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Prevalence of, and predictors of, bile acid malabsorption in outpatients with chronic diarrhoea

Gracie D *et al.* Neurogastroenterology & Motility 2012; 24: 983-e538

Prescribing information can be found at the end of this presentation

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08-2017 JB7287 | UK Communication Tool

Background

- Bile acids are produced in the liver, secreted into the biliary system and stored in the gall-bladder
- After meals, cholecystokinin stimulates the release of bile acids into the small intestine where they act to digest and absorb lipids
- Normally, over 95% of the bile acids are absorbed in the terminal ileum and are taken back up by the liver
- Bile Acid Malabsorption (BAM) is a condition in which bile acids are not reabsorbed in the terminal ileum and so continue into the colon
- When larger amounts of bile acids enter the colon, they stimulate water secretion and intestinal motility, resulting in chronic diarrhoea

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Types of Bile Acid Malabsorption

Type I

Failure in the reabsorption of bile acids in the terminal ileum caused by resection or localised disease

Type II

Idiopathic- in the absence of any of those etiologies

Now known to be associated with defective feedback inhibition instead of malabsorption. Also it is known to be highly represented in patients with diarrhoea predominant irritable bowel syndrome (IBS-D).[1]

Type III- BAM following:

Cholecystectomy, Acute enteric illness , Radiotherapy or in the presence of biopsy proven celiac disease/microscopic colitis

1. Mottacki N, Simrén M, Bajor A et al. Alliment Pharmacol Ther 2016; 43 (8): 884-98.

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Background data

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- Chronic diarrhoea is a very common concern with prevalence between 2 and 9%[1]
- Abnormalities of the enterohepatic circulation of bile acids can be assessed with a SeHCAT scan
- In a recent meta-analysis, an abnormal SeHCAT scan was found in more than 30% of patients who met criteria for diarrhoea-predominant irritable bowel syndrome (D-IBS)[2]
- This data suggest that type II (idiopathic) BAM is the cause

1. Basaranoglu M *et al*. Digestion 2008; 77: 10-5.

2. Wedlake L *et al*. Aliment Pharmacol Ther 2009; 30: 707-17.

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Use of SeHCAT™

Some clinicians do not perform SeHCAT

The SeHCAT scan may be used more appropriately amongst Gastroenterologists if there were greater awareness of:

- Likely prevalence of BAM among chronic diarrhoea patients undergoing SeHCAT
- Predictors of a positive test
- Yield of scanning in those with compatible IBS-D symptoms

Aim of the study

- If the demand for SeHCAT scanning is increasing (suggesting increased awareness)
- The yield of testing in patients with chronic diarrhoea
- Factors that may predict a positive test
- Characteristics of patients with bile acid malabsorption according to type and severity

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Participants and Setting

- Retrospective review
- Consecutive patients with chronic diarrhea referred for SeHCAT
- 7-year period
- Leeds General Infirmary and St James' University Hospital, Leeds
- Recruited individuals representative of the local secondary care population

Data collection and Synthesis

Institutional radiology information system (IRIS) was used to identify data collected prospectively from all subjects who had received SeHCAT scanning

Data collected January 2005-December 2011

Medical records reviewed retrospectively

- Data recorded:
- Date of scan
- Requesting clinician (physician/surgeon)
- Age of patient at time
- Patient sex
- Percentage retention of SeHCAT scan

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Data collection and Synthesis

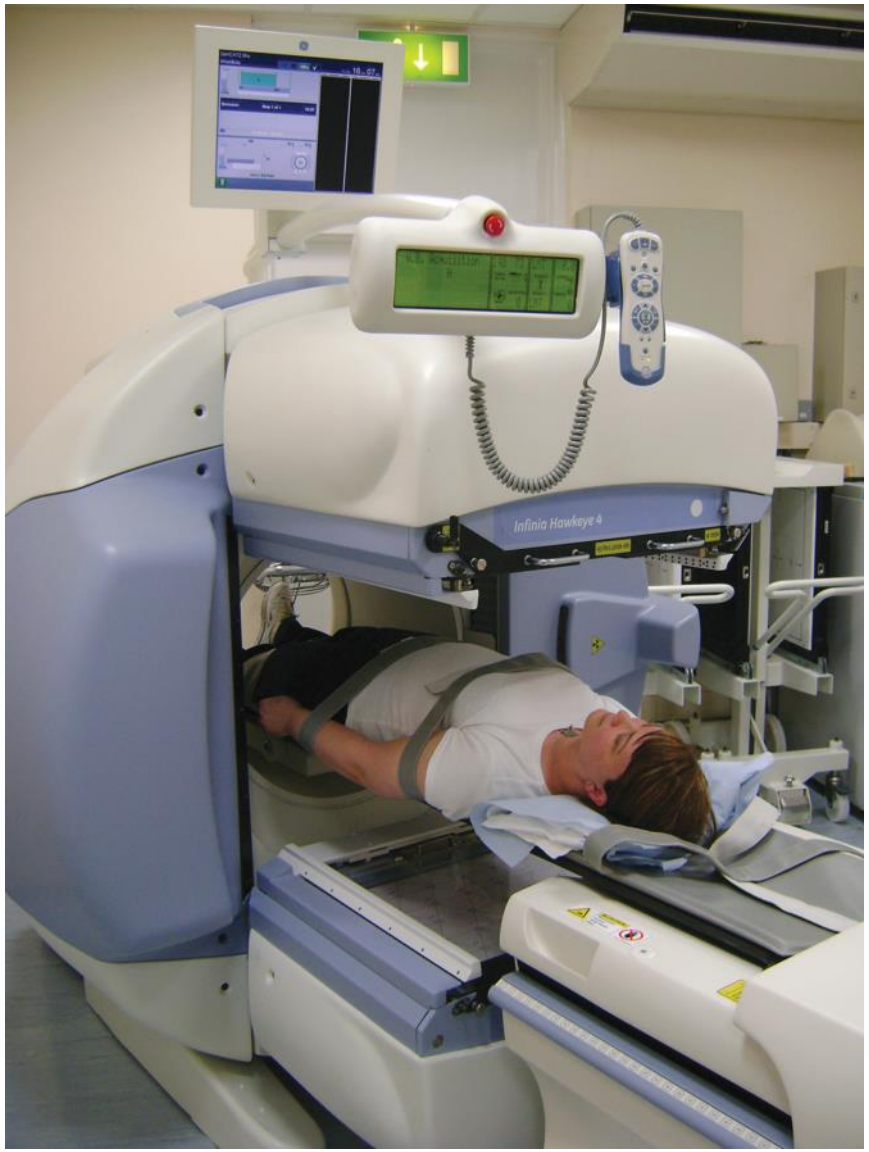
A complete medical history prior to the SeHCAT scan being requested were recorded:

- Cholecystectomy
- Terminal ileal Chron's disease
- Terminal ileal resection or right hemicolectomy for Chron's disease or for reasons other than Chron's disease
- Acute enteric illness
- Radiotherapy
- Biopsy-proven celiac disease or microscopic colitis

Scanning Protocol

Data acquired on a Hawkeye Infinia™ dualheaded gamma camera

- 370 KBq capsule of SeHCAT
- Oral administration at day 1
- 10 minute patient and background count acquisitions at 3 hours and 7 days



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Retention Data

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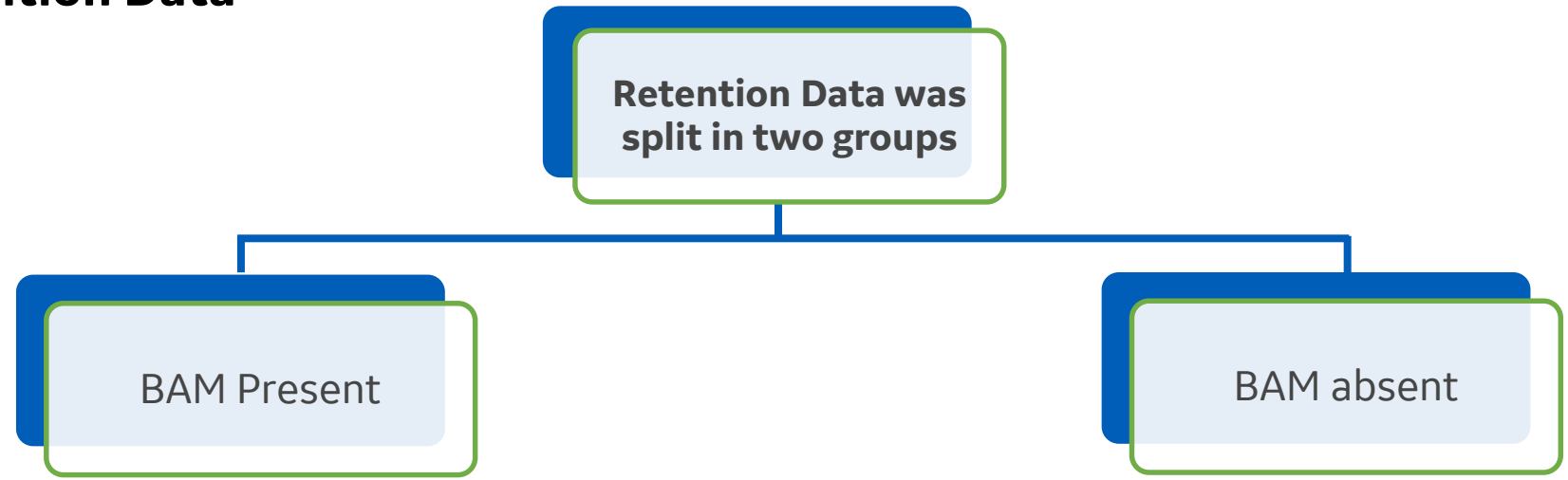

Using thresholds of:

- Mild BAM 10 – 15%
- Moderate BAM 5 – 10%
- Severe BAM <5%

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Statistical Analysis

Categorical demographic data were compared between those:

- With and without BAM
- Between each of the 3 severities (mild, moderate, severe)
- Between each of the three subtypes (Type I, II and III)

Statistical Analysis

- Logistic regression analysis was used to determine independent predictors of a positive SeHCAT test
- P value < 0.01 was considered as statistically significant
- Results expressed as odds ratios (ORs) with 99% confidence intervals (CIs)

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Results

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- 373 individuals with chronic diarrhoea underwent SeHCAT
- 293 requested by gastro/80 requested by colorectal/upper gastrointestinal surgeon
- Mean age of 48.0 years (range 17-90 years)
- 258 (69.2%) female

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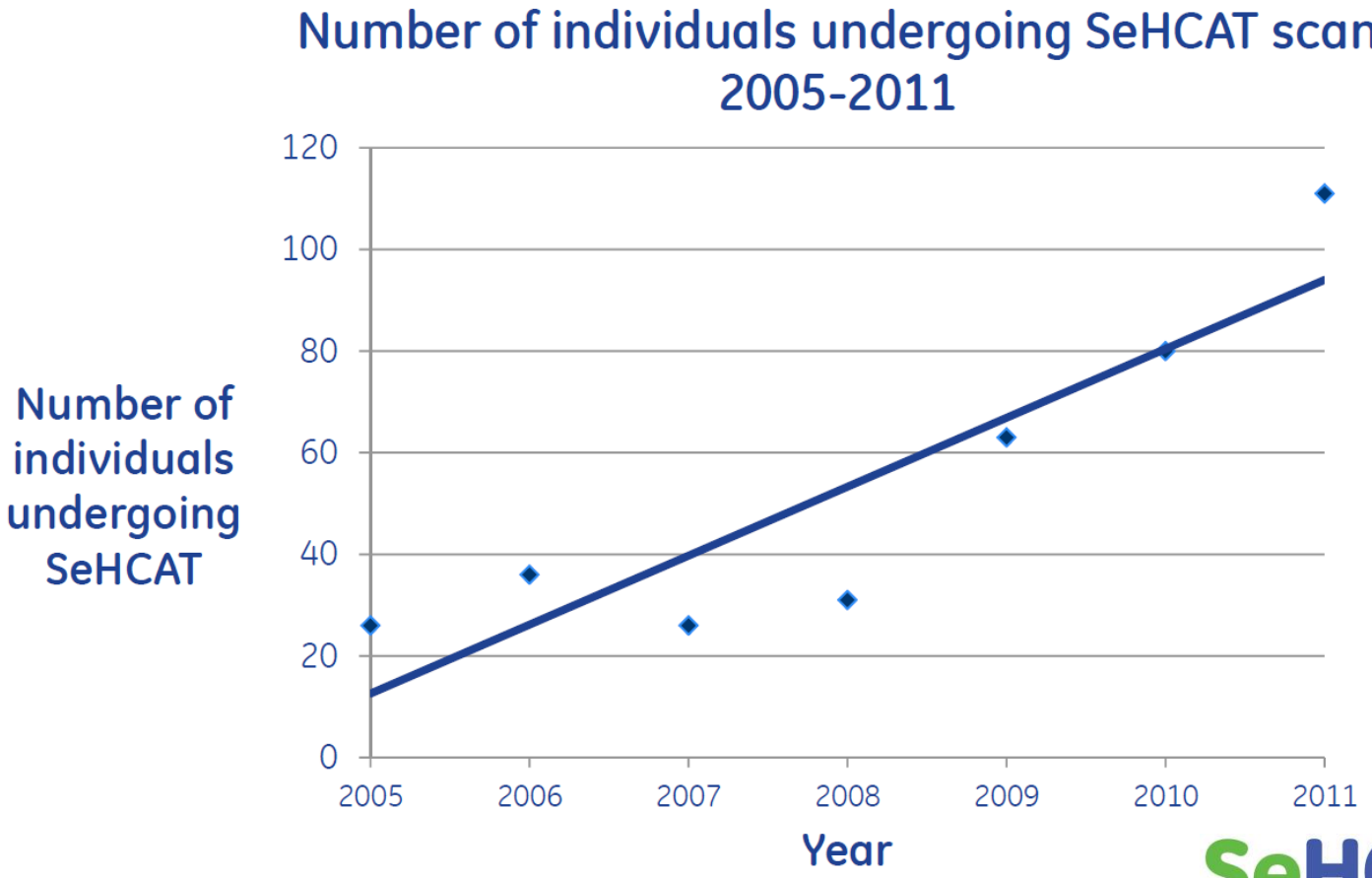
Number of SeHCAT™ scans

Number of scans increased from 26 in 2005 to 111 in 2011,

more than a four-fold increase



This increase was statistically significant (p=0.01)

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Prevalence of, and risk factors for, BAM

50.9% (190/373) showed some degree of BAM

A significantly greater proportion of individuals who with BAM had undergone:

- Cholecystectomy (27.4% vs 13.3% p=0.003)
- Terminal ileal resection or right hemicolectomy for Crohns (18.4% vs 1.6% p<0.001)
- Terminal ileal resection or right hemicolectomy for other reasons (7.4% vs 1.6% p=0.008)

These are therefore associated with presence of BAM

Prevalence of, and risk factors for, BAM

Previous procedure or identified risk factor	Number of Patients	No evidence of bile acid malabsorption n (%)	Evidence of bile acid malabsorption n (%)
Cholecystectomy	76	24 (31.6)	52 (68.4)
Terminal ileal resection or right hemicolectomy for Crohn's disease or other reasons	55	6 (10.9)	49 (89.1)
Acute enteric illness	22	13 (59.1)	9 (40.9)
Celiac disease	6	5 (83.3)	1 (16.7)
Collagenous colitis	18	12 (66.6)	6 (33.3)
Lymphocytic colitis	6	3 (50.0)	3 (50.0)

Patients Results

Patients with no risk factors

- 45.0% (168/373) individuals with no obvious risk factors other than chronic diarrhea
- Of these 168, 63 (37.5%) had some degree of BAM
- Of these 63, 18 (28.6%) had severe BA

Patients with IBS-D compatible symptoms

- 77 patients reported symptoms compatible with IBS-D
- Of these 77, 21 (27.3%) showed a positive SeHCAT test

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Prevalence of, and risk factors for, BAM according to severity

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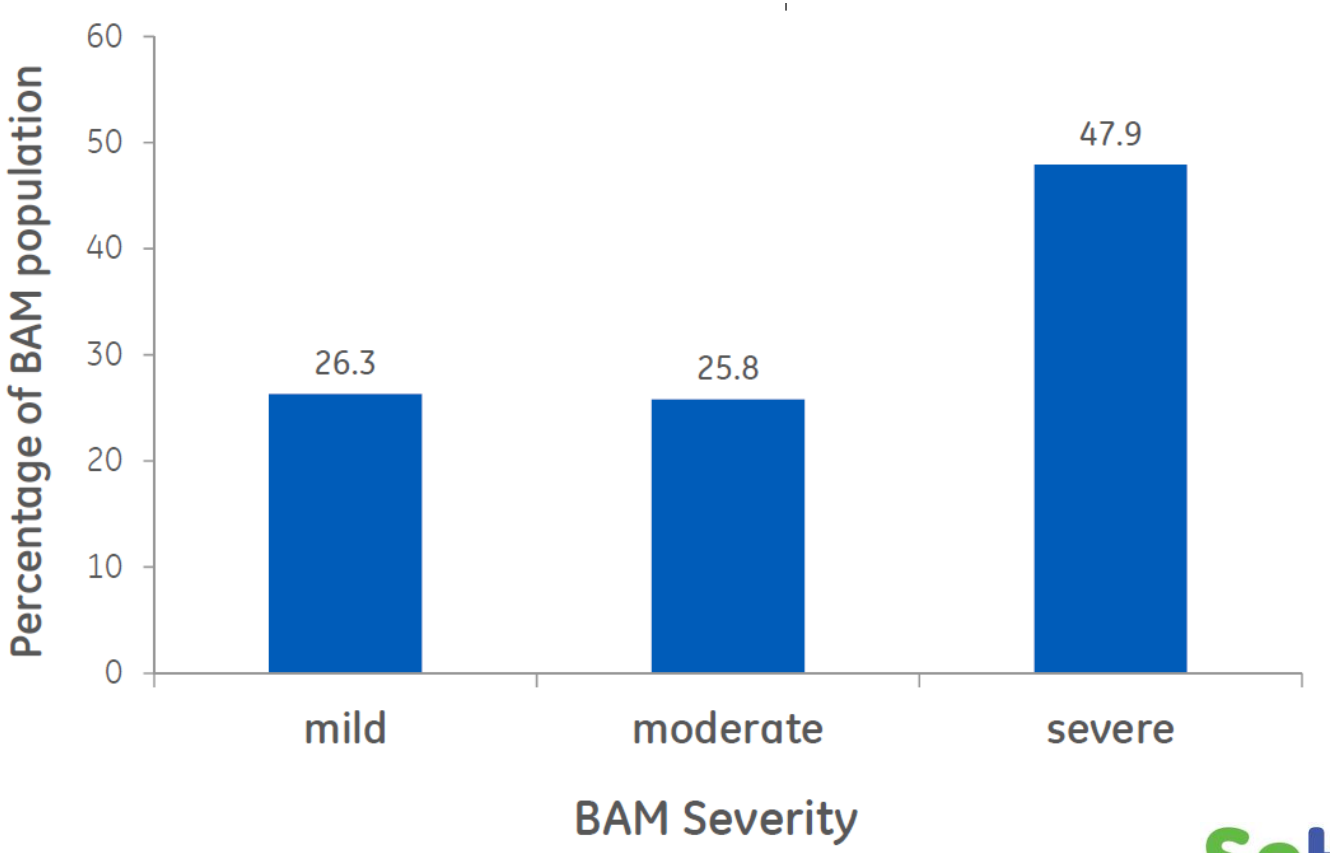
Of the 190 individuals with BAM



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Severe BAM

There were significantly more patients with severe BAM with:

- Terminal ileal resection or right hemicolectomy for Crohn's disease (33.0%, $p < 0.001$)
- Terminal ileal resection of right hemicolectomy for other reasons (12.1%, $p = 0.05$)

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Prevalence of, and risk factors for, BAM according to subtype

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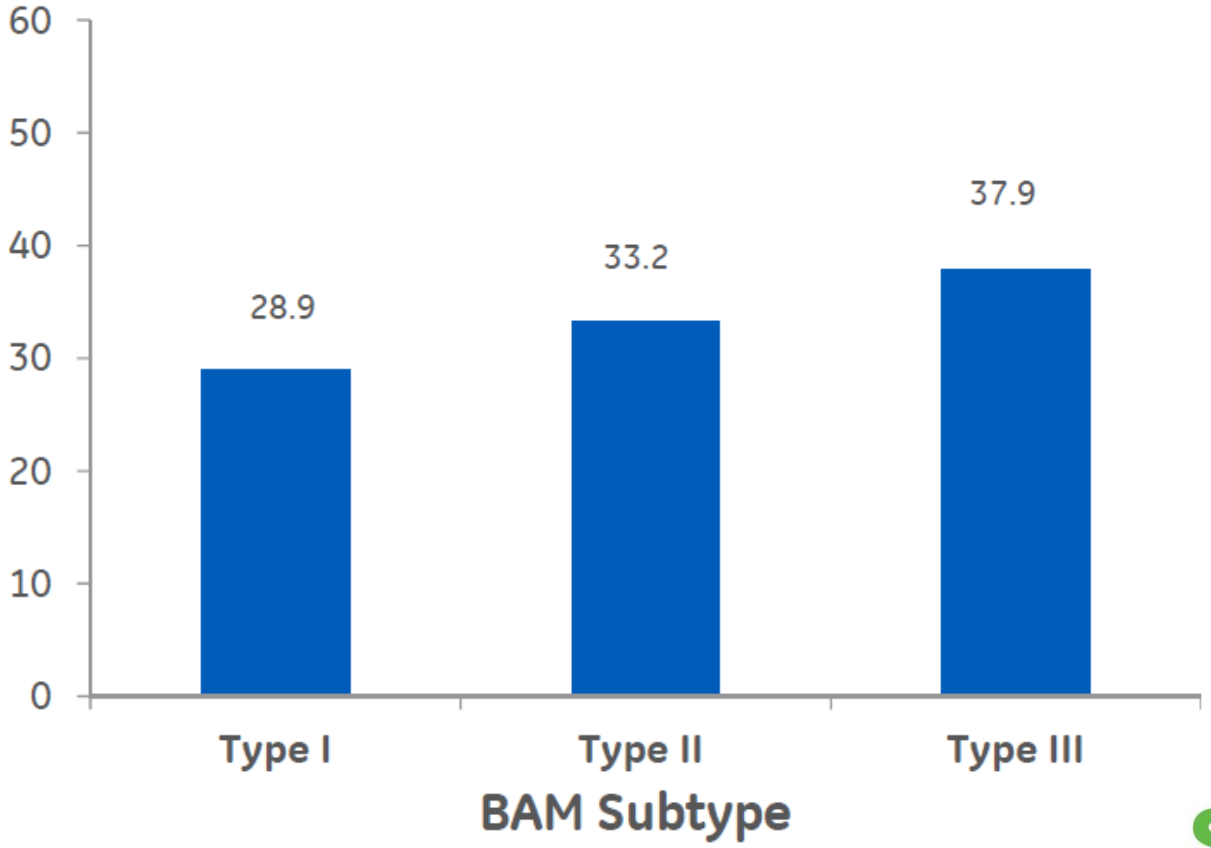
Of the 190 individuals with BAM



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Prevalence of, and risk factors for, BAM according to subtype

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- 80% of patients with Type I BAM were severe compared with 28.6% and 40.3% in those with Types II and III BAM respectively ($p<0.001$)
- Type II BAM more likely to report bloating
- Out of the 63 with Type II BAM, 21 (33.3%) met criteria for IBS-D

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Conclusions

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- Bile acid malabsorption was present in 50% of patients undergoing SeHCAT scanning
- Almost 40% of those without risk factors had evidence of BAM
- In patients meeting criteria for IBS-D, prevalence of BAM was almost 30%
- BAM should be considered as a potential cause for all patients with chronic diarrhoea, regardless of age, sex, symptoms or proposed risk factors

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PRESCRIBING INFORMATION SeHCAT 370kBq Capsules ([^{75}Se]tauroselcholic acid)
Please refer to full national Summary of Product Characteristics (SPC) before prescribing.
Indications and approvals may vary in different countries. Further information available on request.

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PRESENTATION Hard gelatin capsule containing [^{75}Se]tauroselcholic acid [370kBq at the activity reference date].

INDICATIONS This medicinal product is for diagnostic use only. Used for the investigation of bile acid malabsorption and measurement of bile acid pool loss. It may be used in the assessment of ileal function, in the investigation of inflammatory bowel disease and chronic diarrhoea and in the study of entero-hepatic circulation.

DOSAGE AND METHOD OF ADMINISTRATION Normal adult and elderly dose is one capsule administered orally. No paediatric dosage form or clinical experience of the use of this product in children. The same dose used adults should be used in children. A careful assessment of the risk/benefit ratio should be undertaken before use of the product in children due to increased effective dose equivalent. Careful consideration of the activity to be administered to patients with hepatic impairment is required since increased radiation exposure is possible. Drinks of 15 ml of water are recommended before, during and after swallowing capsule to ensure passage to the stomach. Patient should be in standing or sitting position.

CONTRAINDICATIONS Hypersensitivity to the active substance or to any of the excipients.

WARNINGS AND PRECAUTIONS If hypersensitivity or anaphylactic reactions occur, administration must be discontinued immediately and if required, intravenous treatment initiated. The necessary medicinal products and equipment such as endotracheal tube and ventilator must be immediately available. Caution advised in administration of SeHCAT to patients with severe hepatic dysfunction or biliary tract obstruction. Radiation dose to liver will be significantly increased in these patients. Exposure to ionising radiation must be justifiable on the basis of likely benefit. The activity administered must be such that the resulting radiation dose is as low as reasonably achievable bearing in mind the need to obtain the intended diagnostic or therapeutic result. For each patient, the radiation exposure must be justifiable by the likely benefit. The activity administered should be as low as reasonably achievable to obtain the required diagnostic information. Careful consideration of the benefit risk ratio in patients with hepatic impairment is required since increased radiation exposure is possible. No data are available for the paediatric population however careful consideration of the indication is required since the effective dose per MBq is higher than in adults. This medicinal product contains 3.01 mmol (71.04 mg) sodium in each capsule which should be taken into account in patients on a low sodium diet.

INTERACTIONS No interaction studies have been performed and no interactions reported to date.

PREGNANCY AND LACTATION When an administration of radiopharmaceuticals to a woman of childbearing potential is intended, it is important to determine whether or not she is pregnant. Any woman who has missed a period should be assumed to be pregnant until proven otherwise. If in doubt about the potential pregnancy, alternative techniques not using ionising radiation (if there are any) should be offered to the patient. No data are available on the use in human pregnancy. Animal reproduction studies have not been carried out. Radionuclide procedures carried out on pregnant women also involve radiation doses to the foetus. Only essential investigations should therefore be carried out when the likely benefit exceeds the risk to the mother and foetus. Before administration to a breastfeeding mother, consideration should be given as to whether the investigation could be reasonably delayed until after the mother has ceased breastfeeding and as to whether the most appropriate choice of radiopharmaceutical has been made, bearing in mind the secretion of activity in breast milk. If administration is considered necessary, breastfeeding should be interrupted and breast milk discarded for three to four hours after administration, after which breastfeeding can be resumed.

PRESCRIBING INFORMATION SeHCAT 370kBq Capsules ([^{75}Se]tauroselcholic acid)
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UNDESIRABLE EFFECTS Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects. As the effective dose is 0.26 mSv when the maximal recommended activity of 370 kBq is administered these adverse reactions are expected to occur with a low probability.
Immune system disorders: Hypersensitivity (unknown frequency).
DOSIMETRY Effective dose for a healthy adult administered one 370kBq capsule of SeHCAT is typically 0.26mSv. In most clinical investigations for which this substance is used (e.g. Crohn's disease) the effects of impaired ileal absorption and shorter gastrointestinal transit time tend to reduce the dose commitment compared with the normal case. However, in patients with severe cholestatic jaundice, the liver dose has been estimated to be about 100 times the normal value.
MARKETING AUTHORISATION HOLDER GE Healthcare Limited, Amersham Place, Little Chalfont, HP7 9NA, UK.
CLASSIFICATION FOR SUPPLY Subject to medical prescription (POM).
UK MARKETING AUTHORISATION NUMBER PL 0221/0105.
PRICE £195.
DATE OF REVISION OF TEXT 28 April 2017.

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to GE Healthcare.

GE Healthcare Limited, Amersham Place,
Little Chalfont, Buckinghamshire, England HP7 9NA
www.gehealthcare.com

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