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ORIGINAL ARTICLE

Outcomes from treating bile acid malabsorption using a multidisciplinary approach

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Abstract
Background & aim Despite bile acid malabsorption affecting >1 % of the population, the outcomes of treatment are largely unreported. This study evaluated the effectiveness of a structured intervention for this condition.
Method This was a retrospective evaluation of prospectively recorded patient reported outcome measures in a consecutive cohort of patients diagnosed with bile acid malabsorption seen in a cancer centre gastroenterology clinic. Every patient completed a 7-day food diary, a gastrointestinal symptom rating scale questionnaire and Bristol stool chart before the first clinic appointment and the symptom questionnaire and Bristol stool chart before all subsequent appointments. Patients who reported any episodes of type 6 or 7 stool were referred for a ^{75}Selenium (Se) homocholic acid taurine scan. Abnormal gastrointestinal symptoms were investigated and treated systematically using a peer reviewed management algorithm.
Results Between 2011 and 2013, 136 men, 146 women, median age 66 years (range 19–89) underwent a scan. 143 (51 %) had 7-day isotope retention of ≤20 %. 105 (73 %) had previously undergone pelvic radiotherapy and 67 (47 %) GI surgery. 123 (86 %) were treated with low-fat diets, 79 (55 %) with a bile acid sequestrant, 73 (51 %) both. On discharge, 100 (70 %) patients reported an overall symptom improvement (mean −4.2 points, $p<0.0001$). In patients who had only bile acid malabsorption and no other gastrointestinal diagnoses, 77 % (41/53) reported a mean improvement of −5.4 points ($p<0.0005$). Patients reported a clinically significant improvement in urgency, faecal incontinence, wind, nocturnal defaecation, tiredness, abdominal pain, bloating, and steatorrhoea, ($p=<0.0005$). Stool frequency was reduced and stool consistency was improved.
Conclusion In this large cohort of complex patients, bile acid malabsorption is common and a multidisciplinary approach to managing gastrointestinal symptoms is effective.

Keywords Bile acid malabsorption · Dietary fat intake · Sequestrant · Colesevelam · SeHCAT

Introduction

Bile acid malabsorption (BAM) was first described in 1967 [1]. In 2009, a systematic review of 18 studies [2] confirmed that if patients firmly diagnosed with diarrhoea-predominant irritable bowel syndrome (IBS-D) in a gastroenterology clinic then undergo ^{75}Selenium homocholic acid taurine (SeHCAT) scanning, approximately one third will be shown to have been misdiagnosed and have idiopathic BAM instead. If using these data, the prevalence of I-BAM is calculated, it can be shown to be in excess of 1 % of the population, which equates to approximately 10 million people in North America and Europe alone.

However, bile acid malabsorption does not just affect people misdiagnosed as having IBS. There are large, although as yet unquantified, numbers of people who have secondary bile acid malabsorption as a result of surgery, radiotherapy, chemotherapy, and diseases of the gastrointestinal (GI) tract. Indeed, bile acid malabsorption is a condition which is at least as

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common as coeliac disease and twice as common as inflammatory bowel disease [3].

Yet diagnostic criteria for BAM remain controversial [4], and there are almost no guidelines for treatment from national bodies and very few published treatment outcomes. It is therefore not surprising that BAM is commonly undiagnosed. A survey of 437 British gastroenterologists showed only 6 % investigate for BAM as a first-line investigation in patients with chronic diarrhoea, while 61 % consider the diagnosis only in selected patients or not at all [5]. It seems likely that fewer than 1 % of patients suffering from this condition are currently diagnosed.

Bile acids are synthesised in the liver from cholesterol and released into the duodenum in response to cholecystokinin secretion as a result of dietary intake of fat. They aid the emulsification of lipids in the gut, allowing their subsequent absorption. Bile acids are mostly actively reabsorbed in the terminal ileum and returned to the liver via the venous portal system as part of the enterohepatic circulation. In health, less than 3–5 % of bile acids reach the colon where they undergo deconjugation and dehydroxylation by bacteria. If excess bile acids reach the colon, these then stimulate increased fluid and electrolyte secretion and shorten colonic transit time. This causes the characteristic symptoms of BAM-unpredictable loose stool as well as bloating, cramps, wind, urgency, and faecal incontinence [6].

Previously, three types of BAM, primary, secondary, and tertiary, were described [6], but as the underlying mechanisms for BAM have become clearer, the classification has required revision and it is now accepted that there are two completely distinct mechanisms that can give rise to identical symptoms [7]. True bile acid malabsorption occurs in people where there is an issue with adequate bile acid uptake from the lumen in the terminal ileum, either because of disease or mucosal dysfunction at that site or following surgical resection of the ileum. However, there is a second group of patients where ileal absorptive function is normal or even enhanced, but instead hepatic bile acid synthesis is increased to the degree that it overwhelms the absorptive capacity of the small bowel—and this is now increasingly termed bile acid diarrhoea (BAD) [6].

Despite controversy how best to use diagnostic tests for BAM/BAD [4], clinicians with access to the ^{75}Se-homocholyltaurine (SeHCAT) test first described in 1981 [8] consider it the 'gold-standard' for diagnosis, because of its safety, relatively low cost, very low radiation exposure, and very high sensitivity and specificity [9]. However, other investigations can help reach the diagnosis in countries where there is no access to SeHCAT scanning [10].

Pharmacological treatment of BAM primarily involves the use of bile acid sequestrants (BAS): colestyramine, colestipol, colesevelam, and rarely aluminium hydroxide. Budesonide, while not a bile acid sequestrant, may increase uptake of bile in the terminal ileum. A new agent obeticholic acid is undergoing preliminary studies. Antidiarrhoeals and stool bulking agents are also used to help alleviate symptoms [11]. Colestyramine and colestipol are historically the most widely used sequestrants; however, many patients are unable to tolerate these drugs due to poor taste and texture [12, 13]. Colesevelam, a relatively new BAS, first described in the context of treating hyperlipidaemia [14], is better tolerated, has greater affinity for bile acids, and is effective in the presence of steatorrhoea [15, 16]. While large randomised studies have established its safety in patients with hyperlipidaemia and diabetes mellitus, only five small studies have been reported so far in patients treated for BAM [16–19].

It is not common practise to treat BAM by reducing dietary intake of fat although this approach may improve symptoms [20–24]. However, all the studies, which have described the use of dietary fat manipulation, are more than 20 years old, have small sample sizes and confounding factors influencing outcomes. It is therefore unsurprising that clinicians do not offer dietary intervention as routine management, but as BAM is an increasing burden on health care, it is clearly important to define the best management strategy.

With this background in mind, we aimed with this study to evaluate the effectiveness of interventions for bile acid malabsorption in people who have had previous treatment for cancer.

Method

This was a retrospective evaluation of prospectively and systematically recorded data of all patients referred to a specialist GI "consequences-of-cancer-treatment" clinic. In the absence of national guidance regarding management of patients with BAM, we have developed our own algorithm to manage patients with BAM diagnosed in our clinic (Fig. 1). The primary aim of this study was to evaluate the effectiveness of treatment offered for bile acid malabsorption following our algorithm. This study was reviewed and authorised by the Royal Marsden Hospital (RMH) Committee for Clinical Research and approved as a service evaluation which did not require consent from the patients.

Before every clinic appointment, all patients filled out a gastrointestinal symptom rating scale (GSRS) questionnaire. These are routinely used to aid clinical management. The GSRS has been previously validated for gastro-oesophageal reflux disease, peptic ulcer disease, GI surgery (e.g. pancreatectomy), coeliac disease, chronic intestinal pseudoobstruction, chronic non-specific abdominal complaints, and irritable bowel syndrome [25–31].

The GSRS questionnaire we use in our clinic contains 21 questions. For this study, 8 of the 21 gastrointestinal symptoms the questionnaire asks about were deemed disease

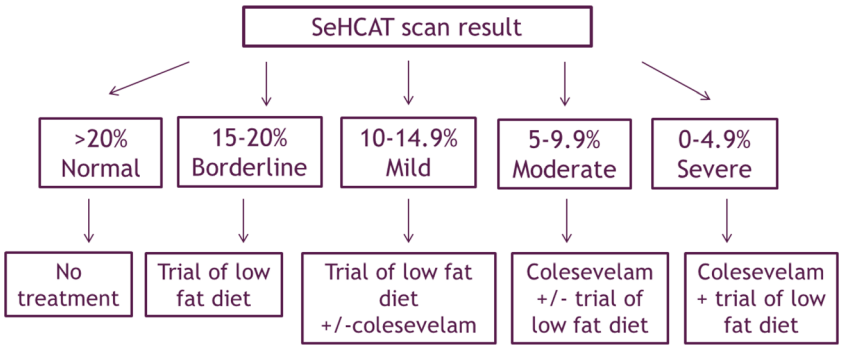

Fig. 1 The Royal Marsden GIaNTs algorithm for managing bile acid malabsorption according to 7-day SeHCAT retention values

specific for BAM. These symptoms were abdominal pain, bloating, wind, urgency, faecal incontinence, steatorrhoea, nocturnal defaecation, and tiredness [6]. Patients can categorise severity of each symptom as "never," "occasionally," or "frequently affecting their life" or causing "major changes their life". We assigned values of 0, 1, 2, and 3, respectively, to each of these severity categories [25]. Therefore, the best symptom score that a patient could report was 0, the worst 24. In this paper, we report only symptom scores recorded at the initial consultation and at time of discharge from the GI clinic.

Patients were also routinely asked to indicate on a Bristol stool chart what stool forms they had experienced in the last 4 weeks. The Bristol stool chart identifies seven different forms of stool [32]. If patients reported any episodes of type 6 (mushy) or 7 (liquid) stool even rarely, they were referred for a SeHCAT scan.

All patients who had any abnormal gastrointestinal symptoms were investigated systematically using the Royal Marsden peer reviewed investigational algorithm version 7, which has been shown to be effective in a randomised clinical trial [33].

A list of all patients who underwent a 7-day SeHCAT scan between September 2011 and September 2013 were obtained and cross-referenced against those prescribed colesevelam by the hospital pharmacy and clinic records. In this cohort of patients we did not use any other bile acid sequestrant. Colesevelam was always initiated by the hospital clinician. Patients were asked to build up to a maximum dose of 6× 625 mg tablets a day, taken with food, and were given written information how to take the medication, its possible side effects and interactions. If patients had a 7-day SeHCAT retention of 10–20 %, they were given an initial trial of a low-fat diet. If this did not improve their symptoms sufficiently, or they found the diet too restrictive, they were offered a trial of colesevelam, a bile acid sequestrant. If patients had a 7-day SeHCAT retention of ≤10 %, Colesevelam was prescribed first and the patients were asked to optimise the dose over a 6-week period. At that stage, they were reviewed. If they still had residual symptoms considered to be due to probable bile acid malabsorption, or patients wanted to try a dietary approach before using a bile acid sequestrant, they were reviewed by one of two Registered Dietitians. Patients were asked to complete a 7-day food diary before that first dietetic appointment. The dietitian calculated their average daily fat intake from the diary and demonstrated to each patient the sources of fat in their diet. Then patients were advised how to reduce their fat intake so that their daily fat dietary intake did not exceed 20 % of their calculated total energy requirements—usually of the order of a maximum of 30–50 g fat per day. Written diet sheets were provided and suggestions were made of alternative foods low in fat that the patient could consider. Patients' careers and partners were invited to the consultation with the dietitian to help the patient make changes in their food choices to meet an overall lower fat intake. Joint follow-up by the dietitian and gastroenterology team was routinely arranged 6 to 8 weeks later, and if required, further joint consultations were arranged at 6- to 8-week intervals until it was felt by the patient and staff that further advice was not required. At that point, they were offered a final out patient review 3 months later to ensure that any improvement in GI symptoms achieved was sustained. This approach is shown diagrammatically in Fig. 1.

Data regarding patient characteristics, previous cancer history, treatment, and concomitant diagnoses possibly affecting gastrointestinal symptoms were extracted retrospectively from electronic patient records and entered into a study database.

Statistical analysis

Change in GSRS score was normally distributed. So in addition to descriptive analysis, the paired *t* test was used to test the overall change in GSRS score, from baseline to discharge, and to see if the mean change in GSRS was significantly different from zero.

Individual symptom change scores were nonparametric, discrete, ordinal data over a limited range (0–3 points). So the Wilcoxon signed-rank test was used to test whether scores significantly changed after intervention.

Results

Patient characteristics

This study included 363 consecutive patients referred for a SeHCAT scan over a 2-year period from September 2011–2013 as a result of reporting occasional, frequent, or continuous type 6 or 7 stool. Reasons why some patients were excluded from this study are shown in Fig. 2. Data from 282 patients (median age 66) were evaluated (Table 1). The majority had been treated with pelvic radiotherapy.

143 (51 %) patients had a 7-day SeHCAT retention of ≤20 %, which is the cutoff at which we consider that the patient warrants a trial of treatment for possible bile acid malabsorption (Fig. 1; Table 2).

Of this group, after systematic investigation, 53 patients had only BAM and no other GI diagnoses causing their symptoms. Of the other 90 patients, 74 had one and 16 had two or more additional major GI diagnoses made, which were considered to be a contributing factor for their symptoms. These additional diagnoses included small intestinal bacterial overgrowth, pancreatic insufficiency, lactose intolerance, or new onset inflammatory bowel disease.

Baseline GSRS scores

The median score for the 282 patients at time of their first consultation in our clinic was 10 (range 2–21). The median score in the 143 who had a 7-day SeHCAT retention of ≤20 % was 11 (range 3–21). In those who had only BAM and no other GI diagnoses made after investigation, the median score was 10 (range 3–21) and in those with BAM and at least one other new GI diagnosis was 12 (range 3–19).

All data reported in this manuscript from here on are related to the changes in the eight symptoms—abdominal pain, bloating, wind, urgency, faecal incontinence, steatorrhoea, nocturnal defaecation, and tiredness—which we considered were potentially due to bile acid malabsorption. However, if we consider the patients' reported responses to all the 21 symptoms asked in the GSRS at baseline, the scores were as follows (Table 3): whole cohort (n=282): median score 18 (range: 2–45); BAM cohort (n=143): 18 (range 5–45); BAM and no other GI diagnoses cohort (n=53): 17 (range 5–33); and BAM+other diagnoses (n=90): 19 (range 6–45).

Change in reported symptoms after treatment

In the 143 patients diagnosed with BAM, 123 (86 %) were treated with dietary intervention, 79 (55 %) were treated with colesevelam, 73 (51 %) were treated with both diet and medication, and 20 received no treatment. Of the 107 patients seen by the dietitian, median daily dietary fat intake at the time of the initial consultation was 60 g/day (range 20–110 g) on the day with the lowest intake and 79 g/day (range 29–190 g) on the day with the highest intake. Patients were prescribed a target intake of <45 g/day (median range 30–65 g/day) and by time of discharge from the clinic their 7-day diary recorded a median intake of 40 g/day (range 10–100 g) on the day with the lowest values and a median of 49 g of fat/day (range 19–109) on the day with the highest intake.

From baseline to discharge, 70 % (100/143) of patients reported a significant overall improvement of symptoms

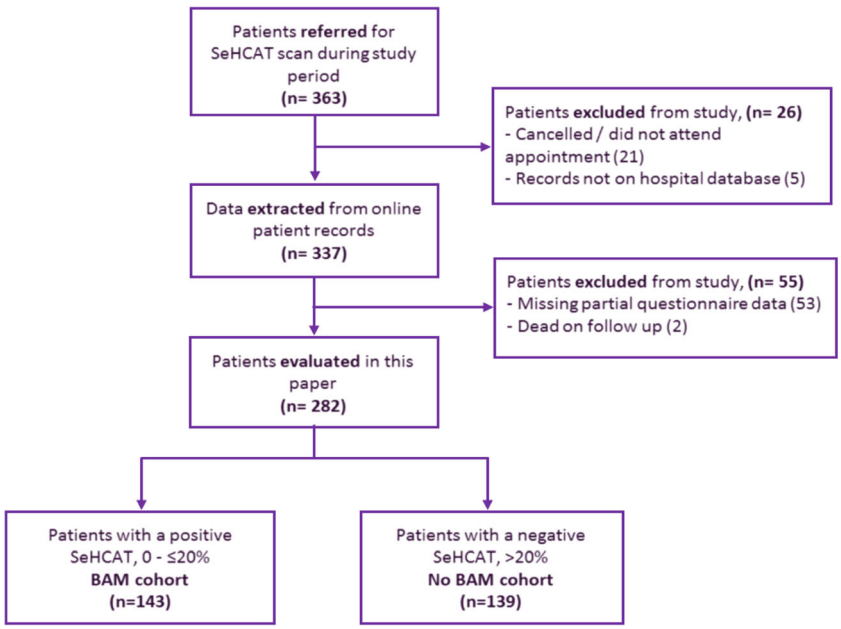

Fig. 2 Flowchart showing patients included and excluded in this study

Table 1 Demographics and clinical characteristics of patients referred to clinic, with a suspected diagnosis of bile acid malabsorption after cancer therapy [*n* (%)]

Characteristics		BAM (*n*=143)	No BAM (*n*=139)	Whole cohort (*n*=282)
Male		57 (40)	79 (57)	136 (48)
Female		86 (60)	60 (43)	146 (52)
Age on referral (median [range])		65 (19–81)	67 (22–89)	66 (19–89)
7-day SeHCAT retention (mean [SD])		8.78 (12.4)	42.69 (12.1)	25.5 (12.3)
Primary tumour site				
Upper GI	Oesophagogastric	9	14	23
	Pancreas	6	6	12
	Hepatobiliary	0	3	3
	Total	15 (10)	23 (17)	38 (13)
Lower GI	Colorectal	21	10	31
	Anal	8	9	17
	Total	29 (20)	19 (15)	48 (17)
Urological	Prostate	26	49	75
	Bladder	1	4	5
	Kidney	0	0	0
	Total	27 (19)	53 (38)	80 (28)
Gynaecological	Cervix	27	9	36
	Endometrial	17	10	27
	Vulva/vaginal	3	5	8
	Ovary	1	1	2
	Total	48 (34)	25 (18)	73 (26)
Haematological	6	3	9	
Lymphoma	9	7	16	
Miscellaneous	Other	9	7	16
	Unknown primary	0	2	2
	Total	9 (6)	9 (6)	18 (6)
Previous treatment				
Radiotherapy		105 (73)	101 (73)	206 (73)
Chemotherapy		89 (62)	71 (51)	160 (57)
GI surgery		67 (47)	41 (29)	108 (38)
Biological therapy		23 (16)	13 (9)	36 (13)
Stem cell therapy		10 (7)	6 (4)	16 (6)
Bowel function before cancer diagnosis				
Normal		105 (73)	90 (65)	195 (69)
Tendency to Diarrhoea		17 (12)	10 (7)	27 (10)
Tendency to Constipation		6 (4)	12 (9)	18 (6)
Other		8 (6)	6 (4)	14 (5)
Unknown		7 (5)	21 (15)	28 (10)

according to the GSRS score (overall mean reduction of score in all 143 patients=−4.2 points, $p<0.0001$) following intervention. Response of symptoms stratified according to SeHCAT treatment groups outlined in Fig. 1 can be seen in Table 4. In the 53 patients who had only BAM and no other GI diagnoses causing their symptoms, 77 % (41/53) reported a mean reduction of −5.4 points, ($p<0.0005$); in the patients who had a SeHCAT 7-day score of >20 %, management of the other causes for their symptoms also led to an improvement in their bowel score 67 % (93/139), with patients reporting a mean reduction of −3.1 points ($p<0.0005$).

Patients with an abnormal SeHCAT scan reported a highly clinically significant improvement in all of the following

Table 2 Response of gastrointestinal symptoms, as recorded in patient questionnaires, after treatment in a study of patients with suspected bile acid malabsorption after cancer therapy

	Change in symptom score [*n* (%)]				Wilcoxon test	
	Improvement	No change	Worse	Did not have symptom	*Z* score	Asymptomatically significant (two-tailed) *p* value
BAM cohort—all patients with a positive SeHCAT (n=143)						
Overall GSRS score	100 (70)	11 (8)	32 (22)	0 (0)		
Urgency	97 (68)	30 (21)	13 (9)	3 (2)	−7.000	0.000
Faecal incontinence	79 (55)	24 (17)	16 (11)	24 (17)	−6.506	0.000
Wind	62 (43)	53 (37)	24 (17)	4 (3)	−4.233	0.000
Nocturnal defaecation	62 (43)	24 (17)	15 (10)	42 (29)	−5.570	0.000
Tiredness	58 (41)	58 (41)	19 (13)	8 (6)	−4.137	0.000
Abdominal pain	57 (40)	50 (35)	17 (12)	19 (13)	−4.994	0.000
Bloating	47 (33)	45 (31)	25 (17)	26 (18)	−4.598	0.000
Steatorrhoea	45 (31)	28 (20)	21 (15)	49 (34)	−3.328	0.001
Pure BAM cohort—no other GI diagnoses (n=53)						
Overall GSRS score	41 (77)	4 (8)	8 (15)	0 (0)		
Urgency	32 (60)	12 (23)	6 (11)	3 (6)	−3.137	0.002
Faecal incontinence	31 (58)	11 (21)	3 (6)	8 (15)	−4.657	0.000
Nocturnal defaecation	26 (49)	7 (13)	2 (4)	18 (34)	−4.337	0.000
Abdominal pain	23 (43)	14 (26)	5 (9)	11 (21)	−3.524	0.000
Bloating	20 (38)	15 (28)	7 (13)	11 (21)	−2.467	0.140
Wind	20 (38)	19 (36)	12 (23)	2 (4)	−1.816	0.069
Tiredness	19 (36)	19 (36)	9 (17)	6 (11)	−1.958	0.050
Steatorrhoea	17 (32)	7 (13)	6 (11)	22 (42)	−2.683	0.007

symptoms by the time they were discharged from our clinic: urgency, faecal incontinence, wind, nocturnal defaecation, tiredness, abdominal pain, bloating, and steatorrhoea (p=<0.0005). Reduction in bowel frequency and an improvement in stool consistency were also reported by the majority of patients (Figs. 3 and 4).

In the cohort of patients (n=53) who had just BAM and no other GI diagnosis made, significant improvements (p=<0.005) were noted in all symptoms except bloating (38 %, p=0.140) and wind (38 %, p=0.069). However, the numbers of patients with these symptoms was small and the study may have not had sufficient power to detect statistically significant improvement.

Discussion

This study which included patients with often very complex problems referred to and treated by the gastrointestinal and nutrition teams (GIaNTs) in a specialist consequences of cancer treatment clinic shows that patients who report even occasional type 6 or 7 stools on a Bristol stool chart, have a high

Table 3 Change in gastrointestinal symptoms, according to overall GSRS score

Cohort	Paired differences (discharge GSRS score−baseline GSRS score)							
	Mean (SD)	Standard deviation	Std. Error Mean	95 % Confidence interval		*t* Value	*df*	*p* Value
				Lower	Upper			
Whole cohort (n=282)	−3.649	6.983	0.416	−4.47	−2.83	−8.776	281	0.000
BAM cohort (n=143)	−4.196	7.036	0.588	−5.36	−3.03	−7.131	142	0.000
No BAM cohort (n=139)	−3.086	6.907	0.586	−4.24	−1.93	−5.268	138	0.000
Pure BAM cohort (n=53)	−5.415	7.234	0.993	−7.45	−3.46	−5.49	52	0.000

Table 4 Response of gastrointestinal symptoms after treatment, according to SeHCAT results

BAM cohort—patients with a positive SeHCAT (n=143)	Change in symptom score [n (%)]				Wilcoxon test	
Symptom	Improvement	No Change	Worse	Did not have symptom	Z score	Asymptomatically significant (two-tailed) p value
Baseline SeHCAT 0 to ≤5 absorption (n=47)						
Overall GSRS score	35 (74)	4 (9)	8 (17)	0 (0)		
Urgency	36 (77)	7 (15)	2 (4)	2 (4)	−4.648	0.000
Faecal incontinence	30 (64)	6 (13)	7 (15)	4 (9)	−4.264	0.000
Nocturnal defaecation	27 (57)	6 (13)	5 (11)	9 (19)	−4.001	0.000
Abdominal pain	25 (53)	11 (23)	6 (13)	5 (11)	−3.532	0.000
Wind	18 (38)	21 (45)	7 (15)	1 (2)	−2.118	0.034
Tiredness	18 (38)	20 (43)	7 (15)	2 (4)	−2.297	0.022
Steatorrhoea	16 (34)	7 (15)	7 (15)	17 (36)	−2.130	0.033
Bloating	8 (17)	24 (51)	7 (15)	8 (17)	−0.677	0.499
Baseline SeHCAT 5 to ≤10 absorption (n=33)						
Overall GSRS score	22 (67)	2 (6)	9 (27)	0 (0)		
Urgency	21 (64)	7 (21)	4 (12)	1 (3)	−3.285	0.001
Tiredness	18 (55)	10 (30)	5 (15)	0 (0)	−2.305	0.021
Wind	16 (48)	9 (27)	7 (21)	1 (3)	−2.047	0.041
Nocturnal defaecation	15 (45)	4 (12)	2 (6)	12 (36)	−3.161	0.002
Bloating	14 (42)	5 (15)	7 (21)	7 (21)	−1.672	0.094
Faecal incontinence	13 (39)	9 (27)	3 (9)	8 (24)	−2.691	0.007
Abdominal pain	12 (36)	15 (45)	3 (9)	3 (9)	−2.501	0.012
Steatorrhoea	9 (27)	4 (12)	6 (18)	14 (42)	−0.766	0.444
Baseline SeHCAT 10 to ≤15 absorption (n=40)						
Overall GSRS score	23 (56)	2 (5)	15 (38)	0 (0)		
Urgency	26 (65)	9 (23)	5 (13)	0 (0)	−3.295	0.001
Faecal incontinence	20 (50)	6 (15)	4 (10)	10 (25)	−2.856	0.004
Wind	16 (40)	14 (35)	9 (23)	1 (3)	−1.512	0.131
Nocturnal defaecation	14 (35)	9 (23)	5 (13)	12 (30)	−2.137	0.033
Bloating	13 (33)	11 (28)	9 (23)	7 (18)	−1.044	0.297
Tiredness	13 (33)	17 (43)	5 (13)	5 (13)	−1.708	0.088
Abdominal pain	12 (30)	17 (43)	5 (13)	6 (15)	−1.882	0.060
Steatorrhoea	10 (25)	13 (33)	5 (13)	12 (30)	−1.414	0.157
Baseline SeHCAT absorption 15 to ≤20 (n=23)						
Overall GSRS score	20 (87)	3 (13)	0 (0)	0 (0)		
Faecal incontinence	16 (70)	3 (13)	2 (9)	2 (9)	−3.257	0.001
Urgency	14 (61)	7 (30)	2 (9)	0 (0)	−2.540	0.011
Bloating	12 (52)	5 (22)	2 (9)	4 (17)	−2.693	0.007
Wind	12 (52)	9 (39)	1 (4)	1 (4)	−2.967	0.003
Steatorrhoea	10 (43)	4 (17)	3 (13)	6 (26)	−2.311	0.021
Tiredness	9 (39)	11 (48)	2 (9)	1 (4)	−2.111	0.035
Abdominal pain	8 (35)	7 (30)	3 (13)	5 (22)	−1.706	0.088
Nocturnal defaecation	6 (26)	5 (22)	3 (13)	9 (39)	−1.155	0.248

frequency of bile acid malabsorption if investigated using a SeHCAT scan. The cohort who had what we consider an abnormal scan, i.e. a 7-day SeHCAT retention of between 0 and 20 %—when managed following an algorithm, improved stool consistency and symptoms of urgency, faecal incontinence, nocturnal defaecation, abdominal pain, bloating, wind, fatigue, steatorrhoea and stool frequency. The greatest improvement was noted for symptoms of urgency and faecal

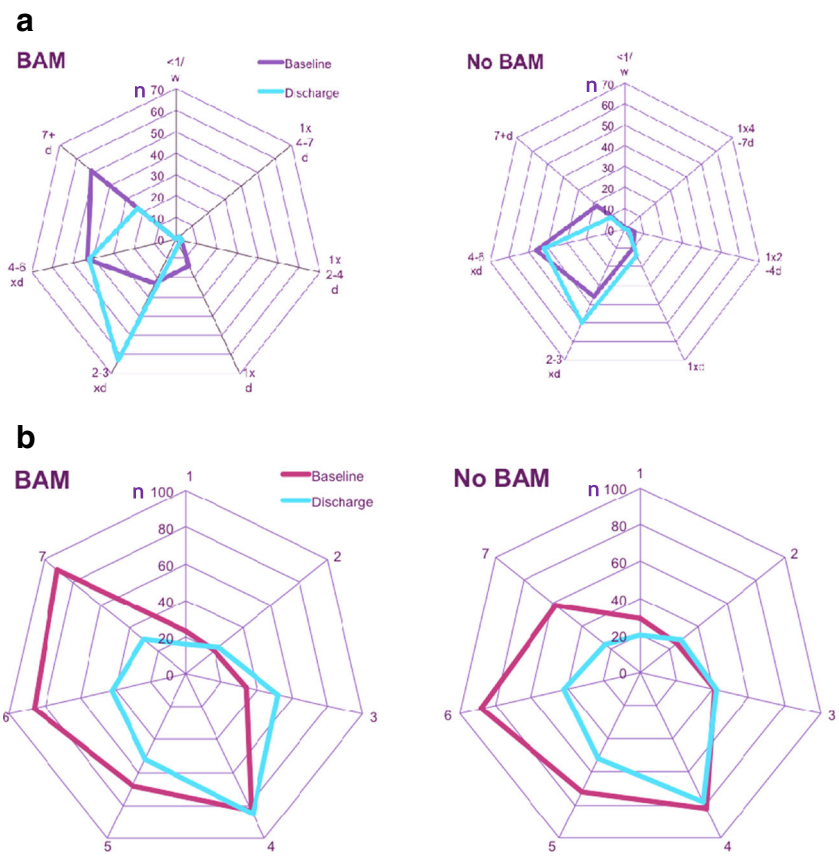

Fig. 3 **a** Spider graph showing change in reported stool frequency [*n* (%)]: Patients had the option to report frequency of bowel actions less than once a week, once every 4–7 days, once every 2–4 days, once per day, two to three times per day, four to six times a day, and seven or more times a day. *d*=day, *w*=week. **b** Spider graph showing change in reported stool consistency as recorded by a Bristol stool chart [*n* (%)]

incontinence, which is reassuring as patients often report these symptoms as the most debilitating of all symptoms [34]. The patients often reported their improvement as considerable.

It is of note that patients with a sole diagnosis of BAM reported the greatest improvement in GSRS symptom score. Furthermore, patients with severe/moderate BAM (SeHCAT retention 0 to ≤10) reported a more significant improvement compared to those with mild borderline BAM (SeHCAT retention 10 to ≤20). This may imply that the management algorithm is particularly effective at treating symptoms specifically attributable to BAM. It is also likely that a greater improvement shown in these patients is due to better compliance with treatment, as noncompliance leads to significantly increased symptom burden. It remains to be seen whether further refinement to the algorithm can lead to improvement in outcomes for GI symptoms due to other causes. However, improvements in bloating and wind did not reach statistical significance and may need to be addressed with better strategies, although these results are perhaps partly explained by flatulence caused by colesevelam, which is a recognised adverse effect of all bile acid sequestrants [35].

This is the largest study to date, and the only study in more than 20 years which evaluates the role of dietary intervention in patients with BAM after cancer therapy. The dietary strategy was to explain to patients the benefits of reducing dietary fat intake to 20 % of total energy and to teach them practical methods by which they could maintain their dietary fat intake at this level long term. From our study, it seems that dietary restriction is a useful approach. BAM and BAD are very common disorders and the recognition that dietary fat reduction improves symptoms is an important therapeutic advance; low-fat dietary lifestyles are cheap to implement, avoid expensive drugs and the risk of side effects from those drugs, and may have significant benefits for the patient (in terms of weight loss and improved cardiovascular status) in addition to the effects it has on their bowel function. However, as this study was retrospective, and a number of different interventions occurred between the first and last clinic visit, we cannot be certain yet as to which patients really benefit from the use of low-fat dietary advice or the degree of that benefit. This needs further urgent study particularly as recent reviews of the management of bile acid malabsorption have completely ignored the relevance of this approach [4].

The retrospective nature of this study poses some limitations, which was most markedly seen as missing patient data. 53 (15 %) of those eligible for this study were excluded due to incompletely recorded/missing questionnaires. Retrospective analysis of records may also result in inaccurate representation of initial findings especially as a small minority of patients misinterpret questions on the GSRS. This may explain why

some patients were discharged from the clinic, and the clinic letter suggested very marked improvement, but their GSRS recorded no benefit.

Patients with consequences of cancer treatment evaluated in this study are a clinically complex group, two thirds or more have GI symptoms arising from multiple causes [36] and in more than a quarter, at least four causes. This complexity is reflected by the fact that patients in whom no diagnosis was made other than BAM seemed to improve more than those with BAM and other causes for GI symptoms.

Finally, not all experts would agree that a SeHCAT scan value between 15 and 20 % accurately diagnoses BAM, and many would consider a value in this range to suggest that the scan is normal. However, by including these patients in this study, it would reduce the magnitude of any benefit seen and not exaggerate it. We believe that BAM cannot be diagnosed by a rigid cutoff value on SeHCAT and symptoms can be treated effectively in some people with such a scan result especially if they have a high dietary intake of fat [37]. In addition, the only study which has looked at the reproducibility of the result of a SeHCAT scan in patients with diarrhoea shows that while it is relatively accurate, it may have sufficient variability to alter the category patients are placed into if repeated [38].

In conclusion, this study in a large cohort of complex patients shows that a systematic multidisciplinary approach to managing GI symptoms related to bile acid malabsorption is effective. Further research is required urgently to investigate the long-term effectiveness of this approach, particularly when and in which patients' dietetic intervention is helpful. This is important in view of the huge population of affected patients with this condition who have never had cancer.

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Conflict of interest HJNA has chaired advisory boards for GE, manufacturers of SeHCAT and for Sanofi Aventis and Genzyme, and manufacturers of Colesevelam and has received honoraria as a speaker and consultant for these companies.

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