopy. The guideline recommends that, in people with functional bowel disease or IBS-D, a positive diagnosis of BAM should be made by either SeHCAT testing or serum bile acid precursor C4 (depending on local availability). It states that a SeHCAT retention of 10–15% at 7 days is usually defined as mild bile acid loss, 5–10% as moderate and 0–5% as severely abnormal. The guideline also notes that these values predict response to therapy with bile acid sequestrants, with very low SeHCAT values most likely to respond to treatment.

A new treatment for IBS-D is now recommended by NICE; Eluxadoline is recommended as an option for treating irritable bowel syndrome with diarrhoea in adults in some scenarios. The NICE committee noted that IBS-D is diagnosed after physicians rule out other conditions, including inflammatory bowel disease, colorectal cancer and bile acid malabsorption.

Literature searches suggest that SeHCAT may now be used for the investigation of bile acid malabsorption in people who have chronic diarrhoea after chemotherapy or radiotherapy treatment for cancer, however it is not certain if SeHCAT is in widespread clinical use for this indication.

6.3 New studies

In the 2015 review, 19 studies were identified which met the inclusion criteria for the original systematic review; 18 primary studies and 1 systematic review. Of the 18 primary studies, all report responses to treatment with bile acid sequestrants following a SeHCAT test and 1 (Kumar et al. 2013) also reports the impact of SeHCAT testing on treatment plans. The systematic review and meta-analysis (Slattery et al. 2015) aimed to establish the prevalence of bile acid malabsorption in adults with diarrhoea predominant irritable bowel syndrome.

In the 2019 review, 13 studies were identified which met the inclusion criteria for the original systematic review; all were primary studies. Of these, 7 reported on response to treatment with bile acid sequestrants following a SeHCAT test, 2

reported on response to dietary changes following a SeHCAT test, 4 reported on SeHCAT usage or care pathways, and 2 reported on cost-effectiveness.

6.3.1 Response to treatment with bile acid sequestrants

The data available on response to treatment with bile acid sequestrants following a SeHCAT scan are summarised in table 1 in appendix 1. Most studies were retrospective cohort studies without any comparator group. In some studies, all included patients had an abnormal SeHCAT scan result and were classified has having BAM. Other studies included all patients that had a SeHCAT scan and reported SeHCAT scan results as well as response to treatment. In this latter group of studies, the proportion of people with a positive SeHCAT scan varied but was typically in the range of 40 to 60%. In terms of the response to treatment with bile acid sequestrants, the proportion of people reporting a good response to treatments showed greater variation between the studies, which could be because of heterogeneity in the study populations, that is they include both people with organic and functional diarrhoea, and differences in the threshold used to determine a positive SeHCAT scan. In general, studies reported a good response to bile acid sequestrants in the range of 40 to 85% of people treated. Intolerance to bile acid sequestrants varied between the studies but was generally around 10%. Some studies reported much higher intolerance of bile acid sequestrants (62%; Arms Williams et al. 2016).

Some studies reported on the correlation between the SeHCAT result (severity of BAM) and the response to bile acid sequestrant treatment. Rubio et al. (2018) found that the response to treatment was 80% in severe BAM, 71% in moderate BAM and 100% in mild BAM (although the latter group only included 3 patients). Puig et al. 2012) reported that in people with a SeHCAT retention rate of less than 5%, 66% had a complete response, 20% had a partial response and 4% had no response. Whereas in people with a SeHCAT retention rate of less than 10%, 85% had a complete response, and 15% had a partial response.

Three studies reported some comparative data and partially address research recommendation 7.3, but the included study populations are small and heterogeneous. Woolson et al. (2014) reported data for people with normal SeHCAT results who were given bile acid sequestrants only 1 person out of 63 reported a partial response compared to 52% of people with an abnormal SeHCAT result who reported a good response. Murray et al. (2017) reported response to bile acid sequestrants in people with normal and abnormal SeHCAT results. Good or partial response was seen in 15% of those with normal SeHCAT result, 65% with mild BAM, 73% with moderate BAM, and 75% with severe BAM. Fernandez-Banares et al. (2015) randomised people with a positive SeHCAT scan to either cholestyramine or

placebo; no statistically significant differences in the percentage of people in clinical remission at week 8 were reported between the groups.

6.3.2 Response to dietary changes

Two studies reported on response to dietary changes following a SeHCAT scan. Jackson et al. (2017) and Watson et al. (2015) evaluated low-fat diets for managing gastrointestinal symptoms due to BAM (SeHCAT retention of less than 20%). Both studies reported that low-fat diets lead to clinically important improvement in gastrointestinal symptoms in people with BAM.

6.3.3 Impact of SeHCAT scan on treatment decisions

Kumar et al. (2013) reported data on the impact of SeHCAT on treatment decisions. In a retrospective audit of 88 people having a SeHCAT scan, treatment decisions were changed in 84% of people with an abnormal result and 33% of people with a normal result. Zanoni et al. (2018) assessed the impact of SeHCAT on treatment decisions in 12 patients suspected of BAM; the SeHCAT result led to a change in treatment for 9 patients.

6.3.4 Use of SeHCAT in the UK

Lim et al. (2019) retrospectively identified 1071 consecutive patients with chronic diarrhoea undergoing SeHCAT testing at 1 UK centre from 2012 to 2016. The following thresholds were used to categorise BAM: <5% was severe, 5% to 9.9% moderate and 10% to 14.9% mild. Due to changes to local referral testing for SeHCAT there was a significant reduction in referrals with terminal ileal Crohn's disease or resection over time.

Murray et al. (2017) retrospectively identified 387 consecutive patients undergoing SeHCAT at 1 UK centre. The authors noted that number of referrals steadily increased from 4 in 2008 to 142 in 2014. Summers et al. (2016) conducted a prospective multicentre survey to investigate the use of SeHCAT for diagnosis of BAM in UK hospitals. In total, 38 centres responded with data on 1036 patients. Authors concluded that that there was a lack of consistent threshold values for an 'abnormal' SeHCAT result. In addition, referral systems, SeHCAT protocols and bile acid sequestrant prescription varied between centres.

Bannaga et al. (2016) reported the results of an anonymous survey of BAM Support UK and the Bile Salt Malabsorption Facebook group members. Responses collected found that 58% of people had been diagnosed with BAM following a SeHCAT test.

6.3.5 Cost effectiveness of SeHCAT

Fernandes et al. (2019) conducted a retrospective study to estimate the economic burden of delayed diagnosis of BAM from the perspective of a UK centre. Authors reported that use of SeHCAT earlier in the pathway reduces healthcare costs. If SeHCAT scanning was ordered at first consultation, symptoms were experienced for 24 months on average and the diagnostic package-of-care cost was £811.40 (range: £625.59 to £1508.20). If SeHCAT scanning was booked later, symptoms were experienced for 30 months on average and the cost was £1568.31 (range: £1200.55 to £1713.18).

Turner et al. (2017) carried out a retrospective longitudinal analysis of data from a prospective study of chronic diarrhoea at 2 UK centres, with the aim of determining whether positive SeHCAT results could lead to lower health care resource use. The authors concluded that a BAM diagnosis made by a SeHCAT test resulted in reduced use of diagnostic investigations (savings would be £46 from CT imaging, £46 from MRI imaging and £102 from ultrasound imaging).

These studies are short term cost studies, looking at the resource use associated with diagnosing BAM. In contrast the economic model for DG7 was a long-term model which incorporated health outcomes and utility for people after a SeHCAT scan.

6.4 NICE's research commissioning activities

A research project was commissioned by NICE to characterise the provision of the SeHCAT service in the UK. The outcome of this study was published as Summers et al. (2016) which is described in section 6.3.4.

7. Summary of new evidence and implications for review

Since the NICE guidance was published in November 2002 there have been no changes to SeHCAT, however, there is a substantial amount of new evidence and SeHCAT is recommended in the British Society of Gastroenterology guidelines on chronic diarrhoea earlier in the diagnostic pathway than previously. Clinical experts have noted that the SeHCAT test is now in routine use in the NHS.

Most new studies reported on the proportion of people diagnosed with bile acid malabsorption (BAM) following a SeHCAT test and on the response to treatment with bile acid sequestrants. However, many of these studies include small numbers of people, are retrospective and heterogeneous in terms of the included populations. Therefore, results from these studies vary quite widely.

Two studies reported on response to dietary changes following an abnormal SeHCAT result, finding that low fat diets led to clinically important improvement in gastrointestinal symptoms in people with BAM. Low fat diets following a diagnosis of BAM were not included in the original economic model for DG7, but authors of these studies conclude that dietary changes should be used more widely in these patients.

Several studies report data on the use of SeHCAT in the UK, for example, number of tests performed, thresholds used, diagnostic yield and impact on treatment decisions. In addition, 2 cost studies identified had a UK perspective and found that use of SeHCAT, especially earlier in the diagnostic pathway, led to lower healthcare costs. However, these models were short-term and did not include health outcomes and utility for people after a SeHCAT scan.

Because of the volume of new evidence, the positive recommendation from the BSG positioning SeHCAT earlier in the diagnostic pathway, the UK specific audit data and the 2 short term cost studies which suggest SeHCAT is cost effective, it is possible that the recommendations could change. Therefore, we propose that a standard update of DG7 is planned into NICE's work programme.

8. Implementation

Expert advice suggests that SeHCAT is currently being used in the NHS. SeHCAT now has a discrete scan code (RN14Z), and the NHS Tariff for administering the diagnostic test is £380.

9. Equality issues

During the assessment it was noted that people with chronic diarrhoea are likely to be classified as having a disability and therefore be protected under the Equality Act 2010. No potential equality issues relating to SeHCAT testing were raised in the original guidance.

Paper sign off by: Rebecca Albrow, Associate Director, 17 January 2020

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Appendix 1

Table 1 Studies reporting SeHCAT use and response to bile acid sequestrants

Study	Design	Population	SeHCAT results	Response to treatment
Arms-Williams et al. (2016)	Single-centre retrospective study UK	269 patients who had a SeHCAT scan	3 groups were identified as having increased risk of BAM: quiescent Crohn's disease (ileal and colonic) cholecystectomy, and RH/IR.	Colestyramine was trialled in 100 people, 84% had a good response and 38% tolerated therapy. Colesevelam was trialled in 64 BAM cases, 84% had a good response and 48% tolerated therapy.
Aujla et al. (2014)	Retrospective cohort study	118 patients with chronic diarrhoea	51 people classed as having BAM 27/118 had severe BAM (<5% SeHCAT retention); 15/118 had moderate BAM (<10% SeHCAT retention); 9/118 had mild BAM (<15% SeHCAT retention	Data available for 68% (n=35) of the 51 people with BAM: 7 had colesevelam 28 had cholestyramine – 43% had a good response, 7% had a partial response and 25% had a poor response.
Bain et al. (2013)	Retrospective cohort study	122 patients referred for a SeHCAT scan	50% of people had a SeHCAT retention of <15%; 30 had <5% SeHCAT retention, 19 had 5.1%-10% SeHCAT retention and 12 had 10.1%-15% SeHCAT retention	84.9% of people with abnormal SeHCAT retention were treated with BAS and reported a good response.
Bajor et al. (2014)	Cohort study	141 patients with IBS	57 people had low SeHCAT retention <20%	27 people with low SeHCAT retention were treated with Colestipol and 55% reported successful treatment.
Bannaga et al. (2017)	Retrospective survey study UK	100 survey respondents from the bile salt	58% of respondents were diagnosed following a SeHCAT scan. 33% were diagnosed following a successful trial of bile binding medication or by	Not reported

Study	Design	Population	SeHCAT results	Response to treatment
		malabsorption Facebook group	symptoms alone. 29% of the respondents who had a SeHCAT scan had severe BAM with a retention score of 5% or less.	
Damsgaard et al. (2018)	Retrospective survey study Denmark	594 patients with BAM verified by SeHCAT scans	Based on retention fractions by SeHCAT, 67% had severe, 18% had moderate and 15% had mild BAM.	Following treatment, diarrhoea improved in 50% of patients, was unaltered in 31%, and was worse in 19%. Lower retention fractions of SeHCAT were associated with loose or liquid stools (OR 1.08 per 1% decrease in SeHCAT retention rates, 95% CI 1.02-1.12, p=0.007).
Dhaliwal et al. (2013)	Retrospective audit	286 patients with structural and functional IBS-D	286 people had a SeHCAT scan.	228 people received BAS and around 70% reported a good response to treatment.
Diana et al. (2013)	Retrospective audit	130 patients with structural and functional chronic diarrhoea	65 people had SeHCAT retention of <15% and were classed as having BAM	84% of people responded to BAS treatment. One third of people discontinued treatment, most commonly because of side effects.
Fernandez-Banares et al. (2015)	Double-blind, multicentre RCT	26 people with chronic watery diarrhoea	All people have a SeHCAT 7-day retention of ≤20%	No statistically significant difference in clinical remission at week 8 between the cholestyramine and placebo groups.
Holmes et al. (2012)	Retrospective audit	55 people attending for SeHCAT scans	44 sets of notes could be analysed: 62% of scans were abnormal with SeHCAT retention of <15%, 32% had mild BAM, 24% had moderate BAM and 44% had severe BAM.	46% of people with BAM had a trial of treatment; 88% reported good response.

Study	Design	Population	SeHCAT results	Response to treatment
Kumar et al. (2013)	Retrospective audit	88 people referred for SeHCAT testing	56% of people were classed as having BAM (SeHCAT retention <15%); 59% had severe BAM, 18% had moderate BAM and 22% had mild BAM.	All people with abnormal SeHCAT scans and a subset (n=13) of people with normal SeHCAT scans received BAS. 55% of people with BAM reported a treatment response and 20% discontinued treatment because of side effects.
Kurien et al. (2014)	Retrospective cohort study	515 people referred for a SeHCAT scan	41% of people had BAM (SeHCAT retention <10%).	51% of people with BAM had BAS. Mean stool frequency decreased from 7.3 stools per day to 3.9 ($p<0.0001$). People who did not have treatment had no change in daily stool frequency.
Lim et al. (2019)	Retrospective study UK	1071 patients with chronic diarrhoea	42.7% patients had BAM and there was no downward trend in yield of SeHCAT over the 5-year study period. 51.6% had type II BAM, 36.1% type III, and 12.3% type I. BAM was mild in 31.7%, moderate in 34.4%, and severe in 33.9%.	Not reported
Lin et al. (2016)	Retrospective audit	515 people with chronic diarrhoea referred for a SeHCAT scan	40% of people had an abnormal SeHCAT scan (retention of <10%)	All people with an abnormal SeHCAT scan were given BAS. 107 people were included in the final analysis. Median stool frequency decreased from 7 stools per day to 3 ($p=0.0008$). Those who did not have treatment had no change in daily stool frequency.

Study	Design	Population	SeHCAT results	Response to treatment
Maisterra et al. (2012)	Single centre observational study	84 people with IBS-D or functional diarrhoea	BAM diagnosed following a SeHCAT retention of <10%	82% of people receiving BAS had a complete response to cholestyramine, 15% had a partial response and 3% had a no response.
Mottacki et al. (2015)	Retrospective cohort	2112 people referred for a SeHCAT scan with chronic diarrhoea	BAM diagnosed following a SeHCAT retention of either <10% or <15%.	People were excluded if no information from on the effect of treatment was available. 74% of people with BAM experienced symptomatic improvement on cholestyramine.
Murry et al. (2017)	Retrospective cohort UK	387 patients undergoing testing for BAM	46.2% of people tested had BAM. 99 patients had severe BAM (<5% SeHCAT retention), 47 moderate BAM (5% to <10% retention), and 33 mild BAM (10% to <15% retention). Predictors of a positive SeHCAT were right hemicolectomy (OR 4.88), cholecystectomy (OR 2.44), and Crohn's (OR 1.86).	A positive SeHCAT predicted a good or partial response to BAS of 66.7% (mild), 78.6% (moderate), or 75.9% (severe BAM).
Notta et al. (2014)	Prospective cohort	78 people with chronic functional diarrhoea	A SeHCAT retention rate of <10% was considered abnormal. The SeHCAT scan was normal in 57% of people and abnormal in 43%. After 3 months SeHCAT retention improved in 14/25 people with complete response and in 3/5 people with partial response to BAS.	People with a positive SeHCAT scan had cholestyramine for 3 months; 74% reported a complete response, 15% a partial response and 2% no response. 9% discontinued treatment.

Study	Design	Population	SeHCAT results	Response to treatment
Orekoya et al. (2015)	Retrospective audit	264 people with chronic diarrhoea referred for a SeHCAT scan	139 people had a SeHCAT retention rate of <15% and were diagnosed with BAM.	123 people with BAM were given cholestyramine as a first line treatment, 56% of whom responded. People who did not report improvement were given second line colesevelam, which was better tolerated than cholestyramine.
Puig et al. (2012)	Cohort study	75 people with chronic diarrhoea	BAM was diagnosed where SeHCAT retention rate was <10%. 45% of patients had BAM – 28% had a retention rate of <5% and 17% had a retention rate of <10%.	57% of people with a SeHCAT retention rate of <5% needed high dose treatment compared with 38% of people with retention rates of <10%. 66% of people with a SeHCAT retention rate of <5% had complete response, 20% partial response and 4% no response. 85% of people with a SeHCAT retention rate of <10% had a complete response, and 15% a partial response.
Rojas et al. (2013)	Retrospective audit	297 people with chronic diarrhoea	A SeHCAT retention rate of <10% was considered abnormal. 44% of people had a SeHCAT retention rate of <10%.	113 people were treated with cholestyramine and 83% reported an improvement in symptoms.
Rubio et al. (2018)	Cohort study	259 patients with chronic diarrhoea	The SeHCAT test was abnormal in 63% of people tested. 82/164 had severe BAM, 42/164 moderate BAM and 41/164 mild BAM	The response to treatment was 79.54% in severe BAM, 71.42% in moderate BAM and 100% in mild BAM (although the mild group only had 3 patients).
Saleem et al. (2013)	Retrospective audit	87 people with chronic diarrhoea	BAM was diagnosed where the SeHCAT retention rate was <15%. 50.1% of people had BAM; 63.6% had severe BAM (SeHCAT retention <5%), 22.7% had moderate BAM (SeHCAT retention <10%) and	78% of people with BAM were treated with BAS (colesevalam or cholestyramine). 70% of people reported good or partial response. 4 people discontinued cholestyramine because of side effects.

Study	Design	Population	SeHCAT results	Response to treatment
			13.6% had mild BAM (SeHCAT retention <15%).	
Sanchez et al. (2016)	Prospective study	29 patients with suspected BAM	In 10 patients, the SeHCAT test was negative and in 19 it was positive.	17 patients with a positive test began treatment with colestyramine. At follow-up, 6 were asymptomatic and 11 showed a decrease in the number of bowel movements and improved abdominal pain.
Sarkodieh et al. (2013)	Retrospective audit	82 people having a SeHCAT scan.	A SeHCAT retention rate of <15% was considered abnormal. 62% of people had an abnormal SeHCAT result – 27% had mild BAM, 12% had moderate BAM and 23% had severe BAM.	49% of people with an abnormal SeHCAT result had BAS; 42% reported improvement in symptoms and 8% reported side effects.
Summers et al. (2016)	Prospective survey UK	1036 patients referred for a SeHCAT test with a clinical suspicion of BAM because of chronic diarrhoea	50% of patients had a SeHCAT retention score of <15%, and 24% had a score of <5%. The mean SeHCAT retention score for all patients was 19% (95% CI 17.8% to 20.3%). But this differed with suspected BAM type. Type 1: 9% (95% CI 6.3% to 11.4%), type 2: 21% (95% CI 19.2% to 23.0%), type 3: 22% (95% CI 19.6% to 24.2%).	BAS treatment was prescribed to only 73% of patients with abnormal results. Patient-reported adherence to BAS treatment was 76%. 21 patients reported side effects from the BAS treatment. A reduction in the severity of diarrhoea symptoms was reported by 71%.
Woolson et al. (2014)	Retrospective audit	121 people having a SeHCAT scan	Of the whole population tested: 78% had a previous colonoscopy; 33% had a previous oesophago-gastro-duodenoscopy; 21% had a previous CT scan	83% of people with a positive SeHCAT scan were given BAS: 52% reported a good response 23% reported no response

Study	Design	Population	SeHCAT results	Response to treatment
			47% of people had a positive SeHCAT scan (cut-off not reported) Crohn's disease and right hemicolectomies were significantly associated with BAM.	10% could not tolerate the treatment 63 people with a negative SeHCAT scan were given BAS: 1 person reported a partial response
Zanoni et al. (2018)	Retrospective study Italy	12 patients with suspected BAM	The mean SeHCAT retention score was 18% (median 10%; range 3-48).	8 patients had BAS therapy, with significant clinical benefit seen in 6 patients.
BAM - bile acid malabsorption; BAS - bile acid sequestrants; CI – confidence intervals; OR – odds ratios; RCT - randomised controlled trial				

Appendix 2 – explanation of options

If the published Diagnostics Guidance needs updating NICE must select one of the options in the table below:

Options	Consequence	Selected – 'Yes/No'
Standard update of the guidance	A standard update of the Diagnostics Guidance will be planned into NICE's work programme.	Yes
Accelerated update of the guidance	An accelerated update of the Diagnostics Guidance will be planned into NICE's work programme. Accelerated updates are only undertaken in circumstances where the new evidence is likely to result in minimal changes to the decision problem, and the subsequent assessment will require less time to complete than a standard update or assessment.	No
Update of the guidance within another piece of NICE guidance	The guidance is updated according to the processes and timetable of that programme.	No

If the published Diagnostics Guidance does not need updating NICE must select one of the options in the table below:

Options	Consequences	Selected – 'Yes/No'
Transfer the guidance to the 'static guidance list'	The guidance remains valid and is designated as static guidance. Literature searches are carried out every 5 years to check whether any of the Diagnostics Guidance on the static list should be flagged for review.	No
Produce a technical supplement	A technical supplement describing newer versions of the technologies is planned into NICE's work programme.	No
Defer the decision to review the guidance to [specify date or trial].	NICE will reconsider whether a review is necessary at the specified date.	No
Withdraw the guidance	The Diagnostics Guidance is no longer valid and is withdrawn.	No

Appendix 3 – supporting information

Relevant Institute work

Published

Crohn's disease: management (2012 – last updated May 2019) CG152

Irritable bowel syndrome in adults: diagnosis and management. (2008 - last updated April 2017) CG61

Faecal calprotectin diagnostic tests for inflammatory diseases of the bowel (2013) diagnostics guidance 11

Eluxadoline for treating irritable bowel syndrome with diarrhoea (2017) NICE technology appraisal 471

Bile acid malabsorption: colesevelam (2013) NICE evidence summary 22

In progress

None

Registered and unpublished trials

Trial name and registration number	Details
Validation of Stimulated FGF19 for Diagnosing Bile Acid Diarrhoea https://clinicaltrials.gov/ct2/show/NCT03059537	Objective: To validate a possible diagnostic test for bile acid diarrhoea prospectively compared to SeHCAT scintigraphy Denmark Completed in December 2017, results unpublished
The Role of Faecal Bile Acids in the Management of Bile Acid Diarrhoea https://clinicaltrials.gov/ct2/show/NCT02848040	Objective: To evaluate a cheaper and simpler laboratory test, which quantifies faecal bile acids (IDK bile acids test). UK Estimated primary completion date: June 2020
Effect of the Sequestrant Colesevelam in Bile Acid Diarrhoea (SINBAD) https://clinicaltrials.gov/ct2/show/NCT03876717	Objective: To validate (i.e. compare) both the C4-test and the SeHCAT test with the colesevelam treatment response as the reference. Denmark Estimated primary completion date: September 2020

Trial name and registration number	Details
The FOCCUS study: "Focusing on Cancers Chemotherapys' Untreated Symptoms" https://clinicaltrials.gov/ct2/show/NCT02121626	Objective: To quantify the incidence, severity, frequency, impact on quality of life, and, where possible, the cause of the full range of chemotherapy-induced GI symptoms. UK Completion: Dec 2017, no results published
Assessment of BAM as a cause of chronic diarrhoea	Objective: To evaluate patients with functional chronic diarrhoea, and to estimate the proportion of cases of bile acid malabsorption in these patients. Spain Completion: October 2018, no results published
Use of SeHCAT to investigate the aetiology of chronic diarrhoea in patients with Crohn's disease after resection surgery	Objective: To establish the usefulness of SeHCAT to diagnose malabsorption of bile acids in Crohn's disease patients after resection surgery, and to determine the usefulness of the test in guiding therapy. Spain Completion: June 2018, no results published
The effectiveness of gastrointestinal intervention during pelvic chemoradiotherapy: A randomised controlled pilot study	Objective: To determine if a gastrointestinal care bundle, including nutritional intervention and detecting and treating lactose intolerance, small bowel overgrowth and BAM, improves GI symptoms in the short-term. UK Completion: January 2016, no results published
Causes of chronic diarrhoea after treatment for cancer in cecum and the ascending colon	Objective: To investigate to what extent chronic post-surgery diarrhoea among right-sided hemicolectomy patients, curatively operated for cancer in cecum and the ascending colon, is caused by bile acid malabsorption. Denmark Expected completion: December 2020

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