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By-Band-Sleeve Collaborative Group

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Extended Research Article

Roux-en-Y gastric bypass, adjustable gastric banding or sleeve gastrectomy for severe obesity: The By-Band-Sleeve randomised controlled trial

By-Band-Sleeve Collaborative Group

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This article

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Abstract

Background: Bariatric surgery can improve health outcomes but high-quality comparative evidence about different procedures is limited.

Objective: To compare the effectiveness and cost-effectiveness of Roux-en-Y gastric bypass (Bypass), adjustable gastric banding (Band) and sleeve gastrectomy (Sleeve) for people living with severe obesity.

Design, setting and participants: Multicentre, parallel-group, randomised controlled trial conducted in 12 National Health Service hospitals. Adults with a body mass index ≥ 35 kg/m^2 with comorbidity or body mass index ≥ 40 kg/m^2 without comorbidity were eligible. Participants were initially randomised 1 : 1 to Bypass or Band. After 32 months of recruitment, the trial was adapted to include Sleeve, and participants were randomised to Bypass, Band or Sleeve thereafter. Participants were followed up for 3 years.

Interventions: Bypass, Band and Sleeve surgery.

Main outcome measures: Primary outcomes were self-reported quality of life (EQ-5D-5L utility score) and weight (at least 50% excess weight lost) at 3 years. Sleeve and Bypass were each considered superior to Band if there was non-inferior excess weight loss (< 12% difference between groups) and superior quality of life. Sleeve was considered superior to Bypass by the same criteria. Secondary outcomes included comorbidities, adverse health events, generic and disease-specific quality of life at 6, 12, 24 and 36 months post randomisation, dietary intake, binge eating behaviour and cost-effectiveness.

Results: One thousand three hundred and fifty-one participants were randomised between December 2012 and September 2019. Five participants withdrew consent to use their data, leaving 1346 (462 Bypass, 464 Band, 420 Sleeve). The mean age was 47.3 years, 1020 (75.9%) were women and the mean weight and body mass index was 129.7 kg and 46.4 kg/m^2, respectively. Overall, 1183 (87.5%) of participants underwent surgery within 3 years, with a median waiting time of 5 months (interquartile range 2.5–10.1 months).

At least 50% excess weight loss at 3 years was achieved for 276/405 (68.1%) participants randomised to Bypass, 97/383 (25.3%) randomised to Band and 142/342 (41.5%) randomised to Sleeve [adjusted risk difference (Bypass–Band) + 40.7%, 98% confidence interval (+ 33.9% to + 47.5%); (Sleeve–Band) + 14.7% (+ 5.2% to + 24.2%), (Sleeve–Bypass) −26.0% (−35.8% to −16.3%)]. Mean EQ-5D scores at 3 years were 0.72 (standard deviation 0.29), 0.62 (0.33) and 0.68 (0.30) for participants randomised to Bypass, Band and Sleeve, respectively [adjusted mean difference (Bypass–Band) + 0.079 (+ 0.040 to + 0.117), (Sleeve–Band) + 0.045 (+ 0.006 to + 0.085), (Sleeve–Bypass) −0.033 (−0.072 to + 0.006)]. Secondary outcomes showed similar trends. The adverse event rate was highest in the Band group and lowest with Sleeve. Bypass was the most cost-effective procedure, with probabilities < 0.3 that Sleeve or Band was the most cost-effective.

Limitations: The study was impacted by the COVID-19 pandemic which prevented some participants having surgery and/or attending hospital for study follow-up appointments, which impacted on the completeness of data for these visits.

Conclusions: Bypass and Sleeve are more effective than Band. Sleeve has inferior excess weight loss and lower mean quality-of-life score than Bypass.

Future work: Longer-term follow-up is needed to determine the sustainability of observed effects and to examine adverse events. A comparison of optimal gastric bypass and optimal medical therapy for severe obesity is now needed to inform decision-making and health policy.

Trial registration: This trial is registered as ClinicalTrials.gov: NCT02841527, ISRCTN00786323.

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List of abbreviations

ALP	alkaline phosphatase
ALT	alanine transaminase
Band	laparoscopic adjustable gastric banding surgery
BiPAP	bilevel positive airway pressure
BMI	body mass index
BNF	*British National Formulary*
BP	blood pressure
BTC	Bristol Trials Centre
Bypass	laparoscopic gastric bypass surgery
CI	Chief Investigator
COMET	Core Outcome Measures in Effectiveness Trials
CONSORT	Consolidated Standards of Reporting Trials
COS	core outcome set
COVID-19	coronavirus disease 2019
CPAP	continuous positive airway pressure
CRF	case report form
CRS	Core Registry Set
DMSC	Data Monitoring and Safety Committee
DVT	deep-vein thrombosis
ELF	enhanced liver fibrosis test
eMIT	electronic market information tool
%EWL	percentage of excess weight loss
GI	gastrointestinal
GIQLI	Gastrointestinal Quality of Life Index
HADS	Hospital Anxiety and Depression Scale
HbA1c	glycated haemoglobin
HDL-C	high-density lipoprotein cholesterol
HDU	high-dependency unit
HRG	Healthcare Resource Group
HRQoL	health-related quality of life
ICER	incremental cost-effectiveness ratio
ICU	intensive care unit
IWQOL-Lite	Impact of Weight of Quality of Life-Lite
LDL-C	low-density lipoprotein cholesterol
MAR	missing at random
MDT	multidisciplinary team
MedDRA	Medical Dictionary for Regulatory Activities
MNAR	missing not at random
NICE	National Institute for Health and Care Excellence
NMB	net monetary benefit
PI	principal investigator
PIL	patient information leaflet
PRO	patient-reported outcome
QALY	quality-adjusted life-year
QRI	QuinteT Recruitment Intervention
RCT	randomised controlled trial
RN	research nurse
SAE	serious adverse event
SAP	statistical analysis plan
SEAR	screened, eligible, approached, randomised
SF-12	12-item Short Form health survey
SIV	site initiation visit
Sleeve	sleeve gastrectomy surgery
SQOT	Standardising Quality of life measures in Obesity Treatment
TMG	Trial Management Group
TSC	Trial Steering Committee
%TWL	percentage total weight loss
VAS	visual analogue scale
WTP	willingness to pay

Plain language summary

Background

People who are overweight or obese may benefit from surgery to lose weight (bariatric surgery), improve quality of life and health. While several operations are available, it is uncertain which procedure leads to the best results for patients and the National Health Service.

Who participated?

One thousand three hundred and forty-six adults with severe obesity referred for bariatric surgery from 12 hospitals in the United Kingdom.

What was involved?

The people who took part were allocated by chance to one of three surgical procedures aimed at achieving weight loss: gastric bypass, gastric band or sleeve gastrectomy. Participants were followed up for 3 years. We collected information on weight loss, blood markers, diet, hospital visits and safety information (e.g. side effects) over this period. Participants were also asked to complete questionnaires about their health-related quality of life and income.

What did the trial find?

The people having bypass surgery and sleeve surgery had greater weight loss and better quality of life at 3 years compared to those people having band surgery. Bypass surgery led to greater weight loss compared to sleeve surgery. There were fewer side effects after sleeve surgery compared to bypass and band surgery. Bypass surgery was found to provide the best value for money for the National Health Service.

Scientific summary

Introduction

Bariatric surgery is an effective treatment for severe and complex obesity. When this study started (2011), adjustable gastric band (Band) and gastric bypass (Bypass) accounted for over 80% of procedures worldwide. By 2015, practice had changed. Sleeve gastrectomy (Sleeve) accounted for over 35% of procedures and Band use had declined. Well-designed randomised controlled trials (RCTs) comparing the procedures were lacking and considered difficult to do because of recruitment challenges. Additionally, outcome heterogeneity in bariatric trials hindered data synthesis.

Objectives

To compare the clinical and cost-effectiveness of Bypass, Band and Sleeve for the treatment of severe and complex obesity. To develop a core outcome set for bariatric surgery.

Methods

Study design

Open parallel-group RCT with an integrated internal pilot and QuinteT Recruitment Intervention (QRI). Initially a two-group trial (Bypass and Band), it was adapted to include Sleeve to ensure the trial remained relevant to clinical practice.

Settings and participants

Hospitals offering all 3 surgical procedures, with a minimum of 2 surgeons with experience of at least 100 Bypass, 50 Band and 50 Sleeve procedures were eligible. Adults referred for surgery according to National Institute for Health and Care Excellence (NICE) guidelines were eligible.

University of Bristol sponsored the trial, which was approved by the Research Ethics Committee Southwest-Frenchay (reference 11/SW/0248).

QuinteT Recruitment Intervention

The QRI was integrated throughout. Recruitment challenges were elicited through recruiter and patient interviews, audio-recordings of recruitment discussions, review of screening/eligibility information, charting recruitment pathways, and observing study meetings. Recruiter-training, site visits, with group and individual feedback on study presentation and equipoise issues, tips documents and newsletters were used.

Interventions

Surgical procedures were protocolised with minimal mandated and prohibited criteria and flexible components. Protocol adherence was monitored throughout.

Randomisation and blinding

Initially participants were randomised 1 : 1 to Bypass or Band. After the adaptation, participants were randomised to Bypass, Band or Sleeve, with the aim of achieving equal-sized groups at the end of recruitment. Randomisation was via a secure internet-based randomisation system, with stratification by site and cohort minimisation to ensure balance by diabetes status and baseline body mass index (BMI). The allocation ratio varied by site to account for site recruitment before the adaptation (i.e. higher site-specific probability of being allocated to Sleeve for sites that recruited to the two-group trial, 1 : 1 : 1 allocation for sites that opened after the trial was adapted). Randomisation was performed once eligibility was confirmed and consent given. Different postoperative care prevented blinding of study personnel or participants.

Follow-up

Participants were followed up at 4 weeks post surgery and 6, 12, 24 and 36 months post randomisation. Participants attended hospital for follow-up except during the pandemic when follow-up was conducted by telephone.

Outcomes

The two primary end points measured 3 years after randomisation were (1) loss of at least 50% excess weight (defined as change in BMI from baseline/BMI at baseline −25) and (2) the EQ-5D-5L utility score. Secondary outcomes were other weight loss measures (change in BMI over time, per cent total weight loss, %TWL), other aspects of quality of life [Short Form questionnaire-12 items physical and mental health component scores, EQ-5D visual analogue scale, Impact of Weight of Quality of Life-Lite (IWQOL-Lite) overall, self-esteem, sexual life and public distress domain scores, Gastrointestinal Quality of Life Index overall and gastrointestinal domain scores, Hospital Anxiety and Depression Scale (HADS) anxiety and depression scores], blood results assessing (1) metabolic control: glycated haemoglobin (HbA1c), fasting glucose, triglycerides, total cholesterol, high-density lipoprotein cholesterol (HDL-C); (2) safety bloods: haemoglobin, 25-hydroxyvitamin D, calcium, ferritin, folate, parathyroid hormone, serum iron and vitamin B12; and (3) liver and kidney function: alkaline phosphatase, alanine transaminase and creatinine, measures of dietary intake assessed using a validated interview process, binge eating behaviour, sleepiness, adverse health events, non-alcoholic fatty liver disease and resource use.

Sample size

We hypothesised that Bypass and Sleeve would have non-inferior weight loss and superior quality of life to Band and that Sleeve would have non-inferior weight loss and superior quality of life to Bypass. The expected proportion achieving least 50% excess weight loss at 3 years was 70% (based on registry data) and the non-inferiority margin (12%) was chosen by clinicians and patient representatives. The target standardised difference for the EQ-5D-5L utility score was 0.2, with correlations between pre- and post-randomisation measures and repeated post-randomisation measures of 0.5 and 0.75, respectively. The sample size was set at 447 per group, which was sufficient to test the two hypotheses with 90% power and 1% (one-sided) statistical significance for the non-inferiority hypothesis and 2% (two-sided) statistical significance for the superiority hypothesis, allowing for 15% loss to follow-up.

Statistical analyses

The analysis population was all randomised participants, excluding withdrawals who were unwilling for their data to be used. Primary analyses were by intention to treat. Analyses were adjusted for diabetes and BMI at baseline and baseline values of the outcome where available. For longitudinal continuous outcomes, hierarchical mixed models with participant nested by site and gradients allowed to vary across time for each participant were fitted. Time was modelled with treatment-specific restricted cubic splines. Generalised linear models were used to assess treatment effects for binary and count outcomes. Pre-specified subgroup analyses and sensitivity analyses were carried out for the primary outcomes. Missing data for the primary weight outcome were imputed. Results are presented as treatment effects with 98% confidence intervals. Analyses were performed using Stata, version 18.0 (StataCorp LP, College Station, TX, USA).

Economic evaluation

The primary objective was to compare the cost-effectiveness of Bypass, Band and Sleeve to 3 years. Costs for the surgical procedures were taken from a micro-costing study. Other healthcare resource use was costed using national UK reference costs. Quality-adjusted life-years (QALYs) were estimated using the EQ-5D-5L utility score, assuming quality of life changed linearly between follow-up points and imputing missing questionnaires. Costs and outcomes after the first year of follow-up were discounted at an annual rate of 3.5%. The cost-effectiveness of the three procedures was compared using the incremental net monetary benefit. The probability of each intervention being the most cost-effective option was calculated. A range of subgroup and sensitivity analyses were carried out.

Results

Patient screening and recruitment

Between December 2012 and September 2019, 6961 patients from 12 NHS hospitals were assessed for eligibility. Overall, 1351 (28.5% of eligible, 32.6% of approached) were recruited and randomised; 463 to Bypass, 468 to Band and

420 to Sleeve. Recruitment was achieved with over 30 interviews, 77 individual and 27 group feedback sessions and 29 training sessions. Sites opening later benefitted from lessons learnt earlier in the trial.

Withdrawals

Ninety participants withdrew, 55 before surgery and 35 after surgery. The most cited reason (when given) was declining surgery. Five participants (one Bypass, four Band) withdrew consent for their data to be used.

Protocol deviations

Overall, 163/1346 (12.1%) participants did not undergo surgery within 3 years of randomisation. Of the remaining 1183, 115 did not receive the allocated surgery and two operations were abandoned. Most crossovers were from Band to Bypass or Sleeve, with few crossovers from Sleeve to another procedure.

Patient follow-up

Overall, 1159 (85.7%) participants remained in follow-up at 3 years.

Numbers analysed

The analysis population consisted of 1346 randomised participants. All participants were included in analyses of the primary weight outcome and 1284 (95.4%) were included in analyses of the primary quality-of-life outcome.

Baseline data and operative characteristics

Baseline characteristics were similar in the three groups. The mean age was 47.3 years and 1020/1344 (75.9%) were women. The mean BMI at recruitment was 46.4 kg/m^2. Most participants were White (1140/1344, 84.8%) and fewer than half (561/1343, 41.8%) were in full time employment. Almost a third had type 2 diabetes (407/1344, 30.3%), and most were on medication (1232/1346, 91.5%).

The median waiting time to surgery was 5 months; 389 participants had a Bypass, 363 Band and 429 Sleeve. All prohibited aspects of surgery were avoided, but in 31/1181 (2.6%) cases not all of the mandated components were adhered to, the most common surgery-specific deviations were not closing mesenteric defects and not reflecting the fad pad. Most participants (1099/1181, 93.1%) had an uneventful (normal) postoperative recovery (Clavien–Dindo grade 0). The median postoperative stay was 2 days.

Primary outcome: percentage excess weight loss at 3 years

In total, 276/405 (68.1%) participants randomised to Bypass achieved at least 50% excess weight loss at 3 years, compared to 97/383 (25.3%) participants in the Band group and 141/342 (41.2%) participants in the Sleeve group [adjusted risk differences: Bypass minus Band + 40.7% 98% confidence interval (+ 33.9% to + 47.5%); Sleeve minus Band + 14.7% (+ 5.2% to + 24.2%), Sleeve minus Bypass −26.0% (−35.8% to −16.3%)]. Sensitivity analyses provided consistent results. There was no evidence to suggest subgroup differences (diabetic status at baseline, $p = 0.90$; baseline BMI, $p = 0.30$).

Primary outcome: EQ-5D utility score at 3 years

The mean utility score was significantly higher in the Bypass group compared to Band [mean difference 0.079 (0.040 to 0.117)] and in the Sleeve group compared to Band [0.045 (0.006 to 0.085)]. The difference between Sleeve and Bypass was not statistically significant [−0.033 (−0.072 to 0.006)]. Comparisons involving Bypass were robust to the sensitivity analyses, with an increase in the difference between Sleeve and Bypass in favour of Bypass when excluding participants who did not have surgery [−0.043 (−0.084 to −0.003)]. All sensitivity analyses favoured Sleeve over Band, some were statistically significant at the 2% level and others were not. No subgroup differences were found (diabetes $p = 0.79$, baseline BMI $p = 0.31$).

Secondary outcomes

Mean BMI and mean %TWL followed the same pattern as the primary weight outcome; the Bypass group had greater weight loss compared to the Sleeve group, which in turn had greater weight loss compared to the Band group.

Scores measuring overall quality of life and physical function mirrored the primary EQ-5D-5L utility score, Bypass and Sleeve were superior to Band; Bypass and Sleeve were not different statistically, but the differences favoured Bypass. Scores measuring mental well-being were similar in the three groups, except for the HADS depression score which was higher (worse) in the Band group compared to the Bypass group. Mean IWQOL-Lite scores with Bypass and Sleeve were superior (better) compared with Band statistically across all domains; scores for Bypass and Sleeve were similar except for self-esteem which was higher with Bypass [+ 6.7 (+1.0 to +12.30)]. The gastrointestinal subscale favoured Bypass over Band, with similar scores for comparisons involving Sleeve.

Metabolic control (mean HbA1c and fasting glucose) was lower with Bypass and Sleeve compared to Band, with no difference between the Bypass and Sleeve. At 3 years, 244/291 (83.8%) of the Bypass group, 200/268 (74.6%) of the Band group and 190/230 (82.6%) of the Sleeve group had a HbA1c < 48 mmol/mol without antidiabetic medication. Triglycerides, total cholesterol and HDL-C followed similar trends; additionally, mean triglyceride and total cholesterol levels were higher in the Sleeve group compared to Bypass. Differences in safety bloods between groups varied, with most differences being between Bypass and Band. The only differences between Bypass and Sleeve were for ferritin and calcium, both of which were higher with Sleeve. Mean vitamin B12 and vitamin D were notably lower in the Band group compared to Bypass and Sleeve, which were similar. At 3 years, 76/285 (26.7%) of the Bypass group, 106/256 (41.4%) of the Band group and 70/238 (29.4%) of the Sleeve group had vitamin D ≤ 50 nmol/l. Alkaline phosphatase and alanine transaminase levels were lower in the Sleeve group compared to the Bypass group.

No differences in dietary intake were found. Mean binge eating scores were consistent with non-binge eating behaviour in all groups. Sleepiness was most common in the Band group. In all groups, most participants had moderate or severe non-fatty liver disease, with < 3% having none or mild disease.

Adverse events

There were 11 deaths, 4 before surgery and 7 following surgery; 1 death could be attributed to Band. Overall, 1905 adverse events were reported, with fewest post-surgery events in participants who had Sleeve (39.3/100 years compared to 51.4 and 57.1/100 years after Bypass and Band, respectively [rate ratio Sleeve : Bypass 0.74 (0.55 to 0.99)]). Post-surgery morbidity was rare with 15 internal hernia repairs after Bypass, 3 leaks from the staple line following Sleeve, and 52 corrective surgeries, removals and/or revisions following Band.

Economic evaluation

The mean costs per participant over the 3 years in the trial, including the costs of the surgery, were £8268 for Bypass; £7695 for Sleeve; and £7357 for Band. Participants randomised to Bypass accrued on average more QALYs over the 3 years than those allocated to Band and Sleeve (2.02 for Bypass; 1.82 for Band, 1.95 for Sleeve). Combining the costs and QALYs, Bypass was the most cost-effective option at the cost-effectiveness thresholds applied by NICE, with probabilities < 0.3 that Sleeve or Band is the most cost-effective option.

Core outcome set

A nine-item core set was developed.

Discussion

Main findings

Bypass and Sleeve were superior to Band, with non-inferior weight loss and superior quality of life. Sleeve was inferior to Bypass in terms of weight loss. Quality of life, while not statistically different, favoured Bypass, with a mean difference that exceeded the 0.03 threshold for clinical significance. Higher proportions of recipients in all three groups achieved a HbA1c of < 48 mmol/mol than is achieved with the new drugs for treating obesity. Rates of adverse events were highest in the Band group followed by Bypass, then Sleeve; serious surgical complications occurred at rates in line with registry reports. Bypass was found to be the most cost-effective surgical option from a UK NHS perspective.

Strengths and limitations

By-Band-Sleeve is the largest multicentre trial to date to assess the impact of the three most common bariatric operations on weight loss, quality of life, comorbidities and cost-effectiveness. The findings are generalisable to the wider NHS.

Despite recruitment challenges, the introduction of Sleeve and decline in Band, the recruitment target was met. Adherence to intervention protocols was high. COVID-19 impacted follow-up, but loss-to-follow-up for the primary outcomes was in line with the power calculation.

Percent excess weight loss is no longer the weight metric of choice, %TWL is preferred. The trial was not blinded. Completeness of data for some secondary outcomes was low. Current internationally recognised definitions of comorbidity resolution, which changed since the trial was designed, could not be applied.

Conclusion

Bypass and Sleeve resulted in significantly more weight loss and better quality of life than Band. Bypass resulted in more weight loss and a higher mean quality-of-life score than Sleeve. These differences between groups were mirrored in most secondary end points. There were fewest adverse events after Sleeve. Bypass was the most cost-effective operation, followed by Sleeve.

Trial registration

The trial is registered as ClinicalTrials.gov: NCT02841527 and ISRCTN00786323.

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Chapter 1 Introduction

Background and rationale

The prevalence of adults living with obesity is increasing around the world, and in the UK rates have trebled during the past 25 years.[6,7] Severe and complex obesity [clinically defined as body mass index (BMI) of 35 kg/m^2 or more with comorbidity or BMI of over 40 kg/m^2 without] is also on the increase. Obesity is associated with health problems, including type 2 diabetes, cardiovascular disease, musculoskeletal disorders, infertility, psychiatric disorders poor quality of life and increased mortality.[8–11] Additionally, it is a major contributor to social inequalities in health, and requires increasing costs to be placed on health services. In the UK NHS, the direct costs of treating diseases associated with overweight and obesity being estimated at £58B per year.[12] The prevention and treatment of obesity is thus a key priority for healthcare providers, but reversal of obesity is uncommon without intervention. Surgery is usually considered after patients have attempted other forms of weight loss without success.[13,14] Over the past two decades, common procedures undertaken worldwide include Roux-en-Y gastric bypass (Bypass), adjustable gastric band (Band), sleeve gastrectomy (Sleeve) and one-anastomosis (mini) gastric bypass.

Roux-en-Y gastric bypass (Bypass)

Bypass achieves weight loss by altering the flow of food through the gut, resulting in hormonal changes to appetite and satiety. Following surgery, patients are required to take vitamin and mineral supplements. Observational studies show that most weight loss occurs within 12 months, alongside improvements in generic aspects of quality of life.[15] Medium- and long-term outcome data show that many people sustain the weight loss, although some problems with generic and disease-specific quality of life are experienced and there may be weight regain.[16] Surgical risks include serious morbidity and death. In a cohort study of patients undergoing mainly Bypass, the risk of death by suicide increased 3 years after surgery (3.63 per 1000 patient-years) compared with 3 years before surgery (2.33 per 1000 patient-years).[17] Reoperation because of internal herniae, intestinal obstruction, symptoms of flatulence and regurgitation and nutritional deficiencies may occur. A variation on the Roux en Y Bypass is the one-anastomosis gastric bypass, which has been taken up by surgeons with increasing frequency in recent years due to its perceived simplicity, as it involves only one anastomosis instead of the two in a conventional Bypass.[18] There is a need for better comparative randomised evidence of the two versions.[19]

Adjustable gastric banding (Band)

Band achieves weight loss by three processes: (1) placement of a band surgically around the top of the stomach to restrict the stomach, (2) postoperative adjustment of the band (at outpatient visits) to help control the appetite and to regulate the degree of gastric restriction (by injection or removal of fluid from the band via a subcutaneous access port) and (3) education and support of patients at band adjustments. Observational studies show that after Band surgery patients experience weight loss that is gradual and that it may take 12–24 months to achieve optimal weight loss.[20] The number, timing and nature of visits for band adjustment are important.[21] Weight loss after Band is associated with improvements in comorbidities and quality of life.[22] After Band, patients may have symptoms of dysphagia and regurgitation, although comprehensive quality-of-life data after Band are lacking. Short-term surgical risks are uncommon but long-term complications are frequent and often result in Band removal. These include band erosion or migration, pouch dilatation, leakage from the circuit or infection.[20] These complications have given rise to an increase in the rates of gastric band removal over the past decade in line with its reduction in popularity, although randomised controlled trials (RCTs) evaluating its effectiveness are sparse.

Sleeve gastrectomy (Sleeve)

Sleeve gastrectomy achieves weight loss by reducing the stomach to about 25% of its original size, with favourable changes to gut hormones that control appetite and satiety. A large portion of the stomach is removed along the greater curvature. The result is a sleeve or tube-like structure. The pyloric valve at the bottom of the stomach is left intact, which means that stomach function and digestion are unaltered. Surgical risks of Sleeve include leakage and bleeding. Data show that after Sleeve most weight loss occurs over the first 12 months and tends to plateau thereafter.[16] Patients may experience more problems with reflux symptoms. Weight loss in the 12 months is associated with improvements in quality of life, but long-term quality-of-life data are lacking. A meta-analysis of weight loss and remission of comorbidities in RCTs between Bypass and Sleeve was limited by a small number of studies and limited follow-up.[23]

Rationale for the trial

This study was funded in 2011. At this time, the two most performed operations worldwide were Bypass and Band, accounting for about 80% of all obesity procedures.[3,24] The prevalence of these procedures changed dramatically in the following 5 years. Rates of Band decreased while Sleeve became more popular. By 2015, Sleeve and Bypass accounted for about 80% of all obesity operations.[25,26] By 2018, Sleeve supplanted Bypass to become the commonest bariatric procedure in the UK mirroring global trends. Decisions to undergo each type of surgery were dependent upon individual surgeon and patient preference. Thus, national, international and regional variations and changes over time are not surprising in view of the limited comparative evidence for the common procedures.[27]

Published evidence for Bypass, Band and Sleeve

Systematic reviews summarising the evidence for Bypass, Band and Sleeve have been published during the trial.[19,23,28–35] Throughout the trial we maintained a systematic review of trials evaluating the effectiveness of at least two of the three interventions in By-Band-Sleeve. This review focused on the methodological quality of reported trials.[36] Of the 15 included studies, 12 compared Bypass with Sleeve. Eleven trials randomised fewer than 200 participants and 11 were single-centre studies. None were conducted in the UK. Three were pragmatic in nature, being multicentre with longer-term clinically relevant outcomes; the remainder were studies from two or three centres with narrow inclusion criteria. Six comprehensively reported how participants were randomised and allocated their surgery. Weight loss was the most common primary outcome, frequently measured < 12 months after randomisation. Few had long-term outcome data collection planned. Due to the limited evidence available, in 2012 when By-Band opened, a well-designed and conducted RCT comparing the effectiveness and cost-effectiveness of Bypass and Band was needed and by 2015 a trial that included Sleeve was needed to inform UK (NHS) practice, health policy and individual surgeon and patient decision-making.

Aims and objectives

The By-Band-Sleeve study aimed to compare the effectiveness, cost-effectiveness and acceptability of Bypass, Band and Sleeve surgery for treatment of severe and complex obesity.

Specific objectives were to estimate the differences in:

1. the coprimary outcomes, namely self-reported EQ-5D-5L utility score and proportion of participants achieving > 50% excess BMI loss at 3 years
2. a range of secondary outcomes including generic, disease-specific and gastrointestinal (GI) symptom-specific measures of health-related quality of life (HRQoL), adverse events and comorbidities
3. the cost-effectiveness of the three surgeries.

We also aimed to explore, in a subsample, patients' experiences of management, outcome and eating behaviour change.

For the primary outcomes, we aimed to test the joint hypotheses of non-inferiority with respect to excess BMI loss and superiority with respect to HRQoL; thus, one surgery would only be considered more effective than another if both non-inferiority in terms of weight loss and superiority in terms of quality of life are demonstrated. We hypothesised that Bypass and Sleeve would be more effective than Band and that Sleeve would be more effective than Bypass.

Chapter 2 Trial methods

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Trial design

A multicentre parallel-group RCT with active follow-up to 3 years. The trial included an internal pilot phase (*Figure 1*). Eligibility criteria for participation in the study are described in *Participants*.

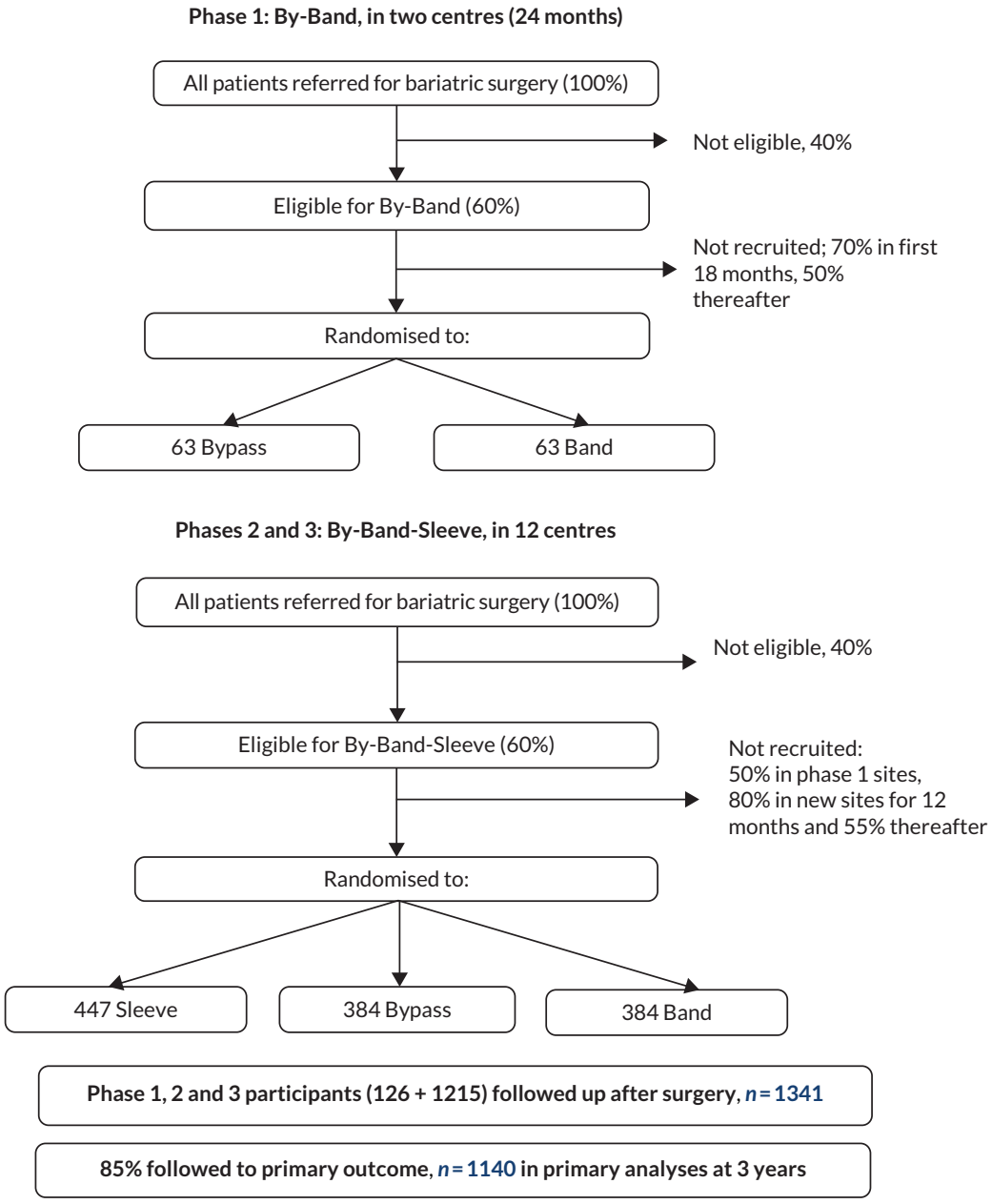

FIGURE 1 Trial schema for the design of the By-Band-Sleeve study. Note: Figure 1 denotes what was planned in terms of number of sites and recruitment, not what happened in the trial.

Criteria for progression from phase 1 to phase 2

During the first phase, processes for trial conduct, including recruitment and consent, were established. A QuinteT Recruitment Intervention (QRI) was included to optimise recruitment as this was anticipated to be difficult.[37] Progression from the internal pilot phase 1 to the full trial phase 2 was dependent on the following criteria being met when assessed after 18 months after the planned start of recruitment:

- twenty patients screened per month across two sites
- sixty per-cent of patients screened for participation considered eligible for the trial (if necessary, by revising the eligibility criteria)
- thirty per-cent of eligible participants consent to randomisation rising to 50% after 18 months of recruitment
- less than 5% fail to receive their allocated treatment
- less than 5% lost to follow-up
- develop a core outcome set (COS) for bariatric surgery
- to reconsider the role of sleeve gastrectomy.

In phase 2, the number of study sites was increased, and all sites used the optimum methods of recruitment established in phase 1.

Changes to trial design after commencement of the trial

There were several substantial amendments made to the study protocol throughout the course of the trial. The design changes are summarised below**.** The protocol version in use when the trial started was version 2.0. The current full trial protocol can be found at https://fundingawards.nihr.ac.uk/award/09/127/53.

The primary change to the design, in May 2015, was to adapt the two-group trial of Bypass versus Band to the three-group trial of Bypass versus Band versus Sleeve. The evidence of and use of Sleeve was considered as part of the progression criteria (see *Criteria for progression from phase 1 to phase 2*). Full details of the rationale for the adaptation and its implementation have been reported elsewhere.[3]

Other design changes included:

- Changing the post-surgery follow-up from 6 to 4 weeks and the addition of a 3-month follow-up (implemented October 2012 before recruitment started). The 3-month follow-up was removed at the next amendment 18 months later (March 2014) when the timing of follow-up assessments was revised (see *below*).
- When the trial was conceived, we anticipated that randomisation would happen once a confirmed surgery date was known (i.e. the time between randomisation and surgery would be minimal) and timed the follow-ups from surgery. However, to facilitate recruitment, allow participants as much time as possible to prepare for their allocated surgery and minimise dropout, sites were encouraged to randomise participants immediately following consent and before a surgery date was set, rather than waiting until the patient had a date for surgery. As surgery could be delayed for a variety of reasons, in March 2014 the protocol was amended, and follow-ups were timed from randomisation apart from the follow-up 4 weeks post surgery. In this amendment, we also clarified that baseline weight should be measured at consent and before randomisation, with weight collected again immediately pre surgery and added completion of the EQ-5D-5L questionnaire pre surgery (2-week window).
- When the trial was adapted to include Sleeve (May 2015), surgeon was removed as a randomisation minimisation factor as we found that most sites used a 'pooled operating list' and the operating surgeon was not known at the time of randomisation.
- In June 2016, the follow-up of participants for the primary outcome measures of weight and quality of life was extended from 3 years (the timing of primary outcome) to a maximum of 8 years, with data collected annually. As part of this amendment, the planned blinded assessment of outcomes at 3 years was removed as this proved to be unfeasible.

- In the first approved version of the protocol, participant questionnaires were completed on paper, the first amendment to the protocol (October 2012), approved before recruitment started, extended this to include e-mail and short message service contact and the option to complete questionnaires on-line.
- Prior to the COVID-19 pandemic participants attended hospital for follow-up, which included collection of participant weight and the taking of blood samples for the measurement of macro- and micronutrients. In July 2020, the protocol was amended to allow follow-up visits to take place either at the hospital or at the participant's home.
- Initially, one subgroup analysis was planned: participants with versus without diabetes mellitus at baseline. In July 2020, a second subgroup analysis was added, baseline BMI < 40 versus 40 or more. In September 2021, the thresholds defining the subgroups were changed to BMI < 40 versus BMI 40–50 versus BMI > 50 at baseline, to better align with international guidelines.

Participants

Patient population

Adults referred for bariatric surgery to one of the participating sites.

Patient eligibility criteria

Patients were eligible to enter the trial if all the following applied:

- 18 years of age or older
- meets National Institute for Health and Care Excellence (NICE) guidelines for bariatric surgery
  - BMI of 40 kg/m^2 or more OR
  - BMI of 35–40 kg/m^2 and other significant disease [e.g. type 2 diabetes or high blood pressure (BP)] OR
  - BMI of 30 kg/m^2 or more and recent-onset diabetes OR
  - Asian family origin with lower BMI and recent-onset diabetes, which could improve with weight loss.
- has been or is willing to receive intensive management in a specialist tier-three obesity service
- fit for anaesthesia and surgery
- committed to follow-up and able to complete quality-of-life questionnaires
- able to provide written informed consent.

Patients were not eligible to enter the study if any of the following applied:

- previous gastric surgery or surgery for severe and complex obesity
- previous abdominal surgery or GI condition that precludes one or more of Band, Bypass or Sleeve
- large abdominal ventral hernia
- pregnancy (women who have given birth and women planning pregnancy were NOT excluded)
- Crohn's disease
- liver cirrhosis and portal hypertension
- systemic lupus erythematosus
- known silicone allergy
- Hiatus hernia > 5 cm
- specified clinical or psychological reason
- active participation in another interventional research study which might interfere with By-Band-Sleeve.

Changes to trial eligibility criteria after commencement of the trial

In the first amendment before recruitment started, hiatus hernia > 5 cm was removed as an exclusion criterion. It was subsequently reinstated in May 2015 when the protocol was adapted to include Sleeve (see *Progression from phase 1 to phase 2 and adaptation to phase 3* for details). The same time the eligibility criteria were revised to reflect updated NICE

guidance and in June 2015 a further amendment was made to remove 'surgeon unwilling' as an exclusion and replace it with a 'clinical or psychological reason' to be specified.

Settings

National Health Service Trusts with an established bariatric service were eligible to participate if the site undertook at least 50 bariatric surgery operations annually and had prior experience of at least 200 Band, 250 Bypass and 200 Sleeve procedures.

Participating surgeons were expected to work within a specialist multidisciplinary bariatric team which included at least two surgeons who were prepared to offer patients participation in the trial. Surgeons were eligible to participate if they had performed more than 100 laparoscopic Bypass procedures, more than 50 laparoscopic Band procedures and more than 50 laparoscopic Sleeve procedures for severe and complex obesity. Also, they had to be willing to carry out all three procedures within the trial according to the randomised allocation.

Trial interventions

Using a typology,[38] the components of the three surgical procedures and concomitant interventions were deconstructed into their component parts and each component and step was classified as mandated, optional or prohibited. The mandated, optional and prohibited components were specified in the trial protocol and data to monitor compliance with the mandated and prohibited components was collected using purpose-designed operative case report forms (CRFs). Non-compliance with the mandated and prohibited components were considered protocol deviations.

Elements common to the three surgeries

All three surgical procedures were carried out laparoscopically. The methods used to create a pneumoperitoneum, the placement of the laparoscopic ports, and retractors were at the discretion of the surgeon. The type of instruments used were also at the surgeon's discretion. Undertaking a hiatal hernia repair and cholecystectomy were permitted but not compulsory. Undertaking an apronectomy was prohibited. Placement of drains was optional.

Adjustable gastric banding (Band)

The type and size of adjustable gastric band were at the discretion of the surgeon. It was mandatory to (1) dissect the lesser curve using the 'Pars flaccida' technique, (2) fix the Band (any fixation method is allowed) and (3) fix the adjustable port to the anterior abdominal wall.

Gastric bypass surgery (Bypass)

Methods used to create the biliary and gastric limbs were flexible, although upper limits of 75 and 150 cm were recommended for the biliary and gastric limbs, respectively. Routing of the Roux limb (antecolic or retrocolic) was flexible. The pouch could be created according to the surgeon's usual practice, except that a horizontal gastric pouch that includes fundus was prohibited. Use of a bougie was optional. Anastomoses were performed based on the surgeon discretion (e.g. stapled or sutured, single or double layer). Closure of iatrogenic mesenteric defects was mandatory from April 2018 onwards (see *Changes to trial interventions after commencement of the trial*). Prior to that it was optional. Testing integrity of the anastomoses was optional.

Sleeve gastrectomy (Sleeve)

It was mandated to visualise the left crus after dissection of the fundus. The type of bougie used was not specified but was required to be between 30 and 40 Fr. The type of stapler used was flexible and the use of additional sutures, clips, reinforcement of the staple line was at the discretion of the surgeon. Testing the integrity of the staple line was optional.

Concomitant interventions

Procedures were carried out under general anaesthesia. All patients were to receive perioperative antibiotics and thromboprophylaxis in accordance with local policy. The use of nasogastric tubes, central and arterial lines, and urinary catheters was optional. After surgery, oral intake commenced according to local policy. The decision to discharge a participant home after surgery was at the surgeon's discretion. The use of postoperative contrast swallows was optional.

Post-surgery follow-up care

Adjustable gastric banding

Follow-up appointments in the first 24 post-surgical months were expected to include follow-up at 4 weeks, 3, 6, 9, 12 and 24 months, with appointments at other times according to need (anticipated to be up to 10 appointments). After 24 months follow-up occurred annually.

Follow-up consultations were conducted by a trained research nurse (RN) or surgeon and followed a specific Band protocol**.** The participant was asked how much food they were able to eat, their appetite and whether they felt satisfied between meals. If a band adjustment was indicated, it was filled progressively to reach the so-called 'sweet spot' of optimal restriction. The band was tested for restriction and if the restriction was too great, fluid was withdrawn, to minimise the need for an urgent band defill. Occasionally, the port may not be easily accessible and X-ray control is needed; however, fixing the port to the rectus sheath usually avoids this.

Gastric bypass and sleeve gastrectomy surgeries

Follow-up appointments in the first 12 post-surgical months were expected to include follow-up at 4 weeks, 3, 6, 9 and 12 months. After 12 months follow-up occurred annually.

Changes to trial interventions after commencement of the trial

There were two significant changes to the intervention protocol during the trial, the first in March 2014 to reduce the length of the biliary and gastric limbs from 100 and 200 cm to 75 and 150 cm, respectively (decided collectively by the study investigators following discussion due to concern that longer limb lengths could cause malabsorption), and the second was to mandate the closure of iatrogenic mesenteric defects for participants having Bypass surgery. This was added in April 2018 following publication of an RCT by Stenberg *et al.*[39] which supported the routine closure of the mesenteric defects in Bypass surgery. Other protocol changes were to clarify the mandatory and optional components of surgery and concomitant interventions.

Outcomes

Primary outcomes

The two primary end points were

1. loss of more than 50% of excess weight at 3 years after randomisation
2. HRQoL measured using the EQ-5D-5L utility score at 3 years after randomisation.

Percentage of excess weight (BMI) lost was defined as

$$100 \times \left[BMI\ at\ 3\ years\ -\ BMI\ at\ randomisation^{1} \right] / \left[BMI\ at\ randomisation\ -\ 25 \right].$$

where a BMI of 25 kg/m^2 was considered an 'ideal' weight.

[1] Weight recorded at baseline, after consent and before randomisation.

Percentage of excess weight loss (%EWL) was chosen because it was the most reported weight loss metric at the time the trial was designed. In the 11 years that have followed, this measure has become less popular, with more recent studies favouring percentage total weight lost (%TWL). %TWL has increased in popularity because it is conceptually easier to understand and less influenced by starting weight. In 2021, the trial team considered changing the primary weight loss measure from %EWL to %TWL, but on reflection and after discussion with the Trial Steering Committee (TSC) decided to leave it as is. %TWL is a secondary outcome which will be reported and available for inclusion in future systematic reviews and meta-analyses. Three years was chosen as the primary outcome time point to allow for a fair comparison between the three operations that have different weight loss trajectories in the early years following surgery.

The EQ-5D-5L is used to assess generic quality of life (https://euroqol.org/wp-content/uploads/2023/11/EQ-5D-5LUserguide-23-07.pdf). It comprises five questions covering five dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression), each of which rated using a five-point scale (no problems, slight problems, moderate problems, severe problems, unable/extreme problems). The five responses are used to derive an overall utility measure of health. Each dimension is scored from 1 (no problems) to 5 (extreme problems) to give a five-digit response (e.g. 11123) which was then mapped to a utility score.[40] A score of 1 denotes perfect health (11111), and lower scores less than perfect health (0 = death, score < 0 state worse than death). Participants also rate their health on vertical visual analogue scale (VAS) ranging from 0 (worst health) to 100 (best health).

Secondary outcomes

Secondary outcomes were selected to assess the effectiveness of the three procedures. They were:

- Change in BMI over time adjusted for BMI at randomisation.
- Percentage total weight loss at 3 years.
- Generic and symptom specific HRQoL to 3 years, namely:
  - Short Form 12 (SF-12) overall physical and mental health component scores. The SF-12 is a 12-item self-completed questionnaire which assesses generic HRQoL, with higher scores indicating better HRQoL (www.qualitymetric.com/sf-12v2-pro-health-survey-lp).
  - EQ-5D VAS.
  - Impact of Weight of Quality of Life-Lite (IWQOL-Lite) overall score and self-esteem, sexual life and public distress domain scores. The IWQOL-Lite is a validated obesity-specific questionnaire that assesses HRQoL issues perceived by people to be related to weight. It is a 31-item self-completed questionnaire developed directly from commonly expressed concerns of obese people as well as from clinicians' experience (www.qualityoflifeconsulting.com/iwqol-lite.html). Each item has five response options from 1 (never true) to 5 (always true), with higher scores indicating poorer HRQoL over the preceding week.[41]
  - Gastrointestinal Quality of Life Index (GIQLI) overall and GI domain scores. The GIQLI is a 36-item self-completed questionnaire which assesses the impact of specific GI symptoms associated with bariatric surgery and obesity on HRQoL.[42] Each item is scored on a five-point scale (0–4) with lower scores indicating greater symptom burden over the preceding 2 weeks.
  - Hospital Anxiety and Depression Scales (HADS). The HADS a 14-item scale self-completed questionnaire, 7 of which relate to anxiety and 7 to depression. Each item is scored from 0 to 3 with higher score indicating poorer HRQoL. A total score of 8 or more on each scale indicates anxiety or depression.[43]
- Resource use to 3 years, including healthcare use, related to hospital admissions, outpatient visits, accident and emergency visits, surgeries, primary care visits, and use of medication and supplements as recorded by RNs in the CRFs.
- Standard blood test results [i.e. haemoglobin, fasting glucose, glycated haemoglobin (HbA1c), alkaline phosphatase (ALP), alanine transaminase (ALT), total cholesterol, high-density lipoprotein cholesterol (HDL-C), triglycerides, 25-hydroxyvitamin D, calcium, ferritin, folate, parathyroid hormone, serum iron, vitamin B12 and creatinine] measured from blood samples taken at each assessment.
- Measures of dietary intake via 24-hour recall using a standardised and validated interview process, namely dietary protein, fat, and carbohydrate (% total energy of each); energy intake (kcal/day); dietary fibre (g/day); vitamins B1 (thiamin), B12, and E; folate (folic acid), calcium and iron.
- Binge eating behaviour using a validated questionnaire.
- Adverse health events including the need for reoperation.

- Epworth sleepiness scale to 3 years.
- Non-alcoholic fatty liver disease at 3 years assessed using the enhanced liver fibrosis (ELF) test.

The outcomes listed above were identified as those that would be statistically compared between the three groups. A range of other outcomes were collected in the trial. These outcomes are described by group but were not subject to formal statistical analysis. The outcomes described are:

- waist circumference at 3 years
- time taken from randomisation to reach first loss of at least 50% of excess BMI
- time taken from first losing 50% excess BMI to first relapse (defined as weight regain such that the target of at least 50% of excess weight loss is no longer met)
- domains (excluding those listed above) in the HRQoL instruments: SF-12, IWQOL-Lite, and GIQLI to 3 years
- nutritional blood tests [i.e. haematocrit, mean cell haemoglobin, mean cell volume, albumin, bilirubin, total protein, low-density lipoprotein-cholesterol (LDL-C), phosphate, potassium, sodium, urea]
- dietary macro- and micronutrients obtained from 24-hour dietary recall [i.e. dietary protein, fat, saturated fat, and carbohydrate (g/day), % total energy from saturated fat, vitamins A, B2 (riboflavin), and D, potassium, magnesium, phosphorus, zinc and selenium]
- weight in kilogram to 3 years
- BP – systolic BP and diastolic BP to 3 years
- proportion of participants at each follow-up with each of the following:
  - systolic BP < 130 mmHg AND diastolic BP < 85 mmHg
  - total cholesterol ≤ 5.0 mmol
  - HbA1c < 48 mmol/mol
  - HbA1c < 48 mmol/mol and not taking antidiabetic medication
  - on continuous or bilevel positive airway pressure (CPAP/BiPAP)
  - obstructive sleep apnoea diagnosis and unable to tolerate CPAP/BiPAP
- duration of time taking antidiabetic medication over the 3 years from randomisation, including and excluding metformin
- crossover between interventions
- waiting time from randomisation to surgery
- pre- and postoperative care including:
  - use of anti-deep-vein thrombosis (DVT) prophylaxis
  - transfusion after surgery
  - length of hospital stay, including intensive care unit (ICU) and high-dependency unit (HDU) stay
  - Clavien–Dindo classification of postoperative recovery
  - medication at discharge after surgery
  - discharge destination
- fertility details.

Changes to trial outcomes after commencement of the trial

There have been amendments to the secondary outcomes since the trial was first designed. In particular,

- Initially, the Epworth sleepiness scale and HADS questionnaire were not included, and these were added as part of the first amendment (October 2012) before recruitment began.
- In March 2014, discontinuation of CPAP was removed as a criterion for the resolution of sleep apnoea and a sleep study at 3 years for participants with sleep apnoea at recruitment was added. Sleep studies were removed from the protocol as part of the amendment submitted in September 2022, as these had not proved feasible.
- When the protocol was first written in 2012, several outcomes were defined in terms of resolution of symptoms or comorbidities. In 2021, all secondary outcomes and their definitions were reviewed in order to determine if they were still fit for purpose. During this review, it became apparent that many of the internationally accepted definitions had been updated during the life cycle of trial and that the current accepted definitions could not be applied to the data collected in the trial. It was therefore decided that resolution of and time to resolution of comorbidities would be removed and replaced with longitudinal analyses of the measures that are markers

of a reduction in comorbidity (e.g. HbA1c for type 2 diabetes) and that the proportion of participants below the clinically accepted threshold(s) (e.g. < 48 mmol/mol for HbA1c) would be described. The secondary outcomes (over 70 in all) were also reviewed to prioritise those outcomes to compare statistically across the three groups and those that would be presented descriptively in order to reduce the likelihood of type I errors. These decisions were made by the Trial Management Group (TMG) in discussion with trial investigators, the patient advisory group (quality-of-life outcomes only) and the TSC; everyone was blinded to the trial data. This protocol amendment was approved in October 2022.

Sample size

We hypothesised that (1) Bypass and Sleeve would each be non-inferior to Band and that Sleeve would be non-inferior to Bypass in terms of the proportion of participants achieving an excess weight loss of at least 50% at 3 years, and that (2) the HRQoL at 3 years for participants receiving a Bypass or Sleeve would be superior to Band and that Sleeve would be superior to Bypass, with respect to HRQoL at 3 years as measured using the EQ-5D-5L utility score. The sample size was chosen to test both these hypotheses. Data from the literature[44] and from a registry of patients treated at the Taunton site were used to inform the power calculation. These estimates were unchanged when the trial was adapted from two to three groups.

The power calculation for weight loss requires the estimation of two parameters, that is, the total proportion of participants that are expected to have lost at least 50% of their excess weight at 3 years and the difference in proportions achieving this target that would be considered clinically important (the non-inferiority margin). The expected proportion of participants losing at least 50% of their excess weight at 3 years was set at 70% (conservative estimate), based on data from the Taunton registry where 73% of Band and 75% of Bypass patients in the target weight range for the trial had lost at least 50% of their excess weight at 3 years. The non-inferiority margin (12%) was chosen based on the opinions of the clinical applicants and patient representatives.

The power calculation for HRQoL requires the estimation of six parameters, that is, the within-group standard deviation (SD), the difference in mean HRQoL that would be considered clinically important, the number of pre- and post-randomisation measures, and the correlations between pre- and post-randomisation scores and between repeated post- randomisation scores. The estimates used were chosen on the basis of the published literature[45,46] and, in order to estimate correlations between different time points, on data from a surgical trial in spine injury. The target mean difference and SD were set at 0.06 and 0.3, respectively (standardised difference 0.2). Conservative estimates were chosen for the other parameters (one pre- and three post-randomisation measures, correlations between pre- and post-randomisation measures and repeated post-randomisation measures of 0.5 and 0.75, respectively), because the calculation assumes the treatment difference is similar at the three time points, which we anticipated may not hold true.

The sample size for the original two-group trial was set at 724 participants (362 per group), which was sufficient to test two hypotheses with 90% power and 2.5% (one-sided) statistical significance for the non-inferiority hypothesis and 5% (two-sided) statistical significance for the superiority hypothesis, allowing for 15% loss to follow-up at 3 years. This sample size also provided > 80% power to test for superior HRQoL using just the outcome at 3 years.

When the trial was adapted to include Sleeve as a third group, the sample size was increased to 1341 (447 per group). The only change from the initial calculation was that the significance levels were adjusted from the conventional 2.5% and 5% levels for non-inferiority and superiority to 1% and 2%, respectively, to account for the three hypotheses.

Interim analyses

There were no interim analyses planned nor undertaken for By-Band-Sleeve.

Randomisation

Randomisation was carried out after trial eligibility had been confirmed and consent given, usually within 2 weeks of consent. Patients were informed of the surgery allocated straight away to allow them sufficient time to prepare for their surgery and make arrangements for support at home afterwards, which is different between the three procedures.

Randomisation was performed by an authorised member of the local research team using a secure internet-based randomisation system. In phase 1, participants were allocated 1 : 1 to Band or Bypass. After the trial was adapted to include Sleeve, the allocation was 1 : 1 : 1 for sites that opened after the trial was adapted. For sites that recruited to both By-Band and By-Band-Sleeve, the allocation ratio was adjusted to give a higher probability of being allocated to Sleeve with the aim of achieving three equal-sized groups at the end of the trial. The allocation ratio applied at each site was based on their recruitment prior to the adaptation and their projected recruitment going forward. The exact ratio chosen for each site was not disclosed to maintain allocation concealment. The allocations were computer-generated and stratified by site. Cohort minimisation (with a random element incorporated) was used to ensure balance across the groups, by diabetes status (any type/none), and BMI 50 or more (yes/no).

Blinding

By-Band-Sleeve was an open trial without blinding of participants or clinicians or research personnel. Blinding was not feasible due to the differences in postoperative care for the three procedures.

Data collection

Overview

Data collection for the trial participants included the following elements:

1. a log of patients screened for suitability for the trial and the date when patients were given or sent the patient information leaflet (PIL)
2. a log of patients assessed against the eligibility criteria and reason(s) if ineligible
3. audio recording and transcription of consultations between surgeons and potential participants (see *QuinteT Recruitment Intervention* for further details)
4. semistructured interviews with a sample of eligible patients, to include patients who accept or decline to join the trial
5. approach and consent details, including reason(s) for non-approach or decline
6. baseline data including the participant's medical history, socioeconomic status obtained at the baseline consultation with the RN, and HRQoL obtained from questionnaires completed at this visit prior to randomisation
7. operative details extracted from medical records
8. postoperative care, including band adjustments extracted from medical records and collected at follow-up
9. adverse events and resource use in the period from randomisation to 3 years extracted from medical records and collected at follow-up
10. anthropometric and nutritional data, participant responses to HRQoL questionnaires, and comorbidity assessment collected at follow-up.

An overview of the schedule of data collection is given in *Appendix 4*, *Table 34*.

Height, weight and waist circumference data

The participant's height in centimetres was measured after removal of shoes using a calibrated stadiometer. When participants attended hospital, their weight in kilograms was measured using calibrated electronic clinic scales. Participants were weighed fully clothed after removal of shoes, jackets and any heavy items in pockets. Waist circumference was measured with outer layers of clothing removed. Further information on how measurements were taken is given in the trial protocol (https://fundingawards.nihr.ac.uk/award/09/127/53).

Blood pressure data

Blood pressure measurements were taken after the participant had been sitting for at least 5 minutes. Two readings were taken, if they differed by more than 10 mmHg, a third reading was taken. All readings were captured on the CRF.

Health-related quality-of-life data

Health-related quality-of-life data at baseline were collected on paper; participants had the option of completing the questionnaires during their appointment or later at home and returning them by post. Subsequent questionnaires were completed on paper or online according to participant preference. Questionnaires were administered by the central co-ordinating centre. Participants who failed to complete the questionnaire within 3 weeks were sent a reminder. If they still failed to respond, the participant was telephoned by the central research team and the data collected over the telephone. Site staff were also able to see if questionnaires were outstanding via the study database and offered participants the opportunity to complete an outstanding questionnaire during a study visit.

In April 2018, the protocol was amended to include £10 voucher to participants for the completion of the questionnaires as an incentive. Initially, it was planned to reimburse participants for completing the questionnaires at each follow-up time point (6 months and annually to 3 years, £40 in total), but in December 2018, this was reduced to payments at the 1- and 3-year time points only, due to limited funding available.

Twenty-four-hour dietary recall

Dietary intake was assessed using a single 24-hour dietary recall audio-recorded interview. Interviews were structured and standardised and included standard neutral probing questions to assist patients with their recall. All foods and beverages consumed over the previous day were recorded on the CRF, including time of consumption, amounts, brand names and preparation methods. Portion sizes were estimated using household measures, package weights, brands and a photographic food atlas. Interviews were conducted in person by RNs/dietitians trained by the nutrition lead (JLT). Audio recordings were used to ensure quality control of the interview process, as well as to clarify and confirm data recorded on the CRF.

Binge eating behaviours were assessed using the self-reported 16-item Binge Eating Scale.[47] Eight items describe behavioural aspects (e.g. eating fast or consuming large amounts of food), and the other eight items focus on associated feelings (e.g. fear of not stopping eating). Each item is scored from 0 to 3 points where 0 = no symptoms and 3 = serious symptoms. A score of < 17 points indicates minimal or no binge eating problems, while a score of 18 or higher indicates binge eating behaviour.

Adverse event data

Serious and other adverse events were recorded and reported in line with Good Clinical Practice guidelines. Data were collected from the time of consent until 3 years post randomisation. Serious adverse events (SAEs) were graded for severity (mild/moderate/severe).

The three surgical interventions are considered 'low risk', but adverse events related to surgery are not uncommon and were considered *expected*. These *expected* events were listed in the trial protocol. Events that occurred that were not listed in the protocol were considered *unexpected*. The list of expected events was kept under review and was updated several times during the trial; the first amendment in 2012 before recruitment started distinguished between events expected during the postoperative hospital stay and after discharge following surgery, the list expanded and revised to distinguish between reoperations, reinterventions and investigations in June 2015, and in December 2015 it was expanded further to include joint replacement or repair and cosmetic surgery (procedures which commonly occur following bariatric surgery).

Safety data were reviewed regularly by the TMG and at least annually by the Data Monitoring and Safety Committee (DMSC). Reporting to the Sponsor was required only if an adverse event was considered serious (i.e. resulted in a hospital admission, prolonged a hospital admission, was life-threatening, resulted in persistent of significant disability or death) and *unexpected* OR *expected* and fatal. Reporting to the Research Ethics Committee and DMSC was required if an *unexpected* SAE was found to be causally related to the intervention.

QuinteT Recruitment Intervention

Overview and aims

The QRI devised by the Qualitative research integrated within Trials (QuinteT) research group[37] aims to investigate, improve and optimise recruitment to RCTs. It was pioneered in the Prostate testing for cancer and Treatment (ProtecT) study,[48,49] and further developed, refined and applied in nearly 70 RCTs (many involving surgical interventions).[50–53] It was decided to include a QRI in By-Band-Sleeve because recruitment challenges were anticipated related to the wide variations in surgical procedures, expertise among the bariatric surgical community, and expression of preferences by patients about the procedure they preferred. The QRI was integrated into the trial from its inception through to the completion of recruitment, aiming to optimise recruitment and informed consent. During the pilot phase of the trial, the QRI was implemented using research methods developed for this purpose[54] in two phases, as specified in its protocol:[37]

Phase 1: Understanding recruitment challenges as they arose (in 'real time') with a focus on identifying 'clear obstacles and hidden challenges' to recruitment.

Research methods: Recruitment pathway mapping, scrutiny of RCT screening logs, interviews with RCT personnel and patients, observations and/or audio-recordings of recruitment appointments.

Phase 2: Implementing actions to improve recruitment, developed collaboratively with the Chief Investigator (CI), TMG, Clinical Trials and Evaluation Unit [now Bristol Trials Centre (BTC)], principal investigators (PIs), RNs and other recruiting staff in the trial sites.

Actions: Developing a plan of actions, individual and group feedback, training at sites and investigator meetings, and tip sheets.

Over the recruitment period, through integrative working with the trial team, the QRI evolved to understand and optimise recruitment. While the iterative phases to understand recruitment and then implement actions to optimise it continued, the QRI also developed several innovations in approach and implementation to sustain recruitment and reach the trial's enrolment targets. The QRI was undertaken in four major chronological stages, linked to recruitment milestones:

- initial stage – internal pilot (phase 1)
- transitional stage – pilot (phase 1) to main trial (phase 2) and adaptation from two groups to three (phase 3)
- sustaining recruitment stage
- final stage to complete recruitment.

A summary of each of these stages in terms of the research methods employed and implementation actions undertaken is given in *Appendix 2*.

Methods and actions in the initial stage

The QRI at this stage included the full application of all components in the QRI protocol,[2,37] and is summarised here.

QuinteT Recruitment Intervention phase 1: understanding recruitment challenges

As part of the documentation for ethics approval, the QRI team *co-designed patient-facing trial documentation* with the BTC, to ensure the documents presented comprehensive information to ensure patients would be fully informed, with balance to demonstrate equipoise.

Prior to sites opening to recruitment and alongside site set-up, *in-depth interviews* were conducted with a purposive sample of staff responsible for trial design/management and/or recruitment and informed consent. These interviews aimed to identify (anticipated) clear obstacles and hidden recruitment challenges[55] and staff members' intended plans for recruitment at their site. Interviews were transcribed verbatim and in full, and analysed thematically using constant comparison techniques[56,57] to identify similarities, discordance and divergence between participants and sites. Newly identified themes were explored in subsequent interviews and the findings were written up as detailed descriptive accounts.

Sites were requested to routinely carry out *audio-recordings of recruiters' trial discussions with patients*. Key sections of the recordings were transcribed verbatim (e.g. discussions about the trial and surgical options) followed by targeted content and conversation analysis to identify 'hidden challenges' that centred around the ways in which the trial and its related concepts such as randomisation were explained, how uncertainty was conveyed, and noting any imbalances in how the treatments were presented.

Non-participant observations of recruiters' trial discussions with patients were carried out in the initial months of recruitment, with the aim of observing the clinical set-up and context. Detailed field notes were made and analysed thematically, with a focus on understanding the organisational aspects of recruitment and the interaction between patients and clinicians.

Sites were requested to routinely capture detailed information on *eligibility and recruitment logs* for all patients who were screened, eligible, approached, randomised (SEAR) (according to the SEAR framework).[58] These data guided the monitoring of recruitment rates and any changes that occurred in relation to QRI or other trial team actions. The intended *patient pathway* for each site was also mapped out to explore areas of complexity in practice and potential bottlenecks to recruitment.

QuinteT Recruitment Intervention phase 2: actions to optimise recruitment

The analysed data were used to summarise the recruitment challenges and inform *a plan of actions* that was collaboratively developed with key stakeholders, with the aim of overcoming the identified recruitment issues. Actions were implemented, including conducting confidential feedback sessions with recruiters and other clinicians involved in the patient pathway at sites. Recruitment practice and recruitment rates were compared pre and post feedback using audio-recordings and recruitment logs.

Methods and actions in the transitional stage

This stage of the QRI began innovatively with *upfront recruitment training sessions* based on the findings from the initial stage and incorporated within the site initiation visits (SIVs) for new sites. Other phase 1 methods were similar to those used in the initial stage and included further *in-depth interviews*, this time focusing on the exploration of recruiters' views on the new third group (sleeve gastrectomy), and also analysing *audio-recordings of trial discussions*, scrutinising *eligibility and recruitment logs*, mapping *patient pathways* and also developing and implementing a phase 2 *plan of actions* in collaboration with the TMG. New sites (and pilot sites where required) had *group feedback sessions. Individual feedback sessions* were conducted with recruiters across all sites. Data and analytic reports from this stage were uploaded on to MaxQDA-12 (*MAXQDA-12*. Version MAXQDA 12 ed. Berlin: VERBI Software; 2015) to enable data management and the identification of key issues.

Methods and actions in the sustainment stage

The QRI methods employed at this stage were again innovative, being responsive to the recruitment needs of sites rather than the implementation of the two phases of the QRI protocol. The aim was to ensure (1) work focused on sites that required the most recruitment support, and (2) that momentum was maintained in sites that were recruiting well. Some standard QRI methods were employed (*in-depth staff interviews* and analysis of *audio-recordings of trial discussions*). In addition, a key innovation was the development of a strategy to identify sites and recruiters requiring targeted support. This was achieved through the development and use of novel methods of analysing the *eligibility and recruitment logs* and detailed targeted analysis of qualitative data obtained from interviews and audio-recordings.

The *plan of actions* that emerged from the new strategy included *targeted training for sites/recruiters*, depending on past achievements, staff turnover and an assessment of the capacity for improvement. This was discussed and approved

at TMG meetings. The strategy guided the group and individual feedback sessions. The QRI team also developed and disseminated a *recruitment tips document*, and undertook *RN training sessions*, *training sessions at investigator meetings*, and *visits to sites that required additional support*. Site(s) opened during this stage received upfront recruitment training at the SIV, followed by rapid and intensive feedback sessions to ensure smooth adoption of optimised recruitment techniques.

Methods and actions in the final stage

At this stage, the focus was on ensuring that the QRI recommendations from the previous three stages were widely disseminated, especially among RNs. There was no further data collection during this stage. The targeted strategy developed in the previous stage continued to be used to *prioritise the sites/recruiters for more intensive feedback*. *RN refresher training teleconferences* were conducted. These aimed to (1) engage with the RNs who continued to have an important role in recruitment and retention, (2) enable new RNs to understand the RCT and the QRI rapidly and (3) facilitate a greater understanding (and resolution) of the organisational issues hindering a smooth recruitment pathway. The QRI team also made monthly telephone calls to RNs at each site over a period of 3 months to enquire about impending recruitment activities and if there were any specific recruitment issues of concern, with feedback and tips based on previous QRI evidence as required. Key recruitment tips were also disseminated through the TMG, individual feedback sessions, an investigators' meeting, and inserted into regular study newsletters to keep the issues and tips in mind.

Statistical methods

All analyses were directed by a pre-specified statistical analysis plan (SAP), which was finalised before the database was locked for analysis. The data are reported in line with the Consolidated Standards of Reporting Trials (CONSORT) reporting guidelines for superiority and non-inferiority trials.[59,60]

Derivation of outcomes

Health-related quality-of-life questionnaires were scored according to the developer's scoring instructions; summary scales derived from the questionnaires are reported. Dietary data collected from participant interviews were analysed using the nutrient analysis programme Dietplan7 (Forestfield Software Limited, version 7.00.47). Dietary intake is reported. Adverse events were all coded using the Medical Dictionary for Regulatory Activities (MedDRA) and are reported by system organ class and preferred term. Abdominal operations and overnight admissions were coded from reported events with clinical input. Overnight admissions were coded based on notification of use of medical services. Incidences of abdominal pain recorded as unexpected SAEs were all considered to be hospital attendances.

Summary statistics and analysis population

Data were described using summary statistics; mean and SD for continuous variables [or median and interquartile range (IQR) if distributions were skewed] and number and percentage for categorical variables.

For the primary analyses, participants were grouped according to the randomised allocation (intention to treat). The analysis population consisted of all randomised participants, excluding those who withdrew and were unwilling for data already collected to be used. Data from any participant who withdrew and was unwilling for their data to be used were included in the study flow chart but not in any subsequent data tables or figures.

Modelling strategy

Treatment allocation, diabetes at baseline (yes/no) and BMI (under 50 vs. 50 or more) were included in all models as fixed effects. Outcome models were also adjusted for baseline values fitted as a fixed effect, where available.

Longitudinal continuous outcomes (e.g. health-related quality-of-life scores, results of blood tests, dietary intake, sleepiness, binge eating)

For longitudinal continuous outcomes, hierarchical mixed models with participant nested in site and gradients allowed to vary across time for each participant were fitted. Time (i.e. date of visit, blood test, HRQoL questionnaire completion,

dietary review, etc.) was modelled as a restricted cubic spline with four knots placed at the study follow-up points (6, 12, 24 and 36 months), with separate splines fitted for each treatment group. This allowed for the modelling of non-linear surgery-specific responses over time, accounted for variation in the actual timing of follow-up assessments and allowed the primary HRQoL outcome to be estimated from surgery (e.g. 36 months after surgery) as well as from randomisation. Identity covariance structure at the site level and unstructured covariance at the participant level were specified, with alternatives only examined if convergence failed. Model fit was assessed graphically (e.g. plots of predicted values vs. standardised residuals and normal probability plots). If the model was a poor fit, transformations (e.g. log transformation for data following a log-normal distribution) were considered. The impact of suppressing outliers was assessed, especially in cases where the data value was considered implausible. Treatment effects at 36 months were calculated as differences between marginal treatment means for values of the splines corresponding to 36 months, holding all other covariates at their means. Trajectories of outcomes over time by treatment group were estimated from the models by calculating marginal means at each month since randomisation (or time since surgery for sensitivity analysis, see *Sensitivity analyses*), with time increments calculated across the three splines and other covariates held at their means.

Binary outcomes (proportion of participants who achieved 50% excess weight loss at 3 years)

Generalised linear models were used to assess treatment effects for the single binary outcome. Risk ratios were estimated using a Poisson model with a log link, while risk differences were estimated using a binomial model with an identity link. Robust standard errors clustered by site were used to account for the nested structure of the data.

Count outcomes (e.g. total number of adverse events, number of abdominal operations, overnight admissions and hospital attendances for abdominal pain)

Generalised linear models were used to assess treatment effects for count outcomes. Incidence rate ratios were estimated using negative binomial models with a log link, with site included as a random effect. The analyses accounted for exposure time defined as the time from randomisation or surgery (depending on the model) to last follow-up, withdrawal or death as appropriate. The negative binomial model was chosen in preference to the Poisson model because overdispersion was indicated for all outcomes.

Ordered multicategory data (enhanced liver fibrosis results)

Ordered logistic regression was used to assess the treatment effects for the single ordered category outcome. ELF results were grouped: none/mild (Ishak score 0–2), moderate (Ishak score 3–4), severe/cirrhosis (Ishak score 5–6). The proportional odds assumption was checked and held for this outcome. The data were too sparse to allow for site to be fitted as a random effect, so the clustered sandwich estimator was used to account for the nested structure of the data.

Subgroup analysis

Pre-specified subgroup analyses, comparing the primary outcomes by diabetes at baseline (yes, no) and baseline BMI (under 40, 40–50, over 50), were performed. These were implemented by adding a treatment by subgroup interaction term into the models comparing primary outcomes between groups.

Sensitivity analyses

The following sensitivity analyses for the primary outcomes were agreed by the TMG and TSC and pre-specified in the SAP but were not included in the protocol:

1. excluding participants who did not have surgery
2. grouping participants according to the surgery received
3. excluding participants not followed up to 3 years
4. taking date of surgery as the time origin (primary HRQoL outcome only)
5. excluding patients who crossed over (i.e. did not have the surgery to which they were allocated).

Post-hoc analyses

Analyses of the primary outcomes adjusting for design phase (randomisation to two or three groups).

Missing data

Missing data are described in footnotes to all tables. Prior to analysis, the pattern of missingness was examined to determine whether the assumption of a missing at random (MAR) held. For longitudinal outcomes, there is negligible benefit in imputing missing outcome data if it can be assumed to be MAR.[61] Chi-squared tests were used to examine balance of missingness at 36 months. For longitudinal outcomes, homoscedasticity across treatment groups was also assessed using Bartlett's test for normally distributed data and Brown and Forsythe's robust median and trimmed mean test statistics for skewed data. If heteroscedasticity was suggested, a further test examining the homoskedasticity of baseline data for the participants who were missing 36-month measurements was performed.[62] If this final test confirmed heterogeneity of variance in the baseline data of participants who did not provide a 36-month data, then the assumption of MAR was rejected, and the missing data were assumed to be missing not at random (MNAR), and imputation methods for MNAR outcomes were explored.[63]

Missing baseline values were imputed using the overall median or mean value, as appropriate, when missingness was < 5%. Where missingness was 5% or more, multiple imputation was used to impute 50 baseline values via a regression on age, sex, site, diabetes status at baseline, and BMI category at baseline, with results combined using Rubin's rules. The exception to this rule were the dietary intake and ELF outcomes, as the level of missingness at baseline was deemed too high to support imputation (> 20%). Dietary intake outcome data for a given participant were only included if a baseline and at least one follow-up measurement were available, while the ELF analysis was restricted to participants with measurements at both baseline and 36 months.

Missing BMI data at 36 months were imputed by chained equations to generate multiple complete data sets and results were combined using Rubin's rules. The model imputed data for all successive study follow-ups from 4 weeks post surgery to 36 months post randomisation and included age, sex, diabetes at baseline, time from randomisation to surgery/last follow-up for participants who did not receive surgery in months, baseline BMI category, and baseline BMI as independent variables. The imputation was performed on each treatment group separately, was truncated between the minimum and maximum BMI values observed in the overall data set and used 50 imputations.

Significance levels and adjustment for multiplicity

For hypothesis tests, two-tailed *p*-values of < 0.02 were considered statistically significant (adjusted to account for three treatment comparisons). Likelihood ratio tests were used in preference to Wald tests. No other formal adjustment for multiplicity was made; the number of statistical tests performed should be considered when interpreting results.

For comparisons of Band versus Bypass and Band versus Sleeve, Band is the reference group, for comparisons of Bypass versus Sleeve Bypass is the reference group. Results are presented as treatment effects with 98% confidence intervals (CIs).

All statistical analyses were performed with the use of Stata software, version 18.0 (StataCorp LP, College Station, TX, USA).

Economic evaluation

Economic evaluation objective

The primary objective of the health economic evaluation was to estimate and compare the cost-effectiveness of Bypass, Band and Sleeve as part of the trial, from the perspective of the UK NHS. The primary within-trial cost-effectiveness analyses focus on the first 3 years after randomisation and was performed on an intention-to-treat basis, effectively estimating the cost-effectiveness of the decision to perform surgery.

Resource use and costs

Resource use related to healthcare resource use was identified a priori based on literature searches and the Database of Instruments for Resource Use.[64] Healthcare resource use was collected through CRFs with details about the type of healthcare contact, relevant diagnosis and procedures, and corresponding dates. At each follow-up visit, RNs recorded information on hospital admissions, outpatient visits, accident and emergency visits, surgeries, primary care visits,

and use of any medication and supplements (*Table 34*). Data (dates and reason for visit) on all types of hospital visits (excluding research visits) were obtained for the entire study period, increasing the likelihood that information on these events were recorded even if a participant missed a follow-up visit. Information on the total number of contacts with primary care was recorded since the participant's last visit. Costs for the three surgical procedures were taken from a micro-costing study that was undertaken as part of the trial.[65,66] The mean costs for each surgical procedure across three sites that participated in the micro-costing study were used as intervention costs. The unit cost of hospital admissions, outpatient visits, accident and emergency visits were estimated by first assigning Healthcare Resource Groups (HRGs) and then assigning reference costs to the resources.[67] For primary care visits, unit costs were obtained from the Personal Social Services Research Unit data[68] and medication costs from the Drugs and pharmaceutical electronic market information tool (eMIT)[69] and the *British National Formulary* (BNF).[70] The medication cost per participant was estimated by multiplying the cost per day to the number of days the medication was taken. The cost per day was based on actual dose prescribed. The eMIT that has prices for generic drugs was the first source for obtaining medication costs. When the drug cost was not available in eMIT, the BNF was used and the price adopted was the one that was under the brand name of the drug. The BNF was also used to obtain unit costs for the vitamin and mineral supplements recommended after Bypass or Sleeve.[71] Costs are reported as 2021 prices and costs not reported in this year were inflated using the Hospital and Community Health pay and price index in England.

Quality-adjusted life-years

Quality-adjusted life-years (QALYs) were estimated using the EQ-5D-5L questionnaire, administered at baseline, 4 weeks post surgery, 6, 12, 24 and 36 months post randomisation. Health state utility values were derived by mapping the 5 level (5L) descriptive system data onto the English 3-level (3L) value set.[40,72] In the main analysis, results were obtained using the interim mapping proposed by Van Hout *et al.*[40] in line with the analysis plan. In an unplanned sensitivity analysis, the more recently developed mapping function developed by the Decision Support Unit and recently recommended by NICE[72] was used. In the main analysis, we assumed that the HRQoL changes linearly between subsequent visits, where visits that occurred within 45 days of their planned date were assigned the date of the scheduled visit (4 weeks post surgery, 6, 12, 24 and 36 months post randomisation). Where there were no measurements within 45 days before or after a scheduled visit, we used multiple imputation to impute the HRQoL at the time of the scheduled visit (see *Health economic analyses*). Utility at the time of death was estimated by linearly interpolating between participant's last observed utility and the utility imputed in place of the following scheduled questionnaire using multiple imputation. For participants who died, their utility was set to zero after death as per the EQ-5D user guide.

Health economic analyses

The main analyses included all randomised patients, excluding patients withdrawn who did not consent for their data collected to be used. Costs and outcomes that occur after the first year of follow-up were discounted at an annual rate of 3.5%.

The comparative cost-effectiveness of the three surgeries were evaluated by estimating the incremental net monetary benefit (NMB), whereby QALYs gained were monetised by multiplying them by the maximum acceptable incremental cost-effectiveness ratio (ICER),[73,74] viz:

$$NMB = (\Delta E \times \lambda) - \Delta C$$

where λ is the maximum acceptable ICER [more commonly referred to the willingness to pay (WTP) per QALY in the literature], and ΔE and ΔC are incremental QALYs and incremental costs, respectively. The incremental NMB was estimated with gastric band as the reference, where the most cost-effective intervention is the one with the highest incremental NMB.

The incremental NMB over a wider range of WTP thresholds is presented, with the £20,000 and £30,000 per QALY highlighted in the results as these thresholds are used by UK's NICE to support NHS decision-making.[72]

The individual components of the NMB are the total discounted costs and QALYs, whereby each were estimated using regression models that take into account the factors included in the cohort minimisation [i.e. BMI (< 50, 50 or over), and

diabetes (yes, no) at recruitment as fixed effects], treatment allocation, and baseline HRQoL as covariates. For the main analyses, linear regression was used for both costs and QALYs, accounting for potential correlation between the two using bootstrapping. To ensure the non-parametric bootstrap approximates the actual randomisation process including the minimisation, trial participants were resampled within each 'allocated treatment-diabetes-BMI' group with the total number of (re)sampled participants equal to the percentage of people within each category in the trial. Missing data in terms of HRQoL estimates were dealt with by nesting a single imputation within each of the 500 bootstraps. The imputation models implemented using chained equations,[75] implemented separately by allocated treatment, included the covariates included in the regression models, as well as the following auxiliary variables that may be associated with missingness and outcome: age, sex, ethnicity, employment status at baseline, income band, receipt of benefits, height, weight, smoking and timing of surgery.

In the main analyses, we assumed healthcare resource utilisation information was complete, thereby assuming that medication and supplementation use would continue until the end of follow-up unless there was evidence that the patient stopped the drug/supplement of interest.

Given that the surgery that is optimal from a cost-effectiveness point of view, that is the surgery with the highest NMB, is not necessarily the surgery with the highest probability of being cost-effective at any value of the maximum acceptable ICER, we constructed cost-effectiveness acceptability curves to show the probability of each intervention to be the most cost-effective option. In addition, we estimated the net loss statistic (opportunity cost), which is estimated as the difference in the incremental NMB of the intervention of interest and incremental NMB of the cost-effective intervention (i.e. the intervention with the highest NMB).[76] All health-economic analyses were performed in R version 4.0.1 (The R Foundation for Statistical Computing, Vienna, Austria).

Subgroup and sensitivity analyses

The cost-effectiveness of the three bariatric surgeries were also compared between subgroups. The subgroups adopted were participants with and without diabetes mellitus at baseline, and BMI < 40, 40–50 and BMI > 50 at baseline. The subgroup effects were investigated by adding subgroup by treatment allocation interaction terms to the regression models described above.

In addition, various pre-specified sensitivity analyses were performed to evaluate the robustness of the cost-effectiveness results as shown below.

1. We used a one-inflated beta regression model instead of a linear regression model to deal with observations with a utility score of 1 more appropriately, that is, modelling the probability to be in perfect health separately from the average utility score not in perfect health. Because negative values can be observed, the non-one values were first normalised so that they fall between (including) 0 and 1. Next, the non-one values were transformed to ensure they fall between (excluding) 0 and 1: $[score_i \times (N-1) + 0.5]/N$, where N equals the sample size.
2. We used mixed-effects linear models to estimate the impact on QALYs gained using (1) a random intercept and time as modelled categorically as in the main analysis; (2) a random intercept and time modelled using a restricted cubic spline with one inner knot placed at 365 days and boundary knots placed at 182 and 730 days; or (3) a random intercept and a random slope on the spline for time.
3. We used a generalised linear model with a gamma distribution and log link to model costs.
4. We assumed that healthcare utilisation and costs were missing or incomplete if no weight measurement was provided at a visit, censored participants from the time point they had a missing weight measurement and onwards for the estimation of healthcare costs and used inverse probability of censoring weighting – using the same variables as used for the multiple imputation – to account for informative censoring.
5. We analysed participant's data according to their received surgery instead of their randomly allocated surgery.
6. We explored the potential impact of the long-term need of nutritional supplementation on the cost-effectiveness over a longer 20-year time horizon. We conservatively – based on the observation that differences in measured costs and QALYs, if anything, widened over the 3 years within the trial follow-up – assumed that those still alive after 3 years of follow-up would have perfect adherence to recommended nutritional supplementation for all surgeries without accruing any further differences over the 20-year time horizon. In addition, given that some observational studies suggested that there may be higher risk of nutritional deficiency with Bypass versus Sleeve,

suggesting that nutritional supplementation could be most essential with gastric bypass,[77,78] we evaluated the sensitivity of the results to the most extreme scenario where adherence would be 100% for Bypass and 0% adherence of the other surgeries without any further differences over the 20-year time horizon. For these analyses, we assumed participants would use the supplementation recommended by NHS foundation trusts.[79]

7. We assessed the incremental NMB using %TWL reduction instead of QALYs, using a wide range for the maximum acceptable ICER for a percentage reduction in weight loss, given the latter is not known/defined.

We pre-specified a further sensitivity analysis that would include hospitalisation within a 2-month interval (flagging hospitalisations if they occurred ± 30 days from EQ-5D questionnaire date; a 60-day window) as a covariate in the imputation models to capture potential temporary reductions in HRQoL due to acute illness related to the hospitalisations that would not be captured in participants that are hospitalised, for example, 100 days after the 1-year follow-up questionnaire. However, this resulted in too many variables included for the imputation model to converge.

The following sensitivity analyses were not pre-specified but added to further assess the robustness of the results.

1. Using a binary indicator for the period before versus after the date of the introduction of Sleeve to the study to assess to what extent results of the main analysis might be biased due to time trends affecting results, where for example outcomes improved over time and the fact that patients could only be randomised to Sleeve after the addition of this group to the already ongoing trial. This binary indicator was also accounted for in the imputation models.
2. Using the more recently developed mapping function developed by the Decision Support Unit and since recently recommended by NICE.[72]
3. Using the estimated intervention costs from the 2021 NHS cost collection (£7860 for Bypass, £6779 for Sleeve, and £4031 for Band) instead of inflating the micro-costing costs, reflecting that the former costs are substantially higher.

In line with the statistical analyses, 98% CIs were used for the pairwise comparisons to account for the three comparisons. For other estimates, for example total QALYs gained per participant allocated to Band, 95% CIs were reported. CIs were estimated form the bootstraps using the percentile method. The CHEERS statement was adhered to when reporting the methods, results, and conclusions of the within-trial analysis.[80]

Analysis of receipt of benefits

Although not included in the cost-effectiveness analyses from an NHS perspective, separate analyses around the receipt of benefits (any, disability-related, and child-related) were performed.[5] These outcomes were evaluated at 36 months only and analysed in separate logistic regression models using the same covariates as for the regression analyses used for the cost-effectiveness analyses, but additionally including receipt of benefits measured at baseline (any, disability-related, and child-related). Given the high percentage of individuals with missing information about gross household income at baseline,[5] and even more missing data for this variable around 3 years (> 40%) we did not perform pre-planned analyses focusing on the impact on (equivalised) gross household income.

Chapter 3 Development of a core outcome set for bariatric surgery

Introduction and aims

Previous systematic reviews of bariatric surgery have highlighted diversity of outcomes measured across trials as an important limitation affecting the amalgamation of study results within meta-analyses.[19,23,27–29] In two reviews alone, 68 patient-reported outcome (PRO) measures and over 1000 clinical outcomes were identified.[81,82] Reviews, including a Cochrane review, recommended the development of a COS to improve trial conduct.[27]

A COS is defined as an agreed standardised set of outcomes that should be measured and reported, as a minimum, in all clinical trials in specific areas of health or health care.[83] The use of COSs can improve meta-analyses, help to reduce outcome reporting bias and ultimately reduce research waste.[84,85] Outcome reporting bias has been estimated to affect more than a third of Cochrane reviews and has been reported to be more prevalent in surgical trials compared to medical trials.[86,87] The use of a COS can help to ensure all outcomes specified within a trial protocol are reported and can help systematic reviewers establish whether the review will be affected by outcome reporting bias.[85,88] If all trials in a particular area report as a minimum the outcomes in the COS, they would contribute more usable and less biased information, enabling comparison and synthesis within meta-analyses to inform clinical decision-making.[89]

There is no agreed number of outcomes that should be included in a COS, although feasibility of use should be considered and most include around 7–10 outcomes.[90–92] We aimed to develop a COS for bariatric surgery effectiveness trials, undertaken as a nested study within the pilot phase of the By-Band-Sleeve study.[3]

Methods

Development of the COS followed the process recommended by the Core Outcome Measures in Effectiveness Trials (COMET) initiative.[89,93] After agreeing the stakeholders to involve, we created a comprehensive list of bariatric surgery outcomes which informed the development of a questionnaire (phase 1), followed by a consensus process to define the COS (phases 2 and 3). This included a Delphi survey comprising three questionnaire rounds (phase 2) and consensus meetings to agree the final COS (phase 3). These phases are summarised in *Appendix 3*, *Table 26*. The project was registered with the COMET Initiative and reported according to the Core Outcome Set-STAndards for Reporting Statement.[94,95] The results of the COS study have previously been published.[1,96] Figures and tables presented in this chapter and in the supplement have been published previously; the original publications are acknowledged.

Stakeholder involvement including patient and public involvement

Expert bariatric surgery health professionals and research methodologists involved in the By-Band-Sleeve trial, and patient research partners, advised on the design and conduct of the COS. Individuals who had undergone NHS bariatric surgery, and specialist health professionals who were part of multidisciplinary teams (MDTs) involved in bariatric surgery care, were included within the consensus process.

Phase 1: creating a comprehensive list of bariatric surgery outcomes and a questionnaire for a Delphi survey

Outcomes of bariatric surgery were identified from two published systematic reviews of clinical outcomes and PROs in bariatric surgery to create two lists.[81,82] The PRO list was created by examining scales and items from each measure cited. These lists were categorised into health domains.[97] Each outcome was assigned a domain independently by at least two researchers who included expert health professional researchers (surgeons, a dietitian, a specialist nurse, a health psychologist) and methodologists. Domains were generated until saturation, or all outcomes were mapped to a health domain. Outcomes which overlapped or were synonyms of each other were combined. Differences between researchers were resolved by discussion within the study team.

A systematic review of qualitative research studies in bariatric surgery was used to identify any new domains to add to the lists.[98] Finally, patient interviews from a parallel qualitative study investigating the patient's perspective of bariatric surgery were used to elicit additional outcomes of importance to patients not already identified.[99]

Creating the questionnaire for the Delphi survey

The health domains and outcomes identified were developed into a questionnaire presented in four sections: (1) short- and long-term complications of surgery, (2) clinical effectiveness of surgery, (3) physical signs, symptoms and other measures (including haematological/biochemical markers and treatment pathway outcomes) and (4) impact of surgery on quality of life and well-being. A questionnaire item was written for each outcome by two members of the research team. To ensure face validity of the questionnaire, members of the research team, including patient research partners, reviewed iterations of the questionnaire and made suggestions to the wording and layout until it was felt to be acceptable and understandable. The technical terms were included in brackets next to the patient-approved wording where appropriate (in both the professional and patient versions of the questionnaire). Questionnaires asked participants to rate the importance of each item (outcome) on a scale of 1 (not important) to 9 (extremely important) to be included in a COS for bariatric surgery. Basic demographic information of patients and professional background information of professionals were also collected in the questionnaire. The full questionnaires are available from the authors (KC).

Phase 2: Delphi survey

Specialist health professionals involved in bariatric surgery care, including surgeons, nurses, dietitians, psychologists, physicians and anaesthetists (as outlined in The National Confidential Enquiry into Patient Outcome and Death report of bariatric surgery in the UK), were invited to participate in the survey.[100] Invitations were sent through professional societies; the British Obesity and Metabolic Surgery Society, the Association of Physicians Specialising in Obesity UK, The Society for Obesity and Bariatric Anaesthesia, the British Psychological Society, and an informal list of clinical psychologists working in bariatric surgery in the UK, and through sites participating in the By-Band-Sleeve trial.[3]

Patients who had undergone bariatric surgery in the previous 5 years at the sites participating in the pilot phase of the By-Band-Sleeve trial were eligible to receive an invitation to participate in the Delphi survey. To ensure patients with a range of characteristics were invited, patients were purposively sampled (based on sex, type of surgery and time since surgery), to receive a postal invitation from their clinical team. Patients returning a signed consent form to the research team were posted the questionnaire. Non-responding health professionals, and patients providing consent but not returning the questionnaire, were sent a postal reminder. In the absence of agreed methodology to determine a sample size for Delphi surveys, the target sample was 100 professionals and 100 patients.[101,102]

The Delphi process consisted of three sequential rounds of questionnaires with the same group of participants. Those that completed the round 1 questionnaire were eligible to participate in round 2, and those that completed round 2 eligible to participate in round 3. In each questionnaire, participants were asked to rate the importance of each item from 1 (not important) to 9 (extremely important). Responses were summarised and fed back anonymously in subsequent rounds. For each item, participants received their own score from the previous round, the median score of all patients, and the median score of all health professionals. For health professionals, the health professional score was broken down into two scores presented as the median score for (1) their own peer group, and (2) other health professionals (excluding their peer group).

All items on the questionnaire were retained between rounds 1 and 2. At the end of rounds 2 and 3, items were only retained if they met pre-specified criteria (see *Statistical analyses*). Further consideration was given by the research team as to whether any remaining items could be merged. Items retained at the end of round 3 were taken forward to the consensus meetings.

Phase 3: consensus meetings

Consensus meetings were held separately with patients and professionals to ensure that patients felt able to express their views. Meetings were held in Bristol, in autumn 2015. Participants completing all three questionnaire rounds were invited to attend, in addition to health professional members of the By-Band-Sleeve TMG.

Retained items and median scores for the patient and professional groups were presented and participants asked to vote 'Yes' (this item should be included in the COS), 'No' (this item should not be included), or 'Unsure', using anonymised keypad voting with Turning Point software linked to Microsoft PowerPoint (Microsoft Corporation, Redmond, WA, USA; TurningPoint Web. Youngstown, OH: Turning Technologies, LLC; 2020). Item wording was shortened and simplified for the consensus meetings to allow for ease of reading on slides, with verbal clarification provided as needed. The item wording used for consensus meetings is provided in *Appendix 3*, *Table 27*. Voting results for each item were presented immediately as a histogram to the group. Items were retained or dropped when consensus was reached. Discussion and further rounds of voting, restricting the options to 'Yes' or 'No', were undertaken until consensus was reached on all items. Items retained from both meetings were included in the final COS.

Statistical analyses

After each Delphi round the median score for each item was calculated for patients and professionals and each professional subgroup; median scores were presented as feedback in the subsequent round (round 3 presented in the consensus meetings). For merged items, the participants' score was calculated as the mean of the individual items' scores, and group scores were calculated as the mean of the individual items' median scores.

At the end of rounds 2 and 3, the percentage of participants who rated each item 8 or 9 was calculated, and items retained if they were scored 8 or 9 by at least 70% of respondents. These criteria were considered separately for patients and professionals, and items retained if they met these criteria in either group. Items discussed at the meetings were retained if at least 70% of participants voted 'Yes'; items were dropped if at least 70% voted 'No'. Analyses were undertaken using Stata software, version 13.0.

Results

An overview of the development of the COS is presented in *Appendix 3*, *Figure 26*. Two patient research partners, advised on the design and conduct of the COS.

Systematic review and patient interviews

The results of the work to elicit items for inclusion in the COS are shown in *Appendix 3*, *Figure 27*. Seven patient interviews were used to elicit important outcomes that were not identified from the systematic reviews. In total, 130 items (58 'clinical' outcomes and 72 PRO domains) were identified. These 130 items, across 17 health domains were included in the questionnaire used for the Delphi survey.

Delphi survey

Survey respondents

A total of 459 professionals were invited to complete the survey, of which 168 (36.6%) returned the round 1 questionnaire. The round 2 denominator was reduced to 157 as we were unable to send questionnaires to 11 professionals (5 had not provided contact details in round 1, 4 were on maternity leave, and 2 had moved away). Response rates to rounds 2 and 3 were 76.4% (120/157) and 85.0% (102/120), respectively. Characteristics of health professional participants in each survey round are presented in *Appendix 3*, *Table 28*. In round 1, just under

half of professionals were surgeons (48.2%). Characteristics of round 2 and 3 participants were similar, except for anaesthetists.

A total of 465 patients were invited to participate in the survey, of which 112 (24.1%) consented to take part. Of these, 90 (80.4%) completed round 1. One patient withdrew after round 1 and 89.9% (80/89) and 88.8% (71/80) completed rounds 2 and 3, respectively. Characteristics of patient participants in each round are presented in *Appendix 3*, *Table 29*.

Survey results

In round 1, 33/130 items were classed as 'very important'. After providing feedback in round 2, 57 items were classed as 'very important'. These were retained for round 3, as well as six additional 'borderline' items (≥ 65% of either patients or professionals rated these items 8–9), which had been highlighted as very important by patients in the qualitative interviews. The remaining 67 items were not carried forward to round 3. Fourteen of the 63 retained items were merged with other items, leading to 49 items on the round 3 questionnaire (see *Appendix 3*, *Table 30*).

After round 3, 41 items were classed as 'very important' by either patients or professionals and were retained. The remainder were discarded. Given the length of time that would be required to discuss and vote on 41 items within a consensus meeting, items were scrutinised to determine if any could be merged. Six were merged, reducing the total to 35 (see *Appendix 3*, *Table 31*). Three other items ['leaks, fistulas, strictures, and ulcerations at anastomosis', 'mortality (30 day or long term), 'improvement in diabetes'] that had been rated 8 or 9 by at least 90% of either group, were considered important to stakeholders and were not discussed at the meeting but included as definite items in the COS. Additionally, the merged item 'weight' (including both weight reduction and maintenance) was included as a definite item in the COS, as issues with weight re-gain/maintenance were highlighted as very important by patients. This reduced the total number of items to be voted on at the consensus meetings to 31.

Consensus meeting

Thirty-seven patients and 46 professionals who participated in the survey and indicated their interest in attending a meeting were invited to a consensus meeting. Of these, eight patients and one partner attended the patient meeting. Five were female, with a mean age of 55 years. Seven had undergone a Roux-en-Y gastric bypass, and one an adjustable gastric band. Their mean time since surgery was 4.3 years.

Thirty-three professionals attended the professional consensus meeting, including 20 survey participants, and 13 professionals from the By-Band-Sleeve Study. This included 14 (42.4%) surgeons, 10 (30.3%) specialist nurses, 4 (12.1%) dietitians, 3 (9.1%) bariatric physicians, 1 psychologist and 1 'other' health professional. Thirty-two professionals were from the UK and one from Australia.

At each consensus meeting, initially the 4 'definite' items to be included in the final COS were presented, followed by discussion and voting on the remaining 31 items. After the initial round of anonymised voting at the patients' meeting, 6 items were voted 'In', 3 'Out', and 22 'Unsure' (see *Appendix 3*, *Table 32*). At the professionals' meeting, 5 were voted 'In', 7 'Out', and 19 'Unsure' (see *Appendix 3*, *Table 33*). 'Unsure' items underwent further discussion and voting.

Extensive discussion in both meetings revealed that some items overlapped in content and meaning. Thus, some items were merged to form a single item. For example, at the professionals' meeting, the consensus was that the 10 items relating to HRQoL (e.g. 'mobility', 'self-esteem and self-confidence') should be combined into a single item, 'overall quality of life'. Professionals indicated a desire to include all 10 HRQoL items (which would have meant 18 items in the final COS). However, they were aware of the importance of limiting the final COS to approximately 10 items, to ensure feasibility of use in future trials. The consensus was therefore to include one broad HRQoL item which would encompass the more specific items, and the assumption that future work would be undertaken to define and select an appropriate HRQoL measure that would include all aspects important to patients. Similarly, items relating to potential complications of the operation were combined into two items, 'technical complications of the specific operation' and 'any reoperation/reintervention and its classification of severity'.

After further voting and discussion, an additional six items were included by patients, and four items by professionals. Thus, the final COS agreed by patients and professionals included 12 and 9 items, respectively (see *Table 1*). When comparing both COSs, all 12 items included in the patient COS were represented in the health professional COS, as

TABLE 1 Comparison of health professional and patient final COSs

	Health professional COS[a]		Equivalent items included in patient COS
1	Weight	1	Weight
2	Diabetes status	2	Diabetes status
3	Cardiovascular risk		Not included by patients
4	Overall quality of life	3–6	Mobility/ability to carry out usual activities/living a normal life; ability to do your work, or to take up work Feeling in control Self-esteem and self-confidence/depression/having a positive outlook on life and expectations for the future
5	Mortality (30 days or long term)	7	Mortality (30 days or long term)
6	Technical complications of the specific operation	8–10	Leaks, fistulas, strictures, and ulcers at anastomosis/gastric band problems Intraoperative organ injury Internal hernia
7	Any reoperation/reintervention and its classification of severity	8, 10	Leaks, fistulas, strictures, and ulcers at anastomosis/gastric band problems Internal hernia
8	Dysphagia/regurgitation	11	Dysphagia/regurgitation
9	Micronutrient status	12	Micronutrient status

a The final COS as it also includes all the items in the patient COS.

Note
Items 1–4 relate to potential benefits of the surgery, 5–9 relate to potential complications of the surgery.

professionals merged 4 items included by patients as 'overall quality of life'. The only item included by professionals that was not included by patients was 'cardiovascular risk'. Thus, the final COS includes nine items (see *Table 1*).

Discussion

This study developed a COS for use in bariatric and metabolic surgery research studies. A wide range of sources were used to inform a consensus process. The final COS consists of nine outcomes important to a range of different professionals and patients, including weight, diabetes, cardiovascular risk, HRQoL and potential risks of bariatric surgery. It is recommended that researchers use the COS to inform the selection of measures used in future studies evaluating bariatric surgery.

Since this study was completed, there have been other important initiatives related to core data in the field of obesity management. A core set for behavioural (non-surgical) weight management interventions was developed in the UK for both research and clinical practice.[103] Valli *et al.*[104] developed a COS for the evaluation of self-management interventions for patients with obesity. Both core sets included a measure of weight, weight-related comorbidities and PROs including HRQoL. The core set by MacKenzie *et al.*[103] also included adverse events/unintended consequences. Both included cost-effectiveness.

There has been recent work to extend COS methodology to bariatric surgery registries with the recognition that variables collected in different registries vary considerably between countries, making cross-country comparisons difficult.[105–107] The findings from this international project as well as the COS reported here formed the basis of a project to develop a core set of items for use in bariatric operations internationally.[108] Findings will be amalgamated with an international project developing core HRQoL measures for obesity treatments – the Standardising Quality of life measures in Obesity Treatment (SQOT) initiative.[109–111] Another recent initiative is the Gastro-intestinal Coordinated

Registry Network established in the USA to define a minimum core data structure for the collection of 'real world' data for obesity endoscopic procedures.[112] There is the potential for data from this COS and the Core Registry Set (CRS) to link in with this data set. Work is now needed to establish consistent wording of items and definitions across both the COS and CRS to allow for comparative effectiveness data from both sources to be combined.

This study has used high-quality methods to develop a COS for research evaluating bariatric and metabolic surgery. This work has since informed the development of a CRS for bariatric surgery registries worldwide. Widespread adoption of the COS and CRS by the bariatric surgery community will improve the quality of data collected within research studies and registries, thus improving meta-analyses and the value to clinical practice.

Chapter 4 Results: trial cohort

Study sites

Two sites took part in pilot phase 1 of the trial and a further 10 were opened in phases 2 and 3. They were well spread geographically and represented a mix of university and NHS trusts that are representative of NHS practice.

Phase 1 (By-Band): study sites and dates opened to recruitment:

Somerset NHS Foundation Trust – 5 November 2012
University Hospital Southampton NHS Foundation Trust – 22 January 2013

Phase 2 (By-Band): study sites and dates opened to recruitment:

Royal Bournemouth and Christchurch Hospitals – 10 July 2014
St James University Hospital, Leeds – 4 November 2014
Sunderland Royal Hospital – 14 January 2015
Royal Cornwall Hospital, Truro – 8 April 2015

Phase 3 (By-Band-Sleeve): study sites and dates opened to recruitment:

Heart of England NHS Foundation Trust, Birmingham – 30 July 2015
Queen Alexandra Hospital, Portsmouth – 7 August 2015
Homerton University Hospital – 11 August 2015
Royal Derby Hospital – 11 August 2015
Imperial College Healthcare NHS Trust – 5 October 2015
North Bristol NHS Trust – 16 November 2017

Patients screened and recruited

Between December 2012 and September 2019, 6961 patients assessed for eligibility, of whom 5610 were excluded; 2221 because they were ineligible, 600 were not approached by the local team, 2763 were approached but declined to take part, and 26 agreed to take part but then withdrew their consent prior to randomisation. Therefore, 1351 (28.5% of eligible patients, 32.6% of patients approached) were recruited and randomised (see *Appendix 4*, *Table 35*). The main reasons for screened patients not being recruited, by study site are shown in *Appendix 4*, *Table 37*. Participant flow through the trial is shown in *Figure 2*. Of those who declined to join the trial, 1277 consented to a single follow-up at 3 years and/or the trial investigators having access to their medical records (see *Appendix 4*, *Table 36*).

Recruitment

Between 16 January 2013 and 30 September 2019, 1351 participants consented to take part and were randomised, 463 to Bypass, 468 to Band and 420 to Sleeve. Five participants withdrew after randomisation and withdrew consent for their data to be used (see *Figure 2*). The final 3-year follow-up for the last participant was completed on 6 October 2022.

Recruitment rate

When the trial was designed the estimated recruitment rate was expressed in terms of the proportion of eligible patients recruited rather than as a recruitment per site per month [see *Figure 1* and trial protocol (https://fundingawards.

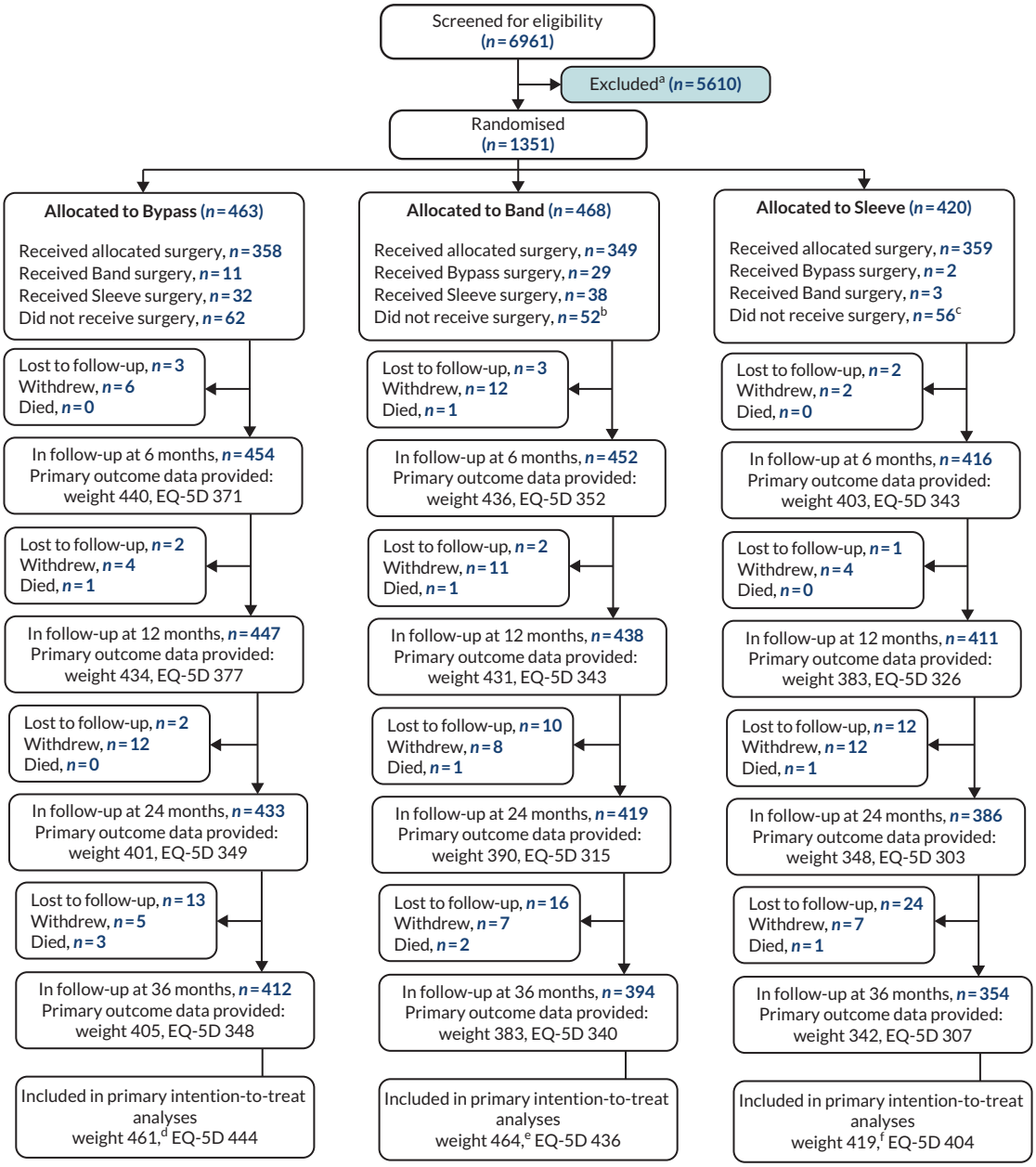

FIGURE 2 The By-Band-Sleeve trial CONSORT flow diagram. a, Reasons for exclusion are provided in *Appendix 4*, *Table 37*. b and c, Includes one surgery that was abandoned in theatre. d, One patient excluded due to withdrawal of consent for data, 1 excluded due to no baseline data. e, Four patients excluded due to withdrawal of consent for data. f, One patient excluded due to no baseline data.

nihr.ac.uk/award/09/127/53)]. The proposed trial sites were asked to estimate the number of surgeries each year and from this the anticipated recruitment rate was derived, allowing for a staggered opening of sites. Recruitment achieved is illustrated in *Appendix 4*, *Figure 28*.

Progression from phase 1 to phase 2 and adaptation to phase 3

Progress against the pre-defined progression criteria was assessed in January 2014. The success criteria were met and the TSC recommended progression to phase 2. In phase 2, the number of study sites was increased, and all sites used the optimum methods of recruitment established in phase 1 (see *QuinteT Recruitment Intervention*).

The review of bariatric surgical practice confirmed the increase in the use of sleeve gastrectomy and the TSC supported the trial team's recommendation that the trial should be adapted to include Sleeve to ensure the trial remained relevant to UK and worldwide practice. The adaptation took several months to implement. Phase 3 of the trial opened in August 2015, thereafter participants were randomised to one of Bypass, Band or Sleeve. The adaptation is discussed in detail elsewhere.[3]

Comparison of randomised and non-randomised patients

The age, sex, BMI and diabetic status of trial participants were similar to those who were eligible, did not join the trial but consented to a single 3-year follow-up and/or access to medical records (see *Appendix 4*, *Table 38*). Demographic information was not collected on ineligible patients or those who did not consent to participate in this way.

Participant withdrawals

In total, 90 randomised participants withdrew following randomisation. The reasons for post-randomisation withdrawal are detailed in *Table 2*. Most withdrawals were participant decisions and occurred before surgery. The most cited reasons were that the participant decided not to have surgery or did not wish to be followed up.

Protocol deviations

Eligibility and surgery

Protocol deviations are summarised in *Table 3*. There were no instances of an ineligible patient being randomised. Overall, 163/1346 (12.1%) participants did not undergo surgery within 3 years of randomisation. Over half of participants who had surgery waited more than 18 weeks from randomisation (the target waiting time when the trial was designed). Of the 1183 participants who did undergo surgery, 117 (9.9%) did not receive the surgery allocated by randomisation. Most crossovers were from Band to Bypass or Sleeve, with few crossovers from Sleeve to the other surgeries. Participant preference was the main reason for crossovers between groups, but there were some crossovers for clinical reasons in all groups (*Table 4*). The preferences for Band over the other procedures were evenly spread across the trial with one or two at most each year, whereas preferences for the other procedures were more common among participants randomised from 2016 onwards (see *Appendix 4*, *Table 39*). The clinical reasons for crossover are summarised in *Table 5*. Eight decisions were made preoperatively and 18 were made perioperatively. Further information on waiting times to surgery and adherence to the mandated and prohibited aspects of the surgical procedure is given in *Operative characteristics*.

Patient follow-up

The number of patients in follow-up and for whom follow-up data on the primary outcomes were available are presented in *Figure 2*. In total, 1160 (86.2%) participants remained in follow-up at 3 years. Of the participants not in follow-up at 3 years, 90 had withdrawn and 11 had died.

Numbers analysed

The analysis population consisted of 1346 randomised participants. Five randomised participants withdrew consent for their data to be used and are excluded. Overall, 1344 participants were included in analyses of the primary weight outcome (two failed to provide baseline weight data) and 1284 (95.4%) participants were included in analyses of the primary HRQoL outcome.

Baseline characteristics

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TABLE 2 Post-randomisation withdrawals

	Randomised to Bypass (*n* = 463)	Randomised to Band (*n* = 468)	Randomised to Sleeve (*n* = 420)	Randomised to Overall (*n* = 1351)
Any withdrawal	**27 (5.8%)**	**38 (81%)**	**25 (6.0%)**	**90 (6.7%)**
Participant decision	20/27 (74.1%)	31/37 (83.8%)	19/25 (76.0%)	70/89 (78.7%)
Clinical decision	7/27 (25.9%)	6/37 (16.2%)	6/25 (24.0%)	19/89 (21.3%)
Withdrawal pre surgery	20/27 (74.1%)	21/38 (55.3%)	15/25 (60.0%)	56/90 (62.2%)
Withdrawal post surgery	7/27 (25.9%)	17/38 (44.7%)	10/25 (40.0%)	34/90 (37.8%)
Type of withdrawal				
Not willing for collected data to be used	1/26 (3.8%)	4/37 (10.8%)	0/25 (0.0%)	5/88 (5.7%)
Willing for collected data to be used only	6/26 (23.1%)	8/37 (21.6%)	6/25 (24.0%)	20/88 (22.7%)
Willing for collected and routine data NHS data to be used	19/26 (73.1%)	25/37 (67.6%)	19/25 (76.0%)	63/88 (71.6%)
Reason for withdrawal				
Does not wish to be followed up	4/27 (14.8%)	5/38 (13.2%)	5/25 (20.0%)	14/90 (15.6%)
Due to allocation	1/27 (3.7%)	4/38 (10.5%)	0/25 (0.0%)	5/90 (5.6%)
Decided not to have surgery	5/27 (18.5%)	8/38 (21.1%)	5/25 (20.0%)	18/90 (20.0%)
Clinical reason	3/27 (11.1%)	3/38 (7.9%)	5/25 (20.0%)	11/90 (12.2%)
No reason given	6/27 (22.2%)	10/38 (26.3%)	2/25 (8.0%)	18/90 (20.0%)
Lost contact (participant moved)	5/27 (18.5%)	4/38 (10.5%)	2/25 (8.0%)	11/90 (12.2%)
Other	3/27 (11.1%)	4/38 (10.3%)	6/25 (24%)	13/90 (14.4%)

Note
Data are *n*/*N* (%).
Other reasons (Bypass, Band, Sleeve): pregnancy (0, 0, 1); length of wait (0, 0, 1), stress (1, 1, 0), poor English (0, 0, 1), no longer interested (0, 0, 1), unhappy with surgery result (0, 1, 0), participant non-compliant (1, 0, 0), unspecified personal reason (1, 2, 1).

TABLE 3 Protocol deviations

	Randomised to Bypass (*n* = 462)	Randomised to Band (*n* = 464)	Randomised to Sleeve (*n* = 420)	Overall (*n* = 1346)
Ineligible but treated in the study	0/462 (0.0%)	0/464 (0.0%)	0/420 (0.0%)	0/1346 (0.0%)
Did not receive surgery	61/462 (13.2%)	47/464 (10.1%)	55/420 (13.1%)	163/1346 (12.1%)
Did not receive allocated surgery	43/401 (10.7%)	68/417 (16.3%)	6/365 (1.6%)	117/1183 (9.9%)
Received surgery > 18 weeks after randomisation	216/401 (53.9%)	195/417 (46.8%)	192/365 (52.6%)	603/1183 (51.0%)

Note
Data are *n*/*N* (%).

The baseline characteristics were similar in the three groups (*Table 6* and *Appendix 4*, *Tables 40–43*). The mean age was 47.3 years (SD 10.6) and 1020/1344 (75.9%) were women. The mean BMI at recruitment was 46.4 kg/m^2 (SD 6.9) and the median waist circumference was 129.3 cm (IQR 120–139.9). Most participants were White (1140/1344, 84.8%) and fewer than half (561/1343, 41.8%) were in full-time employment (see *Appendix 4*, *Table 42*).

Over 80% (1103/1344, 82.1%) had attended commercial slimming clubs previously (see *Appendix 4*, *Table 41*). Comorbidities were common, almost a third had type 2 diabetes (407/1344, 30.3%), which was mainly controlled with oral hypoglycaemics, over 50% had pain from arthritis (724/1343, 53.9%) and approximately 25% suffered from obstructive sleep apnoea (356/1342, 26.5%, *Table 6*). Over 90% were on medication (1232/1346, 91.5%). Details of the medication taken is given in *Appendix 4*, *Table 41*. The By-Band-Sleeve trial population has been discussed in detail elsewhere.[5]

Operative characteristics

The 1183 participants who underwent surgery within 3 years of randomisation waited a median of 5.0 (IQR 2.5–10.1) months for their surgery after randomisation. The waiting times were similar in the three groups (see *Appendix 4*, *Table 44*). Participants operated after the start of the COVID-19 pandemic (*n* = 25 participants) waited a median of 27.1 months for their surgery (see *Appendix 4*, *Table 44* and *Figure 29*).The mean weight at surgery was 125.5 kg (SD 22.4) compared to 129.7 kg (SD 23.6) at recruitment (*Table 7*). Of the 1183 operations started, 1181 were completed, 1 Band and 1 Sleeve procedure were abandoned part way through; the Band participant deteriorated anaesthetically during surgery, while the Sleeve participant became hypotensive 10 minutes after the laparoscopy with a possible cardiac event. In total, there were 389 Bypass, 363 Band and 429 Sleeve procedures completed. Bypass surgery took a median of 132 minutes compared to a median of 70 and 90 minutes for Band and Sleeve, respectively. One hundred and fifty-one participants (13.2%) had an additional procedure alongside their bariatric surgery; over three-quarters of these additional procedures involved the repair of a hiatus hernia, most of which were an anterior rather than posterior repair. Additional surgical details are provided in *Appendix 4*, *Tables 45–48*. All surgeons adhered to the protocol in terms of avoiding the prohibited aspects of surgery but in some cases not all the mandated components were adhered to (*Table 8*). The most common surgery-specific deviations were not closing mesenteric defects (Bypass: 7/129, 5.4%) and not reflecting the fad pad (Band: 8/281, 2.8%). Most participants (1099/1181, 93.1%) had a 'normal' postoperative recovery (Clavien–Dindo grade 0) and the median postoperative stay was 2 days (see *Table 7*).

TABLE 4 Crossovers from allocated surgery

	Randomised to Bypass (*n* = 462)	Randomised to Band (*n* = 464)	Randomised to Sleeve (*n* = 420)	Overall (*n* = 1346)
Received surgery	401/462 (86.8%)	417/464 (89.9%)	365/420 (86.9%)	1183/1346 (87.9%)
Received allocated surgery	358/401 (89.3%)	349/417 (83.7%)	359/365 (98.4%)	1066/1183 (90.1%)
Surgery abandoned in operating theatre	0/401 (0.0%)	1/417 (0.2%)	1/365 (0.3%)	2/1183 (0.2%)
All crossovers	43/401 (10.7%)	67/417 (16.1%)	5/365 (1.4%)	115/1183 (9.7%)
Crossed to Bypass				
Patient preference		20/67 (29.9%)	1/5 (20.0%)	21/115 (18.3%)
Clinical reason		4/67 (6.0%)	1/5 (20.0%)	5/115 (4.3%)
Error		1/67 (1.5%)	0/5 (0.0%)	1/115 (0.9%)
Unclear		4/67 (6.0%)	0/5 (0.0%)	4/115 (3.5%)
Overall		29/67 (43.3%)	2/5 (40.0%)	31/115 (27.0%)
Crossed to Band				
Patient preference	8/43 (18.6%)		2/5 (40.0%)	10/115 (8.7%)
Clinical reason	2/43 (4.7%)		1/5 (20.0%)	3/115 (2.6%)
Error	1/43 (2.3%)		0/5 (0.0%)	1/115 (0.9%)
Overall	11/43 (25.6%)		3/5 (60.0%)	14/115 (12.2%)
Crossed to Sleeve				
Patient preference	12/43 (27.9%)	35/67 (52.2%)		47/115 (40.9%)
Clinical reason	17/43 (39.5%)	1/67 (1.5%)		18/115 (15.7%)
Error	1/43 (2.3%)	0/67 (0.0%)		1/115 (0.9%)
Unclear	2/43 (4.7%)	2/67 (3.0%)		4/115 (3.5%)
Overall	32/43 (74.4%)	38/67 (56.7%)		70/115 (60.9%)

Note
Data are *n*/*N* (%).

TABLE 5 Clinical reasons for crossovers between surgeries

Allocated surgery	Surgery received	Reason for crossover
Decision made preoperatively		
Bypass	Band	Anaemia – concerned bypass will exacerbate
Bypass	Band	Bleeding risk – concerns bypass risky
Band	Bypass	Medically contraindicated (previously unknown)
Band	Bypass	Cardiac problems
Band	Bypass	Hiatus hernia
Band	Bypass	Para oesophageal hernia
Sleeve	Band	Severe reflux
Sleeve	Bypass	MDT decision
Decision made perioperatively		
Bypass	Sleeve	Multiple adhesions (10 cases)
Bypass	Sleeve	Technical reasons (2 cases)
Bypass	Sleeve	Small bowel not suitable
Bypass	Sleeve	Large hernia and adhesions
Bypass	Sleeve	Unable to identify jejunum
Bypass	Sleeve	Cirrhosis
Bypass	Sleeve	Paraumbilical hernia
Band	Sleeve	Aberrant arterial anatomy

TABLE 6 Participant demography and baseline characteristics

Characteristic	Randomised to Bypass (*n* = 462)	Randomised to Band (*n* = 464)	Randomised to Sleeve (*n* = 420)	Overall (*n* = 1346)
Age (years)[a]	47.4 (10.3)	46.8 (10.4)	47.8 (11.0)	47.3 (10.6)
Female sex	345/461 (74.8%)	354/464 (76.3%)	321/419 (76.6%)	1020/1344 (75.9%)
Ethnicity				
White	401/461 (87.0%)	394/464 (84.9%)	345/419 (82.3%)	1140/1344 (84.8%)
Mixed/multiple ethnic groups	11/461 (2.4%)	11/464 (2.4%)	11/419 (2.6%)	33/1344 (2.5%)
Asian/Asian British	10/461 (2.2%)	21/464 (4.5%)	15/419 (3.6%)	46/1344 (3.4%)
Black/African/Caribbean/Black British	30/461 (6.5%)	26/464 (5.6%)	36/419 (8.6%)	92/1344 (6.8%)
Other ethnic group	9/461 (2.0%)	12/464 (2.6%)	12/419 (2.9%)	33/1344 (2.5%)
Weight (kg)[a]	131.4 (23.8)	129.0 (23.1)	128.7 (23.8)	129.7 (23.6)
BMI[a]	46.9 (7.1)	46.1 (6.6)	46.1 (6.9)	46.4 (6.9)
Waist circumference[b]	130.0 (120.3–140.4)	129.5 (120.4–139.3)	128.2 (118.5–139.8)	129.3 (120.0–139.9)
Neck circumference[c]	42.0 (39.0–46.0)	42.0 (39.5–46.0)	42.0 (39.0–45.0)	42.0 (39.0–46.0)
ASA class				
I: Healthy, no medical problems	93/458 (20.3%)	93/463 (20.1%)	91/418 (21.8%)	277/1339 (20.7%)
II: Mild systemic disease	229/458 (50.0%)	222/463 (47.9%)	211/418 (50.5%)	662/1339 (49.4%)
III: Severe systemic disease, but not incapacitating	128/458 (27.9%)	140/463 (30.2%)	113/418 (27.0%)	381/1339 (28.5%)
IV: Severe systemic disease that is a constant threat to life	8/458 (1.7%)	8/463 (1.7%)	3/418 (0.7%)	19/1339 (1.4%)
Diabetes status				
Type 1	1/461 (0.2%)	3/464 (0.6%)	2/419 (0.5%)	6/1344 (0.4%)
Type 2 – Pre-diabetes	8/461 (1.7%)	5/464 (1.1%)	1/419 (0.2%)	14/1344 (1.0%)
Type 2 – Diet controlled	9/461 (2.0%)	14/464 (3.0%)	15/419 (3.6%)	38/1344 (2.8%)
Type 2 – Oral hypoglycaemics	103/461 (22.3%)	90/464 (19.4%)	72/419 (17.2%)	265/1344 (19.7%)
Type 2 – GLP-1 agonist	11/461 (2.4%)	10/464 (2.2%)	6/419 (1.4%)	27/1344 (2.0%)
Type 2 – Insulin	20/461 (4.3%)	22/464 (4.7%)	21/419 (5.0%)	63/1344 (4.7%)
Duration of diabetes (years)[d]	3.6 (1.8, 9.0)	5.0 (2.4, 9.8)	4.8 (2.2, 10.3)	4.7 (2.1, 9.8)
Taking any medication	424/461 (92.0%)	429/464 (92.5%)	379/419 (90.5%)	1232/1344 (91.7%)

Characteristic	Randomised to Bypass (*n* = 462)	Randomised to Band (*n* = 464)	Randomised to Sleeve (*n* = 420)	Overall (*n* = 1346)
Obstructive sleep apnoea	127/460 (27.6%)	135/464 (29.1%)	94/418 (22.5%)	356/1342 (26.5%)
Epworth sleepiness scale[e]	5.0 (3.0, 9.0)	4.0 (2.0, 8.0)	5.0 (2.0, 10.0)	5.0 (2.0, 9.0)
Asthma	127/460 (27.6%)	150/464 (32.3%)	137/419 (32.7%)	414/1343 (30.8%)
Gastro-oesophageal reflux disease/hiatus hernia	209/460 (45.4%)	229/464 (49.4%)	212/419 (50.6%)	650/1343 (48.4%)
Back or leg pain from arthritis	251/460 (54.6%)	247/464 (53.2%)	226/419 (53.9%)	724/1343 (53.9%)

ASA, American Society of Anaesthesiologists; GLP, glucagon-like peptide.
Missing data (Bypass, Band, Sleeve):
a 2 participants (1, 0, 1).
b 16 participants (4, 6, 6).
c 35 participants (13, 14, 8).
d 6 participants (2, 0, 4).
e 5 participants (3, 1, 1).

Note
Data are presented as median (IQR), mean (SD), or *n*/*N* (%).

TABLE 7 Surgical details

Characteristic	Received Bypass (*n* = 389)		Received Band (*n* = 363)		Received Sleeve (*n* = 429)		Overall (*n* = 1181)	
	n	%	*n*	%	*n*	%	*n*	%
Operation details								
Operation length (minutes)[a]	132	(105–171)	70	(55–88)	90	(65–120)	94	(67–129)
Weight on day of surgery	126.1	(21.9)	125.8	(22.8)	124.9	(22.4)	125.5	(22.4)
Additional procedures	**53/369**	**14.4%**	**41/344**	**11.9%**	**57/429**	**13.3%**	**151/1142**	**13.2%**
Hiatus hernia present	32/53	60.4%	35/41	85.4%	48/57	84.2%	115/151	76.2%
Size of defect[b]	20.0	(20.0–30.0)	20.0	(10.0–20.0)	20.0	(20.0–27.5)	20.0	(20.0–25.0)
Length of defect[c]	20.0	(20.0–30.0)	20.0	(10.0–20.0)	20.0	(20.0–20.0)	20.0	(15.0–30.0)
Anterior crural defect	26/31	83.9%	33/34	97.1%	43/48	89.6%	102/113	90.3%
Large posterior defect	5/31	16.1%	5/33	15.2%	6/48	12.5%	16/112	14.3%
Hiatus hernia repair carried out	32/32	100.0%	34/35	97.1%	48/48	100.0%	114/115	99.1%
Anterior repair	26/31	83.9%	32/34	94.1%	39/48	81.3%	97/113	85.8%
Posterior repair	5/31	16.1%	2/34	5.9%	9/48	18.8%	16/113	14.2%
Cholecystectomy	1/53	1.9%	2/41	4.9%	1/57	1.8%	4/151	2.6%
Umbilical hernia repair	0/53	0.0%	0/41	0.0%	1/57	1.8%	1/151	0.7%
Paraumbilical hernia repair	2/53	3.8%					2/151	1.3%
Incisional hernia repair	0/53	0.0%	0/41	0.0%	1/57	1.8%	1/151	0.7%
Other	18/53	34.0%	4/41	9.8%	8/57	14.0%	30/151	19.9%
Recovery								
Time from surgery to discharge (days)[d]	2.0	(2.0–2.0)	1.0	(0.0–1.0)	2.0	(2.0–2.0)	2.0	(1.0–2.0)
Clavien–Dindo classification								
Normal recovery (no complications)	358/389	(92.0%)	347/363	(95.6%)	394/429	(91.8%)	1099/1181	(93.1%)
Grade I	18/389	(4.6%)	14/363	(3.9%)	22/429	(5.1%)	54/1181	(4.6%)
Grade II	6/389	(1.5%)	2/363	(0.6%)	7/429	(1.6%)	15/1181	(1.3%)
Grade IIIa	2/389	(0.5%)	0/363	(0.0%)	2/429	(0.5%)	4/1181	(0.3%)
Grade IIIb	5/389	(1.3%)	0/363	(0.0%)	4/429	(0.9%)	9/1181	(0.8%)

Characteristic	Received Bypass (*n* = 389)		Received Band (*n* = 363)		Received Sleeve (*n* = 429)		Overall (*n* = 1181)	
	n	%	*n*	%	*n*	%	*n*	%
Postoperative care								
Anti-DVT prophylaxis	312/389	(80.2%)	286/360	(79.4%)	355/429	(82.8%)	953/1178	(80.9%)
Flotrons	206/389	(53.0%)	169/361	(46.8%)	245/429	(57.1%)	620/1179	(52.6%)
Heparin	363/388	(93.6%)	293/361	(81.2%)	396/428	(92.5%)	1052/1177	(89.4%)
Discharge care								
Compression stockings	240/388	(61.9%)	218/359	(60.7%)	286/427	(67.0%)	744/1174	(63.4%)
Flotrons	14/388	(3.6%)	3/359	(0.8%)	14/427	(3.3%)	31/1174	(2.6%)
Clexane/heparin	305/388	(78.6%)	169/359	(47.1%)	313/428	(73.1%)	787/1175	(67.0%)
Clexane/heparin duration, (weeks)[e]	1.0	(1.0–2.0)	2.0	(1.0–2.0)	1.0	(1.0–2.0)	1.0	(1.0–2.0)

Missing data (Bypass, Band, Sleeve):
a 8 participants (3, 2, 3).
b 9 participants (3, 2, 4).
c 10 participants (2, 2, 6).
d 1 participant (0, 1, 0).
e 3 participants (1, 0, 2).

Note
Data are presented as median (IQR), mean (SD), or *n*/*N* (%).

TABLE 8 Adherence to mandated components of surgery

Components	Received Bypass (*n* = 389)	Received Band (*n* = 364)	Received Sleeve (*n* = 430)	Overall (*n* = 1183)
Surgery abandoned	0/389 (0%)	1/364 (0.3%)	1/430 (0.2%)	2/1183 (0.2%)
Prohibited surgical components carried out	0/389 (0%)	0/363 (0%)	0/429 (0%)	0/1181 (0%)
Mandated surgical components not carried out	12/389 (3.1%)	13/363 (3.3%)	7/429 (1.6%)	31/1181 (2.6%)
Surgery not carried out laparoscopically	0/389 (0%)	0/362 (0%)	0/429 (0%)	0/1180 (0%)
Prophylactic antibiotics not given	5/389 (1.3%)	0/362 (0%)	7/429 (1.6%)	12/1180 (1.0%)
Inadequate anti-DVT prophylaxis given	0/389 (0%)	0/361 (0%)	0/429 (0%)	0/1179 (0%)
Mesenteric defects not closed[a]	7/129 (5.4%)			
Pars flaccida dissection technique not used		2/361 (0.6%)		
Gastro-gastric tunnelling sutures not used		4/361 (1.1%)		
Fat pad not reflected[b]		8/281 (2.8%)		
Adjustable port not fixed to the anterior abdominal wall		0/360 (0%)		
Left crus not visualised after dissection of fundus			0/426 (0%)	

a Not mandated until April 2018.
b Denominator excludes where reflection of the fat pad was marked not applicable.

Note
Data are *n*/*N* (%).

Band follow-up care

Band participants were expected to have at least three consultations in the first 6 months after surgery, two in the following 6 months and one annually thereafter. The number of consultations reported in the trial and the actions taken at these consultations are summarised in *Table 9*. Almost 85% of participants had at least one consultation in the first 6 months (median 2, rate per participant 2.71 consultations over this period). Two-thirds of consultations involved a band fill of a median 2 ml. Three per cent of participants had a defill in the first 6 months. As the time after surgery increased, the number of participants having a band consultation reduced, with only 40% having a consultation during year 3. The number of band fills also decreased over time as the number of defills increased (see *Table 9*).

TABLE 9 Band consultations during follow-up

Time after surgery	At least one consultation	Total consultations	Consultations per participant	Rate of consultations per participant per time period	Band fill	Fill volume (ml)	Band defill	Defill volume (ml)	Slip/ oesophageal dilation	Suspected slip/ oesophageal dilation
			Median (IQR)			Median (IQR)		Median (IQR)		
First 6 months	307/363 (84.6%)	960	2 (1–4)	2.71/6 months	649/960 (67.6%)	2 (2–4)	31/960 (3.2%)	1 (1–1)	11/363 (3.0%)	11
6–12 months	241/363 (66.4%)	548	1 (0–2)	1.60/6 months	322/548 (58.8%)	1 (1–2)	41/548 (7.5%)	1 (1–2)	7/363 (1.9%)	7
Second year	216/363 (59.5%)	588	1 (0–3)	1.89/year	294/588 (50.0%)	1 (1–1)	84/588 (14.3%)	1 (0–2)	18/363 (5.0%)	20
Third year	147/363 (40.5%)	312	0 (0–1)	1.56/year	134/312 (42.9%)	1 (0–1)	50/312 (16.0%)	1 (1–3)	6/363 (1.7%)	7

Chapter 5 Results: QuinteT Recruitment Intervention

Overview

Here we present the findings of the QRI with documentation of the 'clear obstacles' and 'hidden challenges' to recruitment that were identified, the rationale for the actions and strategies for improvement that were undertaken, and an assessment of the impact of the actions on progress with recruitment, across the four stages of recruitment. An overview of data collection and actions to address recruitment is given in *Table 10*.

Initial stage: April 2012–June 2014

Recruitment challenges

The QRI identified overlapping and unique recruitment challenges in the two pilot sites, as reported fully elsewhere.[2] In brief, a key recruitment challenge in the first site that opened was that the trial was difficult to embed into routine practice. The site had a well-established pathway for service provision and maintained this in the early months of recruitment. The site ran a 'one-stop' clinic in which patients saw multiple healthcare professionals sequentially to assess needs and eligibility for treatment, and, at the end, decide upon future management. Staff found it difficult to fit the trial into the existing pathway, and multiple barriers were noted. For example, eligibility for the trial could only be confirmed when test results became available, so if patients agreed to take part early on, they could not receive their randomised allocation. Staff who saw patients early in the clinic tended to write their perception of the patient's treatment preference on the notes, and this set patients on a treatment pathway and often precluded further discussion of the trial. The trial tended to be mentioned towards the end of the surgical consultation, often in an apologetic tone, making it unattractive to patients. Trial paperwork (follow-up schedules) was presented in a manner that suggested they were an additional burden for patients. Recruiters did not always establish the link between the uncertainty that they believed in and raised in the patient's mind and the need for the study. This meant the study was not presented as a solution to the uncertainty and a preference for a procedure was reached. For details, see Paramasivan *et al.*[2]

The major issues related to the embedding of the trial into routine practice and the complexity of the patient pathway were less problematic in the second pilot site. This site opened to recruitment 3 months after the first site and benefitted from the initial lessons learnt. The second site had the opportunity to set up a new pathway in a way that facilitated recruitment processes (e.g. eligibility assessment preceded the recruitment consultation, perceptions of preferences were not appended to clinical notes).

Challenges that centred around recruiters' equipoise were identified across both sites. In interviews, recruiters articulated ways in which they intended to overcome their treatment biases (often in favour of Bypass), but audio-recordings of their trial discussions with patients showed this was difficult to implement. For instance, recruiters used more favourable terminology to describe Bypass than Band surgery (e.g. permanent vs. temporary solution to obesity; guaranteed vs. requiring additional patient input respectively). Also, despite being familiar with QRI-specific literature on the importance of exploring patient preferences,[48,49,113,114] recruiters found it difficult to implement the suggestions effectively (e.g. they tended to ask 'why' patients had a particular preference as suggested by previous research, but then accepted the preference without further exploration; or attempted to balance the information about the two operations, but without tailoring this to the concerns of the patient). In addition, recruiters sometimes expressed their treatment preference when asked or made a treatment recommendation (as in routine clinical practice).

TABLE 10 Overview of QRI activity across the four stages

Recruitment stages	Initial stage	Transitional stage	Sustaining recruitment	Final stage of recruitment
Phase 1 (data collection and analysis)				
Interviews	12	11	11	–
Audio-recordings	84			
Non-participant observations	19	–	–	–
Eligibility/recruitment logs				
Patient pathway mapping	2	9	1	–
Phase 2 (plan of action/strategies and dissemination)				
Plan of action development				
TMGs/investigator meetings	5	2	3	1
Individual feedback	11	33	31	2
Group feedback	3	11	13	–
Tips document	1	–	1	–
Training at SIVs	–	9	1	–
Training at Investigators' meetings	1	–	2	1
RN training	1	–	3	11
Visits to sites (not SIVs or feedback)	–	–	6	–

In interviews towards the end of the initial stage, surgeons began to discuss Sleeve, a new procedure that was not included in the trial originally but had become more commonly used. Many were asking whether the trial could be adapted into a three-group design to incorporate Sleeve in order to be more acceptable to the surgeons who regularly carried out the procedure, and to include patients who had heard of it.

QuinteT Recruitment Intervention actions and strategies

Solutions developed and implemented through QRI feedback sessions to address the identified recruitment challenges included (for details, see Paramasivan *et al.*[2]) recommendations to:

- mention the trial early in the recruitment consultations
- offer the participation in the trial to all eligible patients (rather than only to those without a preference) and avoid appending a perception of a patient's preference to the clinical notes
- link uncertainty around the best treatment to the need for the trial
- provide a clear explanation of randomisation using QRI advice
- present trial follow-up within the context of what is already offered in the NHS
- develop clear pathways for potentially eligible patients
- avoid loaded terminology or conveying own treatment preferences
- explore patient preferences more thoroughly (beyond the initial 'why') so that any factually incorrect information could be rectified
- request patients to 'keep an open mind' until they had heard all relevant information, especially if they expressed a preference early in the consultation
- provide balanced information on the two operations, tailored to the patient's concerns.

Recruiters' views on the need for Sleeve were conveyed to the CI, who indicated that the TMG was considering including Sleeve in the main trial, after further review of the literature.

Recruitment progress

The first site opened was able to find patients eligible for the study, but none of the first 20 patients consented to take part. The detailed analysis described above identified some key recruitment challenges and QRI actions were put in place to address these. Following feedback sessions and concerted efforts from all key stakeholders, the site's recruitment rate increased from 9% (2/22) in the first 2 months of recruitment to 40% (26/65) in the next 4 months.[2] There were subsequent feedback sessions and a 'tips' document was circulated (February 2014). Recruitment eventually stabilised at about 38% in the first site at the end of the pilot phase. Findings were conveyed to the second pilot site which had delayed opening and was able to avert potential pathway related issues and began with optimised recruitment practices; their recruitment stabilised at about 45% over the next year. At the end of this initial stage, the trial met its recruitment target of 30% of eligible patients being randomised as well as other progression criteria and proceeded to the main trial (see *Progression from phase 1 to phase 2 and adaptation to phase 3*).[2,3] There was some indication that the feedback and site visits had some positive impact on recruitment (*Figure 3*). Lessons learnt were used in a recruitment training session (April 2014) for new investigators in sites likely to be enrolling in the main trial, and in future years.

Transitional stage: July 2014–April 2016

Recruitment challenges and recommended actions/strategies

In addition to the challenges and solutions identified in the initial stage, it was anticipated that the three subsequent trial transitions might also create difficulties for recruitment. Each transition is presented below with its challenges (anticipated and new) as well as recommended QRI actions/solutions:

Progression from pilot to main trial: July 2014

With the progression from pilot to the main trial, there were some changes to the recruitment targets. The eligibility rate (proportion of patients eligible among those screened) remained unchanged at 60%, but the proportion of eligible patients expected to be randomised was increased from 30% (during first 18 months of recruitment) to 50% (later

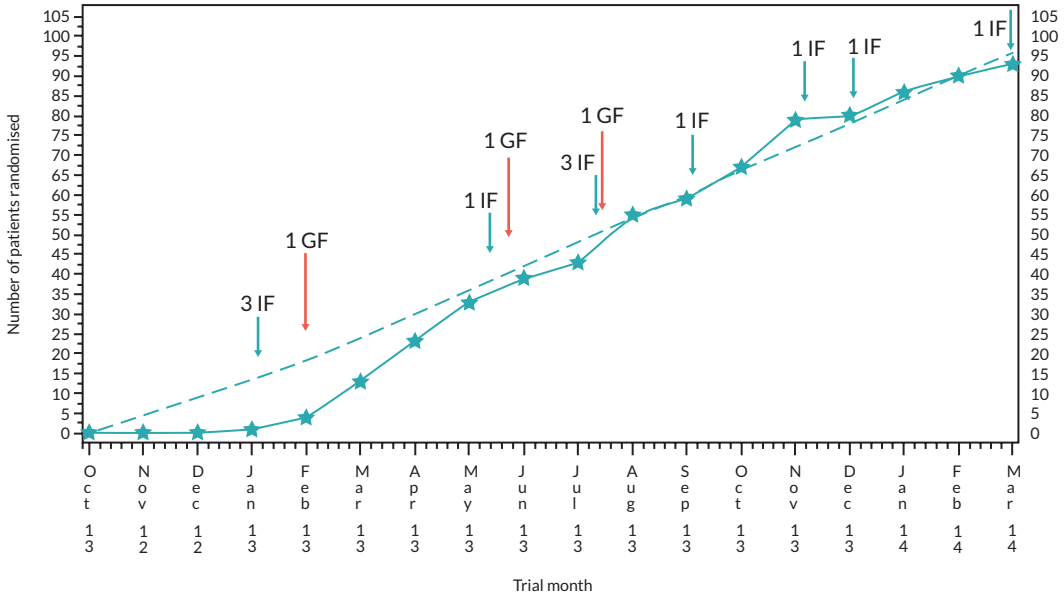

FIGURE 3 Recruitment progress in the initial stage mapped with QRI actions. GF, group feedback; IF, individual feedback.

amended to 45%). Screening logs were scrutinised and the expected versus actual average number of eligible and randomised participants per month was calculated for the existing and nine new sites. These targets were presented to sites at feedback sessions. For instance, at site 3's first group feedback session, held 6 months after they opened for recruitment, the QRI team discussed with the site that although they had sufficient eligible patients (*n* = 36 of 60 screened; 60%), their randomisation rate was low in comparison to the recruitment target (*n* = 4; 11%). This information helped set the stage for a collaborative dialogue at feedback sessions, with discussions around the feasibility of the recruitment targets and changes in sites that could affect recruitment (e.g. staff attrition, nurse availability, MDT arrangements, content of education sessions). The QRI team also presented the latest findings about the recruitment challenges identified in interviews and audio-recorded consultations, and actions were proposed to overcome these difficulties.

Facilitating recruitment in the nine new sites as well as the two pilot sites

In addition to maintaining recruitment in the two pilot sites, the QRI adapted to having nine new sites opened for recruitment. These all needed input into SIVs as well as group and individual feedback sessions as a routine part of the QRI. The first QRI action was sharing lessons learnt during the internal pilot phase during the pre-recruitment training provided during each SIV. For instance, given the value of integrating the trial and its processes within routine clinical service provision identified in the first site, new sites were requested to map recruitment pathways and adapt their clinical set up to facilitate trial integration and recruitment. Similarly, drawing from the QRI findings in the first site, it was realised that new sites with little or no research experience required additional support and training. There was intense activity with visits to sites and feedback sessions held about 4–8 months after recruitment commenced in each of the new sites.

Data collection and analysis in the transitional stage identified a wide range of recruitment challenges in the new sites, alongside those seen previously. New challenges also emerged. For instance, during the brief QRI training provided at the SIVs, recruiters were informed of the need to be balanced in the discussions of the operations in the trial and to explore and address patient preferences (drawing from the pilot stage findings). While recruiters attempted to do this in their consultations, some did not precede or follow this up with a clear invitation to participate in the study, leading to some confusion regarding the purpose of the discussion for patients. Subsequently, QRI actions to overcome these challenges were regularly incorporated in the first and subsequent group feedback session for each of the new sites. The existing sites were also provided with advanced-level tips. The key items of feedback provided in the transitional stage are displayed in *Table 11*.

TABLE 11 Key items of QRI feedback given to sites in response to recruitment challenges identified in the Transitional Stage

A. Organisational and site-level challenges
Integrating study into routine clinical practice Streamlining eligibility assessment and recruitment pathway Ensuring screening logs are accurate with no missing data Adapting to the increased randomisation targets in the main trial phase Balancing information in the education sessions (e.g. ensuring similar time for all three procedures) Redressing site-level biases (e.g. where most recruiters in a site had a preference for Bypass or Sleeve)
B. Consultations: recruiter–patient interaction-related challenges
1. Overall style
Providing clear and consistent information Demonstrating personal commitment and study ownership Open-ended questioning with questions addressed as they arise and pausing for patients' questions Avoiding leading or closed questions at the start (e.g. asking for patient preference or willingness to participate at the start of consultation before trial information provision) Carrying out empathetic, reassuring and supportive discussions
2. Study discussion
Mentioning study early in the patient pathway Mentioning study early in the consultation (in opening statements) Providing a clear introduction with general and personalised statements of uncertainty linked to study rationale Offering a clear invitation to participate in the study Approaching all eligible patients Using 'study' instead of 'trial' Explaining risks and benefits of study participation for patient and others (not just the risks) Avoiding presenting the study as a quicker route to treatment Optimising study discussion length Simplifying the study explanation Avoiding presenting study as an option for those who do not have an initial treatment preference Avoiding the presentation of the non-randomised follow-up study as an option at the start of the discussion (rather than an option for those who decline) Emphasising the voluntary nature of participation
3. Demonstrating equipoise and balanced treatment discussion
Expressing clear statements of uncertainty Providing balanced information on the operations Highlighting similarities/equivalences across the operations as well as differences[a] Providing reassurance that patient is suitable for all operations (and personalising the study invitation)[a] Using neutral language to describe the operations (avoid biased terms to describe operations) Not divulging personal preferences Spending similar amounts of time explaining risks and benefits of each operation Avoiding presenting Sleeve as an operation for those who cannot have Bypass Reordering of operations presented to balance information (Sleeve, Band, Bypass)
4. Managing patient preferences
Using 'keep an open mind' to open up discussions when patients expressed a preference early in the consultation Exploring and addressing patients' concerns and preferences, tailored to the patients' concerns Listening to patient cues and narrowing down the tailored balancing[a] Providing information on all operations even when patient expresses a preference for one Addressing 'all' or 'most' of patients' concerns and preferences Avoiding reinforcing patient preferences or accepting them at face value
5. Explaining randomisation
Covering the rationale (why) and process (how) of randomisation Offering the study as a solution to the dilemma (created by uncertainty in existing evidence) Avoiding presenting randomisation as lack of choice Avoiding presenting randomisation as a logical decision

continued

TABLE 11 Key items of QRI feedback given to sites in response to recruitment challenges identified in the Transitional Stage (*continued*)

6. Next steps (end of consultation)
Offering to put patients in touch with other patients Confirming willingness to have any of the operations (if patient agrees to participate) Explaining next steps more generally (who to see next) Explaining next steps in relation to the trial – whether or not patient agrees to participate in the study

a Advanced level tips provided for sites/recruiters already employing previous suggestions for good practice.

Qualitative analysis of recruitment appointments in the pilot sites revealed that they were implementing many of the good recruitment practices suggested in *Table 11*. At this stage, these sites were also provided with more advanced recruitment tips (as shown by asterisks in *Table 11*), such as adding personalised statements of uncertainty (e.g. *'you are suitable to have all three operations'*) to the generalised statements of uncertainty that were previously recommended (e.g. *'we do not know which is the best operation for this group of patients'*). Further qualitative analysis also showed that across all sites, most of the recruiters were responding to the recruitment challenges identified by the QRI and using components of good practice that were recommended in *Table 11*. However, it was also clear that these were implemented by some recruiters at some sites in some appointments, but not always or consistently across or even sometimes within appointments. This had not been expected, and so further detailed analyses were undertaken, and solutions developed.

For example, although advanced recruiters were already aware of the need to tailor the information they were providing to patients' concerns, there was a need to reframe the advice with an additional recommendation to listen to patient cues. To illustrate this, in the interaction below, the patient was considering participating in the study but was concerned about the practicalities of a band. Although the recruiter attempted some balancing of information, they did not reassure the patient about their concerns about band readjustments:

> *P: I just want something that can help me change my life. I'm going running, I'm going to dance classes, I'm eating a healthier diet and actually it's kind of my life's not changed but . . . you know coming back to that I'd have to get more childcare if I had to come and get my band readjusted until he starts school so in my head I'd quite like a bypass but obviously I'm open to. . .*
> *R: I'm quite happy to do any operation you'd like and it's just important you, you make decisions with the right information and some people do want that definitive sort of hit of the bypass or sleeve where you lose weight quickly initially hmm but as I say it is possible to put the weight back on and some of the people might (audio-recording, consultation).*

Inconsistencies in good practice manifested in two main ways: within a consultation of a recruiter and related to recruitment issues across different consultations. Examples of these inconsistencies are given in *Table 12*, along with suggestions for improved practice. As can be seen in the excerpts above, across the study, there continued to be issues with equipoise related to surgeons' views of the three procedures and particularly concerns about the band procedure.

These issues were discussed at TMG and investigator meetings. The identification of these issues led to an important change to subsequent feedback sessions which was to incorporate as many elements of good practice as possible as well as ensuring recruiters understood the need to be consistent in their communication and be aware of their potential to communicate non-evidence-based biases.

Addition of sleeve gastrectomy: August 2015

Following the transition from pilot to main trial, discussions about the proposal to add sleeve gastrectomy as a third group increased in intensity. A dip in recruitment was seen in some sites. Interviews with surgeons revealed strong support for adding Sleeve. Many explained the difficulties they had explaining the availability of Sleeve in their site while it was not included in the trial. This was especially the case in sites where Sleeve was included in the group education sessions that patients attended prior to seeing clinicians. Surgeons also reported that some patients had declined trial participation because they preferred sleeve gastrectomy. It was also noted that some surgeons were unhappy to

TABLE 12 Inconsistencies in good practice in the transitional stage

Inconsistencies within consultations	Examples	Suggested recruitment tips
Recruiter explored reasons underpinning a patient's preference and provided tailored and balanced information, but (a) may not subsequently do so later in the same consultation or (b) may undermine previous efforts by recommending a treatment or expressing their own preferences/biases in the same consultation[115]	**Excerpt 1: recruiter had received prior QRI training** Following some excellent (and lengthy) balancing of patient's preference for Bypass, patient asks for recruiter's preference: *R: I really don't know which one is the better operation. Potentially, um, potentially certain reasons for choosing one over another. If I lived a long, long way away from where I was going have my band adjusted, I wouldn't have a band. If my main reason for wanting an operation was to cure my diabetes, I'd probably go slightly in favour of the bypass. If my main reason was just general health, weight loss, I'll toss a coin or let the computer toss a coin.* *P: I just, I think I'd have the computer toss a coin in no circumstances* *R: But certainly some people have particular preferences.* *P: I think this thing that the bypass works really well for diabetes, it can sort of eliminate it and I want to be there.* (patient reinforces what he has just heard and uses it as further justification). *R: Okay, I'm happy with that. This is your stomach (explains bypass operation).*	• Avoid divulging personal preferences • Explore and address patients' concerns and preferences, but ensure this is tailored to the patients' concerns • Avoid reinforcing patient preferences or accepting them at face value • Address 'all' or 'most' of patients' concerns and preferences
Recruiter employed some elements of good practice (e.g. explored and addressed patient preferences well), but may not employ other key components of good practice in the same consultation (e.g. avoiding leading or closed questions at the start; providing a clear invitation to participate in the study).	**Excerpt 2: recruiter had brief upfront QRI training at the SIV** *R: Do you feel that there is an operation that you particularly want or don't want from us?* *P: Bypass, bypass* *R: (. . .) now my questions now aren't about changing your mind they're about making sure that I understand why you're drawn towards the bypass and if there are things that push you away from the other two that are misconstrued, misunderstandings from the information we've given you, so is there anything about bands and by-, sleeves that you, push you away from it?* Patient mentions several reasons related to lifestyle, knowledge that someone who had a Band and did not lose weight, heard someone had died after a Band. Each is carefully balanced by the recruiter, but patient and father (F) perceive this to mean recruiter prefers Band. No link to study given. *F: and it seems like you're, you would like her to have a gastric band rather than the other option.* *R: No not at all. I apologise if that's the impression I come . . . the importance with any treatments in anything that we do is informed consent and having informed consent that means that any other option are fully understood. . ..* There was discomfort, and the patient chose Bypass.	• Avoid leading or closed questions at the start (e.g. asking for patient preference or willingness to participate at the start of consultation before trial information provision) • Provide a clear invitation to participate in the study, linking uncertainty to the study rationale • Establish and reassure the patient that they are suitable for all operations

continued

TABLE 12 Inconsistencies in good practice in the transitional stage (*continued*)

Inconsistencies within consultations	Examples	Suggested recruitment tips
A recruiter who does a thorough job of balancing preferences in one consultation may not do the same in a different consultation. This may apply similarly to other good recruitment practices, such as mentioning the study early on and providing sufficient information about the study.	**Excerpts 3, 4, 5: recruiter had received prior QRI training** **Excerpt 3:** Study mentioned early on with equipoise statements and 'keep an open mind'. *R: Right so you've obviously got a fair bit of information about the different types of surgery that we do, and you know a bit about the study that we're doing at the moment because we don't know which type of surgery is is the best, if if, one is. Um we just know that they work, they work in different ways. So just keep a little open mind about that at the moment (patient randomised).* **Excerpt 4:** Study either not mentioned early on or mentioned too briefly (in two different consultations from above) **Not mentioned:** *R: Have you been to one of our education sessions as well? (P: Yes). Yep. You have. So you've had a lot of information already. You'll be aware there are a number of different operations we can do to help people with their weight (mentions all operations). The commonest operations are band and a bypass. The third commonest operation is the sleeve gastrectomy. The others are pretty much very very small numbers (then examination and history) (patient declined).* **Excerpt 5:** **Mentioned briefly:** *R: Oh right, so there's a little bit of different operations that we can do. Which ones did you know about and which ones didn't you know about? (P: I only knew about the band and the bypass.) Well they're the two commonest ones in the UK. . .. Alright there are a few even more obscure ones than those. So you probably know about this study we've been looking at, at the moment as well. (P: yes yes). OK we'll talk about that a bit later. First of all a little bit about you (patient declined).*	• Mention the study early on in all consultations (excellent examples of this from other consultations of same recruiter).

join the trial unless Sleeve was included. The QRI team was fully supportive of adapting the trial to include Sleeve. In interviews, surgeons indicated that they did not expect their equipoise to change, given that the procedure was already offered in all the study sites. They expressed optimism that its inclusion would have a positive impact on recruitment:

> *A lot of people like the sleeve because it seems to sit somewhere between the band and the bypass in terms of the elements of the operation that they were attracted to and elements of the operation that they were put off by.so the sooner we can start offering people sleeve within the study, the better.*
>
> *Surgeon, interview*

> *I would say our current practice is equally unbiased for those three procedures – band, bypass, and sleeve.*
>
> *Surgeon, interview*

However, interview data also indicated that preference for Bypass among some recruiters (found in the initial stage findings) now evolved into a preference for Bypass and/or Sleeve over Band, while among others there were somewhat clearer expressions of equipoise:

> *Bypasses and sleeves do not require that level of engagement post-surgery as a band does. Mind you, that's just my feeling.*
>
> *Surgeon, interview*

> *I know that gastric bypass patients tend to lose weight more dramatically in the first 6 months than any other procedures. I think that sleeve patients tend to have the more gradual weight loss and I think that band patients have to work the hardest to lose weight but overall I think patients have the potential to do as well with each of them.*
>
> *Surgeon, interview*

> *We'd expect them to lose 65% of their excess weight loss with a bypass, 60% with a sleeve and around about 50% with a band.*
>
> *Surgeon, interview*

These issues about how best to incorporate Sleeve were discussed at TMGs, investigator meetings, SIVs and group feedback sessions. The QRI then focused on how best to communicate with balance in relation to all three weight loss operations.

Recruitment progress and the emergence of new challenges

By the end of the transitional stage, across the 11 open sites, most sites were achieving the target for numbers of patients eligible for By-Band-Sleeve: 64% of those screened were eligible, ranging from 33% to 89% across sites. Four sites had less than the target eligibility rate of 60% (sites 3, 7, 8, 11). The targets for randomisation were set at 20% for new sites initially, moving to 45% when fully operational. In May 2016, 560 had been randomised (29% of those eligible), with sites randomisation rate ranging from 12% to 44%. Four sites had < 30% consent rate of those approached to discuss participation (sites 1, 4, 6, 11). It had become clear that some sites in particular were struggling with recruitment. As shown above, some of this was related to specific organisational challenges at the site, and some to the uptake of initial QRI tips for good practice or inconsistencies in recruitment practice seen across recruiters and sites.

As can be seen from *Appendix 4*, *Figure 28*, recruitment had slipped below the target during the early part of this transitional phase, primarily because of a slow start to recruitment in some new sites, the weaker performance of some of the new sites, and increasing interest in Sleeve before its inclusion in the trial. There was, however, an increase in the rate of recruitment after August 2015, potentially due to the incorporation of Sleeve and increasing recruitment in the new sites. The rate of recruitment approached (even exceeded) the target level, but overall, the recruitment numbers did not catch up to the target. There was thus a mix of needs for recruitment training across the trial as it moved into the sustainment stage.

Sustainment stage: May 2016–June 2018

Recruitment challenges and recruitment actions/strategies

The initial aim of this stage was to complete recruitment by June 2018. As indicated in *Appendix 4*, *Figure 28*, to meet this target, there was a need to accelerate recruitment to catch up after the decline in recruitment during 2015. This was made harder by lower numbers of patients screened than expected, although most sites did meet or exceed the study target of 60% of screened patients deemed eligible. From May to December 2016, the QRI team did a focused review of each site, drawing on recruitment data and existing qualitative findings from audio-recordings, interviews, site visits and calls. These data were supplemented by a programme of 11 interviews with the recruiters at 8 sites. Detailed summaries of the recruitment challenges in each site were produced.

The analyses provided a framework for understanding recruitment issues in each site. There continued to be issues with equipoise, particularly related to concerns about Band, which was rapidly falling out of use in NHS practice. While recruiters tried hard to provide balanced presentations of the groups, they struggled to do so when patients asked direct questions about procedures. It also became apparent that many sites were also still trying to resolve organisational and staffing difficulties. The non-randomised component of the trial continued to cause difficulties in some sites. It was meant to be offered to patients who declined participation in the RCT. However, some recruiters tended to present it as an opportunity for patient participation, which took the focus away from the RCT (and unwittingly gave the randomised and non-randomised studies equal weight). The conclusion was that all sites required tailored support and feedback, except for the one site that continued to recruit at or above target (45% of eligible patients). However, it was decided to develop a prioritisation process to ensure QRI work, and resources could be focused where the greatest anticipated benefit could occur. Eight sites were included in this new QRI prioritisation strategy which employed SEAR framework[58] data triangulated with qualitative data analysis[54] in a novel way to facilitate targeted and intensive support and training. This was made possible by the 'real-time' data provided by the trial team, and rapid qualitative analysis and triangulation by the QRI team.[3,54]

Sites were ranked according to numbers of patients screened, eligibility rate, recruitment rate, number of months without any recruitment, numbers of cases of withdrawals or crossovers following randomisation, availability of audio-recorded consultations, and concerns expressed about data capture, pathway issues, or recruitment practice. This allowed sites/recruiters to be prioritised for feedback in terms of their capacity to improve, in discussion with the CI. The strategy is outlined in *Figure 4*.

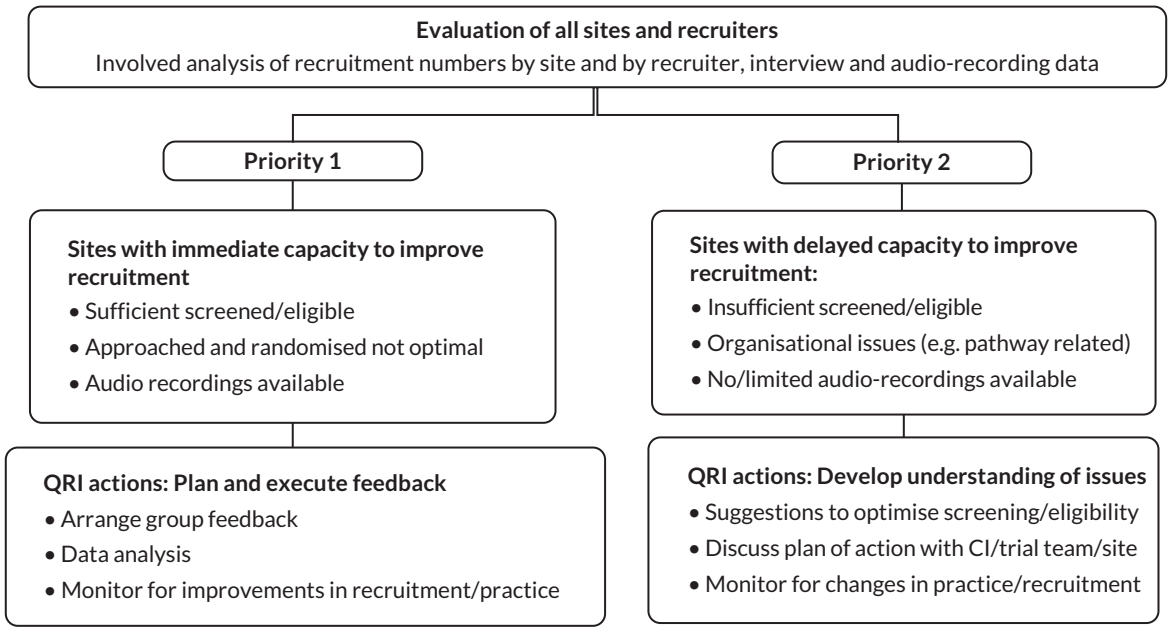

FIGURE 4 QuinteT Recruitment Intervention strategy for site and recruiter prioritisation for feedback.

Visits and telephone feedback sessions were undertaken with the high-priority sites in 2017 by the QRI team and sometimes the CI when that was possible. A group meeting of RNs was also held. A separate set of calls and feedback was focused on sites with higher-than-average crossovers. The prioritisation plan was re-evaluated in July 2017 and a new programme of intensive support was planned for the final site that aimed to open to recruitment in the autumn.

The visits, meetings and feedback sessions yielded important information. For example, two of the highest recruiting sites had periods of several months with no enrolment because of staff shortages and departmental reorganisations. There were also two sites that had not managed to incorporate their MDT early in the recruitment pathway as had been repeatedly advised. This was essential in advance of the final recruitment appointment with the patient, otherwise the discussion with the patient would be provisional and if they agreed to participate, this could be overruled by the MDT. Consequently, both sites had very low recruitment rates. In one of these sites, a lack of representation from study staff on the MDT meant that this could not be changed and so recruitment could not be improved, even following several visits from the CI and QRI team. In the other site, after the visit, the local PI worked hard to change the pathway and eventually it was changed, and, following group and individual feedback to several surgeons, there was an increase in recruitment. The information was also used to provide a 'top tips' document that was circulated to all recruiters, with support for how to start and finish the recruitment consultation efficiently while also providing optimal balanced information.

The plan was further reviewed and sites re-prioritised for visits and feedback in early 2018. There were follow-up visits to sites visited in 2017, and several with the new site to optimise its recruitment. Remote feedback sessions were also planned with recruiters with the lowest recruitment rates in sites where other recruiters had greater success.

Recruitment progress

Over the course of this stage, five sites were recruiting well or satisfactorily. These sites were followed up to monitor the implementation of changes suggested by the QRI and to ensure recruitment was sustained. The QRI team redirected attention towards the four remaining sites with ongoing recruitment issues. The prioritisation strategy meant that some sites were given much more support and training than others. However, overall recruitment remained at around 30%. Most sites had settled into a recruitment pattern, with the best sites able to recruit 40–45% of eligible patients, but the majority around 30–35% (including the largest site), and a small number were below 30%, with insurmountable difficulties. The site that opened in 2017 was able to take on board all the previous knowledge and began well and continued at a high level. Recruitment was thus sustained, but at a similar level as at the end of the transitional stage. Despite recruiting more than 1000 patients by the end of June 2018, the trial was still short of its target, and so a 15-month costed extension to September 2019 was agreed by the funder, with the QRI continuing to work with sites and individual recruiters to achieve the final recruitment target.

Final stage of recruitment: July 2018–September 2019

Recruitment challenges and recruitment actions/strategies

During this final year of recruitment, the key focus was on re-emphasising the main QRI recruitment strategies described above. A revised 'top tips' document was written, presented at an investigator meeting in a session titled 'the final push' for recruitment, and circulated to all recruiters. A series of refresher training teleconferences were held with RNs across the study to reinforce good recruitment practices and try to resolve issues around recruitment pathways. The non-randomised follow-up study, which had been identified early on as hindering RCT recruitment in some sites (*Table 36*), and continued to cause difficulties in some sites, was closed in the final year to direct all efforts on recruitment into the RCT.

Recruitment outcome

The trial achieved its target and closed to recruitment on 30 September 2019 (*Appendix 4*, *Figure 28*). Eleven of the 12 sites reached the study target for eligibility – over 60% of screened patients deemed eligible (see *Appendix 4*, *Table 35*). One site exceeded the study target of 45% of eligible patients randomised, with five sites below 30% of eligible patients, and the final overall average was 28.5% (see *Appendix 4*, *Table 35*). It was notable that the final site to join, site 12, had the highest randomisation rate of patients approached (65%), having received intensive training and support based on all earlier findings.

Chapter 6 Results: primary and secondary outcomes

Primary outcome: percentage excess weight loss at 3 years

Primary analysis

The completeness of the weight data by randomised group is shown in *Appendix 4*, *Figure 30*. Less than 2% (25/1346) of participants failed to provide any data at follow-up, 1012/1346 (75.2%) participants provided data at 6 months, 1, 2 and 3 years and 1130/1346 (84.0%) participants provided data at 3 years. The weight loss trajectory estimated from the data for participants in the three randomised groups is shown in *Figure 5*. In total, 276/405 (68.1%) participants randomised to Bypass achieved at least 50% excess weight loss at 3 years, compared to 97/383 (25.3%) participants in the Band group and 141/342 (41.2%) participants in the Sleeve group (*Table 13*). Comparing the risk relative to the pre-defined 12% non-inferiority margin both Bypass and Sleeve were found to be non-inferior (and superior) to Band, and Sleeve was inferior to Bypass (*Figure 6*). Estimates of the risk ratio for each analysis and treatment comparison are shown in *Appendix 4*, *Table 49*.

Sensitivity analyses

A complete case analysis, omitting participants with missing data at 3 years, gave consistent results. Excluding participants who did not have surgery, grouping those who had surgery according to the allocation and according to the procedure received, and excluding crossovers also provided results consistent with the primary analysis, as did the post hoc analysis adjusting for trial design phase (see *Table 13*). Estimates of the risk ratio for each analysis and treatment comparison are shown in *Appendix 4*, *Table 49*.

Subgroup analyses

Results for participants with and without diabetes at baseline are shown in *Figure 7*. The CIs for the treatment differences are wider for the diabetic subgroup due to fewer participants in this subgroup. As a result, the upper limit for the CI for the Sleeve versus Bypass comparison straddles the non-inferiority margin. However, there was no statistical evidence to suggest that the treatment effects differed between participants with and without diabetes (p = 0.90). Estimates of the risk ratio for each subgroup treatment comparison are shown in *Appendix 4*, *Table 50*.

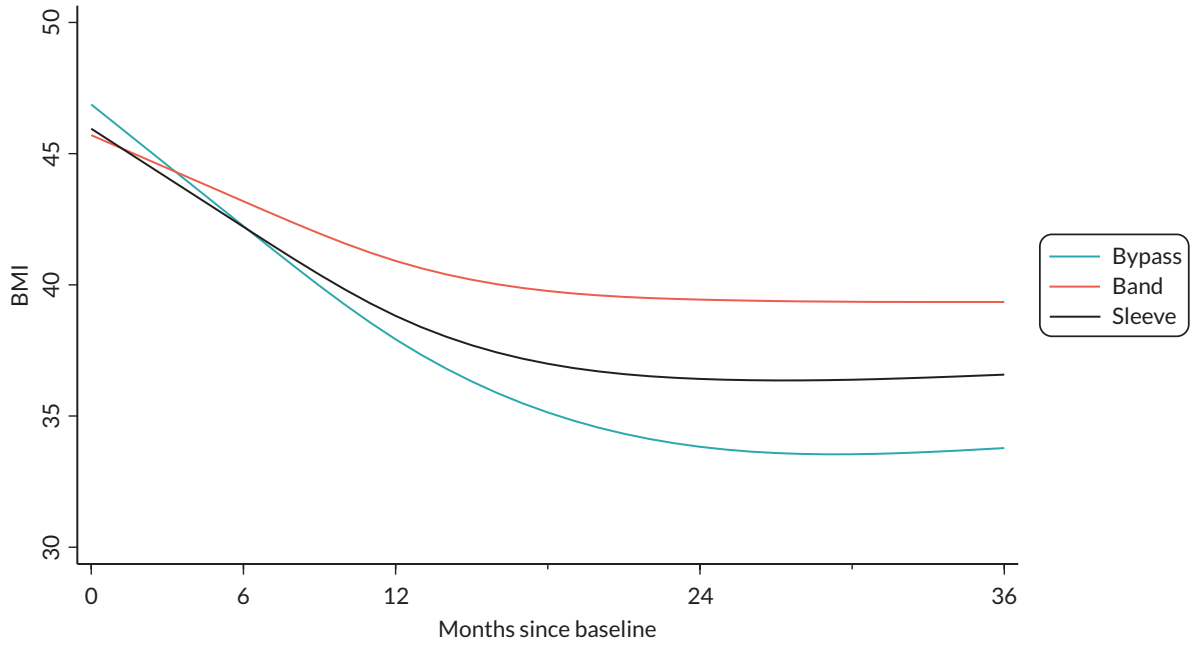

FIGURE 5 Body mass index over time by randomised group. Trajectories are estimated from a regression model and represent the predicted mean BMI.

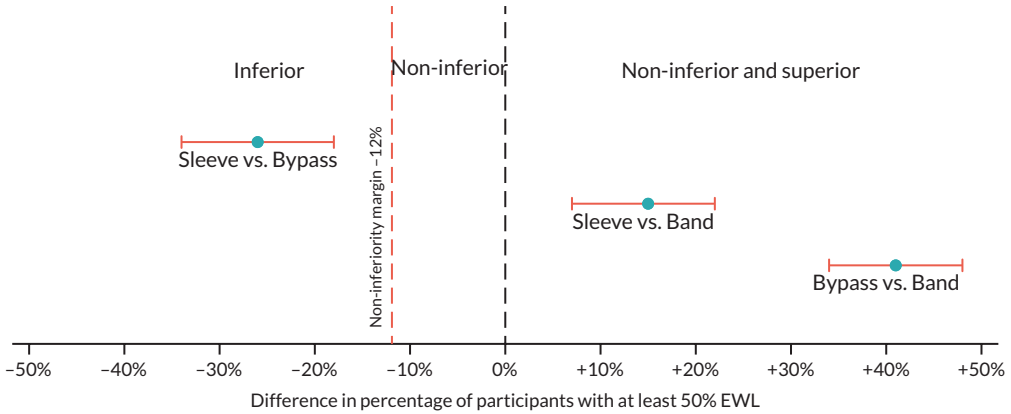

FIGURE 6 Difference in percentage of participants with at least 50% excess weight loss at 3 years by randomised group.

TABLE 13 Percentage of participants with at least 50% excess weight loss at 3 years

Achieved at least 50% EWL[a]	Randomised to Bypass	Randomised to Band	Randomised to Sleeve	Bypass minus Band RD (98% CI)	Sleeve minus Band RD (98% CI)	Sleeve minus Bypass RD (98% CI)
Primary analysis	276/405 (68.1%)	97/383 (25.3%)	142/342 (41.5%)	0.407 (0.339 to 0.475)	0.147 (0.052 to 0.242)	−0.260 (−0.358 to −0.163)
Adjusting for design phase[b]	276/405 (68.1%)	97/383 (25.3%)	141/342 (41.5%)	0.410 (0.341 to 0.478)	0.144 (0.031 to 0.258)	−0.265 (−0.381 to −0.15)
Excluding participants with missing outcome[c]	229/338 (76.7%)	84/325 (20.8%)	123/290 (44.1%)	0.423 (0.364 to 0.481)	0.158 (0.064 to 0.252)	−0.265 (−0.365 to −0.165)
Excluding crossovers	258/363 (71.1%)	62/328 (18.9%)	137/336 (40.8%)	0.490 (0.427 to 0.553)	0.201 (0.099 to 0.302)	−0.289 (−0.385 to −0.194)
Excluding participants who did not have surgery	274/375 (73.1%)	96/363 (26.5%)	140/314 (44.6%)	0.457 (0.395 to 0.519)	0.175 (0.077 to 0.273)	−0.282 (−0.384 to −0.181)
	Received Bypass	**Received Band**	**Received Sleeve**			
Excluding participants who did not have surgery	276/356 (77.5%)	67/322 (20.8%)	167/374 (44.7%)	0.556 (0.472 to 0.639)	0.227 (0.110 to 0.345)	−0.328 (−0.433 to −0.223)

RD, risk difference.
a Multiple imputation (50 imputed data sets) was used to account for missing outcome in analyses, counts exclude imputed observations. Models could not be adjusted for site.
b Post hoc, design phase 1 – before addition of Sleeve (two groups), design phase 2 – after the addition of Sleeve (three groups).
c Multiple imputation not used as primary outcome complete.

Note
Differences of < −12% (i.e. with the lower limit of the CI above −0.12) are considered non-inferior.
Time to achieving at least 50% excess weight loss, and time to relapse in those achieving 50% excess weight loss is shown in *Appendix 4*, *Table 51*.

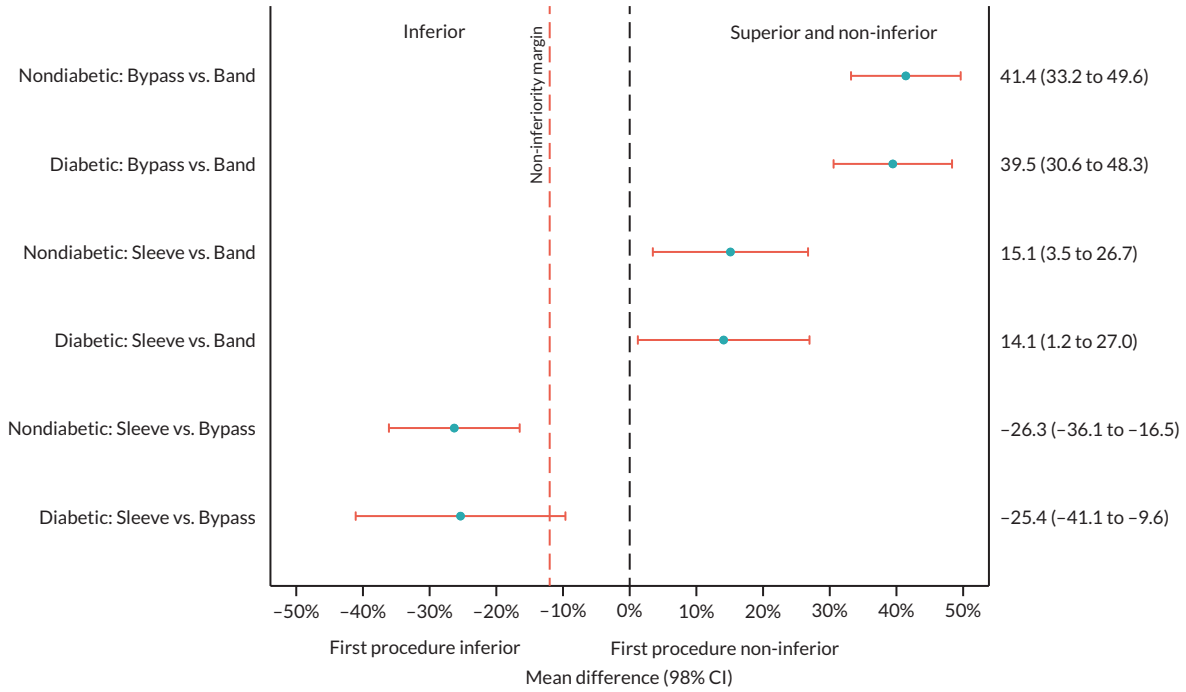

FIGURE 7 Difference in percentage of participants with at least 50% excess weight loss at 3 years – by diabetes status at recruitment.

Results of the analyses by BMI at recruitment are shown in *Figure 8*. Again, there was no statistical evidence to suggest that the treatment effects differed between the different and subgroups of BMI (p = 0.30). The difference between Bypass and Band and Bypass and Sleeve was greatest for the participants with a starting BMI of < 40 kg/m^2 and least for those with a BMI over 50 kg/m^2 at recruitment.

Primary outcome: EQ-5D utility score

Primary analysis

Completeness of the EQ-5D questionnaire is shown in *Appendix 4*, *Figure 30*. Less than 6% (62/1346) of participants failed to provide any data at follow-up and 667/1346 (49.6%) participants provided data at 6 months, 1, 2 and 3 years. The trajectory of EQ-5D utility scores over time is shown in *Figure 9*. The raw data underpinning these trajectories are summarised in *Appendix 4*, *Table 52*. At 3 years, the mean utility score was higher in the Bypass group compared to Band (mean difference 0.079, 98% CI 0.040 to 0.117) and higher in the Sleeve group compared to Band (mean difference 0.045, 98% CI 0.006 to 0.085). The difference between Bypass and Sleeve was not statistically significant (mean difference −0.033, 98% CI −0.072 to 0.006) but did exceed the 0.03 threshold for clinical significance (*Table 14*).

The target treatment effect, unpinning our sample size calculation, was 0.2 SD (see *Sample size*). Our observed unadjusted treatment effect at 3 years was higher at 0.32 SD for the Bypass versus Band comparison and slightly lower for the two comparisons involving Sleeve (0.14 SD and 0.18 SD for the comparisons with Bypass and Band, respectively).

Sensitivity analyses

A complete case analysis, omitting participants with missing data at 3 years, gave consistent results for comparisons involving Bypass. The CI for the Sleeve versus Band comparison rather than just excluding zero as in the primary analysis just included zero in this analysis which included 332 fewer participants. However, the estimated treatment effect was similar (see *Table 14*). In contrast, when participants who did not have surgery were excluded the Sleeve versus Band comparison was in line with the primary results, favouring Sleeve over Band. Excluding participants who did not have surgery also increased the difference between Bypass and Sleeve slightly in favour of Bypass, but the difference between Sleeve and the other procedures was reduced when scores were estimated 3 years after surgery

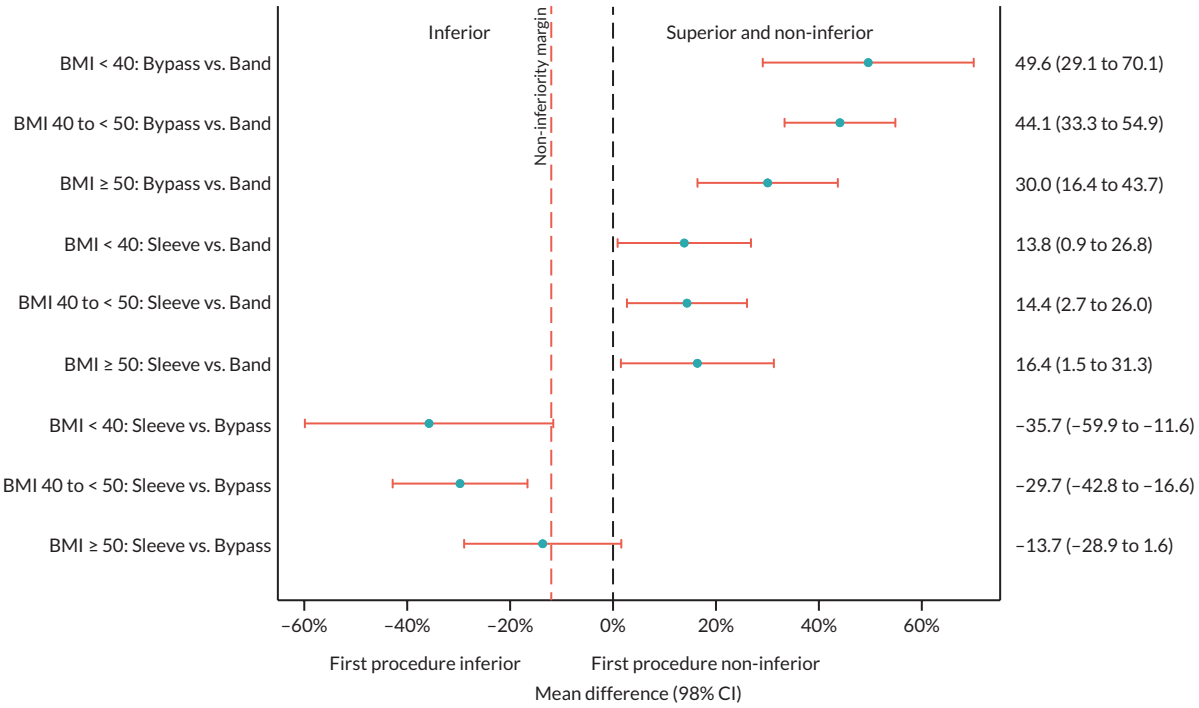

FIGURE 8 Difference in percentage of participants with at least 50% excess weight loss at 3 years – by BMI status at recruitment.

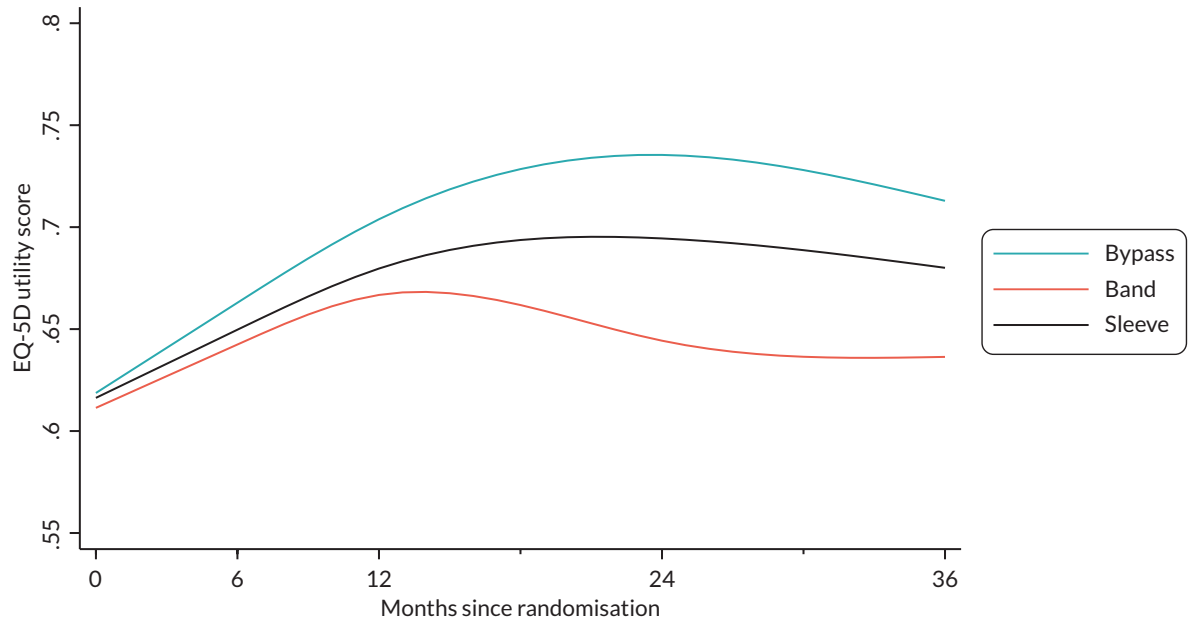

FIGURE 9 EQ-5D utility score over time by randomised group. Trajectories are estimated from the model and represent the predicted mean scores.

rather than 3 years after randomisation (see *Table 14*). Excluding crossovers provided results consistent with the primary analysis, as did the post hoc analysis adjusting for trial design phase (see *Table 14*).

Subgroup analyses

Results of the diabetic versus non-diabetic subgroup analysis are shown in *Figure 10*. The difference in mean EQ-5D scores between Band and the other procedures is slightly less in diabetic participants compared to non-diabetic

TABLE 14 EQ-5D utility score at 3 years

EQ-5D utility score at 5 years	Randomised to Bypass, mean (SD)	Randomised to Band, mean (SD)	Randomised to Sleeve, mean (SD)	Bypass minus Band MD (98% CI)	Sleeve minus Band MD (98% CI)	Sleeve minus Bypass MD (98% CI)
Primary analysis	0.718 (0.288)	0.619 (0.330)	0.676 (0.297)	0.079 (0.040 to 0.117)	0.045 (0.006 to 0.085)	−0.033 (−0.072 to 0.006)
Adjusting for design phase[a]	0.718 (0.288)	0.619 (0.330)	0.676 (0.297)	0.079 (0.040 to 0.117)	0.052 (0.011 to 0.092)	−0.027 (−0.067 to 0.013)
Excluding participants with missing outcome at 3 years	0.721 (0.287)	0.617 (0.330)	0.673 (0.300)	0.082 (0.040 to 0.123)	0.043 (−0.00 to 0.086)	−0.039 (−0.081 to 0.004)
Excluding crossovers	0.725 (0.279)	0.606 (0.333)	0.677 (0.297)	0.093 (0.051 to 0.134)	0.060 (0.018 to 0.101)	−0.033 (−0.073 to 0.008)
Excluding participants who did not have surgery	0.734(0.280)	0.628 (0.322)	0.677 (0.295)	0.089 (0.050 to 0.129)	0.046 (0.006 to 0.086)	−0.043 (−0.084 to −0.003)
Three years from surgery	0.734 (0.280)	0.628 (0.322)	0.677 (0.295)	0.067 (0.022 to 0.112)	0.030 (−0.016 to 0.076)	−0.037 (−0.083 to 0.009)
	Received Bypass	**Received Band**	**Received Sleeve**			
Excluding participants who did not have surgery	0.741 (0.274)	0.617 (0.324)	0.678 (0.299)	0.104 (0.063 to 0.145)	0.061 (0.021 to 0.101)	−0.043 (−0.082 to −0.004)

MD, mean difference.
a Post hoc, design phase 1 – before addition of Sleeve (two groups), design phase 2 – after the addition of Sleeve (three groups).

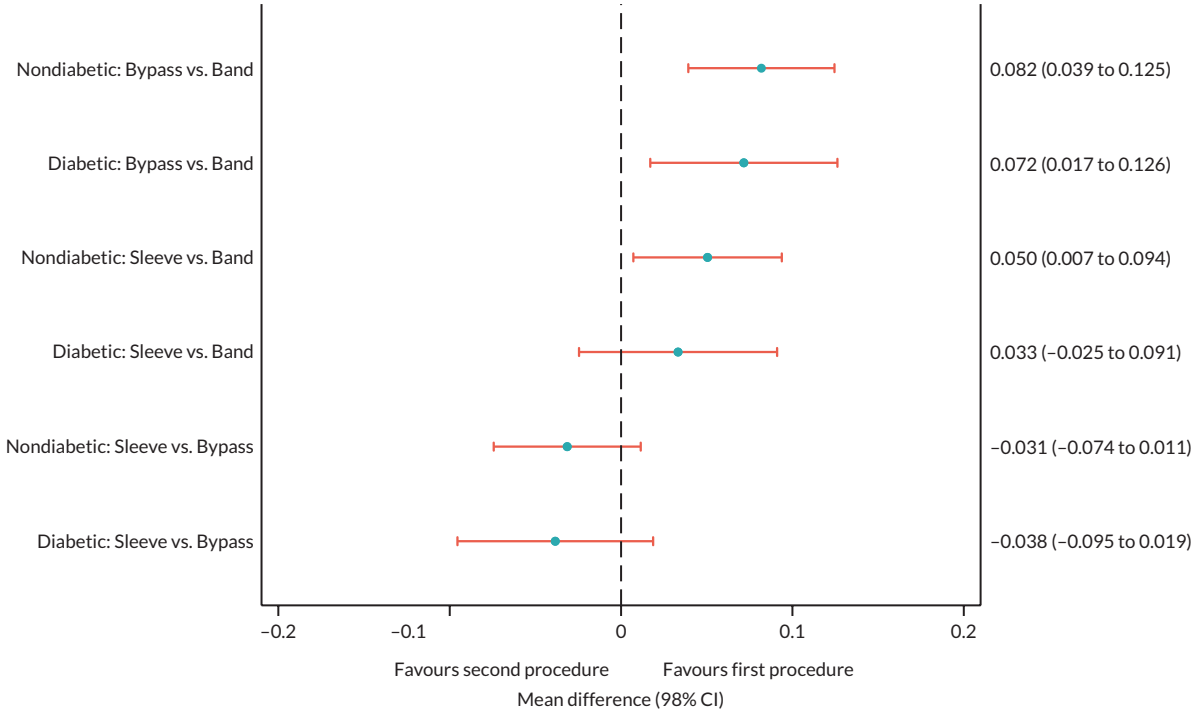

FIGURE 10 Difference in mean EQ-5D scores at 3 years – by diabetic status at recruitment.

participants, but this difference is neither clinically nor statistically significant; there was no statistical evidence to suggest a difference between the subgroups (p = 0.79).

Results of the analyses by BMI at recruitment are shown in *Figure 11*. Again, there was no statistical evidence to suggest that the treatment effects differed between the different subgroups of BMI (p = 0.31).

Interpretation of the primary outcome results

Based on the primary analyses of each outcome, we can conclude that:

- Bypass is superior to Band (non-inferior weight loss and superior HRQoL)
- Sleeve is superior to Band (non-inferior weight loss and superior HRQoL)
- Sleeve is not superior to Bypass (inferior weight loss and not superior HRQoL).

The sensitivity analyses, while showing differences in terms of statistical significance for quality of life for some comparisons, demonstrated that the findings are robust; the mean differences showed little variation, the Bypass versus Sleeve estimates all favoured Bypass and none of the estimates favoured Band. Subgroup analyses showed little variation for both outcomes.

Secondary outcomes related to weight at 3 years

Body mass index

Trajectory of weight loss over time is shown in *Figure 5*. At 3 years, the mean BMI of participants in the Bypass group was lower than the mean BMI in the Sleeve group, which in turn was lower than the mean BMI in the Band group (*Table 15*).

Percentage total weight loss

The mean %TWL of participants in the Bypass group was greater than the mean %TWL in the Sleeve group, which in turn was greater than the mean %TWL in the Band group (*Table 15*). Trajectory of %TWL over time is shown in *Appendix 4*, *Figure 31*.

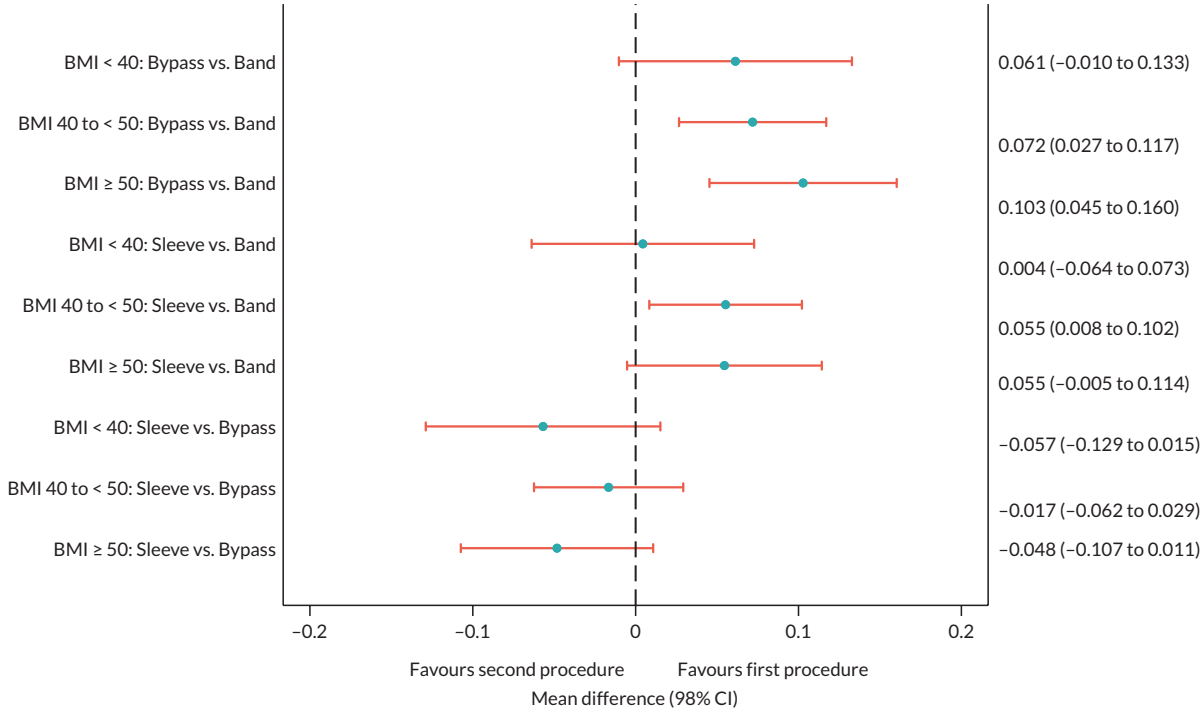

FIGURE 11 Difference in mean EQ-5D scores at 3 years – by BMI at recruitment.

Weight and waist circumference

Weight and waist circumference at each follow-up are summarised in *Appendix 4*, *Table 53*. At 3 years, the median weight was 91.8, 108.8 and 99.9 kg and the mean waist circumference was 104.4, 116.4 and 109.9 cm in the Bypass, Band and Sleeve groups, respectively.

Secondary outcomes related to quality of life

Completeness of the HRQoL questionnaires is shown in *Appendix 4*, *Figure 32*. Overall, 150/1346 participants (11.1%) failed to provide any questionnaire data at follow-up and 510/1346 participants (37.9%) provided data at 6 months, 1, 2 and 3 years.

EQ-5D visual analogue scale

As was seen for the primary outcome, Bypass and Sleeve were superior to Band with a mean score approximately eight points higher with Bypass and six points higher with Sleeve compared to Band at 3 years. The mean scores for Bypass and Sleeve were similar (*Figure 12* and *Table 16*). Trajectory of the VAS scores over time is shown in *Appendix 4*, *Figure 33*.

Short Form 12 physical and mental component scores

The differences in physical component scores between the groups mirrored the EQ-5D scores (see *Figure 12* and *Table 16*). In contrast, there were no differences in mental component scores between the groups (see *Figure 12* and *Table 16*). Trajectories of SF-12 physical and mental component scores over time are shown in *Appendix 4*, *Figure 33*.

Hospital Anxiety and Depression Scale anxiety and depression scores

The trajectories of HADS anxiety and depression scores over time are shown in *Appendix 4*, *Figure 33*. The proportion of participants with anxiety and depression using the clinically defined thresholds is shown in *Appendix 4*, *Table 54*. At 3 years, 22% of respondents had probable anxiety and 14% had probable depression. The differences in mean anxiety scores at 3 years mirrored the SF-12 mental component score with no differences between groups. However, the mean

TABLE 15 Weight outcomes at 3 years

Weight outcomes at 3 years	Randomised to Bypass, mean (SD)	Randomised to Band mean (SD)	Randomised to Sleeve mean (SD)	Bypass minus Band	Sleeve minus Band	Sleeve minus Bypass
				MD (98% CI)	MD (98% CI)	MD (98% CI)
BMI	34.0 (7.64)	39.6 (8.19)	37.0 (7.60)	−5.93 (−7.02 to −4.85)	−2.75 (−3.87 to −1.64)	3.18 (2.07 to 4.29)
%TWL	−26.8 (13.5)	−14.0 (13.5)	−19.4 (13.1)	−12.7 (−14.9 to −10.4)	−5.82 (−8.12 to −3.52)	6.83 (4.55 to 9.11)

MD, mean difference; %TWL, percentage total weight loss.

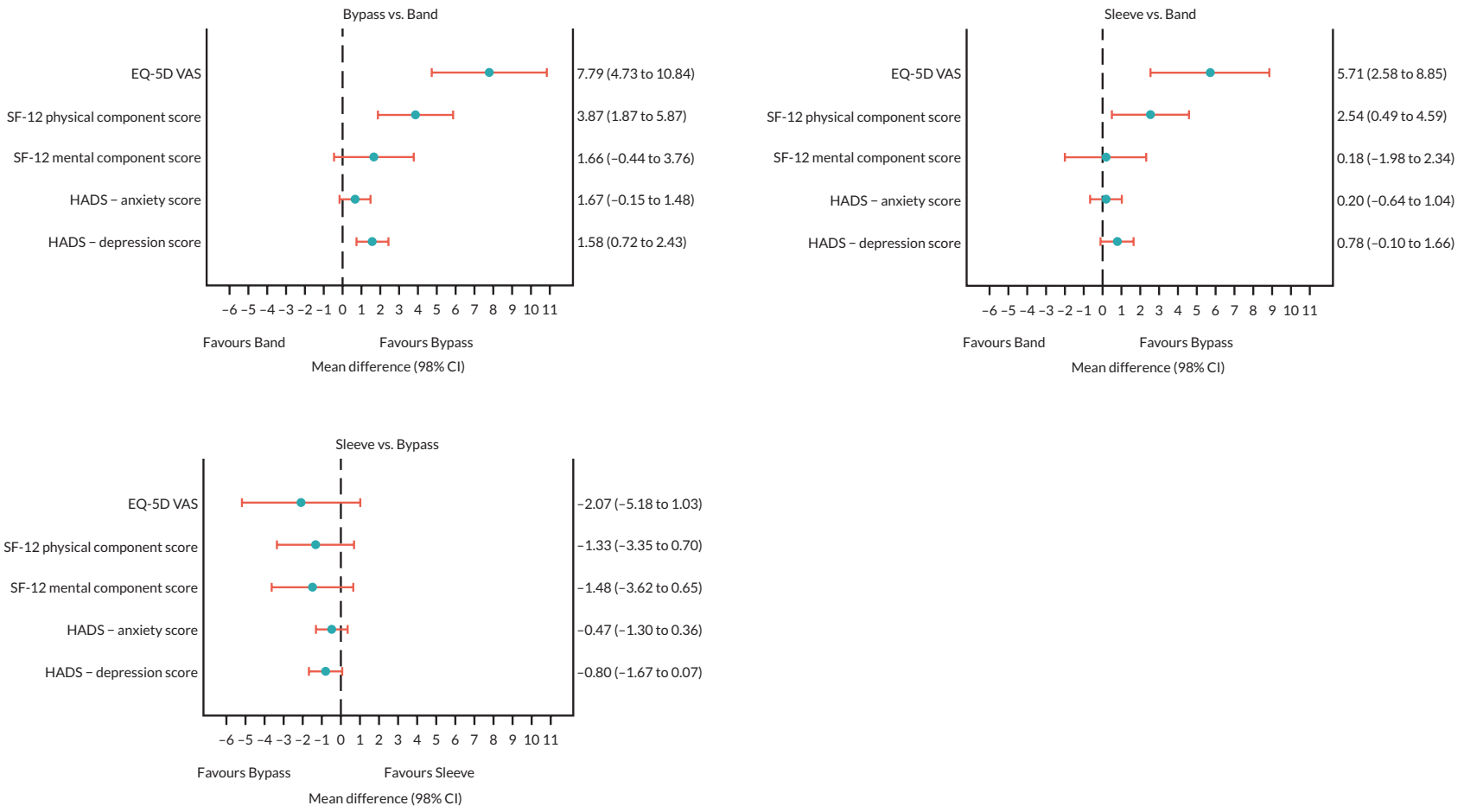

FIGURE 12 Differences in generic QoL outcomes at 3 years. Higher scores equate to better QoL. HADS scores are reversed as higher HADS scores equate to poorer QoL.

TABLE 16 Quality-of-life outcomes at 3 years

QoL outcomes at 3 years	Randomised to Bypass, mean (SD)	Randomised to Band, mean (SD)	Randomised to Sleeve, mean (SD)	Bypass minus Band	Sleeve minus Band	Sleeve minus Bypass
				MD (98% CI)	MD (98% CI)	MD (98% CI)
EQ-5D VAS	75.1 (19.6)	67.9 (22.5)	72.8 (20.6)	7.79 (4.73 to 10.84)	5.71 (2.58 to 8.85)	−2.07 (−5.18 to 1.03)
SF-12 physical component score	48.8 (11.2)	44.2 (12.3)	46.9 (11.4)	3.87 (1.87 to 5.87)	2.54 (0.49 to 4.59)	−1.33 (−3.35 to 0.70)
SF-12 mental component score	46.7 (10.7)	45.6 (12.3)	45.9 (12.3)	1.66 (−0.44 to 3.76)	0.18 (−1.98 to 2.34)	−1.48 (−3.62 to 0.65)
HADS – anxiety	6.38 (4.58)	6.91 (5.09)	6.71 (5.08)	−0.66 (−1.48 to 0.15)	−0.20 (−1.04 to 0.64)	0.47 (−0.36 to 1.30)
HADS – depression	4.36 (4.63)	5.47 (5.14)	4.73 (4.83)	−1.58 (−2.43 to −0.72)	−0.78 (−1.66 to 0.10)	0.80 (−0.07 to 1.67)
GIQLI overall	99.3 (17.9)	92.8 (18.0)	97.2 (17.1)	5.70 (2.53 to 8.87)	4.41 (1.14 to 7.67)	−1.29 (−4.51 to 1.93)
GIQLI gastrointestinal symptoms	58.6 (9.9)	56.3 (9.3)	58.1 (9.6)	2.10 (0.39 to 3.82)	1.96 (0.19 to 3.72)	−0.15 (−1.89 to 1.60)
IWQOL overall	78.6 (22.0)	67.1 (25.4)	74.4 (22.2)	11.4 (6.98 to 15.8)	7.60 (3.04 to 12.2)	−3.81 (−8.32 to 0.71)
IWQOL self-esteem	72.2 (28.5)	57.8 (31.1)	65.0 (30.4)	14.0 (8.43 to 19.6)	7.35 (1.63 to 13.1)	−6.65 (−12.3 to −1.00)
IWQOL sexual life	70.4 (33.4)	64.9 (33.0)	69.1 (33.6)	8.07 (1.88 to 14.26)	8.2 (1.80 to 14.61)	0.13 (−6.16 to 6.43)
IWQOL public distress	82.6 (23.2)	71.5 (28.5)	80.0 (24.0)	11.83 (7.00 to 16.66)	9.00 (4.02 to 13.97)	−2.83 (−7.75 to 2.08)

MD, mean difference; QoL, quality of life.

depression score was higher in the Band group compared to the Bypass group (mean difference −1.58, 98% CI −2.43 to −0.72, *Table 16*).

Gastrointestinal Quality of Life Index overall and gastrointestinal scores

The pattern for these scores followed the generic HRQoL scores, with the highest mean scores in the Bypass group followed by Sleeve and the lowest mean score with Band. For the overall score, Band was lower than both Bypass and Sleeve but for the GI subscale score only Bypass and Band were different from each other (*Figure 13* and *Table 16*). The trajectories of GIQLI scores over time are shown in *Appendix 4*, *Figure 34*.

Impact of Weight of Quality of Life-Lite overall, self-esteem, sexual life and public distress scores

Across all the four domains considered (overall score, self-esteem, sexual life, public distress), the scores were lower in the Band group compared to the Bypass group and Sleeve group, indicating worse QoL in the Band group at 3 years (*Table 16*). The means scores in the Bypass and Sleeve groups were similar overall and for the sexual life and public distress domains, but the score for self-esteem was on average 6.7 points (98% CI 1.0 to 12.3) higher with Bypass compared to Sleeve, indicating better QoL with Bypass for this domain (*Figure 13* and *Table 16*). The trajectories of four scores are shown in *Appendix 4*, *Figure 34*.

Other scores derived from the Short Form 12, Gastrointestinal Quality of Life Index and Impact of Weight of Quality of Life-Lite questionnaires

Other domain scores derived from the three questionnaires are summarised in *Appendix 4*, *Table 55*.

Secondary outcomes: blood results

The completeness at 3 years of the outcomes measured in the blood was lowest for the bloods that required the participant to fast (e.g. fasting glucose). Nonetheless, 1254/1346 (93%) participants provided at least one fasting glucose measure during follow-up and were included in the analysis. Other analyses of markers in the blood included between 1260 and 1303 participants.

Metabolic control: glycated haemoglobin, fasting glucose, triglycerides, total cholesterol and high-density lipoprotein cholesterol

Trajectories of mean levels over time for these outcomes are shown in *Appendix 4*, *Figure 35*. For HbA1c and fasting glucose, the mean in the Bypass and Sleeve groups was lower (better) than the mean in the Band group at 3 years, with no difference between the Bypass and Sleeve groups (*Table 17* and *Figure 14*).

At 3 years, 779/897 participants (86.8%) had a HbA1c < 48 mmol/mol (Bypass 90.7%; Band 82.1%; Sleeve 87.6%), and 634/789 participants (80.4%) had a HbA1c below this threshold and were not taking any antidiabetic medication. The proportion of participants free of diabetes was highest in the Bypass group and lowest in the Band group (Bypass 83.8%, Band 74.6%, Sleeve 82.6%, *Table 18*). A similar pattern was seen for participants with diabetes at baseline; overall 47.9% of participants with diabetes at baseline were free of diabetes at 3 years (see *Appendix 4*, *Table 56*). The proportion of participants with a fasting glucose < 7 mmol/l and the proportion taking antidiabetic medication are also shown in *Table 18*. Numbers of participants taking antidiabetic medication at any point during trial participation and the duration the medication was taken are shown in *Appendix 4*, *Table 57*.

The mean triglycerides and total cholesterol levels were lower (healthier) in the Bypass group compared to Band and the HDL cholesterol was higher (expected). The mean HDL cholesterol was also higher (healthier) in the Sleeve group compared to Band, but the mean triglycerides and total cholesterol levels were similar. In contrast, the mean HDL cholesterol was similar in the Bypass and Sleeve groups, but the mean triglycerides and total cholesterol were higher in the Sleeve group compared to Bypass at 3 years (see *Table 17*, *Figures 14* and *15*). The proportion of participants taking anti-hyperlipidaemic medication at 3 years was lower than a baseline (a positive outcome) and was similar in the three groups (see *Table 19*).

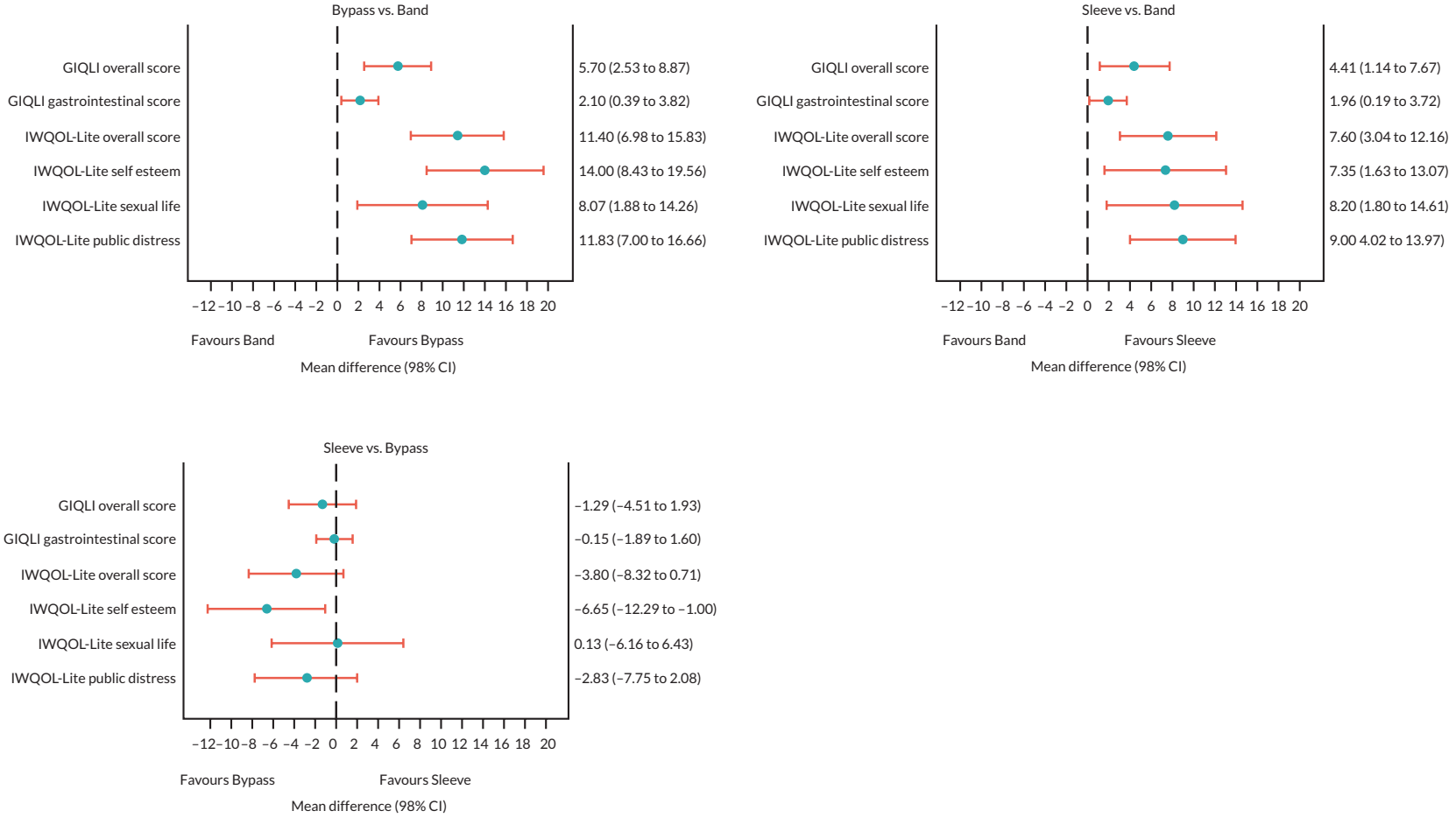

FIGURE 13 Differences in disease-specific QoL outcomes at 3 years. Higher scores equate to better QoL.

TABLE 17 Outcomes measured in the blood at 3 years

Outcomes at 3 years	Randomised to Bypass, median (IQR)	Randomised to Band, median (IQR)	Randomised to Sleeve, median (IQR)	Bypass minus Band	Sleeve minus Band	Sleeve minus Bypass
				GMR (98% CI)	GMR (98% CI)	GMR (98% CI)
HbA1c (mmol/mol)	36 (33–40)	38 (34–44)	36 (33–40)	0.94 (0.91 to 0.97)	0.96 (0.93 to 0.99)	1.02 (0.99 to 1.06)
Fasting glucose (mmol/l)	4.9 (4.4–5.6)	5.0 (4.6–5.6)	4.8 (4.4–5.2)	0.94 (0.89 to 0.98)	0.95 (0.91 to 1.00)	1.02 (0.97 to 1.06)
Triglycerides (mmol/l)	1.01 (0.8–1.4)	1.30 (0.9–1.8)	1.20 (0.9–1.7)	0.82 (0.76 to 0.88)	0.94 (0.87 to 1.01)	1.15 (1.07 to 1.24)
HDL-C (mmol/l)	1.5 (1.30–1.88)	1.34 (1.13–1.57)	1.5 (1.23–1.82)	1.14 (1.09 to 1.19)	1.09 (1.04 to 1.13)	0.96 (0.92 to 1.00)
Ferritin (µg/l)	59 (21–112)	57 (30–121)	73 (32–150)	0.95 (0.81 to 1.11)	1.13 (0.96 to 1.33)	1.19 (1.02 to 1.40)
Serum iron (µmol/l)	16.1 (12.1–20.9)	15.0 (12.0–18.8)	16.9 (13.0–21.0)	1.05 (0.96 to 1.14)	1.09 (1.00 to 1.19)	1.04 (0.95 to 1.13)
Folate (µg/l)	13.1 (6.3–19.1)	9.1 (5.0–15.4)	10.8 (5.5–18.1)	1.23 (1.09 to 1.40)	1.11 (0.97 to 1.26)	0.90 (0.79 to 1.02)
Vitamin B12 (ng/l)	501 (334–833)	348 (259–482)	606 (374–979)	1.36 (1.22 to 1.52)	1.46 (1.30 to 1.64)	1.07 (0.95 to 1.20)
25 hydroxyvitamin D (nmol/l)	64.0 (48.6–82.0)	55.0 (40.0–72.0)	69.5 (47.3–88.7)	1.16 (1.06 to 1.27)	1.15 (1.05 to 1.27)	0.99 (0.91 to 1.09)
Parathyroid hormone (pmol/l)	5.65 (4.4–8.2)	5.6 (4.25–7.75)	5.6 (4.2–8.2)	1.04 (0.95 to 1.13)	0.98 (0.90 to 1.07)	0.95 (0.87 to 1.03)
ALT (IU/l)	19 (15–28)	19 (14–26)	17 (13–23)	1.09 (1.00 to 1.18)	0.95 (0.87 to 1.03)	0.87 (0.80 to 0.95)
ALP (IU/l)	83.5 (70–103)	79 (65–95)	74 (62–91)	1.07 (1.03 to 1.12)	0.96 (0.91 to 1.00)	0.89 (0.85 to 0.93)
Creatinine (µmol/l)	63 (55–71)	66 (57–74)	64 (57–71)	0.98 (0.95 to 1.00)	1.00 (0.98 to 1.03)	1.03 (1.00 to 1.05)
	Mean (SD)	Mean (SD)	Mean (SD)	MD (98% CI)	MD (98% CI)	MD (98% CI)
Total cholesterol (mmol/l)	4.42 (0.98)	4.77 (1.09)	4.96 (1.00)	−0.31 (−0.46 to −0.15)	0.08 (−0.08 to 0.24)	0.39 (0.22 to 0.55)
Haemoglobin (g/dl)	13.4 (1.34)	13.6 (1.32)	13.5 (1.32)	−0.31 (−0.49 to −0.13)	−0.15 (−0.34 to 0.04)	0.16 (−0.03 to 0.35)
Calcium (mmol/l)	2.32 (0.10)	2.36 (0.11)	2.35 (0.11)	−0.027 (−0.045 to −0.010)	−0.003 (−0.021 to 0.015)	0.024 (0.007 to 0.042)

GMR, geometric mean ratio; MD, mean difference.

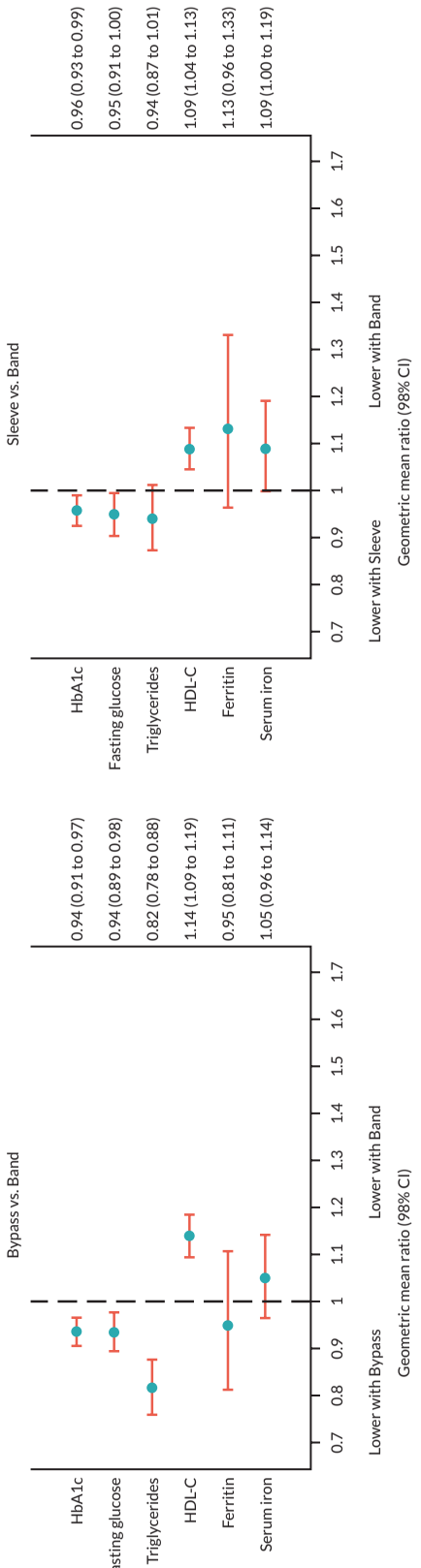

FIGURE 14 Differences in HbA1c, fasting glucose, triglycerides, HDL cholesterol, ferritin and serum iron at 3 years.

TABLE 18 Proportions of participants achieving glycaemic targets and taking of antidiabetic medication

	Randomised to Bypass (*n* = 462)	Randomised to Band (*n* = 464)	Randomised to Sleeve (*n* = 420)	Overall (*n* = 1346)
HbA1c < 48 mmol/mol (with or without antidiabetic medication)				
Baseline	343/447 (76.7%)	350/450 (77.8%)	328/413 (79.4%)	1021/1310 (77.9%)
4 weeks post operative	326/374 (87.2%)	313/372 (84.1%)	301/338 (89.1%)	940/1084 (86.7%)
6 months	344/404 (85.1%)	307/377 (81.4%)	312/368 (84.8%)	963/1149 (83.8%)
12 months	353/391 (90.3%)	299/372 (80.4%)	291/329 (88.4%)	943/1092 (86.4%)
24 months	308/339 (90.9%)	248/312 (79.5%)	249/279 (89.2%)	805/930 (86.6%)
36 months	293/323 (90.7%)	253/308 (82.1%)	233/266 (87.6%)	779/897 (86.8%)
HbA1c < 48 mmol/mol and not taking antidiabetic medication at the stated time point				
Baseline	259/412 (62.9%)	274/415 (66.0%)	259/373 (69.4%)	792/1200 (66.0%)
4 weeks post operative	264/325 (81.2%)	254/338 (75.1%)	248/298 (83.2%)	766/961 (79.7%)
6 months	286/370 (77.3%)	246/334 (73.7%)	266/330 (80.6%)	798/1034 (77.2%)
12 months	294/358 (82.1%)	250/335 (74.6%)	251/299 (83.9%)	795/992 (80.1%)
24 months	253/309 (81.9%)	210/286 (73.4%)	206/245 (84.1%)	669/840 (79.6%)
36 months	244/291 (83.8%)	200/268 (74.6%)	190/230 (82.6%)	634/789 (80.4%)
Fasting glucose < 7 mmol/l (with or without antidiabetic medication)				
Baseline	361/423 (85.3%)	381/442 (86.2%)	342/402 (85.1%)	1084/1267 (85.6%)
4 weeks post operative	315/342 (92.1%)	284/320 (88.8%)	280/301 (93.0%)	879/963 (91.3%)
6 months	342/381 (89.8%)	307/355 (86.5%)	309/344 (89.8%)	958/1080 (88.7%)
12 months	331/359 (92.2%)	289/331 (87.3%)	272/297 (91.6%)	892/987 (90.4%)
24 months	252/269 (93.7%)	209/241 (86.7%)	195/214 (91.1%)	656/724 (90.6%)
36 months	213/237 (89.9%)	198/222 (89.2%)	170/191 (89.0%)	581/650 (89.4%)
Taking antidiabetic medication (any glycaemic level)				
Baseline	145/424 (34.2%)	135/429 (31.5%)	110/379 (29.0%)	390/1232 (31.7%)
4 weeks post operative	46/349 (13.2%)	71/369 (19.2%)	38/322 (11.8%)	155/1040 (14.9%)
6 months	73/397 (18.4%)	81/378 (21.4%)	56/365 (15.3%)	210/1140 (18.4%)
12 months	58/392 (14.8%)	64/378 (16.9%)	41/347 (11.8%)	163/1117 (14.6%)
24 months	48/360 (13.3%)	65/345 (18.8%)	35/313 (11.2%)	148/1018 (14.5%)
36 months	46/350 (13.1%)	64/323 (19.8%)	32/297 (10.8%)	142/970 (14.6%)

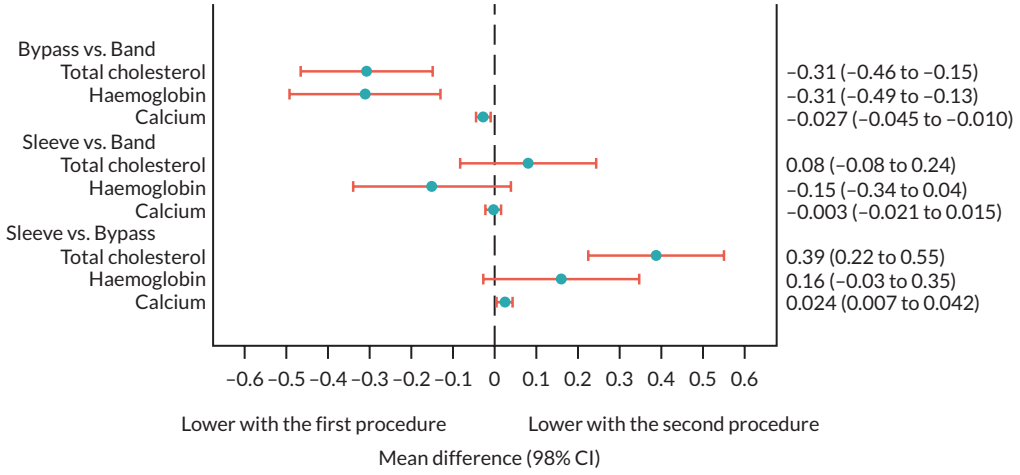

FIGURE 15 Differences in total cholesterol, haemoglobin and calcium at 3 years.

TABLE 19 Proportion of participants taking anti-hyperlipidaemic medication

	Randomised to Bypass (*n* = 462)	Randomised to Band (*n* = 464)	Randomised to Sleeve (*n* = 420)	Overall (*n* = 1346)
Baseline	131/424 (30.9%)	127/429 (29.6%)	110/379 (29.0%)	368/1232 (29.9%)
4 weeks post operative	74/349 (21.2%)	74/369 (20.1%)	62/322 (19.3%)	210/1040 (20.2%)
6 months	91/397 (22.9%)	97/378 (25.7%)	86/365 (23.6%)	274/1140 (24.0%)
12 months	75/392 (19.1%)	81/378 (21.4%)	73/347 (21.0%)	229/1117 (20.5%)
24 months	78/360 (21.7%)	72/345 (20.9%)	65/313 (20.8%)	215/1018 (21.1%)
36 months	78/350 (22.3%)	76/323 (23.5%)	73/297 (24.6%)	227/970 (23.4%)

Safety bloods: haemoglobin, ferritin, serum iron, folate and vitamin B12, vitamin D, calcium, parathyroid hormone

Trajectories over time for these measures are shown in *Appendix 4*, *Figure 35* (haemoglobin), *Appendix 4*, *Figure 36* (ferritin, serum iron, folate, vitamin B12, vitamin D and calcium) and *Appendix 4*, *Figure 37* (parathyroid hormone). The mean haemoglobin was lower in the Bypass group compared to Band (mean difference −0.31, 98% CI −0.49 to −0.13), but Sleeve was similar to both Bypass and Band for this outcome (see *Table 17* and *Figure 15*). Ferritin levels were highest in the Sleeve group, they were on average 19% higher than in the Bypass group (98% CI + 2% to + 40%) and 13% higher compared to Band (98% CI −4% to + 33%). Levels in the Band and Bypass groups were similar. Mean serum iron levels were similar in the three groups (see *Table 17* and *Figure 14*).

Mean folate levels were highest in the Bypass group and lowest in the Band group (see *Table 17*). The Band group also had the lowest mean vitamin B12 and vitamin D levels (see *Table 17*). The mean levels for folate, vitamin B12 and vitamin D were similar in the Bypass and Sleeve groups (see *Figure 16*), while Band was lower than Bypass for folate, vitamin B12 and vitamin D and lower than Sleeve for vitamin B12 and vitamin D (see *Figure 16*). The proportion of participants with vitamin D levels 50 or less is shown in *Appendix 4*, *Table 58*.

Calcium levels were statistically lower in the Bypass group compared to Band and Sleeve which were similar at 3 years, but the mean differences were small (see *Table 17* and *Figure 15*). Levels of parathyroid hormone were similar in the three groups (see *Table 17* and *Figure 16*).

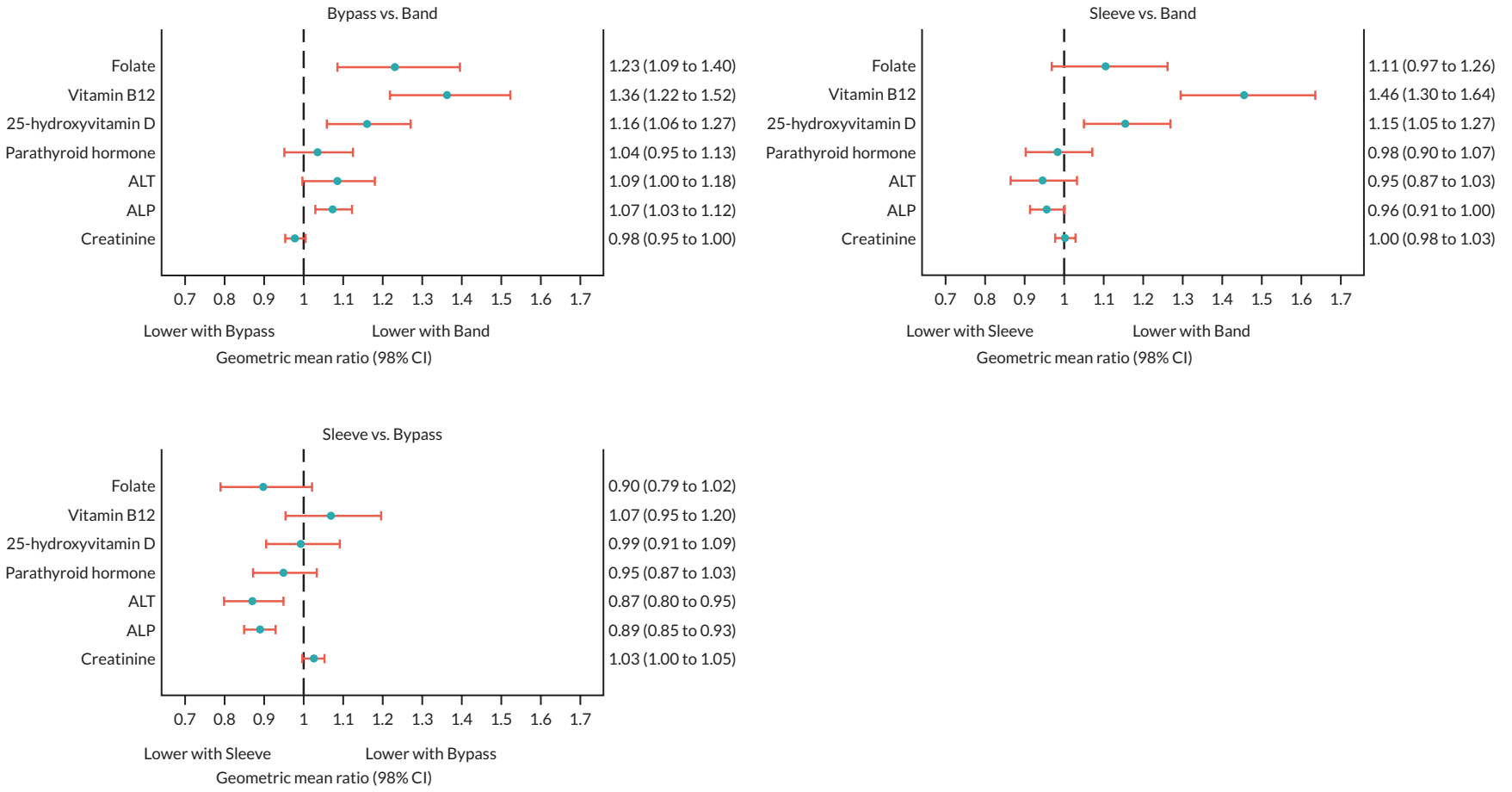

FIGURE 16 Differences in folate, vitamin B12, vitamin D, parathyroid hormone, ALT, ALP and creatinine at 3 years.

Liver and kidney function: alkaline phosphatase, alanine transaminase and creatinine

Trajectories of mean ALT, ALP and creatinine levels over time are shown in *Appendix 4*, *Figure 37*. Statistically there were no differences between Band and Sleeve for these outcomes. On average, the Bypass group had 7% higher ALP levels (98% CI + 3% to + 12%) compared to Band and 2% lower mean creatinine levels (98% CI −5% to 0%). Comparing Bypass and Sleeve, the creatinine levels were similar in the two groups but the ALT and ALP levels were lower in the Sleeve group (ALT: −13%, 98% CI −23% to −2% and ALP: −11% 98% CI −15% to −7%, *Table 17* and *Figure 16*).

Other markers measured in the blood

Other markers measured in the blood, namely haematocrit, mean cell haemoglobin, mean cell volume, albumin, bilirubin, total protein, LDL cholesterol, phosphate, potassium, sodium and urea, are summarised in *Appendix 4*, *Table 59*.

Secondary outcomes measured in food consumed and binge eating behaviour

The completeness of dietary interviews, from which nutrient intake in the diet was obtained, was significantly lower than for other outcomes. The reasons for this were varied including availability of staff at the trial sites to conduct the interviews and the participant not attending the site for follow-up, which was a particular issue during the pandemic. Overall, 864/1346 participants (64.2%) provided dietary information during least one follow-up assessment and 277/1346 participants (20.6%) provided dietary data at baseline and 3 years. Fewer participants in the Sleeve group provided data at baseline and 3 years (66 participants) compared to the Bypass and Band groups (117 and 94 participants, respectively).

Energy intake and percentage energy from protein, fat and carbohydrate were similar in the three groups (*Table 20*, *Figures 17* and *18*). Intake of folate, vitamins B1 and B12, calcium and iron were also similar (see *Table 20* and *Figure 18*). Vitamin E intake was on average 56% higher in the Sleeve group compared to Band (98% CI + 12% to + 117%) but was similar between the Bypass and Band and Bypass and Sleeve groups (see *Table 20* and *Figure 18*).

Details of other nutrients in the food consumed at 3 years are summarised in *Appendix 4*, *Table 60*. Dietary data collected at other follow-up points are available from the authors.

Binge eating scores were highest in the Band group and lowest in the Bypass group. The mean differences between groups were small (< 3 points) but Band had a statistically higher mean score than Bypass and Sleeve. The means in all three groups were consistent with non-binge eating behaviour (i.e. < 17) (*Table 20*).

Secondary outcome of liver fibrosis

Liver fibrosis, assessed using the ELF test, was measured at baseline and 3 years. Overall, samples were provided at baseline for 786/1346 participants (58.5%) and of these 786 participants, 291 (111 Bypass, 104 Band and 76 Sleeve) also provided samples for analysis at 3 years. The analysis was restricted to the 291 participants with results for both time points (21.7% of the 1346 participants). The proportion of participants with none/mild, moderate and severe liver fibrosis at 3 years is shown in *Table 21*. In all groups, most participants had moderate or severe disease with < 3% having none or mild disease; this compares with 13.1% (103/786) of all participants assessed classified as having none or mild disease at baseline and 9.8% (77/786) classified as having severe disease (with the same pattern for those included in the outcome analysis). The odds ratio for more severe liver fibrosis was similar across the three groups (see *Table 21*).

Secondary outcome of sleepiness

Sleepiness at 3 years, as measured by the Epworth scale, is summarised in *Table 22*. In total, 1284 participants were included in the analysis, with data at 3 years available for 850 participants (Bypass 302, Band 284, Sleeve 264). The mean score was higher (more sleepiness) in the Band group compared to the Bypass and Sleeve groups, which were

TABLE 20 Outcomes related to diet at 3 years

Outcomes at 3 years	Randomised to Bypass, median (IQR)	Randomised to Band, median (IQR)	Randomised to Sleeve, median (IQR)	Bypass minus Band	Sleeve minus Band	Sleeve minus Bypass
				GMR (98% CI)	GMR (98% CI)	GMR (98% CI)
Energy intake (kcal/day)	1115 (762–1470)	983.5 (686–1492)	1010 (734–1409)	1.06 (0.92 to 1.22)	1.09 (0.92 to 1.28)	1.03 (0.87 to 1.20)
Dietary fibre (g/day)	9.3 (6.6–13.3)	8.9 (5.2–14.5)	10.0 (6.6–13.8)	1.14 (0.94 to 1.39)	1.14 (0.91 to 1.44)	1.00 (0.80 to 1.25)
% energy from protein	17.7 (14.5–22.9)	17.2 (14.3–22.2)	17.7 (14.4–21.7)	0.97 (0.88 to 1.07)	0.93 (0.83 to 1.05)	0.96 (0.86 to 1.07)
Total folate (µg/day)	127.0 (93.0–177.0)	132.5 (87.0–218.0)	131.5 (87.0–207.0)	0.97 (0.79 to 1.19)	1.12 (0.88 to 1.43)	1.15 (0.92 to 1.46)
Vitamin B1 (mg/day)	0.78 (0.47–1.09)	0.77 (0.48–1.26)	0.83 (0.62–1.33)	1.02 (0.82 to 1.27)	1.24 (0.96 to 1.60)	1.21 (0.95 to 1.55)
Vitamin B12 (mg/day)	2.2 (1.2–3.8)	2.0 (1.0–3.5)	2.4 (1.4–3.5)	1.21 (0.91 to 1.61)	1.25 (0.89 to 1.76)	1.03 (0.74 to 1.43)
Vitamin E (mg/day)	3.0 (1.4–4.8)	2.5 (1.2–5.0)	3.4 (2.1–6.9)	1.19 (0.90 to 1.57)	1.56 (1.12 to 2.17)	1.31 (0.95 to 1.80)
Calcium (mg/day)	483 (316–725)	470 (292–841)	478 (384–612)	0.97 (0.81 to 1.16)	1.03 (0.84 to 1.28)	1.06 (0.87 to 1.30)
Iron (mg/day)	5.9 (3.8–8.7)	5.3 (3.2–8.3)	5.9 (4.5–9.6)	1.06 (0.88 to 1.28)	1.20 (0.96 to 1.49)	1.13 (0.91 to 1.39)
	Mean (SD)	**Mean (SD)**	**Mean (SD)**	**MD (98% CI)**	**MD (98% CI)**	**MD (98% CI)**
% energy from fat	33.6 (11.4)	32.6 (10.5)	34.6 (10.5)	1.60 (−1.59 to 4.78)	2.03 (−1.73 to 5.80)	0.44 (−3.17 to 4.05)
% energy from carbohydrate	46.6 (13.4)	48.4 (13.9)	45.9 (13.0)	−1.98 (−5.71 to 1.75)	−2.00 (−6.40 to 2.40)	−0.01 (−4.23 to 4.20)
Binge eating score	10.83 (8.87)	12.56 (8.61)	11.09 (8.47)	−2.78 (−4.48 to −1.08)	−1.78 (−3.54 to −0.02)	1.00 (−0.75 to 2.74)

GMR, geometric mean ratio; MD, mean difference.

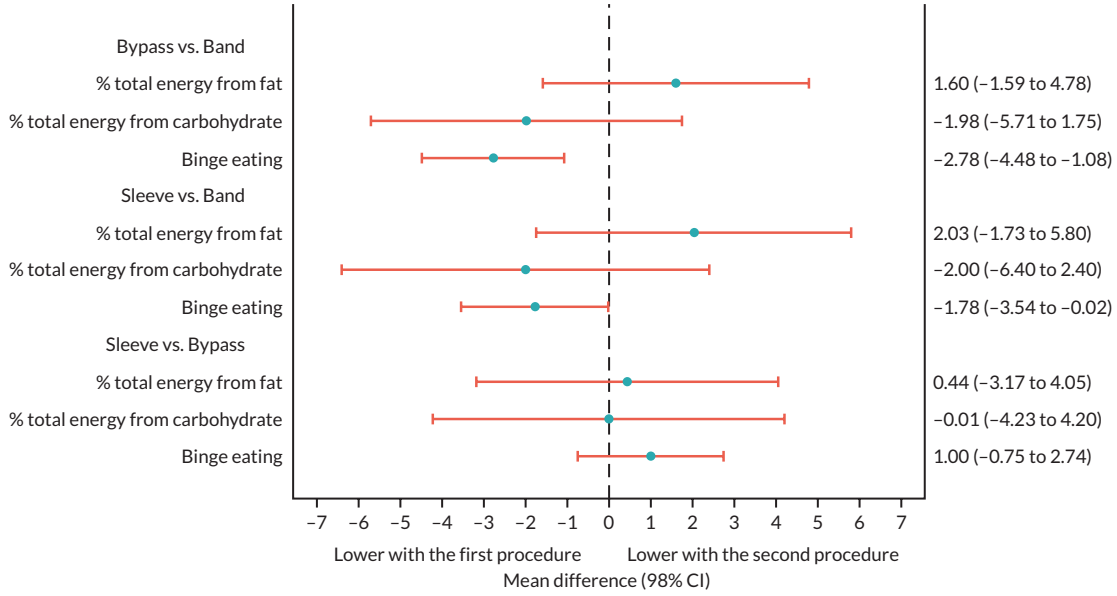

FIGURE 17 Differences in percentage total energy from fat and carbohydrate and in binge eating at 3 years.

similar. As well as a higher mean score, the proportion of participants on CPAP/BiPAP was also highest in the Band group (see *Appendix 4*, *Table 61*).

Blood pressure, medication use and fertility

Blood pressure measurements at each follow-up are given in *Appendix 4*, *Table 62*. The proportion of participants with a systolic BP < 130 mmHg and a diastolic BP < 85 mmHg (i.e. without hypertension) and the proportion taking anti-hypertensive medication are shown in *Table 23*. The Bypass group had the highest proportion of participants with BP below the 130 mmHg/85 mmHg threshold and the lowest proportion taking anti-hypertensive medication. The proportion without hypertension was lowest for the Band group and the Band and Sleeve groups had a similar proportion of participants taking anti-hypertensive medication. Other medication and supplements taken by participants during follow-up are summarised in *Appendix 4*, *Table 63*. Fertility data are summarised in *Appendix 4*, *Table 64*.

Secondary outcome of adverse events

Adverse events in the period from randomisation to 3 years

During participation in the trial, a total of 1905 adverse events were reported (675 in the Bypass group, 705 in the Band group and 525 in the Sleeve group) giving an incidence rate per 100 participant years of follow-up of 56.8 in the Bypass group, 62.0 in the Band group and 50.2 in the Sleeve group. The incidence rate ratios comparing the three groups are shown in *Table 24*. The rate in the Bypass group was similar to the Band and Sleeve groups statistically, but the rate in the Sleeve group was lower than in the Band group (incidence rate ratio 0.78, 98% CI 0.62 to 0.98). An overview of the adverse events reported by MedDRA system organ class is given in *Figure 19*. It is important to note that not all the events reported were 'adverse'. Any event that results in an hospital admission is classified as a (serious) adverse event even if it is a 'positive' event such as the birth of a child or a joint replacement. The number of such events was small (18 births and 73 joint replacements) and they were balanced across the groups (Bypass, Band, Sleeve: joint replacements 26, 30, 17; births 5, 6, 7).

There were 11 deaths within 3 years of randomisation, 4 in the Bypass group, 5 in the Band group and 2 in the Sleeve group. Four of the deaths occurred in participants who had not undergone surgery. One death could be attributed to

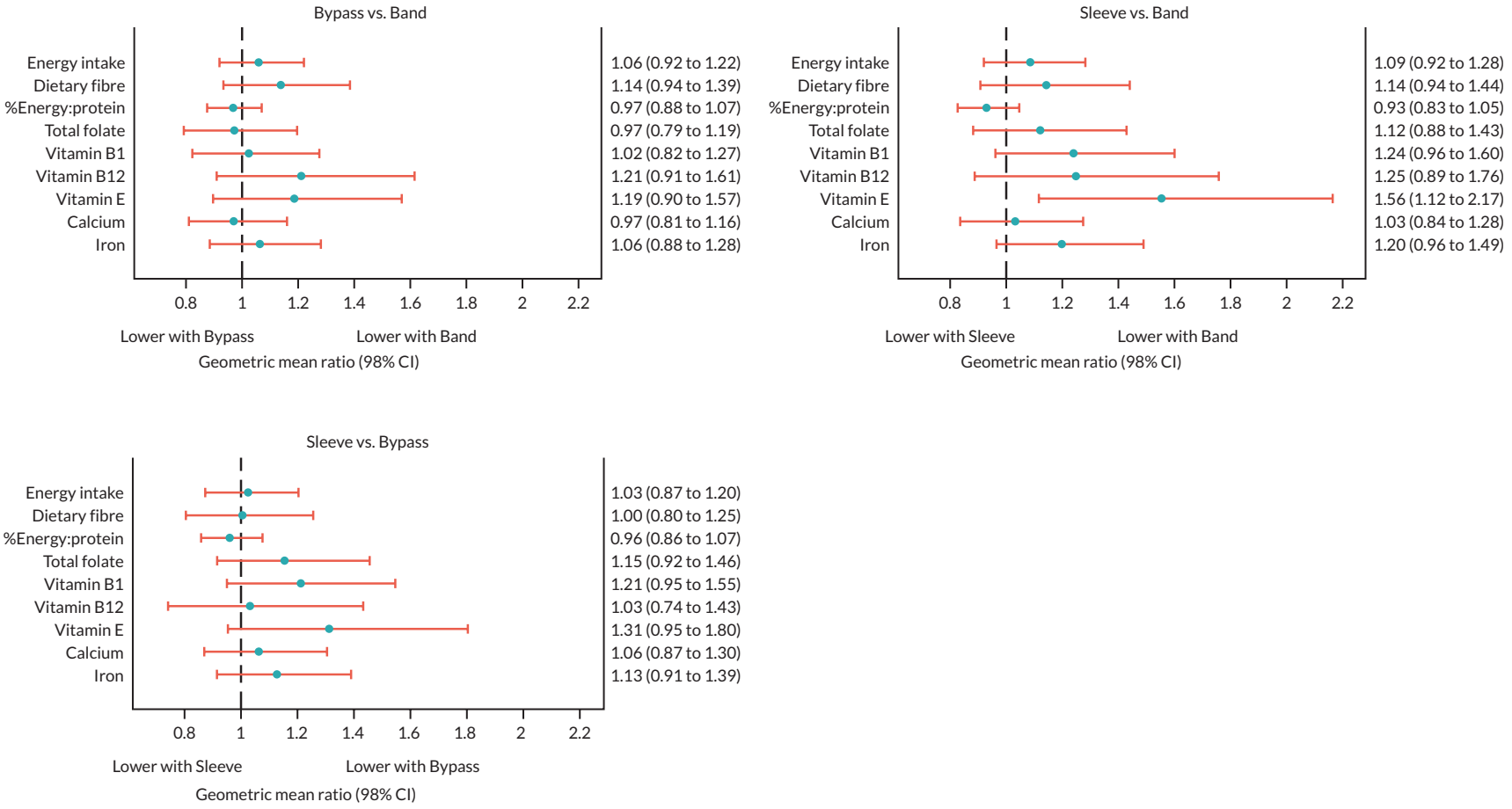

FIGURE 18 Differences in dietary outcomes at 3 years.

TABLE 21 Liver fibrosis at baseline and 3 years

Liver fibrosis	Randomised to Bypass	Randomised to Band	Randomised to Sleeve	Bypass minus Band	Sleeve minus Band	Sleeve minus Bypass
				Odds ratio (98% CI)	Odds ratio (98% CI)	Odds ratio (98% CI)
Baseline						
None/mild (Ishak < 3)	15/111 (13.5%)	13/104 (12.5%)	13/76 (17.1%)			
Moderate (Ishak 3–4)	89/111 (80.2%)	81/104 (77.9%)	60/76 (79.0%)			
Severe (Ishak > 4)	7/111 (6.3%)	10/104 (9.6%)	3/76 (4.0%)			
Three years						
None/mild (Ishak < 3)	3/111 (2.7%)	3/104 (2.9%)	2/76 (2.6%)	1.26 (0.54 to 2.92)	1.44 (0.51 to 4.08)	1.14 (0.47 to 2.79)
Moderate (Ishak 3–4)	86/111 (77.5%)	84/104 (80.8%)	60/76 (79.0%)			
Severe (Ishak > 4)	22/111 (19.8%)	17/104 (16.3%)	14/76 (18.4%)			

TABLE 22 Epworth sleepiness scale at 3 years

Sleepiness	Randomised to Bypass	Randomised to Band	Randomised to Sleeve	Bypass minus Band	Sleeve minus Band	Sleeve minus Bypass
				MD (98% CI)	MD (98% CI)	MD (98% CI)
Sleepiness	3.58 (3.77)	4.26 (4.23)	4.06 (4.24)	−1.02 (−1.66 to −0.38)	−0.68 (−1.34 to −0.02)	0.34 (−0.31 to 1.00)

MD, mean difference.

Note
Scale ranges from 0 to 24, higher scores indicate more sleepiness.

TABLE 23 Blood pressure and anti-hypertensive medication

	Randomised to Bypass (*n* = 462), *n*/*N* (%)	Randomised to Band (*n* = 464), *n*/*N* (%)	Randomised to Sleeve (*n* = 420), *n*/*N* (%)	Overall (*n* = 1346), *n*/*N* (%)
BP < 130 mmHg AND diastolic BP < 85 mmHg				
Baseline	104/422 (24.6%)	126/417 (30.2%)	98/384 (25.5%)	328/1223 (26.8%)
4 weeks post operative	152/310 (49.0%)	124/312 (39.7%)	113/261 (43.3%)	389/883 (44.1%)
6 months	153/357 (42.9%)	127/336 (37.8%)	122/319 (38.2%)	402/1012 (39.7%)
12 months	155/345 (44.9%)	126/326 (38.7%)	123/282 (43.6%)	404/953 (42.4%)
24 months	122/246 (49.6%)	85/233 (36.5%)	90/201 (44.8%)	297/680 (43.7%)
36 months	97/225 (43.1%)	76/202 (37.6%)	72/173 (41.6%)	245/600 (40.8%)
On anti-hypertensives				
Baseline	210/424 (49.5%)	178/429 (41.5%)	176/379 (46.4%)	564/1232 (45.8%)
4 weeks post operative	126/349 (36.1%)	130/369 (35.2%)	120/322 (37.3%)	376/1040 (36.2%)
6 months	150/397 (37.8%)	142/378 (37.6%)	148/365 (40.5%)	440/1140 (38.6%)
12 months	124/392 (31.6%)	131/378 (34.7%)	131/347 (37.8%)	386/1117 (34.6%)
24 months	108/360 (30.0%)	123/345 (35.7%)	113/313 (36.1%)	344/1018 (33.8%)
36 months	107/350 (30.6%)	117/323 (36.2%)	108/297 (36.4%)	332/970 (34.2%)

TABLE 24 Adverse event rates

Period	Randomised to Bypass, events (rate)	Randomised to Band, events (rate)	Randomised to Sleeve, events (rate)	Bypass minus Band IRR (98% CI)	Sleeve minus Band IRR (98% CI)	Sleeve minus Bypass IRR (98% CI)
Any adverse event						
Randomisation to 3 years (rate per 100 years)	675 (56.8)	705 (62.0)	525 (50.2)	0.89 (0.72 to 1.12)	0.78 (0.62 to 0.98)	0.87 (0.69 to 1.10)
Surgery to 30 days post surgery (rate per 100 days)	183 (1.53)	155 (1.26)	140 (1.30)	1.20 (0.85 to 1.68)	1.01 (0.71 to 1.45)	0.84 (0.59 to 1.20)
30 days post surgery to 3 years (rate per 100 years)	410 (48.8)	485 (57.5)	290 (40.7)	0.81 (0.61 to 1.07)	0.65 (0.49 to 0.88)	0.81 (0.60 to 1.10)
Post-surgery abdominal procedure[a]						
Surgery to 3 years (rate per 100 years)	47 (5.39)	79 (9.01)	29 (3.91)	0.56 (0.31 to 1.01)	0.41 (0.21 to 0.78)	0.72 (0.36 to 1.44)
Hospital attendance for abdominal pain						
Randomisation to 3 years (rate per 100 years)	38 (3.20)	37 (3.25)	31 (2.96)	1.00 (0.51 to 1.97)	0.90 (0.44 to 1.83)	0.90 (0.45 to 1.82)
Surgery to 3 years (rate per 100 years)	35 (4.01)	37 (4.22)	24 (3.24)	0.96 (0.47 to 1.96)	0.77 (0.35 to 1.66)	0.80 (0.37 to 1.73)
Overnight admission for any reason						
Randomisation to 3 years (rate per 100 years)	179 (15.1)	189 (16.6)	161 (15.4)	0.90 (0.66 to 1.21)	0.89 (0.65 to 1.21)	0.99 (0.73 to 1.35)
Surgery to 3 years (rate per 100 years)	153 (17.5)	164 (18.7)	127 (17.1)	0.90 (0.66 to 1.25)	0.85 (0.61 to 1.20)	0.94 (0.67 to 1.33)
	Received Bypass	**Received Band**	**Received Sleeve**			
Any adverse event						
Surgery to 30 days post surgery (rate per 100 days)[b]	175 (1.51)	120 (1.11)	181 (1.44)	1.38 (0.96 to 1.98)	1.27 (0.89 to 1.83)	0.92 (0.66 to 1.29)
30 days post surgery to 3 years (rate per 100 years)[b]	412 (51.4)	443 (57.1)	320 (39.3)	0.85 (0.64 to 1.14)	0.63 (0.47 to 0.85)	0.74 (0.55 to 0.99)
Post-surgery abdominal procedure[a]						
Surgery to 3 years (rate per 100 years)[b]	52 (6.24)	74 (9.19)	29 (3.41)	0.64 (0.36, 1.15)	0.35 (0.18, 0.67)	0.54 (0.28, 1.06)

continued

TABLE 24 Adverse event rates (*continued*)

Period	Randomised to Bypass, events (rate)	Randomised to Band, events (rate)	Randomised to Sleeve, events (rate)	Bypass minus Band IRR (98% CI)	Sleeve minus Band IRR (98% CI)	Sleeve minus Bypass IRR (98% CI)
Hospital attendance for abdominal pain						
Surgery to 3 years (rate per 100 years)	38 (4.56)	31 (3.85)	27 (3.18)	1.22 (0.59 to 2.55)	0.81 (0.37 to 1.74)	0.66 (0.31 to 1.39)
Overnight admission for any reason						
Surgery to 3 years (rate per 100 years)	157 (18.8)	142 (17.6)	143 (16.8)	1.03 (0.74 to 1.44)	0.90 (0.64 to 1.26)	0.87 (0.63 to 1.21)

IRR, incidence rate ratio.

a Abdominal procedures include the following: appendicectomy, caesarean section, cholecystectomy, hernia repair (abdominal, hiatus, incisional, umbilical, unspecified), hysterectomy, jejunostomy, laparoscopy, laparotomy, oophorectomy (unilateral bilateral, unspecified), hysterosalpingo-oophorectomy, salpingectomy, salpingo-oophorectomy (bilateral, unilateral), peritoneal adhesions division, small intestinal resection, splenectomy, liposuction, gastrostomy, wound drainage, enteral nutrition, abdominoplasty, adhesiolysis, peritoneal lavage, abdominal cavity drainage, gastric banding, gastric bypass, gastric operation, GI surgery, gastric banding reversal, drain placement, stoma closure, stoma creation, intestinal plication surgery.

b Two surgeries (one Band, one Sleeve) were attempted but abandoned; these two surgeries are included in the analyses by randomised allocation but are excluded from the analyses by surgery received. Reasons for the surgeries being abandoned were: Band – participant deteriorated anaesthetically and Sleeve – participant became hypotensive 10 minutes after the laparoscopy with a possible cardiac event.

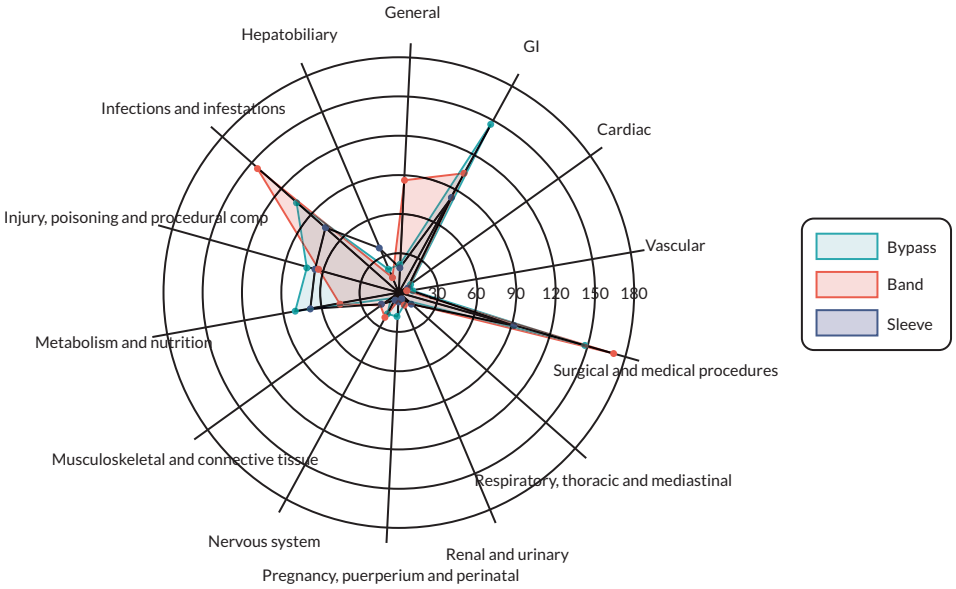

FIGURE 19 Overview of the total number of adverse events reported from randomisation to 3 years by randomised allocation. MedDRA system organ classes with 20 or fewer events in total are excluded. General: general disorders and administration site conditions, Injury, poisoning and procedural comp, injury, poisoning and procedural complications.

bariatric surgery; the participant died from peritonitis caused by a leak from the gastric band sutures. For causes of death, see *Appendix 4*, *Table 65*.

Adverse events in the period from randomisation to surgery

In total, 242/1905 (12.7%) adverse events were reported in the period from randomisation to surgery (82 in the Bypass group, 65 in the Band group and 95 in the Sleeve group). An overview of the adverse events reported in this period by MedDRA system organ class is given in *Figure 20*. The 47 surgical and medical procedures included 7 joint arthroplasties, 4 hernia repairs, 4 cholecystectomies, 3 cardiac procedures and 4 mineral supplementations. Most

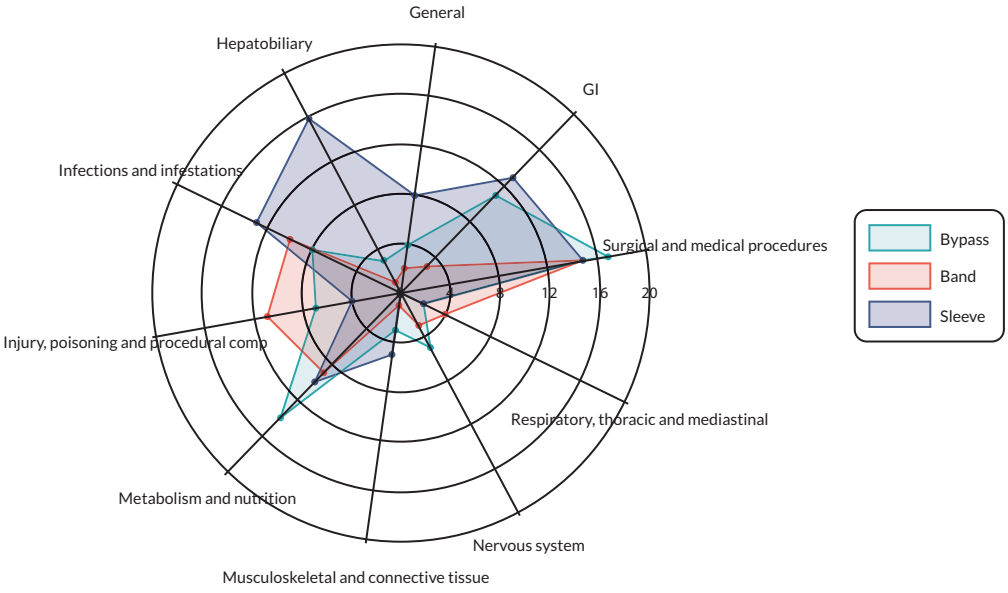

FIGURE 20 Overview of the number of adverse events reported pre surgery by randomised allocation. MedDRA system organ classes with five or fewer events in total are excluded. General: general disorders and administration site conditions; injury, poisoning and procedural comp, injury, poisoning and procedural complications.

of the GI disorders were abdominal pain (10/27 events) or hernias (5 events) and most hepatobiliary disorders were cholelithiasis (12/20 events). The general disorders included chest and hernia pain (10/14 events), and the most commonly reported infections were respiratory tract infections (8/31 events) and cellulitis (6 events). Most injuries were musculoskeletal in nature (7/22 events) and the nutritional issues were mainly related to iron deficiency (30/33 events).

Adverse events in the period from surgery to 30 days

In the 30 days following surgery, 478 adverse events were reported in the 1183 participants in whom surgery was started. In two cases, the surgery was abandoned, and these two participants are excluded from the analyses grouping participants by the surgery received. When participants were grouped by surgery received rather than randomised allocation, the incidence rate per 100 days of follow-up was unchanged in the Bypass group (1.53 vs. 1.51), decreased in the Band group (1.26 vs. 1.11) and increased in the Sleeve group (1.30 vs. 1.44), but statistically the rates were similar in the three groups for both analyses (see *Table 24*). An overview of the adverse events reported in each surgical group in this period by MedDRA system organ class is given in *Figure 21*. The most common adverse events in this period were infections and infestations (154 events in 144 participants) and GI disorders (93 events in 75 participants) followed by injury, poisoning and procedural complications (76 events in 58 participants) and metabolism and nutrition disorders (64 events in 56 participants). Most infections were wound infections (122 events, which occurred with similar frequency in each group), followed by urine and respiratory tract infections (9 and 8 events, respectively). The most commonly reported GI-related events were abdominal pain (26 events, mainly after Bypass and Sleeve surgery), vomiting (13 events, most commonly after Bypass) and abdominal distension (8 events, 6 after Bypass). The most frequently reported procedure-related events were haemorrhage, transfusion and urinary retention, all of which occurred most frequently after Sleeve followed by Bypass. As was seen pre surgery, most nutrition-related events were iron deficiency followed by electrolyte imbalance. A breakdown of the events by MedDRA system organ class for events that occurred in at least five participants is given in *Appendix 4*, *Table 66*.

Adverse events in the period from 30 days post surgery to 3 years

Most adverse events occurred in the period from 30 days after surgery to 3 years after randomisation. In total, 1185 events were reported in this period. The incidence rate per 100 years of follow-up was similar when participants were grouped by randomised allocation and by surgery received. Both analyses suggested that the incidence rate of adverse events was lower after Sleeve surgery compared to Band (incidence rate ratio 0.63, 98% CI 0.47 to 0.85 grouping by surgery received, and 0.65, 98% CI 0.49 to 0.88 grouping by allocation). A similar pattern was seen when comparing Sleeve and Bypass (incidence rate ratio 0.74, 98% CI 0.55 to 0.99 grouping by surgery received, and 0.81, 98% CI 0.60

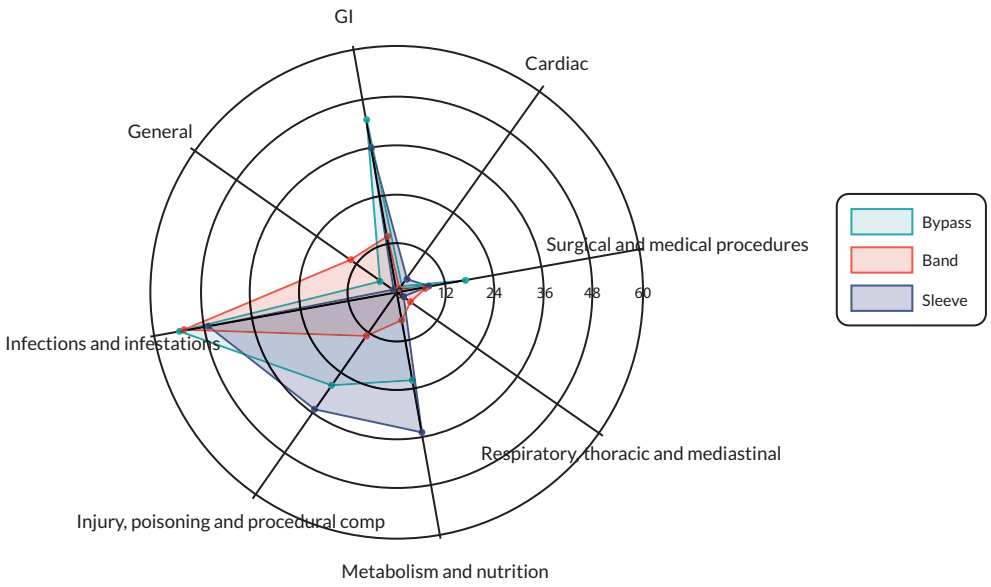

FIGURE 21 Overview of the number of adverse events reported in the first 30 days following surgery by surgery received. MedDRA system organ classes with five or fewer events in total are excluded. General: general disorders and administration site conditions; injury, poisoning and procedural comp, injury, poisoning and procedural complications.

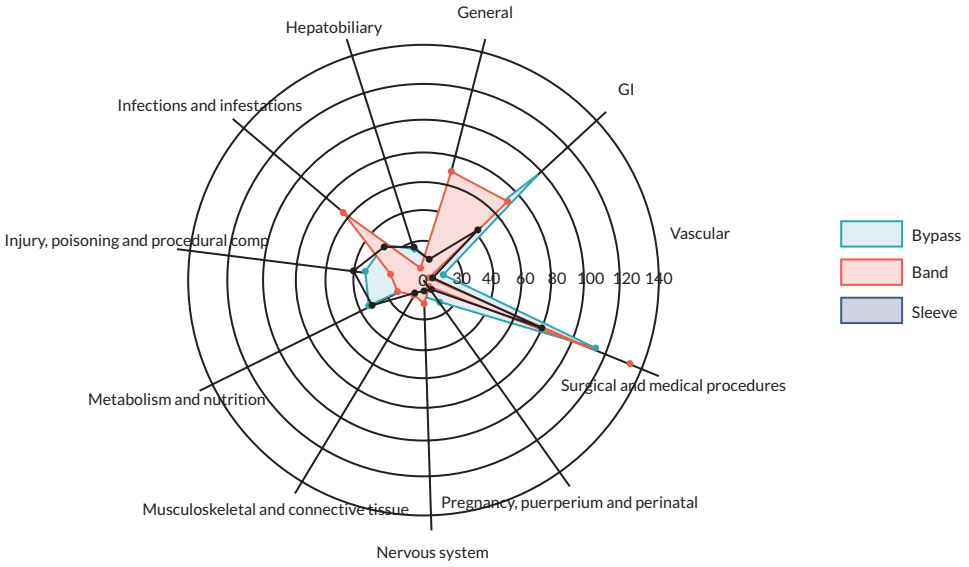

FIGURE 22 Overview of the number of adverse events reported in period from 30 days post surgery to 3 years by surgery received. MedDRA system organ classes with 20 or fewer events in total are excluded. General: general disorders and administration site conditions; injury, poisoning and procedural comp: injury, poisoning and procedural complications.

to 1.10 grouping by allocation). The rates in the Bypass and Band groups were similar (see *Table 24*). An overview of the adverse events reported in surgical groups in this period by MedDRA system organ class is given in *Figure 22*. The most commonly reported events were surgical and medical procedures (313 events in 212 participants, most frequent after Band) and GI disorders (202 events in 119 participants, most frequent after Bypass), followed by infections infestations (124 events in 92 participants, most frequent after Band). A breakdown of the events by MedDRA system organ class for events that occurred in at least five participants is given in *Appendix 4*, *Table 67*.

Adverse events in the period from surgery to 3 years

Abdominal procedures

In total, 155 of the 1663 events reported following surgery were abdominal procedures; 52 occurred in participants who had received Bypass surgery, 74 in those who had received Band and 29 following Sleeve. The incidence rates per 100 years of follow-up by allocation and by surgery received are shown in *Table 24*. Both analyses suggested that the incidence rate of adverse events was lower after Sleeve surgery compared to Band (incidence rate ratio 0.35, 98% CI 0.18 to 0.67 grouping by surgery received, and 0.41, 98% CI 0.21 to 0.78 grouping by allocation). In both analyses, the rates in the Bypass versus Band groups and in the Sleeve versus Bypass groups were statistically similar (see *Table 24*).

Hospital attendance for abdominal pain

In total, 106 of the 1905 adverse events were reported hospital attendances for abdominal pain; 10 occurred before surgery and the remaining 96 were after surgery. Of the attendances following surgery, 38 occurred in participants who had received Bypass surgery, 31 in those who had received Band and 27 following Sleeve. The incidence rates per 100 years of follow-up by allocation and by surgery received are shown in *Table 24*. All analyses suggested that the incidence rates of attendances for abdominal pain were statistically similar across the three groups (see *Table 24*).

Overnight hospital admission for any reason

In the period from randomisation to 3 years, there were 529 overnight admissions excluding the admission for bariatric surgery, 179 admissions in the Bypass group, 189 in the Band group and 161 in the Sleeve group. Of these 529 admissions, 85 occurred before the participant had their bariatric surgery and 444 occurred following surgery. Statistically, the incidence rates were similar in the three groups, both overall, after surgery and when grouping post-surgery events by allocation and surgery received (see *Table 24*).

TABLE 25 Surgery-specific morbidity

Event	Received Bypass (*n* = 389)	Received Band (*n* = 363)	Received Sleeve (*n* = 429)
Surgery-related			
Intra-abdominal haematoma requiring surgery or drain placement	1		3
Internal hernia (in meso-colic space) requiring repair	15		0
Hiatal hernia repair not at time of initial intervention	2		1
Adhesion obstruction requiring surgery ± small bowel resection	4		
Anastomotic obstruction/perforation requiring revision surgery or dilatation at:	4		
Jejuno-jejunostomy[a]	1		
G-J anastomosis[b]	3		
GI leak requiring surgery and/or drain placement			
From sleeve staple line (fistula)			3
From G-J anastomosis	0		
From J-J anastomosis	0		
From band sutures		1	
Corrective surgery for maintaining the band[c]		16	
Band removal (not revision)		22	
Revision surgery			
Band to Bypass		10	
Band to Sleeve		2	
Sleeve to Bypass			4
Bypass reversal to normal anatomy	0		
Medically related			
Need for total parenteral nutrition/enteral feeding	5	–	1
Malnutrition	2	–	
Neuropathy	–	–	–
Wernicke's encephalopathy	–	–	–
Hyperglycaemia		1	4

TABLE 25 Surgery-specific morbidity (*continued*)

Event	Received Bypass (*n* = 389)	Received Band (*n* = 363)	Received Sleeve (*n* = 429)
Hypoglycaemia	1	–	2
Abdominal pain	38	31	27
Diarrhoea	1	–	1
Electrolyte imbalance	10	5	16
Ketoacidosis	1	1	
Dehydration	1	–	2
Iron deficiency	44	18	46
High turnover osteopathy	1	–	–
Dry skin or hair	–	–	–
Death within 3 years	2	4	1

a Obstruction at 1 week, redone.
b Stricture within 12 months, redone at 24 months; Ulcer perforation at G-J anastomosis at 10 months; G-J revision at 36 months.
c Slippage, erosion, infection, and/or leak.

Note
Data are number of events

Surgery-specific morbidity

Surgery-specific surgical morbidity is summarised in *Table 25*. There were 15 internal hernias requiring repair, 4 anastomotic obstructions/perforations requiring revision surgery or dilatation, 3 GI leaks from the sleeve staple line requiring surgery and/or drain placement, 16 band corrections and 21 band removals. Ten participants who had a Band and four participants who had a Sleeve subsequently underwent Bypass surgery. One Band participant went on to have a Sleeve. There were no Bypass reversals.

The most common medically treated complications were abdominal pain (see *above*), iron deficiency and electrolyte imbalance. Both iron deficiency and electrolyte imbalance were more common after Bypass and Sleeve surgery than after Band. Five Bypass recipients and one Sleeve recipient required total parenteral nutrition/enteral feeding.

Summary of outcomes in the core outcome set

The COS was developed during the first phase of By-Band-Sleeve and the Core Measurement Set was not developed (see *Chapter 3*). It was therefore necessary to use outcomes we identified to collect before the trial started to capture data for the COS domains. *Appendix 4*, *Table 68* shows how the COS domains were measured in the trial.

Chapter 7 Results: economic evaluation

Main analysis

Out of 1351 patients randomised, 5 withdrew consent for their data to be used, leaving 1346 patients for the cost-effectiveness analyses. Trial participants had lower household incomes, received more benefits, and were more likely to live in areas with high deprivation than the general population.[5] However, similar observations have been made for people living with obesity in the general UK population.[5]

The costs for the surgeries were highest for Bypass (accounting for inflation, £5403 in 2021 prices), followed by Sleeve (£4651), and Band (£2730).[66] These higher procedural costs for Bypass and Sleeve compared to Band were partly offset by lower other healthcare costs per participant over the 3 years considered. The mean costs per participant in the trial excluding the surgery procedure were £3708, 95% CI £3285 to £4194 for participants receiving Bypass; £3696, 95% CI £3171 to £4309 for Sleeve; and £4593, 95% CI £4120 to 5119 for Band. When the costs of the surgical interventions were included, the mean costs per participant increased to £8268, 95% CI £7786 to £8813 for Bypass; £7695, 95% CI £7143 to £8451 for Sleeve; and £7357, 95% CI £6865 to £7905 for Band, respectively. The mean difference in total costs including intervention costs were 911 (98% CI £76 to £1813) when comparing Bypass versus Band; £337 (98% CI −£626 to £1396) comparing Sleeve versus Band; and −£574 (98% CI −£1486 to £526) comparing Sleeve versus Bypass.

Participants randomised to Bypass accrued on average more QALYs over the 3 years than those allocated to Band (2.02, 95% CI 1.95 to 2.09 for Bypass; 1.82, 95% CI 1.75 to 1.90 for Band; mean difference of 0.20, 98% CI 0.08 to 0.31 QALYs). In comparison, those allocated to Sleeve accrued fewer QALYs than those allocated to Bypass (1.95, 95% CI 1.88 to 2.03, mean difference of −0.07, 98% CI −0.20 to 0.05), but more than those allocated to Band (mean difference of 0.13, 98% CI 0.02 to 0.27).

Combining these effects and their uncertainties into an incremental NMB analysis, Bypass was the most cost-effective option at both the lower and upper limit (£20,000 and £30,000 per QALY, respectively) of the cost-effectiveness threshold generally applied by NICE when identifying cost-effective interventions (*Figure 23*) with the incremental NMB of Bypass (vs. Band) ranging between £3149 and £5241, whereas these values ranged between £2288 and £3587 for Sleeve (vs. Band). When using these same thresholds, the probability that the intervention with the highest expected incremental NMB is also the most cost-effective option is relatively high for Bypass (*Figure 24*) at £20,000 and

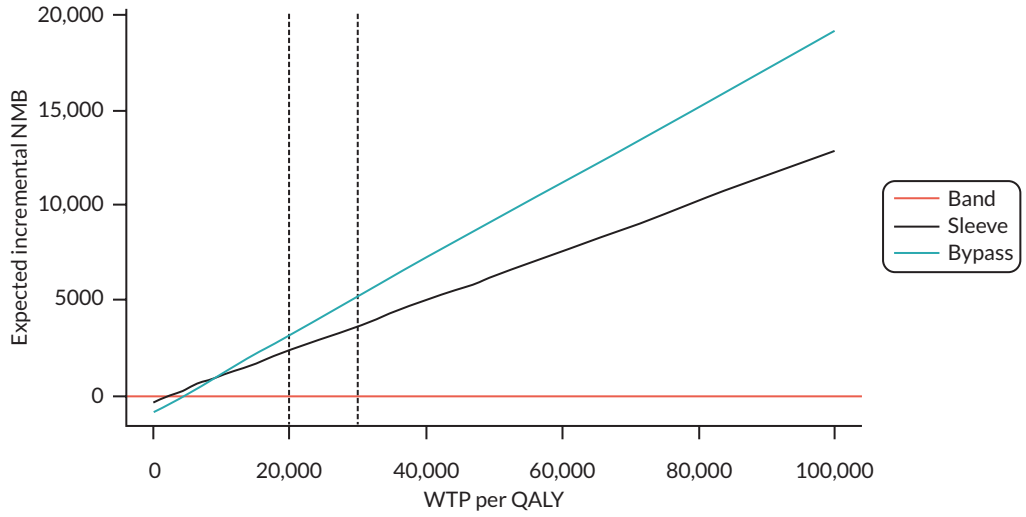

FIGURE 23 Expected incremental NMB for Sleeve and Bypass vs. Band in the UK NHS. Results are based on *n* = 500 bootstrap samples, WTP per QALY (maximum acceptable ICER) and the expected incremental NMB are expressed in 2021 Great British pounds (GBP). The dashed vertical lines represent the £20,000 and £30,000 per QALY thresholds generally used by NICE.

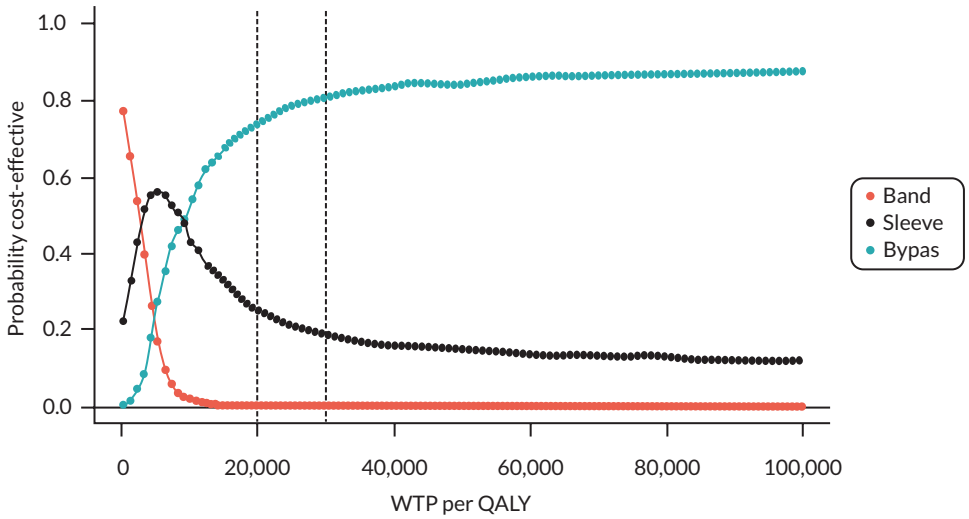

FIGURE 24 Cost-effectiveness acceptability curves for the three surgeries in the UK NHS. Results are based on *n* = 500 bootstrap samples, WTP per QALY (maximum acceptable ICER) is expressed in 2021 GBP. The dashed vertical lines represent the £20,000 and £30,000 per QALY thresholds generally used by NICE.

£30,000 per QALY (0.75 and 0.81, respectively), with zero probability for Band being the most cost-effective option at these thresholds.

Figure 25 shows how much better the most cost-effective options are compared to their alternatives, by estimating the net monetary loss of each intervention by taking difference in incremental NMB of that intervention with the incremental NMB of the most cost-effective intervention (i.e. Bypass at most thresholds). At the £20,000 and £30,000 thresholds generally used by NICE, using Band instead of Sleeve is expected to lead to larger net monetary losses (or net health losses) than choosing Sleeve instead of Bypass.

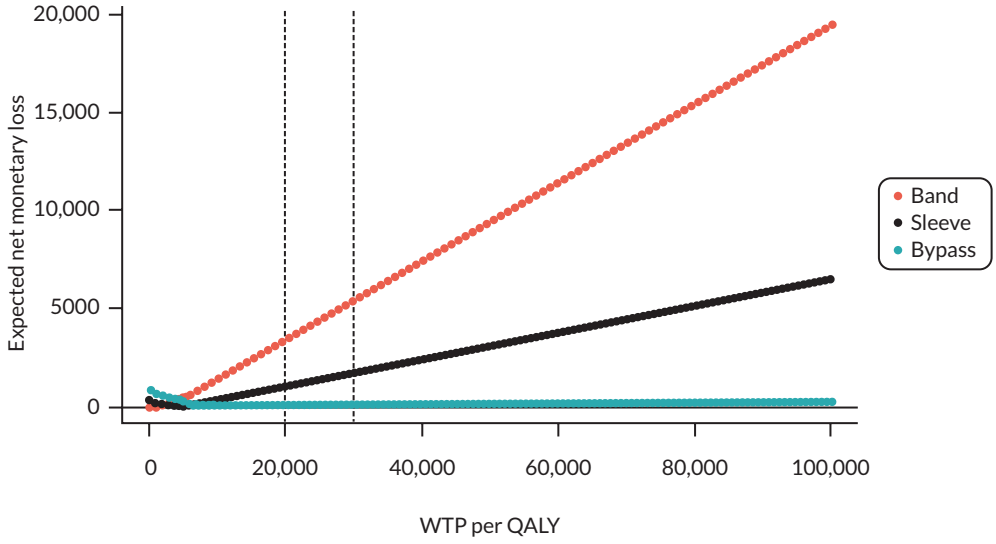

FIGURE 25 Expected net monetary loss for the three surgical options in the UK NHS. Results are based on *n* = 500 bootstrap samples, WTP per QALY and the expected net monetary loss are expressed in 2021 GBP. The dashed vertical lines represent the £20,000 and £30,000 per QALY thresholds generally used by NICE.

Subgroup and sensitivity analyses

Bypass remained the most cost-effective option, with the highest incremental NMB, across the subgroup analyses by BMI (< 40, 40–50 and > 50) and diabetes (see *Appendix 4*, *Figures 38* and *39*) and when grouping participants by the surgery received (see *Appendix 4*, *Figure 40*) at the £20,000 and £30,000 per QALY thresholds. Using different statistical approaches to estimate QALYs gained or healthcare costs incurred during the trial follow-up, including using inverse probability weighting to address potential missing healthcare utilisation and associated costs, had little impact on the results (see *Appendix 4*, *Tables 69* and *70*). The most noticeable difference was observed when using one-inflated beta regression for QALYs instead of a linear model which resulted in smaller differences between surgeries (Bypass vs. Band 0.13, 98 CI 0.03 to 0.25 instead of 0.20, 98% CI 0.08 to 0.31; Sleeve vs. Band 0.10, 98% CI 0.00 to 0.22 vs. 0.13, 98% CI 0.02 to 0.27; Sleeve vs. Bypass −0.03, 98% CI −0.13 to 0.07 instead of −0.07, 98% CI −0.20 to 0.05). Further sensitivity analyses that were not pre-specified, including (1) adding a binary indicator to address potential bias introduced by time trends combined with Sleeve only being added to the study after patients had been already randomised to either Bypass or Band; (2) an alternative mapping algorithm to derive HRQoL estimates from the EQ-5D-5L questionnaire; and (3) using intervention costs as estimated by the NHS cost collection, all led to similar results as the main analysis (see *Appendix 4*, *Figures 41*–*43*).

Focusing on %TWL and ignoring QALYs gained, Bypass was estimated to be the most cost-effective option if the WTP per %TWL reduction (26.8% for Bypass, 19.4% for Sleeve, 14.0% for Band, *Table 15*) is at least £10,317. However, it is important to note that this secondary analysis does not capture relevant differences in HRQoL between the different surgeries. Indeed, the gap in measured costs and QALYs was widening over the years within the first 3 years of follow-up (see *Figure 9*). When assuming perfect adherence to nutritional supplementation in all groups between year 4 and year 20, while conservatively – given the widening of difference between groups over time – not modelling any differences in health outcomes beyond year 3 between the allocated surgeries, these additional required supplementation costs would be higher for Bypass and Sleeve (£1217) than for Band (£415). However, adding this difference (£802) is smaller than the difference in incremental NMB of the main analysis at a threshold of £20,000 per QALY (£3149 for Bypass and £2288 for Sleeve), meaning that conclusion of the main analysis still holds after adding longer-term nutritional supplementation costs. However, longer-term follow-up is needed to estimate the longer-term cost–utility beyond 3 years more accurately.

Impact on receipt of benefits

Given the health-economic analyses were performed from an NHS perspective, the potential impact of allocating to the different bariatric surgeries on benefits were estimated separately from the cost-effectiveness analyses. There was no evidence that any of the surgeries had a different impact on the receipt of benefits 3 years after randomisation, with over a third of participants receiving any benefits in the group randomly allocated to Bypass (38%, 95% CI 32% to 45%), Band (44%, 38% to 51%) and Sleeve (38%, 95% CI 32% to 44%, *Appendix 4*, *Table 71*).

Chapter 8 Patient and public involvement

Trial design

A patient representative contributed to the study design, especially supporting the idea that a RCT comparing Band and Bypass was important and acceptable. She was a co-applicant on the grant application. There was also patient support for the adaptation of the trial to three groups when it was presented to two members of the patient and public involvement (PPI) group during the TSC and TMG meetings and at a PPI meeting in 2014.

Trial set up

There was a patient representative on the TMG throughout. They advised on the By-Band press release and reviewed all the patient-related documents prior to submission to the Research Ethics Committee. The PPI member also engaged with and organised a meeting with Commissioners on behalf of the research team to raise awareness of By-Band. The patient representative left the UK (and the TMG) in July 2012 and was replaced by two new PPI members who had been bariatric patients; both joined the TMG, reviewed patient information sheets, as well as a draft of the protocol paper and provided feedback on the By-Band study logo. They remained active on the TMG until the death of one member in 2021.

Recruitment

To support recruitment, the trial manager and CI set up a PPI group. The group was set up in liaison with the nurses from each recruiting site. The group included 12 patients, the lead RN from Taunton and a research dietitian from the University of Bristol (for about 3 years) and the Trial Manager. The first PPI meeting was held in November 2014 and was attended by five bariatric patients from the Taunton and Southampton area and included trial participants and others who had undergone bariatric surgery. As this was the first PPI meeting the CI and two members of the QRI team attended. The PPI group drafted a lay summary of the By-Band study and offered suggestions on how best to describe the trial. They voiced concerns about follow-up medications and their struggles to maintain weight loss post surgery. They were pleased to know that the trial followed everyone for 3 years (because only 2-year follow-up is routinely available in the NHS). The PPI group met annually throughout recruitment. Meetings included a minimum of four trial participants, the lead RN and the Trial Manager. Members of the QRI team attended sometimes. The CI attended the first few meetings, meetings when the SAP was discussed and the results feedback meetings. TMG PPI representation continued, and one member agreed to join the TSC, which they attended annually. Six PPI meetings were held in total. These were held in Taunton, Exeter, Bristol (three times) and once online.

During recruitment, we received excellent PPI feedback about trial conduct, the key points which informed the trial were:

- Successful maintenance of weight loss is dependent upon regular follow-up, emotional and practical help from the RNs, dietitians and surgeons after surgery, and belonging to patient support groups. The patient support groups should include a healthcare professional who can address biases and provide accurate information on the three surgeries. The help patients required most after surgery was from the nurses and dietitians. During the trial, the RNs and dietitians attended investigators meetings, and these points were regularly raised to optimise follow-up.
- A significant concern among the PPI group was the lack of ongoing support beyond the 3-year trial period; in the absence of regular appointments with the bariatric nurses, many patients might struggle to keep their weight off. There was general agreement among participants that follow-up should extend up to 10 years to ensure weight loss is maintained; the lack of clinical and psychological support experienced by bariatric patients a few years after their surgery is a major barrier to maintaining weight loss. In light of this feedback, the trial team modified the protocol and received research ethics approval to allow long-term follow-up (to 8 years post randomisation) to explore these issues.

- Excess skin following weight loss is a major concern for many bariatric patients; for some, this becomes a psychological and emotional issue which might stop them from losing further weight. They all indicated they would have plastic surgery if it was offered by the NHS. One participant said:

  I suffer from self-loathing due to my excess skin; it limits what I can wear and I find medical appointments embarrassing and awkward. I am saving money to have cosmetic surgery to remove my excess skin, but I think this surgery should be provided by the NHS.

The same participant also told us:

Bariatric surgery has been my lifeline and the By-Band-Sleeve team my emotional crutch.

- All participants agreed that following surgery the resolution of comorbidities which are associated with obesity is the most positive outcome, followed by the ability to live 'normal' lives and do 'normal' everyday activities. Success after surgery is not just about losing weight but is very much associated with feeling healthier and being socially accepted. Overall, participants were very happy with the surgery they received and would recommend it to potential patients. They were also happy to be part of By-Band-Sleeve. To quote one participant, *'after surgery my mental state of mind improved, I became more positive, my health improved, I had lots of energy, and I completed a 10-mile race'*.
- Certain words used in the GIQLI questionnaire were deemed inappropriate and were replaced with acceptable terminology following Research Ethics Committee approval.
- Participants advised us on how to simplify and clarify the wording in the health-economics diaries.
- They provided tips and feedback on a poster designed for patients and advised us on how to explain the trial in lay terms and where best to advertise the poster in hospitals.
- Participants suggested that we create a frequently-asked-questions document providing information on life after surgery including facts around nutrition, diet, dumping syndrome, vitamin B12, general health improvements and changes in lifestyle.
- Participants encouraged us to circulate at least one participant newsletter each year to keep participants updated and engaged; numerous PPI members contributed to each newsletter by sharing their experience in the By-Band-Sleeve trial and explaining to their fellow participants the importance of providing data in follow-up. Eight newsletters were written and circulated by e-mail and/or by post to participants. The newsletters were also posted to our recruiting sites so they could be shared with bariatric patients during their hospital visits.

Follow-up

Once recruitment ended in September 2019, our focus turned entirely on retaining participants in the trial. Our PPI members advised us on how to keep participants engaged and collect data in follow-up; their recommendations and feedback included the following key points:

- Participants should see the same nurse(s) during their follow-up care; this allows them to build a rapport with the nurse(s) and encourages them to attend their research assessments.
- Bypass and Sleeve participants should receive better follow-up care, in the same way that Band participants continue to attend regular hospital visits. PPI members who received Bypass or Sleeve surgery said they lost a vital link when they stopped seeing their RNs and this has had a negative impact on continued engagement with the service at their hospital.
- Provide dietary advice and guidance as well as physical and emotional support; provide more dietitians for participants seeking information on postoperative diets.
- Circulate annual newsletters; these keep participants engaged throughout the trial, help retain participants and encourages them to attend visits and complete questionnaires. Participants are keen to read personal stories on how gastric surgery can change a person's life.
- Newsletters should point out that hospital visits can be tailored to participants' schedules whenever possible and that travel expenses are reimbursed.
- Newsletters reach participants who have had a negative experience after surgery. Participants who have struggled with weight loss are often embarrassed and feel they have let the research team and the NHS down; newsletters can reach these participants and encourage them to remain in the trial.

- The newsletter sent during the COVID-19 pandemic was particularly important to remind participants that follow-up and data collection were continuing.
- Once results are published, and participants are keen to see a leaflet comparing outcomes of all three surgeries.
- Participants stressed that to maintain weight loss it is important to be monitored for at least 5 years and ideally for up to 10 years.

Dissemination of results

Patient and public involvement TMG members joined an investigator meeting held in May 2023 when preliminary trial results were shared for the first time. The CI also presented the main results to six PPI group members at two online meetings held in June 2023. A newsletter giving the main findings was prepared with extensive advice from the PPI TMG representative and PPI involvement, to ensure the results were as simple and clear way as possible. The newsletter was sent by post to all trial participants. The leaflet included an invite and a QR code to attend an online meeting where results would be presented and there was an opportunity to ask questions. These took place in October and November 2023. The PPI TMG member contributed to the meetings. Only 10 trial participants attended, although the discussion was very insightful and methods to better engage participants with trial results emerged.

Patient and public involvement contributions to oversight committees and trial meetings

Patient and public involvement members attended oversight committee meetings such as the TMG and TSC as well as the annual PPI meetings. Their engagement and contributions led to changes, some of which have been outlined above. Other specific contributions arising from meetings included:

- a letter sent to participants explaining the potential delay between randomisation and surgery and that the first By-Band-Sleeve follow-up may be pre surgery
- a glossary of commonly used terms, which was included in a participant newsletter
- a reward for participants once they completed their HRQoL questionnaires at 1 and 3 years. Participants were sent a shopping voucher.

In addition to positive feedback, participants flagged areas for improvement, and these included:

- stopping asking participants to complete health-economic diaries because they were too time-consuming to complete
- making sure all PPI members have the opportunity to contribute to discussions and are encouraged to have the confidence to speak to an audience of health professionals.

Patient and public involvement contributions to the statistical analysis plan

At a meeting held in April 2021, the CI explained to the PPI group the importance of pre-planned analyses to reduce the chance of false-positive findings. Following the discussion, the PPI group were asked how they valued the HRQoL domains within the questionnaires being used in the trial and to prioritise the important domains from a participant perspective. The domains chosen formed part of a protocol amendment that established which outcomes would be compared statistically (see *Changes to trial outcomes after commencement of the trial*). The PPI members agreed that the most important outcomes after bariatric surgery are physical function, mental health, self-esteem, sexual life and public distress.

Discussion

As outlined above there was active PPI engagement throughout the trial from the planning stage through to the dissemination of results. The PPI contributions were numerous, thoughtful and constructive. Members gave the trial investigators insight into the experiences and life values of individuals undergoing bariatric surgery, that greatly benefitted the conduct of the trial.

Chapter 9 Discussion

Trial conduct

Trial recruitment was achieved with support of the QRI and a short extension. The average proportion of screened patients eligible ranged from 56% to 82% with 11 of the 12 sites reaching the target of 60% of patients eligible. The lead study site (Taunton) recruited consistently throughout the study at just over 30% of eligible patients (a total of 244 participants randomised) and Southampton (also in the study throughout) exceeded the target of 45% of eligible patients randomised despite pausing recruitment completely for 6 months due to staffing issues. The overall average proportion of eligible recruited participants was 28.5%. After the adaption in 2015, it became apparent some sites struggled to offer patients Band due its decline internationally despite data showing its safety, durability and effectiveness and data to show it could be safely revised.[116] It was criticised for causing adverse effects, lacking efficacy and its need for revision.[117] These difficulties were discussed with the TMG and TSC. It was decided to continue to recruit into the three-group trial because while Band was becoming unpopular, the evidence was limited and there were concerns that some of the reasons it was frequently removed or revised were because surgeons were able to do this, whereas surgical revision of Sleeve and Bypass was more complex.

Adherence to intervention protocols was achieved for over 97% of participants; while some mandated components were missed, none of the prohibited components were reported as being undertaken. All mandated components were complete for 97%, 97% and 98% of participants in Bypass, Band and Sleeve groups, respectively. Early on an issue with Band fixation was identified in one site and following discussion with the site this was rectified. An important change to the surgical protocol was made in 2018 following publication of a trial which showed a benefit to routine closure of the iatrogenic mesenteric defect in Bypass surgery.[39] In By-Band-Sleeve, data captured on the CRFs were used to monitor adherence to the surgical protocols. Recent evidence, however, suggests that digital images of interventions provide more accurate information than surgeon-completed CRFs. It is possible that CRF data are misleading (with surgeons being overly optimistic about their surgery).[118] We recommend that future surgical trials include surgical quality assurance measures using digital imaging to monitor intervention fidelity to the protocol and to examine performance bias. Surgical quality assurance could also be important for implementation of trial results. It would demonstrate adherence to the intervention protocol in order to counter cynical surgical views that results would have differed if the quality of surgery was better. Additional procedures were infrequently performed at the time of bariatric surgery; hiatal hernia repair was the most common (48 repairs with Sleeve, 34 with Band and 32 with Bypass). Surgical recovery was good – with inpatient stays of 1 or 2 days. Thirty-day recovery and complication rates mirrored those of national audit sets. Few participants suffered any complication. Serious complications (i.e. Clavien–Dindo category > IIIb) occurred in only five Bypass and four Sleeve participants. There was one death in the Band group due to sepsis and peritonitis following leakage from the band sutures. This is an incredibly rare event.

Recruitment to trials in bariatric surgery has historically been difficult, with few RCTs initiated and even fewer completing recruitment. It was anticipated that recruitment to By-Band-Sleeve would be difficult, potentially impossible, because of polarised views across the community about the procedures, strong patient preferences and a lack of experience of conducting trials in the speciality. To address this, we employed standard and novel QRI methods that were dynamic and responsive of recruitment and context of the site at different periods of time. The internal pilot (initial stage) confirmed anticipated recruitment challenges – the first site found over 20 eligible patients, but none agreed to be randomised. Intensive QRI analysis of interview, observational, and audio-recorded consultation data identified organisational and presentational barriers to recruitment. QRI feedback sessions with individual recruiters and the site changed this, and patients responded to the streamlined processes and improved presentations by agreeing to participate in the trial.

Transferable insights from the initial pilot were incorporated into the main trial and informed the pre-recruitment training provided at SIVs for the new sites. For instance, new sites were advised to ensure their clinical set-up facilitated RCT integration and recruitment, and personnel with little or no research experience were given additional support. QRI data collection was initiated in each new site to identify challenges unique to that site. Audio-recordings and

eligibility/recruitment data were routinely analysed. Each site reported similar challenges to those found in the first two sites, but there were also new challenges related to MDT involvement and equipoise following the emergence of Sleeve and the gradual falling out of favour of Band. Advanced, layered and detailed recruitment tips were developed, with a focus on the need for consistent application of good practice. Some momentum with recruitment was lost early following the adaptation to include Sleeve but then picked up. To further encourage recruitment and reach completion, a novel QRI prioritisation strategy was developed to focus training/feedback on sites/recruiters who would most benefit from additional support, while also continuing to encourage those that were recruiting well. This sustainment stage maintained recruitment at a level similar to the transitional stage, but recruitment could not be completed by the original target date. During the recruitment extension, there was an intense final push towards achieving the recruitment target, achieved 15 months after the original end date.

The recruitment challenges faced in By-Band-Sleeve and the strategies developed to address them included findings that have been previously reported (e.g. in relation to equipoise, patient preferences, complex pathways[49,55,113–115]), findings that have enhanced existing knowledge (e.g. the importance of personalising the invitation to participate or integrating the trial within routine practice[9]), findings that were specific to By-Band-Sleeve (e.g. indication of patient's perceived preferences on their clinical notes early in the pathway, leading to the preclusion of a detailed trial discussion[9]), and the development of new methods (e.g. the prioritisation strategy). The findings from By-Band-Sleeve also identified four different stages of recruitment and it is likely that this could inform recruitment strategies in other long-running trials with an internal pilot. Trialists may want to consider using the prioritisation process and framework of stages to organise recruitment in other trials.

The trial was designed with a review of surgical practice at the end of the pilot phase to ensure that the trial remained relevant to clinical practice. This review led to the addition of Sleeve. Adapting the trial in this way ensured that the resources were used efficiently, but the time taken to implement such a change should not be underestimated. The CRFs, database, randomisation system and all site-specific documentation required to be updated. Furthermore, the sites had to adapt their recruitment processes to include a discussion of Sleeve. Adapting a trial in this way also has implications for the analysis, as these were not contemporaneous to all three groups throughout. Accounting for this design aspect did not affect the conclusions.

Equality, diversity and inclusion

There was good coverage across England in terms of the trial sites; they ranged from large university hospitals to smaller district general hospitals. At the last census in 2021, 18.3% of the population of England and Wales[119] were classified as non-white, that is from a black, Asian, mixed or minority ethnic group. In By-Band-Sleeve, 15.2% of participants were classified as non-white. By-Band-Sleeve has been showcased in the INCLUDE ethnicity framework.[120] However, the trial did not recruit participants from Scotland, Wales or Northern Ireland and had limited numbers of people of Asian heritage (3.4%) compared to 9.3% in the UK population. The black ethnic group was well represented at 6.8% compared to 4.0% in the UK population. A good representation of the ethnic groups most affected by obesity was aimed for, as according to the Health Survey for England 2021 there is an increasing prevalence of obesity and excess weight in all ethnic groups, white 64–66%, black 72%, Asian 57% (https://researchbriefings.files.parliament.uk/documents/SN03336/SN03336.pdf). Patient information was only provided in English; it is unknown if providing the information in other languages would have increased participation and resulted in a study more reflective of the diversity of the UK population.

Trial results

The results of By-Band-Sleeve show that for patients with severe and complex obesity referred for bariatric surgery according to NICE guidance, Bypass was associated with better weight loss, improved QoL and greater reduction in comorbidities than Sleeve or Band. Some 68% of participants randomised to Bypass achieved at least 50% excess weight loss at 3 years, compared to 25% and 41% of participants in the Band and Sleeve groups, respectively. All sensitivity analyses confirmed the findings of the primary analysis and subgroup analyses for diabetic status and weight

category at baseline showed no statistical evidence to suggest that treatment effects differed between the different baseline groups. For the HRQoL coprimary outcome, the EQ-5D-5L utility scores were higher (better) in the Bypass group compared to Band and higher in the Sleeve group compared to Band. Although the mean Bypass EQ-5D-5L utility scores were better than Sleeve, the difference did not reach conventional statistical significance but did exceed the 0.03 threshold for clinical significance. Sensitivity analyses were consistent when excluding crossovers, excluding participants with missing data at 3 years and excluding participants who did not have surgery, but when assessing HRQoL 3 years after surgery rather than after randomisation the differences between Sleeve and both Band and Bypass were reduced. Subgroup analyses for diabetic and weight loss category at recruitment showed no statistical evidence to suggest differences.

The metric most used for weight loss has changed since the conception and design of By-Band-Sleeve. Percentage EWL is no longer recommended for use and %TWL is the preferred metric. The TMG and TSC considered this change in detail in 2020 and considered whether to change the weight loss coprimary outcome metric. After lengthy discussion, it was decided not to change the metric because it is not possible to linearly translate the agreed non-inferiority margin selected for at least 50% EWL to an equivalent margin for %TWL without introducing bias. Percentage TWL was always a key secondary outcome, and data would still be useful to inform subsequent meta-analyses. Retaining the coprimary weight loss metric was considered to be critical to maintain the integrity of its original trial design.

Other changes in definitions of key outcomes (e.g. comorbidities) occurred during the decade that the trial was running. The newer definitions required new data items to be collected, and it was not practical to retrospectively collect the data. Despite this, by using the data collected in By-Band-Sleeve it is possible to see the dramatic benefits of bariatric surgery in metabolic indicators of health (hypertension, lipid and glucose control). The proportion of normotensive participants almost doubled in the Bypass group, and it increased in the Sleeve and Band groups. High proportions of patients in all three groups achieved a HbA1c of < 48 mmol/mol. Benefits were seen in people living with and without diabetes at baseline. It is noted that the proportions of participants with diabetes in each group who achieved HbA1c levels below 48 mmol/mol is much higher than that achieved by the new drugs used for treating obesity.

Many of the secondary HRQoL domains showed similar differences between groups and similar trajectories over time as the coprimary generic HRQoL end point. Exceptions to this pattern were the mental health component of the SF-12, anxiety in the HADs, and several of the GIQLI scores where no between-group differences were observed. Others have reported similar findings to those observed in By-Band-Sleeve with no differences in HRQoL between types of surgery, although numbers in the included studies were small and none were conducted in the UK.[121] It is interesting to note that the obesity-specific HRQoL measure, the IWQOL-Lite, showed important between-group differences and marked improvements in nearly all aspects of HRQoL over time except for the sexual life score. It is possible that this disease-specific measure is more sensitive to change after surgery than the generic tools. Few studies have prospectively studied HRQoL outcomes after bariatric surgery for beyond 2 years with such a comprehensive set of measures.[122]

In view of the clinical and HRQoL benefits of Bypass over Sleeve and Band, consideration of safety and health-economic data is critical. Rates of total adverse events during the 3 years from randomisation were highest in the Band group followed by Bypass then Sleeve; participants having Sleeve had fewer adverse events in the period from 30 days after surgery to 3 years from randomisation than either Bypass or Band. The increased risks associated with Band together with its limited effectiveness and cost-effectiveness have important implications for decision-making and practice (see *Potential implications for policy-makers*). It is also important to understand the safety profile differences between Sleeve and Bypass. Differences were specifically found in rates of abdominal surgical procedures performed after surgery. These ranged from 3.4 to 9.2 per 100 years of follow-up, with Sleeve rates being statistically lower than Band (the highest) and almost half rate after Bypass. Serious specific surgical complications of all procedures such as leak from the staple line following Sleeve or internal hernia after Bypass occurred at rates observed in national databases, indicating that the surgical quality control was satisfactory. Likewise, rates of serious nutritional or metabolic problems were low in all groups. Further follow-up is needed to better quantify the longer-term complications.

The health-economic analyses confirmed that Bypass is likely the most cost-effective bariatric surgery from a UK NHS perspective (ranging from over 75% to 81%, *Figure 24*), and has the highest probability of being the most cost-effective option at the £20,000 and £30,000 per QALY cost-effectiveness threshold, as well as the highest expected NMB. The

same conclusions held in the pre-specified BMI and (non-)diabetic subgroups and in a wide range of sensitivity analyses making different assumptions and using alternative statistical models.

The opportunity costs associated with using Band instead of Sleeve led to larger net monetary losses (or net health losses) than choosing Sleeve instead of Bypass; this implies that from the point of view of pure cost-effectiveness Band is clearly the worst option to choose among the surgical interventions. However, it is noticeable that the %TWL reduction for Band (14% at 3 years) is similar to the weight loss reduction observed with once-weekly semaglutide (Wegovy®, Novo Nordisk Limited) after 68 weeks in the STEP 1 trial that was used to recommend this drug for inclusion in the NHS.[123,124] Caution should be applied when directly comparing these estimates as they come from different trials and at different points of follow-up. However, it raises the question what the cost-effectiveness of the different operations is compared to other interventions, including recently approved drugs such as semaglutide, aimed at reducing weight and improving HRQoL among patients with obesity. To answer this question, in the short-term further health-economic modelling is required integrating information from the different trials, taking into account differences between the trials as much as possible. Additional RCTs with longer-term follow-up that directly compare surgical – potentially including one-anastomosis gastric bypass[19] – medical, and/or life-style interventions are warranted.

While the main analysis was a within-trial analysis focusing on 3 years of follow-up, there was evidence that the difference between the three operations in terms of QALYs was widening during the follow-up period, suggesting that longer-term follow up would show greater differences. Indeed, when conservatively assuming that those still alive at 3 years of follow-up would have 100% adherence to recommended nutritional supplementation for each surgery without accruing any further benefits or harms over time, the conclusions would remain the same.

Strengths and limitations

Strengths

The major strength of By-Band-Sleeve is its pragmatic randomised trial design that was adapted to ensure the research remained relevant to UK practice and was successfully integrated in existing usual care pathways across a range of NHS sites. It is also the largest multicentre trial to date to assess the impact of the three most common bariatric surgeries on weight loss, HRQoL, comorbidities and cost-effectiveness. This makes the findings generalisable to the NHS as a whole and ensures it has implications for health policy. The surgical protocols were clearly defined and compliance with the protocols was monitored throughout. Serious surgical complications were rare and in line with registry reports which is testament to the quality of the surgery across the trial.

The target sample size was met despite many believing the trial would be impossible to achieve due to strong patient preferences. Integrating the QRI throughout, working in close collaboration with CI and clinical trials unit staff was key to recruitment success. Flexible and responsive QRI methods, including interviews, observations and audio-recordings of recruitment discussions, combined with screening and recruitment data, identified recruitment challenges that varied over time and by site. These insights were used to develop tailored feedback and training that were delivered to sites and individual recruiters according to a prioritisation strategy, leading to optimised recruitment. The recruitment rate in the final site to open was highest, as it received upfront training based on all previous findings. Other trials (e.g. the VIOLET trial[125]) used upfront QRI training to enable surgeons to start the trial with confidence and recruit strongly. An integrated QRI combined with upfront training and the prioritisation strategy developed for By-Band-Sleeve is recommended for future trials anticipating recruitment difficulties.

Another strength of By-Band-Sleeve is inclusion of a PRO, the EQ-5D utility score as a coprimary end point. This was unique in bariatric surgical trials at the time; we also established the psychometric properties of this instrument in the bariatric surgical population.[126]

In terms of the strengths of the economic evaluation, while several previous cost-effectiveness analyses indicate that bariatric surgery is likely cost-effective compared to non-surgical interventions,[127–133] our results provide more certainty about the comparative cost-effectiveness of different bariatric surgeries. In addition, as far as we are aware, this is the first study to estimate the comparative cost-effectiveness and other economic information such as receipt

of government benefits for patients having of Bypass, Sleeve or Band informed by data from a large RCT. Furthermore, our conclusions held when different assumptions, for example about missing data on healthcare resource, and statistical models were used in a range of sensitivity analyses.

The significant PPI input throughout the trial is another strength. There were few participant withdrawals, but despite advice from the PPI group on how to maximise participant engagement, questionnaire response rates for secondary outcomes were lower than we would have liked. However, the statistical analysis maximised the use of the data; 89% of participants provided data for at least one follow-up time point and these participants were included in the analyses.

Limitations

The use of the %EWL metric is now outdated. Subgroup analyses by baseline category of weight have only been performed for this primary outcome metric. Although %TWL data are presented, subgroup analyses of %TWL by baseline weight category were not included in the protocol or the SAP.

There was a slight imbalance in the numbers of participants allocated to each surgery with fewer participants allocated Sleeve and more participants allocated Bypass and Band than was planned. This arose because collectively the sites who recruited to By-Band recruited fewer participants to By-Band-Sleeve than was predicted when the site-specific allocation ratios were set. This will have led to reduced power for the comparisons involving Sleeve compared to Bypass and Band.

We used the MedDRA hierarchical classification system for categorising adverse events that occurred. It is an internationally accepted classification system for reporting adverse events in pharmaceutical trials, but not widely understood by the surgical community. There are also limitations insofar as MedDRA does not capture the severity of surgical complications. While the Clavien–Dindo classification for assessing severity of surgical complications is widely used, it typically captures in-hospital events; more work is needed to establish its role in assessing severity of long-term complications of surgery. There is also more work to be done in standardising the selection, measurement and reporting of surgical complications in trials to allow better data synthesis and cross-study comparisons to be made.

Outcome assessment was limited in several ways. The trial was not blinded, measures of comorbidities became outdated and insufficient attention was paid to the quality of the large volume outcome data collection during the trial. Blinding of participants and research staff was not undertaken because of the need for Band adjustments and different post-surgery care. The past decade has seen growing expertise in blinding and placebo surgical trials and the need to consider these methods whenever possible.[134] It would have been possible to blind the Bypass and Sleeve participants to treatment allocation to minimise ascertainment bias as both require the same aftercare and this is recommended in a future bariatric surgical trial.

The CRFs used to capture data on complications were designed at the outset by the clinical team. Some of the terms would have benefitted from provision of a definition to improve data collection and validity. For example, during data cleaning it became clear that different interpretations of 'internal hernia' had been made between sites. This required in-depth analysis of clinical notes to verify rates of internal hernia repair and to exclude other sorts of abdominal wall hernia which had been included incorrectly.

The completeness of the data for some secondary outcomes, in particular dietary outcomes, liver fibrosis and income and benefits, was very low. The reasons for these outcomes being so low include (1) staff availability to conduct dietary interviews, (2) during the pandemic, participants were not attending the hospital for follow-up so blood samples and 24-hour dietary recall interviews were missed, and (3) the assessment of liver fibrosis involved samples being stored and then sent to an independent laboratory for analysis, with one site not having storage facilities and thus they did not provide any samples. The analysis of the samples was expensive and there was limited funding available to cover this. Some participants were unwilling to provide information related to income and benefits. On reflection, the large volume of data collected meant that the completeness of some secondary outcomes was not monitored adequately during the trial. More in-depth monitoring may have provided an opportunity to address these deficiencies and is recommended in future studies.

With respect to limitations of the health-economic evaluation, our pre-planned sensitivity analysis including hospitalisation within a 2-month interval as a covariate in the imputation model to capture potentially temporary reductions in HRQoL due to acute illness between planned visits was not done as this resulted in too many variables for the imputation model to converge. This may have slightly overestimated the total QALYs gained in participants who were hospitalised between trial visits and slightly underestimated this for participants hospitalised around the time of the trial visit. Another limitation of the study was the inability to collect detailed diary data about resource use after surgery from participants. Analyses of the pilot data showed large volumes were missing and use of the diaries was abandoned. While in the main analysis, we may have underestimated healthcare utilisation by assuming all healthcare resource use was captured, sensitivity analyses using alternative assumptions around completeness of healthcare resource data addressed using inverse probability weighting resulted in similar incremental NMB. While the intention-to-treat approach we used leads to unbiased estimation – provided all statistical assumptions are met – of the cost-effectiveness of the decision to perform the surgeries of interest, it may underestimate the differences between the cost-effectiveness of actually performing the surgery given crossover between arms and the waiting times experienced in the NHS.

Potential implications for policy-makers

The By-Band-Sleeve study has implications at several levels. As the trial is representative of NHS practice, we recommend that surgeons share the results with patients with severe obesity choosing to have bariatric surgery so as to allow an informed choice. We recommend that written information summarising the data is provided alongside the consultation. The results from the trial could be incorporated into national guidance for bariatric surgery. This is likely to mean that adjustable gastric banding is no longer recommended on the NHS. If Bypass becomes the recommended procedure, there is a need to ensure that surgeons are well trained to carry it out and that aftercare follows guidelines for provision of micronutrients and dietary advice in primary care.

Successful completion of recruitment indicates that it is possible to conduct a very large, pragmatic trial in bariatric surgery, meaning that the results are able to be generalised to the overall population having surgery. Although the trial took more than 12 years to complete, this was partly due to need to adapt the trial to include Sleeve, and the COVID-19 pandemic. A future trial could benefit from the design methodology which used the QRI to enable recruitment, and a surgical quality assurance intervention in a leaner design with more streamlined data collection and fewer secondary outcomes (i.e. the COS) that is still able to produce meaningful generalisable results.

Unanswered questions and future research

1. Probably the most important question that needs to be answered is whether bariatric surgery is more effective and cost-effective than optimal medical management in the treatment of severe obesity in terms of weight loss and HRQoL. The completion of By-Band-Sleeve and the training involved in recruitment means that the UK bariatric community could be ideally placed to design and conduct such trial(s). Medical management is a rapidly changing field, and it is not possible to define what optimal medical management looks like currently. Any future trial(s) needs to focus on the needs for patients and the public. An adaptive design should be considered to ensure that the interventions under evaluation remain relevant.
2. Future research should consider whether the findings identified in the primary analyses are maintained in the longer term. Information about the longer-term complications of surgery, metabolic and nutritional consequences including the need for revision surgery is important. Understanding patient experience and perceptions of weight regain and analyses of reasons behind this would help explore potential mechanisms that contribute to outcomes. Analyses of micronutrients, eating behaviours and comorbidities in the 5–10 years post surgery will inform how to target interventions that healthcare providers can offer if surgery recipients experience problems. Identifying individuals that may be at risk of poor surgical outcomes would also help target treatment selection and interventions to improve HRQoL.
3. Future RCTs in bariatric surgery may consider the effectiveness of one-anastomosis gastric bypass compared to standard Roux-en-Y bypass, although evidence synthesis may be better positioned to answer this question

4. Other areas of research (in priority order) include:
   (a) development of measures to assess the COS domains
   (b) the use of digital imaging to understand surgical intervention fidelity
   (c) modelling of the potential longer-term impact of the surgeries on overall population health and the distribution of health-economic consequences across different (socioeconomic) groups of the population
   (d) work to identify key communication variables to optimise recruitment in the early stages of a trial to improve trial conduct and completion
   (e) research to further understand the relationships between BMI and health by exploring changes in metabolomic profile with weight loss (e.g. after surgery or medical management) and this might help to define BMI effects, characterise interventions and challenge causal inference.

Chapter 10 Conclusion

The By-Band-Sleeve Study shows that in participants undergoing bariatric surgery, Bypass and Sleeve resulted in significantly more weight loss and better HRQoL than Band. Bypass resulted in significantly more weight loss than Sleeve. HRQoL was better with Bypass than Sleeve, but the difference did not reach statistical significance. The differences between groups and trajectories over time seen in the coprimary end points was mirrored in most of the secondary end points. Notable exceptions were the mental health components of the multidimensional HRQoL assessments which showed similar scores in all three groups. Band had an increased risk of the need for abdominal surgical procedures following surgery and Sleeve had fewer adverse events than Bypass across all categories.

In the economic evaluation, differences in costs and QALYs favoured the Bypass, and, when combined, resulted in Bypass being the most cost-effective, with Sleeve the second most cost-effective procedure. This occurred despite the higher intervention costs associated with Bypass. The cost-effectiveness results clearly indicate that Bypass is the most cost-effective across any WTP threshold and there is negligible uncertainty around this finding, so we can be confident of this result.

In conclusion, Bypass is the most cost-effective bariatric surgery. Furthermore, while the difference between Bypass and Sleeve in some sensitivity analyses was not large at the £20,000 per QALY cost-effectiveness threshold, using Band instead of Bypass would most likely result in substantially worse outcomes in terms of weight loss, HRQoL and NMB.

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Patient data statement

This work uses data provided by patients and collected by the NHS as part of their care and support. Using patient data is vital to improve health and care for everyone. There is huge potential to make better use of information from people's patient records, to understand more about disease, develop new treatments, monitor safety and plan NHS services. Patient data should be kept safe and secure, to protect everyone's privacy, and it is important that there are safeguards to make sure that they are stored and used responsibly. Everyone should be able to find out about how patient data are used. #datasaveslives You can find out more about the background to this citation here: https://understandingpatientdata.org.uk/data-citation

Data-sharing statement

Following publication, anonymised individual participant data will be made available upon request to the corresponding author for secondary research, conditional on assurance from the secondary researcher that the proposed use of the

data is compliant with the Medical Research Council (MRC) Policy 2341 on Data Sharing regarding scientific quality, ethical requirements and value for money. Only data from participants who have consented for their data to be shared with other researchers will be provided.

Ethics statement

The trial was given a favourable ethical opinion by the Southwest-Frenchay Research Ethics Committee (reference 11/SW/0248) on 6 December 2011. This included approval for the COS project (*Chapter 3*).

Information governance statement

The University of Bristol is committed to handling all personal information in line with the UK 2310 Data Protection Act (2018) and the General Data Protection Regulation (EU GDPR) 2016/679. Under the Data Protection legislation, the University of Bristol is the Data Processor; and the Data Controller and we process personal data in accordance with their instructions. You can find out more about how we handle personal data, including how to exercise your individual rights and the contact details for University of Bristol Data Protection Officer here: www.bristol.ac.uk/secretary/data-protection/gdpr/data-protection-officer/

Disclosure of interests

Full disclosure of interests: Completed ICMJE forms for all authors, including all related interests, are available in the toolkit on the NIHR Journals Library report publication page at https://doi.org/10.3310/CXSE2951.

Primary conflicts of interest: Jane M Blazeby reports membership of the NIHR HTA Obesity Themed Call Board 2010, the HTA Surgery Themed Call Board 2012–3, the NIHR CTU Standing Advisory Committee 2012–20 and the HTA Clinical Evaluation and Trials Committee 2009–13. She reports funding from the MRC Network of Hubs for Trials Methodology Research (HTMR). ConDuCT and ConDuCT II and NIHR Bristol Biomedical Research Centre. She also reports research grants from the NIHR (refs. NIHR205174, NIHR152268, NIHR151274, NIHR127393, NIHR130547) and Bristol and Weston Hospitals Charity and NIHR Research Capability Fund in the last 3 years.

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James C Hopkins reports honoraria for speaking at meetings and expert panel review into Meshes in hernia surgery from BD Bard and shares in Dr J C Hopkins Ltd.

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Appendix 2 QuinteT Recruitment Intervention actions in By-Band-Sleeve

A summary of activities which involved QRI input

Y	2012											
M	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
QRI	Set-up			Staff interviews (*n* = 12)						SIV: C1 and C2	C1 open	
						TMG				TMG		

Y	2013											
	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
	C2 open	C1: GF			C1: 1IF	C1: GF	C2: GF		C1: 1IF		C2: 1IF	C2: 1IF
	C1: 3IF[a]					TMG	C2: 3IF				TMG	

Y	2014											
M	Jan	Feb	Mar	Apr	May	Jun	July-main	Aug	Sep	Oct	Nov	Dec
QRI		Tips doc		RN-T		SIV: C3, C4	C3 open			SIV: C5	C5 open	
				Inv M	TMG					C1: GF	TMG	
				C1: 1IF						C1: 4IF		

Y	2015											
	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug-Sleeve	Sep	Oct	Nov	Dec
	C4 open	C3: GF	SIV: C6	C6 open	C5: GF		SIV:C7, C8, C9 and C10	SIV: C11	C4 & C6: GF	C10 open	C1: GF	
		C3: 4IF			C5: 4IF		C7 open	C8, C9, C11 open	C4: 2IF; C6: 3IF	C8: 2IF	C7: GF	
					Staff interviews (*n* = 11)			C6: 2IF	TMG		C7: 3IF	

Y	2016											
M	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
QRI	C10: GF	C9: GF	C11: GF	C8: GF	RN-T	C6, C11: GF	C1: GF	C1 visit	C5: GF	C3, C8 visits		
	C10: 3IF	C9: 3IF; C11:1IF		C8: 2IF	TMG	C6: 2IF	C4: GF	C7: 4IF		TMG		
							C4:2IF; C1:1IF			Inv M		
							C1 visit[b]			Staff interviews (*n* = 11)		

Y	2017											
	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
			RN-T	C9: GF		C11: GF	C8: GF			SIV: C12	C5 visit	
				C9: 2IF		C 11: 3IF	C7: GF			Inv M	C5: 1IF	
						TMG	C8: 3IF; C7: 4IF				C12 open	

Y	2018											
M	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
QRI	C12 visit	C12: GF	C11: GF			C12: GF	TMG	RN-T: C3, C2, C7, C8, C9	C9: 1IF	C5: 1IF	Inv M	
	Tips doc		C11: 5IF			C12: 4IF			RN-T: C10, C11	RN-T: C8, C1, C2		
			RN-T									

	2019											
	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
	Newsletter tips						RN-T: C12					
					Monthly telephone calls to RNs				Recruitment target achieved			

C, centre; GF, group feedback; IF, individual feedback; Inv M, investigators' meeting; M, month; RN-T, research nurse training; Y, year.

a The numbers before IF indicate the number of individual feedback sessions carried out. For example, C1: 3IF indicates three individual feedback sessions were carried out at Centre 1.

b Visits to sites that were not SIVs or feedback meetings are indicated separately (these involved other activities such as informal discussions to encourage audio-recordings, discussions on recruitment status, etc.).

Note

Months colour key:
Initial stage;
Transitional stage;
Sustainment stage;
Final stage.

Appendix 3 Core outcome set: additional tables and figures

TABLE 26 Methods to develop a COS

Phase 1	**Creation of a comprehensive list of outcomes to inform a questionnaire**
a.	Systematic literature reviews to identify clinical outcomes and PROs
b.	Semi-structured interviews to elicit additional outcomes of importance to patients
c.	Outcomes from a. and b. were combined to create a long list of outcomes of bariatric surgery
d.	Outcomes were mapped into health domains and overlapping outcomes removed by expert health professionals and researchers, with patient feedback.
e.	The final list of outcomes and domains is used to develop items for a questionnaire
Phase 2	**Prioritisation of outcomes in a three-round questionnaire survey**
a.	Round 1: Stakeholders (patients and health professionals) are recruited and asked to rate the importance of each item on the questionnaire.
b.	Round 2: Results of round 1 are fed back to stakeholders in a second round of the survey (Delphi methodology) and stakeholders re-rate the importance of each item, taking into account this feedback
c.	Round 2 is analysed using predefined criteria to reduce the list of items taken forward to next round of the survey
d.	Round 3: Results of round 2 are fed back to stakeholders in a third round of the survey and stakeholders are asked to re-rate the importance of each item, taking into account this feedback
e.	Round 3 is analysed using predefined criteria to reduce the list of items. This produces a list of 'very important' items to be taken forward to phase 3.
Phase 3	**Stakeholder consensus meetings**
a.	The list of items kept in from round 3 are presented to patients and health professionals separately, and items are voted on anonymously, with three voting options: 'In', 'Out' or 'Unsure'
b.	Voting is analysed using predefined criteria to either include or exclude items from the COS. Items where there is no consensus undergo discussion and further voting.
c.	The process produces two COSs, selected by patients and by professionals. These are compared and combined into one COS.

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TABLE 27 Item wording for consensus meetings

	Outcomes of obesity surgery definitely in the Core Outcome Set (4)
	Improvement in diabetes
	Mortality – 30 day or long term (death within 30 days of surgery or long term)
	Leaks, fistulas, strictures and ulcerations at anastomosis (problems with the new join between the two pieces of bowel)
	Weight
	Outcomes of obesity surgery to be voted on (31)
	Potential benefits of weight loss surgery
1	Reduction in hypertension (reduction in BP)
2	Reduction in cardiovascular risk (reduction in risk of heart problems)
3	Reduction in dyslipidaemia (reduction in blood cholesterol)
4	Reduction in obstructive sleep apnoea (reduction in sleep apnoea)
5	Improvement in joint disease
6	Ability to carry out usual activities
7	Improved mobility
8	Ability to accomplish work tasks or take up work (ability to do your work, or to take up work)
9	Having a healthy/balanced eating pattern
10	Ability to stop eating when feeling full
11	Improved self-esteem and self-confidence
12	Improvement in depression
13	Reduction in anxiety
14	Feeling able to live a ‘normal’ life (living a ‘normal’ life)
15	Feeling in control of health and well-being
16	Having a positive outlook on life and expectations for the future
	Potential complications of the surgery
17	Intraoperative organ injury (damage to other organs during the operation)
18	Intra-abdominal abscess (infection inside the body due to surgery)
19	Septicaemia (infection requiring prolonged admission to hospital)

20	Bleeding problems – includes intra-abdominal, GI and staple line bleeding (bleeding problems)
21	Gastric band problems
22	Port problems
23	Internal hernia (bowel problems that need additional surgery)
24	Needing to go to ITU for ventilation (needing to go to ITU for breathing problems post-surgery)
25	Cardiac problems due to surgery (heart problems due to surgery)
26	Venous thromboembolism (blood clot in the leg or lung)
27	Stroke
28	Renal failure (kidney failure)
29	Dysphagia/regurgitation (problems swallowing or bringing food back up)
30	Problems with micronutrient levels (problems with vitamin and mineral levels)
31	Re-admission rates (unexpected re-admission to hospital)

Note
Exact wording of items used at both consensus meetings shown. Where there is alternative wording in brackets, this was used for the patient consensus meeting instead of the wording not in brackets.

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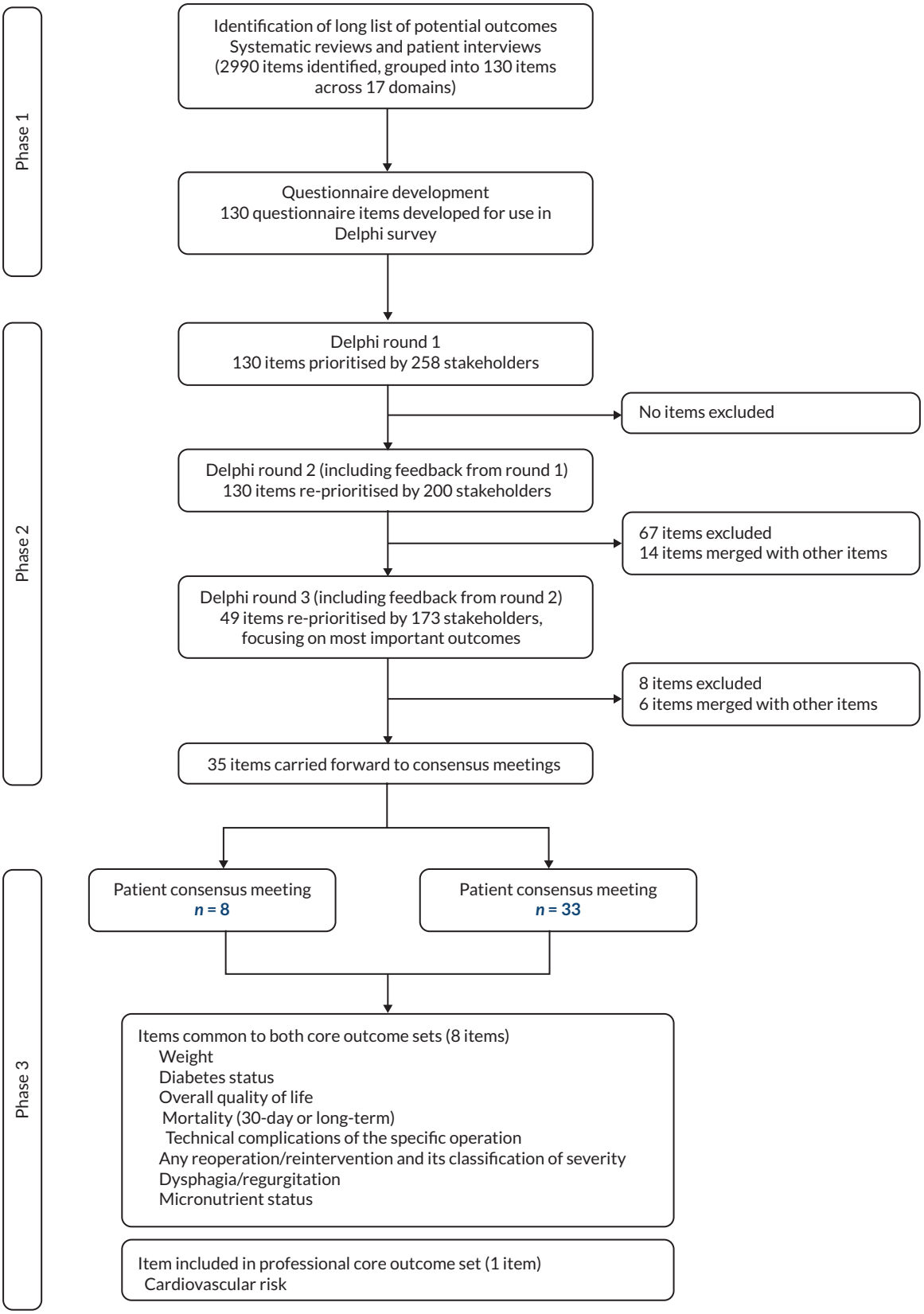

FIGURE 26 Summary of the development of a COS for bariatric and metabolic surgery. Reproduced with permission from Coulman *et al.*[1] This is an Open Access article distributed in accordance with the terms of the Creative Commons Attribution (CC BY 4.0) licence, which permits others to distribute, remix, adapt and build upon this work, for commercial use, provided the original work is properly cited. See: https://creativecommons.org/licenses/by/4.0/. The text below includes minor additions and formatting changes to the original text.

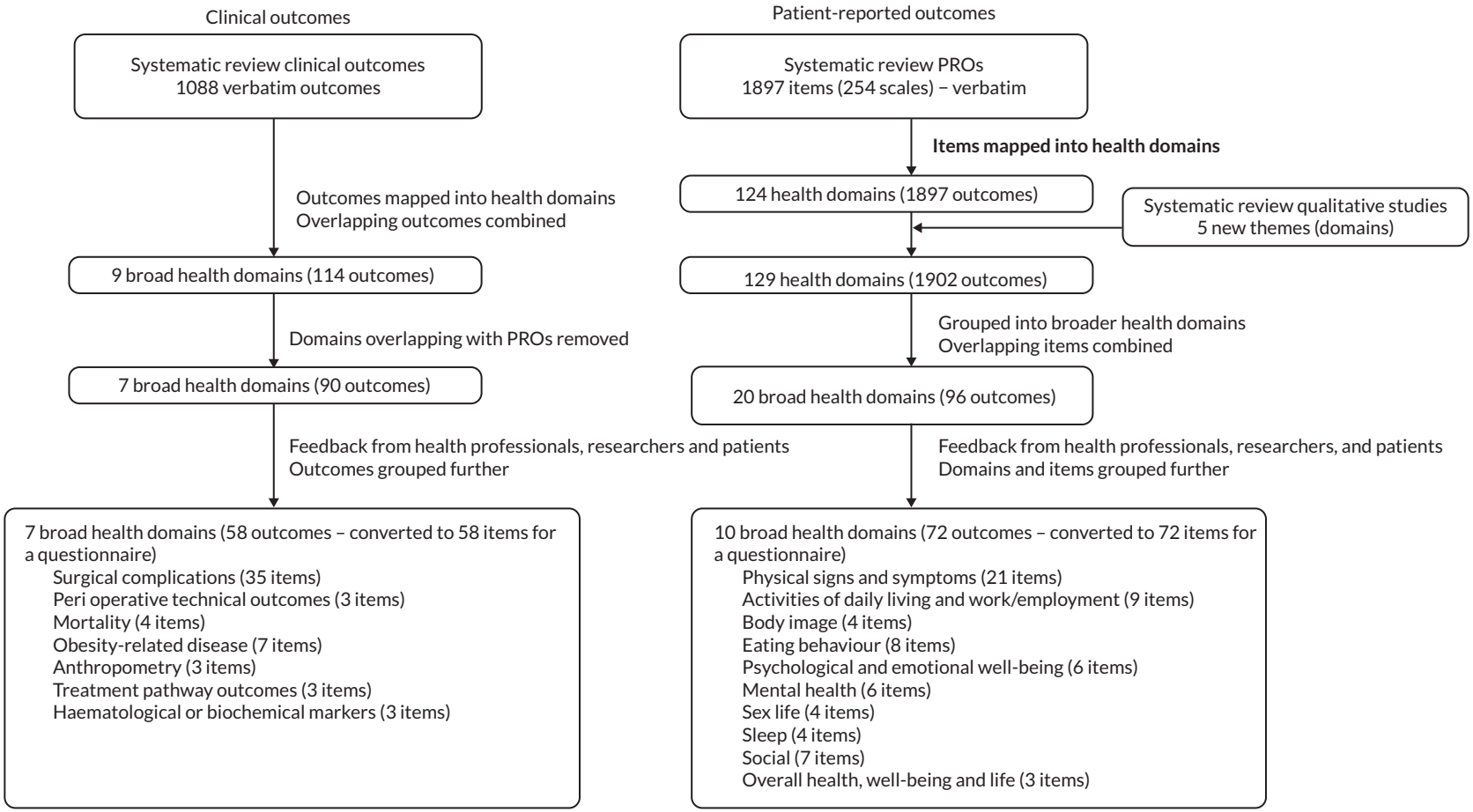

FIGURE 27 Identifying and grouping outcomes of bariatric surgery into domains for a questionnaire study. Reproduced with permission from Coulman *et al.*[1] This is an Open Access article distributed in accordance with the terms of the Creative Commons Attribution (CC BY 4.0) licence, which permits others to distribute, remix, adapt and build upon this work, for commercial use, provided the original work is properly cited. See: https://creativecommons.org/licenses/by/4.0/. The figure includes minor additions and formatting changes to the original text.

TABLE 28 Characteristics of health professionals participating in each round of the survey

Characteristic	Round 1 (*n* = 168)	Round 2 (*n* = 120)	Round 3 (*n* = 102)
Female (%)	77 (45.8)	56 (46.7)	45 (44.1)
Country (%)			
UK	160 (95.2)	115 (95.8)	97 (95.1)
Republic of Ireland	2 (1.2)	2 (1.7)	2 (2.0)
Belgium	1 (0.6)	1 (0.8)	1 (1.0)
Not specified	5 (3.0)	2 (1.7)	2 (2.0)
Type of health professional (%)			
Surgeon	81 (48.2)	59 (49.2)	52 (51.0)
Dietitian	33 (19.6)	26 (21.7)	23 (22.6)
Specialist nurse	24 (14.3)	14 (11.7)	10 (9.8)
Bariatric physician	12 (7.1)	9 (7.5)	8 (7.8)
Psychologist	10 (6.0)	8 (6.7)	7 (6.9)
Anaesthetist	3 (1.8)	0 (0.0)	0 (0.0)
General practitioner	3 (1.8)	2 (1.7)	1 (1.0)
Physiotherapist	1 (0.6)	1 (0.8)	1 (1.0)
Other	1 (0.6)	1 (0.8)	0 (0.0)

TABLE 29 Characteristics of patients participating in each round of the survey

	Round 1 (*n* = 90)	Round 2 (*n* = 80)	Round 3 (*n* = 711)
Female (%)	59 (65.6)	53 (66.3)	48 (67.6)
Mean age in years (SD)	54.4 (9.6)	54.9 (9.1)	55.0 (9.2)
Centre			
Site 1 (%)	56 (62.2)	50 (62.5)	44 (62.0)
Site 2 (%)	34 (37.8)	30 (37.5)	27 (38.0)
'White British' ethnicity (%)	86 (95.6)	77 (96.3)	68 (95.8)
Marital status (%)			
Married	52 (57.8)	47 (58.8)	42 (59.2)
Divorced	18 (20.0)	16 (20.0)	13 (18.3)
Single	14 (15.6)	12 (15.0)	12 (16.9)
Co-habiting	3 (3.3)	2 (2.5)	1 (1.4)
Widowed	3 (3.3)	3 (3.8)	3 (4.2)
Employment status			
Employed full-time	34 (37.8)	28 (35.0)	24 (33.8)
Retired	21 (23.3)	20 (25.0)	18 (25.4)
Employed part-time	11 (12.2)	11 (13.8)	10 (14.1)
Unemployed and seeking work	8 (8.9)	7 (8.8)	6 (8.5)
Unemployed on sickness/disability	7 (7.8)	7 (8.8)	7 (9.9)
Housewife/househusband	5 (5.6)	3 (3.8)	2 (2.8)
Other	4 (4.4)	4 (5.0)	4 (5.6)
Type of operation (%)			
Roux-en-Y gastric bypass	58 (64.4)	55 (68.8)	49 (69.0)
Adjustable gastric band	21 (23.3)	16 (20.0)	14 (19.7)
Sleeve gastrectomy	6 (6.7)	6 (7.5)	5 (7.0)
More than one type of surgery	2 (2.2)	2 (2.5)	2 (2.8)

continued

TABLE 29 Characteristics of patients participating in each round of the survey (*continued*)

	Round 1 (*n* = 90)	Round 2 (*n* = 80)	Round 3 (*n* = 711)
Other	1 (1.1)	0 (0.0)	0 (0.0)
Awaiting surgery	2 (2.2)	1 (1.3)	1 (1.4)
Mean time since surgery in years (SD)[a]	3.5 (2.1)	3.6 (2.1)	3.6 (2.2)

a Data were missing for 5 postoperative patients in all rounds, making *n* = 83 in round 1, *n* = 74 in round 2, and *n* = 66 in round 3.

TABLE 30 Items retained for round 3

No	Item details (n = 63)	% rating item 8–9 in round 2	
		Patients (n = 80)	HCPs (n = 120)
1	Intraoperative organ injury	78.8	62.2
2	Intra-abdominal abscess	76.3	68.1
3	Wound infection or dehiscence	71.3	35.3
4	Septicaemia	87.5	85.7
5	Gastro-intestinal bleeding[a]	72.2	67.8
6	Intra-abdominal bleeding[a]	71.3	78.2
7	Staple line bleed[a]	78.8	77.3
8	Gastric fistula[b]	86.1	89.0
9	Anastomotic leak[b]	91.3	92.4
10	Bowel stricture	80.0	79.7
11	Anastomotic ulceration	76.3	67.2
12	Band infection[c]	78.7	84.9
13	Band erosion[c]	84.0	94.9
14	Band revisions[c]	74.7	78.8
15	Port revisions[d]	70.7	61.3
16	Port infection[d]	73.3	67.2
17	Port malfunction[d]	73.3	41.5
18	Band slippage	82.7	94.9
19	Internal hernia	78.5	89.8
20	Adhesional obstruction	71.8	49.2
21	Requirement for ventilation	73.4	62.7
22	Ischaemic/coronary heart disease[e]	77.2	41.5
23	Arrhythmia[e]	71.8	21.2
24	Venous thromboembolism	84.8	79.7
25	Cerebrovascular accident	83.5	57.6
26	Renal failure	81.0	49.2

continued

TABLE 30 Items retained for round 3 (*continued*)

No	Item details (n = 63)	% rating item 8–9 in round 2	
		Patients (n = 80)	HCPs (n = 120)
27	Perioperative mortality[f]	92.4	94.9
28	In-hospital mortality[f]	91.1	96.6
29	≤ 30-day mortality[f]	91.1	94.8
30	> 30-day mortality	87.3	89.7
31	Dysphagia/regurgitation	65.8	73.3
32	Vitamin levels[g]	67.1	85.8
33	Mineral levels[g]	55.7	80.8
34	Re-admission rates	64.6	79.2
35	Weight[h]	62.0	92.4
36	BMI[h]	53.2	86.4
37	Hypertension	87.5	84.7
38	Cardiovascular risk	88.8	77.1
39	Diabetes	92.5	98.3
40	Dyslipidaemia	70.9	85.6
41	Obstructive sleep apnoea	84.8	90.8
42	Joint disease	86.8	72.9
43	Being able to carry out usual activities	73.4	81.7
44	Mobility	82.3	78.3
45	Fitness	73.4	45.8
46	Being able to accomplish work tasks, or to take up work	75.9	82.5
47	Feeling in control of weight and appearance	77.2	59.7
48	Excess skin or skin folds following weight loss[i]	69.6	52.1
49	Having a healthy/balanced eating pattern	77.2	73.9
50	Being able to stop eating when feeling full	81.0	72.3
51	Feeling satisfied and confident with one's body[j]	70.9	59.7
52	Self-esteem and self-confidence[j]	73.4	58.8
53	Depression	69.6	70.6

No	Item details (n = 63)	% rating item 8–9 in round 2	
		Patients (n = 80)	HCPs (n = 120)
54	Anxiety[i]	65.8	66.4
55	Suicidal thoughts	64.6	73.9
56	Other addictive behaviours[i]	58.2	68.9
57	Overall quality of sleep	77.2	47.9
58	Relationship with partner/spouse[i,k]	61.0	45.0
59	Relationship with children[i,k]	67.9	54.2
60	Relationship with friends[i,k]	44.3	22.5
61	Feeling able to live a normal life	81.0	71.7
62	Feeling in control of health and well-being	79.7	63.0
63	Having a positive outlook on life and expectations for the future	84.8	65.8

HCPs, healthcare professionals.
Items with superscripts[a–j] were merged to create the following single items for round 3:
a 'Intra-abdominal bleeding/GI bleeding/staple line bleed'.
b 'Anastomotic leak/gastric fistula'.
c 'Band infection, erosion, and revisions'.
d 'Port malfunction/revisions/infection'.
e 'Angina/myocardial infarction/arrhythmia'.
f 'Death (during the operation or within 30 days of surgery)'.
g 'Micronutrient levels'.
h Items merged and used to create two new items, 'reduction in weight' and 'maintaining weight loss/preventing weight re-gain'.
i Borderline items (at least 65% of either patients or health professionals rated these items 8–9 in round 2) kept in for round 3.
j 'Self-esteem and self-confidence'.
k 'Relationship with partner/spouse, friends, and/or ability to care for children'.

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TABLE 31 Items brought forward to the consensus meetings

Item details (n = 41)	% rating item 8–9 in round 3	
	Patients (n = 71)	HCPs (n = 102)
Intraoperative organ injury	77.5	55.9
Intra-abdominal abscess	78.9	61.8
Septicaemia	88.7	82.4
Bleeding – includes intra-abdominal, GI and staple line bleeding	80.3	78.4
Anastomotic leak/gastric fistula[a,b]	91.6	90.2
Bowel stricture[a,b]	83.1	67.7
Anastomotic ulceration[a,b]	78.9	52.9
Band infection, erosion and revisions[c]	84.4	84.3
Band slippage[c]	85.9	88.1
Port problems	79.7	58.8
Internal hernia	82.9	81.4
Needing to go to ICU for ventilation	73.2	48.5
Cardiac problems due to surgery	71.8	31.7
Venous thromboembolism	83.1	77.2
Stroke	84.5	59.4
Renal failure	77.5	37.6
≤ 30-day mortality[b,d]	90.1	94.1
> 30-day mortality[b,d]	90.1	86.3
Dysphagia/regurgitation	70.4	57.8
Problems with micronutrient levels	70.4	67.7
Re-admission rates	73.2	72.6
Reduction in weight[b,e]	78.6	88.1
Maintaining weight loss/preventing weight re-gain[b,e]	87.1	89.1
Feeling in control of weight and appearance[b,e]	77.5	50.0
Reduction in hypertension	81.4	74.3

TABLE 31 Items brought forward to the consensus meetings (*continued*)

Item details (n = 41)	% rating item 8–9 in round 3	
	Patients (n = 71)	HCPs (n = 102)
Reduction in cardiovascular risk	84.3	70.0
Improvement in diabetes[b]	87.1	96.0
Reduction in dyslipidaemia	72.9	64.0
Reduction in obstructive sleep apnoea	84.3	77.2
Improvement in joint disease	81.4	61.0
Ability to carry out usual activities	81.7	67.7
Improved mobility	87.3	75.5
Ability to accomplish work tasks, or to take up work	71.8	66.7
Having a healthy/balanced eating pattern	73.2	63.7
Ability to stop eating when feeling full	83.1	59.8
Improved self-esteem and self-confidence	83.1	68.3
Improvement in depression	74.7	58.4
Reduction in anxiety	73.2	48.5
Feeling able to live a 'normal' life	84.3	65.7
Feeling in control of health and well-being	84.5	60.8
Having a positive outlook on life and expectations for the future	87.3	55.9

HCPs, healthcare professionals.
a Merged to create one item, 'Leaks, fistulas, strictures and ulcerations at anastomosis'.
b Included as a definite in the final COS and not voted on at consensus meetings.
c Merged to create one item, 'Gastric band problems'.
d Merged to create one item, 'Mortality (30 days or long term)'.
e Merged to create one item, 'Weight'.

Source

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TABLE 32 Results of the patient consensus meeting

Item	Number of patients (out of 8) voting (%)			Initial views	Final decision
	Item in	Unsure	Item out		
Diabetes status	Definitely in COS – not voted on				Retain item
Mortality (30 days or long term)	Definitely in COS – not voted on				Retain item
Leaks, fistulas, strictures and ulcerations at anastomosis	Definitely in COS – not voted on				Retain 'leaks, fistulas, strictures and ulcers at anastomosis/gastric band problems'[a]
Weight	Definitely in COS – not voted on				Retain item
Hypertension	3 (37.5)	2 (25.0)	3 (37.5)	Unsure	Voted out
Cardiovascular risk	4 (50.0)	1 (12.5)	3 (37.5)	Unsure	Voted out
Dyslipidaemia	0 (0.0)	1 (12.5)	7 (87.5)	Out	Voted out
Obstructive sleep apnoea	1 (12.5)	0 (0.0)	7 (87.5)	Out	Voted out
Joint disease	3 (37.5)	3 (37.5)	2 (25.0)	Unsure	Voted out
Ability to carry out usual activities	5 (62.5)	1 (12.5)	2 (25.0)	Unsure	Retain 'mobility/ability to carry out usual activities/ living a normal life'[a]
Mobility	6 (75.0)	1 (12.5)	1 (12.5)	In	Retain 'mobility/ability to carry out usual activities/ living a normal life'[a]
Ability to do your work, or to take up work	6 (75.0)	1 (12.5)	1 (12.5)	In	Retain item
Having a healthy/balanced eating pattern	5 (62.5)	0 (0.0)	3 (37.5)	Unsure	Retain 'feeling in control'[a]
Ability to stop eating when feeling full	2 (25.0)	3 (37.5)	3 (37.5)	Unsure	Retain 'feeling in control'[a]
Self-esteem and self-confidence	7 (87.5)	0 (0.0)	1 (12.5)	In	Retain 'self-esteem and self-confidence/depression/ having a positive outlook on life and expectations for the future'[a]
Depression	2 (25.0)	2 (25.0)	4 (50.0)	Unsure	Retain 'self-esteem and self-confidence/depression/ having a positive outlook on life and expectations for the future'[a]
Anxiety	0 (0.0)	2 (25.0)	6 (75.0)	Out	Voted out
Feeling able to live a 'normal' life	5 (62.5)	2 (25.0)	1 (12.5)	Unsure	Retain 'mobility/ability to carry out usual activities/ living a normal life'[a]
Feeling in control of health and well-being	5 (62.5)	3 (37.5)	0 (0.0)	Unsure	Retain 'feeling in control'[a]
Having a positive outlook on life and expectations for the future	5 (62.5)	0 (0.0)	3 (37.5)	Unsure	Retain 'self-esteem and self-confidence/depression/ having a positive outlook on life and expectations for the future'[a]

TABLE 32 Results of the patient consensus meeting (*continued*)

Item	Number of patients (out of 8) voting (%)			Initial views	Final decision
	Item in	Unsure	Item out		
Intraoperative organ injury	6 (75.0)	1 (12.5)	1 (12.5)	In	Retain item
Intra-abdominal abscess	2 (25.0)	4 (50.0)	2 (25.0)	Unsure	Voted out
Septicaemia	5 (62.5)	2 (25.0)	1 (12.5)	Unsure	Voted out
Bleeding problems – includes intra-abdominal, GI and staple line bleeding	3 (37.5)	2 (25.0)	3 (37.5)	Unsure	Voted out
Gastric band problems	3 (37.5)	3 (37.5)	2 (25.0)	Unsure	Retain 'leaks, fistulas, strictures and ulcers at anastomosis/gastric band problems'[a]
Port problems	1 (12.5)	5 (62.5)	2 (25.0)	Unsure	Retain 'leaks, fistulas, strictures and ulcers at anastomosis/gastric band problems'[a]
Internal hernia	7 (87.5)	1 (12.5)	0 (0.0)	In	Retain item
Needing to go to intensive therapy unit for ventilation	1 (12.5)	3 (37.5)	4 (50.0)	Unsure	Voted out
Cardiac problems due to surgery	4 (50.0)	0 (0.0)	4 (50.0)	Unsure	Voted out
Venous thromboembolism due to surgery	4 (50.0)	0 (0.0)	4 (50.0)	Unsure	Voted out
Stroke due to surgery	3 (37.5)	2 (25.0)	3 (37.5)	Unsure	Voted out
Renal failure due to surgery	5 (62.5)	2 (25.0)	1 (12.5)	Unsure	Voted out
Dysphagia/regurgitation	6 (75.0)	0 (0.0)	2 (25.0)	In	Retain item
Micronutrient status	5 (62.5)	3 (37.5)	0 (0.0)	Unsure	Retain item
Re-admission rates	5 (62.5)	1 (12.5)	2 (25.0)	Unsure	Voted out

a Item retained and merged with at least two other items.

Note

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TABLE 33 Results of the health professional consensus meeting

Item	Number of professionals (out of 33) voting (%)				Final decision
	Item in	Unsure	Item out	Initial views	
Diabetes status	Definitely in COS – not voted on				Retain item
Mortality (30 days or long term)	Definitely in COS – not voted on				Retain item
Leaks, fistulas, strictures and ulcerations at anastomosis	Definitely in COS – not voted on				Retain 'technical complications of the specific operation', and 'any reoperation/reintervention and its classification of severity'[a]
Weight	Definitely in COS – not voted on				Retain item
Hypertension	17 (51.5)	4 (12.1)	12 (36.4)	Unsure	Voted out
Cardiovascular risk	23 (69.7)	2 (6.1)	8 (24.2)	In	Retain item
Dyslipidaemia	7 (21.2)	5 (15.2)	21 (63.6)	Unsure	Voted out
Obstructive sleep apnoea	16 (48.5)	3 (9.1)	14 (42.4)	Unsure	Voted out
Joint disease	6 (18.2)	2 (6.1)	25 (75.8)	Out	Voted out
Ability to carry out usual activities	14 (42.4)	1 (3.0)	18 (54.5)	Unsure	Retain 'overall quality of life'[a]
Mobility	24 (72.7)	2 (6.1)	7 (21.2)	In	Retain 'overall quality of life'[a]
Ability to do your work, or to take up work	13 (39.4)	4 (12.1)	16 (48.5)	Unsure	Retain 'overall quality of life'[a]
Having a healthy/balanced eating pattern	11 (33.3)	3 (9.1)	19 (57.6)	Unsure	Retain 'overall quality of life'[a]
Ability to stop eating when feeling full	11 (33.3)	3 (9.1)	19 (57.6)	Unsure	Retain 'overall quality of life'[a]
Self-esteem and self-confidence	15 (45.5)	6 (18.2)	12 (36.4)	Unsure	Retain 'overall quality of life'[a]
Depression	10 (30.3)	3 (9.1)	20 (60.6)	Unsure	Retain 'overall quality of life'[a]
Anxiety	1 (3.0)	2 (6.1)	30 (90.9)	Out	Retain 'overall quality of life'[a]
Feeling able to live a 'normal' life	12 (36.4)	6 (18.2)	15 (45.5)	Unsure	Retain 'overall quality of life'[a]
Feeling in control of health and well-being	13 (39.4)	3 (9.1)	17 (51.5)	Unsure	Retain 'overall quality of life'[a]
Having a positive outlook on life and expectations for the future	8 (24.2)	3 (9.1)	22 (66.7)	Unsure	Retain 'overall quality of life'[a]
Intraoperative organ injury	3 (9.1)	2 (6.1)	28 (84.8)	Out	Retain 'technical complications of the specific operation', and 'any reoperation/reintervention and its classification of severity'[a]
Intra-abdominal abscess	6 (18.2)	3 (9.1)	24 (72.7)	Out	Retain 'technical complications of the specific operation', and 'any reoperation/reintervention and its classification of severity'[a]

TABLE 33 Results of the health professional consensus meeting (*continued*)

Item	Number of professionals (out of 33) voting (%)				Final decision
	Item in	Unsure	Item out	Initial views	
Septicaemia	10 (30.3)	2 (6.1)	21 (63.6)	Unsure	Retain 'any reoperation/reintervention and its classification of severity'[a]
Bleeding problems – includes intra-abdominal, GI and staple line bleeding	17 (51.5)	2 (6.1)	14 (42.4)	Unsure	Retain 'technical complications of the specific operation', and 'any reoperation/reintervention and its classification of severity'[a]
Gastric band problems	22 (66.7)	3 (9.1)	8 (24.2)	Unsure	Retain 'technical complications of the specific operation', and 'any reoperation/reintervention and its classification of severity'[a]
Port problems	11 (33.3)	1 (3.0)	21 (63.6)	Unsure	Retain 'technical complications of the specific operation', and 'any reoperation/reintervention and its classification of severity'[a]
Internal hernia	20 (60.6)	0 (0.0)	13 (39.4)	Unsure	Retain 'technical complications of the specific operation', and 'any reoperation/reintervention and its classification of severity'[a]
Needing to go to intensive therapy unit for ventilation	8 (24.2)	3 (9.1)	22 (66.7)	Unsure	Retain 'any reoperation/reintervention and its classification of severity'[a]
Cardiac problems due to surgery	4 (12.1)	2 (6.1)	27 (81.8)	Out	Retain 'any reoperation/reintervention and its classification of severity'[a]
Venous thromboembolism due to surgery	15 (45.5)	2 (6.1)	16 (48.5)	Unsure	Retain 'any reoperation/reintervention and its classification of severity'[a]
Stroke due to surgery	2 (6.1)	2 (6.1)	29 (87.9)	Out	Retain 'any reoperation/reintervention and its classification of severity'[a]
Renal failure due to surgery	2 (6.1)	1 (3.0)	30 (90.9)	Out	Retain 'any reoperation/reintervention and its classification of severity'[a]
Dysphagia/regurgitation	26 (78.8)	0 (0.0)	7 (21.2)	In	Retain item
Micronutrient status	27 (81.8)	0 (0.0)	6 (18.2)	In	Retain item
Re-admission rates	24 (72.7)	2 (6.1)	7 (21.2)	In	Retain 'any reoperation/reintervention and its classification of severity'[a]

a Item retained and merged with at least two other items.

Note

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Appendix 4 Main trial: additional tables and figures

TABLE 34 Schedule of data collection

Item	Pre randomisation	Randomisation	Day of surgery	4 weeks post surgery	Post randomisation (months) 6	12	24	36
Enrolment								
Eligibility	✓							
Audio recording of recruitment consultation	✓							
Informed consent	✓							
Allocation		✓						
Assessments								
Demography	✓							
Height	✓							
Comorbidities	✓							
Socioeconomic status	✓							
Highest ever weight	✓[a]							
Current weight	✓		✓	✓	✓	✓	✓	✓
BP	✓			✓	✓	✓	✓	✓
Waist circumference	✓			✓	✓	✓	✓	✓
HRQoL questionnaires								
SF-12	✓			✓	✓	✓	✓	✓
EQ-5D-5L	✓		✓[b]	✓	✓	✓	✓	✓
IWQOL-Lite	✓			✓	✓	✓	✓	✓
GIQLI	✓			✓	✓	✓	✓	✓
HADS	✓			✓	✓	✓	✓	✓
Eating habits	✓			✓	✓	✓	✓	✓
Resource use	✓			✓	✓	✓	✓	✓
Blood tests for the assessment of comorbidities								
Full blood count	✓		✓	✓	✓	✓	✓	✓
Electrolytes	✓		✓	✓	✓	✓	✓	✓

continued

TABLE 34 Schedule of data collection (*continued*)

Item	Pre randomisation	Randomisation	Day of surgery	4 weeks post surgery	Post randomisation (months)			
					6	12	24	36
Creatinine	✓		✓	✓	✓	✓	✓	✓
Fasting glucose	✓		✓	✓	✓	✓	✓	✓
Lipid profile	✓		✓	✓	✓	✓	✓	✓
HbA1c	✓		✓	✓	✓	✓	✓	✓
Liver function tests	✓		✓	✓	✓	✓	✓	✓
Iron, ferritin, vitamin B12	✓		✓	✓	✓	✓	✓	✓
25-hydroxyvitamin D	✓		✓	✓	✓	✓	✓	✓
Calcium	✓		✓	✓	✓	✓	✓	✓
Parathyroid hormone	✓		✓	✓	✓	✓	✓	✓
24-hour recall eating assessment	✓				✓	✓	✓	✓
Sleep apnoea								
STOPBANG assessment	✓							
Epworth sleepiness scale	✓				✓	✓	✓	✓
ELF test for non-alcoholic fatty liver disease	✓							✓
Interviews (in a purposeful sample of participants)	✓			✓	✓	✓	✓	✓
Blood sample for future research	✓							✓

a Participant reported and from medical notes.
b Posted to participants 2 weeks before surgery.

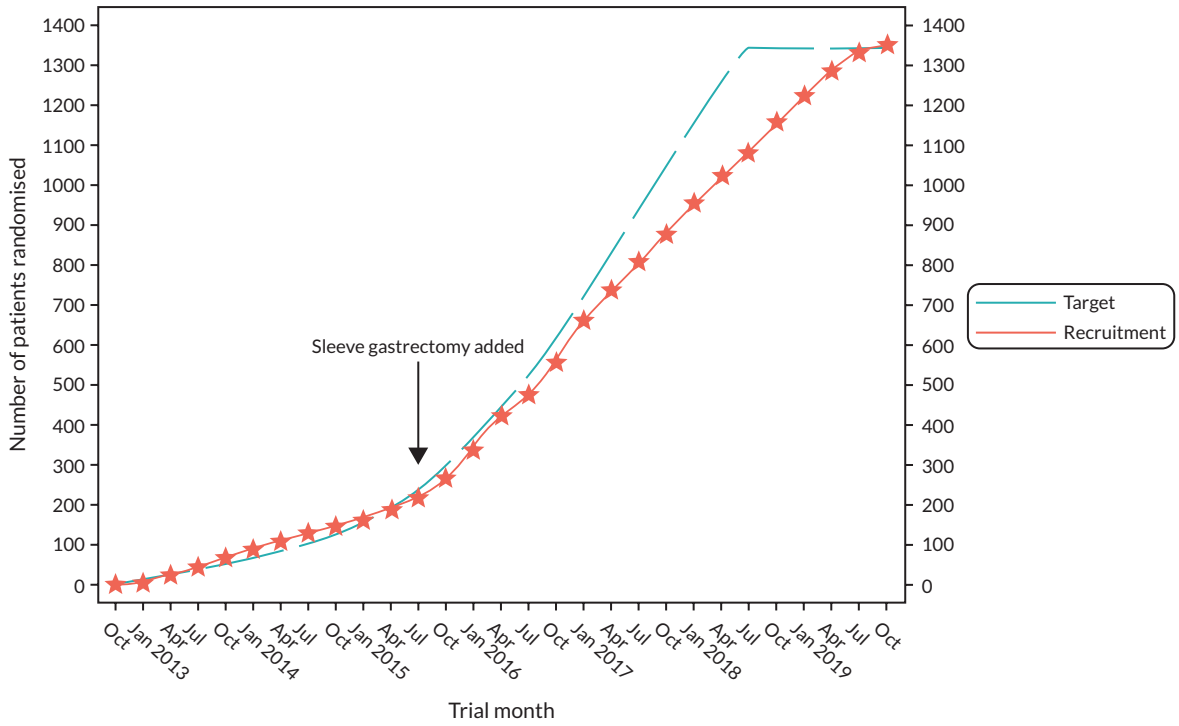

FIGURE 28 Predicted and actual recruitment.

TABLE 35 Screening and recruitment by site

Site	Number of months recruiting	Screened	Eligible (% of screened)	Approached (% of eligible)	Consented (% of eligible)	Randomised	
						(% of eligible)	(% of approached)
1	84	1224	792 (64.7)	769 (97.1)	245 (30.9)	244 (30.8)	244 (31.7)
2	62	470	347 (73.8)	325 (93.7)	160 (46.1)	160 (46.1)	160 (49.2)
3	51	280	188 (67.1)	133 (70.7)	52 (27.7)	52 (27.7)	52 (39.1)
4	56	231	187 (81.0)	163 (86.1)	72 (38.5)	71 (38.0)	71 (43.6)
5	44	326	252 (77.3)	197 (78.2)	75 (29.8)	75 (29.8)	75 (38.1)
6	54	453	365 (80.6)	354 (97.0)	76 (20.8)	76 (20.8)	76 (21.5)
7	51	983	650 (66.1)	593 (91.2)	234 (36.0)	219 (33.7)	219 (36.9)
8	49	910	576 (63.3)	489 (84.9)	102 (17.7)	97 (16.8)	97 (19.8)
9	50	563	347 (61.6)	337 (97.1)	113 (32.6)	113 (32.6)	113 (33.5)
10	48	846	519 (61.3)	300 (57.8)	52 (10.0)	49 (9.4)	49 (16.3)
11	41	543	443 (81.6)	440 (99.3)	169 (38.1)	169 (38.1)	169 (38.4)
12	25	132	74 (56.1)	40 (54.0)	27 (36.5)	26 (35.1)	26 (65.0)
Overall	615	6961	4740 (68.1)	4140 (87.3)	1377 (29.1)	1351 (28.5)	1351 (32.6)

Note
Data are *n* (%).

TABLE 36 Consent to audio-recording recruitment consultations and follow-up

		Declined randomisation		
Site	Eligible	Consent to audio recording (% of eligible)	Consent to follow-up at 3 years (% of eligible)	Consent to access medical records (% of eligible)
1	792	549 (69.3)	197 (24.9)	197 (24.9)
2	347	266 (76.7)	113 (32.6)	114 (32.9)
3	188	126 (67.0)	31 (16.5)	33 (17.6)
4	187	150 (80.2)	68 (36.4)	69 (36.9)
5	252	150 (59.5)	60 (23.8)	58 (23.0)
6	365	262 (71.8)	99 (27.1)	99 (27.1)
7	650	624 (96.0)	211 (32.5)	211 (32.5)
8	576	174 (30.2)	163 (28.3)	164 (28.5)
9	347	250 (72.0)	41 (11.8)	41 (11.8)
10	519	418 (80.5)	35 (6.7)	35 (6.7)
11	443	186 (42.0)	255 (57.6)	256 (57.8)
12	74	47 (63.5)	– (–)	– (–)
Overall	4740	3202 (67.6)	1273 (26.9)	1277 (26.9)

Note
Data are *n* (%).

TABLE 37 Reasons why screened patients were excluded

Exclusion reason	Study site												
	1	2	3	4	5	6	7	8	9	10	11	12	Overall
Excluded	**980 (17.5%)**	**310 (5.5%)**	**228 (4.1%)**	**160 (2.9%)**	**251 (4.5%)**	**377 (6.7%)**	**764 (13.6%)**	**813 (14.5%)**	**450 (8.0%)**	**797 (14.2%)**	**374 (6.7%)**	**106 (1.9%)**	**5610 (100.0%)**
Ineligible	**432 (7.7%)**	**123 (2.2%)**	**92 (1.6%)**	**44 (0.8%)**	**74 (1.3%)**	**88 (1.6%)**	**333 (5.9%)**	**334 (6.0%)**	**216 (3.9%)**	**327 (5.8%)**	**100 (1.8%)**	**58 (1.0%)**	**2221 (39.6%)**
Under 18 years	4 (0.2%)	–	3 (0.1%)	1 (0.0%)	3 (0.1%)	2 (0.1%)	–	5 (0.2%)	–	1 (0.0%)	1 (0.0%)	–	20 (0.9%)
Did not meet NICE guidelines	20 (0.9%)	1 (0.0%)	8 (0.4%)	1 (0.0%)	1 (0.0%)	1 (0.0%)	4 (0.2%)	6 (0.3%)	7 (0.3%)	3 (0.1%)	1 (0.0%)	4 (0.2%)	57 (2.6%)
Not fit for anaesthesia and surgery	45 (2.0%)	13 (0.6%)	3 (0.1%)	2 (0.1%)	2 (0.1%)	7 (0.3%)	15 (0.7%)	22 (1.0%)	8 (0.4%)	7 (0.3%)	–	10 (0.5%)	134 (6.0%)
Not committed to follow-up	93 (4.2%)	29 (1.3%)	9 (0.4%)	3 (0.1%)	12 (0.5%)	35 (1.6%)	77 (3.5%)	48 (2.2%)	24 (1.1%)	81 (3.6%)	2 (0.1%)	2 (0.1%)	415 (18.7%)
Not able to provide written informed consent	13 (0.6%)	6 (0.3%)	10 (0.5%)	2 (0.1%)	5 (0.2%)	2 (0.1%)	6 (0.3%)	9 (0.4%)	6 (0.3%)	41 (1.8%)	3 (0.1%)	6 (0.3%)	109 (4.9%)
History of previous gastric surgery for severe and complex obesity	73 (3.3%)	10 (0.5%)	20 (0.9%)	9 (0.4%)	12 (0.5%)	17 (0.8%)	20 (0.9%)	47 (2.1%)	18 (0.8%)	82 (3.7%)	66 (3.0%)	20 (0.9%)	394 (17.7%)
Large abdominal ventral hernia	20 (0.9%)	–	5 (0.2%)	9 (0.4%)	1 (0.0%)	3 (0.1%)	10 (0.5%)	11 (0.5%)	16 (0.7%)	8 (0.4%)	–	1 (0.0%)	84 (3.8%)
Crohn's disease	3 (0.1%)	3 (0.1%)	4 (0.2%)	1 (0.0%)	–	3 (0.1%)	3 (0.1%)	5 (0.2%)	2 (0.1%)	2 (0.1%)	2 (0.1%)	1 (0.0%)	29 (1.3%)
Liver cirrhosis and/or portal hypertension	9 (0.4%)	3 (0.1%)	5 (0.2%)	3 (0.1%)	–	4 (0.2%)	4 (0.2%)	3 (0.1%)	5 (0.2%)	1 (0.0%)	–	4 (0.2%)	41 (1.8%)
Systemic lupus erythematosus	4 (0.2%)	3 (0.1%)	5 (0.2%)	1 (0.0%)	1 (0.0%)	2 (0.1%)	1 (0.0%)	1 (0.0%)	2 (0.1%)	1 (0.0%)	–	–	21 (0.9%)

TABLE 37 Reasons why screened patients were excluded (*continued*)

Exclusion reason	Study site												
	1	2	3	4	5	6	7	8	9	10	11	12	Overall
Known silicone allergy	3 (0.1%)	1 (0.0%)	1 (0.0%)	2 (0.1%)	–	4 (0.2%)	–	1 (0.0%)	1 (0.0%)	–	–	–	13 (0.6%)
Other clinical/ psychological reason	197 (8.9%)	60 (2.7%)	30 (1.4%)	6 (0.3%)	43 (1.9%)	17 (0.8%)	117 (5.3%)	163 (7.3%)	130 (5.9%)	148 (6.7%)	17 (0.8%)	24 (1.1%)	952 (42.9%)
Active participation in another interventional study	20 (0.9%)	2 (0.1%)	–	1 (0.0%)	1 (0.0%)	3 (0.1%)	15 (0.7%)	–	2 (0.1%)	3 (0.1%)	6 (0.3%)	3 (0.1%)	56 (2.5%)
Pregnancy*	18 (0.8%)	3 (0.1%)	–	1 (0.0%)	–	3 (0.1%)	–	1 (0.0%)	1 (0.0%)	4 (0.2%)	–	1 (0.0%)	32 (1.4%)
Previous abdominal surgery precluding one or more of the three trial groups	26 (1.2%)	11 (0.5%)	1 (0.0%)	3 (0.1%)	3 (0.1%)	3 (0.1%)	24 (1.1%)	24 (1.1%)	24 (1.1%)	16 (0.7%)	43 (1.9%)	–	178 (8.0%)
Hiatus hernia > 5 cm	16 (0.7%)	6 (0.3%)	–	–	3 (0.1%)	3 (0.1%)	13 (0.6%)	17 (0.8%)	12 (0.5%)	11 (0.5%)	9 (0.4%)	–	90 (4.1%)
Not approached	**23 (0.4%)**	**22 (0.4%)**	**55 (1.0%)**	**24 (0.4%)**	**55 (1.0%)**	**11 (0.2%)**	**57 (1.0%)**	**87 (1.6%)**	**10 (0.2%)**	**219 (3.9%)**	**3 (0.1%)**	**34 (0.6%)**	**600 (10.7%)**
Reason not given	4 (0.7%)	5 (0.8%)	6 (1.0%)	5 (0.8%)	1 (0.2%)	4 (0.7%)	14 (2.3%)	15 (2.5%)	–	208 (34.7%)	1 (0.2%)	12 (2.0%)	275 (45.8%)
Patient not interested	2 (0.3%)	4 (0.7%)	5 (0.8%)	7 (1.2%)	–	1 (0.2%)	2 (0.3%)	19 (3.2%)	–	1 (0.2%)	–	10 (1.7%)	51 (8.5%)
Scheduling error/no staff available	–	–	1 (0.2%)	6 (1.0%)	18 (3.0%)	–	6 (1.0%)	4 (0.7%)	–	4 (0.7%)	–	–	39 (6.5%)
Patient did not attend appointment	–	–	2 (0.3%)	2 (0.3%)	18 (3.0%)	4 (0.7%)	3 (0.5%)	–	–	–	–	–	29 (4.8%)
Patient prefers bypass	6 (1.0%)	3 (0.5%)	10 (1.7%)	1 (0.2%)	2 (0.3%)	1 (0.2%)	1 (0.2%)	1 (0.2%)	1 (0.2%)	–	–	1 (0.2%)	27 (4.5%)

continued

TABLE 37 Reasons why screened patients were excluded (*continued*)

Exclusion reason	Study site												
	1	2	3	4	5	6	7	8	9	10	11	12	Overall
Consultant/ surgeon's decision	–	2 (0.3%)	–	–	–	–	1 (0.2%)	23 (3.8%)	–	–	–	–	26 (4.3%)
Clinical reason	1 (0.2%)	1 (0.2%)	–	1 (0.2%)	4 (0.7%)	–	2 (0.3%)	2 (0.3%)	3 (0.5%)	1 (0.2%)	1 (0.2%)	3 (0.5%)	19 (3.2%)
Study closed to recruitment	–	–	–	–	–	–	12 (2.0%)	–	–	5 (0.8%)	–	–	17 (2.8%)
Patient left service/ transferred	–	–	11 (1.8%)	–	–	–	–	1 (0.2%)	–	–	–	2 (0.3%)	14 (2.3%)
Patient prefers sleeve	–	2 (0.3%)	7 (1.2%)	–	–	–	1 (0.2%)	–	2 (0.3%)	–	–	1 (0.2%)	13 (2.2%)
Patient ineligible	6 (1.0%)	–	–	1 (0.2%)	–	–	–	3 (0.5%)	1 (0.2%)	–	1 (0.2%)	–	12 (2.0%)
Patient no longer having surgery	–	–	6 (1.0%)	–	1 (0.2%)	–	–	–	3 (0.5%)	–	–	–	10 (1.7%)
Consultant/ surgeon error	–	–	–	–	–	–	1 (0.2%)	7 (1.2%)	–	–	–	–	8 (1.3%)
Administrative error	–	–	–	–	1 (0.2%)	–	6 (1.0%)	–	–	–	–	–	7 (1.2%)
Patient declined band	–	–	3 (0.5%)	–	1 (0.2%)	–	1 (0.2%)	2 (0.3%)	–	–	–	–	7 (1.2%)
Awaiting other clinical input	–	3 (0.5%)	–	–	1 (0.2%)	–	–	–	–	–	–	2 (0.3%)	6 (1.0%)
Patient did not receive PIL	–	–	–	1 (0.2%)	5 (0.8%)	–	–	–	–	–	–	–	6 (1.0%)
Patient declined randomisation	1 (0.2%)	–	–	–	1 (0.2%)	1 (0.2%)	–	2 (0.3%)	–	–	–	1 (0.2%)	6 (1.0%)
Study not discussed	–	–	–	–	–	–	1 (0.2%)	5 (0.8%)	–	–	–	–	6 (1.0%)

TABLE 37 Reasons why screened patients were excluded (*continued*)

Exclusion reason	Study site												
	1	2	3	4	5	6	7	8	9	10	11	12	Overall
Patient discharged	–	–	–	–	1 (0.2%)	–	–	2 (0.3%)	–	–	–	2 (0.3%)	5 (0.8%)
Patient prefers band	1 (0.2%)	–	3 (0.5%)	–	–	–	1 (0.2%)	–	–	–	–	–	5 (0.8%)
Patient not read PIL	–	2 (0.3%)	–	–	1 (0.2%)	–	–	–	–	–	–	–	3 (0.5%)
Surgeon not on delegation log	–	–	–	–	–	–	3 (0.5%)	–	–	–	–	–	3 (0.5%)
Patient died	–	–	1 (0.2%)	–	–	–	1 (0.2%)	–	–	–	–	–	2 (0.3%)
Personal reasons	1 (0.2%)	–	–	–	–	–	–	1 (0.2%)	–	–	–	–	2 (0.3%)
Consultant/ surgeon biased	1 (0.2%)	–	–	–	–	–	–	–	–	–	–	–	1 (0.2%)
Patient would not quit smoking	–	–	–	–	–	–	1 (0.2%)	–	–	–	–	–	1 (0.2%)
Did not consent	**524 (9.3%)**	**165 (2.9%)**	**81 (1.4%)**	**91 (1.6%)**	**122 (2.2%)**	**278 (5.0%)**	**359 (6.4%)**	**387 (6.9%)**	**224 (4.0%)**	**248 (4.4%)**	**271 (4.8%)**	**13 (0.2%)**	**2763 (49.3%)**
Prefers Bypass	247 (8.9%)	40 (1.4%)	18 (0.7%)	17 (0.6%)	32 (1.2%)	140 (5.1%)	116 (4.2%)	83 (3.0%)	49 (1.8%)	14 (0.5%)	83 (3.0%)	4 (0.1%)	843 (30.5%)
Prefers Sleeve	53 (1.9%)	36 (1.3%)	27 (1.0%)	16 (0.6%)	8 (0.3%)	45 (1.6%)	122 (4.4%)	51 (1.8%)	53 (1.9%)	18 (0.7%)	101 (3.7%)	5 (0.2%)	535 (19.4%)
Prefers Band	81 (2.9%)	18 (0.7%)	16 (0.6%)	14 (0.5%)	8 (0.3%)	38 (1.4%)	71 (2.6%)	8 (0.3%)	20 (0.7%)	3 (0.1%)	11 (0.4%)	1 (0.0%)	289 (10.5%)
Does not want Band	67 (2.4%)	20 (0.7%)	2 (0.1%)	22 (0.8%)	20 (0.7%)	12 (0.4%)	2 (0.1%)	59 (2.1%)	36 (1.3%)	22 (0.8%)	3 (0.1%)	–	265 (9.6%)
Wants own choice	13 (0.5%)	13 (0.5%)	2 (0.1%)	4 (0.1%)	15 (0.5%)	13 (0.5%)	6 (0.2%)	106 (3.8%)	44 (1.6%)	5 (0.2%)	24 (0.9%)	–	245 (8.9%)
No reason given	12 (0.4%)	9 (0.3%)	7 (0.3%)	4 (0.1%)	7 (0.3%)	11 (0.4%)	25 (0.9%)	40 (1.4%)	5 (0.2%)	75 (2.7%)	39 (1.4%)	–	234 (8.5%)
Does not want to be randomised	–	10 (0.4%)	–	2 (0.1%)	5 (0.2%)	17 (0.6%)	1 (0.0%)	11 (0.4%)	1 (0.0%)	31 (1.1%)	2 (0.1%)	2 (0.1%)	82 (3.0%)

continued

TABLE 37 Reasons why screened patients were excluded (*continued*)

Exclusion reason	Study site												
	1	2	3	4	5	6	7	8	9	10	11	12	Overall
Not interested	7 (0.3%)	3 (0.1%)	3 (0.1%)	2 (0.1%)	13 (0.5%)	1 (0.0%)	1 (0.0%)	7 (0.3%)	4 (0.1%)	14 (0.5%)	4 (0.1%)	1 (0.0%)	60 (2.2%)
Personal reasons	13 (0.5%)	4 (0.1%)	–	1 (0.0%)	8 (0.3%)	–	–	14 (0.5%)	1 (0.0%)	9 (0.3%)	–	–	50 (1.8%)
Does not want Bypass	20 (0.7%)	5 (0.2%)	1 (0.0%)	6 (0.2%)	1 (0.0%)	–	3 (0.1%)	3 (0.1%)	2 (0.1%)	5 (0.2%)	–	–	46 (1.7%)
Awaiting MDT	–	–	–	–	–	–	–	–	–	29 (1.0%)	–	–	29 (1.0%)
Does not want surgery	6 (0.2%)	–	4 (0.1%)	–	1 (0.0%)	–	1 (0.0%)	1 (0.0%)	5 (0.2%)	1 (0.0%)	1 (0.0%)	–	20 (0.7%)
Undecided	–	1 (0.0%)	–	–	–	–	2 (0.1%)	–	–	14 (0.5%)	–	–	17 (0.6%)
Does not want Sleeve	4 (0.1%)	1 (0.0%)	–	1 (0.0%)	2 (0.1%)	–	1 (0.0%)	2 (0.1%)	1 (0.0%)	–	–	–	12 (0.4%)
Clinical decision	–	2 (0.1%)	1 (0.0%)	–	–	1 (0.0%)	2 (0.1%)	1 (0.0%)	1 (0.0%)	3 (0.1%)	1 (0.0%)	–	12 (0.4%)
Medical reason	–	2 (0.1%)	–	1 (0.0%)	–	–	1 (0.0%)	–	–	2 (0.1%)	1 (0.0%)	–	7 (0.3%)
Unsure about surgery	1 (0.0%)	1 (0.0%)	–	–	1 (0.0%)	–	1 (0.0%)	–	1 (0.0%)	–	1 (0.0%)	–	6 (0.2%)
Patient preference	–	–	–	–	–	–	3 (0.1%)	–	–	–	–	–	3 (0.1%)
Did not return to consent	–	–	–	–	–	–	1 (0.0%)	1 (0.0%)	–	–	–	–	2 (0.1%)
Language barrier/did not understand study	–	–	–	–	–	–	–	–	–	2 (0.1%)	–	–	2 (0.1%)
Unable to have surgery	–	–	–	–	1 (0.0%)	–	–	–	1 (0.0%)	–	–	–	2 (0.1%)
Reason unclear	–	–	–	–	–	–	–	–	–	1 (0.0%)	–	–	1 (0.0%)
Recruitment closed	–	–	–	1 (0.0%)	–	–	–	–	–	–	–	–	1 (0.0%)

TABLE 37 Reasons why screened patients were excluded (*continued*)

Exclusion reason	Study site												
	1	2	3	4	5	6	7	8	9	10	11	12	Overall
Other reason	**1 (0.0%)**	**0 (0.0%)**	**0 (0.0%)**	**1 (0.0%)**	**0 (0.0%)**	**0 (0.0%)**	**15 (0.3%)**	**5 (0.1%)**	**0 (0.0%)**	**3 (0.1%)**	**0 (0.0%)**	**1 (0.0%)**	**26 (0.5%)**
Patient withdrew post-consent pre randomisation	1 (3.8%)	-	-	1 (3.8%)	-	-	15 (57.7%)	5 (19.2%)	-	3 (11.5%)	-	1 (3.8%)	26 (100.0%)

* Female patients only.

Note
Data are *n* (%).

TABLE 38 Characteristics of randomised and non-randomised participants

		Randomised (*n* = 1351)	Declined randomisation but consented to follow-up/access to medical records (*n* = 1251)[a]	Overall (*n* = 2602)
Sex[b]	Female	1020/1344 (75.9%)	947/1251 (75.7%)	1967/2595 (75.8%)
Age[c]	Median (IQR)	48.5 (39.9–54.6)	46.0 (36.8–53.7)	47.2 (38.6–54.3)
BMI[d]	Mean (SD)	46.4 (6.9)	46.8 (7.3)	46.6 (7.1)
	Proportion overweight (BMI 25–29)	1/1344 (0.1%)	0/1233 (0.0%)	1/2577 (0.0%)
	Proportion obese (BMI 30–39)	234/1344 (17.4%)	216/1233 (17.5%)	450/2577 (17.5%)
	Proportion severely obese (BMI > 39)	1109/1344 (82.5%)	1017/1233 (82.5%)	2126/2577 (82.5%)
Diabetes[e]	Type 1	6/1344 (0.4%)	20/1242 (1.6%)	26/2586 (1.0%)
	Type 2 – pre-diabetes	14/1344 (1.0%)	22/1242 (1.8%)	36/2586 (1.4%)
	Type 2 – diet controlled	38/1344 (2.8%)	32/1242 (2.6%)	70/2586 (2.7%)
	Type 2 – oral hypoglycaemics	265/1344 (19.7%)	225/1242 (18.1%)	490/2586 (18.9%)
	Type 2 – GLP-1 agonist	27/1344 (2.0%)	7/1242 (0.6%)	34/2586 (1.3%)
	Type 2 – insulin	63/1344 (4.7%)	82/1242 (6.6%)	145/2586 (5.6%)

GLP, glucagon-like peptide.
a Only includes patients where baseline details were taken.
b 7 patients (7, 0).
c 148 patients (7, 141).
d 25 patients (7, 18).
e 16 patients (7, 9).

Note
Missing data (randomised, declined randomisation but consented to follow-up/access to medical records).

TABLE 39 Crossovers by year of randomisation

	Crossover						
Year of randomisation	Bypass to Band	Bypass to Sleeve	Band to Bypass	Band to Sleeve	Sleeve to Bypass	Sleeve to Band	Total
2013	1	0	3	0	0	0	4
2014	3	0	1	1	0	0	5
2015	2	1	2	1	0	1	7
2016	1	14	8	13	1	1	38
2017	0	9	5	7	0	0	21
2018	1	3	6	10	1	0	21
2019	3	5	4	6	0	1	19
Total	11	32	29	38	2	3	115

TABLE 40 Participant past history

Characteristic	Randomised to Bypass (*n* = 462)	Randomised to Band (*n* = 464)	Randomised to Sleeve (*n* = 420)	Overall (*n* = 1346)
Cardiovascular history				
Systolic BP (mmHg)[a]	132.6 (121.5, 144.5)	132.0 (121.0, 145.0)	134.2 (122.5, 145.8)	133.0 (121.5, 145.0)
Diastolic BP (mmHg)[a]	83.5 (76.0, 90.0)	82.0 (76.0, 88.3)	82.4 (75.4, 89.4)	82.5 (76.0, 89.0)
Angina	6/461 (1.3%)	11/464 (2.4%)	8/419 (1.9%)	25/1344 (1.9%)
Myocardial infarction	4/461 (0.9%)	6/464 (1.3%)	7/419 (1.7%)	17/1344 (1.3%)
Coronary artery bypass graft	0/461 (0.0%)	2/463 (0.4%)	1/419 (0.2%)	3/1343 (0.2%)
Stroke	9/461 (2.0%)	13/464 (2.8%)	5/419 (1.2%)	27/1344 (2.0%)
Claudication	4/461 (0.9%)	11/464 (2.4%)	13/419 (3.1%)	28/1344 (2.1%)
NYHA classification				
I	357/459 (77.8%)	349/463 (75.4%)	304/419 (72.6%)	1010/1341 (75.3%)
II	74/459 (16.1%)	84/463 (18.1%)	96/419 (22.9%)	254/1341 (18.9%)
III	26/459 (5.7%)	27/463 (5.8%)	14/419 (3.3%)	67/1341 (5.0%)
IV	2/459 (0.4%)	3/463 (0.6%)	5/419 (1.2%)	10/1341 (0.7%)
Smoking				
Never	200/460 (43.5%)	213/464 (45.9%)	194/419 (46.3%)	607/1343 (45.2%)
Ex-smoker	217/460 (47.2%)	212/464 (45.7%)	184/419 (43.9%)	613/1343 (45.6%)
Rarely	6/460 (1.3%)	6/464 (1.3%)	4/419 (1.0%)	16/1343 (1.2%)
Occasionally	13/460 (2.8%)	11/464 (2.4%)	15/419 (3.6%)	39/1343 (2.9%)
Up to 20 cigarettes/day	22/460 (4.8%)	17/464 (3.7%)	19/419 (4.5%)	58/1343 (4.3%)
> 20 cigarettes/day	2/460 (0.4%)	5/464 (1.1%)	3/419 (0.7%)	10/1343 (0.7%)
Other past history				
Symptomatic history of gallstones	75/460 (16.3%)	80/419 (19.1%)	95/464 (20.5%)	250/1343 (18.6%)
Previous cholecystectomy	58/460 (12.6%)	57/419 (13.6%)	74/464 (15.9%)	189/1343 (14.1%)
DVT or pulmonary embolism	22/460 (4.8%)	27/419 (6.4%)	31/464 (6.7%)	80/1343 (6.0%)
Peptic ulcer	16/460 (3.5%)	10/418 (2.4%)	8/464 (1.7%)	34/1342 (2.5%)
Helicobacter pylori status checked	145/460 (31.5%)	102/417 (24.5%)	142/464 (30.6%)	389/1341 (29.0%)

TABLE 40 Participant past history (*continued*)

Characteristic	Randomised to Bypass (*n* = 462)	Randomised to Band (*n* = 464)	Randomised to Sleeve (*n* = 420)	Overall (*n* = 1346)
Positive result	29/462 (6.3%)	19/420 (4.5%)	24/465 (5.2%)	72/1347 (5.3%)
Number of previous conceptions[b]	2.0 (1.0, 3.0)	2.0 (1.0, 4.0)	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)
Number of children[c]	2.0 (0.0, 2.0)	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)
Treatment for fertility?	25/459 (5.4%)	22/464 (4.7%)	27/418 (6.5%)	74/1341 (5.5%)

NYHA, New York Heart Association.
Missing data (Bypass, Band, Sleeve):
a 17 participants (2, 11, 4).
b 11 participants (4, 1, 6).
c 7 participants (3, 1, 3).

Note
Data are median (IQR) or *n*/*N* (%)

TABLE 41 Participant baseline medication and weight loss methods attempted

Characteristic	Randomised to Bypass (*n* = 462)	Randomised to Band (*n* = 464)	Randomised to Sleeve (*n* = 420)	Overall (*n* = 1346)
Medications and supplements taken				
Antidiabetic medication	137/462 (29.7%)	125/463 (27.0%)	103/416 (24.8%)	365/1341 (27.2%)
Anti-hypertensive medication	210/462 (45.5%)	178/464 (38.4%)	176/420 (41.9%)	564/1346 (41.9%)
Antidepressant medication	165/462 (35.7%)	190/464 (40.9%)	153/420 (36.4%)	508/1346 (37.7%)
Anti-hyperlipidaemia medication	131/424 (30.9%)	127/429 (29.6%)	110/379 (29.0%)	368/1232 (29.9%)
Asthma medication	94/424 (22.2%)	114/429 (26.6%)	107/379 (28.2%)	315/1232 (25.6%)
Medication for gastro-oesophageal reflux disease	158/424 (37.3%)	187/429 (43.6%)	143/379 (37.7%)	488/1232 (39.6%)
Anticoagulants	8/424 (1.9%)	9/429 (2.1%)	9/379 (2.4%)	26/1232 (2.1%)
Analgesia	216/424 (50.9%)	219/429 (51.0%)	204/379 (53.8%)	639/1232 (51.9%)
Other medication	254/424 (59.9%)	263/429 (61.3%)	234/379 (61.7%)	751/1232 (61.0%)
Dietary supplements	179/424 (42.2%)	165/429 (38.5%)	142/379 (37.5%)	486/1232 (39.4%)
Weight loss methods attempted				
Orlistat	309/461 (67.0%)	272/419 (64.9%)	319/464 (68.8%)	900/1344 (67.0%)
Sibutramine	36/460 (7.8%)	22/419 (5.3%)	32/464 (6.9%)	90/1343 (6.7%)
Intragastric balloon	4/461 (0.9%)	6/419 (1.4%)	4/464 (0.9%)	14/1344 (1.0%)
Rimonbant	7/460 (1.5%)	4/419 (1.0%)	7/464 (1.5%)	18/1343 (1.3%)
Topiramate	7/460 (1.5%)	2/419 (0.5%)	5/464 (1.1%)	14/1343 (1.0%)
Very-low-calorie diet	313/461 (67.9%)	271/419 (64.7%)	304/464 (65.5%)	888/1344 (66.1%)
High-protein/low-carbohydrate diet	209/461 (45.3%)	181/419 (43.2%)	208/464 (44.8%)	598/1344 (44.5%)
Commercial slimming clubs	372/461 (80.7%)	349/419 (83.3%)	382/464 (82.3%)	1103/1344 (82.1%)
Medical management clinic	375/461 (81.3%)	334/419 (79.7%)	365/464 (78.7%)	1074/1344 (79.9%)
Metformin	77/461 (16.7%)	65/419 (15.5%)	97/464 (20.9%)	239/1344 (17.8%)
Other	154/461 (33.4%)	129/419 (30.8%)	166/463 (35.9%)	449/1343 (33.4%)

Note

TABLE 42 Participant baseline functional status, quality of life and employment status

Characteristic	Randomised to Bypass (*n* = 462)	Randomised to Band (*n* = 464)	Randomised to Sleeve (*n* = 420)	Overall (*n* = 1346)
Functional status				
Can climb 3 flight of stairs without resting	194/458 (42.4%)	197/463 (42.5%)	177/419 (42.2%)	568/1340 (42.4%)
Can climb 1 flight of stairs without resting	187/458 (40.8%)	179/463 (38.7%)	156/419 (37.2%)	522/1340 (39.0%)
Can climb half a flight of stairs without resting	61/458 (13.3%)	74/463 (16.0%)	71/419 (16.9%)	206/1340 (15.4%)
Requires wheelchair or housebound	16/458 (3.5%)	13/463 (2.8%)	15/419 (3.6%)	44/1340 (3.3%)
HRQoL scores				
EQ-5D-5L utility score	0.61 (0.29)	0.60 (0.28)	0.61 (0.28)	0.61 (0.28)
EQ-5D-5L VAS	61.6 (21.0)	61.6 (19.9)	61.3 (22.0)	61.5 (20.9)
SF-12 physical component score	39.0 (10.6)	38.4 (10.5)	39.0 (10.9)	38.8 (10.7)
SF-12 mental component score	43.1 (11.1)	42.7 (11.3)	43.5 (10.9)	43.1 (11.1)
IWQOL: overall score	42.1 (22.0)	41.2 (21.0)	42.2 (20.3)	41.8 (21.1)
GIQLI: overall score	86.5 (17.8)	84.7 (16.2)	86.0 (16.3)	85.7 (16.8)
HADS: anxiety score	7.6 (4.5)	8.0 (4.4)	7.5 (4.2)	7.7 (4.4)
HADS: depression score	7.8 (4.3)	7.6 (3.9)	7.3 (4.0)	7.6 (4.1)
Employment status				
Full time	191/460 (41.5%)	188/464 (40.5%)	182/419 (43.4%)	561/1343(41.8%)
Part time	81/460 (17.6%)	67/464 (14.4%)	69/419 (16.5%)	217/1343(16.2%)
Self employed	25/460 (5.4%)	27/464 (5.8%)	16/419 (3.8%)	68/1343(5.1%)
Homemaker	39/460 (8.5%)	50/464 (10.8%)	40/419 (9.5%)	129/1343(9.6%)
Student	5/460 (1.1%)	5/464 (1.1%)	4/419 (1.0%)	14/1343(1.0%)
Retired	44/460 (9.6%)	33/464 (7.1%)	31/419 (7.4%)	108/1343(8.0%)
Unable to work	43/460 (9.3%)	62/464 (13.4%)	50/419 (11.9%)	155/1343(11.5%)
Unemployed	32/460 (7.0%)	32/464 (6.9%)	27/419 (6.4%)	91/1343(6.8%)
Income and benefits				
Total income/benefits (£)	28,000 (19,404, 45,000)	26,400 (17,285, 45,000)	26,774 (17,847, 45,000)	26,870 (18,259, 45,000)
Unknown/unwilling to say	93 (20.1%)	101 (21.8%)	78 (18.6%)	272 (20.2%)

continued

TABLE 42 Participant baseline functional status, quality of life and employment status (*continued*)

Characteristic	Randomised to Bypass (*n* = 462)	Randomised to Band (*n* = 464)	Randomised to Sleeve (*n* = 420)	Overall (*n* = 1346)
Any benefits	179/461 (38.8%)	204/464 (44.0%)	165/419 (39.4%)	548/1344(40.8%)
Disability benefits	106/461 (23.0%)	123/464 (26.5%)	97/419 (23.2%)	326/1344(24.3%)
Child benefits	46/461 (10.0%)	48/464 (10.3%)	37/419 (8.8%)	131/1344(9.7%)

Note
Data are median (IQR) or *n*/*N* (%)

TABLE 43 Participant baseline bloods

Characteristic	Randomised to Bypass (*n* = 462)	Randomised to Band (*n* = 464)	Randomised to Sleeve (*n* = 420)	Overall (*n* = 1346)
Fasting glucose (mmol/l)[a]	5.2 (4.7, 6.2)	5.2 (4.7, 5.8)	5.1 (4.7, 5.9)	5.2 (4.7, 5.9)
HbA1c (mmol/mol)[b]	40.0 (36.0, 47.0)	40.0 (36.0, 45.0)	39.0 (36.0, 45.0)	40.0 (36.0, 45.0)
Total cholesterol (mmol/l)[c]	4.8 (1.2)	4.8 (1.0)	4.9 (1.0)	4.8 (1.1)
LDL-C (mmol/l)[d]	2.8 (2.2, 3.4)	2.9 (2.2, 3.5)	2.9 (2.3, 3.5)	2.9 (2.3, 3.5)
HDL-C (mmol/l)[e]	1.2 (1.0, 1.4)	1.2 (1.1, 1.4)	1.2 (1.1, 1.5)	1.2 (1.0, 1.4)
Triglycerides (mmol/l)[f]	1.4 (1.1, 2.0)	1.4 (1.1, 1.9)	1.4 (1.1, 1.9)	1.4 (1.1, 1.9)
Red blood cells (10^{12}/l)[g]	4.8 (4.5, 5.1)	4.8 (4.5, 5.1)	4.8 (4.6, 5.1)	4.8 (4.5, 5.1)
Haematocrit (l/l)[h]	0.45 (0.27)	0.42 (0.04)	0.43 (0.19)	0.43 (0.19)
Haemoglobin (g/dl)[i]	13.9 (13.0, 14.7)	13.9 (13.0, 14.6)	13.8 (13.1, 14.6)	13.9 (13.0, 14.7)
Mean cell haemoglobin (pg)[g]	29.0 (27.8, 30.1)	28.9 (27.7, 30.0)	29.1 (27.6, 30.2)	29.0 (27.7, 30.1)
Mean cell volume (fl)[g]	88.4 (84.9, 91.3)	88.0 (84.6, 91.2)	88.1 (84.3, 91.5)	88.2 (84.6, 91.3)
MCHC (g/dl)[j]	32.7 (31.8, 33.5)	32.8 (31.9, 33.5)	32.7 (31.9, 33.5)	32.7 (31.9, 33.5)
Lymphocytes (10^9/l)[k]	2.2 (1.8, 2.7)	2.2 (1.8, 2.6)	2.1 (1.7, 2.6)	2.2 (1.8, 2.6)
Neutrophils (10^9/l)[l]	4.5 (3.6, 5.8)	4.6 (3.7, 5.7)	4.5 (3.6, 5.6)	4.5 (3.7, 5.7)
Alanine aminotransferase (IU/l)[m]	23.0 (18.0, 32.0)	24.0 (17.5, 33.0)	23.0 (17.0, 32.5)	23.0 (18.0, 32.0)
ALP (IU/l)[n]	81.0 (69.0, 97.0)	81.0 (68.0, 98.0)	82.0 (69.0, 96.0)	81.0 (68.0, 97.0)
Bilirubin (µmol/l)[o]	8.0 (6.0, 11.0)	8.0 (7.0, 11.0)	9.0 (7.0, 12.0)	8.0 (7.0, 11.0)
Albumin (g/l)[p]	40.4 (3.8)	40.3 (3.8)	40.0 (3.8)	40.2 (3.8)
Total protein (g/l)[q]	72.0 (69.0, 74.0)	72.0 (69.0, 75.0)	72.0 (69.0, 75.0)	72.0 (69.0, 75.0)
C-reactive protein (mg/l)[r]	7.0 (3.7, 12.0)	7.0 (4.0, 13.0)	7.1 (4.0, 13.0)	7.0 (4.0, 12.0)
Sodium (mmol/l)[s]	139.0 (138.0, 141.0)	139.0 (138.0, 141.0)	140.0 (138.0, 141.0)	139.0 (138.0, 141.0)
Potassium (mmol/l)[t]	4.3 (4.1, 4.5)	4.3 (4.1, 4.5)	4.3 (4.1, 4.5)	4.3 (4.1, 4.5)
Urea (mmol/l)[u]	4.9 (3.9, 5.8)	4.6 (3.9, 5.7)	4.7 (4.0, 5.7)	4.8 (3.9, 5.8)
Creatinine (µmol/l)[v]	66.0 (58.0, 74.0)	66.0 (58.0, 75.0)	65.0 (59.0, 72.0)	66.0 (59.0, 74.0)
Magnesium (mmol/l)[w]	0.8 (0.8, 0.9)	0.8 (0.8, 0.9)	0.8 (0.8, 0.9)	0.8 (0.8, 0.9)
Serum iron (µmol/l)[x]	13.0 (10.0, 17.0)	12.8 (10.0, 16.0)	13.0 (10.0, 16.6)	13.0 (10.0, 16.5)

continued

TABLE 43 Participant baseline bloods (*continued*)

Characteristic	Randomised to Bypass (*n* = 462)	Randomised to Band (*n* = 464)	Randomised to Sleeve (*n* = 420)	Overall (*n* = 1346)
Ferritin (µgl/l)[y]	59.0 (30.0, 109.0)	67.0 (35.0, 114.0)	71.0 (33.0, 131.5)	66.0 (32.0, 116.0)
Vitamin B12 (ng/l)[z]	308.0 (235.0, 417.0)	296.0 (226.0, 398.0)	319.5 (245.0, 415.5)	310.0 (233.0, 415.0)
Folate (µgl/l)[aa]	6.5 (4.5, 9.3)	5.9 (4.2, 8.8)	5.9 (4.3, 9.2)	6.1 (4.3, 9.2)
25-hydroxyvitamin D (nmol/l)[bb]	42.4 (28.0, 59.0)	44.0 (30.0, 60.6)	42.8 (29.5, 61.1)	43.0 (29.0, 60.0)
Parathyroid hormone (pmol/l)[cc]	5.7 (4.4, 7.9)	5.8 (4.2, 7.9)	5.8 (4.3, 7.9)	5.8 (4.3, 7.9)
Calcium (mmol/l)[dd]	2.4 (2.3, 2.4)	2.4 (2.3, 2.4)	2.4 (2.3, 2.4)	2.4 (2.3, 2.4)
Phosphate (mmol/l)[ee]	1.1 (1.0, 1.2)	1.1 (1.0, 1.2)	1.1 (0.9, 1.2)	1.1 (1.0, 1.2)

MCHC, mean corpuscular haemoglobin concentration.
Missing data (Bypass, Band, Sleeve):
a 79 participants (39, 22, 18).
b 36 participants (15, 14, 7).
c 28 participants (10, 9, 9).
d 65 participants (26, 23, 16).
e 32 participants (11, 11, 10).
f 44 participants (19, 16, 9).
g 22 participants (11, 6, 5).
h 29 participants (15, 7, 7).
i 21 participants (11, 5, 5).
j 28 participants (13, 9, 6).
k 22 participants (11, 5, 6).
l 21 participants (11, 5, 5).
m 24 participants (12, 8, 4).
n 19 participants (9, 6, 4,).
o 25 participants (12, 7, 6).
p 18 participants (9, 6, 3).
q 35 participants (15, 14, 6).
r 71 participants (26, 29, 16).
s 20 participants (11, 6, 3).
t 24 participants (13, 8, 3).
u 21 participants (11, 6, 4).
v 21 participants (12, 6, 3).
w 117 participants (37, 46, 34).
x 62 participants (27, 24, 11).
y 39 participants (13, 14, 12).
z 36 participants (15, 13, 8).
aa 52 participants (21, 19, 12).
bb 43 participants (19, 16, 8).
cc 73 participants (25, 30, 18).
dd 41 participants (19, 16, 6).
ee 49 participants (19, 21, 9).

Note
Data are median (IQR) or mean (SD).

TABLE 44 Time from randomisation to surgery

Waiting time (months)	Randomised to Bypass (*n* = 462)	Randomised to Band (*n* = 464)	Randomised to Sleeve (*n* = 420)	Overall (*n* = 1346)
All participants				
Had surgery	401	417	365	1183
Waiting time	5.3 (2.5, 10.3)	4.2 (2.2, 9.2)	5.1 (2.9, 12.1)	5.0 (2.5, 10.1)
Operated before the COVID-19 pandemic				
Had surgery	394	408	356	1158
Waiting time	5.2 (2.5, 10.1)	4.1 (2.2, 8.9)	5.0 (2.9, 11.2)	4.8 (2.5, 9.7)
Operated after the start of the COVID-19 pandemic				
Had surgery	7	9	9	25
Waiting time	26.8 (18.5, 32.9)	30.6 (17.1, 31.5)	22.0 (17.1, 29.1)	27.1 (17.1, 31.0)

Note
Data are number or median and IQR. Participants who did not have surgery were censored at last follow-up. Start of the COVID-19 pandemic was taken as the date of the first lockdown – 20 March 2020.

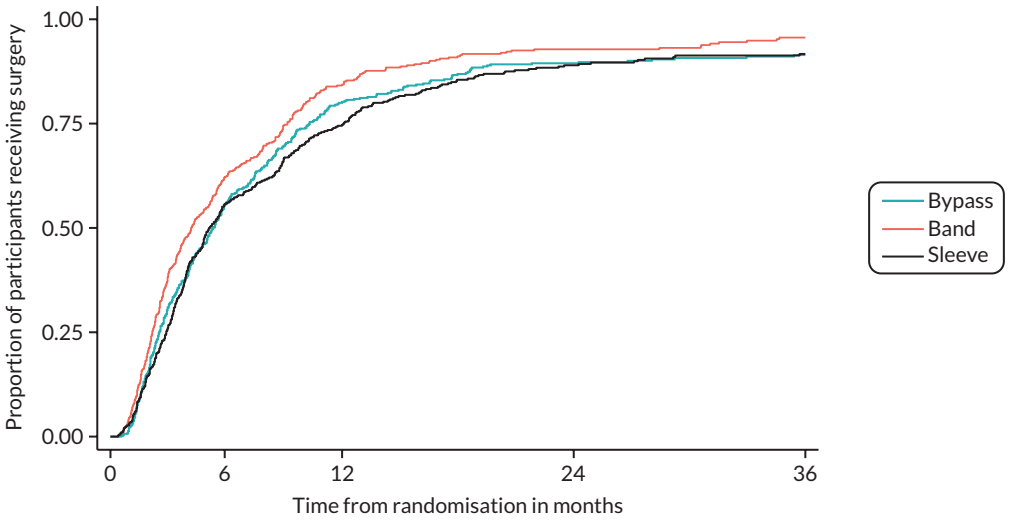

FIGURE 29 Time from randomisation to surgery by randomised group.

TABLE 45 Surgical details: additional information – all surgeries

Characteristic	Received Bypass (*n* = 389)		Received Band (*n* = 363)		Received Sleeve (*n* = 429)		Overall (*n* = 1181)	
	n	%	*n*	%	*n*	%	*n*	%
Additional procedures	53/369	14.4%	41/344	11.9%	57/429	13.3%	151/1142	13.2%
Other	17/53	32.1%	4/41	9.8%	8/57	14.0%	29/151	19.2%
Adhesiolysis	13/53	24.5%	2/41	4.9%	4/57	7.0%	19/151	12.6%
Balloon removal	1/53	1.9%					1/151	0.7%
Lipoma excision			1/41	2.4%			1/151	0.7%
Liver biopsy	2/53	3.8%			1/57	1.8%	3/151	2.0%
Oesophagogastroduodenoscopy	1/53	1.9%					1/151	0.7%
Omentopexy					3/57	5.3%	3/151	2.0%
Skin lesion			1/41	2.4%			1/151	0.7%
Postoperative transfusion	5/389	1.3%	0/363	0%	8/429	1.9%	13/1181	1.1%
Units of red blood cells	2	(2, 4)			2	(1.5, 4)	2	(2, 4)
Recovery time								
Admitted to ICU	20/388	5.2%	17/361	4.7%	15/428	3.5%	52/117	4.4%
Time in ICU (hours)	20.9	(8.7, 43.5)	18.0	(4.4, 19.5)	20.1	(5.1, 45.3)	19.2	(4.8, 34.2)
Admitted to HDU	49/388	12.6%	27/361	7.5%	46/428	10.7%	122/1177	10.4%
Time in HDU (hours)[a]	20.5	(4.6, 32.5)	11.1	(1.2, 20.7)	21.0	(4.3, 44.8)	19.0	(3.0, 24.5)
Admitted to ward	358/387	92.5%	335/361	92.8%	408/428	95.3%	1101/1176	93.6%
Time in ward (hours)[b]	42.8	(23.5, 46.6)	18.0	(2.0, 21.3)	44.0	(40.2, 48.0)	40.5	(19.0, 45.6)
Discharge destination								
Home	389/389	100%	362/363	99.7%	426/429	99.3%	1177/1181	99.7%
Other ward or hospital	0	0%	1/363	0.3%	3/429	0.7%	4/1181	0.3%

Missing data (Bypass, Band, Sleeve):
a 15 participants (7, 1, 7).
b 29 participants (7, 11, 11).

Note
Data are median (IQR), mean (SD), or *n*/*N* (%).

TABLE 46 Surgical details: gastric bypass

	Bypass received (*n* = 389)
	n/*N* (%)
Dissection	
Gastric pouch	
Vertical lesser curve	387/387 (100%)
Horizontal including fundus	0/387 (0%)
Reconstruction	
Roux limb > 150 cm[a]	1/388 (0.3%)
Biliary limb > 75 cm[a]	90/388 (23.2%)
Opening of the retro-colic window	
Ante-colic/ante-gastric	239/386 (61.9%)
Retro-colic/ante-gastric	124/386 (32.1%)
Retro-colic/retro-gastric	23/386 (6.0%)
Other	0/386 (0.0%)
Anastomoses	
Gastro-jejunostomy	
Circular stapler	28/388 (7.2%)
Linear stapler and sewn enterostomy	330/388 (85.1%)
Fully linear stapler	6/388 (1.5%)
Hand sewn	24/388 (6.2%)
Jejuno-jejunostomy	
Triple linear stapler	129/388 (33.2%)
Double linear stapler	7/388 (1.8%)
Single linear stapler	252/388 (64.9%)
Hand sewn	0/388 (0.0%)
Closure	
Optional[b]	
Peterson's space	205/258 (79.5%)
Jejuno-jejunostomy	207/258 (80.2%)
Mesocolon	118/257 (45.9%)
Mandatory[b]	
Peterson's space	119/129 (92.2%)
Jejuno-jejunostomy	114/129 (88.4%)
Mesocolon	41/129 (31.8%)

TABLE 46 Surgical details: gastric bypass (*continued*)

	Bypass received (*n* = 389)
	n/*N* (%)
Other	
Bougie size	
No bougie	32/388 (8.2%)
30 Fr	10/388 (2.6%)
32 Fr	29/388 (7.5%)
33 Fr	4/388 (1.0%)
34 Fr	288/388 (74.2%)
36 Fr	23/388 (5.9%)
Other (no details)	2/388 (0.5%)
Testing of anastomosis	273/275 (99.3%)

a Recommended lengths prior to 25 March 2014 were 100 and 200 cm for biliary and roux limbs, respectively.
b Closure of mesenteric defects became mandatory on the 23 April 2018.

TABLE 47 Surgical details: gastric band

	Band received (*n* = 363)
	n/*N* (%)
Dissection	
Pars flaccida technique	359/361 (99.4%)
Peri gastric technique	2/361 (0.6%)
Insertion	
Band insertion	
Manufacturer 1	275/361 (76.2%)
Manufacturer 2	48/361 (13.3%)
Manufacturer 3	38/361 (10.5%)
Gastro-gastric tunnelling sutures	357/361 (98.9%)
Port fixing method	
Stitches	257/360 (71.4%)
Integral device	102/360 (28.3%)
Other	1/360 (0.3%)
Band directly approximated to serosa	347/360 (96.4%)
Fat pad reflected	273/281 (97.2%)
Fat pad not applicable	80/361 (22.2%)

TABLE 48 Surgical details: sleeve gastrectomy

	Sleeve received (*n* = 429)
Dissection	
Visualisation of left crus	426/426 (100%)
Resection	
Distal staple height	
Blue (1.5 mm)	5/422 (1.2%)
Gold (1.8 mm)	37/422 (8.8%)
Green (2.0 mm)	153/422 (36.3%)
Black (2.25–2.3 mm)	124/422 (29.4%)
Tan (0.88–1.8 mm)	3/422 (0.7%)
Purple (1.5–2.25 mm)	96/422 (22.7%)
Other	4/422 (0.9%)
Proximal staple height	
Blue (1.5 mm)	67/416 (16.1%)
Gold (1.8 mm)	98/416 (23.6%)
Green (2.0 mm)	38/416 (9.1%)
Black (2.25–2.3 mm)	11/416 (2.6%)
Tan (0.88–1.8 mm)	54/416 (13.0%)
Purple (1.5–2.25 mm)	136/416 (32.7%)
Other	12/416 (2.9%)
Distance of start of staple line from pylorus > 2 cm	401/424 (94.6%)
Reinforcement of staple line	
None	173/426 (40.6%)
Bioabsorbable	167/426 (39.2%)
Suturing[a]	44/426 (10.3%)
Clipping	33/426 (7.8%)
Other	9/426 (2.1%)
Bougie size	
No bougie	1/390 (0.3%)
30 Fr	13/390 (3.3%)
32 Fr	18/390 (4.6%)
33 Fr	3/390 (0.8%)
34 Fr	308/390 (79.0%)
36 Fr	38/390 (9.7%)
38 Fr	5/390 (1.3%)
40 Fr	39/390 (10.0%)
Testing of staple line	323/382 (84.6%)

a Includes two participants recorded as also having clips and four participants recorded as also having bioabsorbable reinforcements.

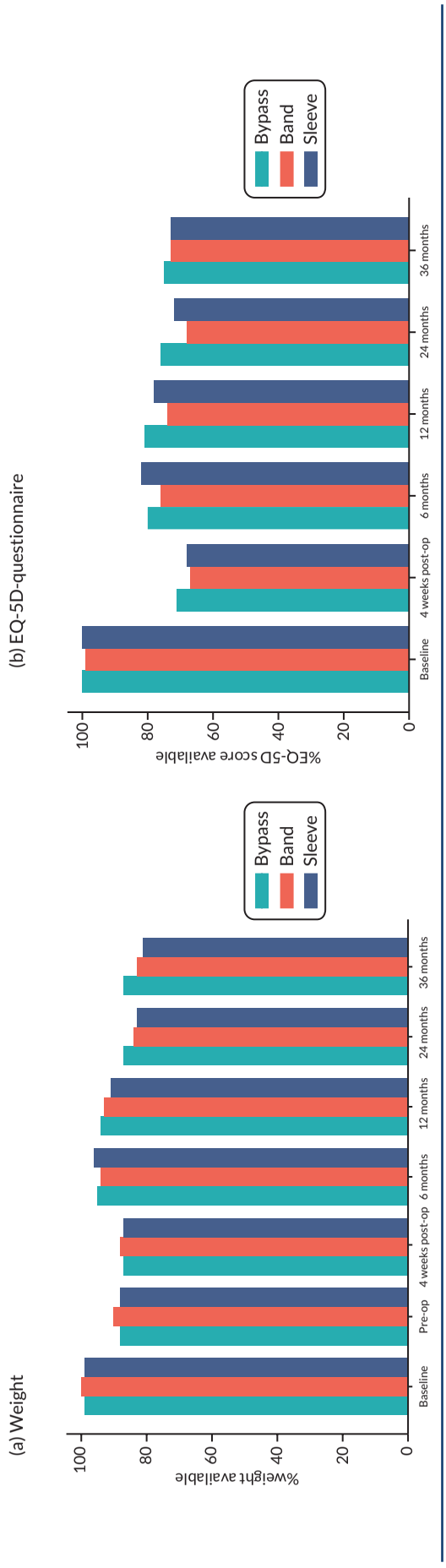

FIGURE 30 Completeness of the primary outcomes over time. (a) Weight; and (b) EQ-5D-questionnaire.

TABLE 49 Percentage of participants with at least 50% excess weight loss at 3 years

Achieved at least 50% EWL[a]	Randomised to Bypass (*n* = 462)	Randomised to Band (*n* = 464)	Randomised to Sleeve (*n* = 420)	Bypass vs. Band RR (98% CI)	Sleeve vs. Band RR (98% CI)	Sleeve vs. Bypass RR (98% CI)
Primary analysis	276/405 (68.1%)	97/383 (25.3%)	142/342 (41.5%)	2.58 (2.09 to 3.20)	1.58 (1.25 to 2.00)	0.61 (0.47 to 0.79)
Excluding participants with missing outcome[b]	229/338 (76.7%)	84/325 (20.8%)	123/290 (44.1%)	2.65 (2.18 to 3.21)	1.62 (1.33 to 1.97)	0.61 (0.47 to 0.80)
Excluding crossovers	258/363 (71.1%)	62/328 (18.9%)	137/336 (40.8%)	3.50 (2.61 to 4.69)	2.04 (1.53 to 2.73)	0.58 (0.45 to 0.76)
Excluding participants who did not have surgery	274/375 (73.1%)	96/363 (26.5%)	140/314 (44.6%)	2.71 (2.19 to 3.35)	1.66 (1.32 to 2.10)	0.61 (0.48 to 0.78)
	Received Bypass	**Received Band**	**Received Sleeve**			
Excluding participants who did not have surgery	276/356 (77.5%)	67/322 (20.8%)	167/374 (44.7%)	3.70 (2.77 to 4.95)	2.14 (1.52 to 3.00)	0.578 (0.455 to 0.734)

RR, risk ratio.
a Multiple imputation (50 imputed data sets) was used to account for missing outcome in analyses, counts exclude imputed observations.
b Excludes participants who had missing data for both coprimary outcomes at 3 years.

Note
Two participants were excluded from the imputation as they withdrew following consent and before providing any weight data.

TABLE 50 Percentage of participants with at least 50% excess weight loss at 3 years by subgroup

Achieved at least 50% EWL	Randomised to Bypass (*n* = 462)	Randomised to Band (*n* = 464)	Randomised to Sleeve (*n* = 420)	Bypass vs. Band	Sleeve vs. Band	Sleeve vs. Bypass	Test for treatment by subgroup interaction
				RR (98% CI)	RR (98% CI)	RR (98% CI)	
Nondiabetic	197/270 (73.0%)	75/264 (28.4%)	112/246 (45.5%)	2.40 (1.99 to 2.88)	1.51 (1.16 to 1.97)	0.63 (0.50 to 0.80)	*p* = 0.22
Diabetic	79/135 (58.5%)	22/119 (18.5%)	29/96 (30.2%)	3.25 (2.09 to 5.07)	1.81 (1.17 to 2.81)	0.56 (0.34 to 0.91)	
BMI < 40	47/60 (78.3%)	19/72 (26.4%)	26/66 (39.4%)	2.76 (1.74 to 4.37)	1.48 (1.03 to 2.13)	0.54 (0.34 to 0.85)	*p* = 0.74
BMI 40 to < 50	169/238 (71.0%)	55/208 (26.4%)	79/193 (40.9%)	2.66 (2.01 to 3.52)	1.54 (1.17 to 2.03)	0.58 (0.43 to 0.79)	
BMI > 50	60/107 (56.1%)	23/103 (22.3%)	36/83 (43.4%)	2.34 (1.56 to 3.51)	1.74 (1.13 to 2.69)	0.74 (0.51 to 1.07)	

Note
RR, risk ratio.
a Multiple imputation (50 imputed data sets) was used to account for missing outcome in analyses, counts exclude imputed observations.

TABLE 51 Time to achieving 50% excess weight loss

Outcome	Randomised to Bypass (*n* = 462)	Randomised to Band (*n* = 464)	Randomised to Sleeve (*n* = 420)	Overall (*n* = 1346)
	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)
Time from randomisation to first loss of 50% excess BMI (months)	14.9 (11.6–27.0)	35.9 (24.5,)	24.2 (12.2–35.8)	25.0 (12.3, -)
Time from first loss of 50% excess BMI to first relapse (months)	- (28.2, -)	24.6 (8.6, -)	28.4 (16.8–32.6)	32.6 (17.9–32.6)

The - symbol indicates times that could not be estimated.

Note
Some event times could not be estimated due to insufficient numbers of participants with the outcome. These estimates are derived from the observed participant weights reported and do not include any imputation for missing data. The - symbol indicates times that could not be estimated

TABLE 52 EQ-5D questionnaire responses

	Randomised to Bypass (*n* = 462)	Randomised to Band (*n* = 464)	Randomised to Sleeve (*n* = 420)	Overall (*n* = 1346)
EQ-5D utility score	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**
Baseline[a]	0.68 (0.44–0.80)	0.66 (0.46–0.80)	0.68 (0.44–0.77)	0.68 (0.44–0.80)
Preoperative[b]	0.66 (0.51–0.77)	0.65 (0.42–0.77)	0.68 (0.42–0.77)	0.66 (0.48–0.77)
4 weeks postoperative[c]	0.77 (0.64–0.88)	0.73 (0.58–0.84)	0.74 (0.59–0.84)	0.74 (0.60–0.85)
6 months[d]	0.73 (0.54–0.84)	0.69 (0.47–0.84)	0.71 (0.52–0.84)	0.71 (0.52–0.84)
12 months[e]	0.77 (0.62–0.88)	0.73 (0.53–0.88)	0.75 (0.55–0.88)	0.77 (0.56–0.88)
24 months[f]	0.84 (0.64–1.00)	0.73 (0.45–0.84)	0.77 (0.60–0.88)	0.77 (0.56–0.88)
36 months[g]	0.77 (0.59–1.00)	0.72 (0.43–0.85)	0.75 (0.55–0.88)	0.74 (0.55–0.88)

Missing data (Bypass, Band, Sleeve):
a 15 patients (1, 10, 4).
b 677 patients (229, 258, 190).
c 416 patients (132, 151, 133).
d 280 patients (91, 112, 77).
e 300 patients (85, 121, 94).
f 379 patients (113, 149, 117).
g 351 patients (114, 124, 113).

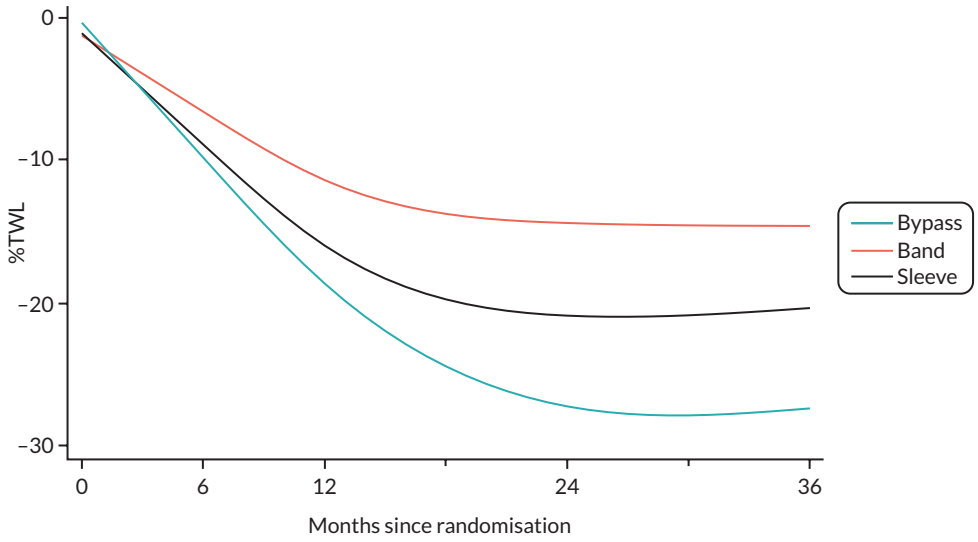

FIGURE 31 Percentage total weight loss over time. Trajectories are estimated from the model and represent the predicted mean scores.

TABLE 53 Weight and waist circumference over time

	Randomised to Bypass (*n* = 462)	Randomised to Band (*n* = 464)	Randomised to Sleeve (*n* = 420)	Overall (*n* = 1346)
Weight (kg)	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**
Baseline[a]	127.8 (114.1–145.8)	125.8 (112.4–143.1)	124.0 (111.2–144.0)	126.3 (112.4–144.4)
Preoperative[b]	124.0 (110.0–143.1)	123.0 (110.4–139.8)	121.0 (108.0–140.0)	122.6 (109.5–140.2)
4 weeks postoperative[c]	112.4 (98.8–128.8)	115.5 (104.3–132.0)	110.8 (98.5–127.1)	113.0 (100.0–130.0)
6 months[d]	115.1 (98.0–131.6)	116.3 (104.8–133.7)	114.0 (98.0–130.0)	115.0 (100.4–131.8)
12 months[e]	100.8 (84.4–120.0)	111.8 (99.6–129.1)	103.0 (87.8–123.0)	106.0 (90.4–125.0)
24 months[f]	91.6 (77.4–107.6)	107.7 (93.2–124.1)	97.8 (84.1–115.6)	99.5 (84.0–116.4)
36 months[g]	91.8 (77.2–107.0)	108.8 (94.4–125.1)	99.9 (86.0–117.0)	99.6 (85.0–118.0)
Waist circumference (cm)	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**
Baseline[h]	130.9 (14.9)	130.6 (14.6)	129.8 (15.1)	130.5 (14.8)
4 weeks postoperative[i]	120.2 (14.6)	123.4 (15.0)	119.4 (15.7)	121.1 (15.2)
6 months[j]	119.2 (17.9)	122.8 (16.1)	120.3 (17.0)	120.7 (17.1)
12 months[k]	109.9 (18.0)	119.3 (15.7)	112.4 (18.0)	113.8 (17.7)
24 months[l]	101.6 (17.8)	115.0 (17.1)	108.5 (16.9)	108.3 (18.1)
36 months[m]	104.4 (17.1)	116.4 (18.2)	109.9 (17.1)	110.2 (18.2)

Missing data (Bypass, Band, Sleeve):
a 2 participants (1, 0, 1).
b 154 participants (57, 47, 50).
c 168 participants (60, 55, 53).
d 67 participants (22, 28, 17).
e 98 participants (28, 33, 37).
f 207 participants (61, 74, 72).
g 216 participants (57, 81, 78).
h 37 participants (14, 10, 13).
i 444 participants (152, 130, 162).
j 308 participants (100, 116, 92).
k 387 participants (113, 139, 135).
l 677 participants (226, 232, 219).
m 785 participants (263, 270, 252).

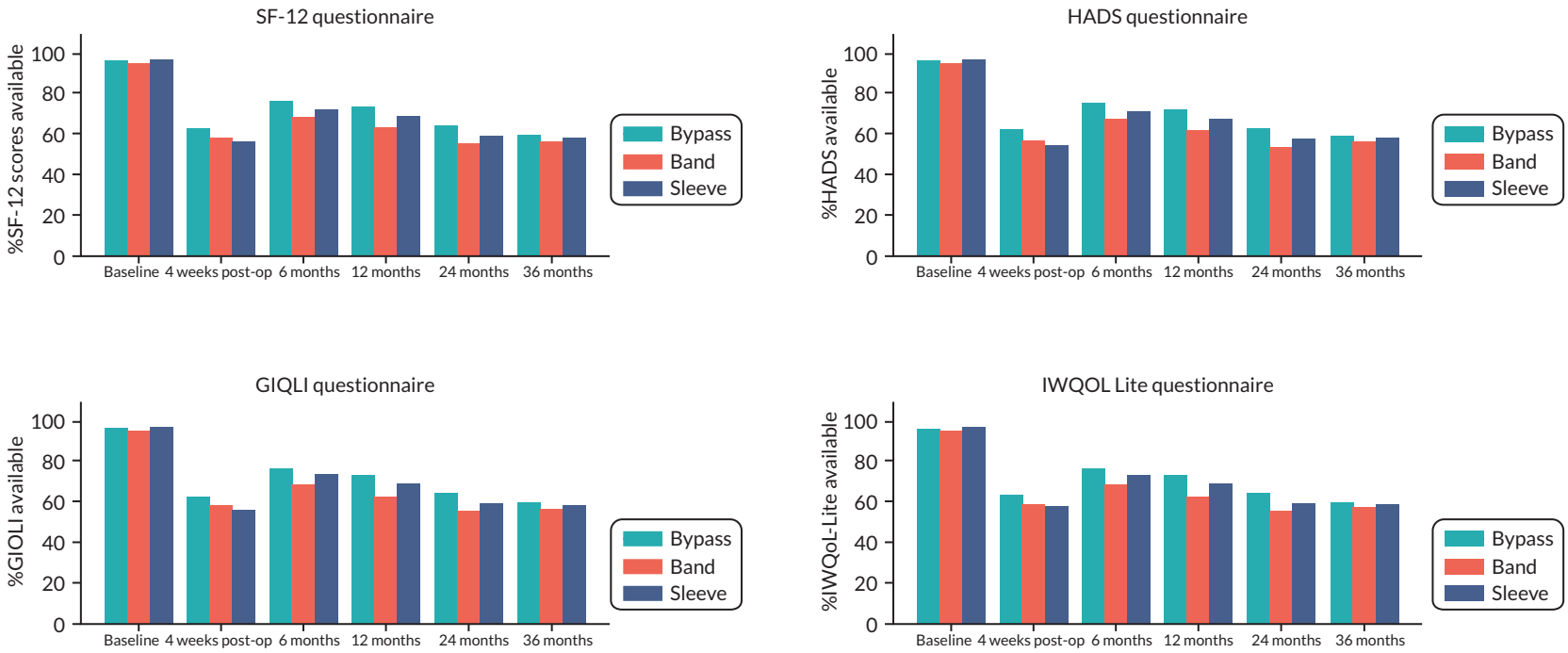

FIGURE 32 Completeness of the SF-12, HADS, GIQLI and IWQOL-Lite questionnaires.

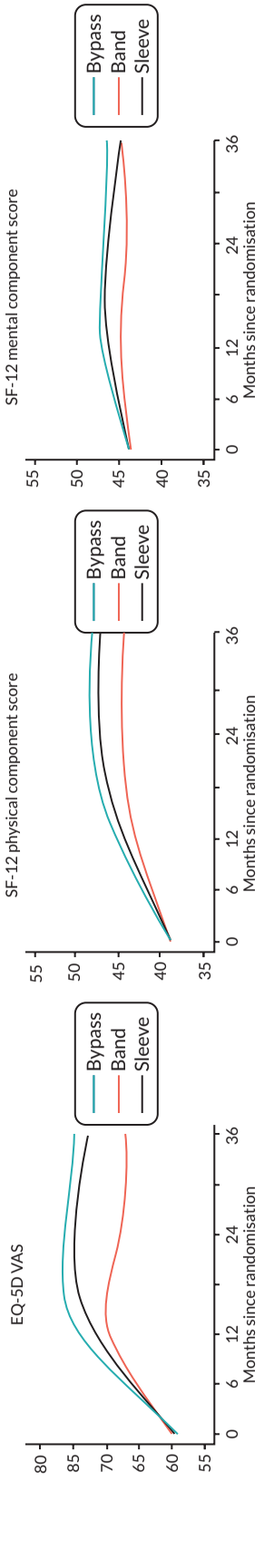

FIGURE 33 Trajectories of generic quality-of-life outcomes over time. Trajectories are estimated from the model and represent the predicted mean scores.

TABLE 54 Proportion of participants with anxiety and depression as assessed using the HADS questionnaire

	Randomised to Bypass (*n* = 462)	Randomised to Band (*n* = 464)	Randomised to Sleeve (*n* = 420)	Overall (*n* = 1346)
	n/*N* (%)	*n*/*N* (%)	*n*/*N* (%)	*n*/*N* (%)
Possible anxiety (score 8–10)				
Baseline	103/430 (24.0%)	88/418 (21.1%)	82/383 (21.4%)	273/1231 (22.2%)
4 weeks postoperative	48/281 (17.1%)	56/256 (21.9%)	47/218 (21.6%)	151/755 (20.0%)
6 months	55/340 (16.2%)	67/305 (22.0%)	63/284 (22.2%)	185/929 (19.9%)
12 months	50/318 (15.7%)	44/275 (16.0%)	50/269 (18.6%)	144/862 (16.7%)
24 months	40/273 (14.7%)	44/238 (18.5%)	33/232 (14.2%)	117/743 (15.7%)
36 months	41/261 (15.7%)	41/252 (16.3%)	36/232 (15.5%)	118/745 (15.8%)
Probable anxiety (score > 10)				
Baseline	101/430 (23.5%)	121/418 (28.9%)	91/383 (23.8%)	313/1231 (25.4%)
4 weeks postoperative	39/281 (13.9%)	58/256 (22.7%)	28/218 (12.8%)	125/755 (16.6%)
6 months	72/340 (21.2%)	74/305 (24.3%)	62/284 (21.8%)	208/929 (22.4%)
12 months	68/318 (21.4%)	78/275 (28.4%)	55/269 (20.4%)	201/862 (23.3%)
24 months	48/273 (17.6%)	63/238 (26.5%)	42/232 (18.1%)	153/743 (20.6%)
36 months	52/261 (19.9%)	60/252 (23.8%)	55/232 (23.7%)	167/745 (22.4%)
Possible depression (score 8–10)				
Baseline	117/431 (27.1%)	103/418 (24.6%)	97/386 (25.1%)	317/1235 (25.7%)
4 weeks postoperative	45/277 (16.2%)	42/253 (16.6%)	28/221 (12.7%)	115/751 (15.3%)
6 months	70/340 (20.6%)	52/298 (17.4%)	57/284 (20.1%)	179/922 (19.4%)
12 months	34/318 (10.7%)	46/276 (16.7%)	39/272 (14.3%)	119/866 (13.7%)
24 months	35/279 (12.5%)	34/243 (14.0%)	31/235 (13.2%)	100/757 (13.2%)
36 months	29/261 (11.1%)	40/252 (15.9%)	28/231 (12.1%)	97/744 (13.0%)

TABLE 54 Proportion of participants with anxiety and depression as assessed using the HADS questionnaire (*continued*)

	Randomised to Bypass (*n* = 462)	Randomised to Band (*n* = 464)	Randomised to Sleeve (*n* = 420)	Overall (*n* = 1346)
	n/*N* (%)	*n*/*N* (%)	*n*/*N* (%)	*n*/*N* (%)
Probable depression (score > 10)				
Baseline	112/431 (26.0%)	103/418 (24.6%)	90/386 (23.3%)	305/1235 (24.7%)
4 weeks postoperative	33/277 (11.9%)	47/253 (18.6%)	23/221 (10.4%)	103/751 (13.7%)
6 months	57/340 (16.8%)	63/298 (21.1%)	52/284 (18.3%)	172/922 (18.7%)
12 months	49/318 (15.4%)	59/276 (21.4%)	36/272 (13.2%)	144/866 (16.6%)
24 months	30/279 (10.8%)	43/243 (17.7%)	31/235 (13.2%)	104/757 (13.7%)
36 months	29/261 (11.1%)	43/252 (17.1%)	32/231 (13.9%)	104/744 (14.0%)

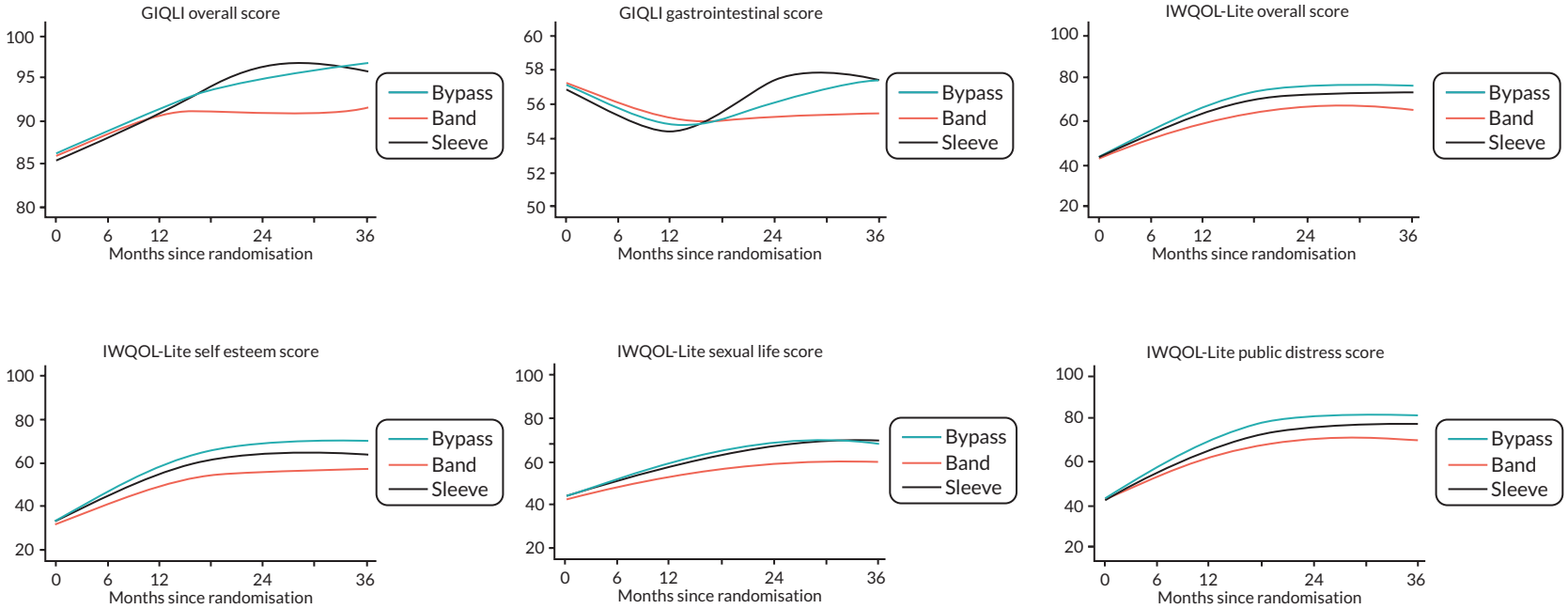

FIGURE 34 Trajectories of disease-specific quality-of-life outcomes over time. Trajectories are estimated from the model and represent the predicted mean scores.

TABLE 55 Quality-of-life questionnaire responses

	Randomised to Bypass (*n* = 462)	Randomised to Band (*n* = 464)	Randomised to Sleeve (*n* = 420)	Overall (*n* = 1346)
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
SF-12 physical function				
Baseline[a]	39.1 (10.4)	38.8 (10.2)	39.3 (10.2)	39.1 (10.3)
4 weeks postoperative[b]	41.8 (10.8)	39.8 (10.3)	42.2 (11.0)	41.2 (10.7)
6 months[c]	42.4 (11.1)	40.6 (10.8)	41.5 (11.3)	41.5 (11.1)
12 months[d]	46.6 (11.7)	42.9 (11.5)	45.3 (11.4)	45.0 (11.6)
24 months[e]	49.1 (10.6)	44.5 (11.4)	47.1 (11.0)	47.0 (11.2)
36 months[f]	48.3 (10.9)	44.6 (12.0)	46.8 (11.1)	46.6 (11.4)
SF-12 role limitation (physical)				
Baseline[g]	39.7 (10.9)	39.2 (10.4)	39.8 (10.9)	39.6 (10.7)
4 weeks postoperative[h]	39.9 (10.7)	40.0 (10.1)	39.9 (10.3)	39.9 (10.3)
6 months[i]	43.1 (11.0)	41.8 (11.3)	42.4 (11.6)	42.5 (11.3)
12 months[j]	46.8 (11.7)	44.0 (11.2)	45.2 (11.6)	45.4 (11.6)
24 months[k]	48.4 (10.9)	44.8 (11.1)	47.4 (10.5)	46.9 (11.0)
36 months[l]	48.5 (10.8)	45.0 (11.6)	46.6 (11.0)	46.7 (11.2)
SF-12 bodily pain				
Baseline[m]	40.2 (12.2)	39.6 (12.1)	40.0 (12.1)	39.9 (12.1)
4 weeks postoperative[n]	42.5 (11.0)	40.2 (11.0)	40.1 (11.5)	41.0 (11.2)
6 months[o]	42.9 (12.1)	41.5 (12.4)	41.9 (12.6)	42.1 (12.3)
12 months[p]	46.2 (12.4)	43.1 (12.4)	44.2 (12.2)	44.6 (12.4)
24 months[q]	47.0 (11.8)	42.5 (12.9)	46.1 (11.7)	45.3 (12.2)
36 months[r]	47.3 (11.7)	43.2 (13.0)	45.1 (12.4)	45.2 (12.4)
SF-12 general health				
Baseline[s]	38.2 (11.0)	37.5 (11.3)	38.5 (11.2)	38.0 (11.2)
4 weeks postoperative[t]	43.6 (11.1)	40.2 (10.7)	43.6 (11.1)	42.4 (11.1)
6 months[u]	42.0 (11.8)	39.9 (11.6)	41.9 (12.1)	41.3 (11.9)
12 months[v]	46.2 (11.7)	41.7 (12.0)	44.5 (12.7)	44.2 (12.2)

continued

TABLE 55 Quality-of-life questionnaire responses (*continued*)

	Randomised to Bypass (*n* = 462)	Randomised to Band (*n* = 464)	Randomised to Sleeve (*n* = 420)	Overall (*n* = 1346)
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
24 months[w]	48.2 (11.5)	42.3 (12.5)	47.1 (11.9)	46.0 (12.2)
36 months[x]	48.0 (11.5)	43.1 (12.2)	46.1 (12.2)	45.7 (12.1)
SF-12 vitality				
Baseline[y]	42.1 (9.8)	41.8 (9.9)	42.9 (9.9)	42.2 (9.9)
4 weeks postoperative[z]	45.5 (10.5)	44.2 (9.6)	45.4 (10.2)	45.1 (10.1)
6 months[aa]	45.1 (10.9)	44.4 (11.1)	45.7 (10.6)	45.0 (10.8)
12 months[bb]	48.4 (11.1)	46.6 (10.9)	49.0 (11.2)	48.0 (11.1)
24 months[cc]	49.9 (11.4)	47.0 (11.9)	49.1 (10.9)	48.7 (11.5)
36 months[dd]	49.0 (11.3)	47.0 (10.7)	49.2 (11.1)	48.4 (11.1)
SF-12 social function				
Baseline[ee]	41.0 (11.6)	40.2 (11.1)	40.9 (11.6)	40.7 (11.4)
4 weeks postoperative[ff]	44.0 (11.1)	42.3 (10.2)	43.8 (10.7)	43.4 (10.7)
6 months[gg]	42.5 (11.8)	42.0 (12.0)	42.6 (12.4)	42.4 (12.0)
12 months[hh]	46.0 (11.6)	42.5 (11.7)	44.9 (11.8)	44.5 (11.8)
24 months[ii]	46.9 (11.7)	43.6 (12.3)	46.3 (11.2)	45.6 (11.8)
36 months[jj]	46.4 (11.6)	44.8 (12.1)	45.2 (12.5)	45.5 (12.0)
SF-12 role limitation (mental)				
Baseline[kk]	40.5 (13.3)	40.4 (13.2)	40.5 (13.3)	40.4 (13.3)
4 weeks postoperative[ll]	44.3 (12.4)	41.6 (11.7)	42.5 (12.9)	42.8 (12.4)
6 months[mm]	42.8 (12.9)	41.5 (13.3)	42.5 (13.4)	42.3 (13.2)
12 months[nn]	45.8 (13.0)	42.2 (13.6)	44.4 (13.1)	44.2 (13.3)
24 months[oo]	46.9 (12.1)	43.7 (13.6)	45.8 (12.2)	45.5 (12.7)
36 months[pp]	46.2 (12.2)	43.9 (13.3)	44.4 (12.7)	44.9 (12.7)
SF-12 mental health				
Baseline[qq]	43.0 (10.7)	42.5 (10.6)	43.6 (10.0)	43.0 (10.5)
4 weeks postoperative[rr]	48.5 (10.4)	45.5 (10.5)	48.4 (9.7)	47.5 (10.3)

TABLE 55 Quality-of-life questionnaire responses (*continued*)

	Randomised to Bypass (*n* = 462)	Randomised to Band (*n* = 464)	Randomised to Sleeve (*n* = 420)	Overall (*n* = 1346)
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
6 months[ss]	45.1 (10.8)	43.6 (11.4)	44.8 (11.0)	44.5 (11.1)
12 months[tt]	47.1 (11.8)	44.0 (11.5)	46.3 (11.1)	45.9 (11.6)
24 months[uu]	47.1 (11.4)	43.8 (12.5)	46.8 (11.1)	46.0 (11.7)
36 months[vv]	47.2 (10.5)	45.2 (12.1)	46.3 (11.6)	46.2 (11.4)
IWQOL – physical				
Baseline[ww]	43.1 (24.6)	42.7 (24.0)	42.5 (23.9)	42.8 (24.2)
4 weeks postoperative[xx]	59.6 (24.1)	52.9 (22.9)	59.5 (23.3)	57.3 (23.6)
6 months[yy]	57.2 (29.3)	53.0 (25.3)	56.8 (28.2)	55.7 (27.8)
12 months[zz]	72.0 (26.5)	62.1 (26.2)	68.8 (25.7)	67.9 (26.5)
24 months[aaa]	80.1 (23.0)	69.5 (24.2)	75.7 (22.6)	75.4 (23.6)
36 months[bbb]	80.5 (22.4)	67.8 (26.4)	76.0 (21.6)	74.8 (24.2)
IWQOL – work				
Baseline[ccc]	59.6 (29.0)	57.2 (27.2)	61.1 (26.0)	59.2 (27.5)
4 weeks postoperative[ddd]	65.9 (27.2)	60.9 (26.1)	67.1 (24.4)	64.5 (26.1)
6 months[eee]	68.3 (29.0)	63.2 (27.3)	67.6 (27.0)	66.5 (27.9)
12 months[fff]	78.2 (27.2)	72.2 (25.6)	77.2 (25.2)	76.0 (26.2)
24 months[ggg]	86.2 (23.4)	77.1 (25.9)	82.9 (22.5)	82.3 (24.2)
36 months[hhh]	86.9 (19.4)	77.9 (26.7)	84.6 (20.9)	83.2 (22.8)
GIQLI – emotional				
Baseline[iii]	8.8 (3.8)	8.5 (3.6)	8.5 (3.5)	8.6 (3.6)
4 weeks postoperative[jjj]	11.9 (3.4)	10.5 (3.3)	11.5 (3.3)	11.3 (3.4)
6 months[kkk]	10.6 (4.1)	9.7 (3.9)	10.0 (3.9)	10.1 (4.0)
12 months[lll]	12.0 (3.9)	10.4 (3.9)	11.6 (3.9)	11.4 (3.9)
24 months[mmm]	12.7 (3.5)	11.0 (4.2)	12.1 (3.8)	12.0 (3.9)
36 months[nnn]	12.7 (3.6)	11.1 (4.1)	11.7 (3.6)	11.8 (3.8)

continued

TABLE 55 Quality-of-life questionnaire responses (*continued*)

	Randomised to Bypass (*n* = 462)	Randomised to Band (*n* = 464)	Randomised to Sleeve (*n* = 420)	Overall (*n* = 1346)
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
GIQLI – social				
Baseline[ooo]	7.2 (2.6)	7.0 (2.6)	7.1 (2.6)	7.1 (2.6)
4 weeks postoperative[ppp]	8.7 (2.7)	8.2 (2.8)	8.7 (2.9)	8.6 (2.8)
6 months[qqq]	7.7 (2.6)	7.7 (2.5)	7.6 (2.7)	7.7 (2.6)
12 months[rrr]	7.8 (2.6)	7.7 (2.5)	8.1 (2.6)	7.8 (2.6)
24 months[sss]	8.0 (2.4)	8.0 (2.6)	8.3 (2.4)	8.1 (2.5)
36 months[ttt]	8.2 (2.6)	8.1 (2.6)	8.7 (2.5)	8.3 (2.6)
GIQLI – physical				
Baseline[uuu]	9.7 (5.9)	9.2 (5.4)	9.7 (5.5)	9.5 (5.6)
4 weeks postoperative[vvv]	12.7 (6.1)	11.9 (5.6)	11.9 (5.7)	12.2 (5.8)
6 months[www]	11.9 (6.3)	11.5 (6.3)	11.6 (6.5)	11.7 (6.4)
12 months[xxx]	14.5 (6.9)	13.2 (6.7)	14.3 (6.7)	14.0 (6.8)
24 months[yyy]	16.0 (6.6)	13.6 (6.8)	15.4 (6.3)	15.0 (6.6)
36 months[zzz]	16.3 (6.2)	14.2 (6.8)	15.4 (6.5)	15.3 (6.5)
GIQLI – treatment				
Baseline[aaaa]	2.6 (1.4)	2.6 (1.4)	2.8 (1.3)	2.7 (1.4)
4 weeks postoperative[bbbb]	2.8 (1.2)	2.8 (1.1)	2.9 (1.1)	2.8 (1.2)
6 months[cccc]	2.9 (1.3)	2.7 (1.3)	2.8 (1.3)	2.8 (1.3)
12 months[dddd]	3.1 (1.2)	3.0 (1.2)	3.1 (1.2)	3.1 (1.2)
24 months[eeee]	3.4 (1.1)	2.9 (1.3)	3.4 (0.9)	3.2 (1.1)
36 months[ffff]	3.4 (1.0)	3.0 (1.4)	3.3 (1.1)	3.2 (1.2)

Missing data (Bypass, Band, Sleeve):
a 79 participants (24, 32, 23).
b 553 participants (175, 195, 183).
c 382 participants (114, 149, 119).
d 434 participants (126, 174, 134).
e 556 participants (171, 211, 174).

TABLE 55 Quality-of-life questionnaire responses (*continued*)

f 574 participants (191, 203, 180).
g 81 participants (23, 34, 24).
h 557 participants (175, 196, 186).
i 384 participants (114, 150, 120).
j 435 participants (127, 173, 135).
k 559 participants (171, 212, 176).
l 574 participants (191, 203, 180).
m 80 participants (24, 31, 25).
n 555 participants (176, 195, 184).
o 383 participants (115, 149, 119).
p 435 participants (128, 173, 134).
q 555 participants (168, 212, 175).
r 573 participants (191, 205, 177).
s 80 participants (24, 33, 23).
t 554 participants (176, 194, 184).
u 384 participants (115, 149, 120).
v 434 participants (127, 173, 134).
w 554 participants (170, 211, 173).
x 572 participants (191, 204, 177).
y 93 participants (29, 35, 29).
z 565 participants (177, 199, 189).
aa393 participants (119, 154, 120).
bb 447 participants (129, 179, 139).
cc 563 participants (171, 216, 176).
dd 582 participants (193, 210, 179).
ee 83 participants (26, 31, 26).
ff 551 participants (175, 193, 183).
gg 381 participants (115, 148, 118).
hh 436 participants (128, 173, 135).
ii 554 participants (169, 211, 174).
jj 579 participants (193, 207, 179).
kk 81 participants (24, 34, 23).
ll 555 participants (175, 195, 185).
mm 386 participants (114, 151, 121).
nn 434 participants (126, 173, 135).
oo 560 participants (171, 213, 176).
pp 575 participants (192, 204, 179).
qq 79 participants (24, 31, 24).
rr 551 participants (175, 193, 183).
ss 381 participants (115, 148, 118).
tt 436 participants (128, 173, 135).
uu 553 participants (168, 210, 175).
vv 573 participants (191, 205, 177).
ww 75 participants (22, 30, 23).
xx 545 participants (172, 191, 182).
yy 387 participants (118, 152, 117).
zz 431 participants (124, 172, 135).
aaa 547 participants (167, 211, 169).
bbb 565 participants (190, 199, 176).

continued

TABLE 55 Quality-of-life questionnaire responses (*continued*)

ccc 201 participants (59, 75, 67).
ddd 616 participants (196, 218, 202).
eee 468 participants (138, 186, 144).
fff 494 participants (135, 199, 160).
ggg 608 participants (185, 233, 190).
hhh 621 participants (203, 222, 196).
iii 80 participants (24, 31, 25).
jjj 551 participants (174, 197, 180).
kkk 386 participants (117, 153, 116).
lll 434 participants (127, 173, 134).
mmm 548 participants (168, 209, 171).
nnn 567 participants (188, 204, 175).
ooo 133 participants (42, 46, 45).
ppp 596 participants (193, 210, 193).
qqq 433 participants (134, 167, 132).
rrr 494 participants (146, 194, 154).
sss 589 participants (183, 222, 184).
ttt 620 participants (199, 225, 196).
uuu 87 participants (25, 34, 28).
vvv 553 participants (174, 198, 181).
www 387 participants (118, 153, 116).
xxx 442 participants (130, 174, 138).
yyy 558 participants (172, 212, 174).
zzz 578 participants (190, 206, 182).
aaaa 109 participants (32, 45, 32).
bbbb 556 participants (175, 200, 181).
cccc 402 participants (124, 159, 119).
dddd 442 participants (130, 176, 136).
eeee 555 participants (169, 211, 175).
ffff 578 participants (191, 208, 179).

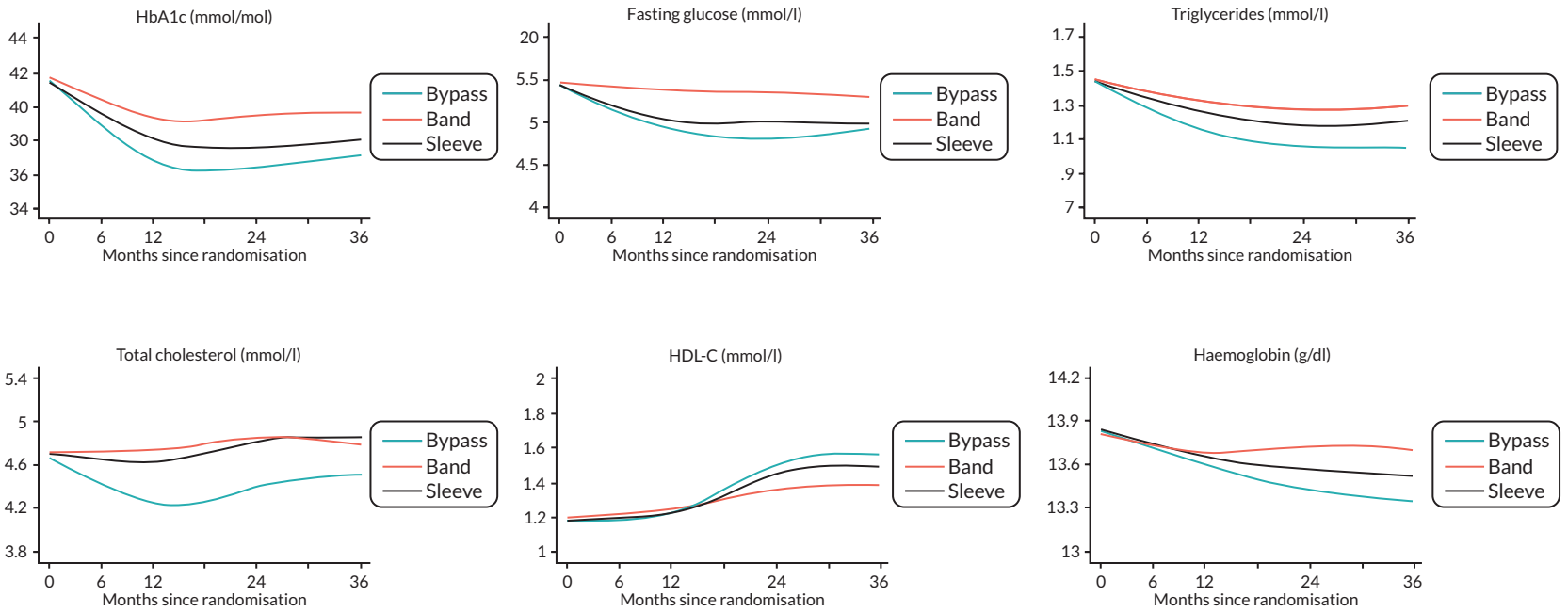

FIGURE 35 Trajectories of outcomes measured in the blood over time – 1. Trajectories are estimated from the model and represent the predicted mean scores.

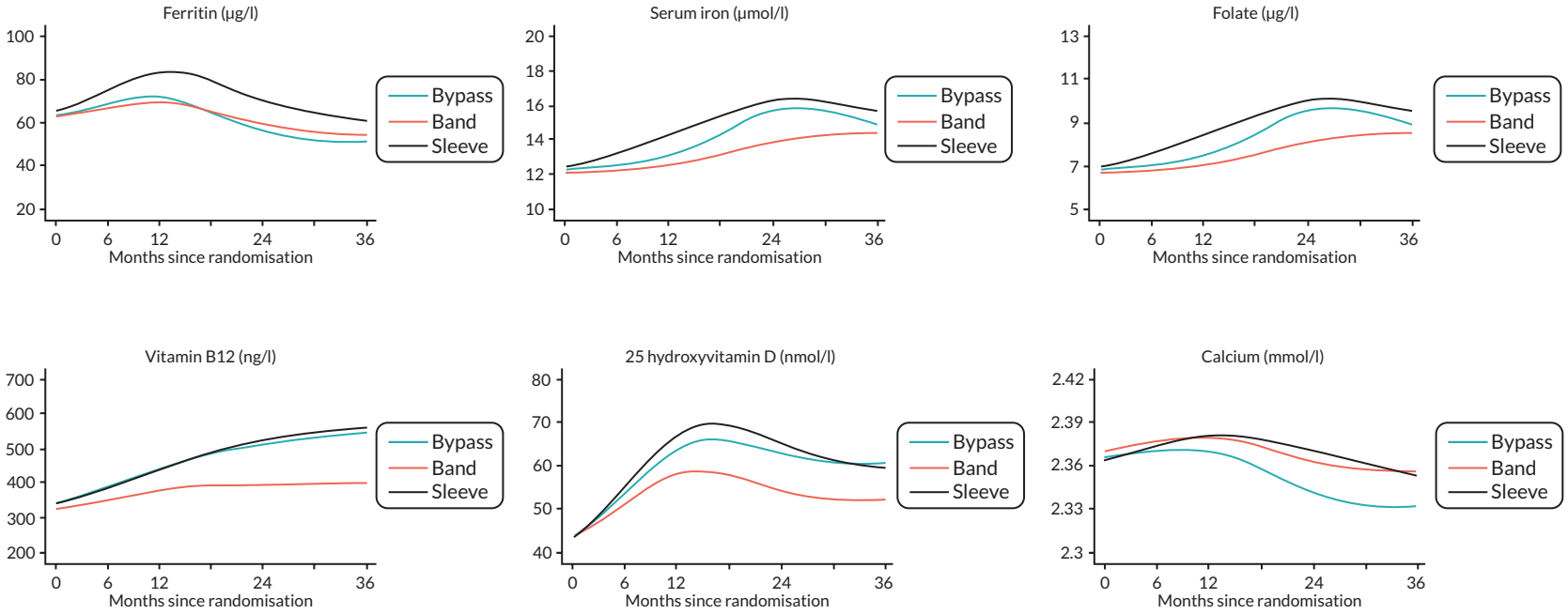

FIGURE 36 Trajectories of outcomes measured in the blood over time – 2. Trajectories are estimated from the model and represent the predicted mean scores.

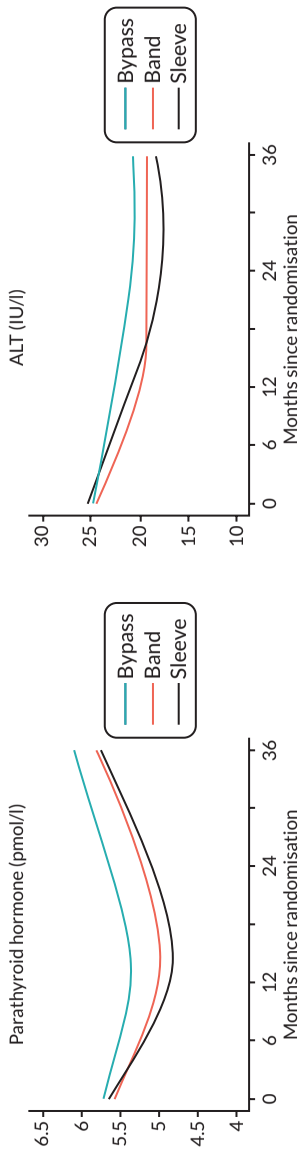

FIGURE 37 Trajectories of outcomes measured in the blood over time – 3. Trajectories are estimated from the model and represent the predicted mean scores.

TABLE 56 Proportions of participants with HbA1c < 48 mmol/mol and not taking of antidiabetic medication, by diabetic status at baseline

	Randomised to Bypass (*n* = 462)	Randomised to Band (*n* = 464)	Randomised to Sleeve (*n* = 420)	Overall (*n* = 1346)
Participants without diabetes at baseline				
HbA1c (mmol/mol)				
Baseline[a]	37.0 (35.0, 40.0)	38.0 (35.0, 41.0)	38.0 (35.0, 41.0)	38.0 (35.0, 41.0)
4 weeks postoperative[b]	36.0 (33.0, 38.0)	36.0 (34.0, 39.0)	36.0 (33.0, 38.0)	36.0 (33.0, 38.0)
6 months[c]	36.0 (32.0, 39.0)	37.0 (34.0, 40.0)	36.0 (33.0, 39.0)	36.0 (33.0, 39.0)
12 months[d]	34.0 (32.0, 37.0)	36.0 (33.0, 39.0)	35.0 (32.0, 38.0)	35.0 (32.0, 38.0)
24 months[e]	34.5 (32.0, 37.0)	36.0 (33.0, 39.0)	35.0 (32.0, 37.0)	35.0 (33.0, 38.0)
36 months[f]	35.0 (33.0, 37.0)	36.0 (34.0, 39.0)	35.0 (33.0, 38.0)	35.0 (33.0, 38.0)
HbA1c < 48 mmol/mol				
Baseline	290/300 (96.7%)	300/309 (97.1%)	288/298 (96.6%)	878/907 (96.8%)
4 weeks postoperative	246/247 (99.6%)	254/256 (99.2%)	243/245 (99.2%)	743/748 (99.3%)
6 months	265/271 (97.8%)	248/253 (98.0%)	262/267 (98.1%)	775/791 (98.0%)
12 months	254/259 (98.1%)	245/247 (99.2%)	227/233 (97.4%)	726/739 (98.2%)
24 months	218/222 (98.2%)	197/202 (97.5%)	192/193 (99.5%)	607/617 (98.4%)
36 months	203/205 (99.0%)	202/205 (98.5%)	183/185 (98.9%)	588/595 (98.8%)
HbA1c < 48 mmol/mol and not taking antidiabetic medication				
Baseline	248/266 (93.2%)	258/275 (93.8%)	249/260 (95.8%)	755/801 (94.3%)
4 weeks postoperative	206/214 (96.3%)	222/229 (96.9%)	210/215 (97.7%)	638/658 (97.0%)
6 months	235/246 (95.5%)	219/227 (96.5%)	234/237 (98.7%)	688/710 (96.9%)
12 months	226/238 (95.0%)	218/223 (97.8%)	206/212 (97.2%)	650/673 (96.6%)
24 months	192/199 (96.5%)	181/187 (96.8%)	164/167 (98.2%)	537/553 (97.1%)
36 months	180/184 (97.8%)	169/180 (93.9%)	157/158 (99.4%)	506/522 (96.9%)

TABLE 56 Proportions of participants with HbA1c < 48 mmol/mol and not taking of antidiabetic medication, by diabetic status at baseline (*continued*)

	Randomised to Bypass (*n* = 462)	Randomised to Band (*n* = 464)	Randomised to Sleeve (*n* = 420)	Overall (*n* = 1346)
Participants with diabetes at baseline				
HbA1c (mmol/mol)				
Baseline[g]	53.0 (44.0, 64.0)	52.0 (44.0, 64.0)	51.0 (44.0, 63.0)	52.0 (44.0, 64.0)
4 weeks postoperative[h]	44.0 (39.0, 54.0)	47.0 (41.0, 57.0)	44.0 (39.0, 49.0)	45.0 (39.5, 54.0)
6 months[i]	44.0 (39.0, 56.0)	48.0 (41.5, 59.0)	48.0 (40.0, 56.0)	47.0 (40.0, 57.0)
12 months[j]	41.0 (36.0, 47.5)	49.0 (40.0, 63.0)	43.0 (38.0, 51.5)	44.0 (38.0, 57.0)
24 months[k]	40.0 (35.0, 46.0)	48.5 (40.0, 65.0)	43.0 (39.0, 52.0)	43.0 (37.0, 54.0)
36 months[l]	40.0 (36.0, 46.0)	48.0 (40.0, 64.0)	44.0 (39.0, 56.0)	43.0 (38.0, 56.0)
HbA1c < 48 mmol/mol				
Baseline	53/147 (36.1%)	50/141 (35.5%)	40/115 (34.8%)	143/403 (35.5%)
4 weeks postoperative	80/127 (63.0%)	59/116 (50.9%)	58/93 (62.4%)	197/336 (58.6%)
6 months	79/133 (59.4%)	59/124 (47.6%)	50/101 (49.5%)	188/358 (52.5%)
12 months	99/132 (75.0%)	54/125 (43.2%)	64/96 (66.7%)	217/353 (61.5%)
24 months	90/117 (76.9%)	51/110 (46.4%)	57/86 (66.3%)	198/313 (63.3%)
36 months	90/118 (76.3%)	51/103 (49.5%)	50/81 (61.7%)	191/302 (63.2%)
HbA1c < 48 mmol/mol and not taking antidiabetic medication				
Baseline	11/146 (7.5%)	16/140 (11.4%)	10/113 (8.8%)	37/399 (9.3%)
4 weeks postoperative	58/111 (52.3%)	32/109 (29.4%)	38/83 (45.8%)	128/303 (42.2%)
6 months	51/124 (41.1%)	27/107 (25.2%)	32/93 (34.4%)	110/324 (34.0%)
12 months	68/120 (56.7%)	32/112 (28.6%)	45/87 (51.7%)	145/319 (45.5%)
24 months	61/110 (55.5%)	29/99 (29.3%)	42/78 (53.8%)	132/287 (46.0%)
36 months	64/107 (59.8%)	31/88 (35.2%)	33/72 (45.8%)	128/267 (47.9%)

Missing data (Bypass, Band, Sleeve):
a 26 participants (10, 11, 5).
b 185 participants (63, 64, 58).
c 142 participants (39, 67, 36).
d 194 participants (51, 73, 70).
e 316 participants (88, 118, 110).

continued

TABLE 56 Proportions of participants with HbA1c < 48 mmol/mol and not taking of antidiabetic medication, by diabetic status at baseline (*continued*)

f 338 participants (105, 115, 118).
g 10 participants (5, 3, 2).
h 77 participants (25, 28, 24).
i 55 participants (19, 20, 16).
j 60 participants (20, 19, 21).
k 100 participants (35, 34, 31).
l 111 participants (34, 41, 36).

Note
Data are *n*/*N*(%) or median (IQR). The diabetes subgroup includes participants with glucose impairment, pre-diabetes, diet-controlled diabetes and medically controlled diabetes.

TABLE 57 Antidiabetic medication taken during trial participation

Medication taken	Randomised to Bypass (*n* = 462)	Randomised to Band (*n* = 464)	Randomised to Sleeve (*n* = 420)	Overall (*n* = 1346)
Metformin included				
Took antidiabetic medication during trial participation	148/462 (32.0%)	145/464 (31.3%)	117/420 (27.9%)	410/1346 (30.5%)
Time taking medication (months)	11.9 (2.8, 35.1)	21.3 (5.5, 35.7)	10.1 (4.0, 25.8)	12.7 (3.8, 35.1)
Metformin excluded				
Took antidiabetic medication during trial participation	86/462 (18.6%)	88/464 (19.0%)	68/420 (16.2%)	242/1346 (18.0%)
Time taking medication (months)	7.6 (3.4, 23.5)	12.4 (4.2, 28.8)	7.3 (3.4, 23.9)	9.3 (3.4, 24.6)

Note
Data are *n*/*N* (%) or median (IQR). All participants are included; duration is based on reported duration(s), no adjustment has been made for participants without full follow-up to 3 years (e.g. if a participant is reported as on medication at 12 months and no further follow-up is provided, the time beyond 12 months is not considered), so estimates are conservative. Discontinuous periods of taking medication are summed.

TABLE 58 Proportions of participants with vitamin D ≤ 50 nmol/l

Time point	Randomised to Bypass (*n* = 462)	Randomised to Band (*n* = 464)	Randomised to Sleeve (*n* = 420)	Overall (*n* = 1346)
Vitamin D ≤ 50 nmol/l				
Baseline	272/443 (61.4%)	273/448 (60.9%)	250/412 (60.7%)	795/1303 (61.0%)
4 weeks postoperative	118/367 (32.2%)	141/367 (38.4%)	88/319 (27.6%)	347/1053 (33.0%)
6 months	129/397 (32.5%)	150/373 (40.2%)	122/358 (34.1%)	401/1128 (35.5%)
12 months	103/378 (27.2%)	125/352 (35.5%)	83/328 (25.3%)	311/1058 (29.4%)
24 months	81/310 (26.1%)	103/283 (36.4%)	56/262 (21.4%)	240/855 (28.1%)
36 months	76/285 (26.7%)	106/256 (41.4%)	70/238 (29.4%)	252/779 (32.3%)

TABLE 59 Markers measured in the blood

Timepoint	Randomised to Bypass (*n* = 462)	Randomised to Band (*n* = 464)	Randomised to Sleeve (*n* = 420)	Overall (*n* = 1346)
Haematocrit (l/l)	***Medium (IQR)***	***Medium (IQR)***	***Medium (IQR)***	***Medium (IQR)***
Baseline[a]	0.42 (0.40–0.45)	0.42 (0.40–0.44)	0.42 (0.40–0.44)	0.42 (0.40–0.44)
4 weeks postoperative[b]	0.42 (0.40–0.44)	0.41 (0.39–0.44)	0.42 (0.39–0.44)	0.41 (0.39–0.44)
6 months[c]	0.42 (0.40–0.44)	0.42 (0.40–0.44)	0.42 (0.39–0.44)	0.42 (0.40–0.44)
12 months[d]	0.41 (0.39–0.43)	0.42 (0.39–0.44)	0.41 (0.39–0.44)	0.41 (0.39–0.44)
24 months[e]	0.41 (0.39–0.43)	0.42 (0.39–0.44)	0.41 (0.39–0.43)	0.41 (0.39–0.44)
36 months[f]	0.41 (0.39–0.43)	0.41 (0.39–0.43)	0.41 (0.39–0.44)	0.41 (0.39–0.43)
Mean cell haemoglobin (pg)	***Mean (SD)***	***Mean (SD)***	***Mean (SD)***	***Mean (SD)***
Baseline[g]	28.8 (2.1)	28.8 (2.0)	29.0 (4.6)	28.9 (3.1)
4 weeks postoperative[h]	29.0 (1.9)	29.0 (3.8)	29.3 (5.0)	29.1 (3.7)
6 months[i]	29.0 (2.1)	28.6 (2.8)	28.9 (2.3)	28.9 (2.4)
12 months[j]	29.4 (2.1)	29.1 (1.7)	29.6 (2.0)	29.4 (1.9)
24 months[k]	29.9 (3.9)	29.3 (2.0)	29.7 (2.2)	29.7 (2.9)
36 months[l]	30.0 (3.7)	29.4 (2.0)	29.6 (2.5)	29.7 (2.9)
Mean cell volume (fl)	***Medium (IQR)***	***Medium (IQR)***	***Medium (IQR)***	***Medium (IQR)***
Baseline[m]	88.4 (84.9–91.3)	88.0 (84.6–91.2)	88.1 (84.3–91.5)	88.2 (84.6–91.3)
4 weeks postoperative[n]	88.9 (85.5–92.2)	88.0 (84.9–91.1)	88.0 (84.8–91.0)	88.2 (85.0–91.5)
6 months[o]	89.0 (85.7–92.4)	88.0 (84.7–91.0)	88.6 (84.9–92.0)	88.5 (85.0–91.9)
12 months[p]	89.9 (86.4–92.8)	88.3 (85.2–91.5)	89.7 (86.2–92.6)	89.3 (86.0–92.3)
24 months[q]	91.5 (88.0–94.5)	89.3 (85.7–92.6)	90.5 (87.3–93.6)	90.5 (87.0–93.6)
36 months[r]	91.1 (87.8–94.2)	89.2 (86.0–92.3)	90.5 (87.4–93.5)	90.4 (87.0–93.7)
Albumin (g/l)	***Mean (SD)***	***Mean (SD)***	***Mean (SD)***	***Mean (SD)***
Baseline[s]	40.4 (3.8)	40.3 (3.8)	40.0 (3.8)	40.2 (3.8)
4 weeks postoperative[t]	40.2 (3.6)	40.4 (3.4)	39.7 (3.6)	40.1 (3.5)
6 months[u]	39.8 (3.5)	40.1 (3.6)	39.6 (3.6)	39.8 (3.6)
12 months[v]	39.4 (4.1)	40.2 (3.5)	39.6 (3.9)	39.7 (3.9)
24 months[w]	39.7 (3.7)	40.1 (3.5)	39.6 (3.8)	39.8 (3.7)

continued

TABLE 59 Markers measured in the blood (*continued*)

Timepoint	Randomised to Bypass (*n* = 462)	Randomised to Band (*n* = 464)	Randomised to Sleeve (*n* = 420)	Overall (*n* = 1346)
36 months[x]	39.7 (3.5)	40.1 (3.8)	39.6 (3.5)	39.8 (3.6)
Bilirubin (µmol/l)	***Mean (SD)***	***Mean (SD)***	***Mean (SD)***	***Mean (SD)***
Baseline[y]	9.5 (4.7)	9.5 (4.7)	9.8 (4.4)	9.6 (4.6)
4 weeks postoperative[z]	11.9 (5.5)	10.3 (4.9)	11.7 (4.9)	11.3 (5.2)
6 months[aa]	10.8 (5.6)	9.8 (5.3)	10.9 (4.7)	10.5 (5.3)
12 months[bb]	11.0 (5.1)	10.1 (4.7)	11.5 (6.6)	10.8 (5.5)
24 months[cc]	11.2 (5.9)	10.2 (5.0)	10.9 (6.8)	10.8 (5.9)
36 months[dd]	10.7 (5.8)	10.2 (5.9)	10.5 (5.9)	10.5 (5.8)
Total protein (g/l)	***Mean (SD)***	***Mean (SD)***	***Mean (SD)***	***Mean (SD)***
Baseline[ee]	72 (69, 74)	72 (69, 75)	72 (69, 75)	72 (69, 75)
4 weeks postoperative[ff]	69 (66, 72)	70 (68, 73)	69 (66, 72)	69 (67, 72)
6 months[gg]	69 (66, 72)	71 (68, 74)	70 (67, 73)	70 (67, 73)
12 months[hh]	68 (65, 71)	71 (68, 73)	70 (67, 73)	70 (66, 73)
24 months[ii]	68 (65, 71)	70 (67, 73)	69 (67, 72)	69 (67, 72)
36 months[jj]	68 (65, 71)	70 (67, 73)	70 (67, 73)	69 (67, 72)
LDL-C (mmol/l)	***Mean (SD)***	***Mean (SD)***	***Mean (SD)***	***Mean (SD)***
Baseline[kk]	2.8 (2.2, 3.4)	2.9 (2.2, 3.5)	2.9 (2.3, 3.5)	2.9 (2.3, 3.5)
4 weeks postoperative[ll]	2.4 (1.9, 2.9)	2.8 (2.2, 3.3)	2.8 (2.2, 3.4)	2.6 (2.0, 3.2)
6 months[mm]	2.5 (1.9, 3.2)	2.8 (2.2, 3.5)	2.8 (2.3, 3.5)	2.7 (2.1, 3.4)
12 months[nn]	2.4 (2.0, 3.0)	2.8 (2.2, 3.4)	2.8 (2.2, 3.5)	2.7 (2.1, 3.3)
24 months[oo]	2.4 (1.8, 2.9)	2.8 (2.2, 3.4)	2.8 (2.2, 3.4)	2.6 (2.0, 3.3)
36 months[pp]	2.3 (1.9, 2.9)	2.8 (2.2, 3.4)	3.0 (2.2, 3.5)	2.6 (2.0, 3.3)
Phosphate (mmol/l)	***Medium (IQR)***	***Medium (IQR)***	***Medium (IQR)***	***Medium (IQR)***
Baseline[qq]	1.1 (1.0–1.2)	1.1 (1.0–1.2)	1.1 (0.9–1.2)	1.1 (1.0–1.2)
4 weeks postoperative[rr]	1.1 (1.0–1.2)	1.1 (1.0–1.2)	1.1 (0.9–1.2)	1.1 (1.0–1.2)
6 months[ss]	1.1 (1.0–1.2)	1.1 (1.0–1.2)	1.1 (1.0–1.2)	1.1 (1.0–1.2)
12 months[tt]	1.2 (1.0–1.3)	1.1 (1.0–1.2)	1.1 (1.0–1.2)	1.1 (1.0–1.2)
24 months[uu]	1.1 (1.0–1.3)	1.1 (1.0–1.2)	1.1 (1.0–1.2)	1.1 (1.0–1.2)

Timepoint	Randomised to Bypass (*n* = 462)	Randomised to Band (*n* = 464)	Randomised to Sleeve (*n* = 420)	Overall (*n* = 1346)
36 months[vv]	1.1 (1.0–1.2)	1.1 (1.0–1.2)	1.1 (1.0–1.2)	1.1 (1.0–1.2)
Potassium (mmol/l)	***Medium (IQR)***	***Medium (IQR)***	***Medium (IQR)***	***Medium (IQR)***
Baseline[ww]	4.3 (4.1–4.5)	4.3 (4.1–4.5)	4.3 (4.1–4.5)	4.3 (4.1–4.5)
4 weeks postoperative[xx]	4.2 (3.9–4.4)	4.2 (4.0–4.5)	4.2 (4.0–4.5)	4.2 (4.0–4.4)
6 months[yy]	4.3 (4.1–4.5)	4.3 (4.1–4.5)	4.3 (4.1–4.5)	4.3 (4.1–4.5)
12 months[zz]	4.3 (4.1–4.5)	4.3 (4.1–4.5)	4.3 (4.1–4.5)	4.3 (4.1–4.5)
24 months[aaa]	4.3 (4.1–4.5)	4.3 (4.1–4.6)	4.3 (4.1–4.5)	4.3 (4.1–4.5)
36 months[bbb]	4.3 (4.0–4.5)	4.3 (4.1–4.5)	4.3 (4.1–4.5)	4.3 (4.1–4.5)
Sodium (mmol/l)	***Medium (IQR)***	***Medium (IQR)***	***Medium (IQR)***	***Medium (IQR)***
Baseline[ccc]	139 (138–141)	139 (138–141)	140 (138–141)	139 (138–141)
4 weeks postoperative[ddd]	141 (139–142)	140 (139–141)	141 (139–142)	140 (139–142)
6 months[eee]	140 (139–142)	140 (138–141)	140 (139–142)	140 (139–141)
12 months[fff]	140 (139–142)	140 (138–141)	140 (139–142)	140 (139–142)
24 months[ggg]	140 (139–142)	140 (138–141)	140 (139–142)	140 (139–142)
36 months[hhh]	140 (139–142)	140 (139–141)	140 (139–141)	140 (139–141)
Urea (mmol/l)	***Medium (IQR)***	***Medium (IQR)***	***Medium (IQR)***	***Medium (IQR)***
Baseline[iii]	4.9 (3.9–5.8)	4.6 (3.9–5.7)	4.7 (4.0–5.7)	4.8 (3.9–5.8)
4 weeks postoperative[jjj]	3.7 (3.0–4.6)	4.1 (3.4–5.0)	3.8 (3.0–4.8)	3.9 (3.1–4.8)
6 months[kkk]	4.2 (3.5–5.2)	4.6 (3.7–5.6)	4.3 (3.5–5.5)	4.4 (3.6–5.4)
12 months[lll]	4.2 (3.5–5.3)	4.6 (3.7–5.4)	4.6 (3.8–5.5)	4.5 (3.6–5.4)
24 months[mmm]	4.6 (3.8–5.4)	4.4 (3.7–5.7)	4.9 (3.9–5.8)	4.6 (3.7–5.7)
36 months[nnn]	4.5 (3.8–5.5)	4.5 (3.6–5.6)	4.7 (3.9–5.7)	4.6 (3.8–5.6)

Missing data (Bypass, Band, Sleeve):
a 29 participants (15, 7, 7).
b 227 participants (76, 81, 70).
c 153 participants (41, 74, 38).
d 214 participants (59, 83, 72).
e 336 participants (99, 120, 117).
f 382 participants (110, 137, 135).
g 22 participants (11, 6, 5).

continued

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TABLE 59 Markers measured in the blood (*continued*)

h 223 participants (75, 80, 68).
i 147 participants (41, 71, 35).
j 207 participants (59, 81, 67).
k 325 participants (97, 115, 113).
l 372 participants (110, 132, 130).
m 22 participants (11, 6, 5).
n 223 participants (75, 80, 68).
o 147 participants (41, 71, 35).
p 205 participants (57, 81, 67).
q 321 participants (95, 114, 112).
r 369 participants (109, 132, 128).
s 18 participants (9, 6, 3).
t 224 participants (72, 81, 71).
u 143 participants (39, 68, 36).
v 191 participants (54, 73, 64).
w 327 participants (96, 119, 112).
x 367 participants (109, 135, 123).
y 25 participants (12, 7, 6).
z 249 participants (80, 90, 79).
aa154 participants (40, 72, 42).
bb 212 participants (60, 82, 70).
cc 355 participants (102, 129, 124).
dd 385 participants (113, 143, 129).
ee 35 participants (15, 14, 6).
ff 252 participants (83, 86, 83).
gg 173 participants (52, 72, 49).
hh 242 participants (72, 90, 80).
ii 428 participants (130, 155, 143).
jj 489 participants (149, 178, 162).
kk 65 participants (26, 23, 16).
ll 325 participants (103, 117, 105).
mm 242 participants (68, 109, 65).
nn 317 participants (95, 118, 104).
oo 528 participants (167, 190, 171).
pp 585 participants (188, 204, 193).
qq 49 participants (19, 21, 9).
rr 271 participants (85, 95, 91).
ss 216 participants (64, 94, 58).
tt 271 participants (78, 102, 91).
uu 485 participants (151, 176, 158).
vv 586 participants (177, 215, 194).
ww 24 participants (13, 8, 3).
xx 225 participants (74, 81, 70).
yy 149 participants (44, 69, 36).
zz 199 participants (55, 78, 66).
aaa 311 participants (88, 112, 111).
bbb 348 participants (100, 125, 123).
ccc 20 participants (11, 6, 3).
ddd 216 participants (71, 78, 67).
eee 141 participants (42, 67, 32).
fff 195 participants (51, 78, 66).

TABLE 59 Markers measured in the blood (*continued*)

ggg 304 participants (87, 109, 108).
hhh 344 participants (99, 124, 121).
iii 21 participants (11, 6, 4).
jjj 226 participants (75, 81, 70).
kkk 158 participants (49, 71, 38).
lll 223 participants (59, 86, 78).
mmm 348 participants (102, 122, 124).
nnn 399 participants (121, 145, 133).

TABLE 60 Dietary nutrient intakes from food at 3 years

Nutrients	Randomised to Bypass (*n* = 462) Median (IQR)	Randomised to Band (*n* = 464) Median (IQR)	Randomised to Sleeve (*n* = 420) Median (IQR)	Overall (*n* = 1346) Median (IQR)
Protein (g)[a]	53.4 (35.3–71.6)	48.8 (29.6–61.2)	42.9 (32.5–58.5)	47.9 (32.4–67.2)
Fat (g)[a]	40.7 (25.8–63.1)	33.6 (22.3–55.0)	37.8 (25.1–55.5)	38.1 (23.5–58.0)
Carbohydrate (g)[a]	120.9 (79.2–177.4)	116.1 (77.8–166.3)	111.9 (76.6–147.4)	116.0 (77.8–170.3)
Starch (g)[b]	51.9 (29.2–85.0)	46.0 (24.8–80.1)	53.2 (35.7–69.8)	50.5 (29.2–79.2)
Total sugar (g)[a]	47.2 (25.8–73.7)	44.6 (26.4–72.3)	41.9 (25.8–74.3)	45.5 (26.0–73.2)
Non-milk extrinsic sugars (g)[c]	5.5 (1.5–13.7)	7.9 (0.8–17.9)	8.3 (2.4–25.0)	7.2 (1.1–16.9)
Glucose (g)[d]	4.2 (1.5–10.2)	4.5 (1.7–10.3)	5.7 (1.9–11.6)	4.5 (1.7–10.7)
Fructose (g)[e]	5.4 (1.5–11.3)	5.0 (1.4–10.7)	4.7 (1.8–11.9)	4.8 (1.5–11.6)
Sucrose (mg)[f]	11.4 (3.1–23.0)	12.1 (4.2–22.9)	10.0 (2.8–18.6)	11.4 (3.4–21.8)
Maltose (g)[g]	1.8 (0.8–3.3)	1.3 (0.6–3.2)	1.5 (0.8–2.2)	1.6 (0.7–3.0)
Lactose (g)[h]	7.8 (3.7–13.5)	6.9 (4.3–13.5)	8.0 (3.7–11.1)	7.6 (4.0–13.0)
Non-starch polysaccharides (g)[i]	7.0 (5.2–10.4)	7.0 (3.9–10.9)	7.5 (4.4–10.3)	7.2 (4.6–10.5)
Saturated fats (g)[a]	15.0 (7.3–23.0)	12.2 (7.3–20.6)	14.1 (8.3–19.9)	13.6 (7.7–21.3)
Monounsaturated fats (g)[a]	13.7 (8.1–20.7)	10.9 (5.9–16.5)	12.4 (7.0–18.6)	12.4 (6.8–19.1)
Polyunsaturated fats (g)[a]	5.0 (2.5–7.1)	4.1 (2.1–6.8)	4.2 (2.5–7.4)	4.5 (2.3–7.1)
Trans fatty acids (g)[j]	0.4 (0.2–1.0)	0.5 (0.2–1.0)	0.4 (0.2–0.7)	0.5 (0.2–0.9)
Cholesterol (mg)[a]	126.7 (68.0–233.7)	88.7 (53.6–199.4)	122.9 (68.1–264.8)	115.6 (60.2–228.7)
Sodium (mg)[a]	1595.5 (1022.5–2364)	1321 (725–1975)	1254.5 (811.5–1756.5)	1349 (807–2132)
Potassium (mg)[a]	1947.5 (1239–2517)	1538 (1184–2207)	1430 (990–1888)	1582 (1158–2319)
Magnesium (mg)[a]	172.5 (121.5–228.5)	157 (109–213)	156.5 (117–209)	162 (113–216)
Phosphorus (mg)[a]	746.5 (556–1024)	723 (487–991)	737.5 (539–953)	743 (532–981)
Copper (mg)[a]	0.6 (0.4–1.0)	0.5 (0.3–1.0)	0.6 (0.4–0.9)	0.6 (0.4–0.9)
Zinc (mg)[a]	4.9 (3.4–7.6)	4.4 (3.1–6.4)	5.1 (3.4–6.8)	4.8 (3.3–6.9)
Chloride (mg)[a]	1815.5 (1014.5–2914.5)	1476 (877–2241)	1326 (1001.5–1997.5)	1534 (969–2491)
Manganese (mg)[a]	1.8 (1.2–2.5)	1.7 (1.1–2.8)	1.8 (1.3–3.0)	1.8 (1.2–2.6)

TABLE 60 Dietary nutrient intakes from food at 3 years (*continued*)

Nutrients	Randomised to Bypass (*n* = 462) Median (IQR)	Randomised to Band (*n* = 464) Median (IQR)	Randomised to Sleeve (*n* = 420) Median (IQR)	Overall (*n* = 1346) Median (IQR)
Selenium (µg)[b]	19.5 (7.9–35.5)	19.5 (9.0–35.0)	19.8 (9.8–39.4)	19.5 (9.0–35.5)
Iodine (µg)[a]	69.0 (36.5–121.8)	67.1 (33.9–115.5)	57.6 (38.9–83.9)	63.1 (36.2–109.8)
Retinol (µg)[k]	120 (50–227)	118 (60–248)	138 (54–302.5)	122 (54–251)
Carotene (µg)[l]	468.5 (140–1151)	349.5 (86–1395)	195 (56–770)	339 (84–1115)
Vitamin D (µg)[m]	0.9 (0.3–1.9)	0.6 (0.2–1.4)	1.3 (0.4–2.6)	0.8 (0.3–1.9)
Thiamine (mg)[a]	0.8 (0.5–1.2)	0.7 (0.5–1.2)	0.8 (0.6–1.3)	0.8 (0.5–1.2)
Riboflavin (mg)[a]	1.0 (0.7–1.5)	1.0 (0.6–1.3)	1.0 (0.7–1.3)	1.0 (0.7–1.4)
Niacin (mg)[a]	10.8 (6.5–15.7)	9.6 (5.2–15.5)	10.3 (6.1–17.7)	10.0 (5.8–16.2)
Tryptophan (mg)[a]	6.2 (3.6–10.0)	6.8 (4.4–9.6)	7.1 (4.3–10.1)	6.5 (4.1–10.0)
Vitamin B6 (mg)[a]	1.0 (0.7–1.4)	0.9 (0.5–1.3)	0.9 (0.5–1.5)	0.9 (0.6–1.4)
Panothen (mg)[a]	2.8 (2.0–4.6)	2.6 (1.9–4.0)	2.7 (1.8–4.7)	2.8 (1.9–4.4)
Biotin (µg)[n]	24.4 (14.5–35.9)	19.9 (12.8–32.2)	21.3 (13.2–32.0)	21.8 (13.7–33.6)
Vitamin C (mg)[o]	32 (15–77.5)	33 (12–85)	26 (8–71)	30.5 (12–78)
% total energy from saturated fat[a]	12.1 (8.4–16.9)	12.2 (8.0–16.0)	12.7 (8.7–16.1)	12.2 (8.3–16.3)

Missing data (Bypass, Band, Sleeve):
a 1017 participants (330, 351, 336).
b 1020 participants (332, 352, 336).
c 1232 participants (410, 417, 405).
d 1023 participants (330, 354, 339).
e 1020 participants (330, 353, 337).
f 1025 participants (331, 355, 339).
g 1065 participants (350, 367, 348).
h 1029 participants (337, 352, 340).
i 1018 participants (330, 352, 336).
j 1026 participants (334, 354, 338).
k 1019 participants (332, 351, 336).
l 1019 participants (330, 352, 337).
m 1040 participants (337, 361, 342).
n 1018 participants (330, 351, 337).
o 1024 participants (330, 355, 339).

TABLE 61 Prevalence of sleep apnoea and excessive sleepiness

Time point	Randomised to Bypass (*n* = 462) *n/N* (%)	Randomised to Band (*n* = 464) *n/N* (%)	Randomised to Sleeve (*n* = 420) *n/N* (%)	Overall (*n* = 1346) *n/N* (%)
On CPAP/BiPAP				
Baseline	107/460 (23.3%)	117/464 (25.2%)	82/418 (19.6%)	306/1342 (22.8%)
4 weeks postoperative	72/344 (20.9%)	88/354 (24.9%)	58/304 (19.1%)	218/1002 (21.8%)
6 months	78/405 (19.3%)	92/386 (23.8%)	72/365 (19.7%)	242/1156 (20.9%)
12 months	55/386 (14.2%)	90/378 (23.8%)	60/331 (18.1%)	205/1095 (18.7%)
24 months	42/319 (13.2%)	65/306 (21.2%)	39/283 (13.8%)	146/908 (16.1%)
36 months	37/303 (12.2%)	50/287 (17.4%)	36/267 (13.5%)	123/857 (14.4%)
Obstructive sleep apnoea diagnosis, but unable to tolerate CPAP/BiPAP				
Baseline	17/460 (3.7%)	15/464 (3.2%)	10/418 (2.4%)	42/1342 (3.1%)
4 weeks postoperative	24/344 (7.0%)	16/354 (4.5%)	17/304 (5.6%)	57/1002 (5.7%)
6 months	24/405 (5.9%)	18/386 (4.7%)	16/365 (4.4%)	58/1156 (5.0%)
12 months	25/386 (6.5%)	20/378 (5.3%)	17/331 (5.1%)	62/1095 (5.7%)
24 months	13/319 (4.1%)	14/306 (4.6%)	18/283 (6.4%)	45/908 (5.0%)
36 months	6/303 (2.0%)	13/287 (4.5%)	11/267 (4.1%)	30/857 (3.5%)
Excessive sleepiness (Epworth sleepiness scale score > 10)				
Baseline	2/459 (17.9%)	78/463 (16.8%)	82/419 (19.6%)	242/1341 (18.0%)
4 weeks postoperative	36/340 (10.6%)	34/349 (9.7%)	31/299 (10.4%)	101/988 (10.2%)
6 months	48/404 (11.9%)	44/386 (11.4%)	46/360 (12.8%)	138/1150 (12.0%)
12 months	35/385 (9.1%)	40/374 (10.7%)	39/327 (11.9%)	114/1086 (10.5%)
24 months	28/315 (8.9%)	36/305 (11.8%)	24/276 (8.7%)	88/896 (9.8%)
36 months	15/302 (5.0%)	32/284 (11.3%)	27/264 (10.2%)	74/850 (8.7%)

TABLE 62 Blood pressure during follow-up

Time point	Randomised to Bypass (*n* = 462), Median (IQR)	Randomised to Band (*n* = 464), Median (IQR)	Randomised to Sleeve (*n* = 420), Median (IQR)	Overall (*n* = 1346), Median (IQR)
Systolic BP (mmHg)				
Baseline[a]	134.0 (123.5–145.0)	132.5 (123.5–146.0)	135.0 (124.8–146.0)	134.0 (123.5–146.0)
4 weeks postoperative[b]	125.0 (117.0–134.0)	128.3 (119.6–138.2)	125.3 (117.0–137.5)	126.0 (117.5–137.0)
6 months[c]	127.0 (118.0–140.7)	128.4 (119.0–141.0)	129.7 (120.0–141.0)	128.5 (119.0–141.0)
12 months[d]	127.0 (115.0–138.0)	128.5 (119.5–142.0)	128.6 (117.5–140.0)	128.0 (118.0–140.0)
24 months[e]	126.0 (116.0–140.0)	131.5 (119.5–146.0)	128.5 (117.5–144.5)	128.6 (117.5–143.5)
36 months[f]	128.5 (118.0–143.0)	131.5 (122.0–147.5)	131.0 (119.0–140.5)	130.0 (119.0–144.2)
Diastolic BP (mmHg)				
Baseline[a]	87.0 (79.0–97.3)	85.0 (78.0–94.5)	85.0 (78.0–94.4)	86.0 (78.5–95.0)
4 weeks postoperative[b]	82.0 (75.5–89.5)	83.5 (76.5–91.0)	81.7 (74.5–90.5)	82.5 (75.5–90.3)
6 months[c]	83.0 (75.5–90.7)	83.5 (76.5–92.4)	83.0 (76.0–92.5)	83.0 (76.0–92.0)
12 months[d]	81.5 (73.5–90.5)	83.0 (76.0–91.0)	82.3 (73.5–90.0)	82.5 (74.0–90.7)
24 months[e]	80.5 (72.5–88.0)	84.0 (76.5–93.5)	81.0 (74.0–91.0)	81.5 (74.0–90.8)
36 months[f]	82.0 (72.0–91.0)	83.8 (75.5–93.0)	81.5 (73.5–91.0)	82.4 (74.0–91.0)

Missing data (Bypass, Band, Sleeve):
a 123 participants (40, 47, 36).
b 463 participants (152, 152, 159).
c 334 participants (105, 128, 101).
d 393 participants (117, 138, 138).
e 666 participants (216, 231, 219).
f 746 participants (237, 262, 247).

TABLE 63 Medication and dietary supplements taken during follow-up

	Randomised to Bypass (*n* = 462)	Randomised to Band (*n* = 464)	Randomised to Sleeve (*n* = 420)	Overall (*n* = 1346)
	n/*N* (%)	*n*/*N* (%)	*n*/*N* (%)	*n*/*N* (%)
On asthma medication				
Baseline	94/424 (22.2%)	114/429 (26.6%)	107/379 (28.2%)	315/1232 (25.6%)
4 weeks postoperative	61/349 (17.5%)	85/369 (23.0%)	73/322 (22.7%)	219/1040 (21.1%)
6 months	69/397 (17.4%)	83/378 (22.0%)	85/365 (23.3%)	237/1140 (20.8%)
12 months	63/392 (16.1%)	78/378 (20.6%)	79/347 (22.8%)	220/1117 (19.7%)
24 months	47/360 (13.1%)	65/345 (18.8%)	63/313 (20.1%)	175/1018 (17.2%)
36 months	48/350 (13.7%)	67/323 (20.7%)	57/297 (19.2%)	172/970 (17.7%)
On GORD medication				
Baseline	158/424 (37.3%)	187/429 (43.6%)	143/379 (37.7%)	488/1232 (39.6%)
4 weeks postoperative	277/349 (79.4%)	233/369 (63.1%)	257/322 (79.8%)	767/1040 (73.8%)
6 months	180/397 (45.3%)	153/378 (40.5%)	194/365 (53.2%)	527/1140 (46.2%)
12 months	162/392 (41.3%)	151/378 (39.9%)	174/347 (50.1%)	487/1117 (43.6%)
24 months	129/360 (35.8%)	123/345 (35.7%)	158/313 (50.5%)	410/1018 (40.3%)
36 months	125/350 (35.7%)	120/323 (37.2%)	137/297 (46.1%)	382/970 (39.4%)
On anticoagulants				
Baseline	8/424 (1.9%)	9/429 (2.1%)	9/379 (2.4%)	26/1232 (2.1%)
4 weeks postoperative	65/349 (18.6%)	61/369 (16.5%)	63/322 (19.6%)	189/1040 (18.2%)
6 months	19/397 (4.8%)	19/378 (5.0%)	20/365 (5.5%)	58/1140 (5.1%)
12 months	10/392 (2.6%)	12/378 (3.2%)	16/347 (4.6%)	38/1117 (3.4%)
24 months	13/360 (3.6%)	7/345 (2.0%)	15/313 (4.8%)	35/1018 (3.4%)
36 months	11/350 (3.1%)	9/323 (2.8%)	12/297 (4.0%)	32/970 (3.3%)
On antidepressants				
Baseline	165/424 (38.9%)	190/429 (44.3%)	153/379 (40.4%)	508/1232 (41.2%)
4 weeks postoperative	111/349 (31.8%)	140/369 (37.9%)	103/322 (32.0%)	354/1040 (34.0%)
6 months	140/397 (35.3%)	153/378 (40.5%)	129/365 (35.3%)	422/1140 (37.0%)
12 months	123/392 (31.4%)	145/378 (38.4%)	108/347 (31.1%)	376/1117 (33.7%)

TABLE 63 Medication and dietary supplements taken during follow-up (*continued*)

	Randomised to Bypass (*n* = 462)	Randomised to Band (*n* = 464)	Randomised to Sleeve (*n* = 420)	Overall (*n* = 1346)
	n/*N* (%)	*n*/*N* (%)	*n*/*N* (%)	*n*/*N* (%)
24 months	120/360 (33.3%)	129/345 (37.4%)	106/313 (33.9%)	355/1018 (34.9%)
36 months	130/350 (37.1%)	129/323 (39.9%)	105/297 (35.4%)	364/970 (37.5%)
On analgesia medication				
Baseline	216/424 (50.9%)	219/429 (51.0%)	204/379 (53.8%)	639/1232 (51.9%)
4 weeks postoperative	169/349 (48.4%)	189/369 (51.2%)	164/322 (50.9%)	522/1040 (50.2%)
6 months	169/397 (42.6%)	179/378 (47.4%)	173/365 (47.4%)	521/1140 (45.7%)
12 months	164/392 (41.8%)	172/378 (45.5%)	154/347 (44.4%)	490/1117 (43.9%)
24 months	135/360 (37.5%)	159/345 (46.1%)	125/313 (39.9%)	419/1018 (41.2%)
36 months	139/350 (39.7%)	144/323 (44.6%)	125/297 (42.1%)	408/970 (42.1%)
Other medication				
Baseline	254/424 (59.9%)	263/429 (61.3%)	234/379 (61.7%)	751/1232 (61.0%)
4 weeks postoperative	223/349 (63.9%)	227/369 (61.5%)	207/322 (64.3%)	657/1040 (63.2%)
6 months	219/397 (55.2%)	230/378 (60.8%)	217/365 (59.5%)	666/1140 (58.4%)
12 months	210/392 (53.6%)	227/378 (60.1%)	201/347 (57.9%)	638/1117 (57.1%)
24 months	193/360 (53.6%)	199/345 (57.7%)	192/313 (61.3%)	584/1018 (57.4%)
36 months	184/350 (52.6%)	188/323 (58.2%)	175/297 (58.9%)	547/970 (56.4%)
Dietary supplements				
Baseline	179/424 (42.2%)	165/429 (38.5%)	142/379 (37.5%)	486/1232 (39.4%)
4 weeks postoperative	315/349 (90.3%)	294/369 (79.7%)	291/322 (90.4%)	900/1040 (86.5%)
6 months	309/397 (77.8%)	264/378 (69.8%)	282/365 (77.3%)	855/1140 (75.0%)
12 months	348/392 (88.8%)	304/378 (80.4%)	293/347 (84.4%)	945/1117 (84.6%)
24 months	324/360 (90.0%)	278/345 (80.6%)	285/313 (91.1%)	887/1018 (87.1%)
36 months	318/350 (90.9%)	249/323 (77.1%)	266/297 (89.6%)	833/970 (85.9%)

GORD, gastro-oesophageal reflux disease.

TABLE 64 Fertility details: female participants

	Randomised to Bypass (*n* = 462)	Randomised to Band (*n* = 464)	Randomised to Sleeve (*n* = 420)	Overall (*n* = 1346)
Female	345/461 (74.8%)	354/464 (76.3%)	321/419 (76.6%)	1020/1344 (75.9%)
Baseline				
Previous unsuccessful attempt to get pregnant?	57/345 (16.5%)	51/353 (14.4%)	53/321 (16.5%)	161/1019 (15.8%)
Polycystic ovarian syndrome				
No	291/345 (84.3%)	290/354 (81.9%)	267/321 (83.2%)	848/1020 (83.1%)
Diagnosis: no medication	42/345 (12.2%)	51/354 (14.4%)	43/321 (13.4%)	136/1020 (13.3%)
On medication	11/345 (3.2%)	9/354 (2.5%)	11/321 (3.4%)	31/1020 (3.0%)
Infertility	1/345 (0.3%)	4/354 (1.1%)	0/321 (0.0%)	5/1020 (0.5%)
Normal periods				
Baseline	117/345 (33.9%)	115/353 (32.6%)	115/321 (35.8%)	347/1019 (34.1%)
4 weeks postoperative	76/258 (29.5%)	77/260 (29.6%)	73/230 (31.7%)	226/748 (30.2%)
6 months	88/304 (28.9%)	81/293 (27.6%)	89/273 (32.6%)	258/870 (29.7%)
12 months	80/294 (27.2%)	83/277 (30.0%)	74/248 (29.8%)	237/819 (28.9%)
24 months	57/241 (23.7%)	59/226 (26.1%)	53/219 (24.2%)	169/686 (24.6%)
36 months	55/224 (24.6%)	48/218 (22.0%)	52/206 (25.2%)	155/648 (23.9%)
Trying to conceive				
4 weeks postoperative	6/258 (2.3%)	1/260 (0.4%)	1/231 (0.4%)	8/749 (1.1%)
6 months	4/305 (1.3%)	3/294 (1.0%)	3/273 (1.1%)	10/872 (1.1%)
12 months	5/294 (1.7%)	2/278 (0.7%)	5/247 (2.0%)	12/819 (1.5%)
24 months	7/242 (2.9%)	7/226 (3.1%)	5/219 (2.3%)	19/687 (2.8%)
36 months	9/224 (4.0%)	3/218 (1.4%)	6/206 (2.9%)	18/648 (2.8%)
Pregnant				
4 weeks postoperative	1/305 (0.3%)	2/295 (0.7%)	1/274 (0.4%)	4/874 (0.5%)
6 months	1/294 (0.3%)	2/278 (0.7%)	4/249 (1.6%)	7/821 (0.9%)
12 months	3/242 (1.2%)	3/226 (1.3%)	3/219 (1.4%)	9/687 (1.3%)
24 months	4/225 (1.8%)	4/218 (1.8%)	3/206 (1.5%)	11/649 (1.7%)
36 months	1/305 (0.3%)	2/295 (0.7%)	1/274 (0.4%)	4/874 (0.5%)

TABLE 64 Fertility details: female participants (*continued*)

	Randomised to Bypass (*n* = 462)	Randomised to Band (*n* = 464)	Randomised to Sleeve (*n* = 420)	Overall (*n* = 1346)
Had a baby since last visit				
12 months	0/295 (0.0%)	0/278 (0.0%)	0/249 (0.0%)	0/822 (0.0%)
24 months	3/243 (1.2%)	2/225 (0.9%)	4/219 (1.8%)	9/687 (1.3%)
36 months	9/225 (4.0%)	5/218 (2.3%)	3/207 (1.4%)	17/650 (2.6%)
If yes, number of children				
24 months	1.0 (1.0, 1.0)	2.0 (1.0, 3.0)	1.0 (1.0, 1.0)	1.0 (1.0, 1.0)
36 months	1.0 (1.0, 1.0)	1.0 (1.0, 1.0)	1.0 (1.0, 1.0)	1.0 (1.0, 1.0)

Note
Data are *n*/*N* (%) or median (IQR)

TABLE 65 Causes of death

Randomised to Bypass (*n* = 4)	Randomised to Band (*n* = 5)	Randomised to Sleeve (*n* = 2)
Underwent surgery		
• Global bowel ischemia (not related to Bypass) • Myocardial fibrosis and fatty liver disease	• Ischaemic heart disease (*n* = 2) • Sepsis from soft tissue abscess (diabetic) • Peritonitis due to leak from gastric band sutures	• Metastatic renal cell cancer
Did not undergo bariatric surgery		
• Pulmonary embolus and DVT • Metastatic vulval cancer (DVT and GI bleed)	• COVID-19 pneumonia	• Metastatic breast cancer

Note
Participants who underwent surgery received the allocated surgery.

TABLE 66 Adverse events following surgery: surgery to 30 days

Event	Received Bypass (*n* = 389)			Received Band (*n* = 363)			Received Sleeve (*n* = 429)			Overall (*n* = 1181)		
	Participants *n* (%)	Events (*n*)	SAE (*n*)	Participants *n* (%)	Events (*n*)	SAE (*n*)	Participants *n* (%)	Events (*n*)	SAE (*n*)	Participants *n* (%)	Events (*n*)	SAE (*n*)
All events	**112 (28.8%)**	**175**	**75/175**	**83 (22.9%)**	**120**	**37/120**	**110 (25.6%)**	**181**	**74/181**	**305 (25.8%)**	**476**	**186/476**
Cardiac disorders	**2 (0.5%)**	**2**	**1/2**	**1 (0.3%)**	**1**	**1/1**	**3 (0.7%)**	**4**	**3/4**	**6 (0.5%)**	**7**	**5/7**
GI disorders	**34 (8.7%)**	**43**	**25/43**	**13 (3.6%)**	**14**	**8/14**	**28 (6.5%)**	**36**	**24/36**	**75 (6.4%)**	**93**	**57/93**
Abdominal pain	10 (2.6%)	10	7/10	3 (0.8%)	3	2/3	13 (3.0%)	13	11/13	26 (2.2%)	26	20/26
Vomiting	8 (2.1%)	9	3/9	1 (0.3%)	1	1/1	3 (0.7%)	3	1/3	12 (1.0%)	13	5/13
Abdominal distension	6 (1.5%)	6	4/6	2 (0.6%)	2	1/2	0 (0.0%)	0	0/0	8 (0.7%)	8	5/8
Constipation	2 (0.5%)	3	2/3	2 (0.6%)	2	1/2	3 (0.7%)	3	2/3	7 (0.6%)	8	5/8
Dysphagia	2 (0.5%)	2	2/2	2 (0.6%)	2	1/2	2 (0.5%)	2	1/2	6 (0.5%)	6	4/6
Intra-abdominal fluid collection	1 (0.3%)	1	1/1	0 (0.0%)	0	0/0	5 (1.2%)	5	4/5	6 (0.5%)	6	5/6
General disorders and administration site conditions	**5 (1.3%)**	**5**	**2/5**	**14 (3.9%)**	**14**	**4/14**	**1 (0.2%)**	**1**	**0/1**	**20 (1.7%)**	**20**	**6/20**
Complication associated with device	0 (0.0%)	0	0/0	10 (2.8%)	10	2/10	0 (0.0%)	0	0/0	10 (0.8%)	10	2/10
Hepatobiliary disorders	0 (0.0%)	0	0/0	0 (0.0%)	0	0/0	2 (0.5%)	2	2/2	2 (0.2%)	2	2/2
Immune system disorders	1 (0.3%)	1	0/1	0 (0.0%)	0	0/0	1 (0.2%)	1	0/1	2 (0.2%)	2	0/2
Infections and infestations	51 (13.1%)	54	13/54	48 (13.2%)	53	13/53	45 (10.5%)	47	6/47	144 (12.2%)	154	32/154
Wound infection	39 (10.0%)	39	6/39	38 (10.5%)	42	4/42	40 (9.3%)	41	1/41	117 (9.9%)	122	11/122
Urinary tract infection	5 (1.3%)	5	1/5	1 (0.3%)	1	1/1	3 (0.7%)	3	3/3	9 (0.8%)	9	5/9
Respiratory tract infection	0 (0.0%)	0	0/0	6 (1.7%)	6	6/6	2 (0.5%)	2	1/2	8 (0.7%)	8	7/8
Abscess	5 (1.3%)	5	1/5	1 (0.3%)	1	0/1	0 (0.0%)	0	0/0	6 (0.5%)	6	1/6
Injury, poisoning and procedural complications	**22 (5.7%)**	**28**	**13/28**	**11 (3.0%)**	**13**	**3/13**	**25 (5.8%)**	**35**	**20/35**	**58 (4.9%)**	**76**	**36/76**
Haemorrhage	5 (1.3%)	5	1/5	2 (0.6%)	2	0/2	6 (1.4%)	7	5/7	13 (1.1%)	14	6/14
Transfusion	5 (1.3%)	5	3/5	0 (0.0%)	0	0/0	8 (1.9%)	8	7/8	13 (1.1%)	13	10/13
Urinary retention	4 (1.0%)	4	1/4	1 (0.3%)	1	0/1	8 (1.9%)	8	0/8	13 (1.1%)	13	1/13
Iatrogenic injury	4 (1.0%)	4	1/4	4 (1.1%)	4	0/4	1 (0.2%)	1	0/1	9 (0.8%)	9	1/9
Upper GI haemorrhage	4 (1.0%)	4	2/4	0 (0.0%)	0	0/0	2 (0.5%)	2	2/2	6 (0.5%)	6	4/6
Metabolism and nutrition disorders	**18 (4.6%)**	**22**	**7/22**	**6 (1.7%)**	**7**	**0/7**	**32 (7.5%)**	**35**	**8/35**	**56 (4.7%)**	**64**	**15/64**

continued

TABLE 66 Adverse events following surgery: surgery to 30 days (*continued*)

Event	Received Bypass (*n* = 389)			Received Band (*n* = 363)			Received Sleeve (*n* = 429)			Overall (*n* = 1181)		
	Participants *n* (%)	Events (*n*)	SAE (*n*)	Participants *n* (%)	Events (*n*)	SAE (*n*)	Participants *n* (%)	Events (*n*)	SAE (*n*)	Participants *n* (%)	Events (*n*)	SAE (*n*)
Iron deficiency	14 (3.6%)	14	3/14	3 (0.8%)	4	0/4	14 (3.3%)	15	1/15	31 (2.6%)	33	4/33
Electrolyte imbalance	5 (1.3%)	5	2/5	2 (0.6%)	2	0/2	12 (2.8%)	12	5/12	19 (1.6%)	19	7/19
Hyperglycaemia	0 (0.0%)	0	0/0	1 (0.3%)	1	0/1	4 (0.9%)	4	0/4	5 (0.4%)	5	0/5
Musculoskeletal and connective tissue disorders	**1 (0.3%)**	**1**	**0/1**	**3 (0.8%)**	**3**	**0/3**	**0 (0.0%)**	**0**	**0/0**	**4 (0.3%)**	**4**	**0/4**
Nervous system disorders	**1 (0.3%)**	**1**	**0/1**	**2 (0.6%)**	**2**	**2/2**	**0 (0.0%)**	**0**	**0/0**	**3 (0.3%)**	**3**	**2/3**
Renal and urinary disorders	**0 (0.0%)**	**0**	**0/0**	**0 (0.0%)**	**0**	**0/0**	**2 (0.5%)**	**2**	**2/2**	**2 (0.2%)**	**2**	**2/2**
Respiratory, thoracic and mediastinal disorders	**0 (0.0%)**	**0**	**0/0**	**3 (0.8%)**	**4**	**3/4**	**2 (0.5%)**	**2**	**2/2**	**5 (0.4%)**	**6**	**5/6**
Surgical and medical procedures	**10 (2.6%)**	**17**	**14/17**	**7 (1.9%)**	**8**	**2/8**	**5 (1.2%)**	**8**	**5/8**	**22 (1.9%)**	**33**	**21/33**
Drain placement	4 (1.0%)	4	4/4	0 (0.0%)	0	0/0	1 (0.2%)	1	1/1	5 (0.4%)	5	5/5
Vascular disorders	**1 (0.3%)**	**1**	**0/1**	**0 (0.0%)**	**0**	**0/0**	**4 (0.9%)**	**4**	**0/4**	**5 (0.4%)**	**5**	**0/5**
Eye disorders	**0 (0.0%)**	**0**	**0/0**	**0 (0.0%)**	**0**	**0/0**	**1 (0.2%)**	**1**	**1/1**	**1 (0.1%)**	**1**	**1/1**
Psychiatric disorders	**0 (0.0%)**	**0**	**0/0**	**1 (0.3%)**	**1**	**1/1**	**0 (0.0%)**	**0**	**0/0**	**1 (0.1%)**	**1**	**1/1**
Skin and subcutaneous tissue disorders	**0 (0.0%)**	**0**	**0/0**	**0 (0.0%)**	**0**	**0/0**	**3 (0.7%)**	**3**	**1/3**	**3 (0.3%)**	**3**	**1/3**

Note
Events within a system organ class are listed where the **event occurred in at least five participants.**

TABLE 67 Adverse events following surgery: 30 days post surgery to 3 years

Event	Received Bypass (*n* = 389)			Received Band (*n* = 363)			Received Sleeve (*n* = 429)			Overall (*n* = 1181)		
	Participants *n* (%)	Events (*n*)	SAE (*n*)	Participants *n* (%)	Events (*n*)	SAE (*n*)	Participants *n* (%)	Events (*n*)	SAE (*n*)	Participants *n* (%)	Events (*n*)	SAE (*n*)
All events	**157 (40.4%)**	**412**	**208/412**	**171 (47.1%)**	**443**	**247/443**	**154 (35.9%)**	**320**	**173/320**	**482 (40.8%)**	**1175**	**628/1175**
Cardiac disorders	**3 (0.8%)**	**3**	**2/3**	**7 (1.9%)**	**10**	**8/10**	**6 (1.4%)**	**6**	**5/6**	**16 (1.4%)**	**19**	**15/19**
GI disorders	**52 (13.4%)**	**91**	**52/91**	**38 (10.5%)**	**68**	**41/68**	**29 (6.8%)**	**43**	**26/43**	**119 (10.1%)**	**202**	**119/202**
Abdominal pain	19 (4.9%)	29	21/29	20 (5.5%)	28	16/28	11 (2.6%)	14	7/14	50 (4.2%)	71	44/71
Vomiting	15 (3.9%)	18	5/18	13 (3.6%)	13	10/13	5 (1.2%)	5	4/5	33 (2.8%)	36	19/36
Internal hernia	11 (2.8%)	11	7/11	0 (0.0%)	0	0/0	0 (0.0%)	0	0/0	11 (0.9%)	11	7/11
Gastric ulcer	8 (2.1%)	9	2/9	1 (0.3%)	1	1/1	0 (0.0%)	0	0/0	9 (0.8%)	10	3/10
Oesophagitis	1 (0.3%)	1	0/1	2 (0.6%)	2	1/2	6 (1.4%)	7	1/7	9 (0.8%)	10	2/10
Dysphagia	3 (0.8%)	3	3/3	3 (0.8%)	3	3/3	0 (0.0%)	0	0/0	6 (0.5%)	6	6/6
General disorders and administration site conditions	**12 (3.1%)**	**12**	**3/12**	**41 (11.3%)**	**66**	**26/66**	**10 (2.3%)**	**11**	**5/11**	**63 (5.3%)**	**89**	**34/89**
Complication associated with device	0 (0.0%)	0	0/0	30 (8.3%)	48	20/48	0 (0.0%)	0	0/0	30 (2.5%)	48	20/48
Chest pain	4 (1.0%)	4	1/4	5 (1.4%)	6	2/6	6 (1.4%)	7	3/7	15 (1.3%)	17	6/17
Hepatobiliary disorders	**16 (4.1%)**	**18**	**9/18**	**6 (1.7%)**	**7**	**2/7**	**14 (3.3%)**	**20**	**10/20**	**36 (3.0%)**	**45**	**21/45**
Cholecystitis acute	10 (2.6%)	11	6/11	5 (1.4%)	5	1/5	11 (2.6%)	13	5/13	26 (2.2%)	29	12/29
Cholangitis	6 (1.5%)	6	2/6	1 (0.3%)	1	0/1	6 (1.4%)	6	4/6	13 (1.1%)	13	6/13
Immune system disorders	**1 (0.3%)**	**1**	**0/1**	**1 (0.3%)**	**1**	**0/1**	**0 (0.0%)**	**0**	**0/0**	**2 (0.2%)**	**2**	**0/2**
Infections and infestations	**24 (6.2%)**	**32**	**14/32**	**44 (12.1%)**	**62**	**30/62**	**24 (5.6%)**	**30**	**25/30**	**92 (7.8%)**	**124**	**69/124**
Wound infection	6 (1.5%)	7	2/7	13 (3.6%)	16	3/16	3 (0.7%)	3	1/3	22 (1.9%)	26	6/26
Respiratory tract infection	1 (0.3%)	2	2/2	8 (2.2%)	9	5/9	6 (1.4%)	6	5/6	15 (1.3%)	17	12/17
Urinary tract infection	6 (1.5%)	7	0/7	8 (2.2%)	10	2/10	1 (0.2%)	1	1/1	15 (1.3%)	18	3/18
Pneumonia	1 (0.3%)	1	1/1	2 (0.6%)	2	2/2	3 (0.7%)	3	2/3	6 (0.5%)	6	5/6
Abscess	3 (0.8%)	3	0/3	2 (0.6%)	3	0/3	0 (0.0%)	0	0/0	5 (0.4%)	6	0/6
Cellulitis	2 (0.5%)	2	1/2	2 (0.6%)	2	2/2	1 (0.2%)	1	1/1	5 (0.4%)	5	4/5
Pneumonia pneumococcal	3 (0.8%)	4	4/4	2 (0.6%)	2	1/2	0 (0.0%)	0	0/0	5 (0.4%)	6	5/6

continued

TABLE 67 Adverse events following surgery: 30 days post surgery to 3 years (*continued*)

Event	Received Bypass (*n* = 389)			Received Band (*n* = 363)			Received Sleeve (*n* = 429)			Overall (*n* = 1181)		
	Participants *n* (%)	Events (*n*)	SAE (*n*)	Participants *n* (%)	Events (*n*)	SAE (*n*)	Participants *n* (%)	Events (*n*)	SAE (*n*)	Participants *n* (%)	Events (*n*)	SAE (*n*)
Injury, poisoning and procedural complications	**25 (6.4%)**	**35**	**9/35**	**16 (4.4%)**	**20**	**6/20**	**35 (8.2%)**	**42**	**12/42**	**76 (6.4%)**	**97**	**27/97**
Fall	5 (1.3%)	5	1/5	7 (1.9%)	7	1/7	9 (2.1%)	9	2/9	21 (1.8%)	21	4/21
Musculoskeletal injury	6 (1.5%)	8	0/8	2 (0.6%)	3	0/3	8 (1.9%)	8	0/8	16 (1.4%)	19	0/19
GI anastomotic stenosis	3 (0.8%)	3	0/3	0 (0.0%)	0	0/0	4 (0.9%)	4	1/4	7 (0.6%)	7	1/7
Upper GI haemorrhage	3 (0.8%)	3	1/3	1 (0.3%)	1	1/1	2 (0.5%)	2	1/2	6 (0.5%)	6	3/6
Metabolism and nutrition disorders	**34 (8.7%)**	**37**	**7/37**	**18 (5.0%)**	**18**	**3/18**	**33 (7.7%)**	**35**	**4/35**	**85 (7.2%)**	**90**	**14/90**
Iron deficiency	27 (6.9%)	28	3/28	14 (3.9%)	14	1/14	29 (6.8%)	31	1/31	70 (5.9%)	73	5/73
Electrolyte imbalance	4 (1.0%)	4	2/4	3 (0.8%)	3	1/3	3 (0.7%)	3	2/3	10 (0.8%)	10	5/10
Musculoskeletal and connective tissue disorders	**3 (0.8%)**	**3**	**0/3**	**10 (2.8%)**	**13**	**6/13**	**8 (1.9%)**	**10**	**1/10**	**21 (1.8%)**	**26**	**7/26**
Back pain	1 (0.3%)	1	0/1	2 (0.6%)	3	0/3	4 (0.9%)	5	1/5	7 (0.6%)	9	1/9
Arthralgia	1 (0.3%)	1	0/1	2 (0.6%)	2	0/2	3 (0.7%)	3	0/3	6 (0.5%)	6	0/6
Nervous system disorders	10 (2.6%)	11	4/11	7 (1.9%)	15	8/15	7 (1.6%)	7	2/7	24 (2.0%)	33	14/33
Renal and urinary disorders	6 (1.5%)	10	3/10	3 (0.8%)	6	4/6	2 (0.5%)	2	0/2	11 (0.9%)	18	7/18
Nephrolithiasis	3 (0.8%)	4	0/4	2 (0.6%)	4	3/4	0 (0.0%)	0	0/0	5 (0.4%)	8	3/8
Respiratory, thoracic and mediastinal disorders	**6 (1.5%)**	**7**	**1/7**	**4 (1.1%)**	**5**	**3/5**	**7 (1.6%)**	**8**	**4/8**	**17 (1.4%)**	**20**	**8/20**
Asthma	3 (0.8%)	4	1/4	1 (0.3%)	2	1/2	2 (0.5%)	3	1/3	6 (0.5%)	9	3/9
Dyspnoea	1 (0.3%)	1	0/1	1 (0.3%)	1	1/1	3 (0.7%)	3	2/3	5 (0.4%)	5	3/5
Surgical and medical procedures	**71 (18.3%)**	**108**	**78/108**	**82 (22.6%)**	**130**	**96/130**	**59 (13.8%)**	**75**	**54/75**	**212 (18.0%)**	**313**	**228/313**
Joint arthroplasty	12 (3.1%)	12	10/12	15 (4.1%)	15	11/15	14 (3.3%)	16	9/16	41 (3.5%)	43	30/43
Gastric banding reversal	0 (0.0%)	0	0/0	30 (8.3%)	36	22/36	0 (0.0%)	0	0/0	30 (2.5%)	36	22/36
Cholecystectomy	6 (1.5%)	6	5/6	4 (1.1%)	4	4/4	10 (2.3%)	10	9/10	20 (1.7%)	20	18/20
Gastric bypass	0 (0.0%)	0	0/0	10 (2.8%)	10	8/10	4 (0.9%)	4	2/4	14 (1.2%)	14	10/14
Knee arthroplasty	6 (1.5%)	6	6/6	5 (1.4%)	6	5/6	3 (0.7%)	3	3/3	14 (1.2%)	15	14/15

TABLE 67 Adverse events following surgery: 30 days post surgery to 3 years (*continued*)

Event	Received Bypass (*n* = 389)			Received Band (*n* = 363)			Received Sleeve (*n* = 429)			Overall (*n* = 1181)		
	Participants *n* (%)	Events (*n*)	SAE (*n*)	Participants *n* (%)	Events (*n*)	SAE (*n*)	Participants *n* (%)	Events (*n*)	SAE (*n*)	Participants *n* (%)	Events (*n*)	SAE (*n*)
Therapeutic procedures NEC	5 (1.3%)	5	4/5	4 (1.1%)	4	3/4	1 (0.2%)	1	1/1	10 (0.8%)	10	8/10
Abdominal hernia repair	9 (2.3%)	9	4/9	0 (0.0%)	0	0/0	0 (0.0%)	0	0/0	9 (0.8%)	9	4/9
Skin cosmetic procedure	4 (1.0%)	4	3/4	2 (0.6%)	2	0/2	3 (0.7%)	3	1/3	9 (0.8%)	9	4/9
Hip arthroplasty	2 (0.5%)	2	2/2	2 (0.6%)	3	3/3	3 (0.7%)	3	2/3	7 (0.6%)	8	7/8
Hysterectomy	2 (0.5%)	2	2/2	4 (1.1%)	4	4/4	1 (0.2%)	1	0/1	7 (0.6%)	7	6/7
Mineral supplementation	5 (1.3%)	9	1/9	0 (0.0%)	0	0/0	0 (0.0%)	0	0/0	5 (0.4%)	9	1/9
Vascular disorders	**11 (2.8%)**	**12**	**2/12**	**3 (0.8%)**	**3**	**1/3**	**6 (1.4%)**	**6**	**3/6**	**20 (1.7%)**	**21**	**6/21**
Circulatory collapse	6 (1.5%)	6	1/6	1 (0.3%)	1	1/1	1 (0.2%)	1	0/1	8 (0.7%)	8	2/8
DVT	2 (0.5%)	3	1/3	2 (0.6%)	2	0/2	1 (0.2%)	1	0/1	5 (0.4%)	6	1/6
Blood and lymphatic system disorders	**4 (1.0%)**	**6**	**2/6**	**1 (0.3%)**	**1**	**1/1**	**1 (0.2%)**	**1**	**1/1**	**6 (0.5%)**	**8**	**4/8**
Ear and labyrinth disorders	**1 (0.3%)**	**1**	**0/1**	**1 (0.3%)**	**1**	**1/1**	**0 (0.0%)**	**0**	**0/0**	**2 (0.2%)**	**2**	**1/2**
Eye disorders	**1 (0.3%)**	**1**	**0/1**	**0 (0.0%)**	**0**	**0/0**	**0 (0.0%)**	**0**	**0/0**	**1 (0.1%)**	**1**	**0/1**
Neoplasms benign, malignant and unspecified (incl. cysts and polyps)	**1 (0.3%)**	**1**	**1/1**	**1 (0.3%)**	**1**	**1/1**	**4 (0.9%)**	**6**	**6/6**	**6 (0.5%)**	**8**	**8/8**
Pregnancy, puerperium and perinatal conditions	**7 (1.8%)**	**18**	**18/18**	**4 (1.1%)**	**6**	**6/6**	**5 (1.2%)**	**7**	**7/7**	**16 (1.4%)**	**31**	**31/31**
Delivery	5 (1.3%)	5	5/5	5 (1.4%)	5	5/5	5 (1.2%)	5	5/5	14 (1.2%)	14	14/14
Psychiatric disorders	**2 (0.5%)**	**2**	**0/2**	**4 (1.1%)**	**6**	**2/6**	**4 (0.9%)**	**5**	**4/5**	**10 (0.8%)**	**13**	**6/13**
Reproductive system and breast disorders	**3 (0.8%)**	**3**	**3/3**	**1 (0.3%)**	**1**	**1/1**	**4 (0.9%)**	**6**	**4/6**	**8 (0.7%)**	**10**	**8/10**
Skin and subcutaneous tissue disorders	**0 (0.0%)**	**0**	**0/0**	**2 (0.6%)**	**3**	**1/3**	**0 (0.0%)**	**0**	**0/0**	**2 (0.2%)**	**3**	**1/3**

Note
Events within a system organ class are listed where the **event occurred in at least five participants.**

TABLE 68 Core outcome set domains and metrics used to assess these in By-Band-Sleeve

	COS Domain	Core Outcome Metric (s) used in the trial
1	Weight	BMI and %TWL
2	Diabetes status	HbA1c, changes in diabetic medication
3	Cardiovascular risk	Hypertension, and anti-hypertensive medication
4	Overall quality of life	EQ5D-5L, SF-12, GIQLI and IWQoL Lite
5	Mortality (30 days or long term)	Death within 3 years post randomisation
6	Technical complications of the specific operation	These were identified by the surgeons in the TMG
7	Any reoperation/reintervention and its classification of severity	These were identified by the surgeons in the TMG, the Clavien–Dindo classification of severity was used for complications occurring in hospital
8	Dysphagia/regurgitation	Items in the GIQLI index and use of anti-reflux medication
9	Micronutrient status	Blood levels of vitamin D, B12 and self-reported dietary intake of vitamins and minerals

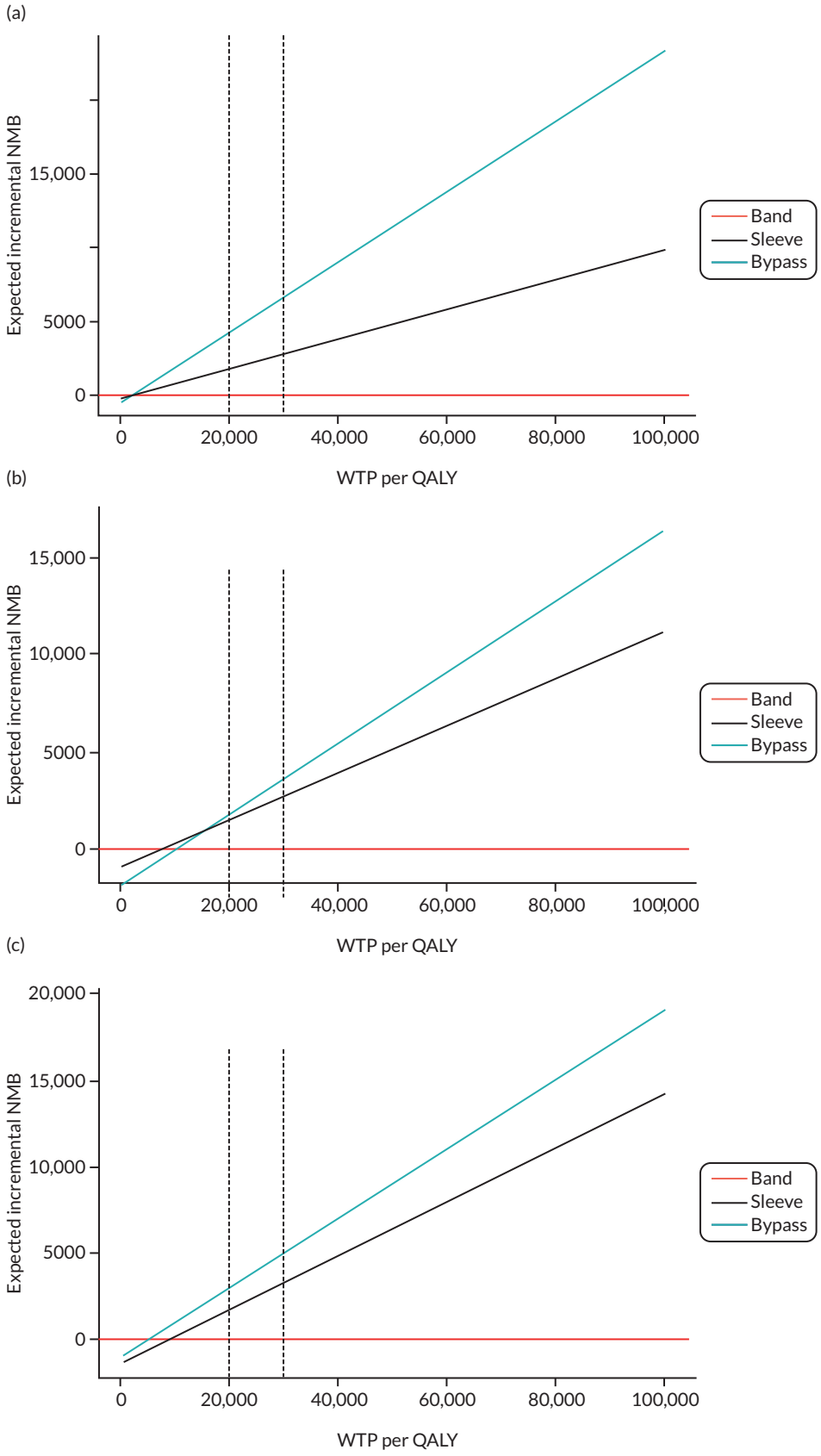

FIGURE 38 Expected incremental NMB of Bypass and Sleeve vs. Band in the UK NHS by BMI at baseline. (a) BMI < 40; (b) BMI 40–50; and (c) BMI> 50. Results are based on *n* = 500 bootstrap samples, WTP per QALY (maximum acceptable ICER) and the expected incremental NMB are expressed in 2021 GBP. The dashed vertical lines represent the £20,000 and £30,000 per QALY thresholds generally used by.

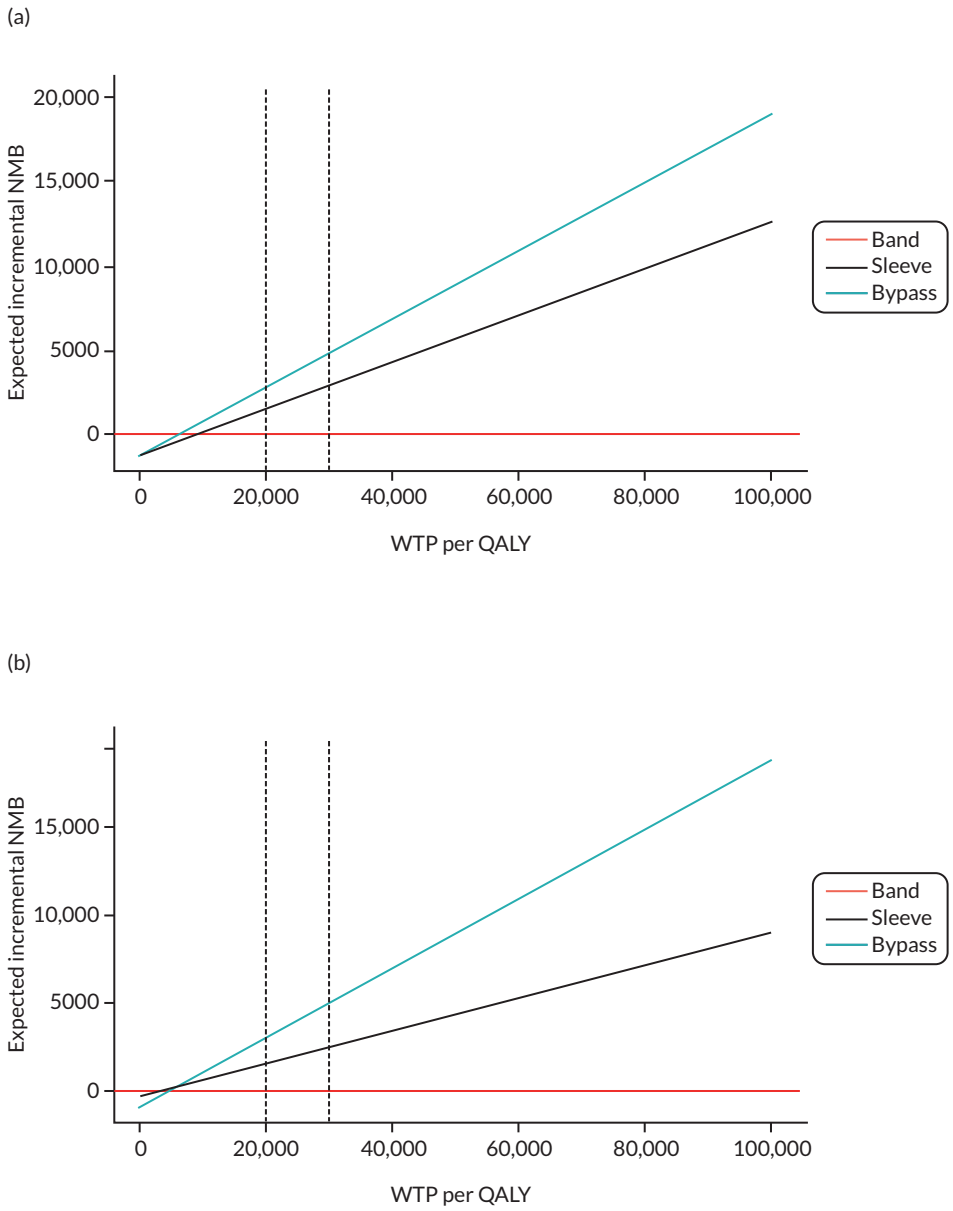

FIGURE 39 Expected incremental NMB of Bypass and Sleeve vs. Band in the UK NHS by diabetes status at baseline. (a) No diabetes; and (b) Diabetic. Results are based on *n* = 500 bootstrap samples, WTP per QALY (maximum acceptable ICER) and the expected incremental NMB are expressed in 2021 GBP. The dashed vertical lines represent the £20,000 and £30,000 per QALY thresholds generally used by NICE.

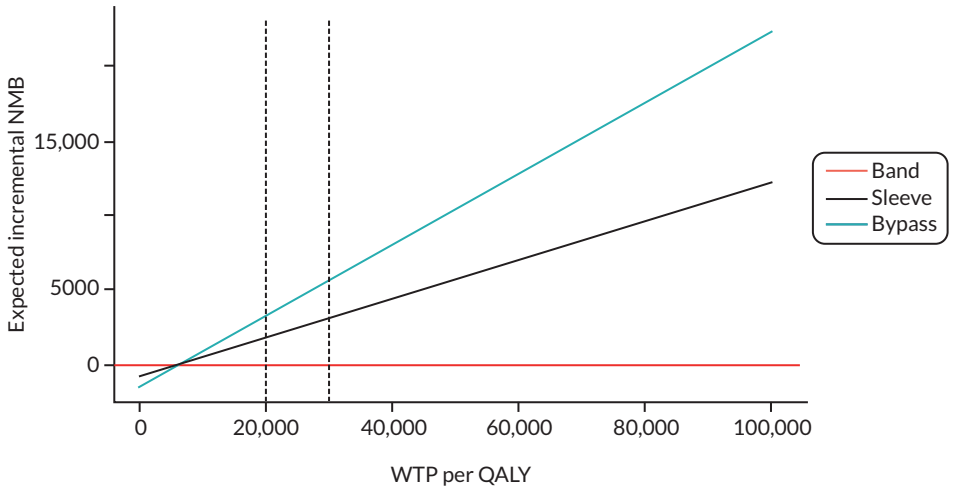

FIGURE 40 Expected incremental NMB of Bypass and Sleeve vs. Band in the UK NHS by surgery received. Results are based on *n* = 500 bootstrap samples, WTP per QALY (maximum acceptable ICER) and the expected incremental NMB are expressed in 2021 GDP. The dashed vertical lines represent the £20,000 and £30,000 per QALY thresholds generally used by NICE.

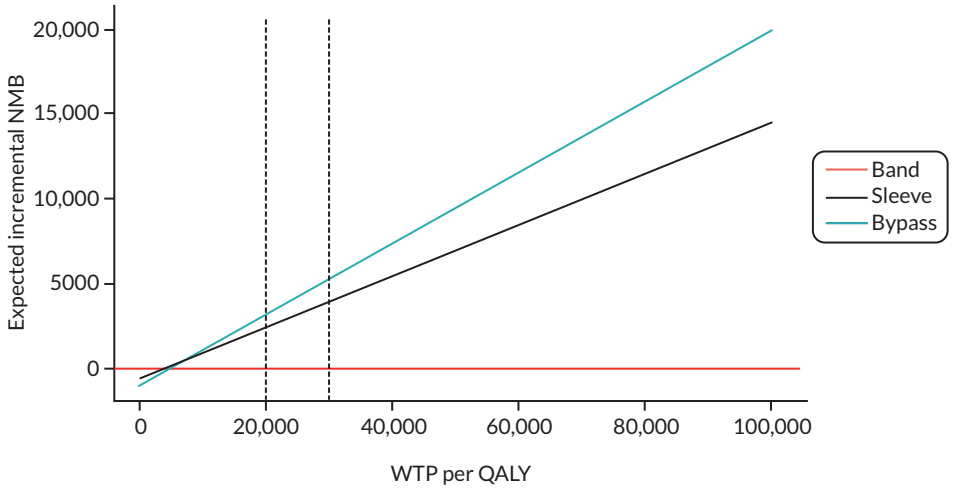

FIGURE 41 Expected incremental NMB of Bypass and Sleeve vs. Band in the UK NHS using a binary indicator to address a potential time-trend bias. Results are based on *n* = 500 bootstrap samples, WTP per QALY (maximum acceptable ICER) and the expected incremental NMB are expressed in 2021 GBP. The dashed vertical lines represent the £20,000 and £30,000 per QALY thresholds generally used by NICE.

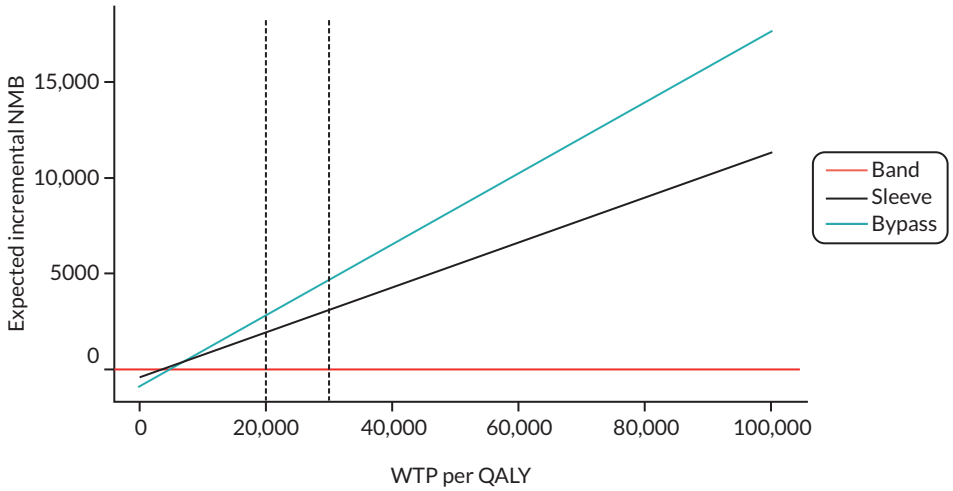

FIGURE 42 Expected incremental NMB of Bypass and Sleeve vs. Band in the UK NHS using alternative mapping algorithm for deriving HRQoL. Results are based on *n* = 500 bootstrap samples, WTP per QALY (maximum acceptable ICER) and the expected incremental NMB are expressed in 2021 GBP. The dashed vertical lines represent the £20,000 and £30,000 per QALY thresholds generally used by NICE.

TABLE 69 Impact of sensitivity analyses on estimated costs including intervention costs

	Main analysis – linear regression			Gamma regression			Assuming costs data are incomplete when weight is missing and using inverse probability of censoring weighting to address selection bias after censoring participants with missing weight data		
Group	Mean costs per participant (95% CI)	Cost per participant vs. band (98% CI)	Cost per participant vs. bypass (98% CI)	Mean costs per participant (95% CI)	Cost per participant vs. band (98% CI)	Cost per participant vs. bypass (98% CI)	Mean costs per participant (95% CI)	Cost per participant vs. band (98% CI)	Cost per participant vs. bypass (98% CI)
Band	7357 (6865 to 7905)	–	–	7365 (6879 to 7023)	–	–	7716 (7200 to 8269)	–	–
Sleeve	7695 (7143 to 8451)	337 (−626 to 1396)	−574 (−1486 to 526)	7790 (7217 to 7398)	425 (−502 to 1310)	−523 (−1426 to 375)	8045 (7419 to 8788)	328 (−649 to 1346)	−431 (−1469 to 651)
Bypass	8268 (7786 to 8813)	911 (76 to 1813)	–	8313 (7855 to 7982)	948 (142 to 1787)	–	8476 (7952 to 9044)	759 (−103 to 1674)	–

TABLE 70 Impact of sensitivity analyses on estimated difference in HRQoL

	Main analysis		Beta-one-inflated regression		Mixed-effect regression with a spline for time and a random intercept		Mixed-effect regression with a random slope and intercept and time modelled using a spline		Mixed-effect regression with time modelled as a categorical variable and a random intercept	
Group	Incremental QALYs per participant vs. band (98% CI)	Incremental QALYs per participant vs. Bypass (98% CI)	Incremental QALYs per participant vs. band (98% CI)	Incremental QALYs per participant vs. Bypass (98% CI)	Incremental QALYs per participant vs. band (98% CI)	Incremental QALYs per participant vs. Bypass (98% CI)	Incremental QALYs per participant vs. band (98% CI)	Incremental QALYs per participant vs. Bypass (98% CI)	Incremental QALYs per participant vs. band (98% CI)	Incremental QALYs per participant vs. Bypass (98% CI)
Sleeve	0.13 (0.02 to 0.27)	−0.07 (−0.20 to 0.05)	0.10 (−0.00 to 0.22)	−0.03 (−0.13 to 0.07)	0.10 (−0.01 to −0.21)	−0.08 (−0.20 to 0.03)	0.10 (−0.01 to 0.21)	−0.08 (−0.19 to 0.03)	0.13 (0.00 to 0.27)	−0.07 (−0.20 to 0.04)
Bypass	0.20 (0.08 to 0.31)	–	0.13 (0.03 to 0.25)	–	0.18 (0.06 to 0.29)	–	0.18 (0.06 to 0.30)	–	0.20 (0.08 to 0.32)	–

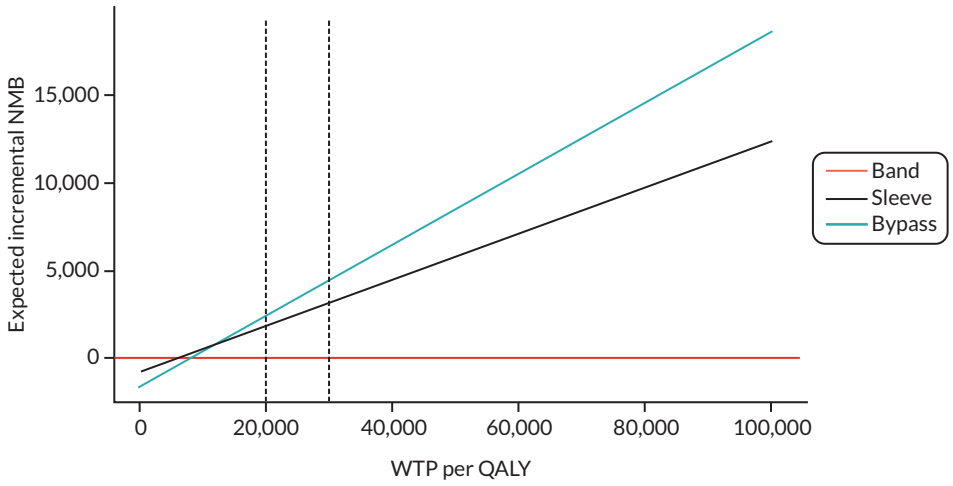

FIGURE 43 Expected incremental NMB of Bypass and Sleeve vs. Band in the UK NHS using intervention costs as reported by NHS Cost Collection. Results are based on *n* = 500 bootstrap samples, WTP per QALY (maximum acceptable ICER) and the expected incremental NMB are expressed in 2021 GBP. The dashed vertical lines represent the £20,000 and £30,000 per QALY thresholds generally used by NICE.

TABLE 71 Receipt of benefits 3 years after randomisation

Group	Percentage receiving disability-related benefits at 3 years (95% CI)	Compared to Band (98% CI)	Compared to Bypass (98% CI)	Percentage receiving child-related benefits at 3 years (95% CI)	Compared to Band (98% CI)	Compared to Bypass (98% CI)	Percentage receiving any benefits at 3 years (95% CI)	Compared to Band (98% CI)	Compared to Bypass (98% CI)
Band	22 (17 to 28)			14 (8 to 20)			44 (38 to 51)		
Sleeve	18 (13 to 23)	−4 (−12 to 4)	−3 (−11 to 5)	7 (3 to 11)	−7 (−15 to 0)	−3 (−11 to 3)	38 (32 to 44)	−6 (−16 to 3)	−1 (−11 to 10)
Bypass	21 (16 to 27)	−2 (−10 to 9)		10 (6 to 15)	−3 (−12 to 5)		38 (32 to 45)	−6 (−16 to 5)	

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