

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

Diagnostics guidance

Published: 28 November 2012

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1 Recommendations

- 1.1 SeHCAT (tauroselcholic [⁷⁵selenium] 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.

2 The technology

- 2.1 SeHCAT is a radiopharmaceutical that is licensed for use in measuring bile acid pool loss and investigating bile acid malabsorption. It can also be used in the assessment of ileal function, to investigate inflammatory bowel disease (IBD) and chronic diarrhoea, and to study enterohepatic circulation.

3 Clinical need and practice

The problem addressed

- 3.1 The aim of this evaluation is to determine the clinical and cost effectiveness of SeHCAT in diagnosing bile acid malabsorption in people with chronic diarrhoea who have been diagnosed with IBS-D and people with Crohn's disease without ileal resection.

The condition

Bile acid malabsorption

- 3.2 The target condition for this assessment is chronic diarrhoea due to bile acid malabsorption. Diarrhoea is defined as the abnormal passage of loose or liquid stools more than 3 times daily or a volume of stool greater than 200 g/day. Diarrhoea is considered to be chronic if it persists for more than 4 weeks.
- 3.3 Chronic diarrhoea is one of the most common reasons for referral to a gastrointestinal clinic and can account for as many as 1 in 20 referrals. Estimates of the prevalence of chronic diarrhoea in western populations are between 4% and 5%. The cause of chronic diarrhoea in adults is difficult to ascertain, and people may have several investigations without a definitive cause being identified.
- 3.4 Bile acid malabsorption is one of several causes of chronic diarrhoea. Bile acids are synthesised in the liver from cholesterol before being transferred in conjugated form to the bile ducts, where they accumulate and are stored in the gall bladder. After a meal, the gall bladder contracts and bile acids flow into the intestinal lumen. Most of the bile acids are then reabsorbed by the distal ileum into the portal circulation and returned to the liver. The bile acids are later secreted into the bile again as part of a recycling process called enterohepatic circulation. Although a small proportion of bile acids (3%) are excreted in the faeces, about 97% of bile acids are recycled.
- 3.5 In people with bile acid malabsorption, excess bile in the colon stimulates electrolyte and water secretion, which results in chronic watery diarrhoea. Bile

acid malabsorption causes diarrhoea by one or more of the following mechanisms:

- inducing secretion of sodium and water
- increasing colonic motility
- stimulating defecation
- inducing mucus secretion
- damaging the mucosa, thereby increasing mucosal permeability.

3.6 Bile acid malabsorption has been divided into 3 types depending on aetiology:

- type 1: following ileal resection, disease or bypass of the terminal ileum
- type 2: primary idiopathic malabsorption
- type 3: associated with cholecystectomy, peptic ulcer surgery, chronic pancreatitis, coeliac disease or diabetes mellitus.

3.7 Type 2 bile acid malabsorption has no known cause. In people with type 2 bile acid malabsorption, there is a history of diarrhoea that can be either continuous or intermittent.

3.8 Although not life threatening, bile acid malabsorption can have a considerable impact on lifestyle and quality of life because the associated increased frequency of bowel motions often limits the person's ability to travel or leave the house.

Populations included in the evaluation

3.9 This evaluation included 2 populations associated with bile acid malabsorption:

- people with chronic diarrhoea considered likely to have IBS-D
- people with chronic diarrhoea who have been diagnosed with Crohn's disease and have not had an ileal resection.

- 3.10 Several other populations with chronic diarrhoea were considered but excluded from this evaluation, for example, people with an ileal resection, cholecystectomy or radiation-induced bowel damage.

Irritable bowel syndrome

- 3.11 IBS is one of the most common functional gastrointestinal disorders. It is a chronic, relapsing and often life-long disorder, characterised by abdominal pain or discomfort associated with defecation, disordered defecation (constipation or diarrhoea, or both), and the sensation of abdominal distension. It can include associated non-colonic symptoms such as lack of sleep, backache, urinary frequency, anxiety and lethargy. Consequences of IBS include time taken off work, avoidance of stressful or social situations, and substantial reduction in quality of life.
- 3.12 IBS most commonly presents for the first time between the ages of 20 and 30 years and is twice as common in women as in men. People with IBS are the largest group of patients seen in general gastroenterology clinics (1 in 20 referrals). The prevalence of the condition in the general population is estimated to be between 10% and 20%. Recent trends indicate that the prevalence of IBS in older people is considerable, so that the condition is a possible diagnosis whenever an older person presents with unexplained abdominal symptoms. The true prevalence of IBS in the whole population may be higher than estimated because it is thought that many people with IBS symptoms do not seek medical advice. NHS Direct online data suggest that 75% of people with IBS symptoms using this service rely on self-care. Extrapolating these data suggests that around 1.6–3.9 million people in England and Wales seek medical help for IBS.
- 3.13 There are 3 types of IBS: IBS with constipation (IBS-C), IBS with diarrhoea (IBS-D), and IBS with alternating constipation and diarrhoea (IBS-A). People with chronic diarrhoea are often given a diagnosis of IBS-D if a definitive cause for the diarrhoea has not been identified. There is evidence suggesting that up to a third of people with a diagnosis of IBS-D have bile acid malabsorption. On this basis, around half a million people who are currently being treated for IBS-D in the NHS may actually have bile acid malabsorption for which potential diagnosis and treatment are available.

Crohn's disease

- 3.14 Crohn's disease is a common form of IBD. It is a chronic severe condition characterised by inflammation, ulcers and bleeding that can affect any part of the gastrointestinal tract but mostly commonly affects the small intestine, the colon or both. Crohn's disease can directly cause chronic diarrhoea, but people with the condition can also develop bile acid malabsorption. Crohn's disease is estimated to affect about 60,000 people in the UK, around 100 per 100,000 population.
- 3.15 Crohn's disease is sometimes treated by ileal resection. The prevalence of bile acid malabsorption in people with Crohn's disease in clinical remission who have had ileal resection is high (97%), so this group was excluded from this assessment because testing before treatment was considered not to be necessary. In people with Crohn's disease in clinical remission who have not had ileal resection, the prevalence is 54%.

The diagnostic and care pathways

Diagnostic pathway

- 3.16 In current practice, the main pathway that includes SeHCAT is set out in the 2003 British Society of Gastroenterology (BSG) guidelines for the investigation of chronic diarrhoea. These guidelines are currently being updated.
- 3.17 There is uncertainty about whether using SeHCAT reduces the use of other diagnostic tests and clinician visits. Some clinical specialists suggest that placing SeHCAT earlier in the pathway would not stop additional tests such as colonoscopy or flexible sigmoidoscopy being done. Other clinical specialists thought that a positive SeHCAT test earlier in the pathway would result in cost savings because people with chronic diarrhoea would then not have additional tests, which is currently the case.

Treatment

- 3.18 After a definitive diagnosis of bile acid malabsorption, people can be treated with bile acid sequestrants that bind with bile acids in the small bowel and prevent the secretory action of bile acids on the colon. There are currently 3 bile acid sequestrants available: colestyramine, colestipol and colesevelam.

- 3.19 Colestyramine and colestipol are anion exchange resins that have a high affinity for bile acids in the gastrointestinal tract, and form complexes with them. An important disadvantage of colestyramine and colestipol is an unpleasant taste, which can lead to poor tolerance of and adherence to treatment. Other side effects include constipation, nausea, borborygmi, flatulence, bloating and abdominal pain.
- 3.20 Colesevelam is a newer bile acid sequestrant that forms a polymeric gel in the gastrointestinal tract. It binds to bile acids with higher affinity than colestyramine or colestipol. Colesevelam is available in tablet form, whereas colestyramine is only available in powder form, which some people find unpleasant. Colesevelam is much more expensive than colestyramine and colestipol, and it is not licensed to treat bile acid malabsorption.
- 3.21 The response to bile acid sequestrants varies among people who have diarrhoea due to bile acid malabsorption. For people with Crohn's disease and ileal resection, the response to bile acid sequestrants has been reported to be 60%. In people with Crohn's disease without ileal resection, the estimate of response to bile acid sequestrants was 40% and in people with a diagnosis of IBS-D the estimate was 70% (Smith et al. 2000). These estimates are derived from case-series data. The effectiveness of SeHCAT and the treatment of bile acid malabsorption have not been widely assessed in randomised trials.

4 The diagnostic test

The intervention

SeHCAT

- 4.1 SeHCAT (GE Healthcare) is a radiopharmaceutical that is licensed for measuring bile acid pool loss and investigating bile acid malabsorption. It can also be used to assess ileal function, to investigate IBD and chronic diarrhoea, and to study the enterohepatic circulation.
- 4.2 SeHCAT consists of a capsule containing a synthetic analogue of the natural conjugated bile acid tauroselcholic acid and ⁷⁵Selenium (a gamma-emitter). The radionuclide tracer atom allows SeHCAT to be easily detected in a whole body scan using a standard gamma camera. The technology is used to test the function of the bowel by measuring how well the compound is retained or lost from the body into the faeces. SeHCAT is the only test currently used to diagnose bile acid malabsorption.
- 4.3 The SeHCAT test involves 2 scans, 1 week apart, carried out as outpatient appointments. During the first appointment, the SeHCAT capsule is administered orally and, once localised in the body (which takes 1–3 hours), the radionuclide tracer atom is detected in a whole-body baseline scan using a standard gamma camera. This gives an initial count that is used to provide a zero-time or 100% value. During the second appointment, the patient is scanned to produce a second count, and the retained activity is expressed as a percentage of the original value. In general practice, retention values of less than 15% have been considered abnormal and indicative of bile acid malabsorption. However, there is no definitive cut-off between normal and abnormal. In this assessment, 3 cut-off points were evaluated, 5%, 10% and 15%.
- 4.4 Although the models used in the assessment assumed no treatment differences based on the results of tests using SeHCAT, clinicians have used SeHCAT results to grade the severity of the bile acid malabsorption as follows:
- retention values of 10–15% (mild bile acid malabsorption)
 - retention values of 5–10% (moderate bile acid malabsorption)

- retention values of 0–5% (severe bile acid malabsorption).

The comparator

- 4.5 There is no commonly used direct comparator for this diagnostic test. Current diagnostic options include analysis of a person's history of symptoms, investigations to exclude 'red flag' symptoms, and a variety of other diagnostic tests such as blood tests and lactose tolerance tests. The main comparator used in the assessment was the protocol of tests and clinical observations contained in the BSG guidelines for the investigation of chronic diarrhoea.

5 Outcomes

The Diagnostics Advisory Committee ([appendix A](#)) considered evidence from a number of sources ([appendix B](#)), but primarily used the assessment performed by the External Assessment Group.

How outcomes were assessed

- 5.1 A de novo model was constructed by the External Assessment Group to assess the clinical and cost effectiveness of SeHCAT in people presenting with symptoms suggesting IBS-D and people with Crohn's disease without ileal resection. A systematic literature review was performed to obtain parameters for the model. For parameters for which no evidence was identified, a survey was carried out to elicit expert opinion.

Modelling approach

- 5.2 The model consisted of 2 parts: a decision model reflecting the diagnostic and initial treatment phase, and a Markov model to estimate long-term costs and effects. The model was used for both the IBS-D and Crohn's populations but with different parameter values.
- 5.3 In the population with IBS-D, the decision-tree component of the model used response to treatment, dependent on test outcome, to compare 2 strategies that did not use SeHCAT with 3 strategies that did use SeHCAT. The 3 strategies using SeHCAT had percentage reabsorption at cut-off points of 5%, 10% and 15%, with a normal (negative) test result being higher than the cut-off points. The 2 strategies that excluded the use of SeHCAT were 'no-SeHCAT' (meaning everybody was treated for IBS-D) and 'trial of treatment' with bile acid sequestrants.
- 5.4 In the population with Crohn's disease, the outline of the decision-tree component of the model was essentially the same as that for the IBS-D model with 2 exceptions. First, if SeHCAT was not used, if the test was negative, or if there was no response to 'trial of treatment', people were treated for Crohn's disease (that is, with therapy to control diarrhoea not caused by bile acid malabsorption). Second, the truncated model (for the population with Crohn's disease) did not include the SeHCAT strategy with a cut-off at 5% because no

data on the probability of a positive test result were available for this cut-off point.

- 5.5 The Markov component of the model allowed the costs and effects of the various strategies to be assessed throughout the person's lifespan. People whose condition responded to treatment entered the Markov model in the 'no diarrhoea' state and people whose condition did not respond entered in the 'diarrhoea' state. Because the model is a lifetime horizon, the third state was death.
- 5.6 People could move between the 'no diarrhoea' state and the 'diarrhoea' state from 1 cycle to another, stay the same or die. The cycle length used was 6 months. The general Markov component of the model was given parameters according to treatment, which resulted in multiple models based on the same structure. This meant that, in the population with IBS-D, people who received bile acid sequestrants entered the bile acid sequestrant Markov model, and those who received IBS-D treatment entered the IBS-D Markov model. Likewise, in the population with Crohn's disease, people who received bile acid sequestrants entered the bile acid sequestrant Markov model, and people who received treatment for Crohn's disease with chronic diarrhoea entered the Crohn's Markov model.
- 5.7 Each Markov model included 6 transition probabilities. These were from 'diarrhoea' to 'no diarrhoea' and from 'no diarrhoea' to 'diarrhoea', from 'diarrhoea' to 'death' and from 'no diarrhoea' to 'death', and to 'stay in diarrhoea' or to 'stay in no diarrhoea'.

Systematic review for effect parameter values

- 5.8 Searches or systematic reviews were carried out to obtain evidence to estimate the parameter values for inclusion in the model. Twenty-four publications of 21 studies met the inclusion criteria and were included in the review. Of these, 20 studies provided data either on the accuracy of SeHCAT in predicting treatment response (in which treatment response was the reference standard), or on treatment effect in groups with positive or negative SeHCAT tests. Out of the 20 SeHCAT studies, 19 studies included people with chronic diarrhoea of unknown cause and 2 studies included people with Crohn's disease and chronic

diarrhoea. The remaining study was a randomised placebo-controlled trial of the bile acid sequestrant colesevelam for IBS-D.

- 5.9 Three studies were identified that contained usable data on the accuracy of SeHCAT in assessing response to treatment in people with chronic diarrhoea. Merrick et al. (1985) estimated the sensitivity of SeHCAT in predicting a positive response to treatment to be 0.67 (95% confidence interval [CI] 0.22 to 0.96) and the specificity to be 0.97 (95% CI 0.85 to 0.10) using a cut-off of 8% for the test. Using a cut-off of 15%, the sensitivity was 1.00 (95% CI 0.54 to 1.00) and the specificity 0.91 (95% CI 0.76 to 0.98). Sciaretta et al. (1986) estimated the sensitivity of SeHCAT in predicting a positive response to be 0.86 (95% CI 0.42 to 0.10) and the specificity to be 1.00 (95% CI 0.541 to 1.000) using a cut-off of 5% for the test. However, only 13 people were included in this analysis. Sciaretta et al. (1987) estimated the sensitivity of SeHCAT in predicting a positive response to be 0.95 (95% CI 0.75 to 0.10) and the specificity to be 0.96 (95% CI 0.80 to 0.10) using a cut-off of 8% for the test.
- 5.10 Two studies were identified that contained data on the accuracy of SeHCAT for assessing response to treatment in people with Crohn's disease. Neither study presented data for people with a negative SeHCAT test. Moreover, neither study explained why certain people received treatment and others did not.
- 5.11 For the effectiveness of bile acid sequestrants in treating chronic diarrhoea, 1 controlled clinical trial compared colesevelam with placebo for people with IBS-D. No controlled trials that assessed the effectiveness of bile acid sequestrants in terms of bowel function in people with chronic diarrhoea of unknown cause were identified. In addition to the randomised controlled trial, data on the effectiveness of bile acid sequestrants for treating bile acid malabsorption were also obtained from the 19 studies described above. All 19 studies provided data on the effectiveness of bile acid sequestrants given after a positive SeHCAT test. Only 3 of the studies provided data on the effectiveness of bile acid sequestrants given after a negative SeHCAT test.
- 5.12 Two studies looked at the effectiveness of bile acid sequestrants in treating diarrhoea in people with Crohn's disease. Neither study presented data for people with a negative SeHCAT test. In addition, it was not clear why certain people were treated and others were not. From both studies, those with a

positive SeHCAT test had a response rate of 95% at a cut-off of 5% and 87% at a cut-off of 10%.

Additional model parameters

- 5.13 Most of the model parameters used represent the probability of events occurring in the care pathway. The model was populated with estimates of these probabilities, which were obtained from the systematic review when data were available, supplemented with expert opinion when objective data could not be found. Based on the data retrieved, a random effects meta-analysis was performed to find a pooled estimate for each of the 3 cut-off values (5%, 10% and 15%).
- 5.14 The probabilities of a positive SeHCAT test in the population with IBS-D for cut-off points of 5%, 10% and 15% were 0.22, 0.36 and 0.38 respectively.
- 5.15 For the population with Crohn's disease, there were no studies identified with a SeHCAT 5% cut-off point. The External Assessment Group only estimated the probability of a positive SeHCAT test in this population for cut-off points of 10% and 15%, which were 0.54 and 0.63 respectively.
- 5.16 In the population with IBS-D, the probability of a positive response to bile acid sequestrants was 0.88 for SeHCAT 5%, 0.76 for SeHCAT 10% and 0.73 for SeHCAT 15%.
- 5.17 For the population with Crohn's disease, no data were available on response to bile acid sequestrants in people with a positive SeHCAT test. The External Assessment Group therefore assumed that the response rate for this population would be the same as that in people with IBS-D (0.76 for SeHCAT 10% and 0.73 for SeHCAT 15%).
- 5.18 Rates of response to treatment in people with IBS-D who had not had a SeHCAT test were not found in the literature. A questionnaire was sent to clinical specialists asking what percentage of people would eventually be successfully treated with the usual IBS-D treatment options, and what would be a plausible range for this percentage. Based on the responses received, a pooled mean of a 52% response to IBS-D treatment was calculated.

- 5.19 In the strategies in which a SeHCAT test was performed, only those with a negative SeHCAT test received IBS-D treatment. This implies that most people who have bile acid malabsorption are no longer part of the group receiving IBS-D treatment. The External Assessment Group assumed that the response rate to IBS-D treatment in the population with a negative SeHCAT test may therefore be higher than in the population who did not have SeHCAT test. In the base-case analysis, an assumption was made that, at cut-off points of 15%, 10% and 5%, the response rates to IBS-D treatment in the SeHCAT-negative population are higher by 10%, 8% and 5% respectively. In the 'trial-of-treatment' strategy, it was assumed that the response rate to IBS-D treatment is the same as in the strategy with a SeHCAT cut-off of 15%.
- 5.20 For people with Crohn's disease without ileal resection, there were no data in the literature about how often the condition responds to treatment for diarrhoea. The External Assessment Group asked clinical specialists what percentage of people would eventually be treated. Based on responses received, a pooled mean of 62% response to treatment was calculated.
- 5.21 The External Assessment Group assumed that response to treatment for diarrhoea may be higher in people with Crohn's disease who had a negative SeHCAT test than in the population who did not have a SeHCAT test. No data were available to test this assumption. The External Assessment Group made the same assumption as it did in the population with IBS-D, which is that the response rate is 10% higher than in the population who did not have a SeHCAT test for a cut-off of 15% and 8% higher for a cut-off of 10%.
- 5.22 The External Assessment Group assumed that there is no excess mortality associated with IBS-D and bile acid malabsorption, and concluded that the overall mortality in the UK population is relevant. Data on mortality were derived from England and Wales Interim Life Tables 1980–82 to 2008–10. In addition, the average age and gender distribution in the model cohort was 47 years and the ratio of men to women was 0.71.
- 5.23 For the population with Crohn's disease, no reports were found that suggested the chronic diarrhoea caused by the condition leads to excess mortality. However, people with Crohn's disease have a shorter life expectancy compared with the general population. This shorter life expectancy was included in the

modelling and no additional reduction was assumed for those people who also have chronic diarrhoea.

5.24 No data were available about the transition probabilities from 'diarrhoea' to 'no diarrhoea' and vice versa. A range of plausible scenarios were used to show the impact of the assumptions on the model estimates of health and cost outcomes.

Quality of life

5.25 For the population with IBS-D, the following utilities were estimated by the External Assessment Group based on multiple studies:

- for the health state 'diarrhoea', utility was 0.71
- for the health state 'no diarrhoea' (IBS-D), utility was 0.78
- for the health state 'no diarrhoea' (bile acid malabsorption), utility was 0.76.

5.26 For the population with Crohn's disease, the following utilities were similarly estimated:

- for the health state 'diarrhoea', utility was 0.70
- for the health state 'no diarrhoea' (IBS-D), utility was 0.76
- for the health state 'no diarrhoea' (bile acid malabsorption), utility was 0.74.

Economic analysis

Costs

5.27 Table 1 shows the cost estimates that were used in the model.

Table 1: Cost estimates used in the model

Description	Cost (£)
Cost per day of IBS-D ^a medication	0.17
Diet costs per 6 months associated with IBS-D	46.05
Psychological costs per 6 months associated with IBS-D	129.81

Cost per day of BAS ^b medication (IBS-D model)	0.63
Cost of SeHCAT capsule	195.00
Cost for administering SeHCAT test	186.00
Maintenance and service costs of SeHCAT test	0.00
Cost per day associated with health state 'diarrhoea'	0.06
IBS-D medication cost per day associated with health state 'no diarrhoea'	0.17
BAS cost per day associated with health state 'no diarrhoea' (IBS-D model)	0.63
Cost per day of Crohn's medication	1.78
Cost per day of BAS medication (Crohn's model)	0.63
Crohn's medication cost per day associated with health state 'no diarrhoea'	1.08
BAS cost per day associated with health state 'no diarrhoea' (Crohn's model)	0.63
^a IBS-D, diarrhoea-predominant irritable bowel syndrome ^b BAS, bile acid sequestrant	

Cost effectiveness

Results of analysis for IBS-D

- 5.28 No information was available to estimate the transition probabilities in the Markov models other than for all-cause mortality. Therefore, a range of scenarios were used to show the impact of the assumptions on the model estimates of health and cost.
- 5.29 In some scenarios, the use of SeHCAT was cost effective. In others, it was not cost effective. The results of the economic evaluation showed that there is considerable uncertainty about the cost effectiveness of SeHCAT testing for people diagnosed with IBS-D.
- 5.30 An additional analysis was carried out to explore the impact of the cost of additional testing for people whose disease does not respond to IBS-D treatment in all of the scenarios. This additional testing resulted in no change in any of the scenarios in terms of whether SeHCAT testing was found to be cost effective.

Results of analysis for Crohn's disease

- 5.31 No information was available to estimate the transition probabilities in the Markov models other than for all-cause mortality. Therefore, a range of scenarios were used to show the impact of the assumptions on the model estimates of health and cost.
- 5.32 Again, in some scenarios, the use of SeHCAT was cost effective. In others, it was not cost effective. The results of the economic evaluation showed that there is considerable uncertainty about the cost effectiveness of SeHCAT testing for people diagnosed with Crohn's disease who have not had ileal resection.

6 Considerations

- 6.1 The Committee considered the prevalence of bile acid malabsorption in people with chronic diarrhoea diagnosed with either IBS-D or Crohn's disease without ileal resection. Although studies have shown that as many as 30% of people with IBS-D have bile acid malabsorption, it is not clear whether the bile acid malabsorption is a primary idiopathic condition or secondary to another condition, which can determine the effectiveness of subsequent treatment. The Committee was informed that there are several causes of bile acid malabsorption, including that it may be a consequence of the decreased transit time associated with diarrhoea.
- 6.2 The Committee considered the diagnostic accuracy of SeHCAT. The Committee was informed that there are no clinical validity results for SeHCAT, and that the diagnostic accuracy of SeHCAT has only been determined by response to treatment with bile acid sequestrants, which may be open to assessment bias because of an inability to blind patients and clinicians.
- 6.3 The Committee considered how good the repeatability is for SeHCAT testing. The Committee was informed that, in people with IBS-D, the result of a SeHCAT test may vary depending on when in the course of the condition it is administered, because the disease is quite variable over time. The Committee was informed that there is likely to be less variability with other conditions but, because of the nature of the test (namely dependency on the use of radio-isotopes with relatively long half-lives), formal repeatability assessments would be difficult.
- 6.4 The Committee discussed the effectiveness of bile acid sequestrants in treating bile acid malabsorption. The Committee was informed that there is little evidence on the clinical effectiveness of bile acid sequestrants. Moreover, it is not clear whether, in people with bile acid malabsorption, bile acid sequestrants work by binding bile acids, by a more direct constipating effect, or by a placebo effect. The Committee was also informed that a soon-to-be published study suggests that bile acid sequestrants may reduce bile acid malabsorption by reducing transit time rather than through binding bile acids, which may imply other more tolerable treatments could be effective.

- 6.5 The Committee considered the validity of a trial of treatment with bile acid sequestrants as a comparator to SeHCAT. The Committee was informed that a trial of treatment may work if the clinician persuades the person to adhere to the treatment. But a trial may not be suitable for the population groups included in this assessment because the efficacy of treatment is dose sensitive and because the treatment is not well tolerated. This means that achieving adherence during the treatment trial can be challenging. The Committee was informed that the results of a SeHCAT test help to guide the clinician in the titration of the dose of bile acid sequestrants and to provide an incentive for adherence to treatment. The Committee was also informed that a positive diagnosis is likely to increase adherence among people prescribed bile acid sequestrants. The Committee was also informed that no studies were identified that quantified the accuracy and effectiveness of a trial of treatment.
- 6.6 The Committee considered what other options are available for diagnosing bile acid malabsorption. The Committee was informed that there are currently laboratory-based tests being developed, whereas older methods such as faecal bile acid measurements are not routinely practised.
- 6.7 The Committee was informed by the manufacturer that 30–40% of gastrointestinal centres in the country use SeHCAT and that the number is rising. The Committee was informed by clinical specialists that SeHCAT is mostly used in teaching hospitals and universities. The specialists also agreed that the use of SeHCAT has increased substantially in the past 2 years.
- 6.8 The Committee considered the cost-effectiveness analysis in the diagnostic assessment report. The report contained multiple scenario analyses because of the paucity of the evidence. SeHCAT use in the populations under evaluation was variably cost effective depending on the assumptions used in the scenario. The Committee was informed that it is extremely difficult to establish transition probabilities from 'diarrhoea' to 'no diarrhoea'. As such, the Committee was unable to establish the relative plausibility of these scenarios.
- 6.9 The Committee concluded that, given the apparent prevalence of undiagnosed bile acid malabsorption, there is the potential for patient and system benefit associated with using SeHCAT. But the Committee concluded that there is currently insufficient evidence to determine whether and under what circumstances SeHCAT is a cost-effective option for diagnosing bile acid

malabsorption in people with chronic diarrhoea who have been diagnosed with IBS-D or Crohn's disease without ileal resection. The Committee agreed that a programme of research was needed to evaluate this technology, the condition and the effects of treatment, and that its research recommendations would stimulate the collection of evidence about the potentially important clinical benefits and potential harms of using SeHCAT and treating bile acid malabsorption.

- 6.10 The Committee was aware that people with chronic diarrhoea are likely to be classified as having a disability and therefore be protected under the Equality Act 2010. The Committee considered the potential impact a negative recommendation or a recommendation for further research could have on this population. It was felt that given the cost of the test and the unpleasantness of the treatment, research was essential to establish cost effectiveness and benefit for this population, and that the population would be best served by research, including research to address the acceptability of treatment, before the recommendation of widespread adoption of this test.

7 Recommendations for further research

- 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.

8 Implementation

NICE will support this guidance through a range of activities to promote the recommendations for further research. The research proposed will be passed to the NICE Medical Technologies Evaluation Programme research facilitation team for the development of specific research trial protocols as appropriate. NICE will also incorporate the research recommendations in [section 7](#) into its guidance research recommendations database (available on the NICE website at www.nice.org.uk) and highlight these recommendations to public research bodies. A costing report will not be developed.

9 Related NICE guidance

Published

- Crohn's disease: Management in adults, children and young people. NICE clinical guideline 152 (2012)
- Irritable bowel syndrome in adults: diagnosis and management of irritable bowel syndrome in primary care. NICE clinical guideline 61 (2008)

10 Review

NICE will update the literature search at least every 3 years to ensure that relevant new evidence is identified. NICE will contact product sponsors and other stakeholders about issues that may affect the value of the diagnostic technology. NICE may review and update the guidance at any time if significant new evidence becomes available.

Andrew Dillon
Chief Executive
November 2012

Appendix A: Diagnostics Advisory Committee members and NICE project team

Diagnostics Advisory Committee

The Diagnostics Advisory Committee is an independent committee consisting of 22 standing members and additional specialist members. A list of the Committee members who participated in this assessment appears below.

Standing Committee members

Dr Trevor Cole

Consultant Clinical Geneticist, Birmingham Women's Hospital Foundation Trust

Dr Paul Collinson

Consultant Chemical Pathologist, St George's Hospital

Professor Ian Cree

Senior Clinical Advisor, NIHR Evaluation Trials and Studies Coordinating Centre, University of Southampton

Professor Erika Denton

National Clinical Director for Imaging, Department of Health

Dr Simon Fleming

Consultant in Clinical Biochemistry and Metabolic Medicine, Royal Cornwall Hospital

Professor Elizabeth (Lisa) Hall

Professor of Analytical Biotechnology, Institute of Biotechnology, Department of Chemical Engineering and Biotechnology, University of Cambridge

Professor Chris Hyde

Professor of Public Health and Clinical Epidemiology, Peninsula College of Medicine and Dentistry

Professor Noor Kalsheker

Professor of Clinical Chemistry, Molecular Medical Sciences, University of Nottingham

Dr Mark Kroese

Consultant in Public Health Medicine, PHG Foundation and UK Genetic Testing Network

Professor Adrian Newland (Chair)

Consultant Haematologist, Barts and the London NHS Trust

Dr Richard Nicholas

Consultant Neurologist, Heatherwood and Wexham Park Hospital, Imperial Healthcare Trust

Ms Margaret Ogden

Lay member

Dr Diego Ossa

Director Market Access Europe, Novartis Molecular Diagnostics

Mr Stuart Saw

Director of Finance and Procurement, Tower Hamlets Primary Care Trust

Professor Mark Sculpher

Professor of Health Economics, Centre for Health Economics, University of York

Dr Steve Thomas

Senior Lecturer and Consultant Radiologist, University of Sheffield

Mr Paul Weinberger

CEO, Diasolve Ltd, London

Mr Christopher Wiltsher

Lay member

Specialist Committee members

Dr Kevin Bradley

Consultant in Nuclear Medicine & Radiology, Oxford Radcliffe Hospitals

Dr Matthew Brookes

Consultant Gastroenterologist, Royal Wolverhampton NHS

Dr Annelies Maenhout

Consultant in Nuclear Medicine, Chelsea and Westminster NHS Foundation Trust and Royal Brompton and Harefield NHS Trust

Professor John McLaughlin

Consultant Gastroenterologist, Salford Royal Hospitals NHS Foundation Trust

Dr Nick Read

Chair and Medical Advisor, IBS Network

Dr Richard Thompson

Senior Lecturer in Paediatric Hepatology, Institute of Liver Studies, King's College London

NICE project team

Each diagnostics assessment is assigned to a team consisting of a Technical Analyst (who acts as the topic lead), a Technical Adviser and a Project Manager.

Farouk Saeed

Topic Lead

Hanan Bell

Technical Adviser

Jackson Lynn

Project Manager

Appendix B: Sources of evidence considered by the Committee

The diagnostics assessment report for this assessment was prepared by Kleijnen Systematic Reviews:

- Riemsma R, Al MJ, Corro Ramos I, et al. SeHCAT (tauroselcholic [⁷⁵selenium] acid) for the investigation of bile acid malabsorption (BAM) and measurement of bile acid pool loss: a systematic review and cost-effectiveness analysis. April, 2012.

Registered stakeholders

The following organisations and/or their members accepted the invitation to participate in this assessment as stakeholders. They were invited to attend the scoping workshop, and to comment on the diagnostics assessment report and the diagnostic consultation document:

Manufacturers/sponsors:

- GE Healthcare

Professional/specialist, patient/carer and other groups:

- British Nuclear Medicine Society
- British Society of Gastroenterology
- Chelsea and Westminster NHS Foundation Trust and Royal Brompton and Harefield NHS Trust
- Institute of Nuclear Medicine
- NHS Grampian
- Pelvic Radiation Disease Association
- Royal College of Nursing
- Rotherham NHS Foundation Trust
- Royal College of Physicians
- The Royal Marsden NHS Foundation Trust

About this guidance

NICE diagnostics technologies guidance is designed to help the NHS adopt efficient and cost effective medical diagnostic technologies more rapidly and consistently.

The programme concentrates on pathological tests, imaging, endoscopy and physiological measurement, since these represent most of the investigations performed on patients. The types of products which might be included are medical diagnostic technologies that give greater independence to patients, and diagnostic devices or tests used to detect or monitor medical conditions. Diagnostic technologies may be used for various purposes: diagnosis, clinical monitoring, screening, treatment triage, assessing stages of disease progression, and risk stratification.

This guidance was developed using the NICE [diagnostic technologies guidance](#) process.

We have produced a [summary for patients and carers](#).

Changes since publication

December 2014: Minor maintenance

December 2012: NICE Accreditation logo added

Your responsibility

This guidance represents the view of NICE, which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity, and foster good relations. Nothing in this guidance should be interpreted in a way which would be inconsistent with compliance with those duties.

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ISBN: 978-1-4731-0914-8

Accreditation

