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## SYSTEMATIC REVIEW

# Guide to managing persistent upper gastrointestinal symptoms during and after treatment for cancer

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► Additional material is published online only. To view please visit the journal online (<http://dx.doi.org/10.1136/flgastro-2016-100714>).

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Received 20 April 2016  
Revised 30 June 2016  
Accepted 18 July 2016  
Published Online First  
14 October 2016



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**To cite:** Andreyev HJN, Muls AC, Shaw C, et al. *Frontline Gastroenterology* 2017;**8**:295–323.

**ABSTRACT**

**Background** *Guidance: the practical management of the gastrointestinal symptoms of pelvic radiation disease* was published in 2014 for a multidisciplinary audience. Following this, a companion guide to managing upper gastrointestinal (GI) consequences was developed.

**Aims** The development and peer review of an algorithm which could be accessible to all types of clinicians working with patients experiencing upper GI symptoms following cancer treatment.

**Methods** Experts who manage patients with upper GI symptoms were asked to review the guide, rating each section for agreement with the recommended measures and suggesting amendments if necessary. Specific comments were discussed and incorporated as appropriate, and this process was repeated for a second round of review.

**Results** 21 gastroenterologists, 11 upper GI surgeons, 9 specialist dietitians, 8 clinical nurse specialists, 5 clinical oncologists, 3 medical oncologists and 4 others participated in the review. Consensus (defined prospectively as 60% or more panellists selecting 'strongly agree' or 'agree') was reached for all of the original 31 sections in the guide, with a median of 90%. 85% of panellists agreed that the guide was acceptable for publication or acceptable with minor revisions. 56 of the original 61 panellists participated in round 2. 93% agreed it was acceptable for publication after the first revision. Further minor amendments were made in response to round 2.

**Conclusions** Feedback from the panel of experts developed the guide with improvement of occasional algorithmic steps, a more user-friendly layout, clearer time frames for referral to other teams and addition of procedures to the appendix.

**INTRODUCTION**

This guide is designed for all clinicians who look after people who have been treated for upper gastrointestinal (GI) cancer. It is also designed for patients who are experiencing upper GI symptoms following any cancer treatment. Some of these will be doctors, others may be senior nurses and increasingly, other allied health professionals.

Some lower GI symptoms are also included because these are common after treatment for upper GI cancers. However, for more detailed advice about managing lower GI symptoms please refer to *Guidance: The practical management of the gastrointestinal symptoms of pelvic radiation disease*.<sup>1</sup>

The GI consequences of chemotherapy, radiotherapy and resectional surgery are not that different. Historically, clinicians have associated specific clusters of symptoms with typical diagnoses especially in patients who have been treated for upper GI and hepatopancreatobiliary cancer. Research increasingly suggests that specific symptoms are not reliable indicators of the underlying cause, hence, this algorithmic approach.

This guide defines best practice although not every investigation modality or treatment may be available in every hospital.

Those using the guide, especially if non-medically qualified, should identify a senior gastroenterologist or other appropriately qualified and experienced professionals whom they can approach easily for advice if they are practicing in an unsupervised clinic.

Practitioners should not use this guide outside the scope of their competency

and must identify from whom they will seek advice about abnormal test results which they do not fully understand before using the guide.

Specific therapies are usually not listed by name but as a ‘class’ of potential drugs as different clinicians may have local constraints or preferences as to the medications available.

Arranging all first line suggested investigations required by the symptom(s) at the first consultation reduces follow-up and allows directed treatment of all causes of symptoms at the earliest opportunity. Timely review of requested investigations is required so that further investigations can be requested if required. If worrying symptoms are elicited or potentially abnormal findings are present on clinical examination, then the order of investigations suggested in the algorithm may no longer be appropriate.

Practitioners seeing these patients are encouraged to consider providing patients with symptom questionnaires including nutritional screening questions to complete before or during the consultation as this may help improve the choice of investigations and identify when referral is required.

This guide has three parts:

1. An introduction, instructions how to use the algorithm, guide to blood tests and taking a history.
2. An algorithm detailing the individual investigations and treatment of each of the 28 GI symptoms.

3. Appendices with brief descriptions of the diagnosis, treatment and management techniques available.

**HOW TO USE THE ALGORITHM**

1. Up to 28 symptoms have been described in this patient group.
2. Each symptom may have more than one contributing cause.
3. Symptoms must be investigated systematically otherwise causes will be missed.
4. Identify the symptoms by systematic history taking.
5. Examine the patient appropriately.
6. Use the algorithm to plan investigations.
7. Most patients have more than one symptom and investigations need to be requested for each symptom.
8. Usually all investigations are requested at the same time and the patient reviewed with all the results.
9. When investigations should be ordered sequentially, the algorithm indicates this by stating first line, second line, etc.
10. Treatment options are generally offered sequentially but clinical judgement should be used.

**GUIDE TO USING BLOOD TESTS**

Routine blood tests include: full blood count, urea and electrolytes, liver function, glucose, calcium (table 1).

Additional blood tests are indicated depending on the presenting GI symptoms and differential diagnoses as outlined in the algorithm (table 2).

**Table 1** Routine blood tests: responding to results

Anaemic and symptomatic	<ul style="list-style-type: none"> <li>▶ Consider blood transfusion (checking ferritin, transferrin saturation, RBC folate and vitamin B<sub>12</sub> before transfusion).</li> <li>▶ If iron deficient: consider iron supplements and coeliac screen (ie tissue transglutaminase and IgA levels), OGD, SI biopsy, colonoscopy and renal tract evaluation.</li> </ul>
Anaemic but not symptomatic	<ul style="list-style-type: none"> <li>▶ Check ferritin, transferrin saturation, RBC folate and vitamin B<sub>12</sub>. Replace if necessary, monitor response. If unexplained consider coeliac screen, OGD, SI biopsy and colonoscopy and renal tract evaluation.</li> <li>▶ If anaemia is unexplained, refer to haematology.</li> </ul>
Abnormal urea, electrolytes	<ul style="list-style-type: none"> <li>▶ Urine dipstix.</li> <li>▶ Discuss with supervising clinician within 24 hours.</li> <li>▶ Consider appropriate intravenous fluid therapy/oral replacement.</li> <li>▶ If K<sup>+</sup> &lt;3 mmol/L or &gt;6 mmol/L, this is an emergency.</li> <li>▶ If Na<sup>+</sup> &lt;120 or &gt;150 mmol/L, this is an emergency.</li> </ul>
Abnormal liver function tests (new onset)	<ul style="list-style-type: none"> <li>▶ Discuss with supervising clinician within 24 hours.</li> <li>▶ Check thyroid function</li> <li>▶ Patient will need a liver ultrasound and liver screen including hepatitis A, B, C and E serology, EBV and CMV, ferritin, α feta protein, α 1 antitrypsin, coeliac serology, liver autoantibodies, total Igs, cholesterol, triglycerides, caeruloplasmin (&lt;50 years old only).</li> </ul>
Abnormal liver function tests (long standing)	<ul style="list-style-type: none"> <li>▶ Refer for further evaluation to a hepatologist.</li> </ul>
Abnormal glucose level	<ul style="list-style-type: none"> <li>▶ If no history of diabetes:                             <ul style="list-style-type: none"> <li>Between 7–11 mmol/L: refer to GP.</li> <li>&gt;11 mmol/L and ketones in urine: this is an emergency.</li> <li>&gt;11–20 mmol and no ketones in urine: discuss with supervising clinician within 24 hours.</li> <li>&gt;20 mmol/L and no ketones in urine: this is an emergency.</li> </ul> </li> <li>▶ If known diabetic:                             <ul style="list-style-type: none"> <li>Do not check glucose levels.</li> <li>Consider checking glycosylated haemoglobin (HbA1C).</li> </ul> </li> </ul>
Abnormal corrected calcium level	<ul style="list-style-type: none"> <li>▶ If 2.6–2.9 mmol/L: discuss with supervising clinician within 24 hours.</li> <li>▶ If &lt;1.8 mmol/L or &gt;3.0 mmol/L: this is an emergency.</li> <li>▶ Check parathyroid hormone levels.</li> </ul>

CMV, cytomegalovirus; EBV, Epstein-Barr virus; GP, general practitioner; K, potassium; Na, sodium; OGD, upper GI endoscopy (oesophago-gastroduodenoscopy); RBC, red blood cell; SI, small intestine.

**Table 2** Additional blood tests: responding to results

Elevated ESR/CRP	<ul style="list-style-type: none"> <li>▶ Consider the following possibilities:                             <ul style="list-style-type: none"> <li>– Infection.</li> <li>– Inflammation (including IBD).</li> <li>– Recurrent malignancy.</li> <li>– Non-GI causes (eg, rheumatoid arthritis, vasculitis, connective tissue disorders).</li> </ul> </li> </ul>
RBC folate deficiency	<ul style="list-style-type: none"> <li>▶ Consider referral to dietitian for dietetic advice/supplementation.</li> <li>▶ Check coeliac screen.</li> </ul>
Iron deficiency: ferritin, % transferrin saturation, red cell indices	<ul style="list-style-type: none"> <li>▶ If iron is low and iron saturation is low, discuss with supervising clinician and oncology team within 2 weeks.</li> <li>▶ If intolerant of oral iron: consider intravenous iron infusion.</li> </ul>
If excess iron=raised ferritin with transferrin saturation>45%	<ul style="list-style-type: none"> <li>▶ Consider haemochromatosis: Discuss with supervising clinician and consider genetic testing.</li> </ul>
Low vitamin B <sub>12</sub>	<ul style="list-style-type: none"> <li>▶ Exclude the possibility of inadequate dietary intake (especially vegans)—if this is the probable cause, consider trial of oral vitamin B<sub>12</sub> supplements. Dietetic referral.</li> <li>▶ Consider possibility of pernicious anaemia—check parietal cell and intrinsic factor antibodies.</li> <li>▶ Exclude SIBO (p. 27). Recheck result after treatment with antibiotics.</li> <li>▶ Check coeliac screen.</li> <li>▶ If confirmed on repeat testing and not treatable with oral replacement, eg, after gastrectomy, ask GP to arrange lifelong intramuscular replacement.</li> <li>▶ Metformin therapy.</li> </ul>
Abnormal thyroid function tests	<ul style="list-style-type: none"> <li>▶ If TSH suppressed (&lt;0.5 mIU/L), recheck result with thyroid auto antibodies.</li> <li>▶ If TSH suppression confirmed, request GP to organise/refer for radiological imaging and treatment.</li> <li>▶ If TSH elevated (&gt;4.0 mIU/L), recheck result. Also check 09:00 cortisol if Na ≤135 mmol/L and K<sup>+</sup> &gt;4 mmol/L or raised urea or creatinine.</li> <li>▶ If TSH elevation confirmed: start thyroid replacement medication. Request GP to monitor long-term. Review bowel function after 6–8 weeks.</li> </ul>
Abnormal coeliac serology	<ul style="list-style-type: none"> <li>▶ If IgA deficient, request IgG coeliac screen.</li> <li>▶ If TTG elevated, confirm with SI biopsy.</li> <li>▶ Refer for dietetic advice once diagnosis is confirmed.</li> <li>▶ Refer to coeliac clinic.</li> </ul>
Serum Mg <sup>2+</sup>	<ul style="list-style-type: none"> <li>▶ If &lt;0.3 mmol/L, this is an emergency.</li> <li>▶ Check K<sup>+</sup> and Ca<sup>2+</sup>, if low, will also need replacement.</li> <li>▶ If 0.3–0.5, consider intravenous replacement if symptomatic or fall in Mg<sub>2</sub> level has been acute. If oral replacement is given, check for response after 5–7 days with repeat blood tests.</li> <li>▶ If oral replacement is used, Mg Oxide or Mg aspartate provide better bioavailability and cause less diarrhoea than other Mg preparations.</li> <li>▶ If associated with refeeding syndrome, also monitor PO<sub>4</sub> and K<sup>+</sup> closely and give intravenous vitamin replacement.</li> </ul>

Ca, calcium; CRP, C reactive protein; ESR, erythrocyte sedimentation rate; GI, gastrointestinal; GP, general practitioner; IBD, inflammatory bowel disease; K, potassium; Mg, magnesium; Na, sodium; PO<sub>4</sub>, phosphate; RBC, red blood cell; SIBO, small intestinal bacterial overgrowth; TSH, thyroid stimulating hormone; TTG, tissue transglutaminase.

**Table 3** Specific blood tests: responding to the results

Any malabsorptive syndromes, eg, Pancreatic insufficiency, BAM	<ul style="list-style-type: none"> <li>▶ Check vitamin D, trace elements (selenium, copper and zinc) and INR (for vitamin K).</li> <li>▶ If deficient: start appropriate supplementation and recheck levels in 3 months</li> <li>▶ Request yearly monitoring via GP.</li> </ul>
Short bowel syndrome	<ul style="list-style-type: none"> <li>▶ Check vitamin D, trace elements (selenium, copper and zinc) and INR (for vitamin K).</li> <li>▶ Spot urine sodium.</li> <li>▶ If deficient: start appropriate supplementation and recheck levels in 3 months</li> <li>▶ Request yearly monitoring via GP.</li> </ul>
If bleeding	<ul style="list-style-type: none"> <li>▶ Check full blood count and INR.</li> <li>▶ Discuss immediately with supervising clinician and gastroenterologist/GI surgeon/haematologist.</li> </ul>
When on a bile acid sequestrant	<ul style="list-style-type: none"> <li>▶ Check triglyceride levels annually.</li> <li>▶ Check vitamin D and INR (for vitamin K) annually.</li> <li>▶ Check trace elements (selenium, zinc, copper) annually.</li> </ul>
Cortisol level	<ul style="list-style-type: none"> <li>▶ 09:00 am level needed. If low, arrange synacthen test. If abnormal, needs immediate discussion with endocrinologist.</li> </ul>
Severe acute abdominal pain	<ul style="list-style-type: none"> <li>▶ Amylase. If elevated this is an emergency.</li> </ul>
Neuroendocrine tumour	<ul style="list-style-type: none"> <li>▶ Urinary 5HIAA.</li> <li>▶ Chromogranin A+B.</li> </ul>

5HIAA, 5-hydroxyindole acetic acid; BAM, bile acid malabsorption; GI, gastrointestinal; GP, general practitioner; INR, international normalised ratio.

They potentially include: erythrocyte sedimentation rate, C reactive protein, red cell folate, iron studies, vitamin B<sub>12</sub>, thyroid function test, coeliac serology (tissue transglutaminase IgA), magnesium, amylase (table 2).

Specific tests are indicated depending on the symptoms/diagnosis as outlined in the algorithm.

They may include fat soluble vitamins, trace elements, fasting gut hormones, international normalised ratio, haematinics (table 3).

**TAKING AN APPROPRIATE HISTORY**

Patients cannot be helped without an accurate history being taken.

- ▶ Taking a history of GI symptoms is a skill that must be learnt.
- ▶ Specialist units find that symptom questionnaires completed by the patient before the consultation often help clarify which issues are really troubling the patient.
- ▶ Take a broad approach: for example, after treatment for upper GI cancer, patients also frequently develop troublesome lower GI symptoms.

**Taking a history needs to elicit**

- ▶ What was GI function like before the cancer emerged?
- ▶ How have the symptoms changed over time and how severe are they?
- ▶ If the patient has received multimodality treatment, how did symptoms change after each treatment component was delivered?
- ▶ Are key features indicative of potentially serious underlying pathology present, for example,

- Rapid progressive worsening of symptoms?
- Rapid weight loss?
- Has the patient noticed any masses?
- ▶ Are there key features possibly indicative of reversible underlying pathology present, for example,
  - Sudden onset symptoms?
  - Nocturnal waking from the symptom?
  - Development of steatorrhoea?
- ▶ Is there a consistent impact of a specific component of diet on their symptoms, especially:
  - Alcohol intake?
  - Are they eating/drinking too much at each sitting?
  - Are they eating erratically?
  - Fat intake?
  - Fibre: how much are they eating—too much/too little?
  - Gluten-containing foods?
  - Lactose-containing foods?
  - Other carbohydrates intake?
- ▶ Is there an association between the start of specific medication or increase in its dose and their symptoms—for example, metformin, lansoprazole, β-blockers?
- ▶ Ask specifically about the presence of intermittent steatorrhoea (see p. 22). After upper GI cancer, this commonly indicates the development of one or more of the following:
  - Small intestinal bacterial overgrowth.
  - Pancreatic insufficiency.
  - Severe bile acid malabsorption (BAM).

**THE GI SYMPTOMS**

**APPETITE: POOR/REDUCED** (*anorexia*) (supplementary figure 1 and table 4)

**Table 4** Investigation and management of anorexia

Investigations	Potential results	Clinical management plan
<b>Actions from history, medication and dietary assessment</b>		
History findings	Weight loss/sweats/fatigue	Routine and additional blood tests. CT chest, abdomen, pelvis. Refer for dietetic advice.
	Depression, sadness, anxiety	Refer for psychological support.
	Underlying eating disorder	Refer for psychiatric assessment.
	Pre-existing comorbidities, eg, Cardiac failure COPD Chronic kidney disease Chronic liver disease	Refer for dietetic advice and appropriate GP/specialist advice to optimise these conditions.
	Constipation	See management of constipation (p. 26).
Medication findings	Antibiotics, eg, cotrimoxazole, metronidazole, chemotherapy, eg, cytarabine, hydroxyurea, opioids, metformin, NSAID	Discuss possible alternative medications and adequate antiemetics while on treatment.
<b>First line</b>		
Routine and additional blood tests	Infection	Treat with antibiotics within level of confidence or discuss with microbiologist/supervising clinician within 24 hours.
	Endocrine dysfunction	Refer the patient to the GP or endocrinology team for further management.
	Other abnormalities	Follow treatment for abnormal blood results (p. 2).

Continued

**Table 4** Continued

Investigations	Potential results	Clinical management plan
<b>Second line</b>		
OGD and SI aspirate (p. 25)	Inflammation (acid/bile) Gastric dysmotility	See management of acid or bile related inflammation (p. 25). Consider prokinetic medication (p. 26). ± pyloric dilatation.
	SIBO	Management of SIBO (p. 27).
	Malignancy/tumour recurrence	Discuss and refer urgently to the appropriate cancer MDT requesting an appointment within 2 weeks. Refer for dietetic advice.
Glucose hydrogen methane breath test	SIBO	Management of SIBO (p. 27).
CT/MRI/PET	Malignancy/tumour recurrence	Discuss and refer urgently to the appropriate cancer MDT requesting an appointment within 2 weeks. Refer for dietetic advice.
	Infection	Treat with antibiotics within level of confidence or discuss with a microbiologist and supervising clinician immediately.
	Small bowel obstruction	If acute, this is an emergency. Discuss immediately with a GI surgeon. If subacute/chronic discuss immediately with supervising clinician.
<b>Third line</b>		
If normal investigations/no response to intervention		Reassure.

CT, computerised tomography; GI, gastrointestinal; GP, general practitioner; MDT, multidisciplinary team; NSAID, non-steroidal anti-inflammatory drug; OGD, upper GI endoscopy (oesophago-gastroduodenoscopy); MRI, magnetic resonance imaging; PET, positron emission tomography; SI, small intestine; SIBO, small intestinal bacterial overgrowth.

**BELCHING/BURPING** (*eructation*) (Supplementary [figure 2](#) and [table 5](#))

**Table 5** Investigation and management of belching/burping

Investigations	Potential results	Clinical management plan
<b>Actions from history, medication and dietary assessment</b>		
History findings	Aerophagia (excessive swallowing of air)	Eat slowly. Reduce chewing gum and temperature of hot drinks.
	Carbohydrate sensitivity	Assess for carbohydrate malabsorption (p. 26). Psychological support.
Medication findings	Use of effervescent medications	Discuss alternatives available.
	Sedatives, eg, temazepam	Discuss alternatives available.
	Metformin	Change to long-acting preparation.
Dietary findings	Excessive use of carbonated drinks	Advise regarding reducing carbonated drinks intake.
	Eating/drinking too much in one sitting	Eat/drink little and often.
<b>First line</b>		
OGD and SI aspirate (p. 25)	Malignancy/tumour recurrence	Refer to appropriate MDT requesting an appointment within 2 weeks.
	SIBO	Management of SIBO (p. 27).
	Stricture formation	Dilatation of anastomosis (p. 25)±dilatation of pylorus (if evidence of delayed gastric emptying) with careful biopsy.
Glucose hydrogen methane breath test	SIBO	Management of SIBO (p. 27).
<b>Second line</b>		
If normal investigations/no response to intervention		<ul style="list-style-type: none"> <li>▶ Refer to dietitian for trial of low FODMAPS diet.</li> <li>▶ Reassure.</li> </ul>

FODMAPS, fermentable oligo-di-monosaccharides and polyols; MDT, multidisciplinary team; OGD, upper GI endoscopy (oesophago-gastroduodenoscopy); SI, small intestine; SIBO, small intestinal bacterial overgrowth

**BLOATING**

An uncomfortable feeling that the abdomen is full or distended or visibly swells (Supplementary figure 3 and table 6).

**Table 6** Investigation and management of bloating

Investigations	Potential results	Clinical management plan
<b>Actions from history, medication and dietary assessment</b>		
History findings	Constipation Dumping syndrome	See management of constipation (p. 26). See p. 20 (postprandial symptoms).
Medication findings	Opioids Metformin Statins NSAIDs	Consider stopping or alternative medications.
Dietary findings	Eating/drinking too much in one sitting Inadequate/excessive fluid or fibre intake Excessive sorbitol Excessive caffeine	1. Dietary advice. 2. Referral to a dietitian with a 7-day food diary.
<b>First line</b>		
Routine and additional blood tests	Abnormal results	Follow treatment for abnormal blood results (p. 2).
In women, also check Ca 125	Raised	Refer to gynaecology requesting an appointment within 2 weeks.
AXR	Faecal loading Ileus/obstruction  Bone fracture Gall stones Air in biliary tree Pleural effusion	See management of constipation (p. 26). This is an emergency. Discuss immediately with GI surgeon and arrange urgent CT scan.  Discuss with supervising clinician within 24 hours.
<b>Second line</b>		
OGD and SI aspirate and SI biopsies (p. 25)	SIBO Inadequate gastric emptying Coeliac disease	Management of SIBO (p. 27). Prokinetics (p. 26). Consider formal gastric emptying studies. Refer to coeliac clinic/dietitians/gastroenterology.
Glucose hydrogen methane breath test	SIBO	Management of SIBO (p. 27).
Stool sample for faecal elastase	EPI	Management of EPI (p. 26).
Carbohydrate challenge	Carbohydrate intolerance/ malabsorption	Management of carbohydrate malabsorption (p. 26).
CT/MRI abdomen and pelvis	Intra-abdominal pathology, eg, ascites Malignancy/tumour recurrence	Discuss with supervising clinician within 24 hours. Refer to appropriate MDT requesting an appointment within 2 weeks.
<b>Third line</b>		
US biliary tree and Doppler	Suggestive of gallstones, tumour recurrence Malignancy/tumour recurrence Ascites	Discuss with supervising clinician and refer as clinically appropriate to a GI surgeon/gastroenterologist/oncology team. Refer to appropriate MDT requesting an appointment within 2 weeks. Discuss with supervising clinician within 24 hours.
MRI small bowel/enteroclysis/enterogram	Small bowel disease	Discuss with supervising clinician and refer as clinically appropriate to a GI surgeon/gastroenterologist/oncology team.
<b>Fourth line</b>		
If normal investigations		Refer to dietitian for a trial of low FODMAPs diet.
<b>Fifth line</b>		
If no response to intervention		Referral for gastroenterology for small bowel motility studies. Reassure.

AXR, abdominal X-ray; CT, computerised tomography; EPI, exocrine pancreatic insufficiency; FODMAPs, fermentable oligo-di-monosaccharides and polyols; GI, gastrointestinal; MDT, multidisciplinary team; MRI, magnetic resonance imaging; NSAID, non-steroidal anti-inflammatory drug; OGD, upper GI endoscopy (oesophago-gastroduodenoscopy); SI, small intestine; SIBO, small intestinal bacterial overgrowth; US, ultrasound.

**BORBORYGMI**

Rumbling/gurgling noises in the abdomen (Supplementary figure 4 and table 7).

**Table 7** Investigation and management of borborygmi

Investigations	Potential results	Clinical management plan
<b>Actions from history, medication and dietary assessment</b>		
History findings	Faecal loading	Plain AXR.
	Obstruction	
	Mass	CT scan.
	Fibre excess/inadequacy	Refer for dietetic advice.
<b>First line</b>		
Routine and additional blood tests	Abnormal results	Follow treatment for abnormal blood results (p. 2).
Glucose hydrogen methane breath test	SIBO	Management of SIBO (p. 27).
OGD and SI aspirate (p. 25) and biopsies	Enteric infection	Treat as recommended by microbiologist.
	SIBO	Management of SIBO (p. 27).
	Coeliac disease	Refer to coeliac clinic/dietitians/gastroenterology.
Carbohydrate challenge	Carbohydrate malabsorption	Management of carbohydrate malabsorption (p. 26).
<b>Second line</b> , if borborygmi are present in combination with other symptoms: flushing, abdominal pain, diarrhoea, wheezing, tachycardia or fluctuations in BP		
Fasting gut hormones	Functioning NET eg, carcinoid syndrome or pancreatic NET	Discuss and refer urgently to the appropriate neuroendocrine MDT requesting an appointment within 2 weeks.
Chromogranin A+B		
Urinary 5-HIAA		
CT chest, abdomen, pelvis		
Plain AXR	Ileus/obstruction	This is an emergency. Discuss immediately with a GI surgeon and arrange urgent CT scan.
	Faecal loading	See management of constipation (p. 26).
<b>Third line</b>		
Colonoscopy	Inflammatory bowel disease	Send stool culture. If mild or moderate, refer urgently to gastroenterology. If severe, this is an emergency. Discuss immediately with a gastroenterologist.
<b>Fourth line</b>		
If normal investigations/no response to intervention		Reassure.

5HIAA, 5-hydroxyindole acetic acid; AXR, abdominal X-ray; CT, computerised tomography; GI, gastrointestinal; MDT, multidisciplinary team; NET, neuroendocrine tumour; OGD, upper GI endoscopy (oesophago-gastroduodenoscopy); SIBO, small intestinal bacterial overgrowth.

**CHANGE IN SENSE OF SMELL** (hyposmia, anosmia or parosmia)

The reduced ability, inability or distortion of sensation of odour (Supplementary figure 5 and table 8).

**Table 8** Investigation and management of change in smell

Investigations	Potential results	Clinical management plan
<b>Actions from history, medication and dietary assessment</b>		
Medication findings	Chemotherapy related	1. Reassure.
	Opioid related	2. Consider alternative medications. 3. Consider referral to psychological medicine. 4. Inform patient about the charity Fifth Sense. <sup>2</sup>
<b>First line</b>		
Testing of the olfactory nerve	Neurological defect	Refer to neurology team.
	Olfactory hallucinations	1. Consider neurological referral. 2. Consider referral to psychological medicine.
Blood test for zinc and vitamin B <sub>12</sub>	Deficient	Arrange replacement.
<b>Second line</b>		
Refer to ENT team	Eg, nasal polyps, sinus infection	

Continued

**Table 8** Continued

Investigations	Potential results	Clinical management plan
CT/MRI head/PET	Base of skull disease	Refer to the appropriate MDT requesting an appointment within 2 weeks.
<b>Third line</b>		
If normal investigations/no response to intervention		Reassure.

CT, computerised tomography; ENT, ear, nose and throat; MDT, multidisciplinary team; MRI, magnetic resonance imaging; PET, positron emission tomography.

**CHANGE IN SENSE OF TASTE** (hypogeusia, ageusia or dysgeusia)

The reduced ability, inability or distortion of sensation of taste (Supplementary figure 6 and table 9).

**Table 9** Investigation and management of change in taste

Investigations	Potential results	Clinical management plan
<b>Actions from history, medication and dietary assessment</b>		
History findings	Smoking	Smoking cessation advice.
Medication findings (see p. 80)	Chemotherapy/radiotherapy induced	1. Reassure patient. 2. Refer for dietetic advice around appropriate foods. 3. Inform patient about the charity Fifth Sense. <sup>2</sup>
	Medication induced	Discuss alternative options available. See 'Medications that may induce mucositis or change in sense of taste' (p. 27).
Dietary findings	Nutritional compromise	Refer for dietetic advice.
<b>First line</b>		
Visual inspection of mouth	Oral candidiasis Dental problems/poor oral hygiene	Antifungal therapy. Refer to dentist/oral hygienist.
Blood test for vitamin B <sub>12</sub> , zinc and selenium	Deficient	Arrange replacement.
<b>Second line</b>		
OGD	GORD	Start PPI or H2 antagonist. If following oesophagectomy, consider promotility agents (see p. 26).
	Candidiasis	Antifungal therapy.
If rapid/progressive unexplained changes, then CT/MRI head/PET	Base of skull disease	Refer to the appropriate MDT requesting an appointment within 2 weeks.
<b>Third line</b>		
If normal investigations/no response to intervention		Reassure.

CT, computerised tomography; GORD, gastro-oesophageal reflux disease; H2, histamine receptor 2; MDT, multidisciplinary team; OGD, upper GI endoscopy (oesophago-gastroduodenoscopy); PET, positron emission tomography; PPI, proton pump inhibitor.

**CHRONIC COUGH** (*tussis*) lasting longer than 3 weeks (Supplementary figure 7 and table 10)

**Table 10** Investigation and management of chronic cough

Investigations	Potential results	Clinical management plan
<b>Actions from history, medication and dietary assessment</b>		
History findings	After food	Follow guideline for dysphagia (see tables 14 and 16).
	Allergic rhinitis	Refer the patient to GP for further management.
	Smoking	Advise smoking cessation.
	COPD	Refer the patient to the GP for further management.
	Obstructive sleep apnoea	Refer the patient to the GP for further management.
	Upper airway conditions:	Refer to ENT team.
	Chronic tonsil enlargement	
	Irritation of external meatus	
	Laryngeal problems	

Continued

Table 10 Continued

Investigations	Potential results	Clinical management plan
Medication findings	Cough with excess secretions in pharynx or globus ACE inhibitors	OGD, look specifically for inlet patch. SLT assessment including a contrast swallow. Reassure patient and suggest discussing possible alternatives with the GP or cardiology team.
<b>First line</b>		
Auscultation chest and heart	Cardiac conditions eg, left ventricular failure, tachycardia Respiratory conditions: Aspiration	Discuss immediately with supervising clinician.  <ul style="list-style-type: none"> <li>▶ Nil by mouth.</li> <li>▶ SLT assessment.</li> <li>▶ Alternative feeding.</li> </ul>
Routine and additional blood tests CXR	Other respiratory causes Abnormal results Cardiac causes: ▶ Left ventricular failure ▶ Thoracic aortic aneurysm Malignancy/tumour recurrence Aspiration	Discuss with supervising clinician within 24 hours. Follow treatment for abnormal blood results (p. 2).  Refer to GP/cardiology/acute medicine. Refer to cardiothoracic surgery. Refer to appropriate MDT requesting an appointment within 2 weeks.  <ul style="list-style-type: none"> <li>▶ Nil by mouth.</li> <li>▶ SLT assessment.</li> <li>▶ Alternative feeding.</li> </ul>
	Radiation pneumonitis Pulmonary embolism Other respiratory causes	Refer to respiratory physician. This is an emergency. Contact the on-call medical team. Discuss with supervising clinician within 24 hours.
<b>Second line</b>		
OGD	Vocal cord abnormality, eg, polyp GORD	Refer to ENT. Start PPI or H2 antagonist. If following oesophagectomy, consider promotility agents (see p. 26).
	Anastomotic stricture±pyloric stenosis	Consider dilatation (p. 25) with careful biopsy only after agreement from the appropriate MDT.
	Malignancy/tumour recurrence	Refer to appropriate MDT requesting an appointment within 2 weeks.
Trial of PPI	Cervical inlet patch GORD	Treat with PPI or ablation. Consider GORD
Trial of mucaine/sucralfate	Bile reflux	Consider prokinetics (p. 26).
<b>Third line</b>		
CT chest/CTPA	Pulmonary embolism Cardiac causes: Left ventricular failure Thoracic aortic aneurysm Malignancy/tumour recurrence Other respiratory causes	This is an emergency. Contact the on-call medical team. Refer to GP/cardiology/acute medicine.  Refer to cardiothoracic surgery. Refer to appropriate MDT requesting an appointment within 2 weeks. Discuss with supervising clinician within 24 hours.
<b>Fourth line</b>		
Oesophageal manometry/pH/impedance studies	Spasm  Scleroderma	<ol style="list-style-type: none"> <li>1. Start PPI or H2 antagonist.</li> <li>2. Calcium antagonist.</li> <li>3. Low dose antidepressant, eg, citalopram.</li> <li>4. Refer to gastroenterology.</li> </ol> <ol style="list-style-type: none"> <li>1. Start PPI or H2 antagonist.</li> <li>2. Refer to rheumatology.</li> </ol>
<b>Fifth line</b>		
If normal investigations/no response to intervention		Reassure.

ACE, angiotensin converting enzyme; COPD, chronic obstructive pulmonary disease; CT, computerised tomography; CTPA, CT pulmonary angiography; CXR, chest X-ray; ENT, ear, nose and throat; GORD, gastro-oesophageal reflux disease; GP, general practitioner; H2, histamine -2; MDT, multidisciplinary team; OGD, upper GI endoscopy (oesophago-gastroduodenoscopy); PPI, proton pump inhibitor; SLT, speech and language therapy.

**DIARRHOEA**

Stool type 6–7 on the Bristol stool chart.<sup>3</sup> **Not** increased frequency of type 1–5 (Supplementary figure 8 and table 11).

**Table 11** Investigation and management of diarrhoea

Investigations	Potential results	Clinical management plan
<b>Actions from history, medication and dietary assessment</b>		
History findings	Smoking	Lifestyle advice about smoking cessation.
	Anxiety	Consider referral for psychological support.
	Dumping syndrome	See p. 20.
Medication findings	Drug induced: eg, PPIs	Medications advice.
	Laxatives	
	β blockers	
	Metformin	
Dietary findings	Low/high fibre intake, high fizzy drink intake, high use of sorbitol containing chewing gum or sweets, high caffeine intake, high alcohol intake	<ol style="list-style-type: none"> <li>1. Dietary advice about healthy fibre and dietary fat intake.</li> <li>2. Referral to dietitian and ask patient to complete 7-day dietary diary beforehand.</li> <li>3. Lifestyle advice about smoking cessation and alcohol/caffeine reduction.</li> </ol>
<b>First line</b>		
Routine and additional blood tests	Abnormal results	Follow treatment for abnormal blood results (p. 2).
	Mg <sup>2+</sup> low	Follow treatment for abnormal blood results (p. 2).
	Coeliac disease	Refer to coeliac clinic/dietitians/gastroenterology.
Stool sample for microscopy, culture and <i>Clostridium difficile</i> toxin	Stool contains pathogens	Treat as recommended by the microbiologist and local protocols.
Stool sample for faecal elastase	EPI	Management of EPI (p. 26).
OGD and SI aspirate (p. 25) and SI biopsies	SIBO	Management of SIBO (p. 27).
	Coeliac disease	Refer to coeliac clinic/dietitians/gastroenterology.
	Giardiasis	Metronidazole.
Glucose hydrogen methane breath test	SIBO	Management of SIBO (p. 27).
	Carbohydrate challenge	Management of carbohydrate malabsorption (p. 26).
SeHCAT scan	BAM	Management of BAM (p. 25).
Colonoscopy with biopsies (if frail, consider flexible sigmoidoscopy instead of colonoscopy)	Macroscopic colitis	Send stool culture. If mild or moderate, refer urgently to gastroenterology. If severe, this is an emergency. Discuss immediately with a gastroenterologist.
	Microscopic colitis	Refer to gastroenterology.
	Malignancy	Refer urgently to the appropriate MDT requesting an appointment within 2 weeks.
<b>Second line</b>		
Gut hormones	Functioning NET	Refer to the appropriate NET team requesting an appointment within 2 weeks.
<b>Third line</b>		
If normal investigations/no response to intervention		Refer to gastroenterology.

BAM, bile acid malabsorption; EPI, exocrine pancreatic insufficiency; GI, gastrointestinal; MDT, multidisciplinary team; Mg<sup>2+</sup>, magnesium; NET, neuroendocrine tumour; OGD, upper GI endoscopy (oesophago-gastroduodenoscopy); PPI, proton pump inhibitor; SeHCAT, 23-seleno-25-homotaurocholic acid; SI, small intestine; SIBO, small intestinal bacterial overgrowth.

**DRY MOUTH** (*xerostomia*) (Supplementary figure 9 and table 12)

**Table 12** Investigation and management of a dry mouth

Investigations	Potential results	Clinical management plan		
<b>Actions from history, medication and dietary assessment</b>				
History findings	Cancer related <ul style="list-style-type: none"> <li>▶ Tumour infiltration</li> <li>▶ Paraneoplastic syndrome</li> </ul>	<b>General advice</b> Oral hygiene: refer to dentist/oral hygienist. Use fluoridated toothpaste—all dentate patients should use toothpaste with at least 1000 ppm fluoride, while dentate patients with radiation-induced salivary gland dysfunction should use specialist toothpaste with 5000 ppm fluoride. Limit acidic and sugary drinks/foods/medication and rinse mouth after these products. Symptomatic management <sup>4</sup> 1. Consider saliva substitutes, eg, artificial saliva spray or lozenges (mucin based) or a non-porcine alternative, if required for cultural reasons. Note: Glandosane spray, Salivix pastilles and SST tablets are acidic products and may demineralise tooth enamel. 2. Consider mechanical salivary stimulants: <ul style="list-style-type: none"> <li>▶ Sugarless chewing gum/mints.</li> <li>▶ Pilocarpine 5 mg three times a day in patients treated with radiotherapy to the head and neck.</li> </ul> Consider referral for acupuncture. <sup>5</sup>		
	Cancer treatment related: <ul style="list-style-type: none"> <li>▶ Irradiation to the head and neck/salivary glands</li> <li>▶ Iodine-131</li> <li>▶ Surgery</li> <li>▶ Chemotherapy</li> <li>▶ Biological treatment (interleukin 2)</li> <li>▶ Graft vs host disease</li> </ul>			
	Oral infection	Treat according to local guidelines.		
	Inadequate fluid intake/dehydration	Encourage oral fluid intake and oral hygiene.		
	Decreased mastication (liquid/soft diet)	Refer for dietetic assessment and advice. Refer to a speech and language therapist.		
	Diabetes mellitus <sup>6</sup>	Refer to a GP.		
	Sjögren’s syndrome	Refer to the rheumatology team.		
Medication findings <sup>4</sup>	Antidepressants: <ul style="list-style-type: none"> <li>▶ SSRI’s</li> <li>▶ Tricyclic antidepressants</li> </ul>	Many other medications can cause dry mouth. Check, if any doubt, using an Electronic Medicines Compendium <sup>7</sup> .		
	Ace inhibitors			
	Antiemetics			
	Antihypertensives			
	Antimuscarinics			
	Antipsychotics			
	Calcium antagonists			
	Opioids			
	<b>First line</b>			
	If no improvement		Psychological issues	Refer for psychological support.
			Missed organic cause	Refer to oral surgery.

GP, general practitioner; SSRI, selective serotonin reuptake inhibitor; SST, saliva stimulating tablet.

**DUMPING**

For dumping, please refer to the section ‘Postprandial dizziness/sweating/palpitations’ on page 20.

**DYSPHAGIA—HIGH** (oropharyngeal dysphagia).

Difficulty with swallowing/sensation of food sticking (Supplementary figure 10, tables 13 and 14).

**Table 13** Swallowing score

Grade 0	Normal eating
Grade 1	Difficulty swallowing solids
Grade 2	Difficulty swallowing semisolids
Grade 3	Difficulty swallowing liquids
Grade 4	Unable to swallow solids or liquids

**Table 14** Investigation and management of high dysphagia

Investigations	Potential results	Clinical management plan
<b>Actions from history, medication and dietary assessment</b>		
History findings	Dysphagia present	Refer for dietetic support. Refer for SLT assessment.
	Neurological findings	Refer to neurology.
Medication findings	Bisphosphonates NSAID Potassium supplements Tetracyclines Theophyllines	Discuss possible alternative medications.
<b>First line</b>		
Contrast swallow/fluoroscopy	Fistula with aspiration Stricture, if <6 months after upper GI surgery  Stricture, if after radiotherapy or >6 months after upper GI surgery  Malignancy/tumour recurrence  Inflammation (acid/bile) Pharyngeal dysfunction Local infection (viral/fungal)	This is an emergency. Discuss with thoracic surgery OGD±dilatation (p. 25). Consider treatment for acid/bile reflux (p. 25). OGD with careful biopsy and consider treatment for acid/bile reflux (p. 25). CT±PET scan. Then review in MDT before any further treatment/stent/dilatation (p. 25). Refer to appropriate MDT requesting an appointment within 2 weeks. See management of acid or bile related inflammation (p. 25). SLT assessment. Treat infection appropriately.
<b>Second line</b>		
OGD under GA (no endoscopic intervention until discussed at the MDT)	Inflammation (acid/bile) Malignancy/tumour recurrence  Vocal cord palsy	See management of acid or bile related inflammation (p. 25). Refer to appropriate MDT requesting an appointment within 2 weeks. CT scan and refer to cancer MDT within 2 weeks. Referral to SLT.
CT chest	Malignancy/tumour recurrence	Refer to appropriate MDT requesting an appointment within 2 weeks.
<b>Third line</b>		
Referral to ENT	Head and neck pathology	ENT team management.
<b>Fourth line</b>		
If normal investigations/no response to intervention		Reassure.

CT, computerised tomography; ENT, ear, nose and throat; GI, gastrointestinal; MDT, multidisciplinary team; NSAID, non-steroidal anti-inflammatory drug; OGD, upper GI endoscopy (oesophago-gastroduodenoscopy); PET, positron emission tomography; SLT, speech and language therapy.

**DYSPHAGIA—LOW** (oesophageal dysphagia)

Difficulty with swallowing/sensation of food sticking (Supplementary figure 11, tables 15 and 16).

**Table 15** Swallowing score

Grade 0	Normal eating
Grade 1	Difficulty swallowing solids
Grade 2	Difficulty swallowing semi solids
Grade 3	Difficulty swallowing liquids
Grade 4	Unable to swallow solids or liquids

**Table 16** Investigation and management of low dysphagia

Investigations	Potential results	Clinical management plan
<b>Actions from history, medication and dietary assessment</b>		
History findings	Dysphagia present	Refer for dietetic support.
Medication findings	Bisphosphonates NSAID Potassium supplements Tetracyclines Theophyllines	Discuss possible alternative medications.
<b>First line</b>		
If fistula unlikely OGD (no endoscopic intervention until discussed at the MDT)	Stricture, if <6 months after upper GI surgery	OGD±dilatation (p. 25). Consider treatment for acid/bile reflux (p. 25).
	Stricture, if after radiotherapy or >6 months after upper GI surgery	OGD with careful biopsy and consider treatment for acid/bile reflux (p. 25). CT±PET scan. Then review in MDT before any further treatment/stent/dilatation (p. 25).
	Inflammation (acid/bile)	See management of acid or bile related inflammation (p. 25).
	Local infection (viral/fungal)	Treat infection appropriately.
	Eosinophilic oesophagitis	Refer to gastroenterology.
	No obvious cause	Take SI aspirate (p. 25) to exclude SIBO. Arrange glucose hydrogen methane breath test.
<b>Second line</b>		
Contrast swallow/CT	Fistula with aspiration	This is an emergency. Discuss with gastroenterology.
	Stricture	OGD with careful biopsy. Refer to appropriate MDT requesting an appointment within 2 weeks to consider dilatation (p. 25)/stent insertion/other management.
	Malignancy/tumour recurrence	Refer to appropriate MDT requesting an appointment within 2 weeks.
	Achalasia	Refer to gastroenterology.
CT/MRI/PET	Malignancy/tumour recurrence	Refer to appropriate MDT requesting an appointment within 2 weeks.
	Other	Discussion supervising clinician within 24 weeks.
<b>Third line</b>		
Oesophageal manometry/pH/impedance studies	Acid/bile reflux	See management of acid/bile related inflammation (p.25).
	Bile reflux	
	Spasm	Calcium antagonist. Low dose antidepressant, eg, citalopram. Refer to gastroenterology.
	Scleroderma	Start PPI or H2 antagonist. Refer to rheumatology.
<b>Fourth line</b>		
If normal investigations/no response to intervention	Psychological factors	Refer to psychology.

CT, computerised tomography; GI, gastrointestinal; H2, histamine receptor 2; MDT, multidisciplinary team; NSAID, non-steroidal anti-inflammatory drug; OGD, upper GI endoscopy (oesophago-gastroduodenoscopy); PET, positron emission tomography; PPI, proton pump inhibitor; SIBO, small intestinal bacterial overgrowth; SLT, speech and language therapy.

**EARLY SATIETY**

Feeling full after eating a small amount of food (Supplementary figure 12 and table 17).

**Table 17** Investigation and management of early satiety

Investigations	Potential results	Clinical management plan
<b>Actions from history, medication and dietary assessment</b>		
History findings	After gastrectomy or oesophagectomy	1. Reassure in the postoperative period. 2. Refer for dietetic advice.
	History of diabetes and high blood sugar levels	1. Refer the patient to the GP for further management. 2. Refer for dietetic advice.
	Constipation	See management of constipation (p. 26).
Medication findings	Anticholinergic drugs	Discuss potential alternatives.
<b>First line</b>		
OGD and SI aspirate (p. 25)	SIBO	Management of SIBO (p. 27).
	Malignancy/tumour recurrence	Discuss and refer to appropriate MDT requesting an appointment within 2 weeks.
	Biliary gastritis	See management of bile related inflammation (p. 25).
	Delayed gastric emptying	<ul style="list-style-type: none"> <li>▶ Consider gastric emptying studies.</li> <li>▶ Assess for SIBO</li> <li>▶ Consider prokinetics (p. 26).</li> <li>▶ Pyloric dilatation if after oesophagectomy.</li> <li>▶ Referral to dietitian.</li> </ul>
	Pyloric spasm/stricture	Consider dilatation (p. 25) with careful biopsy only after agreement from the appropriate MDT.
Glucose hydrogen methane breath test	SIBO	Management of SIBO (p. 27).
CT chest, abdomen, pelvis	Malignancy/tumour recurrence	Discuss and refer urgently to the appropriate cancer MDT requesting an appointment within 2 weeks.
Routine blood tests	Abnormal results	Follow treatment for abnormal blood results (p. 2).
<b>Second line</b>		
Barium meal	Pyloric spasm/stricture	Consider dilatation (p. 25) with careful biopsy only after agreement from the appropriate MDT.
<b>Third line</b>		
Gastric emptying study	Delayed gastric emptying	<ul style="list-style-type: none"> <li>▶ Assess for SIBO.</li> <li>▶ Consider prokinetic (p. 26).</li> <li>▶ Pyloric dilatation if after oesophagectomy.</li> <li>▶ Referral to dietitian.</li> </ul>
<b>Fourth line</b>		
If normal investigations/no response to intervention		Reassure.

CT, computerised tomography; GP, general practitioner; MDT, multidisciplinary team; OGD, upper GI endoscopy (oesophago-gastroduodenoscopy); SI, small intestine; SIBO, small intestinal bacterial overgrowth.

**EPIGASTRIC PAIN CHRONIC (>2 weeks)**

Pain localised to the region of the upper abdomen immediately below the ribs (Supplementary figure 13 and table 18).

**Table 18** Investigation and management of chronic epigastric pain

Investigations	Potential results	Clinical management plan
<b>Actions from history, medication and dietary assessment</b>		
History findings	Neuropathic postoperative pain	Refer to the pain team.
<b>First line</b>		
Routine and additional blood tests	Abnormal results	Follow treatment for abnormal blood results (p. 2).
OGD and SI aspirate (p. 25)	Inflammation/ulceration	See management of acid or bile related inflammation (p. 25).
	Local fungal infection	Consider treatment with nystatin or fluconazole.
	Oesophageal or pyloric stricture	Consider dilatation (p. 25) with careful biopsy only after discussion with cancer MDT.
	Spasm	<ol style="list-style-type: none"> <li>1. Start PPI or H2 antagonist.</li> <li>2. Calcium antagonist.</li> <li>3. Low dose antidepressant.</li> </ol>
	Malignancy/tumour recurrence	Discuss and refer urgently to the appropriate cancer MDT requesting an appointment within 2 weeks.
	Benign peptic ulceration	<ol style="list-style-type: none"> <li>1. Treat with PPI.</li> <li>2. Arrange follow-up endoscopy if oesophageal or gastric in 6 weeks.</li> <li>3. Consider <i>Helicobacter pylori</i> eradication.</li> </ol>

Continued

**Table 18** Continued

Investigations	Potential results	Clinical management plan
US	Biliary tree obstruction	This is an emergency if any fever. Otherwise discuss with the supervising clinician within 24 hours.
	Gallstones	Discuss with the supervising clinician within 24 hours.
	Pancreatic duct problems	
	Renal stones	Discuss with the supervising clinician and the oncology team within 24 hours.
	Ascites	
	Mesenteric ischaemia	This is an emergency. Discuss with the on-call surgical team immediately.
Malignancy/tumour recurrence/lymphadenopathy		Discuss and refer urgently to the appropriate cancer MDT requesting an appointment within 2 weeks.
	Pancreatitis	Refer to the appropriate MDT
	Acute cardiac ischaemia	This is an emergency. Discuss with cardiology.
ECG	Normal resting ECG but cardiac aetiology suspected	Urgent referral to cardiology.
	Glucose hydrogen methane breath test	Management of SIBO (p. 27).
<b>Second line</b>		
AXR	Faecal loading	See management of constipation (p. 26).
	Ileus/obstruction	This is an emergency. Discuss immediately with the on-call surgical team and arrange urgent CT scan.
CXR	Infection	Discuss with the supervising clinician within 24 hours and treat appropriately.
CT/MRI/PET	Malignancy/tumour recurrence/lymphadenopathy	Discuss and refer urgently to the appropriate cancer MDT requesting an appointment within 2 weeks.
	Consider also	These are emergencies. Refer to the upper GI surgical team
	1. Internal hernia (if Roux-en-Y)	
	2. Jejunal tube complication, eg, volvulus (if still in situ)	
	3. Pancreatitis	
Mesenteric ischaemia	This is an emergency. Discuss with the on-call surgical team immediately.	
Ascites	Discuss with the supervising clinician and the oncology team within 24 hours.	
<b>Third line</b>		
If normal investigations/no response to intervention		Reassure.

AXR, abdominal X-ray; CT, computerised tomography; CXR, chest X-ray; GI, gastrointestinal; H2, histamine receptor 2; MDT, multidisciplinary team; MRI, magnetic resonance imaging; OGD, upper GI endoscopy (oesophago-gastroduodenoscopy); PET, positron emission tomography; PPI, proton pump inhibitor; SIBO, small intestinal bacterial overgrowth; US, ultrasound.

**GI BLEEDING** (haematemesis and/or melaena)

Vomiting blood or ‘coffee grounds’ and/or black ‘tarry’ faeces associated with upper GI bleeding (Supplementary figure 14 and table 19).

**Table 19** Investigation and management of upper GI bleeding

Investigations	Potential results	Clinical management plan
<b>Actions from assessments</b>		
History findings	This is an emergency. Speak immediately to the on-call GI bleeding team and also to the upper GI surgeon if <4 weeks from GI surgery. Routine blood tests. Clotting and crossmatch.	
GI, gastrointestinal.		

**HALITOSIS**

An unpleasant odour emitted from the mouth (Supplementary figure 15 and table 20).

**Table 20** Investigation and management of halitosis

Investigations	Potential results	Clinical management plan
<b>Actions from history, medication and dietary assessment</b>		
History findings	Smoking	Smoking cessation advice.
	Absence of saliva	Follow guidelines for dry mouth (p. 11).
Medication findings	Nitrates	Consider possible alternative options.
	Phenothiazines <sup>8</sup>	
Dietary findings	Strong smelling food	Encourage dental hygiene.
		Reduce dietary foods containing hydrogen sulphide.
<b>First line</b>		
Visual inspection of mouth	Gum disease	Encourage patient to visit a dentist.
	Tooth decay	
	Hairy tongue	
	Candida infection	Antifungal therapy.
	Dry mouth	See page 11.
<b>Second line</b>		
OGD and SI aspirate (p. 25)	Gastric dysmotility	Consider a prokinetic (p. 26).
	Ulceration	Benign: 6 weeks PPI then reassess. Malignant: as below.
	Malignancy/tumour recurrence	Discuss and refer urgently to the appropriate cancer MDT requesting an appointment within 2 weeks.
	Duodenal obstruction	Discuss with the supervising clinician and refer as clinically appropriate to a GI surgeon/gastroenterologist/oncology team within 24 hours.
Glucose hydrogen methane breath test	SIBO	Management of SIBO (p. 27).
<b>Third line</b>		
Contrast swallow	Pharyngeal pouch	Refer to the ENT/oesophageal surgeon.
<b>Fourth line</b>		
If normal investigations/no response to intervention		Refer to oral medicine.

ENT, ear, nose and throat; GI, gastrointestinal; MDT, multidisciplinary team; OGD, upper GI endoscopy (oesophago-gastroduodenoscopy); PPI, proton pump inhibitor; SIBO, small intestinal bacterial overgrowth.

**HICCUPS** (*singultus*) (Supplementary figure 16 and table 21)

**Table 21** Investigation and management of hiccups

Investigations	Potential results	Clinical management plan
<b>Actions from history, medication and dietary assessment</b>		
History findings	Short-term hiccups	Reassure patient.
	Long-term hiccups	Investigate as outlined below.
Medication findings <sup>9</sup>	Corticosteroids	Discuss possible alternative medications.
	Benzodiazepines	
	Barbiturates	
	Opioids	
	Methyldopa	
<b>First line</b>		
Routine blood tests	Infection with vagal irritation:	Treat infection as appropriate.
	<ul style="list-style-type: none"> <li>▶ Pleuritis</li> <li>▶ Pharyngitis</li> </ul>	
	Metabolic:	Treat underlying condition.
	<ul style="list-style-type: none"> <li>▶ Diabetes</li> <li>▶ Hypokalaemia</li> <li>▶ Hypercalcaemia</li> <li>▶ Uraemia</li> </ul>	
Physical examination	Meningitis	This is an emergency. Refer immediately to the acute medicine on-call team.
CT chest/abdomen	Acute gastric distension	This is an emergency. Discuss immediately with an upper GI surgeon.
	Small bowel obstruction	This is an emergency. Discuss immediately with GI surgeon.

Continued

**Table 21** Continued

Investigations	Potential results	Clinical management plan
	Malignancy/tumour recurrence	Discuss and refer urgently to the appropriate cancer MDT requesting an appointment within 2 weeks.
	Chest pathology	Discuss with supervising clinician within 24 hours.
	Intra-abdominal infection	This is an emergency. Discuss immediately with the on-call surgical team.
<b>Second line</b>		
OGD	GORD	Start PPI or H2 antagonist. If following oesophagectomy, consider promotility agents (see p. 26).
<b>Third line</b>		
If normal investigations/no response to intervention		Consider empirical baclofen, PPI, chlorpromazine, haloperidol, gabapentin, pregabalin. Ask for support from palliative care team. Refer to ENT team. Reassure.

CT, computerised tomography; ENT, ear, nose and throat; GI, gastrointestinal; GORD, gastro-oesophageal reflux disease; H2, histamine -2; MDT, multidisciplinary team; OGD, upper GI endoscopy (oesophago-gastroduodenoscopy); PPI, proton pump inhibitor.

**HOARSE VOICE** (*dysphonia*) (Supplementary figure 17 and table 22)

**Table 22** Investigation and management of hoarseness

Investigations	Potential results	Clinical management plan
<b>Actions from history, medication and dietary assessment</b>		
History findings	Hoarseness	Voice hygiene advice: 1. Adequate hydration. 2. Avoid vocal strain (shouting, throat clearing, excessive voice use). 3. Smoking cessation advice if a smoker. 4. Alcohol reduction (alcohol is an irritant and dehydrating). 5. Refer to SLT.
	Dysphagia/aspiration	Discuss with supervising clinician within 24 hours.
	Presence of laryngeal obstruction	This is an emergency. Refer to ENT team immediately.
	Dyspnoea, stridor, wheeze, exertional dyspnoea, anxiety or signs of hypoxia	
	Dysphagia or drooling	
	Facial or oral oedema	
	Presence of other ENT symptoms	Refer to the ENT team requesting an appointment within 2 weeks.
	Throat or ear pain	
	Nasal blockage	
<b>First line</b>		
Laryngoscopy	Vocal cord palsy	CT scan and refer to cancer MDT within 2 weeks. Referral to SLT.
CT chest, abdomen, pelvis	Malignancy/tumour recurrence	Discuss and refer urgently to the appropriate cancer MDT requesting an appointment within 2 weeks.
	Superior vena cava obstruction	This is an emergency. Contact acute oncology service immediately.
<b>Second line</b>		
OGD	GORD	Start PPI or H2 antagonist. If following oesophagectomy, consider promotility agents (see p. 78).
	Cervical inlet patch	Treat with PPI or ablation.
<b>Third line</b>		
If normal investigations/no response to intervention		Reassure.

CT, computerised tomography; ENT, ear, nose and throat; GORD, gastro-oesophageal reflux disease; H2, histamine receptor 2; MDT, multidisciplinary team; OGD, upper GI endoscopy (oesophago-gastroduodenoscopy); PPI, proton pump inhibitor; SLT, speech and language therapy.

**HYPERSALIVATION/DROOLING** (*sialorrhoea*) present longer than 3 weeks

Production of excessive oral secretions which are not swallowed (Supplementary figure 18 and table 23).

**Table 23** Investigation and management of hypersalivation

Investigations	Potential results	Clinical management plan
<b>Actions from history, medication and dietary assessment</b>		
History findings	Problems swallowing saliva Neurological disorders Problems closing mouth  Infection: ▶ Tonsillitis ▶ Mumps	Follow guideline for dysphagia on tables 14 and 16. Consider referral to a speech and language therapist. Refer to neurology. Establish underlying cause: stroke, jaw fracture or dislocation, facial nerve palsy, Parkinson’s disease. Treat according to local guidelines.
Medication findings	▶ Clozapine ▶ Pilocarpine ▶ Potassium ▶ Risperidone	Discuss possible alternative medications.
<b>First line</b>		
OGD	GORD	Start PPI or H2 antagonist. If following oesophagectomy, consider promotility agents (see p. 78).
<b>Second line</b>		
If normal investigations/no response to intervention		1. Advice on oral hygiene. 2. Consider treating with an antimuscarinic medication: <sup>10</sup> Amitriptyline. Glycopyrronium bromide (glycopyrrolate): oral, nebulised and subcutaneous. Hyoscine hydrobromide (scopolamine hydrobromide): oral, topical, subcutaneous and nebulised. 3. Consider referral to psychological support team.

GORD, gastro-oesophageal reflux disease; H2, histamine receptor 2; OGD, upper GI endoscopy (oesophago-gastroduodenoscopy); PPI, proton pump inhibitor.

**JAUNDICE**

Yellowish pigmentation of the skin, the conjunctival membranes over the sclerae and other mucous membranes caused by high blood bilirubin levels (Supplementary figure 19 and table 24).

**Table 24** Investigation and management of jaundice

Investigations	Potential results	Clinical management plan
<b>Actions from history, medication and dietary assessment</b>		
If there is fever		This is an emergency. Discuss with the on-call gastroenterology team immediately.
If there is no fever Blood for FBC, U&E, LFTs, INR, viral serology, glucose, plus full liver screen (p. 2) and amylase. Urgent US abdomen plus Doppler of the portal vein.		Discuss with the gastroenterology or hepatology team within 24 hours. Warn the patient that if they develop a fever they need to seek immediate medical help.

FBC, full blood count; INR, international normalised ratio; LFTs, liver function tests; U&E, urea and electrolytes; US, ultrasound.

**NAUSEA WITHOUT DYSPHAGIA**

Feeling of sickness in the stomach marked by an urge to vomit.

If dysphagia is present with nausea, follow dysphagia guidance in [tables 14](#) and [16](#).

**Table 25** Investigation and management of nausea

Investigations	Potential results	Clinical management plan
<b>Actions from history, medication and dietary assessment</b>		
History findings	Symptoms of heart burn/acid/bile reflux	1. See management of acid or bile related inflammation (p. 25). 2. Reassess after 2–4 weeks as clinically indicated.
	With dizziness/sweating/palpitations	See page 20.
	Headache/neurological symptoms present	Neurological examination. Funduscopy and CT/MRI head.
	Poor fluid intake	Check renal function/encourage fluids.
	Constipation/impaction	AXR. See management of constipation (p. 26).
Medication findings	Opiates NSAID	
	Chemotherapy	Contact team to change antiemetics urgently. If multiple vomiting daily this is an emergency. Contact the on-call acute oncology team.
Dietary findings	Nutritional compromise	Refer for dietetic advice.
<b>First line</b>		
Funduscopy	Raised ICP	This is an emergency. Discuss immediately with the supervising clinician and oncology or neurology team.
Routine and additional blood tests	Metabolic abnormality	Discuss immediately with the supervising clinician.
	Liver/biliary abnormality	Discuss with the supervising clinician within 24 hours.
	Suggestive of infection	Treat with antibiotics within level of confidence or discuss with microbiologist or supervising clinician.
Urine analysis	Metabolic abnormality, eg, glucosuria, ketonuria	Discuss immediately with supervising clinician.
	Infection	Treat with antibiotics within level of confidence or discuss with a microbiologist or supervising clinician within 24 hours.
<b>Second line</b>		
OGD and SI aspirate (p. 25)	Upper GI inflammation/ulceration	See management of acid or bile related inflammation (p. 25).
	Gastric dysmotility	Consider prokinetic medication (p. 26).
	Pyloric stenosis	Refer urgently to the appropriate cancer MDT.
	Bleeding peptic ulcer	This is an emergency. Discuss immediately with the supervising clinician/gastroenterologist.
Glucose hydrogen methane breath test	SIBO	Management of SIBO (p. 27).
	SIBO	Management of SIBO (p. 27).
US liver and pancreas	Biliary/hepatic/pancreatic aetiology	See management of jaundice on p. 18.
Cortisol level	Addison's disease	Confirm with the Synacthen test, start on hydrocortisone and refer to endocrinology.
US/CT/MRI/PET	Malignancy/tumour recurrence/lymphadenopathy	Discuss and refer urgently to the appropriate cancer MDT requesting an appointment within 2 weeks.
	Consider also	These are emergencies. Refer to upper GI surgical team.
	1. Internal hernia (if Roux-en-Y)	
	2. Jejunal tube complication, eg, volvulus (if still in situ)	
	3. Pancreatitis	
	Mesenteric ischaemia	This is an emergency. Discuss with the on-call surgical team immediately.
	Ascites	Discuss with the supervising clinician and the oncology team within 24 hours.
<b>Third line</b>		
If normal investigations/no response to intervention		1. Consider contributing psychological factors. 2. Consider referral for psychological support if there is a possible underlying eating disorder. 3. Consider a routine referral to gastroenterology for further management.

AXR, abdominal X-ray; CT, computerised tomography; GI, gastrointestinal; ICP, intracranial pressure; MDT, multidisciplinary team; NSAID, non-steroidal anti-inflammatory drug; OGD, upper GI endoscopy (oesophago-gastroduodenoscopy); PET, positron emission tomography; SIBO, small intestinal bacterial overgrowth; US, ultrasound.

**PAIN ON SWALLOWING** (*odynophagia*) (Supplementary figure 21 and table 26)

**Table 26**

Investigations	Potential results	Clinical management plan
<b>Actions from history, medication and dietary assessment</b>		
History findings	Previous upper GI stent	Start simple analgesia. Refer to the pain team.
Medication findings	Bisphosphonates NSAID	Discuss alternative medication.
Dietary findings	Nutritional compromise	Refer for dietetic advice.
<b>First line</b>		
OGD (do not biopsy obvious radiation change/ulceration)	Stricture Candidiasis Viral ulceration	See the guidance in tables 14 and 16. Antifungal therapy. Consider antiviral therapy, eg, Aciclovir for HSV. Ganciclovir for CMV.
	Radiotherapy induced ulceration	1. Pain control, eg, fentanyl patch. 2. Regular mucaine/oxetacaine/sucralfate. 3. PPI. 4. Consider low dose of SSRI. 5. Refer to the pain team. 6. Refer for dietetic advice.
	Other causes of ulceration	Malignancy: refer to the appropriate MDT within 24 hours. Acid/bile reflux (p. 25).
<b>Second line</b>		
Oesophageal manometry/pH/impedance studies	Spasm	Calcium antagonist. Low dose antidepressant, eg, citalopram. Refer to gastroenterology.
	Scleroderma	1. Start PPI or H2 antagonist. 2. Refer to rheumatology.
<b>Third line</b>		
If normal investigations/no response to intervention		Reassure.

CMV, cytomegalovirus; GI, gastrointestinal; H2, histamine receptor 2; HSV, herpes simplex virus; MDT, multidisciplinary team; NSAID, non-steroidal anti-inflammatory drug; OGD, upper GI endoscopy (oesophago-gastroduodenoscopy); PPI, proton pump inhibitor; SSRI, selective serotonin reuptake inhibitor.

**POSTPRANDIAL DIZZINESS/SWEATING/PALPITATIONS/SOMNOLENCE AFTER OESOPHAGECTOMY/GASTRECTOMY/PANCREATECTOMY** (Supplementary figure 22 and table 27)

**Table 27** Investigation and management of potential dumping

Investigations	Potential results	Clinical management plan
<b>Actions from history, medication and dietary assessment</b>		
History findings	History of upper GI resectional surgery 30–60 min after eating with sweating, dizziness, tachycardia	Refer for dietetic advice. Refer for dietetic advice: 1. Eat smaller, more frequent meals. 2. Eat slowly. 3. Avoid a lot of fast-acting sugars, eg, cakes, chocolate, sugary drinks and sweets. 4. Advise more longer-acting carbohydrate foods. 5. If no response, trial acarbose/octreotide. 6. Trial of low dose β blocker.
	Somnolence 1–3 hours after eating	1. Monitor blood sugar. 2. Refer for dietetic advice. 3. If mild, reassure.
<b>First line</b>		
ECG/24 hour tape	Cardiac disease	Discuss with the supervising clinician within 24 hours.
OGD and SI aspirate (p. 25)	SIBO	Management of SIBO (p. 27).

Continued

**Table 27** Continued

Investigations	Potential results	Clinical management plan
Glucose hydrogen methane breath test	SIBO	Management of SIBO (p. 27).
Monitor blood glucose	If abnormally high	Refer to GP/endocrinology.
	If abnormally low	Refer for dietetic advice
<b>Second line</b>		
Persisting unexplained symptoms	Consider insulinoma/neuroendocrine tumour	Refer to gastroenterology/endocrinology.
Third line		
If normal investigations/no response to intervention		Reassure.

ECG, electrocardiogram; GI, gastrointestinal; GP, general practitioner; OGD, upper GI endoscopy (oesophago-gastroduodenoscopy); SI, small intestine; SIBO, small intestinal bacterial overgrowth.

**REFLUX (acid/bile)/heartburn**

If dysphagia is present with reflux, follow dysphagia guidance in tables 14 & 16 instead.

In gastro-oesophageal reflux, acid refluxes from the stomach into the oesophagus. In duodenogastric reflux, bile refluxes from the duodenum into the stomach and oesophagus (Supplementary figure 23 and table 28).

**Table 28** Investigation and management of reflux

Investigations	Potential results	Clinical management plan
<b>Actions from history, medication and dietary assessment</b>		
History findings	Previous upper GI surgery	<ol style="list-style-type: none"> <li>Refer to dietitian Avoid eating late at night. Raise head of the bed. Reduce smoking, alcohol, caffeine, fat. Reduce weight if high BMI. Avoid large portions.</li> <li>Assess for SIBO.</li> <li>Trial of PPI (unless after total gastrectomy)</li> <li>Trial of agents to reduce biliary reflux. (p. 25).</li> <li>Trial of prokinetics. (p. 26).</li> </ol>
	Stress related	<ol style="list-style-type: none"> <li>Consider stress management techniques.</li> <li>Consider referral for psychological support.</li> </ol>
<b>First line</b>		
OGD	Inflammation/ulceration	See management of acid or bile related inflammation (p. 25). Lifestyle changes: reduce smoking, alcohol, chocolate, caffeine, fatty food, carbonated drinks, citrus. Assess weight and BMI.
	Malignancy/tumour recurrence	Discuss and refer urgently to the appropriate cancer MDT requesting an appointment within 2 weeks.
	Pyloric stenosis (after upper GI surgery)	Consider dilatation (p. 25) with careful biopsy only after agreement from the appropriate MDT.
Barium swallow	Oesophageal stricture	See the guidance in tables 14 and 16.
	Delayed emptying	<ol style="list-style-type: none"> <li>Assess for SIBO (p. 21).</li> <li>Prokinetics (p. 26).</li> <li>Consider formal gastric emptying studies.</li> <li>Consider dilatation (p. 25) with careful biopsy only after agreement from the appropriate MDT.</li> </ol>
	Oesophageal spasm	<ol style="list-style-type: none"> <li>Start PPI or H2 antagonist.</li> <li>Calcium antagonist.</li> <li>Low dose antidepressant, eg, citalopram.</li> <li>Confirm with oesophageal manometry, pH/impedance studies.</li> </ol>
	ECG/exercise test	Cardiac related
<b>Second line</b>		
Oesophageal manometry/pH/impedance studies	Spasm	Calcium antagonist. Low dose antidepressant, eg, citalopram. Refer to gastroenterology.
	Scleroderma	<ol style="list-style-type: none"> <li>Start PPI or H2 antagonist.</li> <li>Refer to rheumatology.</li> </ol>
<b>Third line</b>		
If normal investigations/no response to intervention		Reassure.

BMI, body mass index; GI, gastrointestinal; MDT, multidisciplinary team; OGD, upper GI endoscopy (oesophago-gastroduodenoscopy); PPI, proton pump inhibitor; SIBO, small intestinal bacterial overgrowth.

**REGURGITATION**

The expulsion of material from the mouth, pharynx or oesophagus, usually characterised by the presence of undigested food (Supplementary figure 24 and table 29).

**Table 29** Investigation and management of resurgitation

Investigations	Potential results	Clinical management plan
<b>Actions from history, medication and dietary assessment</b>		
History findings	History of (partial) gastrectomy or oesophagectomy	<ol style="list-style-type: none"> <li>1. Small but frequent meals.</li> <li>2. Refer for dietetic advice.</li> <li>3. Consider starting prokinetic drugs.</li> <li>4. PPI/H2 antagonist±sucralfate.</li> </ol>
	Rumination (regurgitation with no obvious cause)	<ol style="list-style-type: none"> <li>1. Refer to gastroenterology.</li> <li>2. Consider referral to psychological support.</li> </ol>
<b>First line</b>		
OGD	Oesophageal stricture	See the guidance in tables 14 and 16.
	Malignancy/tumour recurrence	Refer to appropriate MDT requesting an appointment within 2 weeks.
Barium swallow	Pharyngeal pouch	Refer to ENT team.
	Oesophageal stricture	See the guidance in tables 14 and 16.
	Delayed emptying	<ol style="list-style-type: none"> <li>1. Assess for SIBO (p. 21).</li> <li>2. Prokinetics (p. 26).</li> <li>3. Consider formal gastric emptying studies.</li> <li>4. Pyloric dilatation if after oesophagectomy.</li> </ol>
	Oesophageal spasm/motility disorder	<ol style="list-style-type: none"> <li>1. Start PPI or H2 antagonist.</li> <li>2. Calcium antagonist.</li> <li>3. Low dose antidepressant, eg, citalopram.</li> <li>4. Confirm with oesophageal manometry, pH/impedance studies.</li> <li>5. Refer to gastroenterology.</li> </ol>
<b>Second line</b>		
US/CT/MRI/PET	Malignancy/tumour recurrence/lymphadenopathy	Discuss and refer urgently to the appropriate cancer MDT requesting an appointment within 2 weeks.
	Consider also	These are emergencies. Refer to upper GI surgical team
	<ol style="list-style-type: none"> <li>1. Internal hernia (if Roux-en-Y)</li> <li>2. Jejunal tube complication, eg, volvulus (if still in situ)</li> <li>3. Pancreatitis</li> </ol>	
	Mesenteric ischaemia	This is an emergency. Discuss with the on-call surgical team immediately.
	Ascites	Discuss with the supervising clinician and the oncology team within 24 hours.
<b>Third line</b>		
If normal investigations/no response to intervention		Reassure.

ENT, ear, nose and throat; GI, gastrointestinal; H2, histamine receptor 2; MDT, multidisciplinary team; OGD, upper GI endoscopy (oesophago-gastroduodenoscopy); PET, positron emission tomography; PPI, proton pump inhibitor; SIBO, small intestinal bacterial overgrowth; US, ultrasound.

**STEATORRHOEA**

The presence of excess fat in the stool. Stools may float, be difficult to flush away and have an oily appearance. Sometimes pale (chalk/sand) in colour. Sometimes an oily film can be seen in the lavatory water after defaecation (Supplementary figure 25 and table 30).

**Table 30** Investigation and management of steatorrhea

Investigations	Potential results	Clinical management plan
<b>First line</b>		
Stool sample for faecal elastase	Pancreatic insufficiency	Management of EPI (p. 26).
Routine and additional blood tests	Addison's disease Coeliac disease Thyroid dysfunction	Follow treatment for abnormal blood results (p. 2).
Blood tests for malabsorptive symptoms	Malabsorptive pathology	Follow treatment for abnormal blood results (p. 2).

Continued

**Table 30** Continued

Investigations	Potential results	Clinical management plan
SeHCAT scan	BAM	Management of BAM (p. 25).
OGD and SI aspirate and biopsies (p. 25)	SIBO Intestinal parasites	Management of SIBO (p. 27). Treat with antibiotics within level of confidence or discuss with microbiologists and supervising clinician.
Glucose hydrogen methane breath test	SIBO	Management of SIBO (p. 27).
<b>Second line</b>		
Gut hormones (Chromogranin A and B, gastrin, substance P, VIP, calcitonin, somatostatin, pancreatic polypeptide) and urinary 5-HIAA and CT/MRI liver and abdomen	Neuroendocrine tumour	Discuss and refer urgently to the appropriate neuroendocrine MDT requesting an appointment within 2 weeks.
CT abdomen pelvis/capsule endoscopy/MRI enteroclysis	Small intestinal disease	Discuss immediately and refer to the appropriate MDT requesting an appointment within 2 weeks, or if no malignancy to a gastroenterologist.
<b>Third line</b>		
If normal investigations/no response to intervention		1. Trial of empirical antibiotics to exclude test negative SIBO. 2. Trial of low fat diet.

5HIAA, 5-hydroxyindole acetic acid; BAM, bile acid malabsorption; CT, computerised tomography; EPI, exocrine pancreatic insufficiency; MDT, multidisciplinary team; MRI, magnetic resonance imaging; OGD, upper GI endoscopy (oesophago-gastroduodenoscopy); SeHCAT, 23-seleno-25-homotaurocholic acid; SIBO, small intestinal bacterial overgrowth; VIP, vasoactive intestinal protein.

**VOMITING** (emesis)

If dysphagia is present, follow dysphagia guidance in tables 14 and 16 instead (Supplementary figure 26 and table 31).

**Table 31** Investigation and management of vomiting

Investigations	Potential results	Clinical management plan
<b>Actions from history, medication and dietary assessment</b>		
History findings	Symptoms of heartburn/acid reflux:	1. Trial of proton pump inhibitor±trial of antiemetic. 2. Reassess after 2–4 weeks as clinically indicated.
	If within 2 weeks after surgery	Discuss with the surgical team within 24 hours.
	Chemotherapy related	Contact team to change antiemetics urgently.
	Persistent vomiting	This is an emergency. Contact the on-call medical team.
	Nutritional compromise	Refer for dietetic advice.
<b>First line</b>		
Fundoscopy	Raised ICP	This is an emergency. Discuss immediately with the supervising clinician.
Routine and additional blood tests	Metabolic abnormality	Discuss immediately with the supervising clinician.
	Liver/biliary abnormality	Discuss with the supervising clinician within 24 hours.
	Suggestive of infection	Treat with antibiotics within level of confidence or discuss with a microbiologist/supervising clinician.
Urine analysis	Metabolic abnormality, eg, glucosuria, ketonuria	Discuss immediately with the supervising clinician.
	Infection	Treat with antibiotics within level of confidence or discuss with a microbiologist/supervising clinician within 24 hours.
AXR (if with pain)	Small bowel obstruction	This is an emergency. Discuss immediately with a GI surgeon and arrange urgent CT scan.
	Faecal loading	See management of constipation (p. 26).
<b>Second line</b>		
OGD and SI aspirate (p. 25)	Upper GI inflammation/ulceration	See management of acid or bile related inflammation (p. 25). Assess <i>Helicobacter pylori</i> and treat if positive. Discuss with the supervising clinician the need for future repeat endoscopy.
	Gastric dysmotility	Consider prokinetic (p. 26).
	Pyloric stricture	Consider dilatation (p. 25) with careful biopsy only after agreement from the appropriate MDT.
	SIBO	Management of SIBO (p. 27).
	Glucose hydrogen methane breath test	SIBO

Continued

**Table 31** Continued

Investigations	Potential results	Clinical management plan
US liver and pancreas	Biliary/hepatic/pancreatic aetiology	See jaundice (p. 18).
CT/MRI/PET (head/chest/ abdomen/ pelvis)	Malignancy/tumour recurrence/ lymphadenopathy Consider also 1. Internal hernia (if Roux-en-Y) 2. Jejunal tube complication, eg, volvulus (if still in situ) 3. Pancreatitis	Discuss and refer urgently to the appropriate cancer MDT requesting an appointment within 2 weeks. These are emergencies. Refer to the upper GI surgical team.
	Mesenteric ischaemia	This is an emergency. Discuss with the on-call surgical team immediately.
	Ascites	Discuss with the supervising clinician and the oncology team within 24 hours.
<b>Third line</b> If normal investigations/no response to intervention		1. Consider contributing psychological factors. 2. Consider referral for psychological support if there is a possible underlying eating disorder. 3. Consider a routine referral to gastroenterology for further management.

AXR, abdominal X-ray; CT, computerised tomography; GI, gastrointestinal; ICP, intracranial pressure; MDT, multidisciplinary team; OGD, upper GI endoscopy (oesophago-gastroduodenoscopy); PET, positron emission tomography; SI, small intestine; SIBO, small intestinal bacterial overgrowth; US, ultrasound.

**WEIGHT LOSS** (unintentional)

Reduction of the total body mass >5% in 3 months, due to a mean loss of fluid, body fat or lean mass (Supplementary figure 27 and table 32).

**Table 32** Investigation and management of weight loss

Investigations	Potential results	Clinical management plan
<b>Actions from history, medication and dietary assessment</b>		
History findings	No other GI symptoms present	1. Discuss with the supervising clinician. 2. Request blood tests. 3. Request OGD, colonoscopy, CT chest abdomen and pelvis. 4. If all investigations normal and appetite is poor, consider psychological support±appetite stimulant.
Dietary findings	Inadequate dietary intake/ malabsorption	Refer for dietetic advice.
<b>First line</b>		
Routine and additional blood tests	Abnormal results	Follow treatment for abnormal blood results (p. 2).
Stool for faecal elastase	Pancreatic insufficiency	Management of EPI (p. 26).
US/CT/MRI/PET	Malignancy/tumour recurrence/ lymphadenopathy Consider also 1. Internal hernia (if Roux-en-Y) 2. Jejunal tube complication, eg, volvulus (if still in situ) 3. Pancreatitis	Discuss and refer urgently to the appropriate cancer MDT requesting an appointment within 2 weeks. These are emergencies. Refer to the upper GI surgical team.
	Mesenteric ischaemia	This is an emergency. Discuss with the on-call surgical team immediately.
	Ascites	Discuss with the supervising clinician and the oncology team within 24 hours.
<b>Second line</b>		
OGD with SI biopsies	Upper GI tract inflammation (p.25)	1. Proton pump inhibitor/H2 antagonist. 2. Sucralfate suspension. 3. Prokinetics (p. 26).
	Malignancy/tumour recurrence	Refer to the appropriate MDT requesting an appointment within 2 weeks.

Continued

Table 32 Continued

Investigations	Potential results	Clinical management plan
<b>Third line</b>		
PET scan	PET scan positive	Discuss and refer urgently to the appropriate cancer MDT requesting an appointment within 2 weeks. 1. Refer for dietetic advice. 2. Consider psychological causes, eg, depression, underlying eating disorder and refer appropriately for psychological support.
	PET scan negative	
<b>Fourth line</b>		
If normal investigations/no response to intervention		Consider colonoscopy. Refer to gastroenterology.

CT, computerised tomography; EPI, exocrine pancreatic insufficiency; GI, gastrointestinal; H2, histamine receptor 2; MDT, multidisciplinary team; OGD, upper GI endoscopy (oesophago-gastroduodenoscopy); PET, positron emission tomography; SI, small intestine; US, ultrasound.

**APPENDICES**

**Guidelines for dilatation**

For a stricture in the oesophagus that is anastomotic, a tumour or radiation-induced in nature.<sup>11</sup>

1. Should be performed only by experienced endoscopists.
2. If tumour is present, endoscopic intervention should only occur after multidisciplinary team (MDT) discussion.
3. Dilate to a maximum diameter 15–20 mm.
4. Dilate for 20–60 s if using a balloon.
5. Dilatation >12 mm not required for stent insertion.
6. Do not exceed diameter of the stricture by >7–8 mm/session.
7. Risks are increased after chemotherapy/radiotherapy/if tumour is present.

**How to perform a small intestinal aspirate**

1. On intubation with a gastroscope, avoid aspirating oral or oesophageal fluid.
2. Flush 100 mL of sterile saline into the small intestine via the endoscope channel.
3. Follow this by 20 mL of air to ensure no saline remains in the endoscope channel.
4. Turn down the suction.
5. Leave the fluid to equilibrate with the intestinal contents for a few seconds. Aspirate 20 mL of fluid into a sterile trap.
6. Send the aspirate sample directly to microbiology.

**MANAGEMENT OF ACID OR BILE RELATED INFLAMMATION IN THE STOMACH**

**Lifestyle management advice**

1. Avoid eating late at night.
2. Elevate the head of the bed.
3. Treat constipation. (p. 26).
4. Use of an alginate, for example, Gaviscon.

**Management of acid related inflammation**

1. Assess for *Helicobacter pylori*.
2. Proton pump inhibitor.

**Management of bile related inflammation**

1. Fresh orange juice.
2. Mucaïne/oxetacaine.

3. Sucralfate suspension.
4. Altacite.
5. Prokinetics (p. 26).

**MANAGEMENT OF BILE ACID MALABSORPTION/ BILE ACID DIARRHOEA**

**Definition**

Bile is secreted by the liver in direct response to the amount of ingested dietary fat. Bile acid malabsorption (BAM)/bile acid diarrhoea (BAD) is a defect in the enterohepatic circulation of bile acids. BAM occurs in the presence of ileal dysfunction when ability to absorb bile acids in the terminal ileum is impaired. BAD occurs when hepatic overproduction overwhelms terminal ileal absorption capacity.<sup>12</sup>

**Common causes of BAM/BAD**

- ▶ Chemotherapy
- ▶ Ileal disease/resection
- ▶ Upper GI resectional surgery including cholecystectomy
- ▶ Pancreatic disease
- ▶ Pelvic radiotherapy
- ▶ Idiopathic

**Diagnosis**

- ▶ 23-seleno-25-homotaurocholic acid (SeHCAT) scan
- ▶ C4 blood test
- ▶ Trial of bile acid sequestrant

**Severity scores of BAM/BAD when using SeHCAT**

7 day SeHCAT retention BAM/BAD status  
 15–20% borderline BAM/BAD  
 10–15% mild BAM/BAD  
 5–10% moderate BAM/BAD  
 <5% severe BAM/BAD

**Treatment**

Options include:

1. Dietary fat reduction
2. Antidiarrhoeal medication
3. Bile acid sequestrant

Options 1 and 2 may be useful in mild BAM/BAD. Generally bile acid sequestrants are required for moderate BAM/BAD. For severe BAM/BAD, most patients

need a bile acid sequestrant and advice about long-term reduction in dietary fat intake.<sup>13</sup>

Drugs that may be helpful include aluminium hydroxide, budesonide, colessevelam, colestipol and colestyramine.

Patients with steatorrhoea usually require colessevelam.

If dietary intervention is required, advice to reduce dietary fat intake to 20% of total calories can be useful but requires dietetic expertise, patient education and supportive literature.

Many patients with moderate/severe BAM/BAD will be deficient in trace elements and fat soluble vitamins. These should be checked periodically and supplemented as appropriate.

### MANAGEMENT OF CARBOHYDRATE MALABSORPTION

For example, lactose or other disaccharide intolerance.

#### Definition

Intolerance occurs from the inability to digest carbohydrates. Lactose, a component of milk and some other dairy products, is the intolerance most frequently recognised. It is due to lack of the enzyme lactase in the small intestine. Primary hypolactasia affects 70% of the world's population. Lactose or other disaccharide or monosaccharide (eg, fructose) malabsorption may occur de novo during cancer therapies (such as 5-fluorouracil chemotherapy or radiotherapy), due to damage to brush border enzymes and in some patients persists in the long term.<sup>14 15</sup>

#### Diagnosis of carbohydrate intolerance

- ▶ Trial of exclusion of products containing that specific carbohydrate in diet for 1–2 weeks. Patient to keep a record of symptoms before and during the exclusion.
- ▶ Specific carbohydrate breath test. Maybe falsely positive in the presence of small intestinal bacterial overgrowth (SIBO).
- ▶ Small intestine biopsies and assessment for the specific disaccharide or monosaccharide activity.

#### Treatment

- ▶ Long-term exclusion of products containing the carbohydrate in diet.
- ▶ Dietetic assessment to ensure diet remains balanced. With lactose intolerance special attention should be paid to calcium intake. Other bone health risk factors should also be considered and vitamin and mineral supplementation started as appropriate.<sup>14</sup>
- ▶ Consideration of a low fermentable oligo-di-monosaccharides and polyols diet.
- ▶ Oral lactases for isolated lactose intolerance.

### MANAGEMENT OF CONSTIPATION<sup>16</sup>

1. Dietary advice about healthy fibre and fluid intake.
2. Lifestyle advice about daily exercise.

3. Making time to have a toileting routine, correct positioning on the lavatory.
4. Medications advice.
5. Rectal evacuant (eg, glycerine suppositories). More effective if used 30 min after a meal.
6. Non-fermented bulk laxative±rectal evacuant.

#### Further options

1. Consider referral for biofeedback therapy.
2. Consider use of probiotics.
3. Consider use of prucalopride<sup>17</sup>/linaclotide.<sup>18</sup>
4. Consider rectal irrigation.
5. Consider referral to specialist gastroenterology.

### MANAGEMENT OF EXOCRINE PANCREATIC INSUFFICIENCY

#### Definition

Exocrine pancreatic insufficiency is the inadequate production and/or secretion of pancreatic enzymes and may occur after pelvic radiotherapy with para-aortic lymph node irradiation, cancer chemotherapy, acute pancreatitis, pancreatic cancer, upper GI or hepatobiliary surgery and in patients treated with a somatostatin analogue for a neuroendocrine tumour.

#### Diagnosis

Non-liquid stool sample for faecal elastase measurement (<200 µg FE1 per 1 g stool)—falsely low readings may be present in patients with small intestinal bacterial overgrowth.

Clinical response to pancreatic replacement.

#### Treatment

- ▶ Pancreatic enzyme replacement therapy: requires equivalent of at least 200 000 international units Creon per day (other available brands include Nutrizym, Pancrease HL, Pancrex).
- ▶ Starting dose 50 000–75 000 units of lipase with a meal and 25 000–50 000 units with a snack. The final dose of supplement will depend on type of food eaten and symptomatic response.
- ▶ Use pancreatic enzyme replacement therapy with all meals, drinks and snacks, except black tea, black coffee or water.
- ▶ Patients need written guidance on use of enzyme replacement.
- ▶ Consider long-term multivitamin and trace element supplementation.
- ▶ Consider dietetic advice to optimise bowel function.
- ▶ Occasionally addition of proton pump inhibitor is required to reduce loss of replacement enzymes by gastric acid.

#### Long-term management

Ongoing treatment with pancreatic enzyme replacement medication.

## MANAGEMENT OF GASTRIC DYSMOTILITY

May be more effective when used in combination or cyclically

### Effects on stomach

- ▶ Erythromycin: largely ineffective after 4–8 weeks through tachyphylaxis. Recommended dose 250 mg twice daily as a syrup 30 min before food. Or consider azithromycin 250 mg on alternate days.<sup>19</sup>
- ▶ Domperidone: no tachyphylaxis for 8 weeks, may occur after longer use. Recommended dose 10 mg four times a day 30 min before food as a syrup orally or 30 mg four times a day as a rectal suppository. Small increased risk of cardiac arrhythmia. Current MHRA advice<sup>20</sup> is that its use should be restricted to 1 week.
- ▶ Metoclopramide: risk of tardive dyskinesia with use >3 months.
- ▶ Naloxone by subcutaneous infusion.
- ▶ Paroxetine—stimulates small intestinal motility only.
- ▶ Consider gastric pacemaker.

Medicines & Healthcare Products Regulatory Agency (MHRA) has issued a number of warnings about the risks of using some of these medications for a longer period.<sup>20</sup> Prescribers should be aware of local policies with regard to the use of these drugs.

## MANAGEMENT OF SIBO

### Definition

SIBO is the presence of excessive bacteria in the small intestine. Small bowel bacterial overgrowth is a common cause for any GI symptom after chemotherapy and upper GI surgery. For any symptom resistant to conventional treatment, consider the possibility of SIBO.

### Diagnosis

- ▶ There is no gold standard for diagnosing SIBO.<sup>21 22</sup>
- ▶ Glucose hydrogen methane breath testing±small intestine aspirate (p. 25) via upper GI endoscopy.
- ▶ Red blood cell (RBC) folate and total serum bile acid levels may be elevated and vitamin B<sub>12</sub> levels and faecal elastase may be low.
- ▶ 10–15% patients with negative tests still have SIBO.

### Suggested antibiotic treatment options if no growth on culture to direct treatment

(If uncertain, discuss with gastroenterologist/microbiologist)

Seven days to 10 days treatment with:

- ▶ Ciprofloxacin 500 mg twice daily.
- ▶ Clarithromycin 500 mg twice daily.
- ▶ Co-amoxiclav 625 mg three times a day.
- ▶ Doxycycline 200 mg day 1, 100 mg days 2–7/10.
- ▶ Metronidazole 400 mg three times a day.
- ▶ Rifaximin 550 mg twice daily.

- ▶ Vancomycin 250 mg four times a day.

Symptoms can recur any time after antibiotics are stopped because the underlying cause of bacterial overgrowth cannot always be addressed. If symptoms return, repeat treatment with antibiotics for a few days every month or continually at the lowest effective dose may be helpful in managing symptoms in the long term. Some clinicians recommend rotating antibiotics but this may not be effective if the organisms involved are not sensitive to the antibiotics used.

Treatment decisions should be individualised and consider the risks of long-term antibiotic therapy such as *Clostridium difficile* infection, cumulative irreversible neuropathy with metronidazole, Achilles tendon rupture with ciprofloxacin, intolerance, side effects, bacterial resistance and costs.<sup>14 21–24</sup>

## MEDICATIONS THAT MAY INDUCE MUCOSITIS OR CHANGE IN SENSE OF TASTE

Chemotherapy drugs that cause mucositis can cause development of mouth sores. Such drugs include:<sup>25</sup>

- ▶ Alemtuzumab (Campath)
- ▶ Bleomycin (Blenoxane)
- ▶ Capecitabine (Xeloda)
- ▶ Cetuximab (Erbix)
- ▶ Docetaxel (Taxotere)
- ▶ Doxorubicin (Adriamycin)
- ▶ Epirubicin (Ellence)
- ▶ Fluorouracil (5-FU)
- ▶ Methotrexate (Rheumatrex)
- ▶ Vincristine (Oncovin)

Other medicines that have been linked to the development of mouth sores include:

- ▶ Aspirin
- ▶ Gold used to treat rheumatoid arthritis
- ▶ Nicorandil
- ▶ Penicillin
- ▶ Phenytoin
- ▶ Sulfonamides (used in a variety of medications)
- ▶ Streptomycin

Many other medicines have been linked to taste changes:

- ▶ Antibiotics
  - Ampicillin
  - Bleomycin
  - Cefamandole (cephalosporin)
  - Levofloxacin (Levaquin)
  - Lincomycin (treatment for mycoplasma and plasmodium)
  - Metronidazole
  - Tetracyclines
- ▶ Antiepileptics
  - Carbamazepine
  - Phenytoin
- ▶ Antifungals
  - Amphotericin B
- ▶ Antihistamines
  - Chlorpheniramine maleate
- ▶ Antipsychotics

- Lithium
- Trifluoperazine (sometimes also used to treat nausea and vomiting)
- ▶ Asthma medicines
  - Bami­fylline
- ▶ Biological agents
  - Erlotinib (Tarceva)
  - Sunitinib (Sutent)
- ▶ Bisphosphonates
  - Etidronate
- ▶ Blood pressure medications
  - Captopril
  - Diltiazem
  - Enalapril
- ▶ Blood thinners
  - Dipyridamole
- ▶ Cardiac medications
  - Nicorandil
  - Nitroglycerine patch
- ▶ Cancer chemotherapy agents
- ▶ Corticosteroids
  - Dexamethasone
  - Hydrocortisone
- ▶ Diabetes medications
  - Glipizide
- ▶ Diuretics
  - Amiloride
  - Ethacrynic acid (loop diuretic)
- ▶ Glaucoma medications
  - Acetazolamide
- ▶ Gout medications
  - Allopurinol
  - Colchicine
- ▶ Immunosuppressants
  - Azathioprine
- ▶ Iron
  - Iron sorbitex (given by injection)
- ▶ Muscle relaxants
  - Baclofen
- ▶ Parkinson’s disease medications
  - Levodopa
- ▶ Smoking cessation products
  - Nicotine skin patch
- ▶ Thyroid medicines
  - Carbimazole
  - Methimazole

**Acknowledgements** The authors thank the following experts who participated in the Delphi process and provided detailed feedback on this algorithm. Dr Ana Wilson, Mr Paul Wilkerson, Dr Katherine White, Dr Jonathan Wadsley, Mr Timothy Underwood, Mr Sukhbir Ubhi, Dr Jeff Turner, Dr John Todd, Professor Anne Thomas, Mrs Gemma Tham, Dr Kathy Teahon, Miss Nicola Sunderland, Mr Duncan Stewart, Dr Howard Smart, Mr Richard Skipworth, Dr Hamid Sheikh, Dr Charlotte Rutter, Ms Claudia Rueb, Dr Dan Rogers, Ms Alexandra Robson, Miss Briony Robinson, Dr Asad Qureshi, Dr Sue Priestly, Miss Laura Pope, Dr Zinu Philipose, Dr Daniel Pearl, Miss Margaret O’Donnell, Professor Muntzer Mughal, Mrs Karen Morgan, Miss Sarah Moore, Mrs Fiona Mitchell, Ms Laura McGeeney, Dr Astrid Mayer, Dr Thiriloganathan Mathialahan, Dr Mohid Khan, Dr Shanil Kadir, Mrs Elaine

Jones, Professor Sauid Ishaq, Miss Christina Iezzi, Miss Orla Hynes, Mrs Fiona Huddy, Dr Richard Hubner, Dr Jacquelyn Harvey, Mr Richard Hardwick, Dr Emma Greig, Dr John Green, Mr James Gossage, Mr Mike Goodman, Dr Jason Dunn, Miss Louise Davey, Dr Benjamin Colleypriest, Ms Saira Chowdhury, Mrs Emma Chester, Dr Nicola Burch, Ms Melissa Brennan, Mr David Bowrey, Dr Erica Beaumont, Miss Cara Baker and three other reviewers who requested not to be acknowledged

**Contributors** All authors contributed to the study design. Algorithm development was performed by HJNA, ACM and ARD. Guarantor of the article HJNA.

**Funding** National Institute for Health Research and the Royal Marsden Biomedical Research Centre. Some of the work in compiling this guide was facilitated by funding received from Macmillan Cancer Support.

**Competing interests** None declared.

**Provenance and peer review** Not commissioned; externally peer reviewed.

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## REFERENCES

- 1 Andreyev HJ, Muls AC, Norton C, *et al.* Guidance: the practical management of the gastrointestinal symptoms of pelvic radiation disease. *Frontline Gastroenterol* 2015;6:53–72.
- 2 <http://www.fifthsense.org.uk>
- 3 Lewis SJ, Heaton KW. Stool form scale as a useful guide to intestinal transit time. *Scand J Gastroenterol* 1997;32:920–4.
- 4 Davies A, Bagg J, Lavery D, *et al.* Salivary gland dysfunction (‘dry mouth’) in patients with cancer: a consensus statement. *Eur J Cancer Care (Engl)* 2010;19:172–7.
- 5 Meng Z, Garcia MK, Hu C, *et al.* Randomized controlled trial of acupuncture for prevention of radiation-induced xerostomia among patients with nasopharyngeal carcinoma. *Cancer* 2012;118:3337–44.
- 6 Busato IM, Ignacio SA, Brancher JA, *et al.* Impact of clinical status and salivary conditions on xerostomia and oral health-related quality of life of adolescents with type 1 diabetes mellitus. *Community Dent Oral Epidemiol* 2012;40:62–9.
- 7 <https://www.medicines.org.uk/emc>
- 8 Aylıkcı B, Çolak H. Halitosis: from diagnosis to management. *J Nat Sci Biol Med* 2013;4:14–23.
- 9 Marinella M. Diagnosis and management of hiccups in the patient with advanced cancer. *J Support Oncol* 2009;7:122–7, 130.
- 10 NICE Full Guideline. *Parkinson’s Disease Clinical Guideline* 35. 28th June 2006. <http://www.nice.org.uk/nicemedia/live/10984/30087/30087.pdf> (accessed 28 Jun 2012).
- 11 Pasha SF, Acosta RD, Chandrasekhara V, *et al.* ASGE Standards of Practice Committee. The role of endoscopy in the evaluation and management of dysphagia. *Gastrointest Endosc* 2014;79:191–201.
- 12 Walters JR, Pattni SS. Managing bile acid malabsorption. *Therap Adv Gastroenterol* 2010;3:349–57.
- 13 Wedlake L, Thomas K, Lalji A, *et al.* Effectiveness and tolerability of colesevelam hydrochloride for bile acid malabsorption in patients with cancer: a retrospective chart review and patient questionnaire. *Clin Ther* 2009;31:2549–58.

- 14 Andreyev J. Gastrointestinal symptoms after pelvic radiotherapy: a new understanding to improve management of symptomatic patients. *Lancet Oncol* 2007;8: 1007–17.
- 15 Suarez FL Savaiano DA, Levitt MD, *et al*. A comparison of symptoms after the consumption of milk or lactose-hydrolyzed milk by people with self-reported severe lactose intolerance. *N Engl J Med* 1995;333:1–4.
- 16 <http://pathways.nice.org.uk/pathways/constipation>
- 17 *Prucalopride for the treatment of chronic constipation in women*. NICE technology appraisal guidance [TA211] December 2010.
- 18 Irritable bowel syndrome with constipation in adults: linaclotide. NICE advice [ESNM16] April 2013.
- 19 Camilleri M, Parkman H, Shafi MA, *et al*. Clinical guideline: management of gastroparesis. *Am J Gastroenterol* 2013;108:18–37.
- 20 <https://www.gov.uk/drug-safety-update/domperidone-risks-of-cardiac-side-effects>
- 21 Gasbarrini A, Lauritano EC, Gabrielli M, *et al*. Small intestinal bacterial overgrowth: diagnosis and treatment. *Dig Dis* 2007;25:237–40.
- 22 Grace E, Shaw C, Whelan K, *et al*. Small intestinal bacterial overgrowth prevalence, clinical features, current and developing diagnostic tests, and treatment. *Aliment Pharmacol Ther* 2013;38:674–88.
- 23 Andreyev HJ, Davidson S, Gillespie C, *et al*. Practice guidance on the management of acute and chronic gastrointestinal problems arising as a result of treatment for cancer. *Gut* 2012;61:179–92.
- 24 Dukowicz A, Lacy B, Levine G. Small bowel bacterial overgrowth: a comprehensive review. *Gastroenterol Hepatol* 2007;3:112–22.
- 25 <http://www.webmd.com/oral-health/guide/oral-side-effects-of-medications?page=4>