

## Curriculum based clinical review

# Obesity management for the gastroenterologist

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## ABSTRACT

Obesity has reached epidemic levels in the United Kingdom. Obesity is associated with important gastrointestinal and hepatic complications which are common and can present sooner than cardiometabolic disease but often the underlying obesity remains untreated. Given that gastroenterologists and hepatologists will be at the forefront of obesity management we present an overview encompassing obesity pathophysiology, medical and surgical treatment options as well as the role of endobariatrics and the gut microbiome.

## INTRODUCTION

Obesity has reached epidemic levels in the United Kingdom (UK) affecting both the adult and paediatric population. Carrying excess body weight is the norm in the UK as approximately one in four adults are obese and one in three are overweight as defined by body mass index (BMI, [table 1](#)).<sup>1</sup> Ethnic differences for BMI ranges defining overweight and obesity exist especially between Caucasian and Asian populations ([table 1](#)), reflecting the higher risk of cardiometabolic disease at a lower BMI in the latter population.<sup>2</sup> The UK has the second highest prevalence of obesity in Europe and sixth highest worldwide. The National Health Service (NHS) spent approximately £6.3 billion on overweight and obesity-related illness in 2014/2015 and this is predicted to rise to £9.7 billion by 2050.<sup>1</sup>

## Complications of obesity

The excess adiposity that characterises obesity is associated with significant morbidity and mortality. An observational study involving 2.8 million UK adults between January 2000 and July 2018 showed that individuals with a BMI between 40–45 kg/m<sup>2</sup>, when compared with normal weight individuals, had a 50% increased risk of all-cause mortality, a 12-times higher risk of type 2 diabetes

mellitus (T2DM) and were 22 times more likely to develop obstructive sleep apnoea (OSA). The least obese (BMI 30–35 kg/m<sup>2</sup>) had a 70% greater risk of heart failure and were five times more likely to develop T2DM and OSA.<sup>3</sup>

A population-based cohort study involving 3.6 million UK adults demonstrated that cardiovascular disease and cancer were important causes of mortality among overweight and obese patients,<sup>4</sup> and obesity is the second biggest preventable cause of cancer in the UK.<sup>5</sup> Obesity is also associated with significant psychological comorbidity including binge eating, emotionally driven eating, anxiety and mood disorders.<sup>6</sup> Addressing obesity stigmatisation and discrimination is crucial so that patients and healthcare providers appreciate obesity as a disease that requires treatment.

## Gastrointestinal complications of obesity

Obesity is associated with common gastrointestinal and hepatic complications ([table 2](#)) that often present sooner than cardiometabolic diseases<sup>7</sup> and therefore gastroenterologists and hepatologists have a unique opportunity to implement early weight loss interventions and/or to refer to specialist weight management centres. Abdominal obesity is implicated in oesophageal, hepatobiliary and malignant disorders ([table 2](#)) and it is best captured by measuring waist circumference<sup>7</sup>. Indeed, abdominal obesity is also an important predictor of non-alcoholic fatty liver disease (NAFLD) even among patients with a normal BMI.<sup>7</sup>

## Pathophysiology

In the past 50 years, 20%–30% of entire populations have become obese due to environmental changes encouraging increased energy intake and reduced energy expenditure.<sup>8</sup> The availability of large portions of highly palatable



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## Specialty certificate exam style BEST-OF-FIVE questions

**Question 1**

A middle-aged female with a past medical history of obesity and diabetes underwent a laparoscopic Roux-en-Y gastric bypass 1 week ago. She presents to the acute medical take with a fall on a background of a 2-day history of persistent vomiting, confusion and blurred vision.

What micronutrient is most likely to be deficient?

- Vitamin B<sub>1</sub>
- Vitamin B<sub>6</sub>
- Vitamin B<sub>12</sub>
- Calcium
- Potassium

Correct answer a) Vitamin B<sub>1</sub> (Thiamine)

The presentation suggests developing Wernicke's encephalopathy following a recent gastric bypass which places this patient at increased risk of thiamine deficiency because this water-soluble vitamin is absorbed in the duodenum and proximal jejunum. Thiamine can only be obtained from the diet and cannot be endogenously synthesised by human cells.

**Question 2**

A middle-aged female who is asymptomatic is referred to a joint hepatology-diabetology clinic with liver steatosis on abdominal ultrasound, normal liver function tests and a glycosylated haemoglobin (HbA1C) of 59 mmol/mol. She has a past medical history of treated bladder cancer and type 2 diabetes mellitus. She is a non-smoker and does not drink alcohol. She is currently taking metformin 1 g twice a day and gliclazide 80 mg twice a day. On examination, her waist circumference is 102 cm and body mass index (BMI) is 37 kg/m<sup>2</sup>. Her liver screen is unremarkable. She is commenced on a once weekly subcutaneous injection of semaglutide.

What drug class does semaglutide belong to?

- Glucagon-like peptide 1 agonist
- Dipeptidyl peptidase-4 inhibitor
- Sodium-glucose cotransporter 2 inhibitor
- Insulin secretagogues
- Biguanides

Correct answer: a) Glucagon-like peptide 1 agonist (GLP-1)

Semaglutide is a GLP-1 agonist that has effects on the central nervous system, pancreas and intestinal tract. GLP-1 agonists can mediate an incretin effect whereby insulin secretion is enhanced when enteral glucose is given in comparison to parenteral glucose. GLP-1 agonists can have trophic effects on pancreatic beta-cells and are associated with increased satiety, reduced food intake and weight loss. GLP-1 suppresses appetite through vagal-dependent and vagal-independent mechanisms, the latter involving activation of POMC/CART (pro-opiomelanocortin/cocaine and amphetamine regulated transcript) hypothalamic neurones. GLP-1 also delays gastric emptying.

**Question 3**

A middle-aged male presents to your gastroenterology outpatient clinic. He underwent a Roux-en-Y gastric bypass operation for Obesity Class II (BMI 35–39 kg/m<sup>2</sup>) and type 2 diabetes 12 months ago. He has lost 40 kg since his operation and his current glycosylated haemoglobin is 6%. He complains of nausea, abdominal pain, diarrhoea, tremors, sweating and palpitations, especially within 30 minutes of eating sugary snacks for the past 1 month.

What is the most appropriate management option for this patient?

- Inpatient surgical review
- Advise a low glycaemic index carbohydrate diet
- Prescribe antibiotics
- Reassure and advise Fermentable Oligo-, Di-, Mono-saccharides And Polyols (FODMAP) diet
- Colestyramine

Correct answer: b) Advise a low glycaemic index carbohydrate diet

The question gives a history of dumping syndrome which can affect up to 50% of patients at some stage following gastric bypass. It is caused by rapid emptying of gastric contents into the small intestine. This causes fluid to shift into the small intestine due to increased osmolarity. Some patients may also experience an exaggerated postprandial insulin response which can cause hypoglycaemic episodes, especially after eating high glycaemic index carbohydrates and/or eating too fast. Mainstay of management is to adhere to a low GI carbohydrate diet and to eat small frequent meals. Medications such as diazoxide, octreotide or calcium channel antagonists are available for refractory cases of dumping syndrome. GLP-1 analogues have also been trialled as partial agonists.

**Table 1** Classification of weight according to BMI for Caucasian, South Asian and Chinese populations<sup>1</sup>

Classification	BMI (kg/m <sup>2</sup> )	
	Caucasian	South Asian* and Chinese
Healthy or 'normal' weight	18.5–24.9	18.5–23
Overweight or preobesity	25–29.9	23–27.5
Obesity I	30–34.9	≥27.5
Obesity II	35–39.9	
Obesity III	≥40	

\*South Asian = Bangladesh, Bhutan, India, Indian-Caribbean (immigrants of South Asian family origin), Maldives, Nepal, Pakistan and Sri Lanka  
BMI, body mass index.

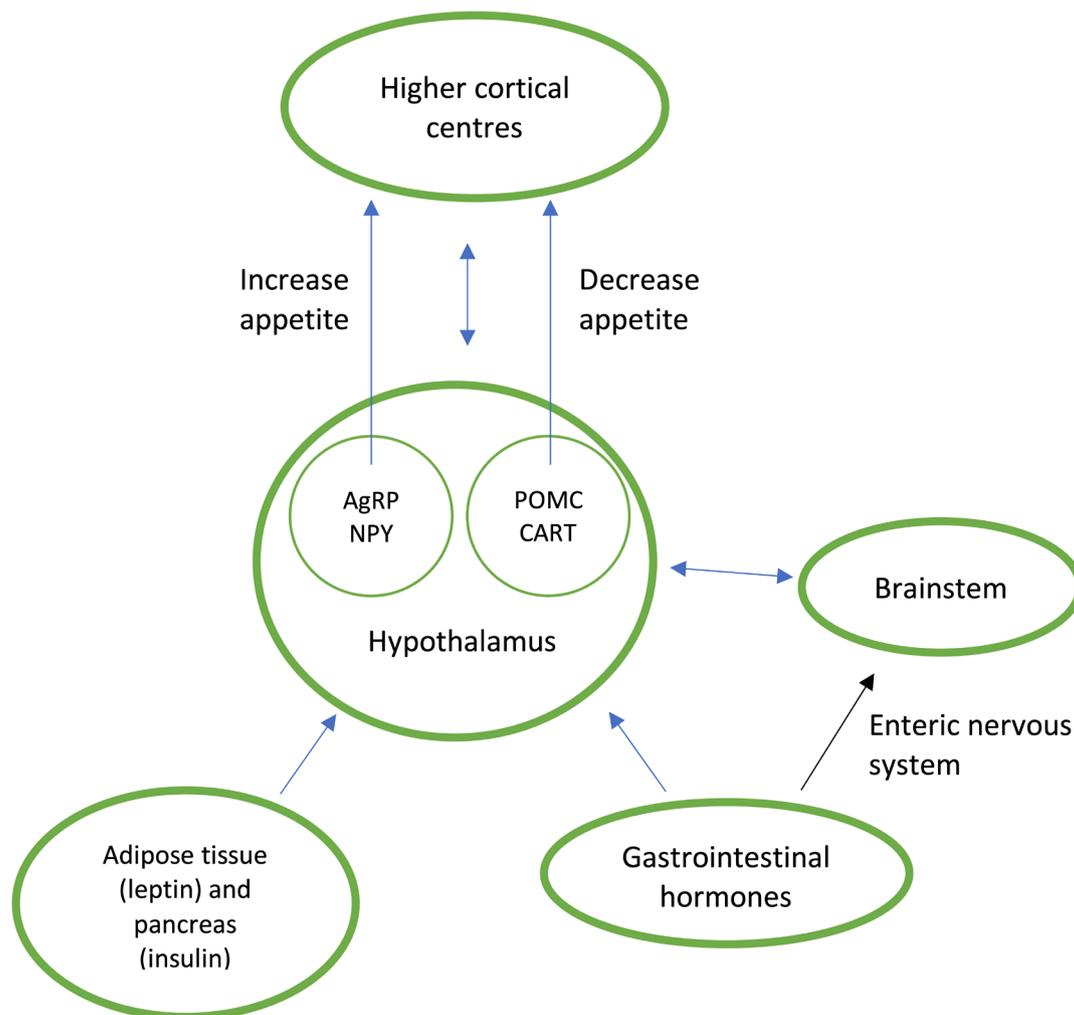
energy-dense processed foods are a key driver for weight gain. Food intake is influenced by external variables such as food palatability and availability and the internal gut–brain axis (figure 1).<sup>8</sup> Hunger and satiety are regulated in the brain via complex reciprocal connections between the hypothalamus, brainstem and higher cortical areas which receive peripheral neuroendocrine signals from the gastrointestinal tract which regulates meal initiation and termination (table 3)<sup>8</sup>. Insulin, leptin and adipokines are involved in the long-term regulation of energy homeostasis mediated by the amount of stored adipose tissue (table 3).<sup>9</sup>

**Table 2** Quantified risk ratios and physiological mechanisms of selected gastrointestinal diseases associated with obesity in adults

Gastrointestinal disease	Obesity as a risk factor		Physiological mechanism by which obesity is associated with gastrointestinal disease
	Risk expressed as OR or RR	95% CI	
<b>Oesophagus</b>			
Gastro-oesophageal reflux disease	OR, 1.94	1.46–2.57	↑ intra-abdominal pressure, ↓ Oesophageal pressure. ↑ Oestrogen
Erosive oesophagitis	OR, 1.87	1.51–2.31	Abdominal adiposity
Barrett's oesophagus	OR, 4.0	1.4–11.1	Abdominal adiposity, ↓ Adiponectin, ↑ Leptin
Oesophageal adenocarcinoma	Men: OR, 2.4 Women: OR, 2.1 RR, 4.8	1.9–3.2 1.4–3.2 3.0–7.7	Abdominal adiposity, ↓ Adiponectin, ↑ Leptin, Insulin-like growth factor
<b>Stomach</b>			
Gastritis	OR, 2.23	1.59–3.11	↓ Adiponectin
Gastric cancer	OR, 1.55 RR (Cardia), 1.8	1.31–1.84 1.3–2.5	Proinflammatory, adipokines, Insulin-like growth factor
<b>Hepatobiliary</b>			
Non-alcoholic fatty liver disease	RR, 4.6	2.5–11.0	Abdominal obesity, ↑ serum free fatty acids, ↑ hepatic triglycerides, hepatic de novo lipogenesis
Liver cirrhosis	RR, 4.1	1.4–11.4	Non-alcoholic fatty liver disease, non-alcoholic steatohepatitis, proinflammatory
Hepatocellular carcinoma	RR, 1.8	1.6–2.1	Non-alcoholic fatty liver disease, non-alcoholic steatohepatitis, proinflammatory
Gallstone disease (gallstones, cholecystitis)	Men: RR 2.51 Women: RR, 2.32	2.16–2.91 1.17–4.57	Abdominal obesity, ↑ Insulin, ↑ leptin, ↑ lipids, insulin resistance, dysmotility
Gallbladder cancer	RR, 1.3	1.2–1.4	↑ risk of gallstones, chronic inflammation
<b>Pancreas</b>			
Acute pancreatitis	RR, 2.20	1.82–2.66	Hyperlipidaemia, chronic inflammation
Pancreatic cancer	Men: RR, 1.10 Women: RR, 1.13 RR, 1.5	1.04–1.22 1.05–1.18 1.2–1.8	Insulin-like growth factor binding protein-1
<b>Intestinal</b>			
Diarrhoea	OR, 2.7	1.10–6.8	↑ Bile acids, accelerated colonic transit,
Diverticular disease	RR, 1.78	1.08–2.94	Chronic inflammation, alteration in gut microbiota
Polyyps	OR, 1.44	1.23–1.70	Chronic inflammation
Colorectal cancer	Men: RR, 1.95 Women: RR, 1.15 RR, 1.3	1.59–2.39 1.06–1.24 1.3–1.4	Chronic inflammation, ↑ adipokines, bile acids, insulin resistance, gut microbiota

Adapted from Camilleri *et al.*<sup>7</sup>

CI, confidence interval; OR, odds ratio; RR, relative risk.



**Figure 1** Neuroendocrine regulation of appetite. Gastrointestinal and peripheral hormones communicate directly (via the blood brain barrier) and indirectly (enteric nervous system) to the subconscious hypothalamus and brainstem to either stimulate appetite via agouti-related peptide (AgRP) and neuropeptide Y (NPY) or suppress appetite via pro-opiomelanocortin (POMC) and cocaine and amphetamine regulated transcript (CART). These signals are conveyed to higher conscious brain centres which regulate eating behaviour.<sup>8</sup>

### Management

The multifactorial nature of obesity requires a multidisciplinary and multicomponent approach that incorporates lifestyle, medical and/or surgical intervention. The National Institute of Clinical Excellence (NICE) use risk stratification to guide treatment acknowledging that high-risk patients require more intensive treatment (table 4).<sup>10</sup>

### Lifestyle

The foundation of obesity management is empowering patients with the skills and strategies to facilitate weight loss (table 5), weight loss maintenance and prevent weight regain, all of which requires different approaches and should be maintained alongside medical and surgical treatment. Psychological therapies for the treatment of obesity can be used in specialist weight management centres and include interpersonal psychotherapy, behavioural therapy and various forms of cognitive behavioural therapy which is effective for bulimia nervosa.<sup>11</sup>

Indeed, input from a clinical psychologist is absolutely necessary before proceeding to surgery.<sup>10</sup>

### Pharmacological

Pharmacotherapy can be considered as an adjunct in patients who are struggling to lose weight (eg, 5–10% after 3–6 months) or maintain weight loss with lifestyle interventions.<sup>10</sup> Orlistat tablets<sup>10</sup> and liraglutide (Saxenda) injections<sup>12</sup> are currently the only medications licenced for the treatment of obesity in the UK, while naltrexone plus bupropion combination is approved by the European Medicines Agency but currently unavailable in the UK (table 6). Patients who fail to lose 5% of their body weight after 12 weeks with orlistat or liraglutide should discontinue use.<sup>10</sup> Like liraglutide, metformin and sodium-glucose cotransporter-2 (SGLT-2) inhibitors are medications used to treat type 2 diabetes which are associated with weight loss but neither are licenced for the treatment of obesity.<sup>12</sup> None of antiobesity drugs are

**Table 3** Summary of the action of selected gastrointestinal hormones, insulin and leptin and how they are altered in obesity<sup>9</sup>

Gut hormone	Gastrointestinal site of secretion	Action on gastrointestinal system	Effect on appetite	Changes in obesity
Ghrelin	X/A-cells in gastric fundus	Increases gastric motility	Increases appetite	Reduced pre-prandial peak levels and reduced postprandial suppression
Peptide YY <sub>3-36</sub>	L-cells in distal intestine	Inhibits gallbladder secretions, inhibits gastric emptying, inhibits pancreatic secretions, enterogastrone effect.	Decreases appetite	Reduced fasting and postprandial secretion
Glucagon-like peptide-1	L-cells in distal intestine	Inhibits gastric emptying, inhibits gastric secretions, promotes pancreatic beta-cell growth, incretin effect.	Decreases appetite	Reduced postprandial secretion
Oxyntomodulin	L-cells in distal intestine	Inhibits gastric secretions, inhibits gastric emptying, incretin effect.	Decreases appetite	–
Cholecystokinin	I cells in small intestine, co-localises with PYY in L-cells of distal intestine	Promotes gallbladder contraction, increases pancreatic secretions, inhibits gastric secretions, inhibits gastric emptying.	Decreases appetite	Not implicated

Peripheral hormone	Site of secretion	Effect on appetite	Changes in obesity
Insulin	Pancreas (beta-cells)	Decreases appetite	Hyperinsulinaemia, insulin resistance
Leptin	Adipocytes	Decreases appetite	Hyperleptinaemia, leptin resistance

licenced in pregnancy and therefore women of child-bearing age should use contraception if these medications are prescribed.<sup>10</sup>

#### Bariatric/metabolic surgery

Randomised controlled trials (RCTs) and prospective cohort studies provide evidence that bariatric surgery is superior to non-surgical interventions for durable weight loss and improvements in comorbidities such as type 2 diabetes, which has led to the term metabolic surgery.<sup>13</sup> The Swedish Obese Subjects Study, a landmark cohort study involving 4047 obese patients

(BMI > 34 kg/m<sup>2</sup>) demonstrated a 23% reduction in body weight 20 years after bariatric surgery when compared with conventional non-surgical management.<sup>14</sup> Two large multicentre RCTs involving lifestyle interventions (Diabetes Prevention Programme, Look AHEAD trial) achieved 7–8 kg weight loss after 1 year, which was regained after 10 years<sup>13</sup>.

Response to bariatric surgery is variable and operation specific but Roux-en-Y gastric bypass (RYGB) and vertical sleeve gastrectomy (VSG) can achieve clinically significant weight loss and metabolic improvements

**Table 4** The level of intervention for obesity is based on BMI, waist circumference and presence of comorbidities.<sup>10</sup>

BMI (kg/m <sup>2</sup> )	Waist circumference (cm)			Comorbidity present*
	Low risk <94 (male) <80 (female)	High risk 94–102 (male) 80–88 (female)	Very high risk >102 (male) >88 (female)	
Overweight (25–29.9)	1	2	2	3
Obesity I (30–34.9)	2	2	2	3
Obesity II (35–39.9)	3	3	3	4
Obesity III (40+)	4	4	4	4

1=general advice on healthy weight and lifestyle.

2=diet and physical activity.

3=diet and physical activity; consider medications.

4=diet and physical activity; consider medications; consider surgery.

\*At least one of the following comorbidities should be present such as type 2 diabetes mellitus, hypertension, dyslipidaemia, ischaemic heart disease, obstructive sleep apnoea polycystic ovarian syndrome, osteoarthritis.<sup>10</sup>

BMI, body mass index.

**Table 5** Summary of NICE guidelines for weight loss through lifestyle changes with selected practical suggestions<sup>10</sup>

	Goal	Practical suggestions
<b>Diet</b>	600kcal/day reduction in energy intake	Encourage a diet rich in colourful vegetables, fruits, beans, pulses, wholegrains and fish
	(Men: 1900kcal/day)	Increase the proportion of high-fibre or wholegrain foods
	Women: 1400kcal/day)	Avoid takeaway and processed foods Avoid sugary drinks and replace them with water or drinks with no or low sugar Avoid energy-dense snacks (biscuits, chocolates, cakes)
<b>Physical activity</b>	Weight neutral: 30 mins/day 5 days a week	Brisk walking or running
	Weight loss: 45–60 mins/day	Stair climbing, avoid escalators and lifts
	Weight loss maintenance: 60–90 mins/day	Cycling
		Gardening Supervised exercise programme Swimming
	Reduce sedentary behaviour	Reduce the amount of time spent sat down, watching TV, using a computer or playing video games
<b>Behavioural</b>	Self-monitoring	Record calorie intake of foods and drinks, record weight loss, slow down the speed of eating Set goals based on what foods to eat, what foods to avoid, calorie intake and amount of physical activity
	Goal setting	Involve family and friends to provide support Plan meals weekly
	Social support	Avoid or be able to manage the sight or smell of high-calorie highly-palatable foods
	Relapse prevention	

Adapted from NICE.<sup>10</sup>

(table 7)<sup>15</sup>. There is on-going research to identify prognostic factors that may predict bariatric surgery outcomes and complications in order to select the right operation for the right patient.<sup>16</sup>

A retrospective UK cohort study in 2016 using 3039 electronic records found that RYGB and VSG are

being favoured over gastric banding which is declining due to complication rates (eg, band slippage or intolerance) and the need for eventual surgery<sup>17</sup>. Biliopancreatic diversion with duodenal switch (BPD-DS) is rarely performed due to its complexity and historical high surgical morbidity and mortality as well as long-term nutritional deficiencies.<sup>17</sup> Bariatric surgery is indicated for severe or morbid obesity among patients fit for surgery and committed to lifelong lifestyle changes and specialist follow-up (Box 1 and 2)<sup>10</sup>.

#### Anatomical description of procedures

During RYGB, the upper part of the stomach is divided to create a small gastric pouch (15–30 mL) which is anastomosed to the mid-jejunum creating the roux or alimentary limb. The remaining stomach, duodenum and proximal jejunum, which form the bilopancreatic limb, are thus bypassed. Small bowel continuity is restored via a distal jejuno-jejunostomy, where the alimentary and bilopancreatic limbs join to form a common channel, where nutrient absorption occurs (figure 2).<sup>18</sup>

VSG involves excising 70–80% of the stomach along the greater curvature to create a banana-sized gastric tube (figure 2). Historically, partial gastrectomy was the first stage of BPD-DS which is a two-stage procedure. The second stage involves dividing the small intestine

proximally at the duodenum and distally approximately 250 cm before the ileocaecal valve. The distal small bowel is anastomosed to the duodenum. The distal end of the excised small bowel, which contains bilopancreatic secretions, is attached approximately 100 cm before the ileocaecal valve thus allowing a long intestinal bypass with a short common channel for nutrient absorption (figure 2).<sup>18</sup> Bilopancreatic diversion with or without duodenal switch is rarely performed but the single anastomosis duodeno-ileal bypass with sleeve gastrectomy is gaining in popularity. Bariatric surgeries are currently described on their anatomical rearrangement but data from mechanistic studies suggest that these operations should be classified according to their metabolic outcomes.<sup>18</sup>

#### Mechanisms of bariatric surgery

Historically bariatric surgery was thought to induce weight loss through caloric restriction, nutrient malabsorption or both. Instead, substantial evidence suggests that the anatomical changes specific to RYGB and VSG differentially alter gastrointestinal signalling to the brain to reduce hunger, increase satiety and change food preferences from high-sugar and high-fat foods to healthier alternatives. It is these subconscious changes in eating behaviour that result in durable weight loss following bariatric surgery.<sup>16 19</sup> This complex gut–endocrine–brain axis is mediated by profound changes in pathways involving gut hormones, bile acids, gut microbiota and the enteric nervous system (table 8).

**Table 6** Medications approved by the EMA for obesity. Indication, drug class, mechanism and side-effects for each medication is included.<sup>13</sup> Risk factors include prediabetes, type 2 diabetes mellitus, hypertension, dyslipidaemia and obstructive sleep apnoea.<sup>10</sup>

	Orlistat	Liraglutide (Saxenda)	Naltrexone plus bupropion
Indication	BMI $\geq$ 30 or $\geq$ 28 kg/m <sup>2</sup> with $\geq$ 1 risk factor	BMI $\geq$ 30 or $\geq$ 27 kg/m <sup>2</sup> with $\geq$ 1 risk factor	BMI $\geq$ 30 kg/m <sup>2</sup> or $\geq$ 27 with $\geq$ 1 risk factor
Drug class	Gastric and pancreatic lipase inhibitor	Glucagon-like peptide-1 agonist	Noradrenaline and dopamine reuptake inhibitor plus opioid antagonist
Mechanism	Reduces dietary fat absorption	Increases satiety, delays gastric emptying	Central appetite suppressant
Side effects	Abdominal pain, flatulence, steatorrhea, anxiety, anorectal haemorrhage, bullous dermatitis, cholelithiasis, diverticulitis, hepatitis, oxalate nephropathy, pancreatitis, renal failure	Nausea, vomiting, constipation, diarrhoea, dizziness, gallbladder disorders, increased risk of infection, insomnia, pancreatitis, tachycardia	Nausea, vomiting, constipation, dry mouth, dizziness, increased blood pressure, insomnia, anxiety, agitation
Contraindications	Cholestasis, chronic malabsorption syndrome, concomitant use with other medications for weight loss	Diabetic gastroparesis, inflammatory bowel disease, severe congestive cardiac failure, $\geq$ 75 years old, obesity due to endocrinological or eating disorders, concomitant use with other medications for weight loss	Uncontrolled hypertension

BMI, body mass index; EMA, European Medicines Agency.

Glucagon-like peptide-1 (GLP-1) and peptide YY<sub>3-36</sub> (PYY) are two potent gut-derived appetite suppressor peptides that are elevated following RYGB and VSG and have been consistently associated with weight loss and blocking these hormones in postoperative bariatric patients leads to increased appetite, food intake and weight gain.<sup>19</sup> Accelerated nutrient presentation to the enteroendocrine L-cells of the distal intestine is a key mechanism explaining the postoperative elevations in GLP-1 and PYY, which has been more consistently demonstrated following RYGB than VSG. Unlike RYGB, VSG has been consistently associated with reduced ghrelin but there is uncertainty whether this is a key driver facilitating weight loss.<sup>19</sup> Following RYGB and VSG, increased bile acid concentration and altered composition are also suggested to contribute towards weight loss and improvements in postprandial glucose metabolism.<sup>19</sup>

#### Metabolic surgery and type 2 diabetes

There is substantial evidence from RCTs that metabolic surgery is superior to medical therapy for the treatment and remission of type 2 diabetes (relative risk 22.1 (3.2–154.2)). There is rapid improvement in glycaemic control among obese patients following RYGB and VSG independent of weight loss and this is discussed elsewhere.<sup>16</sup>

#### Bariatric surgery, NAFLD and non-alcoholic steatohepatitis (NASH)

A systematic review of observational data suggest that bariatric surgery is associated with improvements in NAFLD and NASH using invasive histological and non-invasive markers (eg, NAFLD fibrosis scores).<sup>20</sup> Weight loss is a key mechanism that mediates improvements in inflammation and glucose and lipid metabolism, in NASH and NAFLD respectively. Liver cirrhosis is a relative contraindication to bariatric surgery and large RCTs with long-term follow-up are needed before bariatric surgery can be recommended for NAFLD or NASH.<sup>20</sup>

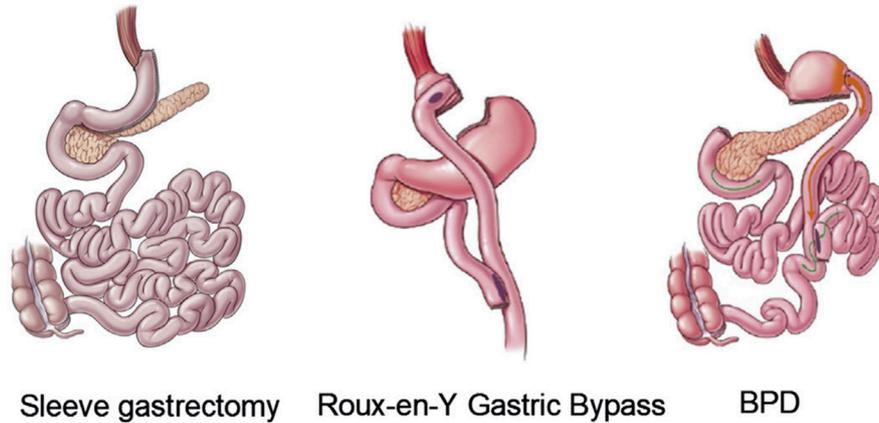
#### Early complications (<30 days)

The safety of bariatric surgery has improved in the past 20 years. Almost all operations are done laparoscopically, increased experience and volume of procedures along with enhanced recovery after surgery programmes have contributed to reduced operation times, length of stay and complications<sup>16</sup>. A meta-analysis of published mortality data (n=84,931) after bariatric surgery reported a <30-day mortality of 0.3% but this varies across subgroups and procedures<sup>16</sup> with data from the US MBSAQIP registry (n=134,142) reporting that perioperative morbidity and mortality after laparoscopic VSG to be half that of

**Table 7** Percentage of excess BMI lost at 1 and 5 year(s) following RYGB and VSG and percentage of patients achieving remission of comorbidities at 5 year follow-up (n=217)<sup>15</sup>.

	% Excess BMI lost after 1 year	% Excess BMI lost after 5 years	% of patients achieving remission of comorbidity at 5 years		
			T2DM	Dyslipidaemia	Hypertension
RYGB	76.70	68.30	67.90	62.30	70.30
VSG	72.40	61.10	61.50	42.60	62.50

There was no significant difference between RYGB and VSG for excess BMI lost at 1 or 5 years or for comorbidity resolution at 5 years.<sup>15</sup> RYGB, Roux-en-Y gastric bypass; T2DM, type 2 diabetes mellitus; VSG, vertical sleeve gastrectomy.



**Figure 2** Schematic diagram of bariatric operations. BPD, biliopancreatic diversion with duodenal switch. Adapted from<sup>16</sup>.

RYGB.<sup>21</sup> Early (<30 days) complications that are fatal include sepsis from anastomotic leak, haemorrhagic hypovolaemic shock and cardiopulmonary events such as venous thromboembolism.<sup>16</sup>

**Late complications (>30days)**

Late complications are procedure specific (table 9). Obstructive symptoms following RYGB may be secondary to a gastro-jejunal anastomotic stricture while after VSG may suggest narrowing at the gastro-oesophageal junction or incisura angularis which can present as gastric outlet obstruction.<sup>22</sup> Endoscopic dilatation can be used to treat upper gastrointestinal stenosis.<sup>22</sup> Internal herniation can also present with obstructive symptoms and is more likely following RYGB.<sup>22</sup> Early recognition is required to avoid life-threatening bowel ischaemia. An abdominal computerised tomography scan is the most sensitive investigation and urgent surgical intervention is needed to reduce the hernia and resect non-viable bowel.<sup>16</sup> At the site of the gastro-jejunostomy following RYGB, ulceration of the unprotected jejunum is due to gastric acid.<sup>16</sup> The incidence of these marginal ulcers is 8% and the majority are treated medically, with proton pump inhibitors, but non-healing symptomatic ulcers

may require surgery.<sup>16</sup> Importantly, RCT and observational data demonstrate that GORD is observed more frequently following VSG compared to RYGB<sup>15 16</sup>.

**Nutritional complications**

Essential vitamin and mineral deficiencies are likely following bariatric procedures, especially RYGB and BPD and their general biochemical monitoring and lifelong supplementation are outlined (tables 10 and 11<sup>2324</sup>). Prolonged vomiting is a risk factor for thiamine deficiency, which can manifest as Wernicke’s encephalopathy. This should be promptly treated, to avoid irreversible neurological deficits, with intravenous thiamine making sure to avoid intravenous glucose containing solutions which can exacerbate thiamine deficiency and precipitate Korsakoff’s psychosis.<sup>25</sup>

**Dumping syndrome**

Dumping syndrome can affect up to 50% of patients post-RYGB<sup>16</sup>. Early dumping presents with gastrointestinal symptoms (abdominal pain, nausea, diarrhoea) and sympathetic nervous system features (tremors, sweating, dizziness, tachycardia) within 15 min of eating large amounts of refined sugars and eating too quickly. These symptoms develop because of rapid emptying of food into the small

**Table 8** Selected physiological changes following RYGB and VSG that are implicated in weight loss and improvements in postprandial glucose metabolism. Adapted from<sup>19</sup>

	RYGB	VSG
Glucagon-like peptide-1	↑↑	↑
Peptide YY 3–36	↑↑	↑
Ghrelin	↓	↓↓
Glucose-dependent insulinotropic polypeptide	↓	–
Oxyntomodulin	↑	–
Neurotensin	↑	–
Bile acids	↑	↑
Gut microbiota composition	‘Lean’ phenotype	–
Vagal afferent signalling	↑	↑

RYGB, Roux-en-Y gastric bypass; VSG, vertical sleeve gastrectomy.

**Table 9** The late complications (>30 days) following RYGB and VSG<sup>29 30</sup>

Operation	Late complications
RYGB	Gastro-jejunal anastomotic marginal ulcer (8%), gastro-jejunal anastomotic stricture (7%), malnutrition of vitamins and minerals (up to 50%), dumping syndrome (up to 50%), gallstones (symptomatic in 2%), internal hernia or small bowel obstruction (4%).
VSG	Gastro-oesophageal reflux disease (33%), gastric dilatation, gastric stenosis leading to gastric outlet obstruction (1–4%), gastric leak.

Prevalence where known is included in brackets.

RYGB, Roux-en-Y gastric bypass; VSG, vertical sleeve gastrectomy.

**Table 10** Haematological and biochemical blood test monitoring schedule following vertical sleeve gastrectomy, roux-en-Y gastric bypass and bilopancreatic diversion with duodenal switch<sup>23,24</sup>.

Blood test	Vertical sleeve gastrectomy	Roux-en-Y gastric bypass Bilopancreatic diversion with duodenal switch
Full blood count	At 3,6 and 12 months in the first year, annually thereafter	At 3,6 and 12 months in the first year, annually thereafter
Urea and electrolytes	At 3,6 and 12 months in the first year, annually thereafter	At 3,6 and 12 months in the first year, annually thereafter
Liver function	At 3,6 and 12 months in the first year, annually thereafter	At 3,6 and 12 months in the first year, annually thereafter
Iron studies, Folate, Ca2+, Vit D, PTH	At 3,6 and 12 months in the first year, annually thereafter	At 3,6 and 12 months in the first year, annually thereafter
Vitamin B <sub>12</sub>	6 monthly first year, annually thereafter. Consider sooner if anaemia or peripheral neuropathy No need to monitor if receiving intramuscular B12 injections	6 and 12 months in first year, annually thereafter. Consider sooner if anaemia or peripheral neuropathy No need to monitor if receiving intramuscular B12 injections
Zinc, copper	Not routinely	Annually. Consider sooner if unexplained anaemia, hair loss, change in taste acuity, poor wound healing
Selenium	Not routinely	Not routinely. Consider if unexplained fatigue, anaemia, metabolic bone disease, diarrhoea, heart failure
Vitamin A	Not routinely	Annually for BPD-DS. Consider in RYGB if steatorrhoea or night blindness
Vitamin E, K	Not routinely	Not routinely. Consider if unexplained anaemia, peripheral neuropathy, coagulopathy

BPD-DS, bilopancreatic diversion with duodenal switch; Ca2+, calcium; PTH, parathyroid hormone; RYGB, roux-en-Y gastric bypass; Vit D, vitamin D.

bowel followed by rapid fluid shifts due to the hyperosmolar food content. Early dumping is often self-limiting.<sup>16</sup> Late dumping or hyperinsulinaemic hypoglycaemia is less common and can present 1 to 3 hours after eating a high glycaemic index carbohydrate meal with neuroglycopenic symptoms. Eating small frequent meals containing low glycaemic index carbohydrates and protein whilst avoiding high glycaemic index carbohydrates is key in early and late dumping syndrome.<sup>16</sup> Medications can be used in refractory late dumping syndrome (eg, diazoxide, octreotide, nifedipine).<sup>16</sup>

#### Future considerations

Gastroenterology has a key role to play in the future of obesity research and management through the human microbiome and endobariatric interventions.

The human microbiome has been implicated in obesity pathogenesis because gut micro-organisms play

a key role in host energy metabolism and immunity.<sup>26</sup> Metagenomics data have shown that obese mice and humans have higher populations of *Firmicutes* and lower populations of *Bacteroidetes* compared with lean equivalents.<sup>26</sup> This combination is associated with more efficient energy harvesting of substrates (eg, short chain fatty acids) from non-digestible carbohydrates and upregulation of genes that enable substrates to be stored as lipids or carbohydrates.<sup>26</sup> The human gut microbiota is differentially altered following RYGB and VSG although more profoundly and favourably after RYGB despite similar weight loss.<sup>19, 26</sup> There is consistent data showing that faecal microbial transplantation from post-RYGB rodents and humans to recipient germ-free mice is associated with reduced adiposity and increased energy expenditure but whether these changes are essential for the metabolic benefits of bariatric surgery remain to be elucidated<sup>19</sup>.

**Table 11** General vitamin and mineral supplementation recommendations following vertical sleeve gastrectomy (VSG), roux-en-Y gastric bypass (RYGB) and bilopancreatic diversion with duodenal switch (BPD-DS)<sup>23, 24</sup>

Supplementation	VSG/RYGB/BPD-DS
Multivitamin	Once or twice daily over the counter multivitamins
Iron	Once daily 200 mg ferrous sulphate or 210mg ferrous fumarate (twice daily for menstruating females)
Folic acid	Supplement only if deficient
Vitamin B <sub>12</sub>	3-monthly intramuscular 1 mg hydroxocobalamin
Calcium and vitamin D	Continue with pre-operative maintenance dose. Likely require 800mg calcium and 20µg vitamin D (eg, Adcal D3). Many patients will likely need additional vitamin D.
Zinc and copper	Not routinely. If additional zinc needed, ratio of 8 to 15 mg per 1 mg copper must be maintained
Thiamine	Not routinely. If prolonged vomiting prescribe thiamine 200–300 mg daily, vitamin B costrong 1–2 tablets and urgent referral to bariatric centre. Intravenous thiamine if symptomatic.

Individualised supplementation regimes may be needed for some patients or patient subgroups (e.g., pregnant women).

**Table 12** Description and weight loss associated with endoscopic bariatric interventions<sup>27</sup>

Site of action	Endoscopic intervention	Endoscopic mechanism	Description	Excess weight loss at 6 or 12 months
Stomach	Intragastric balloon	Reduction in gastric volume	Endoscopic placement of balloons (Orbera or Reshape) that are filled with 400-700mls of blue saline which are removed after 6 months. 1-3 gas-filled balloons (obalon) are swallowed sequentially over a 12-month period and are removed after 3 months.	25%–32% at 12 months (orbera) 27%–31% at 6 months (Reshape) 25% at 6 months (Obalon – not available on the NHS)
	Endoscopic sleeve gastropasty		Endoscopic staples or sutures applied along greater curvature of the stomach to reduce gastric volume by ~70%.	28%–52% at 12 months
	Aspiration therapy	Aspiration of gastric contents	Endoscopic placement of a specialised 26Fr gastrostomy tube that is used to flush water into the stomach before aspirating gastric contents 20–30 mins after a meal	49%–54% at 12 months
Small intestine	Small bowel endobarrier sleeve	Bypass small bowel	A 60 cm nutrient-impermeable sleeve that extends from the duodenal bulb to the distal jejunum and remains in for a maximum of 12 months	35% at 12 months
	Duodenal mucosal resurfacing	Duodenal exclusion	Hydrothermal ablation using a 2 cm long balloon filled with 90°C heated fluid destroys superficial duodenal mucosa distal to the papilla of Vater up to the ligament of Treitz.	2.5% at 12 months

Although bariatric surgery is safe, effective and cost-effective it is not a practical strategy to treat the epidemic levels of obesity. Endoscopic bariatric interventions could be an alternative for unwilling or unsuitable surgical candidates as well as an adjunct to medical therapy. Endobariatric procedures are performed under monitored anaesthetic care and target either the stomach or small bowel (table 12).<sup>27</sup>

A recent multicentre prospective study (n=36) evaluating endoscopic duodenal mucosal resurfacing demonstrated that this procedure was safe, well tolerated and efficacious in reducing glycated haemoglobin by  $10 \pm 2$  mmol/mol (mean  $\pm$  standard error) at 12 months despite only modest weight loss of  $2.5 \pm 0.6$  kg which suggests that the improvement in glycaemia is partly weight loss independent.<sup>28</sup> More data is needed to evaluate long-term weight loss, glycaemic changes, safety and non-weight dependent mechanisms associated with endobariatrics.

## CONCLUSIONS

Gastrointestinal and hepatic diseases are often the first manifestations of obesity. Gastroenterologists and hepatologists will be at the forefront of obesity management and have a unique opportunity to implement timely weight loss interventions or refer to specialist weight management centres. With more patients meeting the criteria for bariatric surgery, awareness of the post-operative complications is essential. Finally,

the potential to manipulate the human microbiome or use the increasing array of endoscopic technologies will allow for less-invasive tools to be added to the armamentarium in tackling obesity, with gastroenterologists set to be key players.

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