BMJ Open

Comparing effects of obesity treatment with very low energy diet and bariatric surgery after 2 years: a prospective cohort study

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To cite: Höskuldsdottir G, Engström M, Rawshani A, *et al*. Comparing effects of obesity treatment with very low energy diet and bariatric surgery after 2 years: a prospective cohort study. *BMJ Open* 2022;**12**:e053242. doi:10.1136/bmjopen-2021-053242

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2021-053242).

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Received 07 May 2021
Accepted 23 March 2022

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ABSTRACT

Objectives To compare long-term effects and complications of medical treatment (MT) of obesity including very low energy diet with bariatric surgery.

Design and setting This prospective study conducted in a clinical setting recruited individuals with body mass index (BMI) ≥35 kg/m^2 referred for obesity treatment. Demographic and anthropometric data, laboratory samples, and questionnaire replies were collected at baseline and 2 years.

Participants and interventions 971 individuals were recruited 2015–2017. 382 received MT, 388 Roux-en-Y gastric bypass (RYGB) and 201 sleeve gastrectomy (SG).

Main outcome measures Primary outcomes included changes in anthropometric measures, metabolic variables and safety. These were analysed using a linear regression model. A logistic regression model was used to analyse composite variables for treatment success (secondary outcomes). A random forest (RF) model was used to examine the importance of 15 clinical domains as predictors for successful treatment.

Results Two-year data were available for 667 individuals (68.7%). Regarding primary outcomes, the decrease in excess BMI was 27.5%, 82.5% and 70.3% and proportion achieving a weight of >10% was 45.3%, 99.6% and 95.6% for MT, RYGB and SG, respectively (p<0.001). The groups were comparable regarding levels of vitamins, minerals and haemoglobin or safety measures. Likelihood for success (secondary outcome) was higher in the surgical groups (RYGB: OR 5.3 (95% CI 3.9 to 7.2) vs SG: OR 4.3 ((95% CI 3.0 to 6.2)) in reference to MT. Baseline anthropometry had the strongest predictive value for treatment success, according to the RF model.

Conclusions In clinical practice, bariatric surgery by RYGB or SG is most effective, but meaningful weight loss is achievable by MT with strict caloric restriction and stepwise introduction of a normal diet. All treatments showed positive effects on well-being, cardiovascular risk factors, and levels of vitamins and minerals at 2-year follow-up and groups were similar regarding safety measures.

Trial registration number NCT03152617.

Strengths and limitations of this study

- The Bariatic surgery Substitution and Nutrition study study is the largest long-term study comparing two surgical methods for the treatment of obesity with structured medical treatment that includes a period of strict caloric restriction.
- The study includes a heterogeneous population of individuals with obesity that is representative for the Region Västra Götaland in Sweden with 1.7 million inhabitants.
- As in many prospective studies, lost to follow-up was observed in our study regarding replies to the questionnaires.
- Pharmaceutical treatment to prevent weight gain in all treatment groups was uncommon.

BACKGROUND

Obesity is one of the major public health challenges of the 21st century due to its role as a major risk factor for cardiovascular, metabolic and renal diseases, cancer, poor mental health and premature death.[1 2] While country-specific strategies to prevent and reduce the disease burden generated by obesity are urgently needed, both medical and surgical treatment of obesity have been demonstrated to lower morbidity and mortality.[3–5] In particular, prospective controlled as well as observational studies have demonstrated that bariatric surgery is effective, resulting in long-term weight loss and improvements in co-morbidities such as type 2 diabetes and cardiovascular disease in comparison with medical treatment (MT) of obesity.[6–8]

There are numerous published studies addressing the effects of obesity treatment, but there are only few addressing long-term consequences. Bariatric surgery alters by definition gastrointestinal anatomy and physiology and is therefore likely to influence

uptake of essential micronutrients. This could eventually result in diseases caused by deficiency of vitamins and minerals like anaemia, bone disease and neuropathies.[9] Furthermore, studies on mental health following bariatric surgery have revealed diverting effects, however, recent data show that there is no difference in mental health at 5-year follow-up in adolescents despite major weight-loss.[10] Other studies have revealed an increase in antidepressant prescription following surgical treatment and increased risk of suicide and non-fatal self-harm.[7 11 12] In patients with obesity and type 2 diabetes, bariatric surgery has been shown to have beneficial effects on cardiovascular and renal disease as well as lower mortality, but might also increase risk of anaemia, malnutrition, psychiatric and alcohol-related diagnoses compared with traditional (non-surgical) treatment.[13 14] Although bariatric surgery has been shown to lead to longer survival in individuals with obesity, the mortality observed in postsurgical populations is still higher than that of the general population.[15] Obesity treatment including very low energy diet (VLED) has been shown to be effective and lead to positive effects on cardiovascular risk factors and plasma glucose. Side effects related to treatment with VLED are generally temporary and directly related to ongoing treatment. These include hair loss, constipation, dizziness, cold intolerance and fatigue, all of which can be generalised to large weight loss. Biliary colic has also been reported but is uncommon.[16 17] The SOS study has a long-term control group with various lifestyle changes and pharmacological interventions.[18] We decided to test a more robust MT with 3–4 months very-low-calory diet, followed by a structured reintroduction of normal food until 12 months.

The Bariatric surgery Substitution and Nutrition study (BASUN) is a prospective non-randomised clinical study including 971 participants with a planned 10-year follow-up aiming to evaluate the long-term outcomes and adverse effects of Roux-en-Y gastric bypass (RYGB), sleeve gastrectomy (SG) and non-surgical treatment of obesity.[19] The overall aim of the BASUN project is to examine the above mentioned knowledge gaps in treatment effects, covering topics such as nutritional status including minerals and vitamins, body composition, bone health, progression of psychiatric disorders, gastrointestinal symptoms, eating disorders, quality of life, levels of physical activity and the influence of socioeconomic status. In the present report, we present an overview of the main results of BASUN after 2 years of follow-up, including the overall weight effects, as well results in subgroups and predictors of successful treatment. Further analysis including bone health, gastrointestinal symptoms, more detailed analysis of vitamin and mineral deficiencies as well as psychiatric health will be presented separately.

METHODS

Study design and participants

The design and patient cohort of the BASUN study have recently been described.[19] To summarise, it is a prospective non-randomised cohort study that recruited 1121 individuals with body mass index (BMI) 35 kg/m^2 or higher referred for treatment of obesity in Region Västra Götaland, Sweden, between May 2015 and November 2017. Follow-up data for the last participant was gathered in March 2019. Power analysis was based on the criteria of allowing 20% drop out and >80% power. Of all the parameters included in the study, ionised calcium was defined as the parameter that would require the highest number of participants to detect a significant and clinically relevant change. Therefore, this parameter was used for power calculation, even if this is not one of the main variables in the study. Based on this, a sample size of 1400 individuals was chosen. The participants were offered medical or surgical treatment and the choice of treatment method was based on clinical guidelines and the preferences of the patients. The MT included VLED for 12 to 20 weeks based on the BMI at baseline, followed by a period of food re-introduction and energy restricted diet for up to 12 months in total.[19] Of those receiving MT at the Regional Obesity Centre, 85% begin with a strict VLED period. The surgical options were RYGB or SG, according to patient characteristics and preferences. Follow-up of participants according to the study protocol is planned 2, 5 and 10 years after start of treatment.

Anthropometric and laboratory measurements

At inclusion and after 2 years, demographic data, blood and urine samples as well as height and weight measurements were collected for all participants. Blood samples that were critical for the choice of treatment were analysed directly, others were stored in a biobank.[19] All participants filled in a booklet that included questions to update demographic data as well as height and weight measurements. Detailed analysis of medical journals was not included.

Questionnaires

Included in the booklet were also the questionnaires used to cover three main areas: gastrointestinal symptoms and eating habits, physical activity and quality of life, and mental health. The questionnaires included to investigate eating habits were the 21-item Three-Factor Eating Questionnaire (TFEQ-R21)[20] and the Questionnaire on Eating and Weight Patterns-Revised (QEWP-R).[21] For information on physical activity and quality of life, the Saltin Grimby physical activity level questionnaire (SGQ),[22] the RAND-36 questionnaire[23] and EuroQol five-dimensional questionnaire (EQ-5D)[24] were included. The Beck Anxiety Inventory (BAI),[25] for the measurement of severity of anxiety and the Patient Health Questionnaire-9 (PHQ-9),[26] a self-reported measure of depression, were also included to investigate psychological health. The Alcohol Use Disorders Identification Test (AUDIT)[27] was used to identify harmful patterns of alcohol consumption.

Outcomes

The primary outcomes analysed were changes in anthropometric measures (weight, BMI and excess BMI (EBMI)) and metabolic variables (glucose, blood lipids, vitamins, minerals and haemoglobin) in the three treatment groups, as well as hospitalisations and all-cause mortality. Four secondary anthropometric outcomes were included: composite variables for successful or unsuccessful outcomes as well as percentage of weight loss of >10% or >20%. Treatment success at was defined as a loss of EBMI of at least 50% or BMI <30 kg/m^2 without any surgical procedures or need for hospitalisation during the follow-up period. Unsuccessful treatment was defined as a reduction of EBMI of less than 25% or the need for surgical treatment or hospitalisation during the follow-up period. Surgical treatment or need for hospitalisation were also seen as complications. Surgical procedures included were re-operations due to complication of bariatric surgery or other surgical procedures involving the gastrointestinal system. Hospitalisations for gastrointestinal disorders, infections, cardiovascular disease, complications of bariatric surgery, malignant disease or psychiatric disorders were also included as safety outcomes. Further secondary outcomes were changes in psychiatric health, levels of physical activity, quality of life, eating habits and alcohol consumption as reported by questionnaires.

Statistical analysis

Continuous variables are reported as mean (SD) and categorical variables as numbers (n) and proportions (%). Standardised mean difference (SMD) is a measure of distance between the group means (difference between sample means divided by pooled SD). Changes in clinical variables were analysed using a linear regression model that was adjusted for age, sex and baseline level of the variable as the absolute change in the outcome may be affected by the baseline value and age and sex are important determinants of the outcomes as well. These were reported as estimated means with 95% CIs. The likelihood of successful or unsuccessful treatment was assessed using a logistic regression model and presented using ORs with 95% CIs. A machine learning algorithm, random forest with conditional variable importance, was used to examine the importance of over 100 clinical variables as predictors for successful or unsuccessful treatment outcomes. Three thousand trees were used for each binary classification model. The variable importance was computed using a conditional permutation scheme to minimise the effect of correlation between variables included and reliably reflect the impact of each variable (party package in R).[28] These variables were divided manually into 15 clinical domains (anthropometry; mental well-being; lifestyle/habits; metabolic disease; biomarkers: vitamins/minerals; biomarkers: cardiovascular)/diabetes mellitus); socioeconomic status; biomarkers: other, age/sex; psychiatric disorders; cardiovascular disease; gastrointestinal disease; musculoskeletal disease; endocrine conditions and other conditions) and the importance of each domain on treatment outcome assessed. The proportion of missing data on BMI (and similar for the other variables) after 2 years were 40%, 27% and 21% in the MT, RYGB and SG groups, respectively. Missing data (online supplemental figure S1 and table S1) was handled using multiple imputation by chained equations algorithm. Data analyses were performed using R (R Foundation for Statistical Computing, V.4.0.3).

RESULTS

Of the 971 individuals that received treatment, 667 were available for follow-up at 2 years (MT 225, RYGB n=284, SG=158). Baseline characteristics of the study population can be seen in table 1. Pharmaceutical treatment of obesity at the 2-year follow-up was reported: 10 individuals used liraglutide (MT: 9, SG: 1), 2 individuals in the MT group used orlistat and 8 individuals used an SGLT2 inhibitor (MT: 6, RYGB: 1, SG: 1). The need for surgery and in-hospital treatment during the follow-up period was similar between the three treatment groups (MT 7.4%, RYGB 8.1%, SG 6.5%; MT 19.4%, RYGB 18.5%, SG 20.3%, respectively, p=0.83 and 0.39). Two patients died in both the MT and the RYGB groups, and there were no fatalities in the SG group (p=0.59). The cause of death was known for two cases (cancer), but unknown for two.

Baseline characteristics

Relevant metabolic comorbidities such as diabetes, hypertension, hyperlipidaemia, sleep apnoea and cardiovascular disease were similar between the groups (SMD <0.1). There were numerically more patients with other cardiac diseases, depression/anxiety and other psychiatric diseases, as well as a larger proportion of patients treated antihypertensive medications in the MT group (table 1). BMI was slightly higher in the RYGB and SG groups than in MT, as well as mean serum triglycerides and low-density lipoprotein (LDL)-cholesterol values, but serum creatinine and urine albumin levels were lower. Measurements of height and weight at baseline were made and registered by healthcare professionals.

Primary outcomes

Changes in anthropometric and laboratory variables after 2 years are given in figure 1. Measurements of height and weight were mainly self-reported at follow-up. The mean BMI at 2-year follow-up was 36.9 kg/m^2 after MT, 28.5 kg/m^2 after RYGB and 30.8 kg/m^2 after SG. The proportion of patients achieving a weight loss of 10% or more was 45.3%, 99.6% and 95.6%, respectively, and the proportion of patients achieving a weight loss of 20% or more was 16.0%, 94.0, and 74.7%, in MT, RYGB and SG, respectively (p<0.001). The largest percentual weight loss was seen after surgical treatment (33.0% after RYGB and 27.6% after SG) as compared with 8.9% after MT. The reported decrease in EBMI was 27.5%, 82.5% and 70.3% for MT, RYGB and SG respectively (p<0.001). There was

Table 1 Characteristics of participants in BASUN at baseline

	MT	RYGB	SG	
N	382	288	201	SMD*
Demographic varibles				
Sex=male (%)	103 (27.0)	87 (22.4)	49 (24.4)	0.12
Age, years—mean (SD)	47.6 (14.2)	42.0 (11.3)	40.8 (11.0)	0.36
Weight at baseline, kg—mean (SD)	118.1 (20.8)	122.4 (17.2)	123.9 (20.7)	0.19
BMI at baseline, kg/m^2—mean (SD)	41.0 (5.39)	42.5 (4.1)	42.8 (4.9)	0.24
Nicotine (%)				0.17
Smoker	24 (8.6)	24 (7.3)	14 (7.8)	
Ex-smoker	85 (30.4)	131 (40.1)	61 (34.1)	
Country of birth=Sweden (%)	226 (80.7)	248 (87.6)	137 (86.7)	0.13
Marital status (%)				0.21
Married	145 (43.7)	142 (40.3)	84 (45.4)	
Cohabitation	61 (18.4)	97 (27.6)	38 (20.5)	
Relationship w/o cohabitation	9 (2.7)	13 (3.7)	10 (5.4)	
Single	115 (34.6)	99 (28.1)	52 (28.1)	
Living w/parents	2 (0.6)	1 (0.3)	1 (0.5)	
Education (%)				0.31
Elementary school	51 (15.5)	42 (12.2)	15 (8.2)	
Vocational secondary education	34 (10.3)	35 (10.2)	24 (13.3)	
Two year secondary education	36 (10.9)	57 (16.6)	27 (14.8)	
Three year secondary education	75 (22.8)	108 (31.6)	47 (26.0)	
Started tertiary education	54 (16.4)	47 (13.7)	38 (21.0)	
University degree	79 (24.0)	55 (16.1)	29 (16.0)	
Diabetes=yes (%)	49 (12.8)	55 (14.2)	26 (12.9)	0.03
Hypertension=yes (%)	90 (23.6)	77 (19.9)	41 (20.5)	0.06
Hyperlipidaemia=yes (%)	14 (3.7)	18 (4.6)	12 (6.0)	0.07
Sleep apnoea=yes (%)	18 (4.7)	14 (3.6)	12 (6.0)	0.08
Cardiovascular disease=yes (%)	6 (1.6)	3 (0.8)	1 (0.5)	0.07
Other cardiac disease=yes (%)	21 (5.5)	11 (2.8)	3 (1.5)	0.15
Renal failure=yes (%)	3 (0.8)	1 (0.3)	1 (0.5)	0.05
Depression/anxiety=yes (%)	42 (11.0)	19 (4.9)	20 (10.0)	0.15
Other psychiatric disease=yes (%)	25 (6.5)	13 (3.4)	13 (6.5)	0.10
Antihyperglycaemics—n (%)	55 (14.4)	56 (14.4)	28 (13.9)	0.01
Antihypertensives—n (%)	141 (36.9)	115 (29.6)	59 (29.4)	0.11
Lipid lowering—n (%)	51 (13.4)	50 (12.9)	26 (12.9)	0.01
Anxiety depression— n (%)	92 (24.1)	71 (18.3)	53 (26.4)	0.13
Laboratory variables:				
Haemoglobin, g/L - mean (SD)	141.5 (12.5)	141.4 (11.0)	141.5 (12.1)	0.01
Calcium, mmol/L—mean (SD)	1.2 (0.0)	1.2 (0.0)	1.2 (0.0)	0.23
HbA1c, mmol/mol—mean (SD)	39.8 (12.1)	39.8 (11.5)	38.8 (9.1)	0.06
Glucose, mmol/L—mean (SD)	6.6 (2.3)	6.7 (2.3)	6.4 (1.7)	0.08
TSH, mIE/L—mean (SD)	2.6 (5.1)	2.7 (4.0)	2.6 (2.3)	0.03
Triglycerides, mmol/L—mean (SD)	1.8 (1.5)	1.9 (1.2)	1.7 (0.8)	0.11
HDL, mmol/L— mean (SD)	1.3 (0.3)	1.2 (0.3)	1.2 (0.3)	0.23
LDL, mmol/L— mean (SD)	3.0 (0.9)	3.10 (0.9)	3.11 (0.8)	0.08

Continued

Table 1 Continued

	MT	RYGB	SG	
N	382	288	201	SMD*
Creatinin, mmol/L—mean (SD)	76.4 (54.1)	71.4 (11.1)	68.2 (9.5)	0.22
U-albumin, mg/L—mean (SD)	54.4 (262.5)	21.5 (38.5)	13.6 (13.8)	0.22

*SMD: values <0.1 are considered non-significant.
BASUN, Bariatric surgery Substitution and Nutrition; BMI, body mass index; HbA1c, glycated haemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; MT, medical treatment; RYGB, Roux-en-Y gastric bypass; SG, sleeve gastrectomy; SMD, standardised mean difference; TSH, thyroid-stimulating hormone.

a significant difference in weight loss in females between the groups with the largest observed weight loss reported in the RYGB group (females: MT kg −19.3, RYGB −37.8 kg and SG −32.9 kg). The difference in males was not significant between the surgical methods (MT −14.2, RYGB −32.3 and SG −34.6). The reduction in BMI was significantly greater in the surgical groups in comparison with MT. The difference between the surgical groups was only statistically significant for females (RYGB: −13.1, SG: −11.5).

Levels of HbA1c decreased in all groups (including all participants, not specifically individuals with diabetes) and there was not a statistically significant difference between the groups. There was a larger reduction in TG in the surgical groups in comparison with the MT group, but the difference was not significant between the surgical groups. The rise in HDL levels was significantly greater in both surgical groups in comparison with MT. The reduction in LDL levels was the greatest in the RYGB group whereas the difference between MT and SG was not significant. There were similar tendencies to reductions in haemoglobin levels and increases in B12 vitamin, folate, and serum iron levels in both surgical groups compared with the MT group. Levels of vitamin D increased in all groups and there was no significant difference between the groups.

Secondary outcomes

The results from the QEWP-R questionnaire reflecting bulimia with or without compensatory behaviour were similar in all treatment groups at baseline. The proportion of patients qualifying for binge eating at 2 years follow-up was lower in the surgically treated groups, as well as reported emotional eating or uncontrolled eating according to TFEQ (table 2). Potential anxiety (BAI) was most common in MT group at baseline and 2 years follow-up. Potential depression, according to PHQ-9, was also most common in the MT group at baseline and remained higher in the MT group after 2 years. Quality of life scores (EQ-5D) were similar at baseline but slightly higher in RYGB and SG groups at follow-up. There were no clear differences in physical activity levels between the groups before treatment (Saltin Grimby questionnaire), but the proportion of physically inactive patients declined in all groups. Light and regular physical activity increased in the two surgically treated groups, after 2 years. The groups did not differ with regard to risk of abuse for alcohol according to AUDIT before and after 2 years of follow-up (table 2).

Successful treatment was more common in the surgical groups (MT 98 (25.7%), RYGB 250 (64.4%) and SG 120 (59.7%), p<0.001). The likelihood for successful treatment was higher in the two surgical groups (OR 5.3 for RYGB and 4.3 for SG), but not significantly different between them in reference to MT (figure 2). The likelihood for unsuccessful treatment was lower after surgical treatment than MT but did not differ significantly between the surgical groups (OR RYGB 0.2, SG 0.2). The differences between MT and surgical treatment regarding likelihood for success was even larger after analysis without imputed data, but still without statistically significant difference between the two surgical methods (OR RYGB 11.8 (7.66, 18.58) and OR SG 8.38 (5.2, 13.8)).

The relative importance of the 15 clinical domains on treatment success in general and for each treatment group, as well as an overview of the individual variables included within each domain, is given in figure 3. Baseline anthropometry had the strongest predictive value for treatment success overall, other important domains were psychiatric disease, lifestyle and habits, biomarkers, mental well-being and socioeconomic status. In the MT group, anthropometry, mental well-being, biomarkers for cardiovascular disease and diabetes as well as lifestyle and habits all exhibited strong predictive values. In the RYGB group biomarkers, anthropometry and musculoskeletal disease had the strongest predictive values while biomarkers, anthropometry and lifestyle and habits were the most important the SG group.

DISCUSSION

The results of this follow-up in clinical routine care 2 years after the start of treatment of almost one thousand people with obesity using medical and surgical methods, show positive results on weight as well as cardiovascular risk factors and minerals. The effect of bariatric surgery with RYGB or SG was observed to be more effective than MT with regard to weight loss and did not lead to a difference in levels of minerals, vitamins or haemoglobin. The reduction in weight and BMI was not significantly different between the surgical groups, and the likelihood

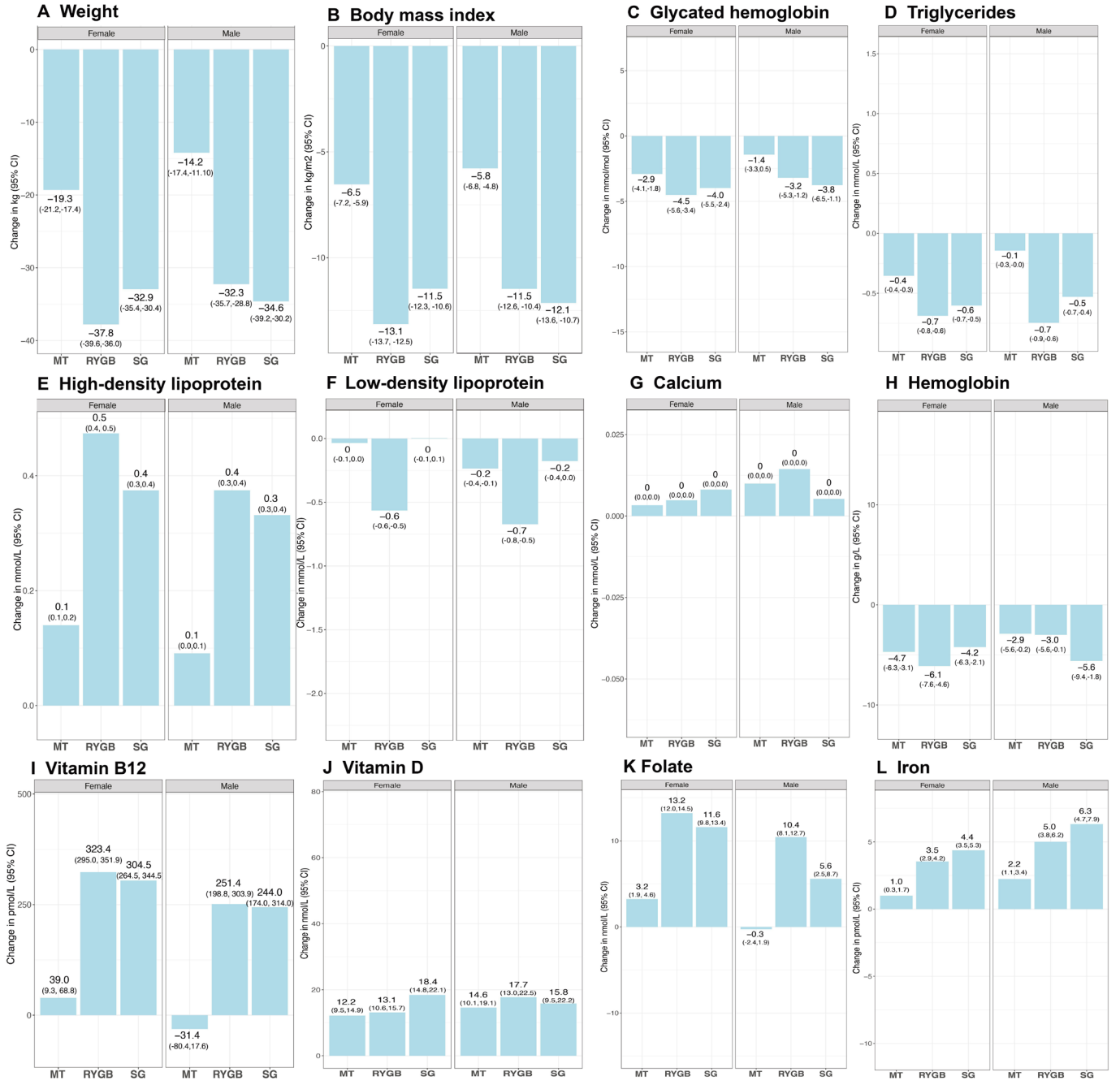


Figure 1 Changes in clinical variables presented as estimated means with 95% CIs. Missing data patterns, before and after imputation with multiple imputation by chained equations. AUDIT, Alcohol Use Disorders Identification Test; BAI, Beck Anxiety Inventory; BE, binge eating; BN, bulimia nervosa; BNC, bulimia nervosa with compensatory behaviour; CR, cognitive restraint; EE, emotional eating; EQ-5D, EuroQol Five-Dimensional Questionnaire; MT, medical Treatment; PHQ-9, Patient Health Questionnaire-9; QEWPR, Questionnaire on eating and weight patterns, revised; RYGB, Roux-en-Y gastric bypass; SG, sleeve gastrectomy; SGQ, Saltin Grimby Questionnaire; TFEQ, three-Factor Eating Questionnaire; UE, uncontrolled eating.

for successful and unsuccessful treatment results was similar in these two groups. MT including VLED was also shown to be effective, with 45% of the individuals maintaining a weight loss of over 10% after 2 years of follow-up.

The BASUN study is clearly the largest long-term study comparing two surgical methods for the treatment of obesity with structured MT that includes a period of strict caloric restriction. TheMT in BASUN included 12–20 weeks of VLED which was followed-by a period of food re-introduction and continued with energy restricted diet for up to 12 months. This method has been shown to be effective. The DIRECT study reported positive effects on weight and diabetes remission in close to half of the participants at 12 months after VLED in primary care practice.[16] However, there is a general lack of studies comparing bariatric surgery and well-structured MT including VLED and long-term strict caloric restriction. Pharmaceutical treatment to support weight loss in the

Table 2 Results from questionnaires, at baseline and 2-year follow-up

	Baseline				Two year follow-up			
	MT	RYGB	SG	P value	MT	RYGB	SG	P value
QEWP BN w CB—n (%)	0 (0.0)	5 (1.4)	0 (0.0)	0.03	4 (1.8)	0 (0.0)	0 (0.0)	0.02
QEWP BN—n (%)	0 (0.0)	0 (0.0)	0 (0.0)	NA	1 (0.4)	2 (0.7)	0 (0.0)	0.58
QEWP BE—n (%)	25 (7.8)	20 (5.7)	14 (7.5)	0.54	18 (8.0)	4 (1.4)	2 (1.3)	<0.01
TFEQ CR—mean (SD)	2.3 (0.7)	2.3 (0.6)	2.3 (0.7)	0.36	2.6 (0.7)	2.5 (0.7)	2.4 (0.7)	0.01
TFEQ EE—mean (SD)	2.5 (1.0)	2.3 (0.9)	2.4 (0.9)	0.07	2.4 (1.0)	1.9 (0.9)	2.0 (0.9)	<0.01
TFEQ UE—mean (SD)	2.3 (0.8)	2.2 (0.8)	2.3 (0.8)	0.63	2.1 (0.8)	1.6 (0.7)	1.6 (0.7)	<0.01
AUDIT score—mean (SD)	2.8 (2.9)	2.8 (2.6)	3.1 (3.0)	0.43	2.6 (2.9)	3.2 (3.3)	3.0 (2.9)	0.08
BAI, potential anxiety—n (%)	97 (27.6)	74 (20.6)	38 (20.3)	0.05	52 (23.4)	54 (19.4)	29 (19.3)	0.48
PHQ-9, potential depression—n (%)	118 (33.9)	82 (23.0)	44 (23.5)	<0.01	67 (30.3)	46 (16.6)	33 (21.9)	<0.01
EQ-5D index score—mean (SD)	0.7 (0.2)	0.7 (0.2)	0.7 (0.2)	0.47	0.7 (0.2)	0.8 (0.2)	0.8 (0.2)	<0.01
SGQ—n (%)				0.41				<0.01
Physically inactive	163 (47.1)	153 (43.1)	74 (40.7)		65 (30.2)	41 (14.8)	41 (27.3)	
Some light physical activity	156 (45.1)	179 (50.4)	94 (51.6)		119 (55.3)	175 (63.2)	84 (56.0)	
Regular physical activity and training	22 (6.4)	22 (6.2)	13 (7.1)		27 (12.6)	57 (20.6)	23 (15.3)	
Regular hard physical training for competition sports	5 (1.4)	1 (0.3)	1 (0.5)		4 (1.9)	4 (1.4)	2 (1.3)	

AUDIT, Alcohol Use Disorders Identification Test; BAI, Beck Anxiety Inventory; BE, binge eating; BN, bulimia nervosa; CB, compensatory behaviour; CR, cognitive restraint; EE, emotional eating; EQ-5D, EuroQol Five-Dimensional Questionnaire; MT, medical treatment; PHQ-9, Patient Health Questionnaire-9; QEWP, Questionnaire on Eating and Weight Patterns; RYGB, Roux-en-Y gastric bypass; SG, sleeve gastrectomy; SGQ, Saltin Grimby Questionnaire; TFEQ, Three-Factor Eating Questionnaire; UE, uncontrolled eating.

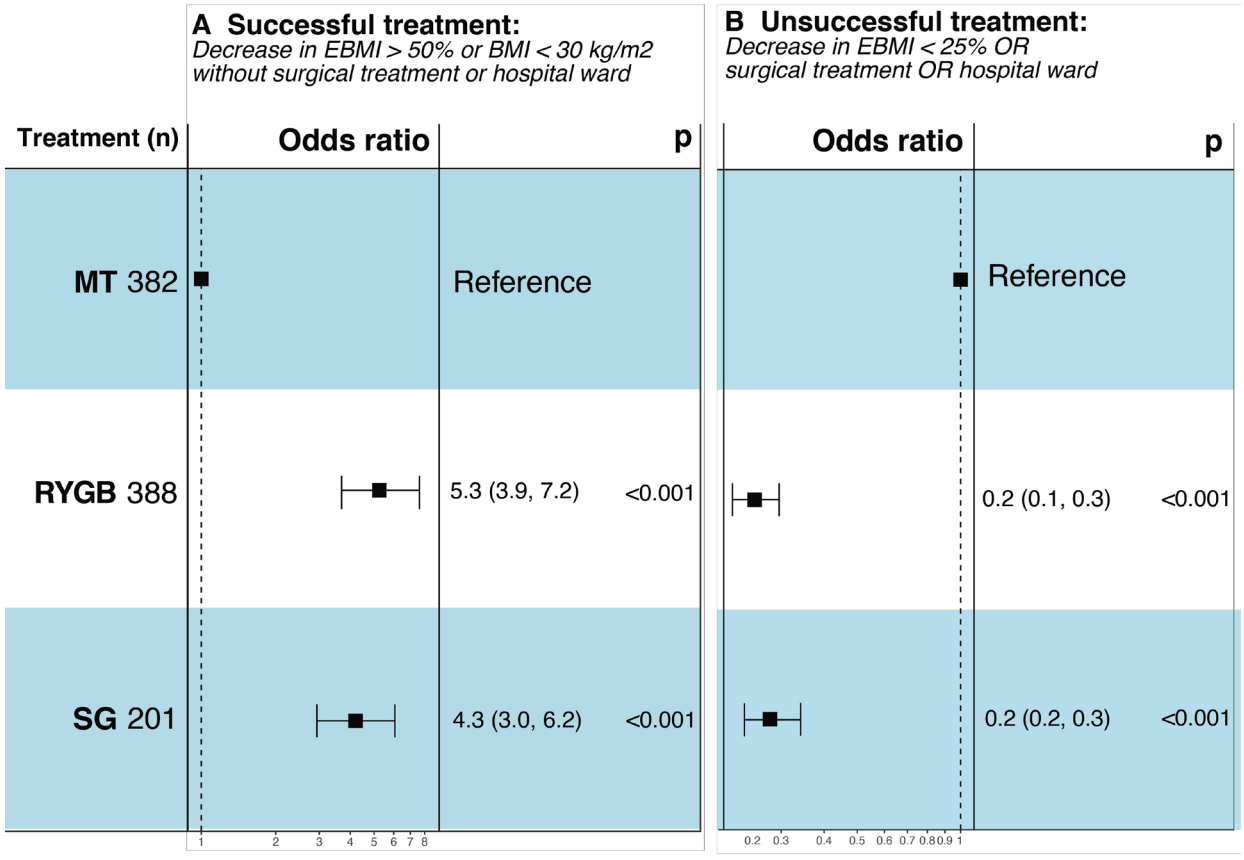


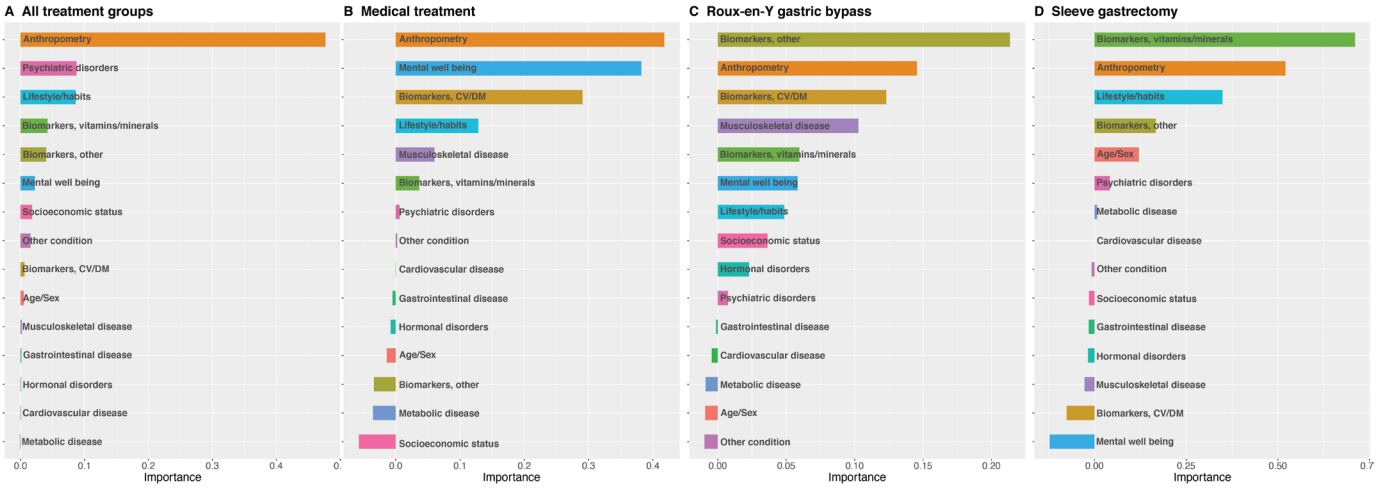
Figure 2 Likelihood for successful or unsuccessful treatment. Successful treatment is defined as as a decrease in excess body mass index (BMI) of at least 50% or a BMI of less than 30 kg/m^2 at 2-year follow-up without the need for surgical treatment or hospital ward during the follow-up period. Unsuccessful treatment is defined as a loss of less than 25% of excess BMI (EBMI) or the need for surgical or hospital ward during the follow-up period. MT, medical treatment; RYGB, Roux-en-Y gastric bypass; SG, sleeve gastrectomy.

medically treated group in our study, as well as in some individuals after surgery, could have been further facilitated. However, only orlistat was reimbursed at the time of this study and costs of other alternatives, such as liraglutide, naltrexon/bupropion were not. It is possible that GLP-1 receptor agonists and similar agents, such as semaglutide or tirzepatide, could play a role in future studies of structured treatment of obesity.[29 30]

Overall, there were positive effects on HbA1c, minerals and vitamins. Blood lipids improved in all treatment groups, and there was a profound effect on LDL-cholesterol after RYGB. There were no observed differences between the groups with regard to need for hospitalisation, surgical treatment or death during the follow-up. Minor positive effects on eating behaviour were also noted, as well as on mental well-being, particularly in the surgically treated groups, with slightly higher quality of life (EQ-5D). Degree of physical activity improved in all treatment groups.

Our results confirm the results of other prospective studies and a new meta-analysis comparing the effects of RYGB and SG. They report absence of statistically significant differences between these methods in terms of weight loss or effects on obesity-related morbidity.[31–33] Previous studies have implied that the risk of complications is somewhat lower after SG,[33] but we did not observe a difference in hospitalisation, need for surgical treatment or deficiencies between the surgical groups. Larger studies, such as the Swedish Obese Subjects trial that includes a general population of obese individuals, as well as the STAMPEDE trial that focuses on individuals with type 2 diabetes, have compared conservative treatment of obesity with addition of pharmaceutical treatment as recommended by clinical guidelines and have also shown superiority of surgical treatment.[18 34] A meta-analysis of randomised control trials comparing bariatric surgery and non-surgical treatment also reported greater effect on weight loss, remission of type 2 diabetes and metabolic variables after bariatric surgery.[35]

The most common postoperative deficiencies described after bariatric surgery are those of vitamin D, iron, B_{12} and folate.[9] Preoperative malnutrition is also common due to suboptimal diet and sequestration of fat-soluble vitamins in adipose tissue. We observed positive changes on B12 vitamin, folate and iron in the surgical groups. Interestingly, levels of vitamin D increased in all groups. It is likely that the positive effects on HbA1c and blood lipids were associated with the weight loss. The observed superiority of the



Individual variables included in each domain:

Biomarkers, CV/DM: cholesterol, HDL, LDL, TG, HbA1c, glucose

Mental well being: results from BAI and PHQ-9 questionnaires

Anthropometry: baseline BMI, baseline weight

Metabolic disease: diabetes, sleep apnea, hypertension, hyperlipidemia, treatment for these disorders

Musculoskeletal disease: analgesics, chronic pain, reumatologic disease, musculoskeletal disease

Biomarkers, vitamins/minerals: vitamin D, iron, cobalamin, folate, calcium

Socioeconomic status: marital status, education, country of birth

Biomarkers, other: hemoglobin, TSH, T4, ASAT, ALAT, creatinine, u-albumin

Cardiovascular disease: anticoagulants, IHD, stroke, arrhythmia, heart failure, valvular disease, VTE

Other condition: previous surgery, cancer, renal failure, vitamin/mineral deficiency, other medical conditions

Gastrointestinal disease: PPI, disease of stomach, gallbladder or intestines

Age/Sex: age, sex

Hormonal disorder: thyroid hormone replacement, hormonal conditions related to obesity

Lifestyle/habits: nicotine, results from QEWPR, EQ5D, TFEQ, AUDIT, SGQ questionnaires

Psychiatric disorders: depression, anxiety, ADHD, other psychiatric disease or treatment for these disorder

Figure 3 Predictive value of 15 clinical domains on the success of obesity treatment (A) and for different treatment groups (B–D). ADHD, attention-deficit/hyperactivity disorder; ALAT, alanine aminotransferase; ASAT, aspartate aminotransferase; AUDIT, Alcohol Use Disorders Identification Test; BAI, Becks Anxiety Inventory; BMI, body mass index; CV, cardiovascular; DM, diabetes mellitus; EQ-5D, EuroQol Five-Dimensional Questionnaire; HbA1c, glycated haemoglobin; HDL, high density lipoprotein; IHD, ischaemic heart disease; LDL, low-density lipoprotein; PHQ-9, Patient Health Questionnaire-9; PPI, proton-pump inhibitors; QEWP, Questionnaire on Eating and Weight Patterns; SGQ, Saltin Grimby Questionnaire; T4, thyroxine; TFEQ, Three-Factor Eating Questionnaire; TG, triglycerides; TSH, thyroid-stimulating hormone; VTE, venous thromboembolism.

effects of RYGB on LDL-cholesterol are similar to that described in previous studies.[36 37] Currently, further studies comparing the effects of RYGB and SG on LDL-cholesterol specifically are ongoing.[38] The reported differences between the groups at follow-up with regard to eating patterns, mainly binge eating, might also reflect an effect of the MT. Individuals in the MT group had monthly visits with nurses or dieticians for a year to discuss eating habits and life-style choices and might therefore have greater awareness of behavioural patterns related to eating. The anatomical restrictions of the surgical methods could also decrease binge eating tendencies.

Patient characteristics with high predictive value for treatment success differed between the groups although anthropometry and lifestyle and habits were important in all groups. Mental well-being was more important in the MT group in comparison with the surgical groups. Variables for psychiatric health (mental well-being and psychiatric disorders) were strong predictors for all treatment groups. This indicates that questionnaires focusing on symptoms of depression and anxiety might be of value when decisions on treatment for obesity are made. According to clinical guidelines, an unstable psychiatric disease is a contraindication for surgical treatment of obesity, and indeed, the choice of treatment in this study in clinical practice, was based not only on clinical guidelines but also on the patients' preferences. Therefore, the differences in patient characteristics before treatment were anticipated, and are likely to affect the results. The BASUN study, however, did include a heterogenous population of individuals with obesity, referred from the region of Western Sweden to the regional obesity centre for the treatment of obesity and is therefore representative for this part of the country, with 1.7 million inhabitants.

Limitations

The fact that the study is largely based on data reported from the participants may cause bias as the participants that are not successful in their treatment are less likely to report back, as well as individuals that have significant psychiatric disorders. The requirement that participants must understand Swedish excluded some participants of other nationalities. The successive lost to follow-up is common in prospective studies, especially with regard to replies to questionnaires. This was also a problem in our study with around 34% of participants that had some information missing at 2-year follow-up. This deficit of information was handled by means of multiple imputations.

Conclusions

In clinical practice, bariatric surgery by RYGB or SG is most effective, but meaningful weight loss is achievable

in many patients by MT with strict caloric restriction and stepwise introduction of a normal diet. All treatments showed positive effects on well-being, cardiovascular risk factors and levels of vitamins and minerals.

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Acknowledgements Dr Malin Werling initiated the BASUN study. Dr Lars Fändriks was PI with Dr Björn Eliasson as coinvestigator until 2020. Dr Karin Mossberg started as PI with Dr My Engström as coinvestigator from 2021.

Contributors All authors contributed to the conception and design of this manuscript. AR and GH performed the statistical analyses. All authors contributed to the interpretation of data. GH and BE drafted the article, and all authors (GH, ME, AR, FL, VW, LF, KM and BE) contributed to the critical revision of the article. KM, LF and BE are the guarantors of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. All authors read and approved with final manuscript.

Funding The study was financed by Region Västra Götaland and by grants from the Swedish state under the agreement between the Swedish government and the country councils (grant number N/A), the ALF-agreement (ALFGBG-725291), as well as the Novo Nordisk Foundation (grant number N/A).

Competing interests BE reports personal fees (expert panels, lectures) from Amgen, AstraZeneca, Boehringer Ingelheim, Eli Lilly, Merck Sharp & Dohme, Mundipharma, Navamedic, NovoNordisk, RLS Global, and grants and personal fees from Sanofi, all outside the submitted work.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval The Ethical Regional Board of Gothenburg approved the protocol (Dr. no 673-14). Informed consent to participate was obtained from all study participants.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request. Availability of data and material: Data and material are not available due to the nature of this prospective study. The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

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