BARI-LIFESTYLE Trial: assessing and maximising the health benefits of bariatric surgery

A thesis submitted for the degree of Doctor of Philosophy

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I, Friedrich Christie Bin Jassil, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

Abstract

Bariatric surgery is the most effective treatment for people living with severe obesity, but weight loss and health outcomes vary markedly from person to person. This thesis aimed to evaluate the efficacy of a post-surgery lifestyle programme in maximising the health benefits of bariatric surgery. One hundred fifty-three patients (78.4% female) with a mean (SD) age of 44.2 (10.6) years and body mass index (BMI) of 42.4 (5.7) kg/m^2 undergoing Roux-en-Y gastric bypass (28.8%), one anastomosis gastric bypass (16.3%) and sleeve gastrectomy (54.9%) were enrolled in a BARI-LIFESTYLE observational study. On the day of surgery, participants were randomised to receive standard post-surgery care (CON) (*n*=74) or the BARI-LIFESTYLE intervention study (INT) (*n*=79), consists of 17 sessions of nutritional-behavioural tele-counselling and 12-week supervised exercise programme. Anthropometric measurements, body composition, bone mineral density (BMD), physical activity levels and sedentary behaviour, physical function and strength, health-related quality of life (HRQoL) and depressive symptomatology were assessed periodically in the first postoperative year. Participants' views and experiences of the lifestyle programme including the tele-exercise classes during the COVID-19 lockdown were assessed qualitatively. Bariatric surgery reduced body weight, fat mass, fat-free mass, and BMD (total hip, femoral neck, and lumbar spine). Physical function and strength, HRQoL, and depressive symptomatology improved following surgery.

Percentage weight loss at 6-month post-surgery (primary outcome), did not differ between groups (mean difference [MD]=-1.0%; 95% CI, -3.4 to 1.4; p=0.39). The improvement in six-minute walk test was higher in INT than CON (MD=+19.6 metres; 95% CI, 0.9 to 38.2; p=0.04). Per-protocol analysis showed favourable impacts of the programme on relative handgrip test (MD=+0.1 kg/BMI; 95% CI, 0.0 to 0.2; p=0.02) and whole-body BMD (MD=+1.5%; 95% CI, 0.1 to 2.8; p=0.04). Patient-reported outcomes support the beneficial impacts of the lifestyle programme including the tele-exercise in helping them adapt to life after bariatric surgery.

Impact Statement

The findings from this thesis have several implications to a wide range of groups including patients, healthcare professionals, the general public, policymakers, service commissioners and clinical decision-makers. The demand for publicly funded bariatric surgery in the United Kingdom (UK) is high, however, capacity is limited by healthcare funding decisions (Welbourn *et al*., 2016). The National Bariatric Surgery Registry is a prospective database of bariatric surgery performed in the United Kingdom that collects limited outcome data such as weight loss, resolution of comorbidities and health-related quality of life (HRQoL) using a generic questionnaire (National Bariatric Surgery Registry, 2020). The BARI-LIFESTYLE observational study provides further data on the effect of bariatric surgery on body composition including bone mineral density (BMD), physical activity levels and sedentary behaviour, physical function and strength, mental health and HRQoL assessed using an obesity-specific questionnaire. Collectively, these data can be used to compare with the outcomes data from the non-surgical weight loss programmes to assess long-term cost-effectiveness. This, therefore, can assist the policymakers, service commissioners and clinical decision-makers in making informed decisions regarding the provision of bariatric surgery in the country. Increasing the number of bariatric surgery could benefit the current obesity crisis in the UK but would require significant investment so that service provision is adequate for demand.

Especially in the present economic climate, there is increased competition for public funds in healthcare services.

Due to a strong weight bias and obesity stigma in society, people living with obesity do not receive adequate health care (Flint, 2021). Furthermore, the stigma attached to bariatric surgery makes access to such effective weight loss treatment difficult (Welbourn *et al*., 2016, Phelan, 2018). Therefore, through various media platforms, data from the BARI-LIFESTYLE observational study will be communicated to the general public to raise awareness regarding the health benefits of bariatric surgery.

Growing evidence has shown that weight loss and health outcomes of bariatric surgery vary from person to person and data from the present observational cohort provide further evidence on this. In 2014, the National Institute for Health and Care Excellence recommended high-quality research to assess the efficacy of lifestyle intervention programmes (exercise, behavioural or dietary) to improve health outcomes of bariatric surgery (NICE, 2014b). The BARI-LIFESTYLE intervention study was conducted to respond to this unmet clinical need as currently, there are no post-surgery lifestyle intervention programmes to help patients adapt to life after bariatric surgery. As presented in this thesis, a combined nutritional-behavioural tele-counselling and tailored supervised exercise programme delivered in the first year of surgery improves physical function and has a favourable impact on physical strength and whole-body BMD. Such a programme is therefore beneficial to counteract the adverse outcomes of bariatric surgery associated with fat-free mass loss and BMD loss. Importantly, patient-reported outcomes support the beneficial impacts of the lifestyle programme in helping them adapt to life after bariatric surgery. The present findings are therefore useful to inform the existing clinical practice guidelines for post-bariatric care.

Finally, this thesis provides further evidence on the potential use of telehealth to be adapted in bariatric care services. Both the nutritional-behavioural tele-counselling and the tele-exercise classes, the latter delivered virtually during the COVID-19 pandemic and assessed in the BARI-LIFESTYLE qualitative study, were perceived to be acceptable. These findings, therefore, support the NHS Long Term Plan that recommends the use of technology in prevention, care and treatment to be mainstreamed across the NHS (National Health Service, 2019).

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This five years of work will not be possible without the trust given to me by my principal supervisor Professor Rachel L. Batterham, to lead the BARI-LIFESTYLE trial, the largest trial to date, undertaken by the Centre for Obesity Research. Thank you so much for this once in a lifetime opportunity that moulded me to be a researcher in obesity field. I would also like to express a huge appreciation to my secondary supervisor, Professor George K. Grimble who was always there to motivate me and keep track of my progress over the years.

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"It is literally true that you can succeed best and quickest by helping others to succeed."

- Napoleon Hill -

..Damit palanad intad daki kumaa dikoyu ngawii..

..Kotohuadan mantad dogo kumaa songovian..

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List of Abbreviations

AGB	Adjustable gastric banding
AUDIT-C	Alcohol Use Disorders Identification Test-C
BDI-II	Beck Depression Inventory-II
BIA	Bioelectrical Impedance Analyser
BOMSS	British Obesity and Metabolic Surgery Society
BMI	Body Mass Index
BPD/DS	Biliopancreatic diversion with duodenal switch
CI	Confidence interval
COVID-19	Coronavirus Disease 2019
CSRI	Client Service Receipt Inventory
CT	Computed tomography
CVD	Cardiovascular disease
DXA	Dual-energy X-ray absorptiometry
EQ-5D-3L	3-Level EuroQol-5D
FFM	Fat-free mass
FM	Fat mass
GLP-1	Glucagon-like peptide-1
HbA_{1c}	Glycated haemoglobin
HGS	Handgrip strength
HRA	Health Research Authority
HRQoL	Health-Related Quality of Life
ISRCTN	International Standard Randomised Controlled Trial Number
ITT	Intention to treat
IWQOL-Lite	Impact of Weight on Quality of Life-Lite

MCID	Minimal clinically important difference
MD	Mean difference
MDT	Multidisciplinary team
MRI	Magnetic resonance imaging
MVPA	Moderate-to-vigorous physical activity
NBSR	National Bariatric Surgery Registry
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
OAGB	One anastomosis gastric bypass
OR	Odd ratio
OSA	Obstructive sleep apnoea
PA	Physical activity
PRO	Patient-related outcome
PYY	Peptide YY3-36
QoL	Quality of life
RCT	Randomised controlled trial
REC	Research Ethics Committee
RYGB	Roux-en-Y gastric bypass
SD	Standard deviation
SF-36	36-Item Short Form Health Survey
SG	Sleeve gastrectomy
SM-BOSS	Swiss Multicentre Bypass or Sleeve Study
STS-test	Sit-to-stand test
T2D	Type 2 diabetes
UCL	University College London
UCLH	University College London Hospitals
UK	United Kingdom
VAS	Visual Analogue Scale
WHO	World Health Organisation
6MWT	6-minute walk test
%EBMIL	Percentage excess BMI loss
%EWL	Percentage excess weight loss
%WL	Percentage weight loss

Chapter 1
Introduction[1]

1.1 Thesis background and rationale

Obesity, defined as Body Mass Index (BMI) of 30 kg/m^2 and above, is characterised by an abnormal or excessive body fat accumulation to the extent that health may be adversely affected (WHO, 2020a). It is linked to the development of several chronic diseases such as type 2 diabetes (T2D), cardiovascular disease (CVD), liver disease, infertility, obstructive sleep apnoea (OSA), musculoskeletal disorders, mental health and certain types of cancer (Jassil and Batterham, 2021). If left without interventions, obesity increases the risk of premature death and shortened life expectancy (Global BMI Mortality Collaboration, 2016). The World Health Organisation (WHO) had declared obesity as a global epidemic over two decades ago (WHO, 2000). However, only in recent years, several countries and international organisations have started to recognise

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[1]The published work related to this chapter is available in Appendix 1. JASSIL, F. C. & BATTERHAM, R. L. 2021. Medical Complications of Obesity. *In:* WASS, J., ARLT, W. & SEMPLE, R. (eds.) *Oxford Textbook of Endocrinology and Diabetes.* Third ed.: Oxford University Press.

obesity as a chronic progressive disease due to its impact upon health (Bray *et al*., 2017). Interestingly, the United Kingdom (UK) is still debating as to whether obesity should be regarded as such (Wilding *et al*., 2019). Since 2019, the Royal College of Physicians has called for obesity to be recognised as a disease so that effective preventative strategies and treatments are adequately prioritised and funded, to tackle stigma and discrimination associated with obesity and remove all barriers to treatment (RCP, 2018).

In 2016, the worldwide obesity prevalence was estimated to have reached 650 million, nearly triple the figure since 1975 (WHO, 2020a). If this trend continues on the same trajectory, the global prevalence of adult obesity is projected to reach 18% in men and 21% in women by 2025. Many countries expected to surpass this prediction (NCD Risk Factor Collaboration, 2016). In the UK, obesity has long been recognised as a major public health concern (Chief Medical Officer, 2002). Despite various strategies and policies implemented at the national level directed to reduce the prevalence of obesity, the number of people affected by obesity continues to grow unabated (Department of Health, 2015a). Currently, in England, 28.7% of adults are living with obesity, 26% and 29% of men and women, respectively (NHS Digital, 2020). It is estimated that the National Health Service (NHS) is spending £6.05 billion annually to treat obesity and its sequelae (Tovey, 2017).

In view of the aetiology of obesity driven by the complex interaction of genetic, biological, environmental, and social factors, achieving and maintaining weight loss over the long term undoubtedly poses a great challenge (Hruby and Hu, 2015, Theilade *et al.*, 2021). The standard approaches for the treatment of obesity incorporate lifestyle modification, pharmacotherapy and bariatric surgery (NICE, 2014b). Lifestyle modification remains the first line of treatment which involves restricting daily energy intake and increasing physical activity with behavioural changes underpinning both elements (Yumuk *et al.*, 2015, Garvey *et al.*, 2016). Unfortunately, many people face difficulties in sustaining weight loss over the long term due to the strong compensatory biological drivers to weight regain (Maclean *et al*., 2011, Busetto *et al*., 2021). Several anti-obesity drugs are available to promote weight loss, however, modest efficacy, safety concerns and cost have made this option less attractive in the past few years (Bessesen and Van Gaal, 2018). In fact, only Orlistat and Liraglutide 3.0 mg (in people with BMI of at least 35 kg/m^2 or at least 32.5 kg/m^2 for members of minority ethnic groups plus pre-diabetes and an additional CVD risk factor) are approved by the National Institute for Health and Care Excellence (NICE) for obesity treatment within the NHS (Manning *et al*., 2014, NICE, 2020). Most recently, NICE recommends Semaglutide 2.4 mg for adults with at least one-weight-related condition and a BMI of at least 35 kg/m^2, in particular for people with a BMI between 30.0 – 34.9 kg/m^2 (NICE, 2022)

Bariatric surgery is currently the most effective treatment for people with severe obesity (Gloy *et al*., 2013). It engenders a remarkable sustained weight loss in the long term and leads to remission or improvement of obesity-associated comorbidities, particularly T2D and increased life expectancy (Colquitt *et al*., 2014). The increased recognition of the sustained long-term beneficial health outcomes of bariatric surgery has led to an increased number of bariatric operations undertaken globally (Angrisani *et al*., 2018). Yet in the UK, the number of people undergoing bariatric surgery has been reduced over the past decade with less than 0.5% of 3.6 million eligible people receiving surgery (Desogus *et al*., 2019). Currently, merely 7000 procedures annually are being performed in the UK (National Bariatric Surgery Registry, 2020), a figure that is significantly lower in comparison to other European counterparts (Booth *et al*., 2016).

Welbourn and colleagues highlighted key factors that contribute to lower provision of bariatric surgery in the UK, even though it is the most effective treatment for obesity (Welbourn *et al*., 2016). For instance, it appears that the UK 4-tiered weight management system hinders access to bariatric surgery (Hazlehurst *et al*., 2020). In fact, some patients remain in the tiered pathway for years before they are referred for surgery. This delay can be off-putting for some (Owen-Smith *et al*., 2017). But the most striking reason for the lower provision of this procedure is the stigma attached to obesity and bariatric surgery, not only by the general public, but also amongst the healthcare professionals (Flint *et al*., 2015, Phelan, 2018). This indirectly affects how this procedure is being funded by the NHS, often considered as the surgical procedure of the lowest priority. Furthermore, the lack of prospective research study evaluating the impact of bariatric surgery delivered in the UK healthcare setting means limited available scientific data that can be used to promote public awareness. The UK National Bariatric Surgery Registry (NBSR) only collects prospective data that are limited to outcomes such as weight loss, resolution of comorbidities and health-related quality of life (HRQoL) using a generic questionnaire (National Bariatric Surgery Registry, 2020). Other important outcome data such as body composition, bone mineral density (BMD), physical activity levels, sedentary behaviour, physical function and strength and cost-effectiveness are not included. In particular, there is an increasing concern regarding bariatric surgery that might has an adverse impact on body composition and increases risk of bone fracture (Gagnon and Schafer, 2018, Nuijten *et al*., 2020). These data are needed by policymakers, service commissioners and clinical decision-makers in making informed decisions to support the increased provision of bariatric surgery and also to inform future clinical guidelines. ***Therefore, the first part of this thesis aims to evaluate the impact of bariatric surgery on body weight, resolution of comorbidities, body composition, BMD, physical activity levels, sedentary behaviour, physical function and strength, HRQoL and mental health from patients undergoing bariatric surgery in the UK NHS setting.***

Whilst in population-level bariatric surgery yields impressive health outcomes, these benefits are unfortunately not universal. There is huge inter-individual variability in weight loss and comorbidities resolution with 20-30% of patients exhibiting poor post-operative outcomes (Manning *et al*., 2015). Difficulty in adapting to the lifestyle changes required after surgery is known to be one of the attributable factors to poor outcomes. This includes increased calorie consumption over time, inadequate protein intake, poor compliance with vitamins and minerals supplements and low physical activity levels, with time spent in sedentary behaviour being still considerably high (Sheets *et al*., 2015, Hood *et al*., 2016). Given the costs and risks of bariatric surgery (accounting for 0.1% mortality and 5% complication) (Gulliford *et al*., 2017, Lim *et al*., 2018), coupled with limited access to surgery (Desogus *et al*., 2019), strategies to maximise the health benefits obtained from bariatric surgery are urgently needed.

Therefore, in 2014 we undertook a pilot study to evaluate the feasibility of a combined nutritional-behavioural and supervised exercise intervention, delivered in a group setting at 3 to 6 months post-surgery (Jassil *et al*., 2015). At one-year post-surgery, the intervention group exhibited greater percentage weight loss (%WL) and higher physical activity levels compared to the matched historical control receiving a standard follow-up care. These preliminary findings coupled with the research recommendation from NICE (NICE, 2014a) and systematic reviews (Bellicha *et al*., 2021, Julien *et al*., 2021) to evaluate postoperative behavioural and exercise interventions provided a strong rationale to undertake a randomised control trial (RCT) in bariatric surgery patients to investigate if an early postoperative nutritional-behavioural and exercise intervention could improve the health outcomes of bariatric surgery. ***Therefore, the second part of this thesis aims to assess the efficacy of a post-surgery lifestyle intervention to maximise the health outcomes of bariatric surgery via a multi-centre RCT.***

1.2 Thesis aims

In light of this, the aims of this doctoral research were:

1. To prospectively assess the impact of bariatric surgery, delivered in the UK healthcare setting, upon health of people with severe obesity.
2. To investigate whether additional support, in the form of a post-surgery lifestyle programme, can further improve upon the health outcomes of bariatric surgery.

Three studies have been conducted to achieve these aims:

Study 1: **The BARI-LIFESTYLE observational study** was a prospective longitudinal cohort study that evaluated the impact of bariatric surgery on weight loss, resolution of obesity-associated comorbidities, body composition, BMD, physical activity levels, sedentary behaviour, physical function and strength, HRQoL and mental health (Jassil *et al*., 2018).

Study 2: **The BARI-LIFESTYLE intervention study** was a multi-centre RCT investigating the efficacy of a combined nutritional-behavioural tele-counselling and tailored supervised exercise programme on weight loss outcome following bariatric surgery. The secondary outcomes included resolution of obesity-associated comorbidities, body composition, BMD, physical activity levels, sedentary behaviours, physical function and strength, HRQoL and mental health.

Study 3: **The BARI-LIFESTYLE qualitative study** was an additional sub study conducted during the coronavirus disease 2019 (COVID-19) pandemic. The face-to-face supervised gym exercise had to be converted to tele-exercise in order to maintain the integrity of the RCT. This qualitative study aimed to assess patients' views and experiences of participation in the tele-exercise classes.

1.3 Thesis layout

The outline of the following chapters is as follows:

Chapter 2: Literature review

Chapter 3: Material and methods

Chapter 4: Weight loss, comorbidities, body composition and bone mineral density outcomes: The BARI-LIFESTYLE observational study

Chapter 5: Physical activity levels, sedentary behaviour, physical function and strength outcomes: The BARI-LIFESTYLE observational study

Chapter 6: Health-related quality of life and mental health outcomes: The BARI-LIFESTYLE observational study

Chapter 7: The impact of a combined nutritional-behavioural and supervised exercise intervention on weight loss and health outcomes following bariatric surgery: The BARI-LIFESTYLE randomised controlled trial

Chapter 8: Patients' views and experiences of live supervised tele-exercise classes following bariatric surgery during the COVID-19 pandemic: The BARI-LIFESTYLE qualitative study

Chapter 9: Implications, conclusions, and future studies

Chapter 2
Literature review

2.1 The NICE guidelines for the management of obesity

In England, the management of obesity is based on a set of evidence-based recommendations developed by NICE (NICE, 2014a). To estimate the degree of adiposity, BMI classification can be used as a proxy (Table 2.1) (WHO, 2000).

Table 2. 1: BMI classification by World Health Organisation.

Classification	BMI (kg/m^2)
Underweight	Less than 18.5
Healthy weight	18.5 – 24.9
Overweight	25 – 29.9
Obesity	
Obesity class I	30 – 34.9
Obesity class II	35 – 39.9
Obesity class III	40 or more

Note: BMI, Body Mass Index.

In certain populations such as Asian origin and older adults, the risk of comorbidities appears to be in a lower BMI range. Hence, an additional measure of waist circumference can be used to identify people who are at risk of excess adiposity-related ill-health (Table 2.2) (NICE, 2014b).

Table 2. 2: Risk classification based on weight circumference for Asian origin and older adults with BMI classified as overweight or obesity class I.

BMI classification	**Waist circumference**		
	Low (males < 94cm; females < 80cm)	**High (males 94 -102cm; females 80 – 88cm)**	**Very High (males > 102cm; females > 88cm)**
Overweight	No increased risk	Increased risk	High risk
Obesity class I	Increased risk	High risk	Very high risk

Note: BMI, Body Mass Index.

Body composition has also been analysed by bioelectrical impedance analyser (BIA), dual-energy X-ray absorptiometry (DXA), computed tomography (CT), and magnetic resonance imaging (MRI) (Thibault and Pichard, 2012). Based on BMI, waist circumference and body composition analysis, patients are offered different treatment options which include a combination of lifestyle modification, weight loss drugs and/or bariatric surgery (Table 2.3) (NICE, 2014b).

Table 2. 3: Treatment recommendations based on BMI classification, waist circumference and the presence of comorbidities.

BMI classification	**Waist circumference**			**Presence of comorbidities**
	Low	**High**	**Very high**	
Overweight	General advice on healthy weight and lifestyle	Lifestyle modification		Lifestyle modification; consider drugs
Obesity Class I	Lifestyle modification			
Obesity Class II	Lifestyle modification; consider drugs			Lifestyle modification and consider drugs; consider surgery
Obesity Class III	Lifestyle modification and consider drugs; consider surgery			

Note: BMI, Body Mass Index.

2.2 Treatment options for obesity

The treatment options for obesity are focusing on addressing the underlying drivers of weight gain. These include lifestyle modification, pharmacotherapy, and bariatric surgery.

Lifestyle modification

The first line of obesity treatment is a lifestyle modification that combines dietary modification and increasing physical activity levels, underpinned by behavioural changes (NICE, 2014b, Yumuk *et al*., 2015, Garvey *et al*., 2016). Diets that promote 600 kcal/day of calorie deficit are recommended or that reduce calories by limiting intake of foods containing high dietary fat (low-fat diet). A low-calorie diet (800-1600 kcal/day) or a very-low-calorie diet (<800 kcal/day) can be considered, but the latter can only be considered as part of a multicomponent weight management strategy (NICE, 2014b). Adults are also advised to meet the recommended physical activity guidelines (Bull *et al*., 2020). Elements of behavioural change form an integral part of the lifestyle modification to promote long-term adherence. On average, lifestyle modification has been shown to induce up to 11.5 kg of weight loss (Hassan *et al*., 2016). However, weight regain is quite common due to the strong compensatory biological responses to dieting (Maclean *et al*., 2011).

Pharmacological treatment

Weight loss drugs can be considered as an adjunct therapy to lifestyle modification rather than a standalone treatment after having undergone a complete risks assessment for eligibility (NICE, 2014b, Bessesen and Van Gaal, 2018). Orlistat is a weight loss drug that has been approved for use in the UK since 2010 (NICE, 2014b).

Orlistat, is a pancreatic lipase inhibitor that reduces fat absorption by ~30% hence resulting in reduced energy intake (Heck *et al*., 2000). In a meta-analysis of 17 RCTs involving 10,435 participants, Orlistat has been shown to induce a weight loss of 3.07 kg. However, the side effects include diarrhoea, flatulence and steatorrhea with deficiency of fat-soluble vitamins (Singh and Singh, 2020). The GLP-1 receptor analogue drug, Liraglutide 3.0 mg (in people with BMI of at least 35 kg/m^2 or at least 32.5 kg/m^2 for members of minority ethnic groups plus pre-diabetes and an additional CVD risk factor) is approved by NICE for obesity treatment within the NHS. Liraglutide binds to, and activates, the GLP-1 receptor to increase insulin secretion, suppresses glucagon secretion, and slows gastric emptying hence reducing appetite and energy intake (NICE, 2020). Another GLP-1 receptor analogue drug, Semaglutide 2.4 mg has been recently licenced and recommended by NICE for adults with at least one-weight-related condition and a BMI of at least 35 kg/m^2, in particular for people with a BMI between 30.0 – 34.9 kg/m^2 (NICE, 2022). Semaglutide supresses appetite, improves control of eating, and reduces food cravings leading to reduction in energy intake (Friedrichsen *et al*., 2021). The amount of weight loss has been shown to be ranging between 5 to 10% in Liraglutide and 10 to 15% in Semaglutide (Pi-Sunyer *et al*., 2015, Wilding *et al*., 2021, Rubino *et al*., 2022). In pharmacological treatment, lesser weight loss is commonly seen in patients with obesity and diabetes compared to those without diabetes. The reason for this is still poorly understood although genetic, metabolic, and environmental factors may play a role (Kahan and Fujioka, 2017).

<u>Surgical treatment</u>

Bariatric surgery is currently the most effective treatment option for people with severe obesity. It involves a surgical manipulation of the gastrointestinal tract that results in altered nutrients and/or biliary flow and changes in the gut physiology (Colquitt *et al*., 2014). Bariatric surgery consists of a few established techniques that modify the anatomy of the gastrointestinal tract such as gastric bypass (Roux-en-Y gastric bypass [RYGB], one anastomosis gastric bypass [OAGB]), sleeve gastrectomy (SG), adjustable gastric banding (ABG), vertical banded gastroplasty (VBG), biliopancreatic diversion with duodenal switch (BPD/DS) and single anastomosis duodenal-ileal bypass (SADI) (Kissler and Settmacher, 2013, De Luca *et al*., 2018). Bariatric surgery results in a substantial weight loss, approximately 25% to 35% of the initial weight that can be sustained up to 20 years as shown by the latest available long-term data (Osland *et al*., 2017, O'Brien *et al*., 2019). Following bariatric surgery, patients also experience resolution or improvement of the obesity-associated comorbidities such as T2D (27.5% to 37.4%), hypertension (48.4% to 60.1%), hyperlipidaemia (55.2% to 68.6%) and OSA (96% to 100%) (Sharples and Mahawar, 2020). As a result, bariatric surgery is considered a cost-effective treatment in the long term (Boyers *et al*., 2021). Therefore, NICE recommends bariatric surgery as a treatment option for people with BMI ≥ 40 kg/m^2 or people with a BMI ≥ 35 kg/m^2 with comorbidities that are weight related, who are unable to achieve and sustain a meaningful weight loss after attempted lifestyle modification and pharmacological therapy. Other criteria that must also be satisfied include had received intensive management in a tier 3 service, fit for anaesthesia and surgery, and committed to the need for long-term follow-up ((NICE), 2014a).

2.3 The NHS 4-tiered weight management system

The management of obesity in England is based on the 4-tiered system (Figure 2.1), (Blackshaw *et al*., 2014). Tier 1 consists of programmes and activities that aim to promote healthy weight by conveying and reinforcing healthy eating and physical activity messages that target the entire population (e.g., public information or educational campaign). Tier 2 refers to weight management services provided by primary care and community teams, normally in a group setting with a limited duration that often lasts for 12 weeks. This also includes referral to a commercial weight loss programme.

Tier 3 are specialist weight management services, the composition of these varies. Eligibility criteria include BMI > 40kg/m^2 or BMI >35 kg/m^2 with comorbidities that can be improved with weight loss or people with obesity with complex needs who has not responded to previous tier intervention. Tier 3 service may be community or hospital-based and delivered by a multidisciplinary team (MDT) providing dietary, medical, psychological and exercise inputs. Access to this service requires a referral from primary care or general practitioner. Tier 3 often includes an assessment of eligibility to access the tier 4 service. Tier 4 is a bariatric surgery service supported by the MDT pre- and post-operatively. Patients must have a prior engagement in tier 3 service in order to access this service. However, patients with T2D or with BMI of 50 kg/m^2 or more can be referred directly to tier 4 and receive an equivalent of tier 3 at the same time as progressing through tier 3 (Peaple, 2016).

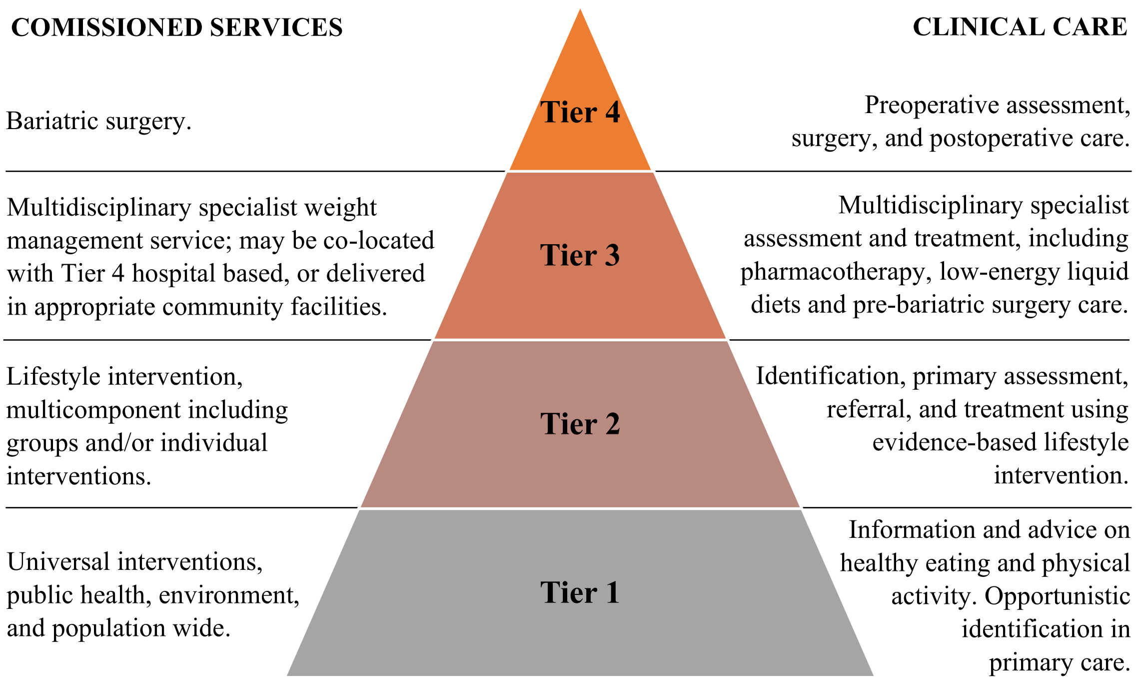


Figure 2. 1: The NHS 4-tiered weight management system.

Image reproduced from (Jennings *et al*., 2014).

2.4 Types of bariatric surgery

Bariatric surgery procedures include RYGB, OAGB, SG, AGB, VBG, BPD/DS and SADI. Each procedure alters the passage of nutrients and gut physiology in distinct ways, hence the procedure-specific variability in weight loss, remission of comorbidities, risk and complications (Neff *et al*., 2013). Procedure selection is a joint decision by bariatric MDT based on informed patients' preference after standardised counselling including details of potential risks and benefits of each procedure that adheres to the international guideline (De Luca *et al*., 2016).

A good balance of benefit to risk ratio has led to gastric bypasses and SG being the preferred choice of bariatric procedures performed both globally and, in the UK (Angrisani *et al*., 2015). Therefore, for the scope of this doctoral research, the literature review will focus on these procedures (Figure 2.2).

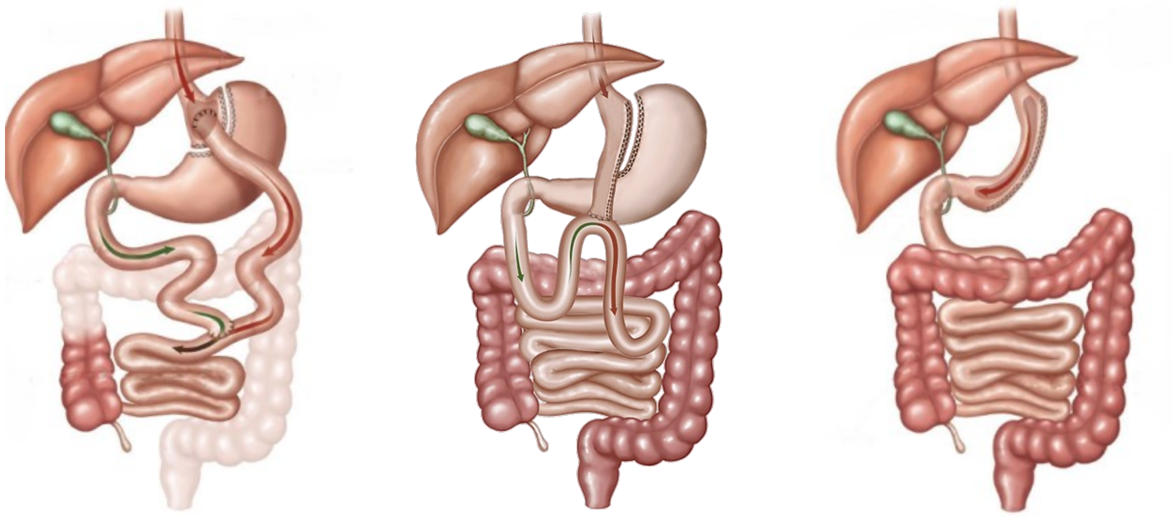
Gastric bypass

RYGB involves creating a small gastric pouch in the upper stomach of approximately 20 mL volume. This pouch is anastomosed with the mid-jejunum to form the Roux limb that allows for the ingested nutrients to bypass the lower stomach, duodenum, and proximal jejunum. The biliopancreatic limb is anastomosed with the jejunum to allow the flow of bile acids and pancreatic secretions that will mix with the nutrients in the jejunum (Figure 2.2) (Olbers *et al.*, 2003).

OAGB is a new procedure that is developed as a simpler alternative to the RYGB that only involves a single anastomosis. This procedure involves the creation of a lesser curvature-based stomach pouch. An anastomosis is constructed between the new stomach pouch and the jejunum, approximately 180-220 distance from the ligament of Treitz. Similar to RYGB, the ingested nutrients bypass the majority of the stomach, duodenum, and proximal jejunum, and mix with the digestive juices at the loop anastomosis (Figure 2.2) (Olbers *et al.*, 2003).

Sleeve gastrectomy

SG is a non-reversible and technically simpler procedure than gastric bypass as it does not involve anastomosis or manipulation of the small bowel. This procedure involves a vertical resection of 80% of gastric fundus along the greater curvature, creating a 'tube-shaped' stomach which results in rapid passage of ingested nutrients into the duodenum (Figure 2.2) (Abu-Jaish and Rosenthal, 2010). SG was initially developed as a first-step procedure for people with BMI > 50 kg/m^2 to achieve sufficient weight before a second procedure, either the RYGB or BPD/DS can be performed safely (Regan *et al.*, 2003). However, owing to the excellent outcomes of SG, most patients do not have to undergo the second stage procedure which eventually leads to the adoption of SG as a stand-alone procedure (Boza *et al.*, 2012).



RYGB **OAGB** **SG**

Figure 2. 2: Anatomical changes in Roux-en-Y gastric bypass (RYGB), one anastomosis gastric bypass (OAGB) and sleeve gastrectomy (SG).

Image source: (Neff *et al*., 2013).

2.5 Mechanisms of weight loss following bariatric surgery

Historically, bariatric procedures were initially thought to induce weight loss by restriction; reducing stomach capacity, with or without malabsorption due to intestinal bypass (Buchwald, 2014). However, the contribution of these effects to weight loss is relatively small and does not fully explain the profound weight loss after surgery (Topart *et al*., 2011, Mahawar and Sharples, 2017).

Following surgery, the primary driver of weight loss is reduced energy intake which is thought to be driven by a combination of changes including reduced hunger, early satiety, altered smell and taste perceptions with a diminished preference for sugary and fatty foods and reduced interest in high-energy-dense foods. These changes lead to lower energy intake that leads to sustained long-term weight loss (Graham *et al*., 2014, Coluzzi *et al*., 2016, Makaronidis *et al*., 2016, Zerrweck *et al*., 2016). Post-surgery changes in circulating gut hormones brought about by the surgical modulation of the gastrointestinal tract are thought to mediate altered eating behaviour (Scott and Batterham, 2011, Miras and le Roux, 2013, Manning *et al*., 2015a, Makaronidis and Batterham, 2016). Elevated circulating nutrient-stimulated anorexigenic hormones peptide YY3-36 (PYY) and GLP-1, with concomitant reduction in circulating levels of the orexigenic hormone ghrelin are associated with a significant weight loss post-surgery (le Roux *et al*., 2006, Peterli *et al*., 2012, Yousseif *et al*., 2014), that were not observed in diet-induced weight-loss subjects (Sumithran *et al*., 2011). Furthermore, the reduction in the hedonic drive for highly palatable, energy-dense foods is caused by the decrease in neural activation of the brain-reward centres as demonstrated in several neuroimaging studies in patients after RYGB (Ochner *et al*., 2011, Ochner *et al*., 2012, Frank *et al*., 2014).

Evidence to date also suggests that other mechanisms such as post-surgery changes in bile acids (Pournaras *et al*., 2012, Ryan *et al*., 2014) and alteration of the gut microbiota (Liou *et al*., 2013, Tremaroli *et al*., 2015) play a role in mediating weight loss and improving glucose metabolism. However, the mechanistic basis underpinning these beneficial outcomes remain to be elucidated. In AGB, it has been suggested the stream of vagal afferent signals arising from the oesophageal-gastric junction resulted in meal termination and satisfaction (Dixon *et al.*, 2012).

2.6 The short- and long-term weight loss outcome of bariatric surgery

The weight loss magnitude following surgery varies across the type of procedures (Table 2.4). Nevertheless, weight loss produced by bariatric surgery is above and beyond the amount of weight loss achieved via non-surgical weight loss interventions (Hassan *et al*., 2016). For example, in the Look AHEAD trial, participants with overweight or obesity with T2D receiving lifestyle intervention (decreasing energy intake and increasing physical activity) only lost an average of 8.6% of their initial weight at 12-month follow-up (Look *et al*., 2007). Furthermore, a systematic review and meta-analysis of RCTs summarising and quantifying the effects of bariatric surgery compared with non-surgical treatment has demonstrated the superiority of bariatric surgery in inducing sustainable weight loss (Gloy *et al*., 2013, Wu *et al*., 2016).

In general, weight loss occurs rapidly in the first year following RYGB and SG, with maximal weight loss achieved at 12 to 24 months post-surgery (Peterli *et al*., 2013, Peterli *et al*., 2017, Miras *et al*., 2018), averaging 25% to 35% of the preoperative weight that accompanied by improvement or complete resolution of comorbidities (Osland *et al*., 2017). Long-term data of ten or more years have shown that the substantial weight loss produced by bariatric surgery is durable, although more data are still needed for OAGB and SG (O'Brien *et al*., 2019).

Table 2. 4: Percentage weight loss following bariatric surgery.

Surgical procedure	**Percentage weight loss (95% CI), %**		
	1-year	**4-year**	**10-year**
RYGB[a]	30.9 (30.2%-31.6%)	27.5 (23.8%-31.2%)	28.6% (19.5%-37.6%)
OAGB[b]	36.1 (7.0)*	n/a	n/a
SG[a]	23.4 (21.8%-24.7%)	17.8 (9.7%-25.9%)	n/a

Note: [a](Maciejewski *et al*., 2016) , [b](Ansar *et al*., 2020), *mean (SD); n/a, not available; CI, confidence interval; OAGB, one anastomosis gastric bypass; RYGB, Roux-en-Y gastric bypass; SD, standard deviation; SG, sleeve gastrectomy

Whilst at the population level bariatric surgery yields an impressive weight loss, this positive outcome is unfortunately, not universal. There is wide inter-individual variability in terms of post-surgery weight loss magnitude (Figure 2.3) (Courcoulas *et al*., 2013, Manning *et al*., 2015b). Moreover, a subset of patients also, unfortunately, experience suboptimal weight loss, arbitrarily defined as weight loss less than 20% at 12 months post-surgery (Manning *et al*., 2015b, Corcelles *et al*., 2016). Whereas in some patients, weight loss is not durable as weight regain starts to occur within the second postoperative year (Chang *et al*., 2014, Osland *et al*., 2017). For instance, Cadena-Obando *et al*. examined the weight loss outcome of 130 patients who underwent either RYGB (38%), OAGB (49%) or SG (13%) and found that 20% of the patients experienced suboptimal weight loss at 12-month post-surgery and this group of patients had an increased risk of weight regain in the second postoperative year (Cadena-Obando *et al*., 2020). Several preoperative baseline characteristics have been previously reported that predict lower weight loss following surgery such as higher baseline BMI, female gender, age more than 45 to 50 years, T2D and lower early postoperative weight loss velocity (Ma *et al*., 2006, Ortega *et al*., 2012, Contreras *et al*., 2013, Ochner *et al*., 2013, Still *et al*., 2014, Manning *et al*., 2015b, Nielsen *et al*., 2020). Furthermore, poor compliance with the recommended dietary intake and physical activity also contributes to poor weight loss outcomes following bariatric surgery (Sheets *et al*., 2015, Hood *et al*., 2016).

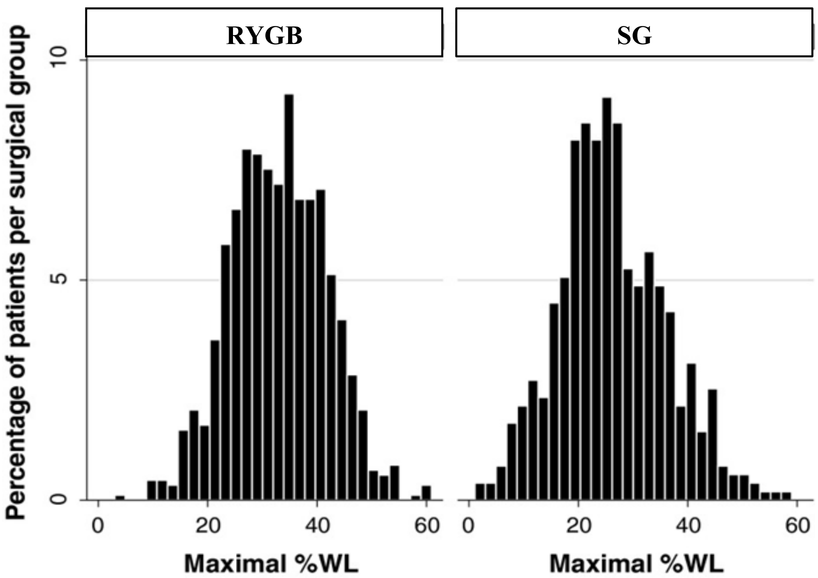


Figure 2. 3: Histogram shows a variability in maximal percentage weight loss in patients undergoing Roux-en-Y gastric bypass (*n*=877) and sleeve gastrectomy (*n*=513) (Manning *et al*., 2015b).

2.7 Remission or improvement of comorbidities following bariatric surgery

Several RCTs have demonstrated a higher proportion of patients achieving T2D remission following bariatric surgery in comparison to the lifestyle and/or medical management available with improved HbA_{1c} level and reduced usage of glucose-lowering medications (Schauer *et al*., 2016). This fact has led bariatric surgery to be part of the treatment pathway for people with T2D of less than 10 years duration with a BMI ≥ 35 kg/m^2 (NICE, 2014a, Yska *et al*., 2015). In addition to weight loss, several other mechanisms of T2D improvement post-bariatric surgery have been proposed. These include altered gut hormones, neural and nutrients signalling, microbiome and bile acid; and reduced glucotoxicity and hepatic/ pancreatic triglycerides (Batterham and Cummings, 2016). However, T2D remission varies between individuals and depends on diabetes duration, the magnitude of weight loss, use of insulin and the severity of T2D (control of HbA_{1c}) (Schauer *et al*., 2014, Ikramuddin *et al*., 2015, Mingrone *et al*., 2015).

Other benefits of bariatric surgery are the remission of hypertension (48.4% to 60.1%), hyperlipidaemia (55.2% to 68.6%) and OSA (96 to 100%), leading to discontinuation of lipid-lowering and antihypertensive medications, and the continuous positive airway pressure (CPAP) machine (Chang *et al*., 2014, Sharples and Mahawar, 2020). Moreover, evidence suggests that bariatric surgery reduces obesity-related cancer risk (Hunsinger *et al*., 2016).

Accumulating data have shown that the extent by which the associated comorbidities improved post-surgery parallels weight loss. For instance, in a multivariate analysis, Lee *et al*. found that patients who achieved more than 25% weight loss had prolonged T2D remission compared to those who did not (Lee *et al*., 2015). Whereas in an RCT, Schauer *et al*. demonstrated an association between greater weight loss achieved in the first postoperative year with durable glycaemic control up to five years of surgery

(Schauer *et al.*, 2017). Furthermore, a long-term remission of the associated comorbidities was also reported to depend on the weight loss magnitude and the ability to sustain weight loss over the long term (Laurino Neto *et al*., 2012). Importantly, weight regain increases the risk of re-emergence or worsening of the existing comorbidities (DiGiorgi *et al.*, 2010, Laurino Neto *et al.*, 2012). Altogether, this evidence suggests that maximising weight loss in the early post-surgery period and sustaining it are crucial to achieving the most beneficial long-term outcomes of bariatric surgery.

2.8 Changes in body composition after bariatric surgery

People living with obesity have a higher amount of both fat mass and fat-free mass compared to those without obesity (Cava *et al*., 2017). Fat-free mass comprises vital organs, fat-free muscles, bones, and water. Thus, maintenance of fat-free mass during the weight loss period is crucial (Heymsfield *et al*., 2014). In any weight loss programmes, including diet and/or exercise or bariatric surgery, it is well-documented that fat mass loss is accompanied by an inevitable loss of fat-free mass, although the latter occurs at a reduced amount (Chaston *et al*., 2007). However, the extent of fat-free mass loss is more prominent in the surgical weight loss approach, given its remarkable effect in inducing rapid weight loss in the short-term (Gloy *et al*., 2013). Fat-free mass plays important physiological roles in energy balance, glucose homeostasis, thermoregulation and functional capacity (Wolfe, 2006). A recent study by Coral *et al*. has demonstrated that fat-free mass loss in the first 6-month following surgery did not affect muscle function and did not correlate with worsening of metabolic profile (Coral *et al*., 2021). However, over a long term, excessive fat-free mass loss was thought to contribute to weight regain and re-emergence of comorbidities; counteracting the long-term benefits of bariatric surgery (Faria *et al*., 2009, Laurino Neto *et al*., 2012). This is in view of the muscle-related factors known as myokines that may directly and indirectly impact feeding behaviours and energy expenditure (Grannell *et al.*, 2022). Furthermore, in the absence of exercise to prevent excessive fat-free mass loss, the metabolic benefits of bariatric surgery tend to be transient and dissipate over time (Gualano *et al.*, 2021). It has been previously shown that the usual parameters used in reporting weight loss after bariatric surgery, such as percentage of Excess BMI Loss (%EBMIL), percentage of Excess Weight Loss (%EWL) and even the %WL, did not reflect the changes in the two compartments of body composition (Maimoun *et al*., 2019). Therefore, analysis of the changes in body composition after surgery is crucial, yet this is not routinely investigated as part of the post-bariatric care in real-world clinical practice.

Generally, the peak fat mass and fat-free mass loss occurred within 3 to 6 months post-surgery with maximal fat mass and fat-free mass loss occurring at 18-month post-surgery (Nuijten *et al*., 2020). In a recent systematic review and meta-analysis quantifying the estimates of fat mass and fat-free mass changes in patients following bariatric surgery of over one year, the mean fat mass loss after RYGB and SG compared to the baseline preoperative were -28.9 kg and -20.8 kg or -12.7% and -8.6%, respectively. Whereas, the mean fat-free mass loss after RYGB and SG relative to the baseline preoperative values were reported to be -9.9 kg and -9.4 kg or 11.7% and 5.7%, respectively (Haghighat *et al*., 2021). Of the 34 studies included in this quantitative synthesis, there were no data derived from patients who have undergone bariatric surgery in the UK and no data regarding the body composition changes following OAGB. There are currently limited data to explain the factors associated with fat-free mass loss following bariatric surgery. An early finding found that older age, male gender, type of procedure, and higher baseline BMI are associated with higher fat-free mass loss at 12- and 24-month post-surgery with a wide interindividual variability (Nuijten *et al*., 2020).

To date, there is still insufficient data to support whether a high protein diet (≥60 g/day) alone helps to counteract lean muscle mass loss following bariatric surgery (Vaurs *et al.*, 2015, Romeijn *et al.*, 2021). Whether exercise training after bariatric surgery promoted higher fat mass loss and prevented fat-free mass loss also remains inconclusive due to the paucity of high-quality studies (Bellicha *et al.*, 2021, Boppre *et al.*, 2021). A combined protein supplementation and exercise prescription assessed in an RCT reduced lean body mass loss (Muschitz *et al.*, 2016). However, in a later RCT by Oppert *et al.*, protein supplementation plus resistance training following RYGB did not mitigate lean body mass loss (Oppert *et al.*, 2018). Taken together, these early findings highlight the need for more integrated well-designed strategies to counteract excessive fat-free mass loss following bariatric surgery.

2.9 Bone health after bariatric surgery

The association between obesity and bone health is complex, known to be one of the components debated in the obesity paradox (Fassio *et al.*, 2018). Whilst obesity is protective against fractures in postmenopausal women and men, skeletal-specific fracture risks vary across gender (Turcotte *et al.*, 2021). In this recent systematic review and meta-analysis, obesity was shown to be protective against hip and wrist fractures by 25% and 15%, respectively, whilst increasing ankle fracture by 60% in postmenopausal women compared with their counterparts without obesity. Furthermore, in men with obesity, hip fracture risk is reduced by 41% compared with men without obesity (Turcotte *et al.*, 2021). Other than gender and postmenopausal status, the differences in fat distribution may also explain the fracture risks variability. As reported in two separate meta-analyses, abdominal obesity increases the risk of hip fracture (Li *et al.*, 2017, Sadeghi *et al.*, 2017).

Whether bariatric surgery increases fracture risk remains inconclusive due to the contradictory findings from the limited number of studies. Two UK population-based retrospective cohort studies have reported no association between bariatric surgery and risk of any fractures (Lalmohamed *et al.*, 2012, Douglas *et al.*, 2015), whilst other studies described a positive association (Nakamura *et al*., 2014, Rousseau *et al*., 2016, Axelsson *et al*., 2018). The heterogeneity across studies that include the differences in matched group comparator, small sample size, different post-surgery follow-up length and various bariatric procedures may likely explain the findings' inconsistencies. Notwithstanding, as the bariatric population ages and more women enter menopause, fracture risk and osteoporosis may likely increase over the long term and eventually become an important clinical concern (Gagnon and Schafer, 2018).

The effects of bariatric surgery on bone health varied between the type of procedures and were inconsistent across studies. Several studies have reported a greater reduction in BMD of the total hip (Bredella *et al.*, 2017, Cadart *et al.*, 2020, Hofso *et al.*, 2021), femoral neck (Bredella *et al.*, 2017, Carrasco *et al.*, 2018, Hofso *et al.*, 2021) and lumbar spine (Guerrero-Perez *et al.*, 2020, Hofso *et al.*, 2021) after RYGB than SG. However, other studies did not find any differences in BMD change between these procedures (Vilarrasa *et al.*, 2013, Maghrabi *et al.*, 2015, Muschitz *et al.*, 2015). Of the studies mentioned above, none were from the UK bariatric population. Whereas to date, only one study has examined the impact of OAGB on BMD, showing a significant reduction in lumbar spine, left hip, and whole-body BMD (Luger *et al*., 2018).

The mechanisms of bone mass loss following bariatric surgery are still poorly understood and likely multifactorial. Among the key candidates are the deficiency in essential nutrients for bone health, mechanical unloading, hormonal factors, and muscle composition (Gagnon and Schafer, 2018). The prevalence of bariatric surgery candidates with pre-existing vitamin D deficiency ranges from 25.4% to 71.3% (de Lima *et al*., 2013), partly explained by the increased level of adiposity that affects the storage and availability of vitamin D, as well as poor diet quality (Wortsman *et al*., 2000). This, along with surgically induced intestinal calcium and vitamin D malabsorption, aggravated the decline in BMD after bariatric surgery (Schafer, 2017).

Another mechanism that explains bone changes after bariatric surgery is the mechanical unloading of the skeleton, owing to the substantial weight loss after surgery (Gagnon and Schafer, 2018). Several studies found a correlation between the extent of weight loss and bone mass loss following surgery (Fleischer *et al.*, 2008, Stein *et al.*, 2013).

Adipose and gut-derived hormonal changes have also been postulated to play a role in the skeletal effects of bariatric surgery (Hage and El-Hajj Fuleihan, 2014). First, Bruno *et al*. reported the decreased leptin level associated with increased bone resorption marker N-telopeptide at 6-month post-RYGB (Bruno *et al*., 2010). In a prospective study, Carrasco *et al*. reported a correlation between increased adiponectin level post-RYGB with decreased total BMD at 1-year follow-up (Carrasco *et al*., 2009). They later reported the association between reduced ghrelin level with total BMD loss in RYGB and lumbar spine BMD loss in RYGB and SG at 1-year follow-up (Carrasco *et al*., 2014). Finally, in a recent 6-month prospective cohort study, Kim *et al.* found the increased PYY level post-RYGB associated with a higher declined in spine volumetric BMD, thus further supporting the concept of a ‘gut-bone’ axis (Kim *et al*., 2020).

Excessive muscle mass loss resulting from bariatric surgery has also been linked with bone mass changes, supporting muscle role in providing anabolic mechanical stimulus to bone tissues (Bonewald *et al*., 2013). Several studies have reported the changes in lean mass that positively correlated with changes in BMD (Vilarrasa *et al.*, 2011, Maghrabi *et al.*, 2015, Shanbhogue *et al.*, 2017). These findings highlight the importance of minimising lean muscle mass loss following bariatric surgery.

2.10 The impact of bariatric surgery on physical function and strength

Obesity is associated with an increased risk of functional limitation which often leads to difficulties in performing activities of daily living such as housework, self-care, family or leisure activities and mobility issue (Forhan and Gill, 2013). In fact, the relationship between obesity and physical inactivity appears to be bidirectional. Obesity leads to a lower level of physical activity caused by reduced mobility, functional impairment, and musculoskeletal pain. Whereas physical inactivity often contributes to a vicious cycle of weight gain and worsening mobility and physical function (Shultz *et al.*, 2014).

One of the beneficial aspects of bariatric surgery, although received less attention, and is often not assessed as part of post-surgery care, are the changes in physical function and strength. Physical functioning can be assessed either subjectively through a physical function scale of the HRQoL questionnaires or objectively through functional assessment tests (Steele *et al.*, 2015, Herring *et al.*, 2016, Hansen *et al.*, 2020, Jabbour and Salman, 2021). There is wide heterogeneity in the type of objective assessments performed to measure improvements in physical function following bariatric surgery, such as walking test, chair rise and treadmill exercise test. Whereas handgrip test, lower limb maximal force and maximal torque have been used to measure the changes in physical strength (Herring *et al.*, 2016, Hansen *et al.*, 2020, Jabbour and Salman, 2021). Although generally bariatric surgery improves physical function, a small proportion of patients continue to have functional limitations (King *et al.*, 2016, Zabatiero *et al.*, 2021). Furthermore, the durability of such improvement over the long term is still poorly understood due to the paucity of 12-month data and beyond (Herring *et al*., 2016). One factor attributed to the persistent functional limitation is the bodily pain that is not completely resolved post-surgery and becomes the barrier for engaging in physical activity (Zabatiero *et al*., 2018).

Muscle strength is defined as *'the amount of force a muscle can produce with a single maximal effort'* (Beaudart *et al*., 2019). Loss of fat-free mass did not affect muscle strength in the first 6-month following surgery (Otto *et al*., 2014, Coral *et al*., 2021), although this favourable outcome was not observed by other (Alba *et al*., 2019). Importantly, the long-term impact of bariatric surgery on muscle strength is still not known.

A combination of both loss of skeletal muscle mass and strength are the characteristics of a pathological disorder known as sarcopenia. Sarcopenic obesity is a risk factor of physical disability, impaired quality of life (QoL), and death (Batsis *et al*., 2014). In an observational study involving 184 patients undergoing SG, the prevalence of patients with sarcopenia increased from 8% at pre-surgery to 32% at 12-month post-surgery (Voican *et al*., 2018). However, recent evidence by Alba *et al*. has shown that when the absolute muscle strength is quantified relative to the changes in body mass, known as a 'relative muscle strength', this parameter of muscle strength improved significantly following bariatric surgery (Alba *et al*., 2019). This result has shed new insights as to whether functional strength should be reported as an absolute or relative measure after bariatric surgery. Nevertheless, more studies are needed to understand the link between the impact of body composition changes on muscle strength, particularly as patients get older, the risk associated with muscle mass and strength loss is likely to increase. Indeed, sarcopenia in older adults is associated with frailty and increases risk of morbidity and mortality (Walowski *et al*., 2020).

2.11 The impact of bariatric surgery on health-related quality of life and mental health

HRQoL is a term used to describe an individual's experiences, beliefs, expectations, and perceptions towards the three distinct domains of health namely physical, psychological, and social. In a simplified form, HRQoL is an individual's subjective perception of health or illness (Testa and Simonson, 1996). Instruments used to assess HRQoL can be categorised into three types which are either generic, disease-specific or preference-based, depending on their utilisation range (Kolotkin *et al*., 2001b). Obesity is known to negatively impacts HRQoL, in particular on physical and psychosocial functioning, with a higher degree of overall impairments seen in people with a greater BMI and those seeking bariatric surgery (Kolotkin and Andersen, 2017). People living with obesity also experience weight bias and societal stigma in various domains, including workplace, educational and healthcare settings (Rubino *et al*., 2020), with the prevalence of weight discrimination being higher in women and people with greater BMI (Spahlholz *et al*., 2016). Therefore, not surprisingly, obesity is linked to negative psychological outcomes, with a bidirectional association involving a vicious cycle of increasing weight and worsening mental illness (Taylor *et al*., 2013). Mental health issues such as depression, anxiety, eating disorders and body image dissatisfaction are also very common in people living with obesity and collectively, these issues contribute to the impairment in HRQoL (Weinberger *et al.*, 2016, Rajan and Menon, 2017). In a systematic review and meta-analysis of RCTs, weight loss following surgical and non-surgical approaches only led to a significant improvement in the physical domain of HRQoL but not in the mental health domain, and the reason for this is still not well understood (Warkentin *et al*., 2014).

Patients undergoing bariatric surgery frequently reported severe impairment in HRQoL (Osterhues *et al*., 2017). The desire to improve aspects of QoL is one of the factors that motivates patients to seek bariatric surgery (Munoz *et al*., 2007, Cohn *et al*., 2019). However, following bariatric surgery, the improvement in HRQoL is still poorly understood due to the limited number of RCTs and well-designed prospective observational studies with long term follow-up (Kolotkin and Andersen, 2017). In addition, the heterogeneity of questionnaires used to measure the impact of bariatric surgery on HRQoL has prevented a robust conclusion from a systematic review and meta-analysis (Coulman *et al.*, 2013, Hachem and Brennan, 2016, Raaijmakers *et al.*, 2017).

To date, limited evidence suggests that the physical domain may improve more than the mental health domain, reaching maximal benefits between one to two years post-surgery (Coulman and Blazeby, 2020). The variability in the durability of HRQoL improvement post-surgery also exist and the reason is yet to be explored further. Previous findings have suggested that factors such as later surgical complications that require further treatments, dissatisfaction with weight loss, weight regain, excess skin and/or scarring may play a role (Tindle *et al*., 2010). Current evidence suggested that the mental health component of QoL did not improve after bariatric surgery (Szmulewicz *et al*., 2019). But this evidence is based on data collected using generic questionnaires that are less sensitive to capturing the real impact of bariatric surgery on the psychological aspects experienced by people living with obesity, such as self-image and social stigma. Therefore, future studies should include specific validated tools to measure mental health conditions to complement the HRQoL questionnaire.

Mental health may play a role in influencing weight loss outcome following bariatric surgery (White *et al*., 2015). Limited studies with inconsistent findings have observed the link between pre- and post-surgery depressive symptomatology with poor post-surgery weight loss (Odom *et al.*, 2010, Dawes *et al.*, 2016). Furthermore, whether this link between depression and weight loss outcome following bariatric surgery is bidirectional is yet to be elucidated (Dixon *et al*., 2003). Importantly, in a recent systematic review of reviews, Kolotkin and Anderson suggested for future studies to explore the factors that mediate HRQoL changes and how they linked with other variables such as physical activity levels (Kolotkin and Andersen, 2017).

2.12 The role of physical activity following bariatric surgery

Physical activity is defined as any bodily movement that results in energy expenditure (Caspersen *et al*., 1985), and based on the level of intensity, can be divided into light, moderate and vigorous (Figure 2.4) (Gibbs *et al*., 2015). Mounting evidence has shown that engaging in regular physical activity provides physiological and psychological health benefits, including weight loss and prevention of weight gain (Warburton *et al*., 2006, Wiklund, 2016, Mandolesi *et al*., 2018). Adults are recommended to accumulate at least 150 to 300 minutes of moderate-intensity aerobic physical activity; or at least 75 to 150 minutes of vigorous-intensity aerobic physical activity; or an equivalent combination of both throughout the week. For additional health benefits, muscle-strengthening activities at a moderate or greater intensity that involve all major muscle groups on two or more days a week are also recommended (WHO, 2020b).

In recent years, sedentary behaviour has become a growing research field. Compelling evidence has revealed its negative impacts upon several health outcomes such as CVD, T2D, metabolic syndrome and early all-cause mortality, regardless of whether people achieve the recommended physical activity levels (de Rezende *et al*., 2014). The term sedentary behaviour is derived from the Latin word *sedentarius*, “sitting, remaining in one place” (Etymology Dictionary), described as any waking behaviours or activities that use a very low energy expenditure in a sitting or reclining position (Figure

2.4). For example, sitting at a workplace for a long period, during leisure/entertainment, while commuting by train, bus, or car, watching television, reading and using a computer, among others (Sedentary Behaviour Research Network, 2012). Sedentary behaviour is distinct from physical inactivity, the latter is described as physical activity levels that are insufficient to meet the physical activity guidelines (WHO, 2020b). Hence, to reduce the health risks of sedentary behaviour, adults are advised to replace the time spent on sedentary behaviour with physical activity of any intensity, even with the light intensity physical activity (WHO, 2020b). It is known that most people living with obesity are physically inactive and highly sedentary. The relationship between obesity and physical inactivity appears to be bidirectional. Obesity leads to a lower level of physical activity caused by reduced mobility, functional impairment, and musculoskeletal pain. While physical inactivity often contributes to further weight gain and a vicious cycle of increasing weight and worsening mobility and physical function (Shultz *et al*., 2014).

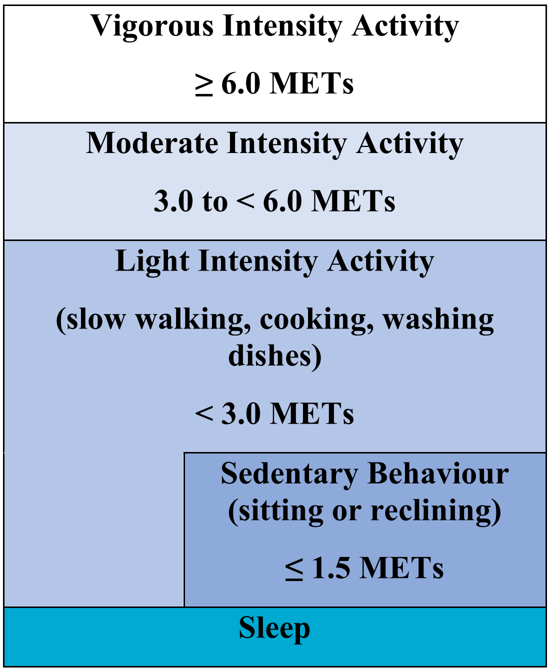


Figure 2. 4: The human movement spectrum.

Note: MET, metabolic equivalent. Image reproduced from (Gibbs *et al*., 2015).

Research examining the role of physical activity as an adjunct therapy for bariatric surgery is accumulating (Coen and Goodpaster, 2016). Initially, it has been reported that following bariatric surgery, the level of physical activity increases relative to pre-surgery (Adil *et al*., 2019). With the advancement in technology to accurately measure objective physical activity, emerging evidence has demonstrated a significant disagreement between data collected using self-reported physical activity questionnaire versus physical activity monitor in patients who have undergone bariatric surgery, with the former tends to overestimate physical activity (Bond *et al*., 2010, Berglind *et al*., 2016). Importantly, it has become more apparent that the changes in physical activity following bariatric surgery varied among individuals. Whilst some patients showed increased physical activity, some did not change whilst some decreased physical activity from pre- to post-bariatric (King *et al*., 2012). Furthermore, evidence has shown that the time spent on sedentary behaviour did not change following bariatric surgery despite a significant weight loss (Berglind *et al*., 2015, Sellberg *et al*., 2019).

Growing evidence, albeit still limited, has shown that increased physical activity through engaging in post-bariatric exercise programme promoted additional health benefits such as improving glucose homeostasis, cardiorespiratory fitness and functional capacity, minimising bone mass loss and promoting greater HRQoL (Pouwels *et al.*, 2015, Coen *et al.*, 2018). Therefore, patients who are physically inactive and highly sedentary post-bariatric would have missed the opportunity to gain these additional health benefits. Currently, there is no specific physical activity recommendations for people who have undergone bariatric surgery (Coen *et al*., 2018). This fact highlights the need for more research to be undertaken to support the future development of evidence-based physical activity recommendations for bariatric surgery.

People living with obesity reported several barriers to physical activity participation, divided into internal and external barriers (McIntosh *et al.*, 2016). The internal barriers encompass physical (excess weight, poor fitness, health problems and injury) and psychological barriers (weight perception, low mood, lack of enjoyment and motivation/ willpower). The external barriers cover aspects such as lack of time and exercise knowledge, poor weather condition and competing demands (McIntosh *et al.*, 2016). Interestingly, despite a significant weight loss following bariatric surgery, most of these barriers to engage in physical activity continue to persist (Zabatiero *et al.*, 2018). Therefore, these barriers should be addressed when planning and developing future interventions to facilitate physical activity participation and for long-term physical activity maintenance.

2.13 Nutritional concern following bariatric surgery

One of the known disadvantages of bariatric surgery is the unintended nutritional deficiencies due to chronically reduced food intake, food avoidance due to intolerance, nausea and vomiting and altered nutrients absorption resulting from gastrointestinal modification (Sawaya *et al.*, 2012, Gletsu-Miller and Wright, 2013). The common macronutrient deficiency reported following surgery is a dietary protein that may exacerbate protein malnutrition due to poor tolerance to a certain food such as meat and poultry (Faria *et al.*, 2011). Whereas for micronutrients, levels of vitamin B12, thiamine, folate, zinc, iron, copper, calcium, and vitamin D are usually compromised that may lead to secondary clinical manifestations such as anaemia, osteoporosis and neuropathy that are potentially irreversible (Gletsu-Miller and Wright, 2013, Sherf Dagan *et al.*, 2017a). The prevalence of nutritional deficiencies post-surgery varies across micronutrients; vitamin D (25%-80%); vitamin B12 (4%-62%); iron (17%-45%); thiamine (up to 49%);

folate (9%-38%) and zinc (SG: 12%, RYGB: 21%-33%) (Stein *et al*., 2014). In light of this, patients are required to commit to a lifelong nutritional supplementation (Mechanick et al., 2013a, O'Kane et al., 2020). Importantly, some patients may have preexisting vitamins and trace elements deficiencies pre-surgery, and it may worsen post-surgery (de Lima *et al*., 2013). Therefore, patients with or at risk of nutritional deficiency preoperatively should be identified and corrected accordingly to prevent postoperative malnutrition with continuous nutritional monitoring after surgery (Mechanick et al., 2013a, O'Kane et al., 2020).

In the early part of the postoperative year, adherence to dietary recommendations has not been shown to associate with better weight loss (Sherf Dagan *et al*., 2017b), owing to the powerful impact of the surgery in inducing weight loss (Hood *et al*., 2016). This fact leads patients to perceive diet as not an essential component and of no consequence on weight loss. As a result of this misconception, it is not surprising that many patients neglect the recommended post-surgery eating practices (Sherf Dagan *et al*., 2017b). Prolonged dietary non-adherence will eventually lead to weight regain at a later stage (Yanos *et al*., 2015). Eating behaviours that can cause poor long term weight loss outcome are snacking, grazing and high consumption of high-calorie drinks (Sheets *et al*., 2015). Furthermore, a gradual increase in calorie consumption over time has also been reported to have impacted upon weight regain (Sarwer *et al*., 2008b).

In terms of nutrients composition, protein intake of a minimum of 60 g daily following surgery is crucial as it is linked to better weight loss and fat mass loss whilst preserving lean muscle mass and bone mass (Ito *et al*., 2017). Despite this standard recommendation, findings from observational studies continue to reveal inadequate intake, in particular, in the first 6 months of surgery (Giusti *et al.*, 2016, Sherf Dagan *et al.*, 2017b). This result could be explained by the poor tolerance towards some protein-rich food like red meat, being reported mainly following RYGB (Moize *et al*., 2003, Nicoletti *et al*., 2015). Therefore, frequent monitoring and dietetic care are essential to guide patients in making appropriate and wise food choices to achieve the suggested recommendation (Kulick *et al.*, 2010, Snyder-Marlow *et al.*, 2010). Indeed, patients provided with diet counselling appeared to have improved several nutritional parameters compared to those without dietetic care (Garg *et al*., 2016). In this sense, higher attendance of dietetic visits has been linked to better post-surgery outcomes (Endevelt *et al*., 2013).

Non-adherence with prescribed vitamin and mineral supplementations is common post-surgery, but the proportion varies considerably across studies. In a study by Welch *et al.*, of 75 patients, only 57.6% adhered to the supplementation regime with suboptimal levels reported for ferritin, haematocrit, thiamine and vitamin D in the study cohort (Welch *et al*., 2011). Whereas a cross-sectional study by Sunil *et al*. has discovered that non-adherence was predominant in males and patients with full-time employment. Furthermore, poorly adherent patients exhibited lower vitamin B12, observed at 6-month after surgery compared to their adherent counterparts (Sunil *et al*., 2017). In contrast, a few studies have shown a higher adherence towards supplementation intake in the early postoperative phase. However, the adherence rate declined over time thus, underscoring the need for continuous reinforcement (Elkins *et al*., 2005, Agaba *et al*., 2015). Forgetfulness and patients perceiving that supplements as unnecessary are the most common identified behavioural barriers to adherence (Agaba *et al.*, 2015, Chan *et al.*, 2015). Taken together, poor adherence with high risk of long-term nutritional deficiencies indicates the need for behavioural interventions that target these barriers.

2.14 Lifestyle interventions as adjunct therapy to bariatric surgery

In light of this, several lifestyle intervention programmes have tested the efficacy and effectiveness of lifestyle changes which might improve weight loss and health outcomes in the earliest post-surgery phase and prevent undesirable nutritional complications.

The nutritional-behavioural interventions

To date, very limited nutritional-behavioural RCTs have been undertaken aimed at optimising weight loss in the first year of bariatric surgery (gastric bypasses and SG) with inconsistent findings (Table 2.5). In a pilot RCT (*n*=84), Sarwer *et al*. investigated the impact of regular dietary counselling delivered by a registered dietitian in the first four months following surgery, but they could not find any significant weight loss difference with a group receiving standard care. Nevertheless, participants in the intervention group exhibited greater dietary cognitive restraint (the intent to reduce energy intake) and disinhibited eating (the tendency to eat in response to social and emotional cues or the availability of palatable foods in the environment) (Sarwer *et al*., 2012). In another pilot RCT (*n*=50) by Lent *et al*., no significant difference was observed in weight loss between patients who received a psychologist-led group-based behavioural intervention programme focusing on dietary and physical activity adherence commenced at 7-month post-surgery compared to the standard post-surgery care group. Notwithstanding, other benefits of the programme were reported, including higher improvement in physical functioning, pain, general health and overall HRQoL (Lent *et al*., 2019). Wild *et al*. conducted an RCT (*n*=117) assessing the efficacy of a one-year videoconferencing-based psychoeducational intervention focusing on diet and physical activity in a group setting but did not find any weight loss difference with the comparative group receiving standard care. However, when participants were stratified based on whether they had clinically significant depressive symptoms at pre-surgery, the intervention programme (*n*=29) helped in promoting better HRQoL, lowering depression scores with a trend towards greater weight loss, albeit not significant, compared to the matched control group (*n*=20) (Wild *et al*., 2015). To date, only one RCT (*n*=162) has been undertaken in the UK assessing the efficacy of psychologist-led behavioural support from 2-week pre-surgery to 3-month post-surgery supporting participants in addressing psychological issues encompassing dietary control, self-esteem, coping and emotional eating. The programme, however, had no impact on weight loss as observed at 12-month post-surgery (Ogden *et al*., 2015). Swenson *et al*. undertook an RCT (*n*=32) investigating whether replacing a standard low-fat diet with a low-carbohydrate high-protein diet through regular counselling from pre- to post-surgery will lead to better weight loss and found no significant weight loss between groups (Swenson *et al*., 2007).

In contrast to these studies, a large RCT involving 144 RYGB patients reported a group-based nutrition and lifestyle educational intervention with frequent contact via telephone calls, e-mail messages, and reminder messages and an option to have frequent individual contacts with healthcare professionals between 6 to 12 months post-surgery period led to a significantly greater excess weight loss compared to the control group (80% versus 64%; $p<0.001$, respectively). The intervention group was also reported to have spent significantly greater time in physical activity and consumed a higher amount of dietary protein at the end of the programme (Nijamkin *et al*., 2012). Interestingly, in another RCT (*n*=56), participants provided with mobile health (mHealth) applications (iPad© mini with the MyFitnessPal© apps) without additional inputs from the healthcare professionals exhibited a greater percentage of excess weight loss at 12- and 24-month post-surgery compared to the control group. However, no difference between groups was observed regarding the improvement in HRQoL (Mangieri *et al*., 2019).

Supervised exercise interventions

The number of RCTs of supervised exercise intervention aiming at optimising weight loss in the first year of bariatric surgery (gastric bypasses and SG) is very limited (Table 2.5). In an RCT (n=128) evaluating a 6-month of once-weekly supervised exercise programme delivered between 1 to 6 months following RYGB, no significant difference in weight loss was observed at the end of the programme compared to the control group receiving six sessions of health education (Coen *et al*., 2015b). Nevertheless, the exercise training improved insulin sensitivity, enhanced mitochondrial respiration, induced cardiolipin remodelling and reduced specific sphingolipids of the skeletal muscle (Coen *et al.*, 2015a, Coen *et al.*, 2015b). Mundbjerg *et al*. conducted a smaller RCT (n= 60) but with a more intense programme which was twice-weekly supervised exercise sessions for 26 weeks and delivered at a later stage from 6 to 12 months post-RYGB. They found no significant difference in weight loss at the end of the exercise programme compared to the control group receiving standard care. However, the exercise training significantly improved high-density lipoprotein cholesterol level, cardiorespiratory fitness, muscle strength of the hip, physical function, and increased fibrinolysis. None of these significant differences were maintained at 24-month post-surgery follow-up except for the exercise training group exhibited lower body weight compared to the control group (91.5 kg versus 94.0 kg; p=0.042, respectively) and a higher score of the general health domain of HRQoL (Mundbjerg *et al.*, 2018a, Mundbjerg *et al.*, 2018b, Stolberg *et al.*, 2018a, Stolberg *et al.*, 2018b).

Other RCTs have been performed evaluating the impact of supervised exercise on body composition, BMD, cardiorespiratory fitness, physical function and strength, and physical balance in the first postoperative year (Castello *et al*., 2011, Castello-Simoes *et al*., 2013, Muschitz *et al*., 2016, Rojhani-Shirazi *et al*., 2016, Daniels *et al*., 2018, Oppert *et al*., 2018, Murai *et al*., 2019, Diniz-Sousa *et al*., 2021, Gil *et al*., 2021). In a small RCT (*n*=16), three times a week of resistance training programme did not elicit any difference in fat-free mass or muscle cross-sectional area but increased muscular strength and quality compared to the usual care group (Daniels *et al*., 2018). In a larger study, Oppert *et al*. randomised 76 post-RYGB women to receive either protein supplementation plus resistance training (PRO+EX), protein supplementation only (PRO) and usual care group (CON). At the end of the programme, no significant difference was seen in lean body mass changes. However, the PRO-EX group exhibited significantly higher lower-limb muscle strength than the PRO and CON groups (Oppert *et al*., 2018).

In contrast, three times a week of a combined aerobic and resistance training programme delivered for six months significantly counteracted the post-surgical loss of muscle mass and function (Gil *et al*., 2021). The programme also significantly reduced loss of BMD at the femoral neck, total hip, distal radius and cortical volumetric BMD at distal radius (Murai *et al*., 2019). This finding corroborated with the earlier results from a larger RCT (*n*=220) which found that supplementing patients with vitamin D, calcium, and protein powder combined with an aerobic exercise programme decelerates the loss of BMD and lean body mass following RYGB and SG. However, it was not clear whether the exercise component of the intervention was supervised sessions (Muschitz *et al*., 2016). The role of exercise in mitigating bone mass loss was further supported by the outcome from the Bariatric Surgery and Exercise Intervention Bone Trial (BaSEIB) that was recently published. In this RCT (*n*=84), three times a week of a supervised multicomponent physical exercise training program (high-impact, balance, and resistance exercises) delivered for 11 months significantly reduced loss of BMD at the lumbar spine and 1/3 radius. In a post-hoc analysis, participants who attended ≥ 50% of the sessions exhibited a favourable impact on the femoral neck BMD (Diniz-Sousa *et al*., 2021).

Other beneficial outcomes reported from RCTs investigating an early post-surgery supervised exercise programme (aerobic and balance exercise programmes) are improvement in cardiac autonomic modulation, heart rate kinetic, functional capacity as well as improvement in the static, dynamic, and functional balance (Castello *et al*., 2011, Castello-Simoes *et al*., 2013, Rojhani-Shirazi *et al*., 2016).

The limitation of the published randomised controlled trials on lifestyle intervention

Based on the reviewed literature, it is still too early to conclude whether a lifestyle programme delivered in the first postoperative year aids in weight loss induced by bariatric surgery. Not only are the number of RCTs, to date, very limited, but the existing published studies have several limitations which reduces their generalisability:

1. There is heterogeneity in the content of the lifestyle programmes. The nutritional-behavioural interventions were delivered in person and/or remotely via telephone or videoconferencing, either individually and/or in a group setting. One study had to be amended from in-person counselling to include telephone counselling at a later stage due to the poor adherence rate (Sarwer *et al*., 2012). The number of sessions varied between 3 to 14 sessions. One study tested the efficacy of mHealth without additional inputs from the healthcare professionals (Mangieri *et al*., 2019), and another study utilised text messaging and email as part of the intervention strategy (Nijamkin *et al*., 2012). The content of the supervised exercise also varied across studies, which included aerobic and/or resistance training or balance exercise. Two studies included additional protein, vitamin, and mineral supplementations to the exercise programme (Muschitz *et al.*, 2016, Oppert *et al.*, 2018). The frequency of the exercise sessions ranges from once weekly to four times a week, with the programme duration between 4 weeks to 24

months. One study did not clearly describe the level of supervision from exercise professionals (Muschitz *et al*., 2016).

2. Some studies have a small sample size that could have led to a type 1 error, and others were pilot RCTs. A few studies did not justify the sample size (Rojhani-Shirazi *et al.*, 2016, Daniels *et al.*, 2018). Of all the RCTs of supervised exercise intervention outlined in Table 2.5, only two studies aimed to investigate the impact of the exercise programme on body weight as a primary outcome (Coen *et al*., 2015b, Mundbjerg *et al*., 2018b).
3. Of eight exercise RCTs, five of the studies recruited only female participants and one RCT only included a homogeneous ethnic background (Nijamkin *et al*., 2012), limiting their generalisability.
4. The majority of the RCTs involved patients who had undergone RYGB. Therefore, the findings might not be generalisable to patients undergoing SG and OAGB, given the difference in surgical outcomes. Note that this review did not include RCTs that assessed the impact of lifestyle interventions in patients undergoing AGB, VBG or BPD/DS, as these procedures are now rarely being performed.
5. There is heterogeneity of the timing of enrolment in the study postoperatively, which influenced the rate of weight loss as well as the degree of improvement in other outcomes of interest. This fact hampered a strong conclusion from systematic reviews and meta-analyses as to whether a post-surgery lifestyle intervention elicited further weight loss (Bellicha *et al.*, 2021, Julien *et al.*, 2021). Note that this review did not include RCTs that enrolled participants in a lifestyle intervention programme beyond 12-month post-surgery as it is out of the scope of this thesis.

To the best of our knowledge, only one RCT (*n*=162) has investigated the impact of a nutritional-behavioural intervention in the first postoperative year in the UK healthcare setting (Ogden *et al*., 2015). Similarly, only one UK RCT (*n*=24) has evaluated the impact of a supervised exercise intervention on physical function and body composition delivered between 12 to 24 months post-surgery period (Herring *et al*., 2017). A further search on ClinicalTrial.gov and the International Standard Randomised Controlled Trial Number (ISRCTN) databases found no other ongoing RCTs in the UK.

In 2015, we undertook a pilot case-control study in bariatric patients to evaluate the impact and feasibility of a combined nutritional-behavioural and supervised exercise intervention, delivered in a group setting at 3 to 6 months post-surgery, upon %WL and physical activity levels. The programme significantly improved functional capacity, increased strenuous intensity exercise, increased consumption of fruits and vegetables, reduced consumption of ready meals and improved 'Change in Health' in the QoL domain. At one-year post-surgery, the intervention group exhibited a greater %WL than the standard care matched historical control. All participants were satisfied with the coaching and exercise input. A once-weekly supervised exercise was acceptable. However, participants preferred a one-to-one session with the dietitian. Overall, all participants agreed for such a programme to be offered to all bariatric patients (Jassil *et al*., 2015). Based on the findings from this pilot study, we developed the protocol for the BARI-LIFESTYLE trial, as reported in the next chapter.

Table 2. 5: Characteristics of RCTs of nutritional-behavioural and supervised exercise interventions in the first year following bariatric surgery.

Study ID and country	Study design	Surgery type	Group allocation	*n*	Time of intervention commencement (intervention period)	Female (%)	Age (years) mean (SD)	Weight (kg) mean (SD)	BMI (kg/m^2) mean (SD)	Length of follow-up from baseline
NUTRITIONAL-BEHAVIOURAL INTERVENTION										
(Sarwer *et al.*, 2012), US	Pilot RCT	RYGB (80%), AGB	A combination of in-person or telephone dietary counselling (8 sessions)	41	Immediately post-surgery for 4 months	63	42 (9.9)	152.7 (33.7)	51.6 (9.2)	24 months
			Usual care	43						
(Lent *et al.*, 2019), US	Pilot RCT	RYGB (66%), SG (28%), BPD	Group-based behavioral intervention for adherence on diet and physical activity (8 sessions)	24	Varied depending on the time of enrollment (mean of 7-month post-surgery for 4 months)	83	47.6 (9.1)	NR	47.1 (6.7)	4 months
			Usual care	26			46.2 (12.0)	NR	50.4 (6.2)	
(Wild *et al.*, 2015), Germany	RCT	SG (58%), RYGB (37%), AGB	A combination of in-person and videoconferencing group-based psychoeducational intervention on diet and physical activity (14 sessions)	58	Immediately post-surgery for 12 months	60	41.2 (9.0)	150.7 (24.2)	50.1 (6.6)	12 months
			Usual care	56		80	41.9 (9.6)	144.2 (22.7)	49.4 (6.2)	
(Ogden *et al.*, 2015), UK	RCT	RYGB	Psychologist-led behavioural counselling including aspect of diet and physical activity (3 sessions)	82	Two weeks pre-op until 3-month post-op	61	45.6 (11.1)	143.8 (29.2)	50.4 (7.3)	12 months
			Usual care	80		61	44.8 (10.6)	140.9 (27.0)	50.9 (8.3)	
(Swenson *et al.*, 2007), US	RCT	RYGB	High-protein, low carbohydrate diet counselling (5 sessions)	19	Pre-op until 12-month post-op	95	41.7 (9.8)	197.5 (85)	50.7 (8.7)	12 months
			Low-fat diet counselling (5 sessions)	13		85	39.7 (7.6)	166.5 (71)	46.3 (9.4)	
(Nijamkin *et al.*, 2012), US	RCT	RYGB	Group-based nutrition and lifestyle education and behavioural-motivational intervention (6 sessions), and frequent contact by telephone calls, e-mails messages, and reminder messages. Options for additional counselling from healthcare professionals	72	6-month post-surgery for 6 months	86	44.2 (12.6)	94.6 (21.2)	35.4 (6.83)	6 months
			Brief printed guidelines for healthy eating and physical activity	72		81	44.8 (14.4)	100.3 (24.9)	36.5 (7.0)	

(Mangieri *et al.*, 2019), US	RCT	SG	The mHealth group was provided with iPad© mini with the MyFitnessPal© apps but without additional inputs	28	Immediately post-surgery for 24 months	84	52.5 (9.0)	NR	35.3 (8.3)	24 months
			Usual care	28		92	53 (10.6)	NR	37.0 (6.9)	
SUPERVISED EXERCISE INTERVENTION										
(Coen *et al.*, 2015b), US	RCT	RYGB	Once-weekly semi-supervised moderate exercise protocol for 6 months	66	Within 1 to 3 months post-surgery	89	41.3 (9.7)	107.3 (19.9)	38.8 (6.1)	6 months
			Control group receiving health education sessions	62		87	41.9 (10.3)	105.7 (25.1)	38.3 (6.9)	
(Mundbjerg *et al.*, 2018b), Denmark	RCT	RYGB	Twice-weekly supervised physical training sessions for 26 weeks	32	6-month post-surgery	66	42.3 (9.4)	129.1 (19.9)	43.1 (6.7)	24 months
			Usual care	28		75	42.4 (9.0)	123.7 (22.0)	42.8 (5.5)	
(Daniels *et al.*, 2018), US	RCT	RYGB	Three times a week of resistance training programme for 12 weeks	8	2-month post-surgery	100	NR	111.8 (15.3)	NR	3 months
			Usual care	8		100	NR	111.9 (16.2)	NR	
(Oppert *et al.*, 2018), France	RCT	RYGB	Three times a week of resistance training for 18 weeks plus whey protein supplementation (48g/day)	23	Immediately post-surgery	100	40.9 (10.8)	116.7 (15.4)	45.2 (5.2)	6 months
			Whey protein supplementation (48g/day) plus usual care	31		100	42.5 (8.7)	115.7 (14.9)	43.3 (6.0)	
			Usual care	22		100	43.9 (10.7)	116.3 (19.3)	43.6 (6.2)	
(Murai *et al.*, 2019), Brazil	RCT	RYGB	Three times a week of aerobic and resistance training for 6 months	35	3-month post-surgery	100	40.0 (7.8)	127.3 (20.4)	49.8 (7.0)	9 months
			Usual care	35		100	42.1 (8.2)	126.1 (21.7)	48.5 (8.1)	
(Diniz-Sousa *et al.*, 2021), Portugal	RCT	RYGB, SG	Three times a week of multicomponent exercise training for 11 months	41	1-month post-surgery	83	41.6 (10.5)	110.0 (17.2)	44.2 (6.8)	12 months
			Usual care	20		80	46.5 (8.5)	114.8 (15.4)	46.1 (4.2)	

(Muschitz *et al.*, 2016), Austria	RCT	RYGB, SG	16,000 IU cholecalciferol/ week and 1000mg calcium monocitrate/ day, daily BMI-adjusted protein supplementation and physical exercise	110	From pre-surgery to 24-month post-surgery	60	41.0* (34.0, 45.0)	119.6* (110.0, 129.0)	44.3* (41.1, 47.9)	24 months
			Usual care	110		56	40.0* (35.0, 45.8)	120.6* (110.4, 131.8)	44.2* (40.7, 47.7)	
(Castello *et al.*, 2011), Brazil	RCT	RYGB	Three times a week of aerobic exercise for 12 weeks	11	1-month post-surgery	100	38.0 (4.0)	117.0 (4.0)	45.6 (1.5)	4 months
			Usual care	10		100	36.0 (4.0)	117.0 (6.0)	44.5 (1.0)	
(Rojhani-Shirazi *et al.*, 2016), Iran	RCT	SG	Four times a week of balance exercise session for 4 weeks	16	5-day post-surgery	100	36.1 (6.7)	109.1 (13.4)	40.5 (5.4)	4 weeks
			Usual care	16		100	36.6 (7.8)	117.3 (22.2)	44.0 (7.2)	

Note: AGB, adjustable gastric banding; BMI, Body Mass Index; BPD, biliopancreatic diversion; IU, International Unit; *n*, number; NR, not reported; RCT, randomised controlled trial; RYGB, Roux-en-Y Gastric Bypass; SD, standard deviation; SG, sleeve gastrectomy; UK, United Kingdom; US, United States. *indicates median and interquartile range.

2.15 Study objectives and hypotheses to be tested

This literature review has revealed that bariatric surgery is effective in promoting significantly sustained long-term weight loss and resolution of obesity-associated comorbidities, with the beneficial health outcomes extended to other aspects relevant to people living with obesity such as improving physical function and HRQoL. However, this literature review has also revealed that most of the published data on the outcomes of bariatric surgery did not come from patients who have undergone bariatric surgery in the UK. The lack of research study evaluating the impact of bariatric surgery delivered in the UK healthcare setting limits data that can be used to support the increased provision of bariatric surgery in the country. To address this information gap, the first part of this thesis (Chapters 4, 5 and 6) will report the results from the one-year longitudinal cohort study. Specifically, the objectives of the BARI-LIFESTYLE observational study were to evaluate the post-surgery changes in:

1. Percentage weight loss (%WL) at 3-, 6- and 12-month post-surgery, relative to baseline pre-surgery weight.
2. Obesity-associated comorbidities (T2D, hyperlipidaemia, hypertension, OSA) at 3-, 6- and 12-month post-surgery, relative to baseline pre-surgery.
3. Fat mass and fat-free mass assessed using DXA scan and BIA at 3-, 6- and 12-month post-surgery, relative to baseline pre-surgery.
4. BMD assessed using DXA scan at 12-month post-surgery, relative to baseline pre-surgery.
5. Physical activity levels (light, moderate, vigorous), percentage achieving 150 minutes of moderate-to-vigorous physical activity (MVPA) in a week and

sedentary behaviour assessed using accelerometer at 3-, 6- and 12-month post-surgery, relative to baseline pre-surgery.

6. Physical function and strength assessed using 6-minute walk test (6MWT), sit-to-stand (STS-test) test and handgrip test (HGS) at 3-, 6- and 12-month post-surgery, relative to pre-surgery.
7. HRQoL assessed using the 3-Level EuroQol-5D (EQ-5D-3L) and Impact of Weight on Quality of Life-Lite (IWQOL-Lite) at 3-, 6- and 12-month post-surgery, relative to baseline pre-surgery.
8. Characteristics of attitude and symptoms of depression assessed using Beck Depression Inventory-II (BDI-II) at 3-, 6- and 12-month post-surgery, relative to baseline pre-surgery.
9. Dietary intake assessed using food diary at 3-, 6- and 12-month post-surgery, relative to baseline pre-surgery.
10. Healthcare resource utilisation and costs assessed using the adapted version of the Client Service Receipt Inventory (CSRI) at 3-, 6- and 12-month post-surgery, relative to baseline pre-surgery.

Hypothesis 1: *For the BARI-LIFESTYLE observational study (objectives 1 to 8), we hypothesise that bariatric surgery, as delivered in a UK healthcare setting, leads to a significant improvement in body weight and body composition, comorbidities, physical activity levels and sedentary behaviour, physical function and strength, HRQoL and the symptoms of depression in the first 12 months following surgery.*

Despite the impressive beneficial outcomes of bariatric surgery at a population level, the current literature review has also revealed that the improvement is not universal for the reasons discussed above. Early findings from RCTs assessing the efficacy of nutritional-behavioural and exercise interventions as adjunct therapy in the first postoperative year, albeit still limited, have shown promise in optimising post-surgery outcomes. However, the implementation of an intensive lifestyle intervention as part of standard care post-surgery will incur additional costs to the NHS and, for that reason, its efficacy needs to be first evaluated in real-world clinical setting. Furthermore, patients' views and acceptance of such service needs to be explored and taken into consideration. Therefore, to address these knowledge gaps, the second part of this thesis (Chapters 7 and 8) will report the efficacy of a combined nutritional-behavioural and supervised exercise programme delivered post-surgery as an adjunct therapy to bariatric surgery. Specifically, the primary objective of the BARI-LIFESTYLE intervention study is to compare the post-surgery %WL at six months after surgery, between people receiving standard care (control group) and people receiving standard care plus a post-surgery lifestyle intervention programme (intervention group). Whereas the secondary objectives of the BARI-LIFESTYLE intervention study were to compare the changes in:

1. %WL at 3-, 6-, and 12-month post-surgery between people receiving standard care and people receiving standard care plus a post-surgery lifestyle intervention programme, relative to baseline pre-surgery.
2. Obesity-associated comorbidities (T2D, hyperlipidaemia, hypertension, OSA) at 12-month post-surgery between people receiving standard care and people receiving standard care plus a postoperative lifestyle intervention programme, relative to baseline pre-surgery.

3. Fat mass and fat-free mass at 3-, 6-, and 12-month post-surgery between people receiving standard care and people receiving standard care plus a post-surgery lifestyle intervention programme, relative to baseline pre-surgery.
4. BMD at 3-, 6-, and 12-month post-surgery between people receiving standard care and people receiving standard care plus a post-surgery lifestyle intervention programme, relative to baseline pre-surgery.
5. Physical activity levels (light, moderate, vigorous), percentage achieving 150 minutes of MVPA in a week and sedentary behaviour at 3-, 6-, and 12-month post-surgery between people receiving standard care and people receiving standard care plus a postoperative lifestyle intervention programme, relative to baseline pre-surgery.
6. Physical function and strength at 3-, 6-, and 12-month post-surgery between people receiving standard care and people receiving standard care plus a postoperative lifestyle intervention programme, relative to baseline pre-surgery.
7. HRQoL scores at 3-, 6-, and 12-month post-surgery between people receiving standard care and people receiving standard care plus a postoperative lifestyle intervention programme, relative to baseline pre-surgery.
8. Characteristics of attitude and symptoms of depression at 3-, 6-, and 12-month post-surgery between people receiving standard care and people receiving standard care plus a postoperative lifestyle intervention programme, relative to baseline pre-surgery.

Hypothesis 2: *For the BARI-LIFESTYLE intervention study, we hypothesise that participants receiving standard post-surgery care plus a lifestyle intervention will achieve greater %WL at 6-month post-surgery and experience favourable impacts on body composition, resolution or improvement in comorbidities, physical activity levels* *and sedentary behaviour, physical function and strength, HRQoL and the symptoms of depression in the first year of surgery, compared to participants receiving standard post-surgery care alone.*

Chapter 3
Material and methods[2]

3.1 Study design

BARI-LIFESTYLE was designed as a two-arm, parallel-group, single-blinded, multi-centre RCT embedded within an observational cohort study (Figure 3.1). A two-stage randomised consent design was employed. This study was conducted by the Centre for Obesity Research, Division of Medicine, University College London (UCL). The study protocol was reviewed and given favourable opinion by London-Dulwich Research Ethics Committee (REC) (Reference: 17/LO/0950) (Appendix 3) and approved by the Health Research Authority (HRA) in July 2017 (Appendix 4). This study was registered at the clinical trial registry of the National Institutes of Health (Reference No: ClinicalTrials.gov NCT03214471), with UCL as the study sponsor.

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[2]The published work related to this chapter is available in Appendix 2. JASSIL, F. C., CARNEMOLLA, A., KINGETT, H., PATON, B., O'KEEFFE, A. G., DOYLE, J., MORRIS, S., LEWIS, N., KIRK, A., PUCCI, A., CHAIYASOOT, K. & BATTERHAM, R. L. 2018. Protocol for a 1-year prospective, longitudinal cohort study of patients undergoing Roux-en-Y gastric bypass and sleeve gastrectomy: the BARI-LIFESTYLE observational study. BMJ Open, 8, e020659.

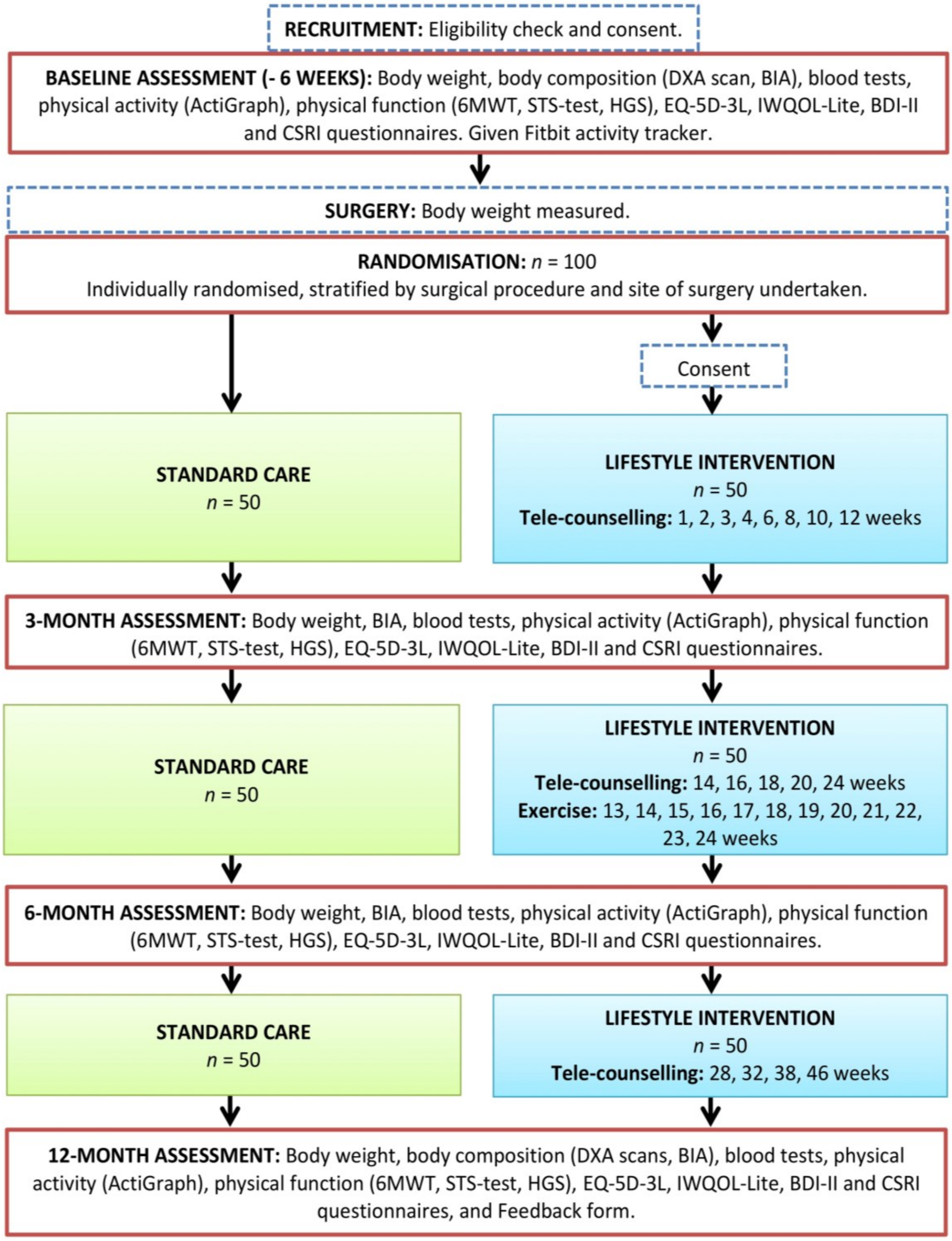


Figure 3. 1: BARI-LIFESTYLE study design.

Note: BDI-II, Beck Depression Inventory-II; BIA, bioelectrical impedance analyser; CSRI, Client Service Receipt Inventory; DXA, dual-energy X-ray absorptiometry; EQ-5D-3L, EuroQol-5D-3L; HGS, handgrip strength; IWQOL-Lite, Impact of Weight on Quality of Life-Lite; STS-test, sit-to-stand test; 6MWT, 6-minute walk test.

Throughout the study period, a total of five protocol amendments (one non-substantial and four substantial amendments) were submitted and approved by REC (Table 3.1). Of particular note, this study was initially designed as a single site, but additional sites were added at a later stage to improve the recruitment rate following the recommendation by the trial steering committee. Other than that, due to the challenges faced in maintaining a low attrition rate, the primary outcome time point was changed from 12-month to 6-month post-surgery, which led to the changes in sample size. Furthermore, during the COVID-19 pandemic, the exercise intervention component and the routine follow-up data collection were modified to maintain the integrity of this RCT (McDermott and Newman, 2020). A detailed explanation of the challenges faced in maintaining good recruitment and low attrition rate, and the impact of the COVID-19 pandemic on this trial are outlined in section 3.6.

Table 3. 1: History of the BARI-LIFESTYLE protocol amendment throughout the study period.

Protocol version	Date	Reasons for amendment
1	01.03.2017	The first version of the study protocol was submitted for approval by London-Dulwich Research Ethics Committee (REC) and Health Research Authority (HRA).
2	27.06.2017	Further information was provided as per requirement by REC and HRA before protocol approval.
3	09.08.2017	Protocol updates for the trial personnel, information regarding electronic data management, list of data collection and changes of the feedback form of the lifestyle intervention programme.
4	24.10.2017	Protocol updates for the contact details of the trial personnel, a list of secondary objectives, a list of questionnaires, and tele-counselling and exercise booklets.
5	14.08.2018	Protocol updates for additional new recruiting sites.
6	10.01.2020	Protocol updates for the changes of the primary outcome time point, the time windows of the follow-up assessment and the changes of sample size.
7	29.09.2020	Protocol updates to address the changes required to conduct the trial during the COVID-19 pandemic and an addition of a new qualitative sub study.

Note: COVID-19, coronavirus disease 2019; HRA, Health Research Authority; REC, Research Ethics Committee.

3.2 Participants

3.2.1 Eligibility criteria

Participants' recruitment was carried out from February 2018 until January 2020 at three London NHS Foundation Trusts: University College London Hospitals (UCLH), Whittington Health and Homerton University Hospital. All patients who were scheduled to undergo bariatric surgery were screened for eligibility to take part in the trial based on the following eligibility criteria:

Inclusion criteria

a) Adult aged between 18 to 65 years old.
b) Planned to undergo either primary gastric bypass surgery or primary SG surgery and fulfilling NICE eligibility criteria for bariatric surgery (NICE, 2014b) .
c) Medically safe to participate in an exercise programme.
d) Able to read and write in English.
e) Willing and able to provide written informed consent.
f) Able to comply with the study protocol.
g) Able to attend a supervised tailored exercise session weekly for 12 weeks.
h) Willing and able to wear a Fitbit wrist-based activity tracker device and an ActiGraph device.

Exclusion criteria

a) More than 200 kg of body weight due to the limitation of the DXA scan.
b) Non-ambulatory.
c) Functional limitation.
d) Medical contraindication for exercise.

3.2.2 Recruitment

In this trial, a two-stage randomised consent design was employed (Figure 3.2). Initially, patients who fulfilled the eligibility criteria as outlined in section 3.2.1 were invited to participate in a one-year prospective, longitudinal cohort study, the BARI-LIFESTYLE observational study (Jassil *et al*., 2018). Detailed information of the study was explained verbally to each potential participant by research staff and a copy of the participant information sheet was given (Appendix 5). Potential participants were also encouraged to ask any questions related to the study. They were given a minimum of 24 hours to decide whether to take part in the study before informed consent is sought. Those who agreed to participate were asked to sign two copies of the consent form (Appendix 6) and keeping one of the copies. Participants were then scheduled to attend a baseline visit (section 3.4), booked within six weeks prior to the planned surgery day.

On the day of surgery, immediately after the surgical procedure was successfully undertaken, all participants enrolled in the BARI-LIFESTYLE observational study were randomised to either continue to receive standard care (control group) following surgery or standard care plus a lifestyle programme (intervention group). Participants randomised to the intervention group were then invited to take part in the BARI-LIFESTYLE intervention study. Detailed information of the lifestyle intervention programme was explained by research staff and a copy of the participant information sheet given (Appendix 7). Those who agreed to participate signed two copies of the consent form before they were discharged (Appendix 8) and keeping one of the copies. Those who declined were asked whether they wanted to continue their participation in the initial BARI-LIFESTYLE observational study.

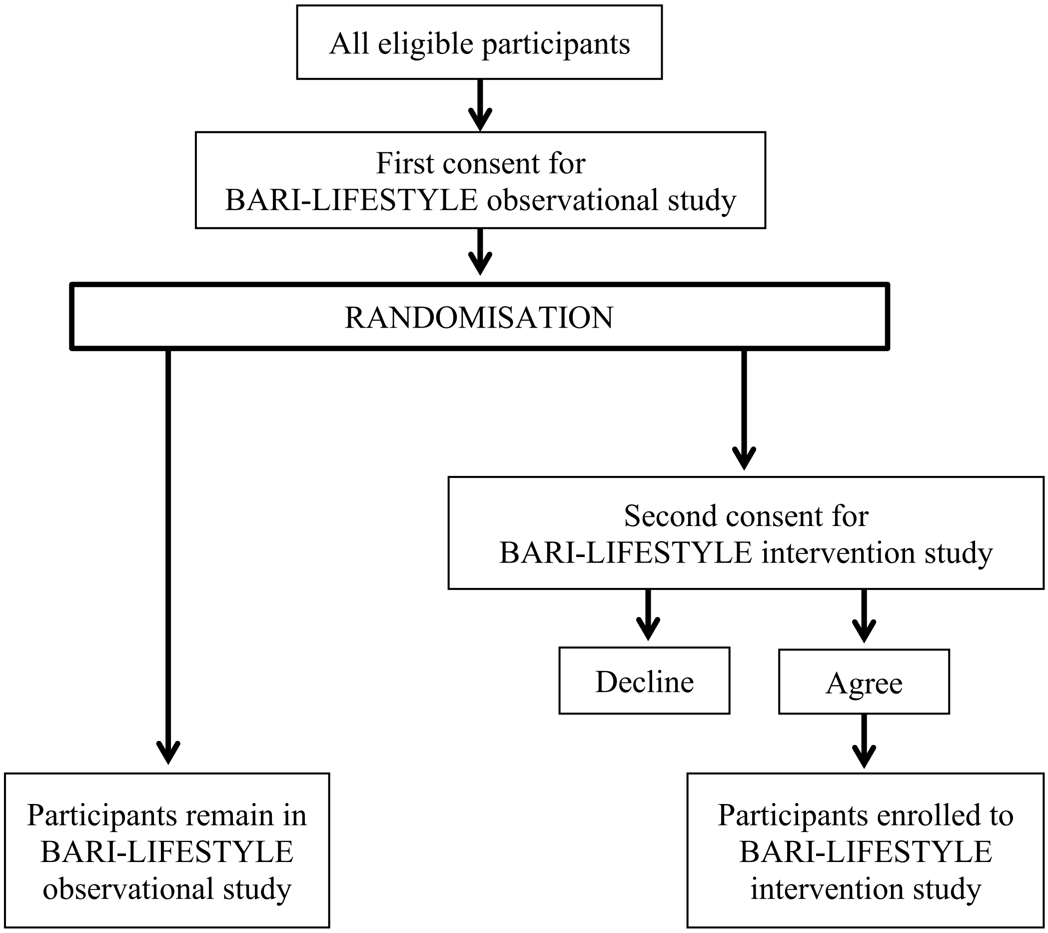


Figure 3. 2: A two-stage randomised consent design employed in the BARI-LIFESTYLE trial.

3.2.3 Randomisation and blinding

Randomisation was carried out via a third-party web-based randomisation service provided by the King's Clinical Trial Unit, King's College London (https://ctu.co.uk/). The randomisation system used multiple block randomisation (two, four and six) of a 1:1 allocation ratio, stratified by type of surgical procedure and study centre. In all centres, the decision for surgical procedure selection was based on informed patient preference after standardised counselling, including details, potential risks, and benefits of each surgical procedure that adhere to the current international guideline for the surgical recommendation for obesity and weight-related disease (De Luca *et al.*, 2016). The randomisation of each participant was carried out immediately post-surgery as occasionally, the decision to undertake gastric bypass or SG could changed intra-operatively.

Participants allocated to the control group were not informed of the existence of the BARI-LIFESTYLE intervention study. The reason behind this was to avoid contamination of the control group, which could potentially dilute the treatment effect in the intention-to-treat (ITT) analysis. The trial statistician and all outcome assessors were blinded to the treatment allocations. However, due to the nature of the study, as commonly occurred in RCTs involving lifestyle intervention programmes (Younge *et al*., 2015), blinding the outcome assessors in this study was challenging.

3.3 Intervention

BARI-LIFESTYLE observational study (control arm)

All participants enrolled in the BARI-LIFESTYLE observational study received the standardised post-bariatric care as stipulated by NICE (NICE, 2014b). Participants underwent regular monitoring of nutritional intake, vitamin and mineral deficiencies, comorbidities and medication review by their respective bariatric team in the first year of surgery. Participants also received verbal physical activity and dietary advice during the post-surgery follow-up visits.

BARI-LIFESTYLE intervention study (intervention arm)

Participants randomised to the BARI-LIFESTYLE intervention study received a 12-month lifestyle intervention programme that ran alongside the standard post-surgery follow-up care (Figure 3.3). The first six months was an intensive phase and the following six months was a maintenance phase. The lifestyle programme comprised of two components, the nutritional-behavioural intervention delivered via tele-counselling and a tailored supervised exercise programme. Both components were participant-centred and individualised. The lifestyle intervention programme focused on providing the support needed by participants to adjust to the dramatic lifestyle changes required following surgery. The programme was designed to address the concerns and difficulties that are typically faced by bariatric patients in the first postoperative year (Sheets *et al.*, 2015, Hood *et al.*, 2016).

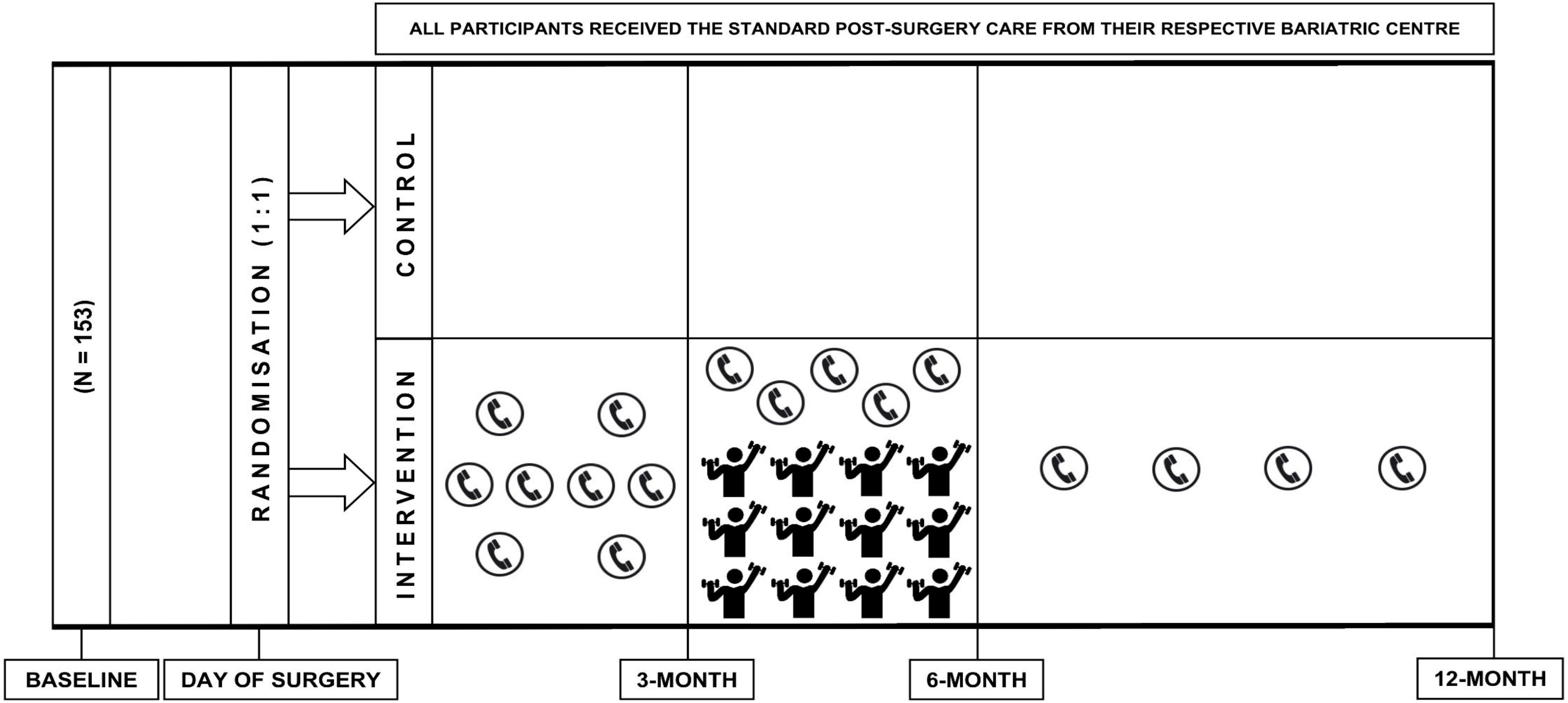


Figure 3. 3: Schematic representation of BARI-LIFESTYLE trial.

Note: The lifestyle intervention programme consisted of a nutritional-behavioural tele-counselling with a dietitian and once weekly tailored supervised exercise classes in the hospital gym for 12 weeks with an exercise therapist. All participants in both arms received the standard post-surgery care from their respective bariatric centre. The outcome analyses are based on the intention-to-treat principle followed by per-protocol analysis (participants who complete more than 50% of the intervention programme).

Tele-counselling programme

Participants received a total of 17 tele-counselling sessions in the first year of surgery that commenced in the first week following surgery. This comprised of 13 tele-counselling sessions in the intensive phase and only four sessions in the maintenance phase. The tele-counsellors were bariatric dietitians trained in behavioural psychological techniques and bariatric clinical psychologists. All tele-counsellors attended a full-day training on the tele-counselling programme. The tele-counselling manual was developed to ensure the sessions were delivered in a standardised format (Appendix 9). Role play that simulated a real tele-counselling session was carried out as part of the training programme to ensure the sessions were delivered according to the tele-counselling manual.

Each participant was assigned with the same tele-counsellor. However, in a situation where the tele-counsellor was not available (e.g., annual leave), another tele-counsellor took over the tele-counselling session. Participants were provided with a tele-counselling booklet containing dietary and exercise recommendations with diaries to self-report their food intake, step count, supplements intake, and body weight (Appendix 10). The information reported by participants in the diaries were used by the tele-counsellor to guide and individualise the content of each tele-counselling session. Participants were also encouraged to raise their preferred subject for discussion and received real-time feedback from the tele-counsellor. All data collected from the tele-counselling sessions were recorded in the trial database. The summary for the tele-counselling content is shown in Table 3.2.

Table 3. 2: Summary of the contents of the tele-counselling sessions.

INTENSIVE PHASE
<u>Week 1 to 12 (8 sessions)</u> The first tele-counselling (week 1) was an introductory session that took 30 minutes, whereas the following sessions took 15 minutes maximum each. The tele-counselling for the first twelve weeks post-surgery focused on ensuring participants achieve adequate nutrition and engage in physical activity. The behavioural aspect of the tele-counselling covered a range of self-regulatory techniques to aid participants to adhere to the post-surgery recommendations. Participants were given goals in relation to four key areas, outlined below. The tele-counsellors ensured that participants understood these recommendations and provided support for adherence. a) **Eating and drinking:** Participants were advised on moving through four phases of eating post-bariatric surgery, from a liquid diet to a soft blended/ pureed diet followed by a soft diet and finally return to solid. The focus was to meet the recommended daily protein intake of a minimum 60g (O'Kane *et al*., 2020). b) **Exercise:** Participants were encouraged to be active, using their Fitbit activity tracker to set goals and monitor their activity. The data from Fitbit was reported to the tele-counsellor for review. Participants were advised to increase their weekly step count by a minimum of 10% each week, aiming to achieve at least 10,000 steps daily. c) **Supplements:** Participants were required to take multivitamin and mineral supplements based on the British Obesity and Metabolic Surgery Society (BOMSS) guideline (O'Kane *et al*., 2020)

d) **Body weight:** The recommended target for weight loss was set to be between 1 to 2 kg per week. Participants were encouraged to report their weight every week to ensure that weight loss fell within the recommended target range.
Week 13 to 24 (5 sessions) From week 13 to 24 post-surgery, the tele-counsellors focused the conversation on maintaining adequate nutrition and protein intake, together with increased physical activity.
MAINTENANCE PHASE
Week 25 to 46 (4 sessions) Finally, from week 25 to 46 post-surgery, the tele-counsellors continued to discuss key targets as outlined above. In relation to exercise, participants were encouraged to achieve and maintain at least 150 minutes of MVPA per week.

Note: MVPA, moderate-to-vigorous physical activity.

Supervised exercise programme

At 3-month post-surgery, participants were enrolled in a once-weekly individually tailored supervised exercise programme for 12 weeks. Participants were free to choose one of three weekly classes based on their preference (Table 3.3). Each session was designed to last for 60 minutes maximum, combining both aerobic and resistance exercises. The programme was delivered by exercise therapists at the hospital gym. In addition to the in-person supervised exercise, participants were encouraged to do at least two additional exercise sessions on their own in a week. Participants were provided with an exercise booklet containing weekly exercise log for 12 weeks (Appendix 11).

Table 3. 3: Weekly schedule for the supervised exercise programme.

Day of the week	Time	Location
Tuesday	10:30 to 11:30 11:30 to 12:30	Physiotherapy Gym, Institute of Sport and Exercise Health (ISEH), UCLH
Thursday	17:30 to 18:30	Physiotherapy Gym, UCLH
Saturday	10:30 to 11:30	Physiotherapy Gym, Homerton Hospital

Note: ISEH, Institute of Sport and Exercise Health; UCLH, University College London Hospitals.

The exercise programme was developed following the protocol and experience learned from the pilot study (Jassil *et al*., 2015). In general, the baseline level of each exercise routine was prescribed based on individualised functional capacity assessed during the first exercise class to ensure suitability, safety, and promote adherence to the programme. Participants were instructed to exercise as long as they did not feel pain and were continuously monitored during the session. Any musculoskeletal problems noted when exercising was considered, and then the exercise programme was then adjusted accordingly to suit individual participants.

Participants were asked to self-report their rating perceived exertion using the Borg's Scale to support monitoring of correct exercise intensity (Borg, 1982). This scale is used to describe the level of perceived exertion. Participants were also given the Borg's Scale to take home, instructed in its use, and advised to work to exertion levels as determined under supervision. Gradual progression in the exercises was achieved by alternately increasing exercise duration and intensity every week. The exercise intensity and duration were modified in individual participants, per the individual's functional capacity and ability to carry out exercise.

The cardio exercise aimed at improving cardiorespiratory fitness, initiated at a level appropriate for each participant. Participants were provided options to exercise on a cycle ergometer, cross-trainer, climbmill and stepper. In addition, the aerobic exercise involving bodily movement in different directions that participants can easily do/replicate at home was also included.

The resistance exercise aimed to improve muscle function and strength. This was performed on either gym weightlifting equipment, body weight, or using resistance bands of various resistance levels. Participants were also provided with three types of resistance bands (PhysioRoom.com, UK) for their home exercise. The resistance exercises were prescribed to target all major muscle groups but were tailored depending on individual functional capacity and contraindications. The resistance exercises were based on the large muscle groups and the practicality and participants' ability to perform them at home. Gradual progression of the resistance training was prescribed as appropriate as the session progressed.

3.4 Outcome measures

Outcome measures were collected at four study time points. The baseline pre-surgery visit was carried out at the main trial site (UCLH) within six weeks prior to the planned surgery day. Then all the follow-up visits at 3-, 6-, and 12-month post-surgery were scheduled to coincide with the standard follow-up care at participants' respective bariatric centre or as preferred by the participants (Table 3.4). All data collected were recorded in the study case report form before being entered into the trial database.

Sociodemographic data and medical history

Participants' sociodemographic data and medical history were collected at the baseline visit. These include information such as age, gender, ethnicity, educational level, marital status, medication intake, weight history, pregnancy history, alcohol consumption using the Alcohol Use Disorders Identification Test-C (AUDIT-C) questionnaire (Bush *et al*., 1998) (Appendix 12), smoking habits and family history of obesity and associated comorbidities (T2D, hypertension, hyperlipidaemia, OSA).

Table 3. 4: BARI-LIFESTYLE timelines and assessments.

Week	-6 Baseline	Day 0 Surgery	1	2	3	4	6	8	10	12	13	14	15	16	17	18	19	20	21	22	23	24	26	28	30	32	38	39/+4	46	52
Visit Number	**1**											**2**												**3**						**4**
Consent 1, Height, Sociodemographic, Medical History, given Fitbit Alta HR	✓																													
Randomisation		✓																												
Consent 2		✓																												
Body Weight	✓	✓										✓												✓						✓
Blood Pressure, Heart Rate	✓											✓												✓						✓
Blood Test	✓											✓												✓						✓
Nurse Review			✓			✓																								
Dietitian Review												✓															✓			
Surgeon Review																								✓						✓
DXA Scan	✓																													✓
BIA	✓											✓												✓						✓
Physical Function & Strength (6MWT, STS-test, HGS)	✓											✓												✓						✓
ActiGraph	✓											✓												✓						✓
Completion of HRQoL questionnaires	✓											✓												✓						✓
Tele-counselling			✓	✓	✓	✓	✓	✓	✓	✓		✓		✓		✓		✓				✓		✓		✓	✓		✓	
Supervised Exercise										✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓									

Note: BIA, bioelectrical impedance analyser; DXA, dual-energy X-ray absorptiometry; HGS, handgrip strength; HRQoL, health-related quality of life; STS-test, sit-to-stand test; 6MWT, 6-minute walk test.

[yellow box] : Intervention arm only
Visit Number 1 : Baseline assessment at approximately within 6 weeks before surgery
Visit Number 2 : Follow-up assessment at week 12 (±4) post-surgery
Visit Number 3 : Follow-up assessment at week 26 (±4) post-surgery
Visit Number 4 : Follow-up assessment at week 52 (-4, +6) post-surgery

3.4.1 Primary outcome

Body weight was measured using BIA (Tanita DC-430MAS; Tanita, Tokyo, Japan) with participants wearing light clothes and without shoes and heavy accessories, to the nearest 0.1 kg. Whereas body weight on the day of surgery was measured using a scale at the respective surgical centres. Height was determined using a stadiometer (Seca 242, Seca, Hamburg, Germany) to the nearest 0.01 metre. %WL was calculated using the following formula: %WL = [(weight on the day of surgery – weight at time point after surgery)/weight on the day of surgery] × 100, measured at each study time point.

3.4.2 Secondary outcomes

Body composition (fat mass, fat-free mass and bone mineral density)

The whole-body composition (fat mass and fat-free mass) and BMD were assessed using DXA scan (Discovery A DXA system, software V.13.4.2; Hologic; Massachusetts, USA) at baseline and 12-month post-surgery (Figure 3.4). BMD was also assessed at the total hip, femoral neck and lumbar spine (L1-L4). DXA scan uses ionising radiation to measure different body compartments. This method is the current reference standard for assessing body composition and a gold standard to diagnose osteopenia and osteoporosis (Lee and Gallagher, 2008). Scans were performed by the same UCLH technologist team, ensuring consistency following the standard quality control procedures. Participants positioning during the DXA scan was standardised according to the manufacturer recommendation. The validity of body composition measurement of DXA compared to CT has been examined in premenopausal women with obesity, anorexia nervosa and normal weight which demonstrated strong correlations ($r=0.77$-0.95, $p<0.001$) (Bredella *et al.*, 2010). A strong correlation ($r=0.89$) was also observed in percentage of body fat in men and women with obesity assessed using DXA and the fourcompartment model as a criterion method (LaForgia *et al.*, 2009). Furthermore, the DXA-assessed lean tissue mass and fat-free mass are highly correlated with both MRI and CT measures of muscle mass with DXA being relatively cheaper than the other two methods (Kim *et al.*, 2002).

Figure 3. 4: Dual-energy X-ray absorptiometry (DXA) scan (Discovery A DXA system, software V.13.4.2; Hologic; Massachusetts, USA).

In addition, the whole-body composition was also determined by BIA (Tanita DC-430MAS; Tanita, Tokyo, Japan) at each study visit (Figure 3.5). BIA is a non-invasive, easy to perform and cheaper option to measure body composition based on the differences in electrical conductivity of fat mass and fat-free mass tissues (Faria *et al*., 2014). The use of BIA to measure body composition in bariatric surgery patients has been previously validated (Savastano *et al*., 2010, Widen *et al*., 2014). However, BIA is less reliable when compared to DXA measurements in people with morbid obesity, overestimating the fat-free mass as the BMI increases (Savastano *et al.*, 2010, Johnson Stoklossa *et al.*, 2016). BIA measurements are also influenced by food and alcohol intake, physical activity, time of day, skin condition (perspiration) and some disease conditions or treatments (Kyle *et al.*, 2004).

Figure 3. 5: Bioelectrical Impedance Analyser (BIA) (Tanita DC-430MAS; Tanita, Tokyo, Japan).

Physical activity levels and sedentary behaviour

Physical activity levels involving the time spent in light, moderate and vigorous physical activities, as well as sedentary behaviour were measured objectively using ActiGraph wGT3X-BT (Pensacola, Florida, USA), an accelerometer-based activity monitor according to the manufacturer's instruction (Figure 3.6) (Migueles et al., 2017a). Participants were instructed to wear the device (~ 27 g; 3.8 × 3.7 × 1.8 cm) using an elastic belt on their hip, daily for 24 hours, for seven consecutive days and remove it only during water-based activities. Participants were instructed to keep an activity diary throughout the wear time period to assist interpretation of data from the device (Appendix 13). Both the device and the activity diary were then returned to the research staff for data analysis using the device software (ActiLife software V.6.13.3, Pensacola, FL, USA).

Figure 3. 6: ActiGraph wGT3X-BT (Pensacola, Florida, USA).

Data were sampled at a frequency of 100 Hz from three axes (vector magnitude [VM]), in (or aggregated to) one-minute epoch. Data were considered valid and included in the analyses if the device was worn for at least 10 hours daily for at least four days, which was validated from the physical activity diary. Non-wear time was defined as at least 60 minutes with no movement (VM = 0 counts per minute [cpm]) with an allowance of a maximum of two minutes of activity (Troiano *et al*., 2008). Therefore, wear time is determined by subtracting non-wear time from 24 hours.

Time spent sedentary was defined as less than 200 cpm, light intensity physical activity as 200 to 2689 cpm, moderate-intensity physical activity as 2690 to 6166 cpm, and vigorous physical activity as 6167 cpm and above (Sasaki *et al*., 2011). Participants were considered compliant with the WHO physical activity guidelines when the total MVPA was ≥ 150 min/week (WHO, 2020b). The methods for data collection and processing criteria were chosen based on the recommendation by Migueles *et al*. (Migueles et al., 2017b).

All participants were given a Fitbit device at the baseline visit (Fitbit, California, USA) (Figure 3.7). Fitbit is a validated wrist-based physical activity tracker that provides real-time feedback, goal-driven prompts and synchronises with smart devices or the internet (Evenson *et al*., 2015). Mobile technologies offer a convenient method for self-monitoring physical activity, sedentary behaviour, calorie intake and body weight, and when aligned with behaviour change, they can improve physical activity and promote weight loss (Wang *et al*., 2020). In addition, they can provide prompts to reduce sedentary behaviour (Bond and Thomas, 2015) and set reminders to take vitamin and mineral supplements. Furthermore, objective data such as the step count reported by participants was used by the tele-counsellor to set a new goal to promote increased physical activity.

Recruitment to BARI-LIFESTYLE will increase awareness of wearable devices with the risk of the control group starting to utilise these. Providing the control group with a Fitbit allowed standardisation of this contaminating effect and monitoring their usage in the absence of ongoing personal contact. The rationale for giving Fitbit prior to the planned bariatric surgery was to enable participants to learn how to use this and for the novelty factor to wear off in the control group.

Figure 3. 7: Fitbit (Fitbit, California, USA).

Physical function and strength

The 6-minute walk test

Participants' functional capacity was assessed using a 6MWT, a self-paced, submaximal assessment of functional capacity that is usually used to prescribe appropriate exercise (Figure 3.8) (A. T. S. Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories, 2002). This test has been validated in people with obesity (Beriault *et al*., 2009) and often used to assess the functional capacity of patients undergoing bariatric surgery (Tompkins *et al*., 2008, de Souza *et al*., 2009). In brief, participants were instructed to walk at their regular pace along an even 30 metres of an undisturbed hospital corridor, marked every five metres. They were asked to cover as much distance as they could, walking back and forth for six minutes, monitored using a stopwatch. During the test, participants were allowed to slow down, stop, rest as necessary and resume walking once they could. Minimal encouragements were given using the standard phrases in the guidelines and patients were asked to self-rate their level of exhaustion based on the 'Talk Test', the Borg's Resting Perceived Exertion scale (Borg, 1982). This test is a simple method used to subjectively measure the intensity of physical activity levels (rated from scale 0 = no exertion at all to scale 10 = maximal exertion). Perceived exertion is based on the person's experience of changes in their heart rate and breathing rate, sweating and muscle fatigue when performing physical activity. This method was considered a good estimate of the actual heart rate during physical activity. The pre- and post-test heart rate, total distance covered, post-test Borg's Resting Perceived Exertion rating, number of stops and any physical problem were recorded in the case report form.

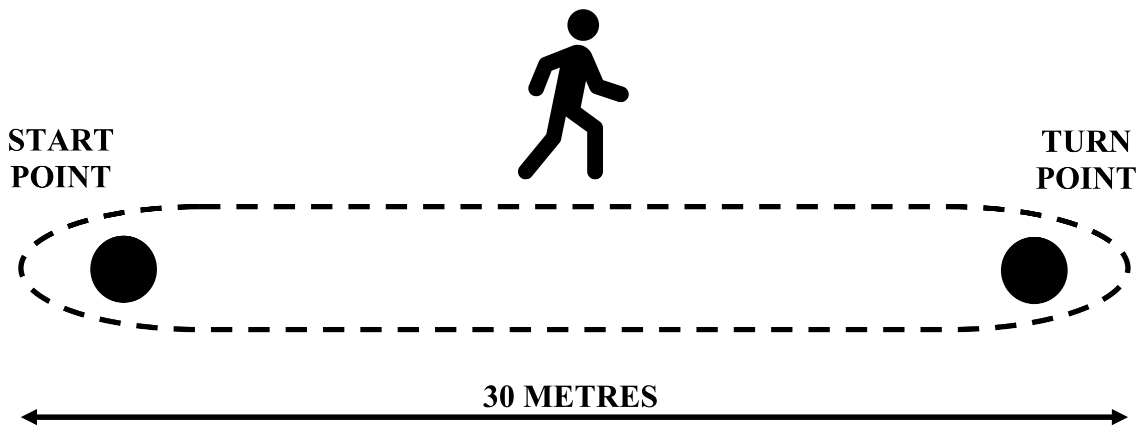


Figure 3. 8: The 6-minute walk test (6MWT).

The sit-to-stand test

The lower body functional capacity and strength were assessed using the STS-test (Figure 3.9) (Pataky *et al*., 2014). In this test, participants were asked to perform five sit-to-stand repetitions as rapidly as possible, starting from a sitting position with arms crossed over the chest. Using a stopwatch, the time taken to complete five repetitions were recorded in the case report form.

Figure 3. 9: The sit-to-stand test (STS-test).

The handgrip test

The static muscle strength of the upper extremities was assessed using Jamar Hydraulic Hand Dynamometer (Patterson Medical; Illinois, USA) (Figure 3.10) (Sousa-Santos and Amaral, 2017). In a sitting position, participants were asked to squeeze the device as hard as possible with each hand, alternately, for three times, with 10 to 20 seconds rest in between each repetition. For the absolute muscle strength, the average of the three measurements of the dominant hand was calculated (Sousa-Santos and Amaral, 2017). Relative muscle strength was calculated using the following formula: absolute muscle strength (kg) divided by BMI (strength/BMI). The relative muscle strength is defined as the muscle force that a person could produce in relation to their body mass (Choquette *et al*., 2010).

Figure 3. 10: The Jamar Hydraulic Hand Dynamometer (Patterson Medical; Illinois, USA).

Dietary intake

All participants were required to keep a 3-day food diary (two working days and one weekend day) at each study time point (Appendix 14). This method has a higher agreement with the nine days food dairy compared to the food frequency questionnaire (Yang *et al*., 2010). This simple food diary also reduced participants' burden and thus promoted better compliance to documenting food intake. The completed food diary was then returned to the research staff with the ActiGraph and the activity diary, using a stamped addressed envelope provided.

Health-Related Quality of Life

HRQoL was assessed using two types of instruments: the generic health status EQ-5D-3L and the obesity-specific questionnaire, IWQOL-Lite.

The EuroQol questionnaire

The EQ-5D-3L descriptive system is a 5-item self-report questionnaire that assesses the following domains: mobility, self-care, usual activities, pain/discomfort and anxiety/depression; from which participants selected the level which most closely matched their health state: no problems, some problems, and extreme problems (Appendix 15). The accompanying visual analogue scale (VAS) records the participants' self-reported health on a vertical scale where the endpoints are labelled 'best imaginable health state' and 'worst imaginable health state.' The point selected on the scale provided a quantitative measure of the health outcome as judged by the participants (Brooks, 1996). The EQ-5D-3L health states were then converted into utility values using a formula that attaches weights to each level in each dimension based on valuations by general population samples. A value set for the UK population was used to calculate utility values at each time point for every participant (Dolan, 1997). The EQ-5D has been used in various health conditions (Rabin and de Charro, 2001) and has good test-retest reliability (van Agt *et al*., 1994). However, despite its popularity and extensive use, the EQ-5D (the 3-level version) has not been validated to assess HRQoL in patients undergoing bariatric surgery (Fermont *et al*., 2017).

The Impact of Weight on Quality of Life - Lite questionnaire

The IWQOL-Lite is a 31-item, self-report, obesity and overweight-specific measure of HRQoL (Appendix 16) (Kolotkin *et al*., 2001a). This tool consists of a total score and the score of five individual scales – physical function, self-esteem, sexual life, public distress, and work; higher scores indicate better HRQoL. Participants were given a series of statements that begin with "Because of my weight…" and then asked to rate whether it was "always true, usually true, sometimes true, rarely true, or never true". The Public Distress subscale, for example, asked whether the participants experience ridicule, teasing, or unwanted attention because of their weight, whether they worry about fitting into seats in public places, aisles and finding chairs that are strong enough or, whether they experience discrimination. This subscale has been shown to have construct validity for capturing "weight stigma". The IWQOL-lite is also scored on a 0 to 100 scale for each subscale; it has excellent psychometric properties and test-retest reliability. This questionnaire has been validated in people living with severe obesity (Kolotkin *et al*., 2001a, Forhan *et al*., 2010).

The Beck Depression Inventory-II questionnaire

Attitude and symptoms of depression were assessed using BDI-II (Appendix 17) (Beck *et al*., 1996). The BDI-II is a 21-item self-report questionnaire (including cognitive-affective and somatic symptoms of depression categories) that assesses mood over the past week. Items rated on an intensity scale of 0 to 3 with a maximum score of 63, and its reliability and validity in mental health contexts are well established. Symptoms of depression are classified by the total score where no symptoms (0 score), minimal (1-13 scores), mild (14-19 scores), moderate (20-28 scores), and severe depressive symptomatology (29-63 scores).

Obesity-associated comorbidities

Comorbidities associated with obesity (T2D, hyperlipidaemia, hypertension, OSA) and medication review were carried out at each study time point. Resolution of hypertension, hyperlipidaemia, and OSA was defined as normalisation of the corresponding characteristics without treatment. Resolution of T2D was defined according to the American Diabetes Association criteria of complete remission: no antidiabetic drug, fasting blood glucose < 5.6 mmol/L, and glycated haemoglobin (HbA1c) in the normal range of at least one years' duration. Partial remission was defined as: no antidiabetic drug, fasting blood glucose between 5.6 – 6.9 mmol/L, and HbA1c < 6.5% of at least one years' duration (Buse *et al*., 2009).

Healthcare resource utilisation and costs

Resource use data were collected using an adapted version of the CSRI (Appendix 18) (Beecham and Knapp, 2001), including the cost of bariatric surgery plus pre-surgery visits, a number of contacts with healthcare professionals, visits to specialist clinics and the emergency department, admissions to the hospital, primary care contacts, and medications. The resource use data were converted into costs using published unit costs (British National Formulary, Curtis and Burns, 2015, Department of Health, 2015b). In addition, information regarding support from informal carers, employment status and time off work was collected. The resource use data were collected for the previous six months at the baseline visit and 'since participants last study visit' at each post-surgery study time point.

Biological parameters

Data on blood test results as part of the post-surgery routine nutritional monitoring was obtained from medical records. Parameters recorded in the study case report form included glucose, lipid, liver and renal profiles, full blood count, bone markers, thyroid function, iron and total iron-binding capacity and other nutritional parameters such as vitamin B12, vitamin D, vitamin B1, zinc and copper. The normal values of the parameters are based on the reference values used by the respective bariatric centres.

Participants' feedback on the lifestyle intervention programme

All participants in the intervention group were asked to complete a feedback form during the final study visit (Appendix 19). This form asked participants to rate the quality of both the tele-counselling and supervised exercise programmes and also captured participants' satisfaction and comments on the programme's contents, length, homework and material. Participants were provided with free text comments. The items also covered self-reported barriers and facilitators that contributed to their compliance with the programme. Overall, this feedback form enabled the identification of processes that may influence the interventions' acceptability and effectiveness.

Assessments of Adverse Events

All adverse events were recorded at each study visit post-randomisation in the case report form. Each adverse event was assessed for severity, causality, seriousness and expectedness as described in Table 3.5. All serious adverse events were reported to the study sponsor (UCL).

Table 3. 5: The classification of adverse events.

Category	Definition
Mild	The adverse events did not interfere with the participant's daily routine and did not require further intervention; it caused slight discomfort.
Moderate	The adverse events interfered with some aspects of the participant's routine, or required further intervention, but was not damaging to health; it caused moderate discomfort.
Severe	The adverse events resulted in alteration, discomfort or disability, which was clearly damaging to health.

3.5 Statistical analysis

3.5.1 Sample size

Initially, the sample size of this trial was calculated based on the findings from our previous pilot study (Jassil *et al.*, 2015) and cohort data of 1064 patients who underwent bariatric surgery at UCLH (555 patients had SG, and 509 patients had RYGB). The mean and standard deviation (SD) of %WL at 12-month post-surgery is 27.8% ± 8.4%. This study was powered to detect a clinically significant change in %WL between the intervention and control groups with a difference of 5%, assuming an SD of 8.4%.

Therefore, this study required a total of 198 participants, 99 participants in each study arm (95% power with 2-sided 5% significance level), after allowing for 25% dropouts throughout the trial period.

However, due to the high attrition rate at 12-month, the primary outcome time point was changed to 6-month post-surgery. Using a mean and SD of %WL of 23.6% ± 6.6% at 6-month post-surgery of the same cohort of patients who underwent bariatric surgery at UCLH, the newly calculated sample size was 100 participants, 50 participants in each trial arm (90% power with 2-sided 5% significance level), after allowing for 25% of dropouts throughout the trial period. This new sample size was powered to detect a clinically significant change in %WL between the intervention and control groups with a difference of 5%, assuming an SD of 6.6%.

3.5.2 Recruitment and retention

A CONSORT diagram is presented in Chapter 7, providing a detailed description of participants numbers at each time point during the trial, including the numbers of drop-outs at each stage of the trial and reasons for drop-out (Moher *et al.*, 2010). All data collected from withdrawn participants were included in the analysis as none of them had specified they wanted their data to be excluded at the point of withdrawal.

3.5.3 Description of demographic variables

Demographic information collected at baseline are presented in Chapters 4 and 7. Categorical variables are presented as raw numbers and percentages. Depending on the data distribution, continuous variables are presented as mean and SD or median and ranges.

3.5.4 Primary outcome analysis

The primary outcome is the percentage loss in weight from the day of surgery until 6-month post-surgery. A negative value of this variable indicates a weight gain and a non-negative value indicates weight loss.

A linear regression model for %WL at 6-month post-surgery was undertaken, with explanatory variables to indicate treatment group (lifestyle intervention or standard care), the explanatory variable 'BMI (kg/m^2) on the day of surgery' and fixed explanatory variables to indicate study centre. The coefficient of the treatment group provided an estimate of the between-group mean difference in %WL. The estimation of this coefficient is reported together with an associated 95% confidence interval (CI). Unless otherwise stated, data are also presented as mean ± SD. A p-value for a test of the null hypothesis that this mean difference is equal to zero against a two-sided alternative is reported using a significance level of 0.05.

Model assumptions/validity was checked using appropriate plots (e.g. normal quantile-quantile plot of model residuals, plot of model residuals against fitted values). The form of the model for the primary outcome is as follows:

$$y_i = \beta_0 + \beta_1 x_{i1} + \beta_2 x_{i2} + \beta_3 x_{i3} + \beta_4 x_{i4} + \epsilon_i$$

where

y_i = %WL at 6-month;

$x_{i1} = 1$ if the patient received surgery at Homerton Hospital, = 0 otherwise;

$x_{i2} = 1$ if the patient received surgery at Whittington Hospital, = 0 otherwise;

$x_{i3} =$ BMI (kg/m^2) on the day of surgery;

$x_{i4} = 1$ if the patient is allocated to the lifestyle intervention group, = 0 otherwise;

$\epsilon_i \sim N(0, \sigma^2)$.

The estimation of β_4, together with its associated 95% CI, provided the intervention effect estimate. A p-value for a test of the null hypothesis that $\beta_4 = 0$ against a two-sided alternative is reported using a 5% significance level. For the sensitivity analysis (model 2), the missing BIA weight at 6-month post-surgery was replaced by the participants' self-reported weight and the primary outcome analysis model was re-fitted. Per-protocol analysis (model 3) was also undertaken by excluding data of participants who did not complete more than 50% of both the tele-counselling and supervised exercise sessions and the primary outcome analysis model was re-fitted.

3.5.5 Secondary outcomes analyses

Other weight-based secondary outcomes (weight at 3-month and weight at 12-month) were analysed in a similar way to the primary outcome. For weight at each time point (3-, 6- and 12-month), additional models were fitted where the weight (rather than the percentage change) is modelled using a normal linear regression model with BMI at surgery, treatment and study centre as explanatory variables. Weight across time were modelled using a longitudinal mixed effects model with weight at surgery, time, treatment and study centre included as fixed effects and a random effect included at the participant level.

Other continuous secondary outcomes (fat mass, fat-free mass, BMD, physical activity levels, sedentary behaviour, physical function and strength, HRQoL and symptoms of depression) were analysed in a similar manner to weight. HRQoL and BDI-II scores were converted into their aggregate scores and domains prior to analysis. For obesity-related comorbidities (T2D, hypertension, hyperlipidaemia, OSA) the proportion of participants with these conditions were reported in a table by treatment group at baseline. In addition, at follow-up, tables were produced to report the number of participants who had new comorbidities and to report the status of comorbidities for participants who had comorbidities at baselines (no change, improvement, remission, worsened).

3.5.6 Analysis of the longitudinal data

The %WL was analysed using a linear mixed-effects model over the three post-surgery time points (3-, 6- and 12-month) after controlling for the baseline BMI. In addition, the overall percentage change in weight since baseline was computed marginally at each of 3-, 6- and 12-month time points. Analyses of secondary outcomes (body composition, BMD, physical activity levels, sedentary behaviour, physical function and strength, HRQoL and mental health) were performed using the similar linear mixed-effects regression models. Model parameter estimates together with the 95% CIs are reported. Unless otherwise stated, data are also presented as mean ± SD. Categorical outcomes (e.g., proportions of participants with comorbidities) are summarised in tabular format at each time point. A p-value of less than 0.05 indicated a statistically significant difference. Analyses for the primary and secondary outcomes of the RCT and the longitudinal data were performed using Stata 17 (StataCorp. 2021. Stata Statistical Software: Release 17. College Station, TX: StataCorp LLC).

3.5.7 Missing Data

Bias owing to missing data were investigated by comparing the baseline characteristics of patients (age, gender, and body weight) with and without missing values for the primary outcome. Depending on the extent of missingness, the predictors of missing values were identified using logistic regression. The primary analysis would then be adjusted for those predictors of missing values (if any) which are related to missingness as a sensitivity analysis.

3.6 Discussion

3.6.1 Rationale for a two-stage randomised consent design

An RCT is a type of study design by which people are allocated at random, by chance alone, to receive one or several clinical interventions. This is a widely used study design to prevent research bias (Hariton and Locascio, 2018). However, RCT has several limitations particularly for a clinical study that involves a lifestyle intervention (Younge *et al*., 2015). In a conventional randomised design, all eligible participants must be fully informed regarding the study pre-randomisation, before informed consent is sought. Unfortunately, in a lifestyle intervention study, participants assigned to the control group may be less likely to participate, because of the disappointment about the allocation, since they perceived the intervention group as more desirable (Corrigan and Salzer, 2003). This is particularly true for people with obesity, as a lifestyle programme involving dietary, behavioural and physical activity support is perceived as beneficial. For such reason, those allocated to the control group may refuse to participate or even if they agreed, the likelihood of dropout, non-compliance and loss to follow-up is high resulted from a 'resentful demoralisation' (Bradley, 1993). Other than that, detailed knowledge of the study may cause participants in the control group to adopt the lifestyle components involved in the intervention arm. This will eventually contaminate the control group and introduce bias to the study as it may dilute the real treatment effect in an ITT analysis (Courneya *et al*., 2002).

To address these problems, the BARI-LIFESTYLE study employed a two-stage randomised consent design, which ethically respects participants' autonomy and at the same time fulfil the scientific rigour (Stott *et al*., 1997). This is a modified version of Zelen's design where participants could decline the experimental intervention and therefore receive the standard treatment (Zelen, 1979). The two-stage randomised consent design has been successfully used previously in randomised trials of a lifestyle intervention (Campbell *et al*., 2005, Land *et al*., 2020).

3.6.2 Rationale for a nutritional-behavioural tele-counselling

Frequent contact with healthcare professionals has been shown to link with better weight loss outcomes following bariatric surgery (Endevelt *et al*., 2013), but delivering regular face-to-face counselling in real-world clinical practice is deemed impractical and challenging. In a behavioural weight loss programme, intervention delivered remotely by telephone has been demonstrated to be equally effective as intervention delivered in-person to promote sustained weight loss (Appel *et al*., 2011). Other than being less costly and requiring lesser manpower, remote intervention would be favourable to patients who find it difficult to commit their time due to working or social support issues or expensive travel costs, especially for those who live geographically far away from their bariatric centre.

Poor adherence to the lifestyle intervention delivered in-person has been previously reported in post-bariatric lifestyle interventions (Nijamkin *et al.*, 2012, Sarwer *et al.*, 2012, Lent *et al.*, 2019). Applying the tele-counselling in this study will address this limitation and improve the adherence rate (Sarwer *et al*., 2012). Also, the application of tele-counselling is in line with the NHS Long Term Plan to promote the use of technology in prevention, care and treatment to be mainstreamed across the NHS (National Health Service, 2019).

3.6.3 Rationale for a supervised exercise programme

People living with obesity generally experience various barriers to engaging in physical activity (McIntosh *et al*., 2016), which continue to persist following bariatric surgery despite a significant weight loss (Zabatiero *et al*., 2016, Zabatiero *et al*., 2018). Post-surgery, patients reported poor motivation to engage in physical activity and most feel uncomfortable in the gym due to inadequate exercise knowledge that leads to poor confidence level to exercise on their own. Patients also experience some issues such as bodily pain that limit their mobility which makes it even difficult for them to do exercise, with some having expressed their fear of getting injuries when exercising (Peacock *et al*., 2014).

The individually tailored supervised exercise programme in this study was designed to address the exercise barriers and supporting patients in meeting the physical activity recommendations after bariatric surgery. Several studies have demonstrated the effectiveness of intensive post-bariatric supervised exercise programmes in promoting better weight loss and other beneficial health outcomes (Bellicha *et al*., 2021). However, implementing an intensive exercise programme (e.g., three times a week of gym supervised exercise) can be very costly and might not be feasible in a real-world clinical setting. Therefore, the current exercise protocol was developed to evaluate whether a lesser intensive form of supervised exercise programme (once weekly gym supervised exercise) can produce similar health benefits.

3.6.4 Challenges with patients' recruitment and retention

In an RCT, failure to reach recruitment target and retain a low attrition rate will lead to scientific, economic and ethical consequences which are common in longer and bigger trials (Gul and Ali, 2010). As such, it is not surprising that we also faced the same issues with BARI-LIFESTYLE. The trial recruitment had progressed slower than expected in the first six months since the commencement of participants' recruitment. Among the reasons were:

a) Change in funding procedure for bariatric surgery from central NHS England to local Clinical Commissioning Groups: this brought about a considerable decrease in both referrals and surgery rate since 2017.

b) UCLH experienced a severe bed crisis since the beginning of 2019. Bariatric surgeries were cancelled to allow for higher priority surgeries to take place.

c) DXA availability: participants' enrolment had to be slowed down due to lack of available DXA scan slots. This led to the loss of a few potential participants as Nuclear Medicine Department was not able to allocate the study enough scanning slots despite having reviewed the study and its requirements before the sign-off.

To counteract this slowdown in recruitment, several amendments to the study protocol and actions were taken that aimed to catch up with the recruitment target. These include converting a participant identification centre to a study site (to allow for study procedure to take place on-site), adding another study site, the Homerton University Hospital to boost recruitment, and employing a research nurse to deliver the study at study sites.

We also experienced difficulties in maintaining a low attrition rate. Frequent monitoring on the 12-month retention rate had revealed that only 65% to 70% of the study participants had come back for the final study visit or had attended this study visit within the expected time frame. Considering the study was powered to account for an attrition rate of 25%, the implication of such observation indicated that the trial might not be able to achieve its target and answer the research question. Conversely, the retention rate at six months surfaced at 75% to 80%. Furthermore, based on the trial protocol, the intensive phase of the study intervention was fully delivered by six months (what's left is only four tele-counselling sessions spread across the remaining six months) hence giving us the possibility to answer the research question of whether or not a lifestyle programme aids weight loss after surgery. Therefore, the evaluation of the primary outcome was brought forward from 12 to 6 months post-surgery and the study protocol was amended accordingly.

Moving the primary outcome from 12 to 6 months post-surgery impacted the required sample size and had brought this down to 100 participants (50 participants per study arm). The original sample size was 198. The study officially closed recruitment in January 2020 with 153 participants enrolled. This is 53% more than the new required sample size.

3.6.5 The impact of COVID-19 pandemic on BARI-LIFESTYLE trial

Following the nationwide lockdown imposed by the UK government due to the COVID-19 crisis effective from the 24th of March (UK Government, 2020), several changes were made to the method of intervention delivery and outcome data collection, replacing the face-to-face research activities. These measures were undertaken to protect the safety of participants and research staff, alongside preserving the integrity of the BARI-LIFESTYLE trial throughout the pandemic period (McDermott and Newman, 2020).

The in-person supervised exercise programme at the hospital gym was converted to home-based tele-exercise classes, delivered virtually via zoom (Zoom Video

Communications, Inc. California, US), with the weekly exercise schedules maintained. The tele-exercise content is detailed in Chapter 8. The delivery of a post-bariatric exercise programme via telehealth has been previously shown to be feasible (Baillot *et al*., 2017). However, patients' acceptability of this method of exercise provision is unknown. Therefore, the protocol amendment during the COVID-19 pandemic included an additional sub study evaluating patients' views and experiences of a live supervised tele-exercise programme using a qualitative study method.

From the beginning of the nationwide lockdown, all data collection was carried out remotely either via telephone or video call. The ActiGraph device, food and physical activity diaries and questionnaires were mailed to the participant's home address together with a self-addressed stamped return envelope. However, several outcome measures such as physical and functional assessments (blood pressure, 6MWT, STS and HGS tests) and body composition measurements (BIA and DXA scan) were not possible to be carried out remotely hence recorded as missing data. The in-person data collection resumed once the COVID-19 restrictions were lifted by the end of June 2020.

Chapter 4
Weight loss, comorbidities, body composition and bone mineral density outcomes: The BARI-LIFESTYLE observational study

4.1 Introduction

As previously outlined in Chapters 1 and 2, bariatric surgery induces a substantial weight loss and comorbidities resolution, particularly T2D. Despite the increasing prevalence of obesity and T2D in the UK, the number of bariatric surgeries performed has not increased in parallel and rates continue to remain low, leading to limited access to bariatric surgery (Booth *et al*., 2016, Desogus *et al*., 2019). Moreover, data on the outcomes of OAGB, the new bariatric procedure that is growingly performed in the UK, is still limited in the literature (Hussain *et al*., 2019). Therefore, more UK prospective studies are needed to assess the outcomes of bariatric surgery that should also include the OAGB procedure. This data is vital for policymakers, service commissioners and clinical decision-makers to make informed decisions to support the increased provision of bariatric surgery and also to inform future clinical guidelines particularly for OAGB procedure.

Similar to diet-induced weight loss, fat mass loss following bariatric surgery is often accompanied by the inevitable loss of fat-free mass (Chaston *et al*., 2007). However, excessive fat-free mass loss post-surgery has been suggested to induce weight regain (Faria *et al*., 2009) which is often accompanied by the re-emergence of comorbidities, counteracting the long-term benefits of bariatric surgery (Laurino Neto *et al*., 2012), given its role in the regulation of energy balance and appetite control (Grannell *et al*., 2019). Monitoring the changes in body composition as part of routine clinical evaluation pre- and post-surgery care is therefore recommended as it provides profound insights into the quality of weight loss after bariatric surgery (Faria *et al*., 2014). The information can assist the bariatric MDT in providing individualised care for patients to maximise outcomes (Gomez-Ambrosi *et al*., 2017, Jimenez *et al*., 2020). However, the usual parameters used in reporting weight loss after bariatric surgery such as percentage of Excess BMI Loss (%EBMIL), percentage of Excess Weight Loss (%EWL) and %WL do not relate to the changes in the two compartments of body composition (Maimoun *et al*., 2019). Apart from that, there is a considerable variation in fat mass and fat-free mass loss between individual post-surgery. However, implementing a body composition assessment as part of standard care also poses a great challenge as access to equipment that can provide an accurate measurement such as DXA, MRI and CT scans are very limited and costly for the public service (Borga *et al*., 2018). BIA on the other hand, has been increasingly used to analyse body composition not only because it is cheap and readily accessible, but this equipment does not require highly skilled personnel to operate and importantly, the assessment procedure is quick, and the result is available instantly (Becroft *et al*., 2019). However, whether BIA can provide an accurate and reliable measurement of body composition especially in people with obesity and those who have undergone bariatric surgery remains to be investigated further.

Another important outcome that is rarely monitored in routine care following bariatric surgery is the changes in BMD. The increased incidence of fractures in patients who have undergone bariatric surgery has been suggested to be caused by post-surgery BMD loss (Gagnon and Schafer, 2018). Indeed, as detailed in Chapter 2, growing scientific research has reported on the impact of bariatric surgery particularly on weight-bearing skeletal regions, such as the total hip, femoral neck and lumbar spine as well as the whole-body BMD, but results are inconsistent across studies. Importantly, such data have never been reported from patients who had bariatric surgery in the UK healthcare setting (Rodriguez-Carmona *et al.*, 2014, Jaruvongvanich *et al.*, 2019). Moreover, studies evaluating the impact of OAGB on BMD are currently very limited in the literature and thus warrant further investigation (Luger *et al*., 2018).

Therefore, the aim of this study is to assess the effect of bariatric surgery upon weight loss, resolution or improvement in comorbidities, and changes in body composition including BMD in the first postoperative year, and to compare the differences of these outcomes between RYGB, OAGB and SG. Specifically, the objectives of this study are:

1. To evaluate changes in %WL at 3-, 6- and 12-month post-bariatric surgery, relative to baseline pre-surgery weight.
2. To identify predictors of weight loss at 12-month post-surgery.
3. To evaluate changes in %WL at 3-, 6- and 12-month post-surgery, relative to baseline pre-surgery weight between RYGB, OAGB and SG.
4. To determine the prevalence of patients with suboptimal weight loss, defined as weight loss less than 20% at 12-month post-surgery (Corcelles *et al*., 2016).

5. To evaluate the changes in obesity-associated comorbidities (T2D, hyperlipidaemia, hypertension, OSA) at 12-month post-surgery, relative to baseline pre-surgery.
6. To evaluate the changes in fat mass and fat-free mass assessed using BIA at 3-, 6- and 12-month post-surgery and DXA scan at 12-month, relative to baseline pre-surgery.
7. To determine the prevalence of patients with excessive fat-free mass loss in the first postoperative year.
8. To identify the predictors of fat-free mass loss at 12-month post-surgery.
9. To assess the differences in fat mass and fat-free mass changes between good and suboptimal weight loss groups.
10. To assess the correlation of body composition measured using BIA and DXA.
11. To analyse the changes in BMD assessed using DXA at 12-month post-surgery, relative to baseline pre-surgery.
12. To identify the predictors of BMD loss at 12-month post-surgery.

4.2 Materials and methods

The study design and setting, eligibility criteria, participant recruitment and data collection for BIA, DXA and obesity-associated comorbidities have been described in detail in Chapter 3. The first participant enrolled in this longitudinal cohort study was in March 2018 and the last participant follow-up was in January 2021. Throughout the nationwide lockdown between April to July 2020, all face-to-face assessments were suspended and DXA scans were cancelled to comply with the government restrictions. Therefore, some BIA and DXA data were missing. Nevertheless, we conducted a remote assessment via both phone and video calls and collected the self-reported body weight and comorbidities status throughout this period. The statistical analysis plan has been previously described in Chapter 3.

4.3 Results

4.3.1 Descriptive characteristics

From 153 participants enrolled in the trial, 74 participants were randomised to remain in the BARI-LIFESTYLE observational cohort (the control arm). Three participants randomised to the intervention group declined the lifestyle programme due to personal reasons hence included in this observational cohort. Throughout the study period, three participants dropped out from further data collection due to pregnancy (*n*=2) and personal reasons (*n*=1). A summary of the flow of participants through the trial is depicted in Chapter 7 (Figure 7.1). The mean ± SD time intervals between the day of surgery to 3-, 6- and 12-month were 13.8 ± 1.6, 26.9 ± 1.9 and 52.8 ± 2.3 weeks, respectively. At the time of surgery, the mean age was 43.4 ± 10.6 years, 80.5% of participants were female and the mean pre-surgery BMI was 42.9 ± 5.8 kg/m^2. Ethnicity included White (62.3%), Black/ Black British (22.1%), Asian/ Asian British (7.8%), mixed-race (3.9%) and other ethnicity backgrounds (3.9%). In terms of educational background, 29.9% had GCSE/O or equivalent, 24.7% had A level or equivalent qualification and, 36.4% held a degree of which 9.1% completed a higher degree. Of all participants, 26% underwent RYGB, 15.6% had OAGB and, 58.4% had SG. Preoperative prevalence of comorbidities includes T2D (26%), hypertension (28.6%), hyperlipidaemia (22.1%) and OSA (24.7%). Participants' characteristics are presented in Table 4.1. Interestingly, participants who completed all study visits were significantly older than participants who did not attend at least one follow-up visit (45.3 ± 10.4 versus 39.7 ± 10.2 years; $p<0.05$). No differences were seen in other baseline characteristics.

Table 4. 1: Participants baseline characteristics.

Participant characteristics	**All, *n*=77**	**RYGB, *n*=20**	**OAGB, *n*=12**	**SG, *n*=45**
Age (years)	43.4 ± 10.6	42.7 ± 10.1	43.7 ± 7.9	43.6 ± 11.6
Gender (%)				
Male	15 (19.5)	3 (20)	4 (26.7)	8 (53.3)
Female	62 (80.5)	17 (27.4)	8 (12.9)	37 (59.7)
Menopause (%)	14 (22.6)	3 (21.4)	0	11 (78.6)
Weight (kg)	117.9 ± 20.7	113.7 ± 15.7	123.9 ± 25.2	118.2 ± 21.4
Height (m)	1.66 ± 0.09	1.67 ± 0.09	1.65 ± 0.08	1.65 ± 0.1
BMI (kg/m^2)	42.9 ± 5.8	40.8 ± 4.2	45.3 ± 7.7	43.1 ± 5.6
Ethnicity (%)				
White	48 (62.3)	12 (60)	6 (50)	30 (66.7)
Mixed race	3 (3.9)	-	2 (16.7)	1 (2.2)
Asian/ Asian British	6 (7.8)	3 (15)	1 (8.3)	2 (4.4)
Black/ Black British	17 (22.1)	4 (20)	3 (25)	10 (22.2)
Other Ethnicity	3 (3.9)	1 (5)	-	2 (4.4)
Education level (%)				
No qualification	3 (3.9)	1 (5)	-	2 (4.4)
GCSE/O equivalent	23 (29.9)	5 (25)	3 (25)	15 (33.3)
A level equivalent	19 (24.7)	3 (15)	2 (16.7)	14 (31.1)
University degree	21 (27.3)	8 (40)	4 (33.3)	9 (20)
Higher degree	7 (9.1)	3 (15)	3 (25)	1 (2.2)
Other	4 (5.2)	-	-	4 (8.9)
Marital status (%)				
Single	29 (37.7)	6 (20.7)	7 (24.1)	16 (55.2)
Married/lives with a partner/ civil partnership	36 (46.8)	9 (25)	4 (11.1)	23 (63.9)
Separated/ divorced	10 (13.0)	4 (40)	1 (10)	5 (50)
Widow	2 (2.6)	1 (50)	0	1 (50)
Employment status (%)				
Employed	52 (67.5)	15 (75)	4 (20)	1 (5)
Unemployed	18 (23.4)	10 (83.3)	2 (16.7)	-
Others	7 (9.1)	27 (60)	12 (26.7)	6 (13.3)
Study site (%)				
UCLH	35 (45.5)	3 (15)	3 (25)	29 (64.4)
Whittington	21 (27.2)	8 (40)	9 (75)	4 (8.9)
Homerton	21 (27.2)	9 (45)	-	12 (26.7)
Smoking status (%)				
Current smoker	1 (1.3)	-	-	1 (2.2)
Past smoker	35 (45.5)	7 (35)	6(50)	22 (48.9)
Never	41 (53.3)	13 (65)	6(50)	22 (48.9)
Comorbidities (%)				
T2D	20 (26)	6 (30)	4 (20)	10 (50)
Hypertension	22 (28.6)	5 (22.7)	3 (13.6)	14 (63.6)
Hyperlipidaemia	17 (22.1)	5 (29.4)	3 (17.7)	9 (52.9)
OSA	19 (24.7)	5 (26.3)	5 (26.3)	9 (47.4)

Note: BMI, Body Mass Index; OAGB, one anastomosis gastric bypass; OSA, obstructive sleep apnoea; RYGB, Roux-en-Y gastric bypass; SG, sleeve gastrectomy; T2D, type 2 diabetes, UCLH, University College London Hospitals.

4.3.2 Weight loss outcome

Of the 77 participants in this cohort, 89.6% have available and valid (collected within time window) body weight measures at 3-month post-surgery, 84.4% at 6-month post-surgery and 74% at 12-month post-surgery. Body weight recorded outside the time window were excluded from the analysis. Overall, body weight and BMI improved significantly throughout the first year of surgery, (body weight/ BMI*time, p<0.001). The changes in mean body weight, BMI and %WL loss are statistically significant at each follow-up visit as compared to baseline pre-surgery (all p<0.001); Table 4.2.

Table 4. 2: Weight loss outcomes at 3-, 6- and 12-month post-surgery relative to baseline pre-surgery.

Study time point	**Day of surgery**	**3-month**	**6-month**	**12-month**	**Change overtime**
Body weight variable	***n*=77**	***n*=69**	***n*=65**	***n*=57**	**p-value**
Weight (kg)	117.9 ± 20.7	102.0 ± 19.1	92.9 ± 18.0	88.9 ± 18.3	<0.001
Change from previous time point	-	-16.9 ± 5.3***	-7.9 ± 3.9***	-4.9 ± 5.5***	
BMI (kg/m^2)	42.9 ± 5.8	37.0 ± 5.6	33.9 ± 5.4	32.2 ± 5.5	<0.001
Change from previous time point	-	-6.1 ± 1.7***	-2.9 ± 1.4***	-1.8 ± 2.0***	
Weight loss (%)	-	14.3 ± 3.9	20.8 ± 5.3	24.6 ± 8.4	<0.001
Change from previous time point	-	-	6.7 ± 3.1***	4.2 ± 4.6***	

Note: ***indicates p<0.001.

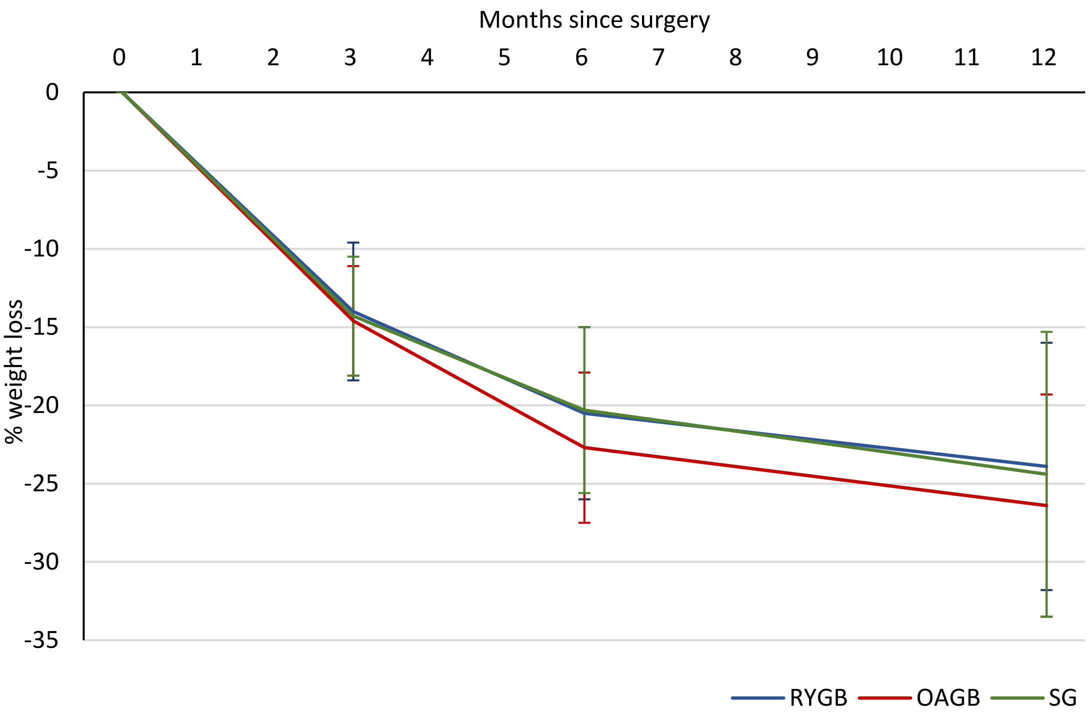
Overall, rapid weight loss occurred in the first 3 months post-surgery (14.3 ± 3.9%). Then, the weight loss velocity slowed down from 3 to 6 months (7.9 ± 3.6%; p<0.001) and from 6 to 12 months post-surgery period (5.4 ± 6.0%; p<0.01). A further exploratory analysis revealed that a subset of participants (12.9%) reached a maximal weight loss as early as in a period between 6 to 12 months post-surgery. These 10 participants had gained a mean percentage weight of 2.7 ± 0.6% in the second half of the year but none of them fulfilled any of the weight regain criteria (El Ansari and Elhag, 2021). Overall, at 12-month post-surgery, a total of 40.2% of participants achieved a BMI <30 kg/m^2. The rest of the participants were still classified, based on their BMI, as obesity: 26.4% (Class I), 24.6% (Class II) and 8.8% (Class III).

4.3.2.1 Predictors of weight loss

To identify the predictors of weight loss in the current cohort, we conducted a linear mixed model regression analysis adjusted for preoperative baseline characteristics including baseline BMI, gender, age, T2D and early postoperative weight loss (3 months post-surgery). From this regression model, we found that T2D (-1.8%; 95% CI, -3.2 to -0.3; p<0.05) and higher postoperative weight loss velocity at 0-3 months post-surgery period (1.2%; 95% CI, 1.1 to 1.4; p<0.001) significantly predicted percentage weight loss throughout the first year of surgery.

4.3.2.2 Weight loss outcome by surgical procedures

When participants were stratified based on the type of surgery undertaken, there were no significant differences observed in %WL throughout the observational period (Figure 4.1). A comparable weight loss was observed between RYGB and OAGB (23.9 versus 26.4%; mean difference [MD]=2.1%; 95% CI, -1.8 to 6.0; p=0.29); RYGB and SG (23.9 versus 24.4%; MD=0.2%; 95% CI, -2.8 to 3.1; p=0.92); as well as OAGB and SG (26.4 versus 24.4%; MD=-1.9%; 95% CI, -5.3 to 1.5; p=0.26).



Enrolled *(n)*	77	76	74	74
Cohort *(n)*	77	69	65	57

Figure 4. 1: Mean percentage weight loss by surgical procedures (RYGB, OAGB and SG) throughout the first year of surgery.

Error bars represent standard deviation. No significant difference in percentage weight loss between surgical procedures was seen at each post-surgery time point. Note: OAGB, one anastomosis gastric bypass; RYGB, Roux-en-Y gastric bypass; SG, sleeve gastrectomy.

4.3.2.3 Prevalence of patients with suboptimal weight loss

A further exploratory analysis confirmed a high variability in weight loss achieved at 12-month post-surgery between individuals (Figure 4.2) (Manning *et al*., 2015b). A total of 35.1% of participants experienced suboptimal weight loss, defined as weight loss less than 20% at 12-month post-surgery (Corcelles *et al*., 2016). Of these, 30% had RYGB, 16.7% had OAGB and 26.7% had SG.

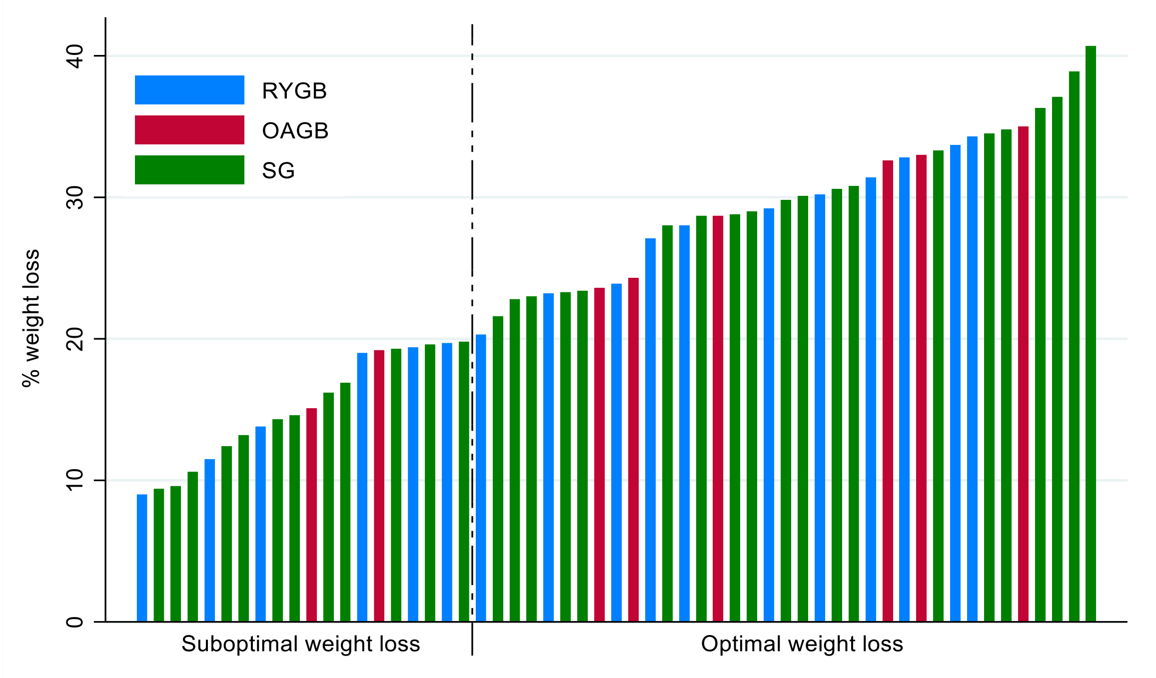


Figure 4. 2: Inter-individual variability in percentage weight loss achieved at 12-month post-surgery.

A total of 35.1% of participants experienced suboptimal weight loss defined as weight loss less than 20% at 12-month post-surgery. Evidence has shown that weight loss of less than 20% was associated with long-term risk for major adverse cardiovascular events (Jimenez *et al.*, 2022). Note: OAGB, one anastomosis gastric bypass; RYGB, Roux-en-Y gastric bypass; SG, sleeve gastrectomy.

When participants were further categorised based on either achieving good or suboptimal weight loss, a significant difference in %WL were observed between groups throughout the study period, (MD=-9.6%; 95% CI, -11.3 to -7.9; $p<0.001$). Interestingly, the difference can be observed as early as 3-month post-surgery (Figure 4.3). No other differences were observed in the baseline characteristics between groups except for participants in the suboptimal weight loss group being older than the good weight loss group ($p<0.01$).

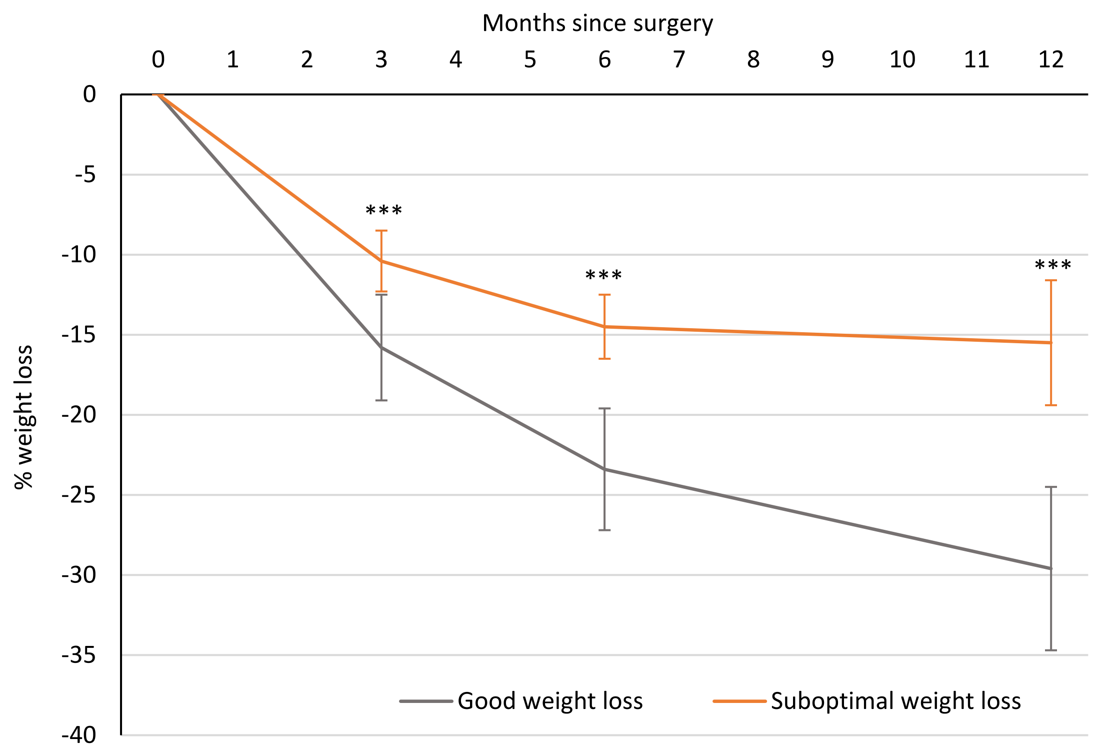


Figure 4. 3: Percentage weight loss between participants with good (*n*=57) versus suboptimal weight loss (*n*=20) throughout the study period.

Error bars represent standard deviation. A significant difference in percentage weight loss was seen between groups at each post-surgery time point. ***indicates $p<0.001$.

4.3.3 Changes in comorbidities

Overall, the rate of T2D complete remission at 12-month post-surgery was 43.8%. Whereas complete resolution of hypertension was 40%, hyperlipidaemia was 20%, and OSA was 46.7% (Table 4.3).

Table 4. 3: Changes in comorbidities status at 12-month post-surgery.

Comorbidities	*n* (%)			
	All (*n*=57)	**RYGB (*n*=17)**	**OAGB (*n*=8)**	**SG (*n*=32)**
Type 2 Diabetes				
Comorbidity present at baseline	16 (28.1)	6 (35.3)	2 (25)	8 (25)
Complete remission	7 (43.8)	3 (50)	1 (50)	3 (37.5)
Partial remission	1 (6.2)	0	0	1 (12.5)
Improved	7 (43.8)	3 (50)	1 (50)	3 (37.5)
Unchanged	0	0	0	0
Worsened	1 (6.2)	0	0	1 (12.5)
Hypertension				
Comorbidity present at baseline	20 (35.1)	5 (29.4)	1 (12.5)	14 (43.8)
Remission	8 (40)	2 (40)	0	6 (42.9)
Improved	8 (40)	2 (40)	1 (100)	5 (35.7)
Unchanged	4 (20)	1 (20)	0	3 (21.4)
Worsened	0	0	0	0
Hyperlipidaemia				
Comorbidity present at baseline	15 (26.3)	5 (29.4)	2 (25)	8 (25)
Remission	3 (20)	1 (20)	1 (50)	1 (12.5)
Improved	10 (66.7)	3 (60)	1 (50)	6 (75)
Unchanged	2 (13.3)	1 (20)	0	1 (12.5)
Worsened	0	0	0	0
Obstructive Sleep Apnoea				
Comorbidity present at baseline	15 (26.3)	5 (29.4)	3 (37.5)	7 (21.8)
Remission	7 (46.7)	0	3 (100)	4 (57.1)
Improved	0	0	0	0
Unchanged	8 (53.3)	5 (100)	0	3 (42.9)
Worsened	0	0	0	0

Note: *n*, number; OAGB, one anastomosis gastric bypass; RYGB, Roux-en-Y gastric bypass; SG, sleeve gastrectomy.

4.3.4 Changes in body composition

Of 77 participants in this cohort, 85.7% have available and valid (collected within time window) BIA measurements at 3-month post-surgery, 67.5% at 6-month post-surgery and 58.4% at 12-month post-surgery. Whereas for DXA, 61% of participants have available repeated measurement at 12-month post-surgery. Assessments undertaken outside the time window were excluded from the analysis. The changes in body composition assessed using BIA and DXA are presented in Table 4.4.

Table 4. 4: Changes in body composition assessed by BIA and DXA in the first year of surgery.

BIA	**Type of surgery**	**Pre-surgery (*n*=77)**	**3-month (*n*=66)**	**6-month (*n*=52)**	**12-month (*n*=45)**	**Change overtime p-value**
Fat mass (kg)	All	57.3 ± 14.7	45.2 ± 13.8	39.3 ± 12.4	34.9 ± 13.5	<0.001
	RYGB	54.4 ± 10.0	42.8 ± 10.3	38.7 ± 10.4	31.4 ± 11.5	<0.001
	OAGB	59.5 ± 18.5	47.5 ± 16.8	39.5 ± 14.8	35.6 ± 16.8	<0.001
	SG	58.1 ± 15.4	45.3 ± 14.1	39.4 ± 12.7	36.7 ± 13.9	<0.001
Body fat (%)	All	46.7 ± 6.5	43.6 ± 7.9	41.6 ± 6.6	38.1 ± 8.5	<0.001
	RYGB	46.2 ± 4.9	43.8 ± 5.6	42.7 ± 5.2	35.6 ± 7.4	<0.001
	OAGB	45.5 ± 7.9	43.9 ± 8.9[b]	39.4 ± 8.6	37.2 ± 10.6	<0.001
	SG	47.2 ± 6.8	43.4 ± 8.3[b]	41.8 ± 6.4	39.8 ± 8.5	<0.001
Fat-free mass (kg)	All	64.6 ± 12.0	57.2 ± 10.4	53.8 ± 9.8	54.6 ± 10.8	<0.001
	RYGB	63.2 ± 11.0	54.6 ± 11.5[a]	51.5 ± 11.9	55.9 ± 13.2	<0.001
	OAGB	69.1 ± 12.3	58.2 ± 9.6[a,b]	58.1 ± 9.2	57.1 ± 9.7	<0.001
	SG	64.0 ± 12.3	57.7 ± 10.5[b]	53.3 ± 8.9	53.3 ± 9.7	<0.001
DXA	**Type of surgery**	**Pre-surgery**			**12-month**	**Change, p-value**
Fat mass (kg)	All	53.8 ± 12.3			90.9 ± 18.2	<0.001
	RYGB	52.4 ± 10.0			33.8 ± 11.6	<0.001
	OAGB	55.1 ± 15.7			30.1 ± 14.4	<0.001
	SG	54.0 ± 12.4			35.2 ± 10.3	<0.001
Body fat (%)	All	43.8 ± 5.6			37.0 ± 7.7	<0.001
	RYGB	44.1 ± 5.3			37.7 ± 8.1	<0.001
	OAGB	42.2 ± 6.2			32.2 ± 8.8	<0.01
	SG	44.0 ± 5.6			37.8 ± 7.0	<0.001
Fat-free mass (kg)	All	68.7 ± 13.0			57.0 ± 1.7	<0.001
	RYGB	66.2 ± 11.5			52.2 ± 3.5	<0.001
	OAGB	74.0 ± 13.8			60.3 ± 4.0	<0.001
	SG	68.5 ± 13.3			57.1 ± 2.2	<0.001

Note: [a]denotes $p<0.05$ and [b]denotes $p<0.01$ between surgical procedures. Note: BIA, bioelectrical impedance analyser; DXA, dual-energy X-ray absorptiometry; *n*, number; OAGB, one anastomosis gastric bypass (*n*=12); RYGB, Roux-en-Y gastric bypass (*n*=20); SG, sleeve gastrectomy (*n*=45).

Based on the body composition assessed using BIA, the mean total weight loss of 21 kg at 3-month post-surgery (*n*=66) was made up of 61.7% fat mass and 38.3% fat-free mass, the mean total weight loss of 28.1 kg at 6-month (*n*=52) consisted of 67.3% fat mass and 32.7% fat-free mass, and the mean total weight loss of 33.5 kg at 12-month (*n*=45) was made up of 70.6% fat mass and 29.4% fat-free mass. Whereas, based on the results from the DXA scan, the mean total weight loss of 31.8 kg at 12-month (*n*=46) was consisted of 60.6% fat mass and 39.4% fat-free mass (Figure 4.4).

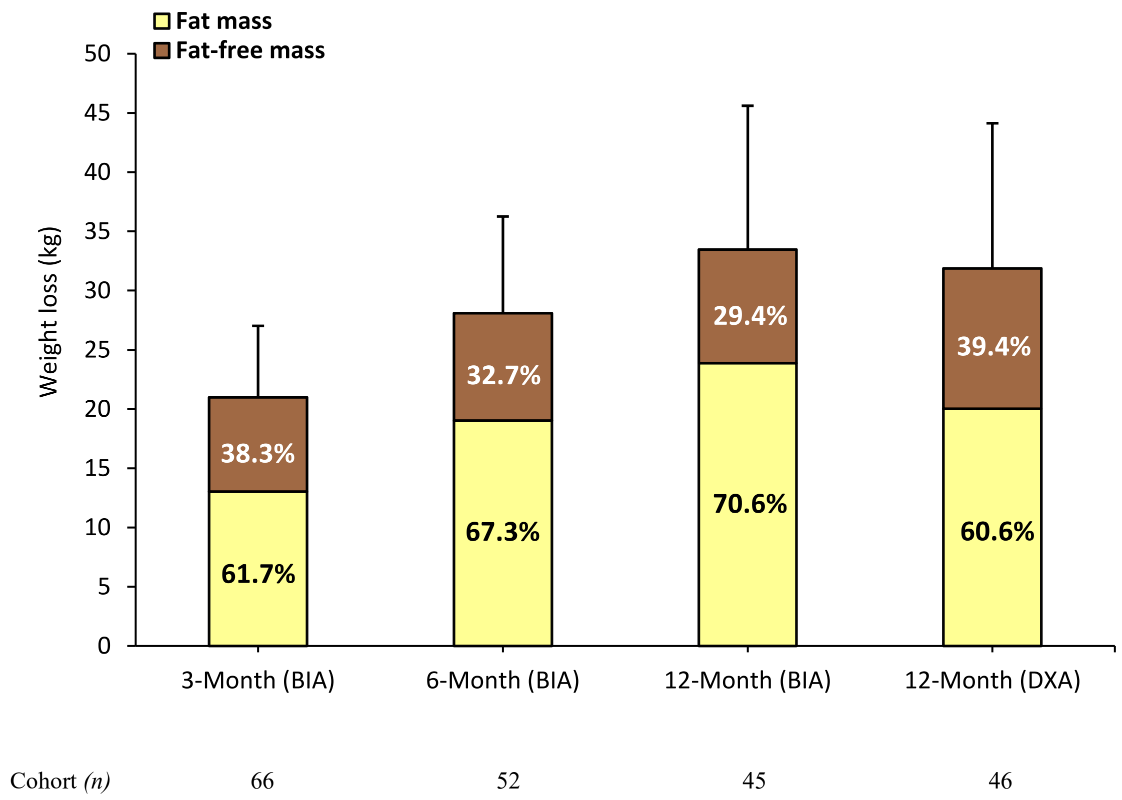


Figure 4. 4: Proportion of fat mass and fat-free mass loss from total weight loss assessed using BIA at 3-, 6- and 12-month and DXA at 12-month post-surgery.

Bars represent total weight loss in kilograms with standard deviation. The proportion of fat mass loss from total weight loss is gradually increasing throughout the first year of surgery. In contrast, the proportion of fat-free mass loss gradually decreasing throughout the year reflecting that the majority of fat-free mass loss occurred in the early post-surgery phase. Note: BIA, bioelectrical impedance analyser; DXA, dual-energy X-ray absorptiometry.

The peak fat mass loss and fat-free mass loss occurred in the first 6-month postoperative period, with the latter occurring at a lesser degree. No significant changes in fat-free mass loss from 6 to 12 months postoperative period were observed (Figure 4.5).

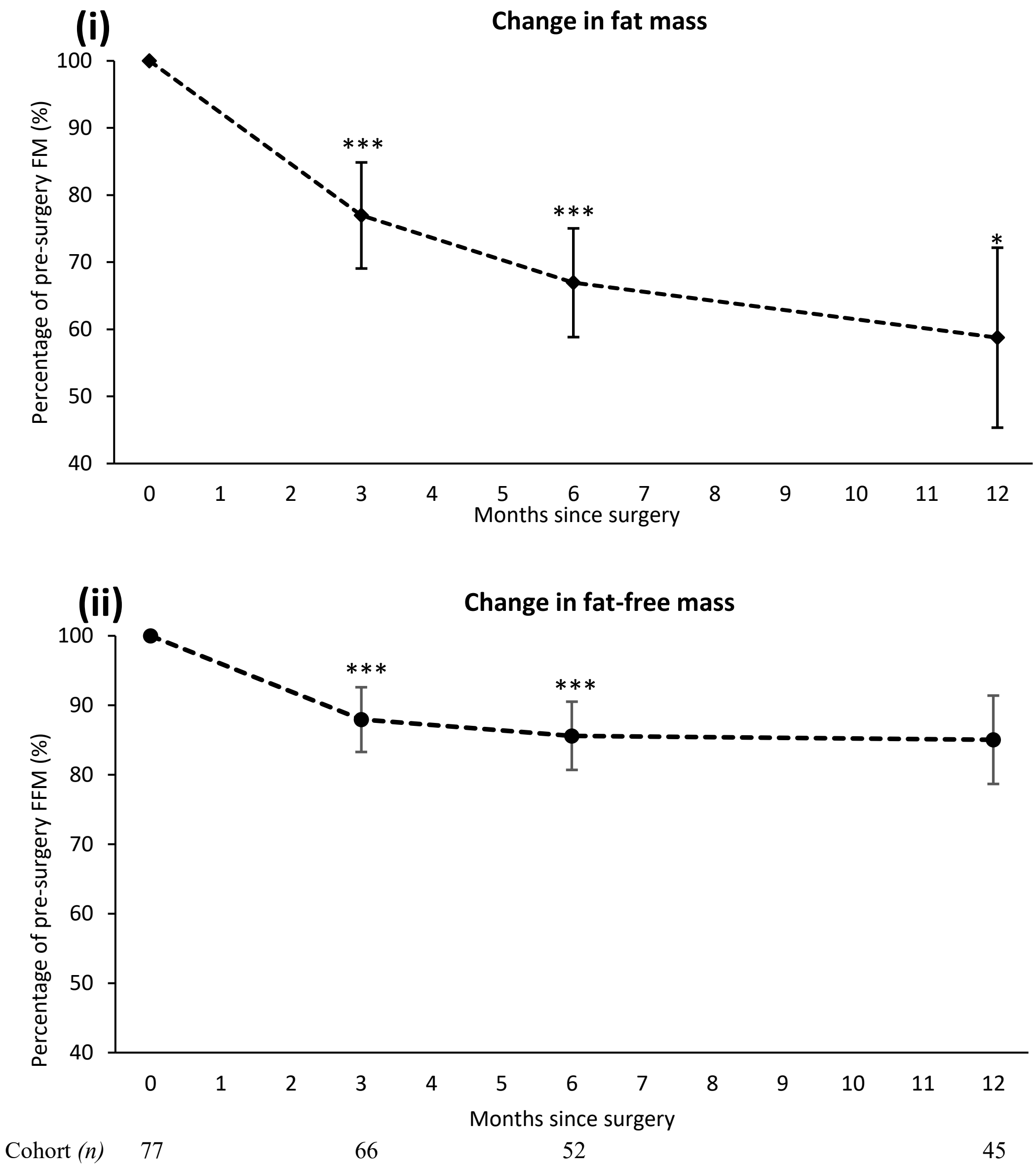


Figure 4. 5: Changes in **(i)** fat mass and **(ii)** fat-free mass in the first postoperative year relative to the baseline pre-surgery assessed using BIA.

Error bars represent standard deviation. ***indicates p<0.001, *indicates p<0.05 relative to the previous follow-up visit. Both components showed a variation in the magnitude of loss by which fat-free mass loss occurred a much lesser degree than fat mass. Note: FFM, fat-free mass; FM, fat mass.

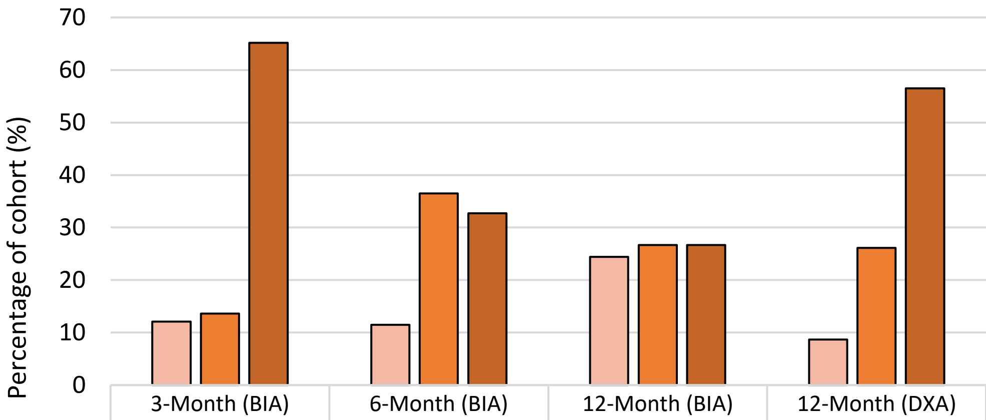
4.3.4.1 Body composition changes by surgical procedures

Between surgeries difference in body composition only exist at 3-month post-surgery, by which the SG group had lower percentage body fat than the OAGB ($p<0.01$).

However, this difference was not observed at later follow-ups. Higher fat-free mass was also seen after OAGB than RYGB ($p<0.05$) and SG ($p<0.01$) within the same time interval, but these differences were not detected at later follow-ups. No differences were observed in other parameters, between surgical procedures, at a different time point (Table 4.4).

4.3.4.2 Prevalence of excessive fat-free mass loss

For this analysis, we adopted three cut-off points identified in a previous study that evaluated the prevalence of fat-free mass loss, categorising fat-free mass loss into ≥25%, ≥30% and ≥ 35% (Nuijten *et al*., 2020). From the BIA results, the prevalence of fat-free mass loss decreased from 90.9% at 3-month to 80.7% at 6-month and 77.8% at 12-month. However, the DXA results showed a higher prevalence (91.3%) of excessive fat-free mass loss at 12-month post-surgery (Figure 4.6).



	3-Month (BIA)	6-Month (BIA)	12-Month (BIA)	12-Month (DXA)
≥25% FFML/WL	12.1	11.5	24.4	8.7
≥30% FFML/WL	13.6	36.5	26.7	26.1
≥35% FFML/WL	65.2	32.7	26.7	56.5

Figure 4. 6: Prevalence of excessive fat-free mass loss assessed by using BIA at 3-, 6- and 12-month and DXA at 12-month post-surgery.

This is based on the cut-off values of ≥25%, ≥30% and ≥35% of fat-free mass loss from total weight loss (FFML/WL). Note: BIA, bioelectrical impedance analyser; DXA, dual-energy X-ray absorptiometry; FFML, fat-free mass loss; WL, weight loss.

4.3.4.3 Predictors of fat-free mass loss

To identify the predictors of the fat-free mass loss at 12-month post-surgery in the current cohort, we conducted a multivariate linear regression analysis. This analysis included age, gender, type of surgery, preoperative BMI, and comorbidities status (T2D, hypertension, hyperlipidaemia, OSA) for both BIA and DXA measurements. From the BIA result, we found that male gender (-11.7%; 95% CI, -19.4 to -3.4; $p<0.01$) and lower preoperative BMI (-0.7%; 95% CI, -1.1 to -0.2; $p<0.05$) predict higher fat-free mass loss at 12-month post-surgery. However, from the DXA result, only lower preoperative BMI (-1.1%; 95% CI, -1.9 to -0.2; $p<0.05$) predicts higher fat-free mass loss at 12-month post-surgery.

4.3.4.4 Body composition changes in suboptimal weight loss versus good weight loss groups

The suboptimal weight loss group had significantly lower fat mass loss at each time point ($p<0.001$) compared to their good weight loss counterparts (Figure 4.7). Although participants in the good weight loss group lost a significantly higher fat-free mass compared to participants in suboptimal weight loss, the magnitude of loss is at a lesser extent compared to fat mass loss.

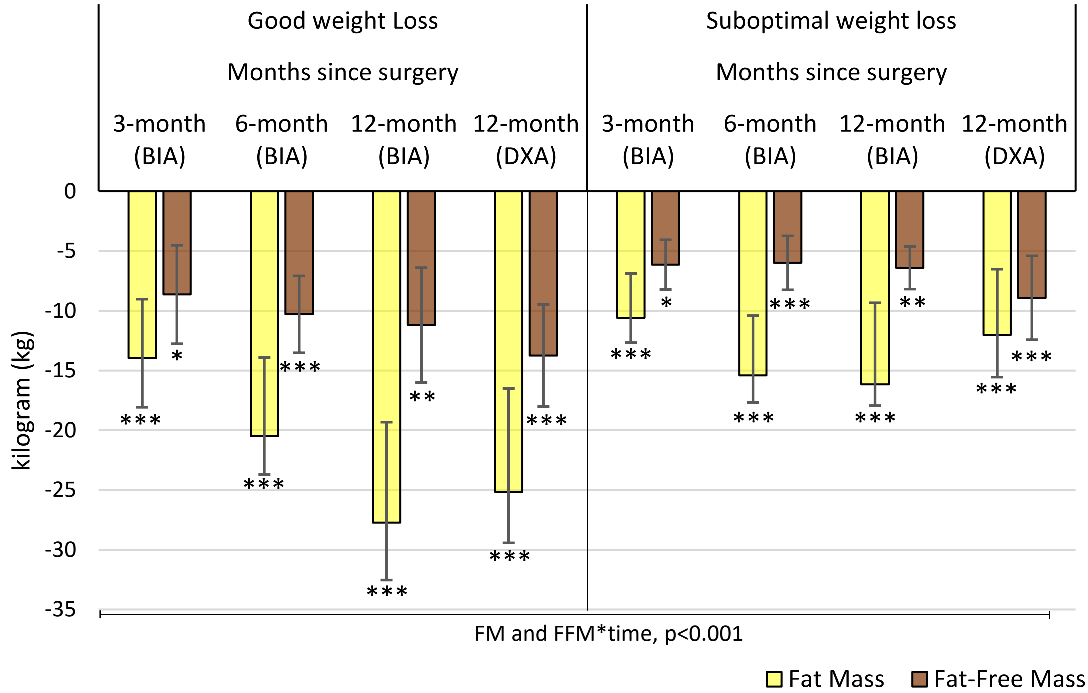


Figure 4. 7: Differences in fat mass loss and fat-free mass loss assessed using BIA and DXA between participants with good weight loss (n=57) versus suboptimal weight loss (n=20).

*indicates p<0.05, **indicates p<0.01, and ***indicates p<0.001 between groups. Note: BIA, bioelectrical impedance analyser; DXA, dual-energy X-ray absorptiometry; FFM, fat-free mass; FM, fat mass.

4.3.4.5 Correlation of body composition assessment between BIA and DXA

Body composition (both fat mass and fat-free mass) assessed by BIA and DXA showed a significant strong linear correlation both at pre-surgery and at 12-month post-surgery, p<0.001. The correlations are as follow: pre-surgery fat mass r=0.917; pre-surgery fat-free mass r=0.895; post-surgery fat mass r=0.931; post-surgery fat-free mass r=0.929. The Bland-Altman plots showed that the BIA method tends to slightly overestimate the fat mass and underestimate the fat-free mass measurements when compared with DXA, pre- and post-surgery (Figure 4.8).

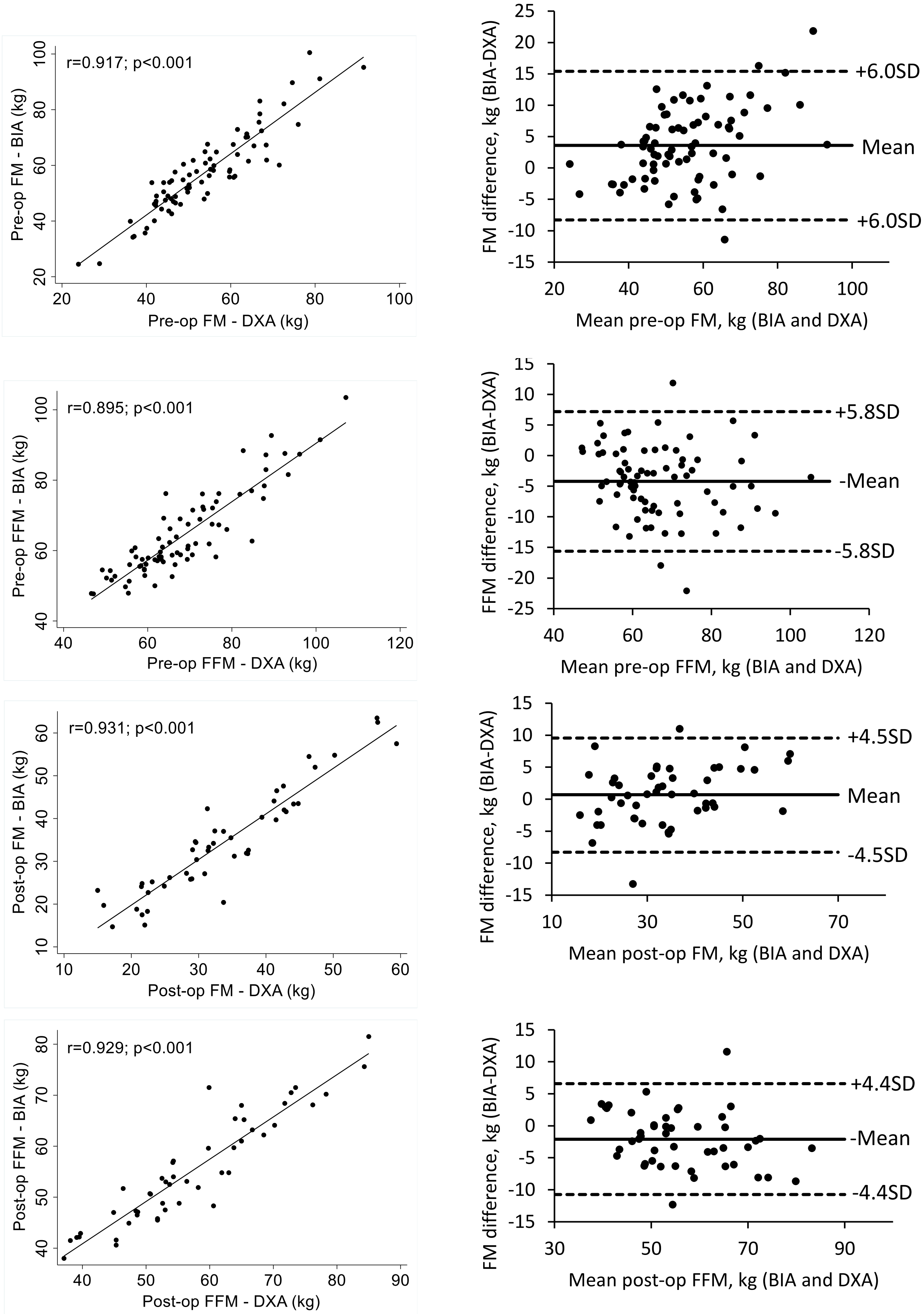


Figure 4. 8: Pearson's Correlation (left) and the respective Bland-Altman plots (right) of BIA and DXA measurements of fat mass and fat-free mass at baseline pre-surgery (*n*=76) and at 12-month post-surgery (*n*=48).

4.3.5 Changes in bone mineral density

The detailed changes in BMD are shown in Table 4.5. All BMD parameters; total hip, femoral neck and lumbar spine decreased significantly (p<0.001) in the first postoperative year, but no changes were observed in the whole-body BMD (p=0.92). The highest mean percentage of BMD loss is at total hip (8.5 ± 4.1%), followed by the femoral neck (5.7 ± 7.0%) and lumbar spine (2.9 ± 4.1%).

Table 4. 5: Changes in bone mineral density by surgical procedures.

Bone mineral density (g/cm²)	Type of surgery	*n*	Pre-surgery	*n*	12-month	Change overtime p-value
Total hip	All	76	1.139 ± 0.111	46	1.036 ± 0.131	<0.001
	RYGB	20	1.130 ± 0.115	15	1.027 ± 0.115	<0.001
	OAGB	12	1.165 ± 0.113	7	0.987 ± 0.091	<0.001
	SG	44	1.135 ± 0.111	24	1.056 ± 0.148	<0.001
Femoral neck	All	76	0.911 ± 0.121	46	0.840 ± 0.116	<0.001
	RYGB	20	0.900 ± 0.116	15	0.839 ± 0.118	<0.01
	OAGB	12	0.919 ± 0.156	7	0.770 ± 0.100	<0.05
	SG	44	0.914 ± 0.115	24	0.862 ± 0.116	<0.001
Lumbar spine	All	77	1.112 ± 0.148	47	0.032 ± 0.046	<0.001
	RYGB	20	1.084 ± 0.154	15	0.052 ± 0.055[a]	<0.01
	OAGB	12	1.132 ± 0.162	7	0.037 ± 0.063	0.18
	SG	44	1.119 ± 0.143	25	0.020 ± 0.030[a]	<0.01
Whole-body	All	76	1.189 ± 0.103	47	1.190 ± 0.111	0.92
	RYGB	20	1.185 ± 0.112	15	1.172 ± 0.114[a]	0.12
	OAGB	12	1.208 ± 0.081	7	1.164 ± 0.088[b]	0.08
	SG	44	1.187 ± 0.106	25	1.208 ± 0.116[a,b]	<0.05

Note: [a,b] denote p<0.05 between surgery. *n*, number; OAGB, one anastomosis gastric bypass; RYGB, Roux-en-Y gastric bypass; SG, sleeve gastrectomy.

4.3.5.1 Changes in bone mineral density by surgical procedures

The mean BMD change for all parameters is considerably less after SG than RYGB and OAGB (Figure 4.9). Twelve-month after RYGB, BMD declined by 9.3 ± 3.6% at total hip, 5.7 ± 6.6% at femoral neck, 4.4 ± 4.8% at lumbar spine and 1.1 ± 2.7% for whole-body BMD, relative to baseline pre-surgery. For OAGB, BMD declined by

10.8 ± 4.2% at total hip, 8.0 ± 9.4% at femoral neck, 3.6 ± 6.1% at lumbar spine and 1.5 ± 2.0% for whole-body BMD after 12-month, relative to pre-surgery baseline. Whereas 12 months after SG, BMD decreased by 7.3 ± 4.1% at total hip, 4.9 ± 6.6% at femoral neck, 1.8 ± 2.5% at lumbar spine with an increase of 1.3 ± 2.2% for whole-body BMD, relative to baseline pre-surgery.

Relative to baseline values, all BMD parameters declined significantly except for whole-body BMD and for lumbar spine after OAGB (Table 4.5). Comparable BMD reductions were seen in total hip and femoral neck between the three types of surgeries. Compared to the SG group, the RYGB group had a significantly higher reduction in lumbar spine, 1.8 ± 2.5 versus 4.4 ± 4.8%, p<0.05, respectively. Furthermore, significant differences were observed in whole-body BMD in SG versus RYGB and OAGB (p<0.05) (Figure 4.9).

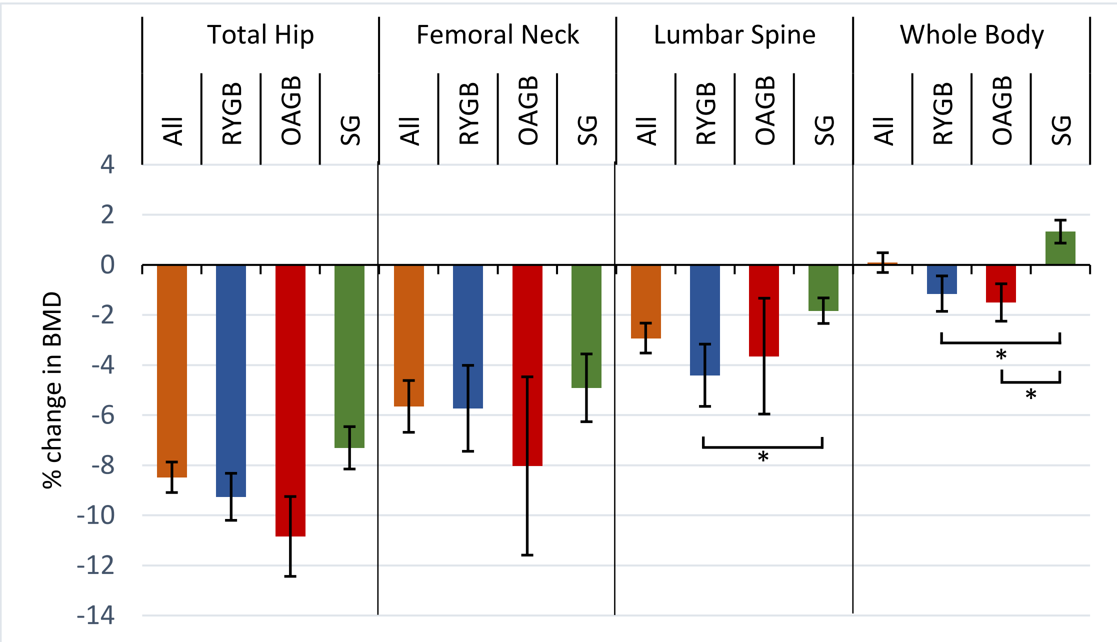


Figure 4. 9: Percentage change in bone mineral density at 12-month post-surgery relative to the baseline pre-surgery.

Note: *indicates p<0.05. OAGB, one anastomosis gastric bypass; RYGB, Roux-en-Y gastric bypass; SG, sleeve gastrectomy.

4.3.5.2 Predictors of bone mineral density loss

To identify the predictors of BMD loss at all skeletal regions, including whole-body BMD at 12-month post-surgery in the current cohort, we conducted a multivariate linear regression analysis that includes age, gender, type of surgery, weight change and fat-free mass change. Based on this regression analysis, %WL was found to predict the total hip BMD loss (p=0.007) at 1-year post-surgery.

4.3.5.3 Correlation between the percentage change in bone mineral density loss with bone markers at 12-month post-surgery

A total of 13 participants has available bone markers at 12-month post-surgery. In a Pearson's Correlation analysis (Table 4.6), percentage change in BMD loss did not correlate with serum calcium, phosphate and 25-Hydroxyvitamin D at 12-month post-surgery. Whereas higher percentage of BMD loss at total hip, lumbar spine and whole-body BMD significantly correlated with increased level of parathyroid hormone at 12-month post-surgery.

Table 4. 6: Correlation between the percentage change in bone mineral density loss with bone markers at 12-month post-surgery analysed using Pearson's Correlation. Data are expressed as correlation coefficient.

Bone markers	Percentage change in BMD			
	Total Hip	**Femoral Neck**	**Lumbar Spine**	**Whole Body**
n	13	13	13	13
Calcium (mmol/L)	-0.23	-0.19	0.84	0.47
Phosphate (mmol/L)	-0.23	-0.52	0.65	0.6
Parathyroid hormone (pmol/L)	-0.58*	-0.17	-0.62*	-0.65*
25-Hydroxyvitamin D (nmol/L)	0.33	0.87	0.18	0.31

Note: *indicated p<0.05; BMD, bone mineral density; *n*, number.

4.3.5.4 Bone mineral density changes in suboptimal weight loss versus good weight loss groups

In a subgroup analysis between participants with good and suboptimal weight loss, the only significant difference in BMD parameter is the total hip with a significant higher decreased in the good weight loss group, MD=-0.030 g/cm^2 [95% CI, -0.059 to 0.001], p=0.04. This further supports the association between the extent of weight loss with total hip BMD loss, as we described earlier.

4.4 Discussion

This study aimed to assess the effect of bariatric surgery upon weight loss and resolution or improvement of comorbidities, as well as the changes in body composition including BMD in the first postoperative period. Additionally, this study aimed to compare the differences of these outcomes between RYGB, SG and OAGB. As previously described, we found that at 12-month post-surgery, weight loss was comparable between surgical procedures with the mean %WL of 24.6%. T2D status and lower weight loss velocity at 0-3 months post-surgery period predicted less weight loss at 12-month post-surgery. A total of 35.1% of patients experienced suboptimal weight loss and this group of patients were older than those in a good weight loss cohort. More than 40% of patients with T2D, hypertension and OSA experienced a complete remission 1-year after surgery. In terms of body composition, comparable changes in fat mass and fat-free mass were observed between surgical procedures with the peak fat-free mass loss observed during the first 6-month of surgery. However, at 12-month post-surgery, more than half of the patients fulfilled the criteria of excessive fat-free mass loss. Male gender and lower baseline BMI significantly predict higher fat-free mass loss. We also found a significant strong linear correlation in body composition measurements between BIA and

DXA. Interestingly, we found a significant reduction in total hip, femoral neck, and lumbar spine BMD at 1-year post-surgery. Specifically, patients who underwent gastric bypass procedures (RYGB and OAGB) showed a tendency towards greater BMD loss in all skeletal regions, albeit not statistically significant, than patients who underwent SG. Furthermore, our data suggest that the changes in BMD are influenced by both the type of surgical procedure and weight loss, but the latter appeared to be in a skeletal-specific manner. This finding is further supported by a significantly higher BMD loss at total hip observed in patients with good weight loss compared to suboptimal weight loss. Higher percentage of BMD loss at total hip, lumbar spine and whole-body BMD correlate with higher level of parathyroid hormone at 12-month post-surgery.

A comparable weight loss results between RYGB and SG in the current cohort are similar to what previously reported by other RCTs (Peterli *et al*., 2018, Salminen *et al*., 2018). In the SM-BOSS RCT involving patients undergoing either SG (*n*=107) or RYGB (*n*=110), no significant difference in weight loss was observed at 1-year after surgery and this comparability continues to persist up to 5-year follow-up (Peterli *et al*., 2018). The SLEEVEPASS RCT also reported a similar weight loss magnitude between RYGB (*n*=119) and SG (*n*=121) from 6-month up until the fifth postoperative year (Salminen *et al*., 2018). This similarity of the effectiveness in inducing weight loss coupled with less operation time and fewer complications rate may explain the increasing number of SG undertaken worldwide since the past few years (Angrisani *et al*., 2018). Nevertheless, beyond 5-year post-surgery, RYGB appeared to produce significantly greater weight loss compared to SG, as reported in the latest systematic review and meta-analysis. However, very long-term RCT data are not available yet to support this finding (Shoar and Saber, 2017). Few RCTs have evaluated the extent of weight loss following OAGB compared to RYGB and SG (Seetharamaiah *et al.*, 2017, Robert *et al.*, 2019, Jain *et al.*, 2021). In the YOMEGA RCT involving patients undergoing either OAGB (n=129) or RYGB (n=124), a comparable weight loss was reported at 2-year post-surgery (Robert *et al.*, 2019). Whereas, in another RCT comparing between OAGB (n=101) and SG (n=100) procedures, a similar weight loss magnitude was observed at 1-year post-surgery (Seetharamaiah *et al.*, 2017) although at 5-year follow-up, weight loss was in favour of OAGB than SG (Jain *et al.*, 2021). Our results corroborated with the findings from these RCTs, which demonstrated comparable short-term (1-year) weight loss outcome after RYGB, OAGB and SG.

Several preoperative baseline characteristics have been reported as predictors of less weight loss following surgery, such as higher baseline BMI, female gender, age > 45-50 years, T2D and lower early postoperative weight loss velocity (Ma *et al.*, 2006, Ortega *et al.*, 2012, Contreras *et al.*, 2013, Ochner *et al.*, 2013, Still *et al.*, 2014, Manning *et al.*, 2015b, Nielsen *et al.*, 2020). In the present cohort, we found that T2D and lower weight loss velocity at 0-3 months post-surgery period appeared to predict less weight loss outcome in the first postoperative year. Indeed, in a recent retrospective study involving a cohort of 714 adults underwent RYGB and SG, the presence of T2D at baseline was associated with 1.6 times less likely to achieve 50% or more of excess body weight loss compared to those without T2D (Luo *et al.*, 2020). A similar observation was also reported in obesity pharmacotherapy, and the reason for this is still poorly understood although genetic, metabolic, and environmental factors may play a role (Kahan and Fujioka, 2017).

Our results also showed that 59.8% of participants still fell within the obesity category of the BMI range at one-year post-surgery. As previously described by Cadena-Obando *et al.*, patients with higher baseline BMI require more than 12 months to lose weight in order to achieve BMI < 30 kg/m^2 (Cadena-Obando *et al.*, 2020). Another key finding from the exploratory analysis was the early maximal weight loss achieved by 12.9% of the cohort. The weight loss trajectory of these participants began to demonstrate some weight regain, although, at 12-month post-surgery, none of these participants met any of the criteria of weight regain (El Ansari and Elhag, 2021). A similar observation has been reported previously in a subset of participants from the Longitudinal Assessment of Bariatric Surgery (LABS) Consortium. Participants who reached the maximal weight loss at 6-month post-surgery had steadily regained their weight over the 3-year follow-up period (Courcoulas *et al*., 2013).

Suboptimal weight loss, defined as weight loss less than 20% at 12-month post-surgery (Corcelles *et al*., 2016), is the emerging area of research interest in bariatric surgery. It is well known that post-surgery weight loss is highly variable between individuals and accumulating numbers of evidence in the literature have reported this (El Ansari and Elhag, 2021). For instance, Cadena-Obando *et al*. examined the weight loss outcome of 130 patients who underwent either RYGB (38%), OAGB (49%) or SG (13%) and found that 20% experienced suboptimal weight loss at 12-month post-surgery, and this group of patients had increased risk of weight regain in the second postoperative years. Furthermore, using a multivariate analysis, they also found that factors such as older age and depression/ anxiety contributed to suboptimal weight loss (Cadena-Obando *et al*., 2020). One-third of participants in the current cohort fulfilled the criteria of suboptimal weight loss and we also found that these patients were older than their counterparts (48.3 ± 10.4 versus 41.6 ± 10.2 years, p=0.01). This finding is in line with a study by Faucher *et al*. which demonstrated that older patients had significantly less weight loss than their matched younger cohort (Faucher *et al*., 2019). Indeed, in most revisional surgery cases, suboptimal weight loss is one of the most common indications reported (Homan *et al*., 2015, Abdulrazzaq *et al*., 2020). Revisional surgery is not only more costly, but it also carries a much higher risk compared to primary surgery (Brolin and Cody, 2008, Ma *et al.*, 2016).

Our results support the existing evidence that bariatric surgery leads to remission or improvement of obesity-associated comorbidities. However, we cannot provide further evidence of whether the remission of comorbidities is associated with the type of surgical procedures per se or the magnitude of weight loss as this study is not powered to detect such differences. As reported by a few systematic reviews and meta-analyses, the remission rate of T2D increases in the following order: SG, RYGB and OAGB. Furthermore, the remission rate of hypertension and hyperlipidaemia are similar after OAGB and RYGB, both procedures are superior to SG (Magouliotis *et al.*, 2017, Magouliotis *et al.*, 2019, Gu *et al.*, 2020), whilst the remission rate of OSA is similar across all procedures (Celio *et al.*, 2017, Magouliotis *et al.*, 2017, Bhandari *et al.*, 2019). Interestingly, the magnitude of weight loss is also strongly correlated with T2D remission with a minimum threshold of 20% weight loss is needed to achieve an initial remission (Barthold *et al*., 2022).

In the present cohort, we observed a substantial decrease in both fat mass and fat-free mass with the peak mass loss occurring during the first 6-month post-surgery, albeit the latter occurred to a less extent. Fat mass continue to decrease in the following 6-month, but no change was observed in fat-free mass. Therefore, our data suggest that participants lost mainly body fat from 6 to 12 months of the postoperative period. Our findings align with previous longitudinal studies (Otto *et al.*, 2016, Marc-Hernandez *et al.*, 2020, Nuijten *et al.*, 2020). Nuijten *et al*. followed up a cohort of 3,596 patients who underwent SG and RYGB for 36 months and reported the highest fat mass and fat-free mass loss at 3- and 6-month from surgery (Nuijten *et al*., 2020). Similarly, Otto *et al*. reported the majority of fat mass and fat-free mass loss occurred at 18 weeks to 6-month post-surgery when patients (n=173) who underwent SG and RYGB assessed periodically in the first postoperative year by using BIA (Otto *et al*., 2016). A similar trend of fat mass and fat-free mass loss was also observed 6-month post-OAGB with little change up to 12-month post-surgery in a recent reported prospective observational study involving 94 patients (Marc-Hernandez *et al*., 2020). In the present cohort, we observed higher fat-free mass loss at 3-month in OAGB than SG and RYGB, but these differences were no more significant at 6-month and 12-month. The small sample size of the OAGB group with relatively higher pre-surgery fat-free mass compared to SG and RYGB may have explained the variability in fat-free mass changes during the first 3-month post-surgery period.

To date, only one study has described the prevalence of excessive fat-free mass loss after bariatric surgery, highlighting the need for in-depth research in this field. In fact, no consensus has yet been reached as to the definition of excessive post-bariatric fat-free mass loss (Nuijten *et al*., 2020). In the present study, we applied the cut-off point used by Nuijten *et al*. to describe excessive fat-free mass and found that 26.7% of our patients experienced fat-free mass loss exceeding 35% of total weight loss at 12-month post-surgery, which is twice the prevalence reported previously (Nuijten *et al*., 2020). The prevalence increases further when evaluated through DXA scan, reaching 56.5% of trial completers. These figures are indeed concerning as fat-free mass is not only playing a critical role in physiological and metabolic processes but it is also important for physical function and activities of daily living (Wolfe, 2006). Therefore, our findings suggest that body composition should be monitored often after surgery in order to prevent further fat-free mass loss. This might be true particularly for patients with lower pre-surgery BMI, as we found that this group of patients experienced a higher loss of fat-free mass.

Another important finding from this study is the high agreement of body composition measurements between BIA and DXA hence confirming the reliability and practicality of BIA to be used in a real-world clinical setting. Previous validation studies that compared BIAs (BIA 101 RJL, Akern Bioresearch, Firenze, Italy, and Inbody 720®, Biospace) against DXA scan in patients following bariatric surgery also showed a high correlation (Savastano *et al.*, 2010, Faria *et al.*, 2014). However, in contrast with the findings from these studies, our results demonstrated that the BIA method tends to slightly overestimate the fat mass and underestimate the fat-free mass measurements when compared with DXA, perhaps due to the difference in the type of equipment used (algorithm embedded in BIA differs across make). Interestingly, the bias between the two methods became smaller at 12-month post-surgery compared to pre-surgery. This might be explained by changes in the hydration status of fat-free mass post-surgery coupled with reduced levels of body fatness following weight loss (Becroft *et al*., 2019).

Our results on the changes in BMD post-surgery are similar to the sub-group analysis of the STAMPEDE trial and a few small observational studies with a follow-up period ranging from 1 to 4 years, showing the reduction in total hip and/or femoral neck BMD did not differ significantly between RYGB and SG at 1-year post-surgery (Vilarrasa *et al.*, 2013, Hsin *et al.*, 2015, Maghrabi *et al.*, 2015, Muschitz *et al.*, 2015, Cadart *et al.*, 2020, Guerrero-Perez *et al.*, 2020). In contrast, several other studies, including an RCT by Hofso *et al*., have reported the reduction in total hip and/or femoral neck BMD differed significantly between RYGB and SG (Bredella *et al*., 2017, Carrasco *et al*., 2018, Hofso *et al*., 2021). Moreover, our study corroborated the findings from two recent RCTs reporting a significantly higher reduction of lumbar spine BMD after RYGB than SG (Guerrero-Perez *et al*., 2020, Hofso *et al*., 2021). Finally, in line with the study by Carrasco *et al*., we found a significantly greater reduction of whole-body BMD in RYGB than SG (Carrasco *et al*., 2018), although this was not observed in other studies (Muschitz *et al.*, 2015, Cadart *et al.*, 2020, Hofso *et al.*, 2021). To our knowledge, only one study has investigated the changes in BMD following OAGB in 50 patients showing a significant decrease in total hip by 13%, lumbar spine by 7% and whole-body BMD by 1% at 12-month post-surgery (Luger *et al*., 2018). Similar trends of BMD loss were also seen in the present study in which total hip reduced by 10.8%, lumbar spine by 3.6% and whole-body BMD by 1.5%, albeit with a smaller sample size (n=7). The differences in the BMD loss outcome across procedures are explained by the anatomical modification of the gastrointestinal tract between gastric bypasses procedures and SG with the former leading to malabsorption of nutrients and hormonal changes associated with bone health (Mahawar and Sharples, 2017).

The percentage change in BMD at total hip, lumbar spine and whole-body BMD significantly correlate with higher level of parathyroid hormone. Secondary hyperparathyroidism is a common observation following surgery with the prevalence reported to be higher after gastric bypasses than SG, as a consequence of vitamin D deficiency (Wei *et al*., 2018, de Holanda *et al*., 2021). The upregulation of parathyroid hormone promotes increased production of vitamin D which enhanced calcium absorption in the intestine and bone resorption (Stein and Silverberg, 2014). Therefore, our findings highlight the importance of patient's compliance with the recommended intake of vitamin and mineral supplementations to maintain bone health.

In the present cohort, we found that %WL significantly predicts BMD loss in total hip, supporting the finding from the STAMPEDE trial and few other observational studies (Maghrabi *et al.*, 2015, Bredella *et al.*, 2017, Cadart *et al.*, 2020). Importantly, our results indicate that fat mass loss ($r=0.447$, $p<0.01$) rather than lean mass loss explains this association which is in line with the finding reported in another recent RCT (Hofso *et al.*, 2021). Several other studies have also reported the associations between weight loss and BMD loss in other skeletal regions (femoral neck, lumbar spine) and whole-body BMD, which were not observed in our cohort (Bredella *et al.*, 2017, Cadart *et al.*, 2020). Using the same regression model (adjusted for age and gender) as Hofso *et al*., we found that both the type of surgery and %WL rather than the type of surgery per se significantly predict BMD loss in total hip but not femoral neck and lumbar spine (Hofso *et al*., 2021). Therefore, our finding supports the notion that mechanical unloading as one of the mechanisms involved in BMD loss post-surgery, but the effect might be rather skeletal-specific. Several factors might have explained the differences in our findings on BMD changes compared with other studies. There is a huge heterogeneity between studies in terms of study design, sample size and differences in demographic characteristics (gender, menopausal status, age, ethnicity, and T2D status) that are known to affect bone health (Eller-Vainicher *et al*., 2020).

This study is not without limitations. As described in chapter 3, BIA and DXA measurements were less accurate compared to CT and MRI. During the nationwide lockdown of the COVID-19 pandemic, all in-person follow-up assessments were carried out remotely hence throughout this period, the BIA and DXA data were missing. The lockdown also may have impacted upon weight loss, physical activity levels and sedentary behaviour so the present results should be interpreted with caution. The unequal sample size that represented each type of bariatric procedure also limited the interpretation of our results. Finally, assessments undertaken outside the time window were excluded from the analysis hence reduced the sample size of the study.

4.5 Conclusions

In conclusion, bariatric surgery delivered in the UK healthcare setting produces substantial weight loss and resolution or improvement of comorbidities. However, a small subset of patients experienced poor weight loss. Furthermore, there is a variability in fat mass loss and fat-free mass loss following surgery, with a substantial number of patients experienced excessive fat-free mass loss. Our data also showed that patients experienced a significant BMD loss following surgery. Taken together, the results from this study highlight the importance of including body composition assessment as part of the routine pre- and post-bariatric care. The findings also indicate that it is important for patients to comply with all lifestyle recommendations after surgery (i.e., diet, physical activity, and intake of nutritional supplements) in order to maximise weight loss and minimise fat-free mass loss including BMD.

Chapter 5

Physical activity levels, sedentary behaviour, physical function and strength outcomes: The BARI-LIFESTYLE observational study[20]

5.1 Introduction

In Chapter 4, we reported that despite a substantial weight loss and resolution or improvement in comorbidities produced by bariatric surgery, patients unfortunately also experienced a significant loss of fat-free mass with a reduction in BMD. In diet-induced weight loss, combining physical activity with energy restriction aided weight loss whilst preserving fat-free mass and mitigating bone mass loss compared to energy restriction alone (Weinheimer *et al*., 2010, Papageorgiou *et al*., 2020). Importantly, physical activity helps in maintaining weight loss and preventing weight regain (Swift *et al*., 2014). Whether similar outcomes are replicated in surgically-induced weight loss is still unclear.

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[20]The work related to this chapter has been accepted for oral presentation at the 13th British Obesity Metabolic Surgery Society (BOMSS) Annual Scientific Meeting, Brighton UK 2022, and available in Appendix 20.

Limited is also the availability of high-quality data on the changes in physical activity levels and sedentary behaviour pre- to post-bariatric surgery (Herring *et al*., 2016, Adil *et al*., 2019).

Following bariatric surgery, patients subjectively reported increased time spent in physical activity (Bond *et al*., 2010, Berglind *et al*., 2016), but when measured objectively, results are inconsistent across studies. Whilst some studies demonstrated positive changes in objectively measured physical activity with a concomitant decrease in sedentary behaviour following surgery (King *et al.*, 2012, King *et al.*, 2015, Bellicha *et al.*, 2019), other studies did not observe any significant changes (Bond *et al.*, 2010, Berglind *et al.*, 2015, Berglind *et al.*, 2016, Crisp *et al.*, 2018, Sellberg *et al.*, 2019, Nielsen *et al.*, 2021). Small sample size, differences in activity monitor used, as well as the method of data collection and accelerometer processing criteria (such as device placement, sampling frequency, filter, epoch length, non-wear-time, what constitutes a valid day and a valid week, cut-points for sedentary time and physical activity intensity classification) may have contributed to the inconsistencies, therefore, warrants more investigation (Migueles et al., 2017b).

Other than physical activity levels, another outcome of bariatric surgery that has not received as much attention from the research community is the changes in physical function and strength. It is well known that most people living with obesity experienced physical impairment, which affect their activities of daily living and thus the overall QoL (Shultz *et al*., 2014). Evidence to support the idea that weight loss following bariatric surgery paralleled improvement in physical function parameters is still limited particularly for the period from 12 months after surgery and beyond (Herring *et al*., 2016, Jabbour and Salman, 2021). Of particular concern, excessive loss of fat-free mass (that mainly consists of ~40% skeletal muscle tissue) and BMD following surgery, as reported in the previous chapter, indicated that physical function and strength might be negatively impacted. Whether this direct relationship exists needs to be investigated.

In this study, we aim to explore whether physical activity levels, sedentary behaviour and functional capacity improved following bariatric surgery and their relationship with weight loss and the changes in body composition. In addition, we aim to elucidate whether fat-free mass loss and reduction in BMD may have an impact upon physical function and strength. The specific objectives of this study are:

1. To evaluate the changes in physical activity levels (light and MVPA), sedentary behaviour, as well as the percentage of participants achieving ≥150 min/week of MVPA, assessed using accelerometer at 3-, 6- and 12-month post-surgery, relative to baseline pre-surgery.
2. To assess the association between the changes in physical activity levels and sedentary behaviour on weight loss and the changes in body composition.
3. To evaluate the changes in physical function and strength assessed using 6MWT, STS-test and handgrip strength (HGS) test at 3-, 6- and 12-month post-surgery, relative to baseline pre-surgery.
4. To determine whether weight loss and the changes in body composition, including BMD, correlates with the changes in physical function and strength at all time points post-surgery.

5.2 Materials and methods

The study design and setting, eligibility criteria, participant recruitment and data collection for physical activity using accelerometer, 6MWT, STS and HGS tests have been described in detail in Chapter 3. Throughout the nationwide lockdown between

April to July 2020, all face-to-face assessments were suspended to comply with the restrictions, which led to several missing data for 6MWT, STS and HGS tests. Nevertheless, throughout this period, we posted the ActiGraph to participants' home address with the detailed instruction on how to wear the device. When the face-to-face assessment resumed, we were unable to do the 6MWT due to the 'one-way system' implemented to keep hospital COVID-safe. The statistical analysis plan has been previously described in Chapter 3.

5.3 Results

5.3.1 Baseline characteristics

Participants' demographic characteristics have been previously described in Chapter 4, section 4.3.1, whereas the pre-surgery baseline characteristics for physical activity levels, sedentary behaviour, and physical function and strength are shown in Tables 5.1 and 5.2. The mean ActiGraph wear time period at baseline was six days with a mean daily wear time of 15 hours. Reasons for missing data at any time points are (i) ActiGraph device not returned, n=55, (ii) missed study visit, n=28, (iii) did not meet the minimum wear time requirement, n=16 and (iv) ActiGraph not provided due to device shortfall, n=1. At baseline, physical activity levels, sedentary behaviour and step count were similar between men and women, except men spent significantly higher time in vigorous-intensity physical activity than women, 5.5 versus 1.0 min/day, p=0.01. No correlation was observed between age and BMI with physical activity levels of any intensity. Overall, prior to surgery, 62.8% of waking time was spent on sedentary behaviour, 32.7% on light physical activity and only 4.5% on MVPA (Figure 5.3). Nevertheless, a total of 86.2% of participants achieved the WHO physical activity guidelines of a total MVPA ≥150 min/week (WHO, 2020b) (Figure 5.4).

Table 5. 1: Changes in physical activity levels, sedentary behaviour and step count assessed periodically from pre- to post-bariatric.

Physical activity behaviours	**Pre-surgery** *n*=65	**3-month** *n*=50	**6-month** *n*=43	**12-month** *n*=42	**Change overtime p-value**
Number of valid days	6.0 ± 1.0	6.4 ± 0.8[a]	6.0 ± 1.0	6.3 ± 1.0	0.23
Wear time (hour/day)	15.7 ± 1.1	15.6 ± 1.1	15.4 ± 1.3[b]	15.6 ± 1.1	0.31
Sedentary (min/day)	593.9 ± 77.0	590.1 ± 106.3	574.2 ± 127.0	570.1 ± 114.9	0.12
Change from baseline		-6.2 ± 78.3	-32.4 ± 106.4	-11.2 ± 108.3	
Light PA (min/day)	309.5 ± 68.9	305.7 ± 90.6	310.5 ± 97.6	326.9 ± 97.7	0.37
Change from baseline		-6.4 ± 10.7	5.4 ± 77.4	7.7 ± 95.5	
MVPA (min/day)	43.2 ± 24.7	39.9 ± 19.9	39.8 ± 20.6	39.2 ± 21.6	0.18
Change from baseline		-2.8 ± 23.5	-5.1 ± 22.8	-6.4 ± 28.9	
Steps/day	5668 ± 1833	5905 ± 2094	6204 ± 2489	5981 ± 2525	0.55
Change from baseline		64 ± 2020	340 ± 1900	44 ± 2529	

Note: [a]denotes p<0.05 and [b]denotes p<0.01 relative to baseline pre-surgery values. MVPA, moderate-to-vigorous physical activity; *n*, number; PA, physical activity.

At baseline, the mean 6MWT was 413.5 metres, with values ranging between 250 and 530 metres (Table 5.2). This is equivalent to a walking pace of 1.15 metres/second. The mean post-test heart rate was 103.0 ± 18.2 beats/min. Whereas the median perceived exertion score was ‘somewhat strong’. Younger participants walked a greater distance compared to their older counterparts (p=0.001). Gender had no impact on walking distance (p=0.46), but the pre-menopausal women had higher walking capacity compared to the post-menopausal counterparts (419.7 ± 54.3 versus 381.6 ± 60.4 metres, p=0.02).

Table 5. 2: Changes in physical function and strength assessed periodically from pre- to post-bariatric.

Physical function and strength	**Pre-surgery**	**3-month**	**6-month**	**12-month**	**Change overtime p-value**
	***n*=77**	***n*=66**	***n*=56**	***n*=26**	
6MWT (m)	413.5 ± 58.1	474.1 ± 61.2	483.9 ± 71.5	492.7 ± 51.6	<0.001
Change from baseline		62.9 ± 39.4[b]	81.1 ± 62.0[b]	92.2 ± 42.6[b]	
Heart rate (beats/min)	103.0 ± 18.2	101.9 ± 19.2	95.8 ± 20.9	84.0 ± 18.3	<0.001
Change from baseline		-1.6 ± 20.6	-7.4 ± 23.1[a]	-21.5 ± 21.4[b]	
Borg's scale (0-10)*	4 (1, 7)	3 (1, 7)	2 (1, 6)[b]	1 (1, 6)[b]	<0.001
	***n*=74**	***n*=67**	***n*=57**	***n*=51**	
STS-test (secs)	10.5 ± 3.4	8.5 ± 2.8	8.4 ± 3.2	7.7 ± 2.5	<0.001
Change from baseline		-2.3 ± 2.8[b]	-2.7 ± 3.4[b]	-3.2 ± 2.8[b]	
	***n*=77**	***n*=66**	***n*=53**	***n*=51**	
HGS-dominant (kg)	32.2 ± 9.3	32.7 ± 8.7	31.4 ± 6.9	31.9 ± 9.4	0.27
Change from baseline		0.0 ± 3.6	0.5 ± 4.0	-0.8 ± 5.2	
Relative HGS (RHGS) (kg/BMI)	0.7 ± 0.2	0.9 ± 0.3	0.9 ± 0.2	1.0 ± 0.3	<0.001
Change from baseline		0.2 ± 0.1[b]	0.2 ± 0.1[b]	0.3 ± 0.2[b]	

Note: *indicates median and interquartile range. [a]denotes p<0.05 and [b]denotes p<0.001 relative to pre-surgery value. 6MWT, 6-minute walk test; HGS, handgrip strength test; *n*, number; STS-test, sit-to-stand test; RHGS, relative handgrip strength.

Higher pre-surgery BMI (r=-0.30, p<0.01) and fat mass (r=-0.29, p=0.01) are negatively correlated with the distance covered in the 6MWT (Figure 5.1) and no association was observed between pre-surgery fat-free mass assessed by DXA scan with the distance covered in the 6MWT (p=0.63). Only 27.3% of participants were able to walk more than 450 metres. This reference cut-off point is based on the 6MWT walking distance ranges from 450 to 800 metres in healthy subjects aged 20 to 75 years old (Camarri *et al.*, 2006, Chetta *et al.*, 2006). Of all participants, 37.7% reported physical problems when performing the test with the frequency of complaint following this order: knee pain (*n*=10), back pain (*n*=6), ankle pain (*n*=6), hip pain (*n*=3), calf pain (*n*=2) and chest pain (*n*=2).

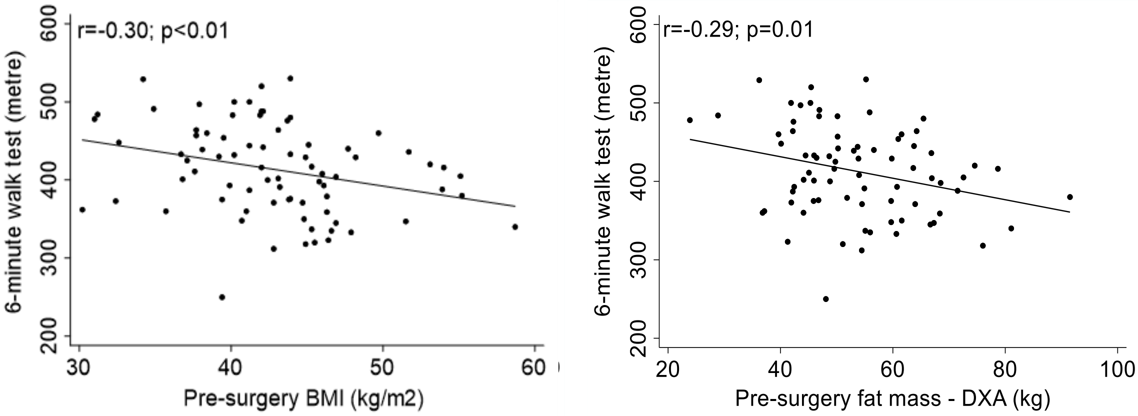


Figure 5. 1: Pearson's correlation between pre-surgery 6MWT with pre-surgery BMI and DXA-assessed fat mass.

Note: 6MWT, 6-minute walk test; BMI, body mass index; DXA, dual-energy X-ray absorptiometry.

Similar to 6MWT, younger participants completed the STS-test more quickly than their older counterparts (p=0.02). There was no difference in the time taken to complete the test between gender (p=0.18) and between pre- and post-menopausal women (p=0.63). Neither pre-surgery BMI nor fat-free mass correlates with the time taken to complete the STS-test, p=0.82 and p=0.66, respectively.

At baseline, men had greater absolute and relative HGS compared to women, ([44.2 ± 10.8 versus 29.3 ± 6.1 kg, p<0.001] and [1.0 ± 0.3 versus 0.7 ± 0.2 strength/BMI, p<0.001]), respectively. Between pre- and post-menopausal women, no significant differences in absolute HGS (30.0 ± 5.2 versus 26.6 ± 8.2 kg, p=0.06, respectively) and relative HGS were observed (0.7 ± 0.1 versus 0.6 ± 0.2 strength/BMI, p=0.12, respectively). Participants who had greater fat-free mass (assessed by DXA scan) had greater absolute and relative HGS (r=0.62, p<0.001; and r=0.35, p<0.01, respectively) (Figure 5.2).

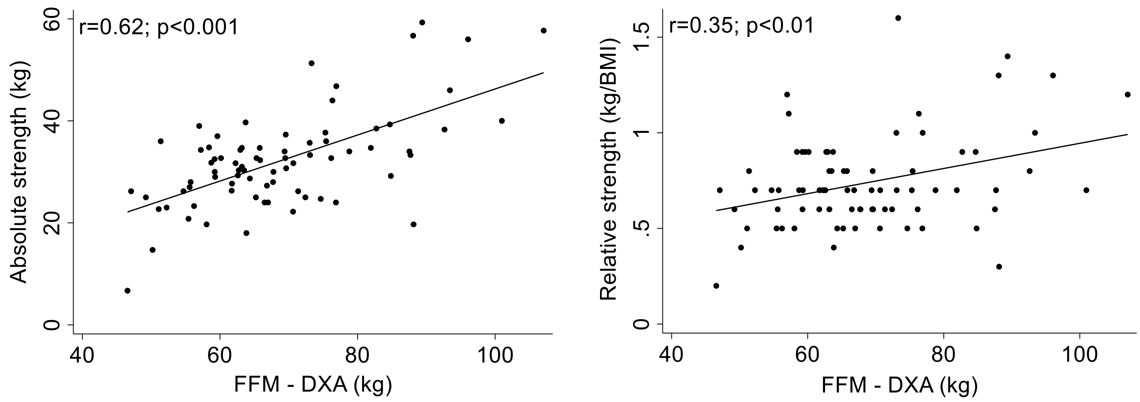


Figure 5. 2: Pearson's correlation between pre-surgery absolute and relative handgrip strengths with DXA-assessed fat-free mass.

Note: DXA, dual-energy X-ray absorptiometry; FFM, fat-free mass.

5.3.2 Changes in physical activity levels and sedentary behaviour

The mean duration of time spent on sedentary, light physical activity and MVPA as well as the step count did not change throughout the time post-surgery, relative to the baseline pre-surgery (Table 5.1). Of the total daily waking period, no significant difference was observed in the time spent on sedentary behaviour, light physical activity and MVPA, at all post-surgery study time points compared to the baseline pre-surgery (Figure 5.3). Furthermore, in the year following bariatric surgery, participants spent most of their daily waking hours accumulating sedentary behaviour (> 60%), with little time spent in light intensity physical activity (~ 32%) and very little time in MVPA (~4%).

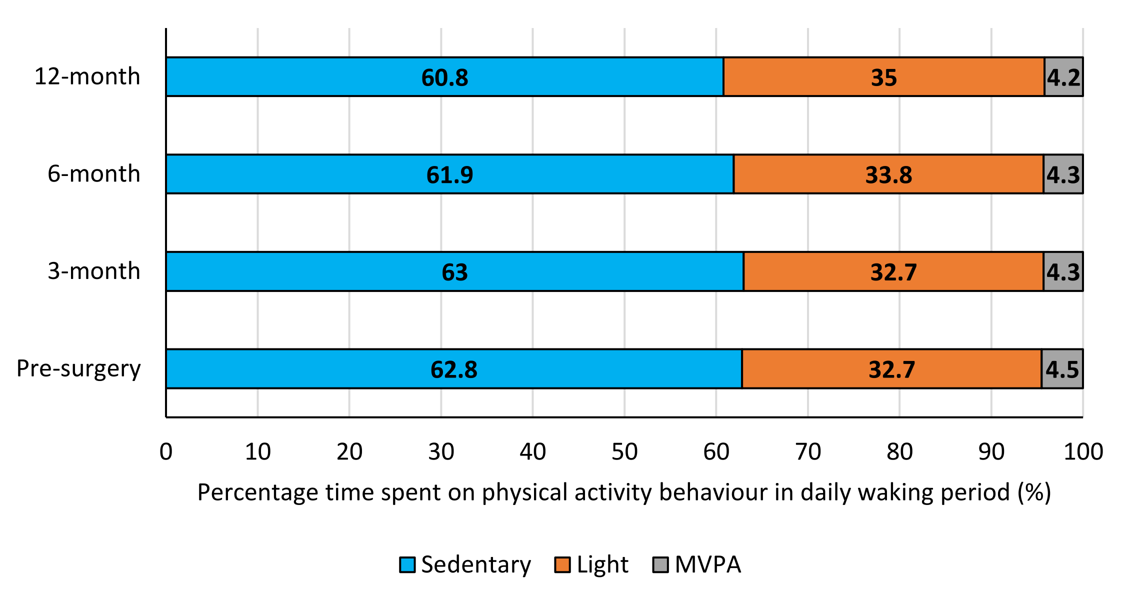


Figure 5. 3: Stacked bar chart illustrating the percentage of waking time spent on sedentary behaviour, light physical activity and MVPA at all study time points.

Of the total daily waking period, no significant difference was observed in the time spent on sedentary behaviour, light physical activity and MVPA, at all study time points post-surgery compared to the baseline pre-surgery. Note: MVPA, moderate-to-vigorous physical activity.

Overall, the proportion of patients compliant to the 2020 WHO physical activity guidelines of accumulating a total MVPA ≥150 mins/week showed a significant decreasing trend overtime, 0.86 OR [0.77 to 0.98], p=0.01. In particular, a significant difference was observed between pre-surgery and at 12-month post-surgery (86.2 versus 69%, p=0.02), Figure 5.4. When looking at the number of participants compliant to a recommendation of walking ≥10,000 daily steps, only 1.5% (*n*=1/65) met the recommendation pre-surgery, 4% (*n*=2/50) at 3-month, 9.3% (*n*=4/43) at 6-month and 4.8% (*n*=2/42) at 12-month post-surgery.

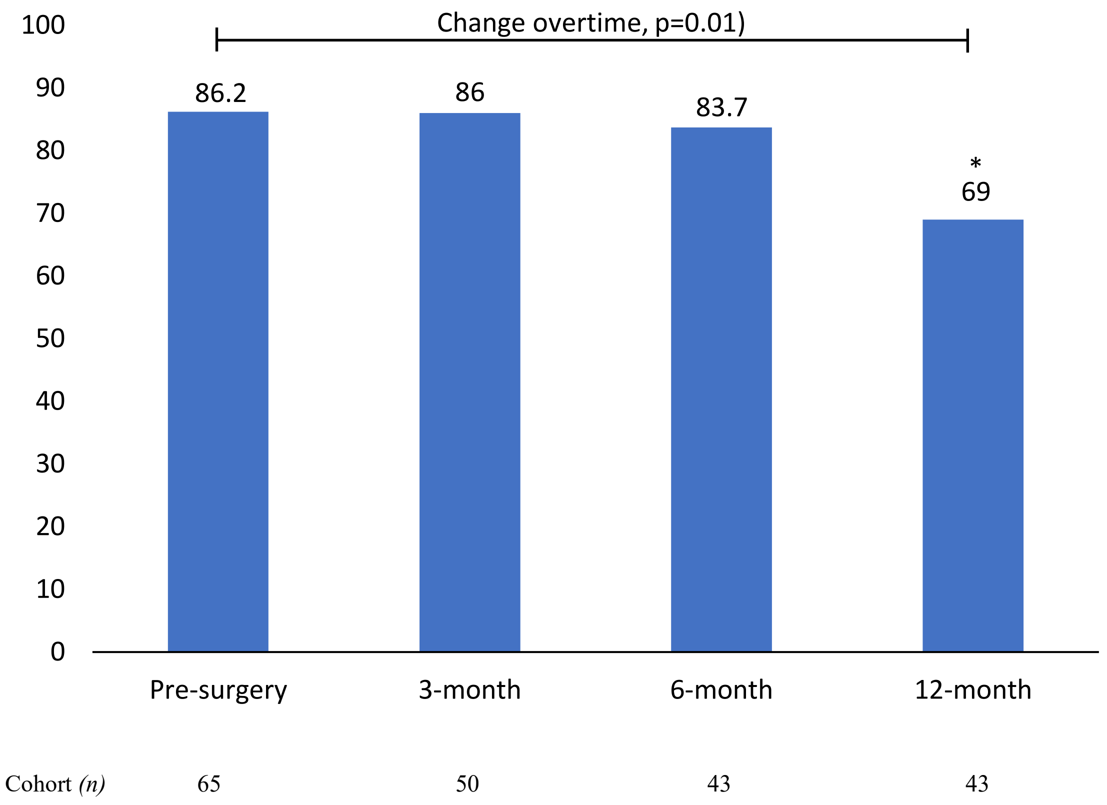


Figure 5. 4: Proportion of participants compliant to the 2020 WHO physical activity guidelines of MVPA ≥150 min/week.

The graph showed a significant decreasing trend overtime, p=0.01. A significant difference was observed between 12-month post-surgery relative to the baseline pre-surgery. Note: *denotes p=0.02; MVPA, moderate-to-vigorous physical activity; WHO, World Health Organisation.

5.3.3 Individual variability in the changes of total physical activity and sedentary behaviour

From pre- to post-surgery, the proportion of participants with improvement in the accumulated total physical activity accounted for 40.9% (*n*=18/44) at 3-month and 51.4% (*n*=19/37) both at 6- and 12-month. The proportions of participants with increased time spent on sedentary behaviour post-surgery relative to baseline pre-surgery are 56.8% (*n*=25/44) at 3-month, 40.5% (*n*=15/37) at 6-month and 46% (*n*=17/37) at 12-month.

5.3.4 Correlation between physical activity levels and sedentary behaviour with weight loss and changes in body composition

In a Pearson's Correlation analysis (Table 5.3), reduced time spent on SB (r=-0.32, p<0.05) with a concomitant increase in the time spent in light physical activity (r=0.43, p<0.01) at 6-month post-surgery appeared to be significantly associated with higher %WL. However, in a multivariate regression analysis adjusted for age and gender, changes in physical activity levels and sedentary behaviour did not predict %WL at any post-surgery time points (Table 5.4).

Table 5. 3: Correlation between physical activity levels and sedentary behaviour with weight loss and changes in body composition at each post-surgery study time point analysed using Pearson's Correlation. Data are expressed as correlation coefficient.

	%WL	**Δ FM (BIA)**	**Δ FFM (BIA)**
3-month	***n*=49**	***n*=48**	
Sedentary activity (min/day)	-0.05	-0.30*	0.00
Light activity (min/day)	0.12	0.22	-0.01
MVPA (min/day)	0.14	0.16	0.12
Total PA (min/day)	0.13	0.24	0.01
6-month	***n*=41**	***n*=36**	
Sedentary activity (min/day)	-0.32*	-0.27	-0.15
Light activity (min/day)	0.43**	0.16	0.24
MVPA (min/day)	0.11	0.33*	0.02
Total PA (min/day)	0.43**	0.22	0.24
12-month	***n*=42**	***n*=34**	
Sedentary activity (min/day)	-0.18	-0.34*	-0.04
Light activity (min/day)	0.06	0.11	-0.06
MVPA (min/day)	-0.00	0.15	-0.11
Total PA (min/day)	0.05	0.13	-0.08
		Δ FM (DXA)	**Δ FFM (DXA)**
12-month		***n*=36**	
Sedentary activity (min/day)	-	0.32	0.04
Light activity (min/day)	-	-0.15	0.09
MVPA (min/day)	-	0.01	0.01
Total PA (min/day)	-	-0.26	-0.01

Note: *indicates p<0.05 and **indicates p<0.01. %WL, percentage weight loss; BIA, bioelectrical impedance analyser; DXA, dual-energy X-ray absorptiometry; FFM, fat-free mass; FM, fat mass; MVPA, moderate-to-vigorous physical activity; PA, physical activity.

In addition, physical activity levels and sedentary behaviour did not correlate with the changes in BIA-assessed fat-free mass. However, higher time spent on sedentary behaviour, at 3- and 12- month post-surgery, was significantly correlated to lower BIA-assessed fat mass loss (kg), r=-0.30 and r=-0.34, both $p<0.05$, respectively. Lastly, higher time spent on MVPA at 6-month post-surgery significantly correlated with higher fat mass loss (kg) (r=0.33, $p<0.05$) (Table 5.3). However, in a multivariate regression analysis adjusted for age and gender, changes in physical activity levels and sedentary behaviour did not predict body composition changes at any of the post-surgery study time points (Table 5.4). No correlation was observed between physical activity behaviours and DXA-assessed fat mass and fat-free mass, analysed through both Pearson's Correlation and multivariate regression analysis.

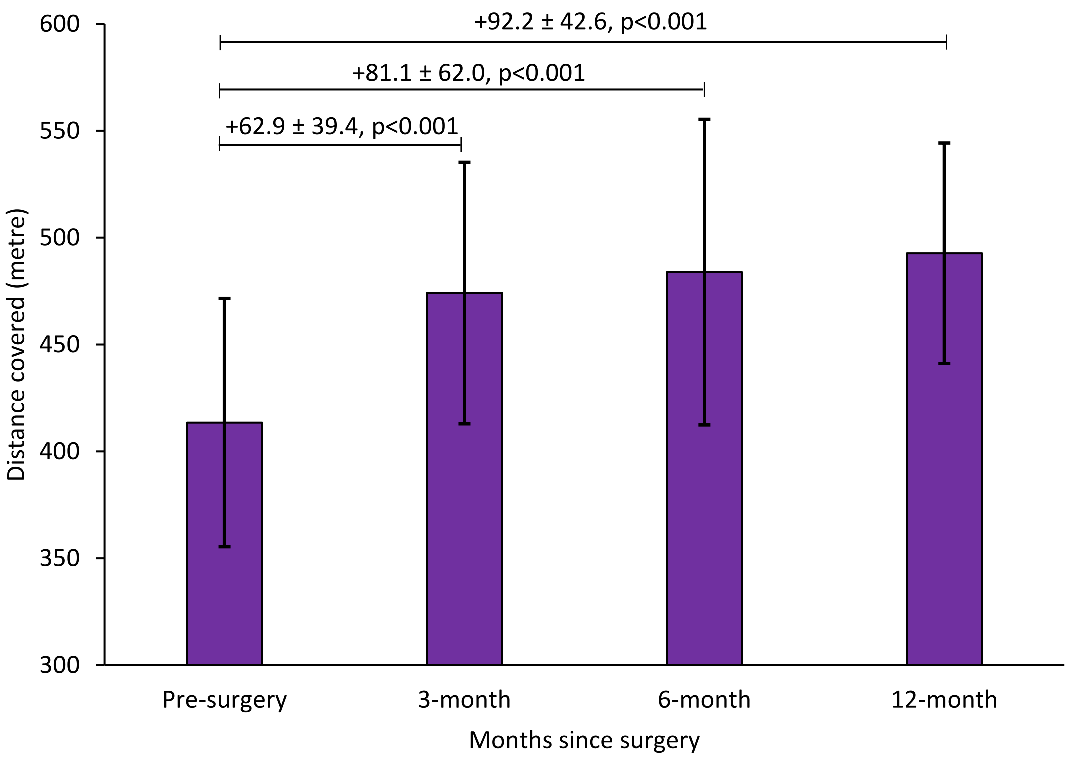
Table 5. 4: Multiple regression analysis adjusted for age and gender. Data are expressed as regression coefficients (β) with 95% CI in parentheses.

	%WL	**%loss from FM (BIA)**	**%loss from FFM (BIA)**
3-month (%)	***n*=43**	***n*=43**	***n*=43**
Δ sedentary	1.65 [-14.19 to 17.49]	0.65 [-64.49 to 65.79]	-0.47 [-65.41 to 64.47]
Δ light PA	1.70 [-14.13 to 17.53]	1.30 [-63.78 to 66.39]	-1.12 [-66.00 to 63.76]
Δ MVPA	1.66 [-14.16 to 17.48]	0.73 [-64.33 to 65.78]	-0.49 [-65.34 to 64.36]
6-month (%)	***n*=35**	***n*=31**	***n*=31**
Δ sedentary	-16.20 [-48.47 to 16.06]	45.27 [-29.57 to 120.17]	-40.76 [-113.50 to 31.95]
Δ light PA	-16.02 [-48.26 to 16.22]	45.27 [-29.57 to 120.11]	-40.76 [-113.45 to 31.93]
Δ MVPA	-16.30 [-48.49 to 15.95]	46.01 [-28.95 to 120.97]	-41.49 [-114.30 to 31.32]
12-month (%)	***n*=37**	***n*=30**	***n*=30**
Δ sedentary	-3.17 [-43.71 o 37.36]	7.48 [-22.50 to 37.46]	-4.23 [-32.71 o 24.25]
Δ light PA	-2.96 [-43.48 to 37.55]	7.59 [-22.38 to 37.56]	-4.35 [-32.82 to 24.12]
Δ MVPA	-3.20 [-43.68 to 37.27]	7.86 [-22.01 to 37.73]	-4.62 [-32.99 to 23.75]
		%loss from FM (DXA)	**%loss from FFM (DXA)**
12-month (%)		***n*=32**	***n*=32**
Δ sedentary		21.75 [-41.14 to 84.65]	-21.75 [-84.65 to 41.14]
Δ light PA		21.71 [-41.15 to 84.57]	-21.71 [-84.57 to 41.15]
Δ MVPA		21.25 [-41.51 to 84.02]	-21.25 [-84.02 t 41.52]

Note: %WL, percentage weight loss; BIA, bioelectrical impedance analyser; DXA, dual-energy X-ray absorptiometry; FFM, fat-free mass; FM, fat mass; MVPA, moderate-to-vigorous physical activity; PA, physical activity.

5.3.5 Changes in physical function

Participants walking capacity improved significantly throughout the first postoperative period with the mean [95% CI] improvement over time of +8.7 metres [7.2 to 10.1], p<0.001. At baseline, the mean distance covered was 413.5 ± 58.1 metres, then improved to 474.1 ± 61.2 metres (p<0.001) at 3-month, 483.9 ± 71.5 metres (p<0.001) at 6-month and 492.7 ± 51.6 metres at 12-month (p<0.001). This improvement in 6MWT is illustrated in Figure 5.5. The proportion of participants achieved a walking distance of ≥ 450 metres increased from 23.7% at baseline to 62.1% at 3-month, 62.1% at 6-month and 73.1% at 12-month. No significant difference in the 6MWT post-test heart rate at 3-month (p=0.53) but significant improvement was seen at 6-month (p=0.02) and 12-month (p<0.001) follow-ups. Although not statistically significant, participants' perceived exertion score at 3-month improved to ‘moderate’ from ‘somewhat strong’ at baseline. The score further improved to ‘weak (light)’ ($p<0.001$) at 6-month, and the walk test became less exerting at 12-month post-surgery with the reported score of ‘very weak’ ($p<0.001$). The proportion of participants reporting physical problem when performing 6MWT at 3-month reduced to 13.6%, consisting of knee pain (*n*=4), hip pain (*n*=3) and chest, ankle and back pain (*n*=1, respectively). At 6-month follow up, the proportion continued to reduce to 10.7% and included knee (*n*=5) and hip pain (*n*=1), and at 12-month, physical problem only accounted for 7.7% that associated with knee pain (*n*=2).

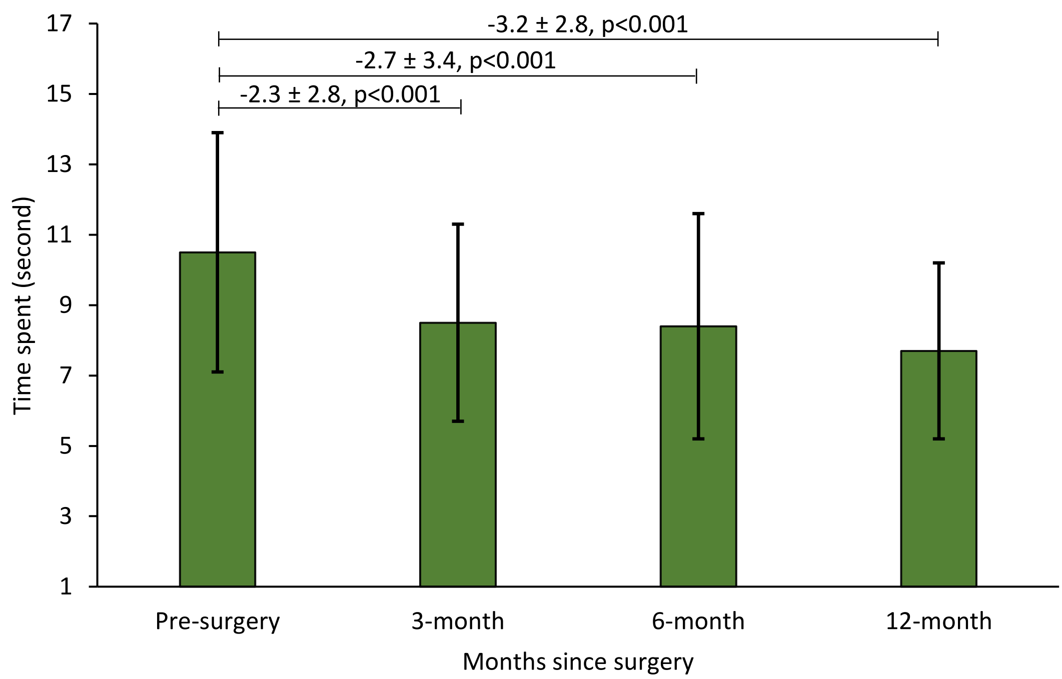


Enrolled *(n)*	77	76	74	74
Cohort *(n)*	77	66	56	26

Figure 5. 5: Graph bar illustrating the significant improvement in walking distance of 6-minute walk test following bariatric surgery. Error bars represent standard deviation.

5.3.6 Changes in physical strength

A total of three participants were unable to perform the STS-test due to functional limitation hence excluded from the analysis. However, two of them completed the test at each post-surgery time point, whereas one participant was lost to follow-up. The time taken to complete the STS-test improved significantly throughout the first postoperative period with a mean [95% CI] improvement over time of -0.2 seconds [-0.3 to -0.2], $p<0.001$. At baseline, the mean time taken to complete the test was 10.5 ± 3.4 seconds, then improved to 8.5 ± 2.8 seconds ($p<0.001$) at 3-month, 8.4 ± 3.2 seconds ($p<0.001$) at 6-month and 7.7 ± 2.5 seconds at 12-month ($p<0.001$). The improvement in the time taken to complete the STS-test is illustrated in Figure 5.6.

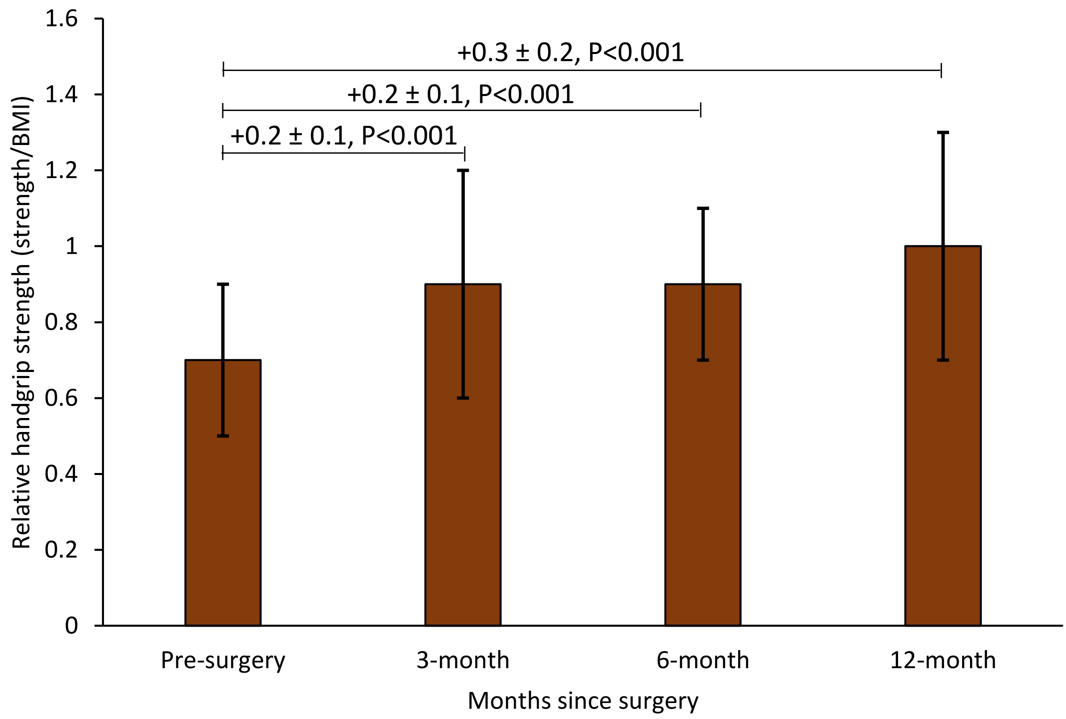


Enrolled *(n)*	77	76	74	74
Cohort *(n)*	74	67	57	51

Figure 5. 6: Graph bar illustrating the significant improvement of the time taken to complete the sit-to-stand test following bariatric surgery. Error bars represent standard deviation.

The absolute HGS did not change throughout the first postoperative period with the mean [95% CI] change over time of -0.1 kg [-0.1 to -0.0], p=0.27. At baseline, the mean HGS was 32.2 ± 9.3 kg. Relative to the baseline value, no significant difference of the HGS at 3-month (32.7 ± 8.7 kg, p=0.87), 6-month (31.4 ± 6.9 kg, p=0.32) and at 12-month post-surgery (31.9 ± 9.4 kg, p=0.21).

In contrast, the relative HGS improved significantly throughout the first postoperative period with the mean [95% CI] improvement overtime of 0.02 strength/BMI [0.02 to 0.03], p<0.001. At baseline, the mean relative HGS was 0.7 ± 0.2 strength/BMI, then improved at 3-month (0.9 ± 0.3 strength/BMI, p<0.001), 6-month (0.9 ± 0.2 strength/BMI, p<0.001) and at 12-month (1.0 ± 0.3 strength/BMI, p<0.001). The improvement in the relative HGS is illustrated in Figure 5.7.



Enrolled *(n)*	77	76	74	74
Cohort *(n)*	77	66	53	51

Figure 5. 7: Graph bar illustrating the significant improvement of the relative handgrip strength following bariatric surgery. Error bars represent standard deviation.

5.3.7 Correlation between changes in BMI and body composition with improvement in physical function and strength

Table 5.5 shows the correlation between changes in BMI and body composition with improvement in physical function and strength at 3-, 6- and 12-month post-surgery. At 3-month post-surgery, higher BMI and higher amount of fat mass are still negatively affecting walking capacity. But these effects were no longer significant at 6- and 12-month post-surgery as participants lost a significant amount of body weight and fat mass. The changes in fat-free mass and BMD post-surgery did not correlate with walking capacity. No significant relationship was found between %WL and percentage improvement in 6MWT at 3-month (r=0.09, p=0.49), 6-month (r=-0.14, p=0.31) and 12-month (r=-0.05, p=0.81) post-surgery.

Having a higher BMI, fat mass and fat-free mass at 3-month, and higher BMI, fat-mass and total hip BMD at 12-month post-surgery were associated with higher time spent to complete the STS-test. The changes in fat-free mass did not correlate with the time taken in completing the STS-test. In all time points post-surgery, having a higher amount of fat-free mass significantly correlated with higher HGS. Furthermore, higher whole-body BMD significantly correlated with higher HGS at 12-month post-surgery.

Table 5. 5: Correlation between 6MWT, STS-test and HGS with changes in BMI and body composition at each post-surgery study time point analysed using Pearson's Correlation. Data are expressed as correlation coefficient with p-value in bracket.

Parameters		6MWT (metre)		STS-test (second)		HGS (kg)
3-month	***n***		***n***		***n***	
BMI (kg/m^2)	64	-0.34 (<0.01)	65	0.36 (<0.01)	66	-0.05 (0.67)
Fat Mass - BIA (kg)	64	-0.33 (<0.01)	64	0.39 (0.001)	66	-0.07 (0.56)
Fat-Free Mass - BIA (kg)	64	0.18 (0.16)	64	0.31 (0.01)	66	0.69 (<0.001)
6-month						
BMI (kg/m^2)	53	-0.12 (0.37)	54	0.11 (0.43)	53	0.16 (0.25)
Fat Mass - BIA (kg)	52	-0.12 (0.42)	52	0.19 (0.18)	52	0.10 (0.46)
Fat-Free Mass - BIA (kg)	52	0.23 (0.09)	52	0.24 (0.09)	52	0.64 (<0.001)
12-month						
BMI (kg/m^2)	26	-0.12 (0.57)	51	0.39 (<0.01)	51	0.11 (0.46)
Fat Mass - BIA (kg)	26	-0.13 (0.53)	45	0.45 (0.001)	45	-0.03 (0.86)
Fat-Free Mass - BIA (kg)	26	0.30 (0.13)	45	0.09 (0.53)	45	0.78 (<0.001)
Fat Mass - DXA (kg)	23	-0.07 (0.74)	44	0.47 (0.001)	44	-0.04 (0.82)
Fat-Free Mass - DXA (kg)	23	0.35 (0.10)	43	0.17 (0.27)	43	0.70 (<0.001)
BMD (g/cm^2)						
Total hip	22	0.03 (0.89)	43	0.32 (0.03)	43	0.28 (0.06)
Femoral neck	22	-0.11 (0.63)	43	0.15 (0.33)	43	0.26 (0.09)
Lumbar spine	23	-0.32 (0.13)	44	0.18 (0.25)	44	0.05 (0.73)
Whole-body	23	-0.06 (0.77)	44	0.11 (0.47)	44	0.29 (0.05)

Note: BIA, bioelectrical impedance analyser; BMD, bone mineral density; BMI, body mass index; DXA, dual-energy X-ray absorptiometry; HGS, handgrip strength test; STS-test, sit-to-stand test; 6MWT, 6-minute walk test.

5.4 Discussion

This study has described the effect of bariatric surgery upon physical activity levels, sedentary behaviour and physical function and strength. Additionally, this study also investigated whether the changes in these parameters correlate with weight loss and the changes in body composition, including BMD. From the present cohort, we found that despite a significant weight loss produced by bariatric surgery, the time spent in any physical activity intensity and sedentary behaviour did not change when assessed periodically in the first postoperative year. Higher time spent on sedentary behaviour was associated with lower %WL at 6-month post-surgery and lower fat mass loss at 3- and

12-month post-surgery. On the other hand, at 6-month post-surgery, higher time spent on MVPA correlated with higher fat mass loss. Physical function and strength assessed as walking capacity, and both functional relative upper and absolute lower extremities strength improved significantly following bariatric surgery. Importantly, our results suggest that maximising weight loss and fat mass loss can optimise the improvement in walking capacity and functional lower extremity strength. Whereas minimising loss of fat-free mass and whole-body BMD following surgery are associated with better maintenance of upper extremity strength.

The lack of favourable improvement in physical activity levels and the time spent in sedentary behaviour observed in the present cohort corroborates with the previously published prospective studies that used a similar 3-axis accelerometer device (ActiGraph GT3X+) to assess physical activity (Berglind *et al.*, 2015, Sellberg *et al.*, 2019). In a longitudinal study involving 56 women who underwent RYGB, Berglind *et al*. found that physical activity levels and sedentary behaviour did not change at 3- and 9-month post-surgery compared to the baseline pre-surgery (Berglind *et al.*, 2015). Interestingly, of those completing the follow-up assessment at 48-month post-surgery (n=26), the time spent on MVPA remained unchanged (Possmark *et al.*, 2020). Similar outcomes were also reported from the ongoing WELL-RYGB RCT (Sellberg *et al.*, 2019). In this sub study analysis, participants assigned to the control group that consists of 66 women who underwent RYGB exhibited no significant changes in physical activity levels and sedentary behaviours at 12-month post-surgery relative to the baseline pre-surgery. In contrast to our result, a sub study analysis undertaken by Bellicha *et al.* involving 54 women underwent RYGB assigned to the control group of a post-surgery exercise RCT (PROMISE trial), found that patients spent significantly higher time in MVPA at 6-month following surgery but no favourable change in sedentary behaviour (Bellicha *et al.*, 2019).

Crisp *et al*. also found that only MVPA level significantly improved at 6-month post-surgery, but this positive change, unfortunately, did not sustain at 12-month post-surgery in a cohort of 34 women underwent RYGB (Crisp *et al*., 2018). Surprisingly, a recently published study by Nielsen *et al*. reported that the time spent on MVPA in 41 patients decreased significantly at 6- and 18-month post-surgery, relative to the baseline pre-surgery (Nielsen *et al*., 2021). Taken together, based upon the findings from our present cohort and the existing literature that had used accelerometer ActiGraph GTX-3+ to measure post-bariatric changes in physical activity, it can be concluded that despite the substantial weight loss produced by bariatric surgery, the time spent on sedentary behaviour remains unchanged.

Existing data to date suggest that the time spent on MVPA, particularly assessed at 6-month post-surgery, varied across studies (either no change, increased or decreased in MVPA, relative to baseline pre-surgery), which might indicate a wide variability in physical activity involvement in the earlier post-bariatric surgery. In fact, data from our cohort revealed that only almost half (47.9%) of the participants spent greater time in total physical activity, with approximately half (47.7%) of participants accumulating more time spent in sedentary behaviour post-surgery as compared to pre-surgery. Importantly, despite all participants in this observational cohort were provided with a wrist-worn physical activity tracker (Fitbit) at baseline pre-surgery, the step count did not significantly improve at any time points post-surgery. This indicates that providing patients with the wearable device alone, without additional input from healthcare professionals to reinforce the use of the device to self-monitor physical activity proved to be insufficient to promote any increase in physical activity (de Vries *et al*., 2016).

Several other methods have been used to measure physical activity in people who have undergone bariatric surgery (Adil *et al*., 2019). In the earlier years, the use of physical activity questionnaires to assess physical activity in the bariatric cohort were very common despite the bias associated with overreporting, particularly when used in people living with obesity (Warner *et al*., 2012). In fact, a few comparative studies have demonstrated a substantial discordant between self-reported subjective physical activity against objectively measured physical activity in patients who have undergone bariatric surgery (Bond *et al*., 2010, Berglind *et al*., 2016, Possmark *et al*., 2020). Bariatric surgery studies then evolved to using pedometers to assess changes in step counts from pre- to post-surgery (Colles *et al.*, 2008, Josbeno *et al.*, 2010, Giusti *et al.*, 2016). However, pedometers do not allow to characterise the different levels of physical activity intensity (frequency, intensity, and duration), hence making it difficult to assess whether patients meet the recommended physical activity guidelines (Bassett *et al*., 2017).

Several other studies have used the types of accelerometer other than the one used in the present cohort to assess physical activity levels in patients who have undergone bariatric surgery. Bond *et al*. did not find any significant change in the 6-month post-bariatric MVPA of 20 patients assessed using RT3 (Stayhealthy, Monrovia, CA), a waist-mounted accelerometer (Bond *et al*., 2010). Afshar *et al*. also assessed physical activity changes before and 6-month after bariatric surgery in 20 patients using a wrist-worn accelerometer (GENEActiv, Activinsights Ltd.) and found the time spent in MVPA and sedentary activity remain unchanged (Afshar *et al*., 2017). In another study using SenseWear Armband (Body-Media Inc., Pittsburgh, PA, USA) and the StepWatch3 Activity Monitor (Orthocare Innovation, Seattle, WA, USA) to assess physical activity changes in 30 adults undergoing bariatric surgery, weight loss did not improve physical activity behaviours assessed three monthly post-surgery at 3-, 6-, 9- and 12-month relative to baseline pre-surgery (Zabatiero *et al*., 2021). Finally, in the Longitudinal Assessment of Bariatric Surgery-2 (LABS-2) (*n*=413), King *et al*. reported modest favourable changes in MVPA and sedentary behaviour from pre- to 1-year post-surgery that were maintained through the third postoperative year assessed using the ankle-worn StepWatchTM 3 Activity Monitor (OrthoCare Innovations, Washington, DC) (King *et al*., 2015).

To date, few studies have attempted to elucidate the link between post-bariatric physical activity behaviours with the magnitude of weight loss and body composition changes (Crisp *et al.*, 2018, Nielsen *et al.*, 2021). In the present cohort, we found a link between higher time spent in MVPA with a larger reduction in fat mass at 6-month post-surgery. This finding is consistent with the study reported by Nielsen *et al*. In their study, a greater increase in total physical activity and MVPA at 6-month post-surgery was associated with higher fat mass loss and weight loss although we did not observe the latter in the present cohort (Nielsen *et al*., 2021). Another important key finding that we identified, which has never been reported thus far, is the link between higher time spent on sedentary behaviour with less favourable outcomes on weight loss and fat mass loss. Specifically, our data suggest that replacing sedentary behaviour with any form of physical activity (regardless of the intensity) is positively associated with better weight loss. Reducing time spent on sedentary activity after surgery has also been shown to promote better preservation of fat-free mass (Crisp *et al*., 2018), although we did not observe this in the present cohort. Collectively, our study supports the previous findings (Crisp *et al.*, 2018, Nielsen *et al.*, 2021) and the latest updated WHO physical activity guidelines (WHO, 2020b) that emphasise the importance of increasing time spent on MVPA and replacing the time spent on sedentary behaviour post-surgery with any form of physical activity intensity to promote better weight loss and fat mass loss as well as protecting against excessive fat-free mass loss.

The latest WHO physical activity guidelines no longer recommend for a continuous aerobic activity to be carried out for a 10-minute minimum duration and advise for “some physical activity is better than none” (WHO, 2020b). Translating this new recommendation into our analysis showed that the proportion of patients with accumulated MVPA at any duration, reduced significantly at 12-month post-surgery compared to pre-surgery (69% versus 86.2%, p=0.01). This substantial reduction in the time spent on MVPA reflects the negative impact of the COVID-19 pandemic on the physical activity levels of the bariatric surgery population. This study was still ongoing by the time the UK government announced the ‘stay-at-home’ order in March 2020 to curb the spread of COVID-19 (UK Government, 2020). The present study included 42 ActiGraph datasets at 12-month post-surgery, 25 were collected during the pandemic. It has been previously reported that bariatric patients who were adherent to the social distancing rules spent significantly more time in accelerometer-assessed sedentary behaviour (+1.1 hour/day) and less time in MVPA (-12.2 minutes/day) compared to their non-adherent counterparts (Rezende *et al*., 2021).

Notably, only approximately one-third of the participants prior to surgery were considered to have met the standard normal range of walking distance. Impaired mobility is a common issue experienced by people living with obesity and it is often associated with musculoskeletal disorders, knee and joint pain as well as reduced postural control and stability (Forhan and Gill, 2013). Compared to people with normal BMI, people with obesity have slower walking speeds, larger steps widths and longer stance durations (Ko *et al*., 2010). Therefore, assessing walking capacity has been recommended as one of the outcome measures to evaluate how participants respond to weight reduction programmes (Ekman *et al*., 2013). The pre-surgery 6MWT revealed poorer walking capacity as BMI increases. Our study demonstrates that bariatric surgery leads to a restoration of the walking capacity, as evidenced by the significant improvement in the walking distance and the increase in the number of participants achieving a distance of ≥450 metres. The improvement in the walking distance observed in the present study is consistent with previously reported studies that range from 35 to 91 metres at 3-month (Tompkins *et al.*, 2008, Josbeno *et al.*, 2010, da Silva *et al.*, 2013, Vargas *et al.*, 2013, Reinmann *et al.*, 2021), 60 to 137 meters at 6-month (Tompkins *et al*., 2008, Lyytinen *et al*., 2013) and 85 to 150 meters at 12-month post-surgery (Maniscalco *et al.*, 2006, de Souza *et al.*, 2009). The mean distance change at 12-month post-surgery in our cohort tripled the minimal clinically important difference (MCID) of 14.0 to 30.5 metres (Bohannon and Crouch, 2017), which indirectly translated to improved cardiorespiratory fitness of participants in this study following bariatric surgery. The improvement in cardiorespiratory fitness is further evidenced by the significant lower 6MWT post-test heart rate with less perceived exertion level reported post-surgery than pre-surgery, with the highest improvement for both variables observed at 12-month follow-up.

Our finding adds to the existing body of evidence collected in systematic review that preliminarily concluded (due to limited existing studies) that the magnitude of weight loss post-surgery does not parallel with the improvement in 6MWT (Herring *et al*., 2016). The lack of correlation might be explained by a few other factors that influenced walking capacity rather than body weight alone, such as participant's height, age, bodily pain (Ekman *et al*., 2013) or external factors such as encouragement during the walking test (A. T. S. Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories, 2002). In this study, we observed the negative effect of higher BMI and fat mass on walking capacity at pre-surgery that persisted up until 3-month post-surgery. Beyond this period, BMI and fat mass did not influence walking capacity. Despite this, almost one-third of participants were still unable to reach the minimal cut-off points of normal walking distance following surgery. The fact that approximately 10% of the participants still reported physical complaints (mainly knee and hip pain) when performing the 6MWT showed that a subset of patients still suffered from poor functional capacity. Taken together, these data suggest that the 6MWT can be used to identify patients who have functional limitations as early as 3-month post-surgery. This group of patients could then be offered additional support, such as a tailored exercise programme to help maximise their functional capacity.

Interestingly, excessive fat-free mass loss, as reported in Chapter 4, does not negatively affect the upper and lower extremities strength as observed from the HGS and STS tests. The absolute HGS did not significantly change in the first postoperative year, in agreement with the results of previous studies (Otto *et al*., 2014, Coral *et al*., 2021) but in contrast with a study by Alba *et al* (Alba *et al*., 2019). In the latter study, Alba and colleagues found the mean absolute strength of 47 adults who underwent RYGB declined significantly by 11.9% at 3-month and 8.8% at 6-month relative to pre-surgery (Alba *et al*., 2019). Whereas in our cohort, assessed at similar time points post-surgery, the mean absolute strength increased by 3.2% at 6-month then followed by a decline by 1.1% at 12-month post-surgery, but these changes are not statistically significant relative to the baseline pre-surgery. The discrepancies with our findings might be explained by the difference in the changes in participants' body composition post-surgery. Whilst Alba *et al*. observed 51% of the total weight loss at 12-month post-surgery came from fat-free mass, this was only accounted for 39.4% in our cohort. Furthermore, we also observed a significant correlation between the HGS with the amount of fat-free mass at all time points post-surgery and the whole-body BMD at 12-month post-surgery that was not observed by Alba *et al*. (Alba *et al*., 2019). Despite these differences, we found a similar significant improvement in the post-surgery relative muscle strength (calculated as HGS divided by BMI), a method used to measure muscle quality. In elderly and other patient populations, handgrip strength has been shown to be a good proxy to measure specific health outcomes such as nutritional status and BMD. Further studies are therefore needed to confirm whether grip strength can be used as a good indicator for overall health in patients following bariatric surgery (Bohannon, 2019).

Only a few studies have used the STS-test to measure lower body extremity strength in patients following bariatric surgery. Alba *et al*. found a significant improvement in the time spent to complete the test from 13.4 ± 3.6 seconds at pre-surgery to 11.6 ± 6.8 seconds at 12-month post-surgery (Alba *et al*., 2019). The same test was performed by Reinmann *et al*. in 33 adults undergoing bariatric surgery, with a significant change seen from 9.78 ± 3.63 seconds at baseline pre-surgery to 8.44 ± 2.74 seconds, 3-month following surgery (Reinmann *et al*., 2021). The findings from both studies are in line with what we observed in the present cohort; a mean improvement between -2 to -4 seconds assessed periodically in the first postoperative year. The changes, although significant, are below the MCID which is between -5 to -7 seconds, a range that was developed from patients with chronic musculoskeletal pain (Benaim *et al*., 2019). One factor that may explain the below-than-MCID range in the present cohort is the fact that patients with functional limitations and non-ambulatory were excluded from this study. These exclusion criteria are part of the requirement in the initial RCT for the supervised exercise programme of the intervention group. Therefore, participants in the current study are considered as not having a severe form of musculoskeletal issues prior to surgery hence were fairly fit when they performed the test pre-surgery. Finally, we also found the correlation between higher BMI, fat mass and total hip BMD (being a weight-bearing joint) with a longer time taken to complete the STS-test at 12-month post-surgery that was not observed by Alba *et al*. (Alba *et al*., 2019).

This study is not without limitations. During the nationwide lockdown of the COVID-19 pandemic, all in-person follow-up assessments were carried out remotely hence throughout this period, the 6MWT, STS test and HGS data were missing. The lockdown also may have impacted upon physical activity levels and sedentary behaviour so the present results should be interpreted with caution. Missing physical activity data was attributed to either participant did not meet the required wear time period; they did not return the device, or the returned device via mail did not reach our department. Assessments undertaken outside the time window were excluded from the analysis hence reduced the sample size of the study. Finally, that associations observed in the present study do not identify causation and do not describe the direction of the relationship.

5.5 Conclusions

Overall, the findings from this study provide further evidence that weight loss following bariatric surgery did not lead to favourable changes in physical activity behaviours but helped improving functional capacity. Nevertheless, our data emphasise the importance of replacing time spent in sedentary behaviour with any form of physical activity intensity to promote better weight loss and fat-mass loss post-surgery. Furthermore, this study highlights the importance of maximising fat mass loss whilst minimising loss of fat-free mass and BMD to optimise walking capacity and maintain both upper and lower extremities strength.

Chapter 6

Health-related quality of life and mental health outcomes: The BARI-LIFESTYLE observational study[21]

6.1 Introduction

In Chapters 4 and 5, bariatric surgery has been shown to be effective in inducing weight loss, remission or improvement of comorbidities as well as improvement in physical function and strength. However, whether the clinical effectiveness of bariatric surgery corresponds with the improvements in how patients' function or feel are less well-understood (Coulman and Blazeby, 2020). Evaluation of patient-related outcomes (PRO) is particularly important following bariatric surgery, as the desire to improve QoL is one of the factors that motivated people to seek bariatric surgery (Munoz *et al*., 2007). Therefore, PRO should be assessed following bariatric surgery but there are few data regarding this collected in real-world clinical practice (Basch *et al*., 2015). Generally,

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[21]Some of the work related to this chapter was presented at UCL Doctoral School Research Poster Competition 2019/2020 and is available in Appendix 21. JASSIL, F. C., BATTERHAM, R. L. & THE BARI-LIFESTYLE TEAM 2020. Health-related quality of life of patients awaiting bariatric surgery: A multi-centre observational study in the United Kingdom.

PRO is assessed either by using validated HRQoL questionnaires which enable responses to be gathered from many patients (Kolotkin and Andersen, 2017) or, by using qualitative research, a type of study design that can provide an in-depth exploration of patients' views and experiences towards the outcomes of bariatric surgery (Coulman *et al.*, 2017).

As previously outlined in Chapter 2, a main cause which limited conclusions from being drawn from systematic reviews of the effect of bariatric surgery on HRQoL was the heterogeneity of questionnaires used (Coulman *et al.*, 2013, Hachem and Brennan, 2016, Raaijmakers *et al.*, 2017). Most studies have used the generic form of the HRQoL questionnaires, particularly the 36-Item Short Form Health Survey (SF-36), which was reported to be less sensitive when studying the impact of weight loss treatments in people living with obesity (Coulman *et al.*, 2013). Therefore, additional use of an obesity-specific questionnaire is recommended as it captures more specific psychosocial outcomes such as body image and social stigma (Kolotkin and Andersen, 2017). Furthermore, it has been recommended that a specific validated measure of mental health conditions should also be used to complement the HRQoL questionnaires, as it is more sensitive to capturing the changes in psychological and mental health following obesity treatments (Fermont *et al.*, 2017, Szmulewicz *et al.*, 2019). It has been previously highlighted that an inappropriate choice of sensitive instruments to assess HRQoL may underestimate the real impact of clinical intervention, hence preventing proper resource allocation and enhancement of patient-centred care (Rothberg *et al.*, 2014, Campbell *et al.*, 2016). Importantly, in a recent systematic review of reviews, Kolotkin and Anderson had highlighted for future studies to explore the factors that mediate HRQoL changes following bariatric surgery, and how they linked with other variables such as physical activity levels (Kolotkin and Andersen, 2017).

To address these knowledge gaps, this study aimed to evaluate the changes in HRQoL following bariatric surgery using a combination of the generic health status, obesity-specific, and mental health questionnaires. In addition, how the changes in HRQoL are linked with other variables will be further explored. The specific objectives of this study are:

1. To evaluate post-surgery changes in HRQoL at 3-, 6- and 12-month post-bariatric surgery, relative to baseline pre-surgery score using a generic health status questionnaire, EQ-5D-3L.
2. To evaluate post-surgery changes in HRQoL at 3-, 6- and 12-month post-bariatric surgery, relative to baseline pre-surgery score using obesity-specific questionnaire, IWQOL-Lite.
3. To evaluate post-surgery changes in the characteristics of attitude and symptoms of depression at 3-, 6- and 12-month post-bariatric surgery, relative to baseline pre-surgery score using BDI-II.
4. To determine the prevalence of depressive symptomatology in patients undergoing bariatric surgery.
5. To assess the link between pre- and post-surgery depressive symptomatology upon weight loss and HRQoL in the first year of bariatric surgery.
6. To explore the correlation between EQ-5D-3L, IWQOL-Lite and BDI-II scores.

6.2 Materials and methods

The study design and setting, eligibility criteria, participant recruitment and data collection for HRQoL and mental health using EQ-5D-3L, IWQOL-Lite and BDI-II have been described in detail in Chapter 3. Throughout the nationwide lockdown between

April to July 2020, all face-to-face assessments were suspended, to comply with the restrictions. Therefore, data for the questionnaires were collected via phone, video call or mailed to the participants. The statistical analysis plan has been previously described in Chapter 3.

6.3 Results

6.3.1 Baseline characteristics

Participants' demographic characteristics have been previously described in Chapter 4, section 4.3.1. The questionnaires completion rates were 92.2%, 89.6% and 72.7% at 3-, 6- and 12-month post-surgery, respectively. The mean baseline EQ-5D-index was 0.68 ± 0.29 and the mean baseline EQ-VAS was 58.3 ± 19.4%. Also, at baseline, only 17 (22.1%) participants had EQ-5D-index score of 1.0, where 1.0 represents perfect health and 0 represents death. Specifically, based on individual dimension of EQ-5D, the proportions of patients who reported having problems with pain/ discomfort were 66.2%, anxiety/ depression were 44.2%, mobility issues were 44.2%, problem performing usual activities such as work, study, housework, family or leisure activities were 39% and having issues with self-care were 11.7%. Participants with older age had significantly lower baseline EQ-5D-index scores compared to their younger counterparts, $p<0.05$. No associations were observed between both the EQ-5D-index and EQ-VAS scores with baseline BMI. Both males and females reported similar scores in both parameters ($p>0.05$).

The mean baseline total score for IWQOL-Lite was 46.1 ± 20.6%, where 100 represents the 'best' score and 0 represents the 'worst' score. A total of 58.4% of participants had a total score below 50%. Specifically, based on the subscales of IWQOL-

Lite, the lowest score was for the self-esteem scale, followed by physical function, public distress, sexual life, and work. Participants of advanced age had significantly lower baseline total IWQOL-Lite and physical function scale scores than their younger counterparts, $p<0.05$. Furthermore, a higher baseline BMI was negatively associated with physical function and public distress scales scores, both $p<0.05$. Both males and females reported similar scores in total IWQOL-Lite and all subscales, all $p>0.05$.

The mean baseline total score for BDI-II was 16.9 ± 11.8. A total of 41.5% of participants were categorised as having none or minimal depressive symptomatology, 22.1% having mild depressive symptomatology, 18.2% having moderate depressive symptomatology and 18.2% having severe depressive symptomatology. Age and gender were not significantly related to the BDI-II total score, the cognitive-affective and the somatic subscales, all $p>0.05$. No difference in BMI was observed in participants with no or minimal to mild versus moderate to severe depressive symptomatology, $p>0.05$. Compared to participants with no or minimal to mild depressive symptomatology, participants with moderate to severe depressive symptomatology had significantly lower EQ-5D-index and total IWQOL-Lite and its subscales, all $p<0.001$.

6.3.2 Impact of bariatric surgery on the generic HRQoL assessed using EQ-5D-3L

The EQ-5D-index improved significantly throughout the first postoperative period with the mean [95% CI] improvement over time of 0.01 [0.01 to 0.02], $p<0.001$ (Table 6.1). The score peaked between 3-month (0.87 ± 0.17) to 6-month (0.87 ± 0.19) post-surgery period and maintained at 12-month post-surgery (0.85 ± 0.23) (Figure 6.1). The proportion of participants who reported having EQ-5D-index score of 1.0 increased to 52.1% at 3-, 55.1% at 6- and 51.8% at 12-month post-surgery. Whereas approximately

65% of participants achieved the MCID of 0.03 points (Luo *et al*., 2010) at all post-surgery time points (Figure 6.2). In terms of the changes in the five health dimensions, significant improvements were observed for mobility ($p<0.001$), physical pain/discomfort ($p<0.05$) and anxiety/ depression ($p<0.05$) at 12-month post-surgery, relative to the baseline pre-surgery scores (Table 6.2).

Table 6. 1: The changes in HRQoL and mental health at 3-, 6- and 12-month post-bariatric surgery, relative to baseline pre-surgery assessed using EQ-5D-3L, IWQOL-Lite and BDI-II.

HRQoL and mental health variables	Pre-surgery *n*=77	3-month *n*=71	6-month *n*=69	12-month *n*=56	Change overtime, p-value
EQ-5D-index (score)	0.68 ± 0.29	0.87 ± 0.17	0.87 ± 0.19	0.85 ± 0.23	0.01 [0.01 to 0.02]
Change from baseline	-	0.16 ± 0.24*	0.17 ± 0.25*	0.16 ± 0.28*	p<0.001
EQ-VAS (%)	58.3 ± 19.4	78.8 ± 14.4	80.8 ± 13.5	85.9 ± 12.6	2.1 [1.7 to 2.5]
Change from baseline	-	18.8 ± 18.9*	21.7 ± 18.6*	27.4 ± 18.5*	p<0.001
IWQOL-Lite total (%)	46.1 ± 20.6	78.6 ± 17.1	85.8 ± 15.4	88.1 ± 15.4	3.4 [2.9 to 3.8]
Change from baseline	-	32.0 ± 18.7*	39.7 ± 19.4*	43.2 ± 18.3*	p<0.001
Scales					
Physical function (%)	46.5 ± 21.3	81.6 ± 16.2	88.6 ± 13.9	88.6 ± 13.6	3.3 [2.9 to 3.8]
Change from baseline	-	35.0 ± 17.9*	42.9 ± 18.5*	43.1 ± 17.2*	p<0.001
Self-esteem (%)	34.3 ± 26.7	72.0 ± 21.9	79.6 ± 22.2	83.8 ± 21.9	3.9 [3.3 to 4.5]
Change from baseline	-	36.7 ± 26.8*	44.7 ± 26.3*	50.3 ± 25.5*	p<0.001
Sexual life (%)	49.1 ± 30.7	76.0 ± 22.3	82.2 ± 23.8	86.6 ± 23.4	3.1 [2.5 to 3.7]
Change from baseline	-	26.0 ± 27.1*	31.9 ± 28.0*	38.6 ± 26.4*	p<0.001
Public distress (%)	48.4 ± 27.7	78.3 ± 23.2	87.0 ± 18.4	91.5 ± 14.4	3.5 [3.0 to 4.0]
Change from baseline	-	29.9 ± 24.3*	38.2 ± 25.1*	45.3 ± 25.6*	p<0.001
Work (%)	60.4 ± 28.0	84.2 ± 21.2	90.0 ± 16.7	91.8 ± 17.6	2.5 [2.1 to 3.0]
Change from baseline	-	23.4 ± 24.4*	29.3 ± 24.7*	32.7± 24.8*	p<0.001
BDI-II total (score)	16.9 ± 11.8	7.5 ± 8.9	6.3 ± 8.6	7.1 ± 10.5	-0.8 [-0.9 to -0.6]
Change from baseline	-	-8.7 ± 9.9*	-10.2 ± 10.1*	-10.0 ± 10.9*	p<0.001
Scales					
Cognitive-affective (score)	5.9 ± 4.8	2.2 ± 3.5	1.8 ± 3.7	2.1 ± 3.8	-0.3 [-0.4 to -0.2]
Change from baseline	-	-3.5 ± 3.5*	-3.9 ± 3.9*	-3.8 ± 4.1*	p<0.001
Somatic (score)	10.9 ± 7.6	5.4 ± 5.7	4.4 ± 5.4	4.9 ± 7.1	-0.5 [-0.6 to -0.1]
Change from baseline	-	-5.2 ± 7.0*	-6.3 ± 6.8*	-6.2 ± 7.2*	p<0.001

Note: * indicates p<0.001relative to baseline pre-surgery value. BDI-II, Beck Depression Inventory-II; HRQoL, health-related quality of life; IWQOL-Lite, Impact of Weight on Quality of Life-Lite; *n*, number; VAS, visual analogue scale.

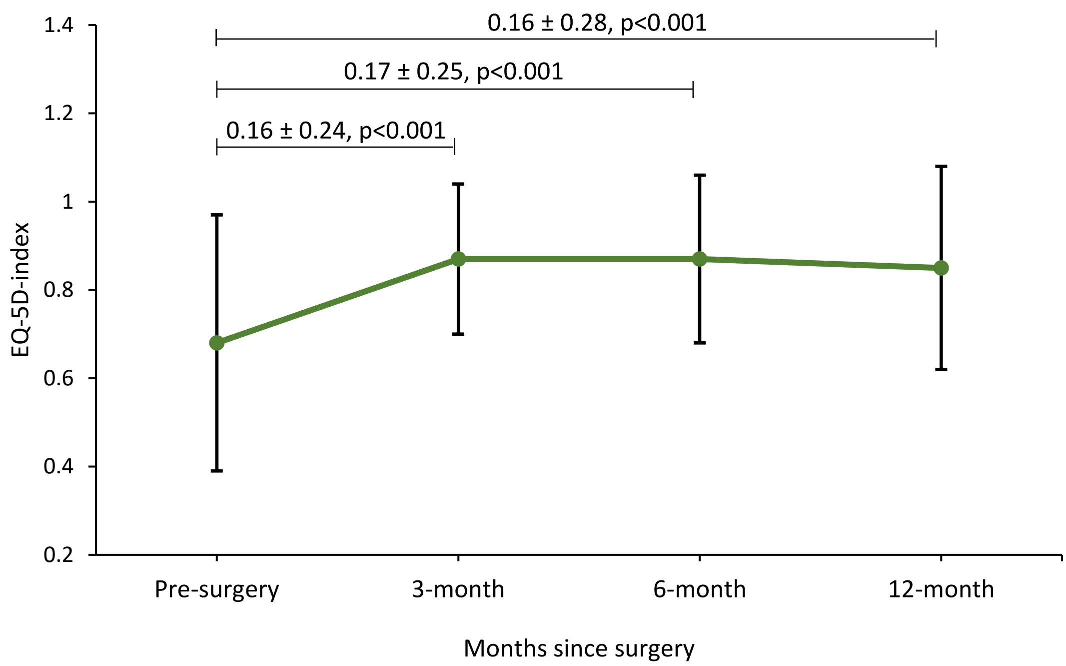
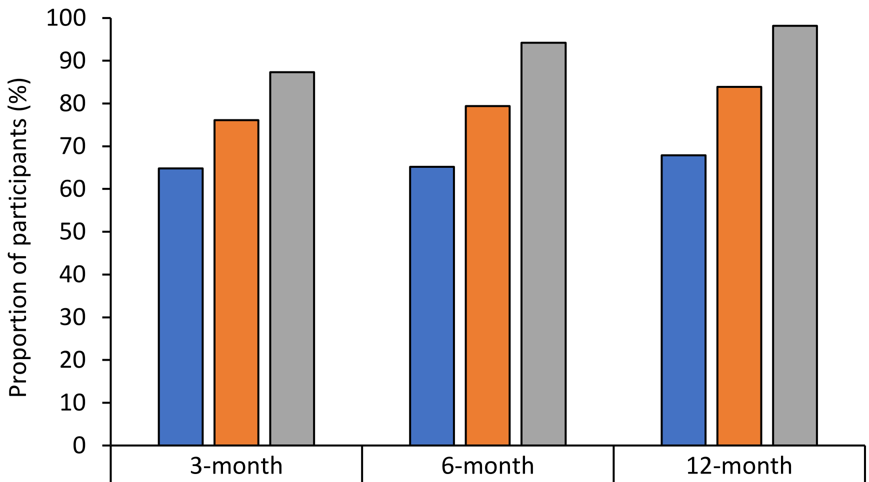


Figure 6. 1: Line graph illustrating the changes in the EQ-5D-index in the first year following bariatric surgery. Error bars represent standard deviation.



	3-month	6-month	12-month
EQ-5D-index MCID	64.8	65.2	67.9
EQ-VAS MCID	76.1	79.4	83.9
IWQOL-Lite Total MCID	87.3	94.2	98.2

EQ-5D-index MCID EQ-VAS MCID IWQOL-Lite Total MCID

Figure 6. 2: The proportion of patients achieving minimal clinically importance differences.

Note: EQ-5D-index MCID = 0.03 points; EQ-VAS MCID = 10 points; IWQOL-Lite total MCID = 12 points; EQ-5D-index, EQ-5D index score; EQ-VAS, EQ visual analogue scale; IWQOL-Lite, Impact of Weight on Quality of Life-Lite; MCID, Minimal clinically importance difference.

Table 6. 2: Numbers and proportions reporting levels within EQ-5D dimensions from pre- to post-surgery.

EQ-5D, *n* (%)	Pre-surgery *n*=77	3-month *n*=71	6-month *n*=69	12-month *n*=56	p-value*
Mobility					
Level 1	43 (55.8)	63 (88.7)	64 (92.8)	47 (83.9)	
Level 2	34 (44.2)	8 (11.3)	5 (7.2)	9 (16.1)	<0.001
Level 3	0	0	0	0	
Self-care					
Level 1	68 (88.3)	68 (95.8)	69 (100)	55 (98.2)	
Level 2	9 (11.7)	3 (4.2)	0	1 (1.8)	0.125
Level 3	0	0	0	0	
Usual activities					
Level 1	47 (61.0)	62 (87.3)	66 (95.7)	51 (91.1)	
Level 2	30 (39.0)	9 (12.7)	3 (4.3)	5 (8.9)	0.147
Level 3	0	0	0	0	
Pain/ discomfort					
Level 1	26 (33.8)	44 (62.0)	46 (66.7)	36 (64.3)	
Level 2	41 (53.2)	26 (36.6)	21 (30.4)	18 (32.1)	0.039
Level 3	10 (13.0)	1 (1.4)	2 (2.9)	2 (3.6)	
Anxiety/ depression					
Level 1	43 (55.8)	56 (78.9)	50 (72.5)	38 (67.8)	
Level 2	30 (39.0)	14 (19.7)	18 (26.1)	16 (28.6)	0.042
Level 3	4 (5.2)	1 (1.4)	1 (1.4)	2 (3.6)	

Note: *Change at 12-month relative to the baseline pre-surgery; EQ-5D, EuroQol 5 dimensions; *n*, number.

The EQ-VAS score improved significantly throughout the first postoperative period with the mean [95% CI] improvement over time of 2.1% [1.7 to 2.5], p<0.001 (Table 6.1). The score increased steadily following surgery with the mean scores of 78.8 ± 14.4% at 3-month, 80.8 ± 13.5% at 6-month and highest at 12-month post-surgery, 85.9 ± 12.6% (Figure 6.3). Whereas 76.1%, 79.4% and 83.9% of participants achieved the MCID of 10 points (Luo *et al*., 2010) at 3-, 6- and 12-month post-surgery, respectively (Figure 6.2).

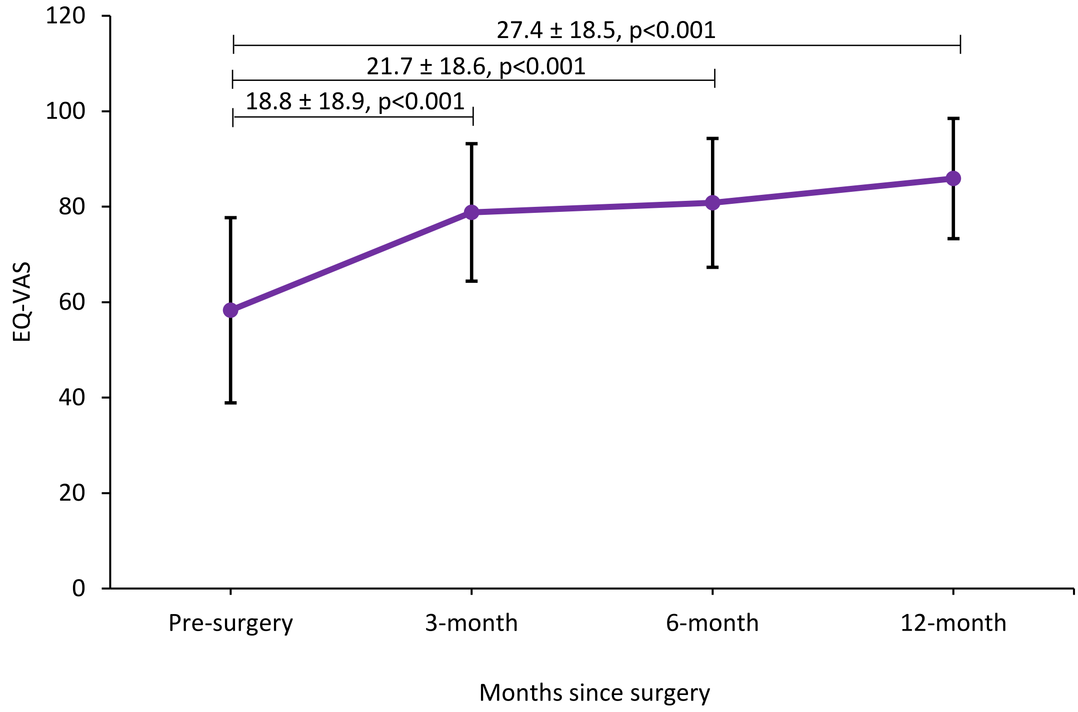


Figure 6. 3: Line graph illustrating the changes in the EQ-VAS in the first year following bariatric surgery. Error bars represent standard deviation.

6.3.3 Impact of bariatric surgery on the obesity-specific HRQoL assessed using IWQOL-Lite

The mean total IWQOL-Lite score improved significantly throughout the first postoperative period with the mean [95% CI] improvement over time of 3.4% [2.9 to 3.8], p<0.001, respectively (Table 6.1). The score increased steadily following surgery with the mean scores of 78.6 ± 17.1% at 3-month, 85.8 ± 15.4% at 6-month and highest at 12-month post-surgery, 88.1 ± 15.4%. The trend of changes in the total IWQOL-Lite is illustrated in Figure 6.4.

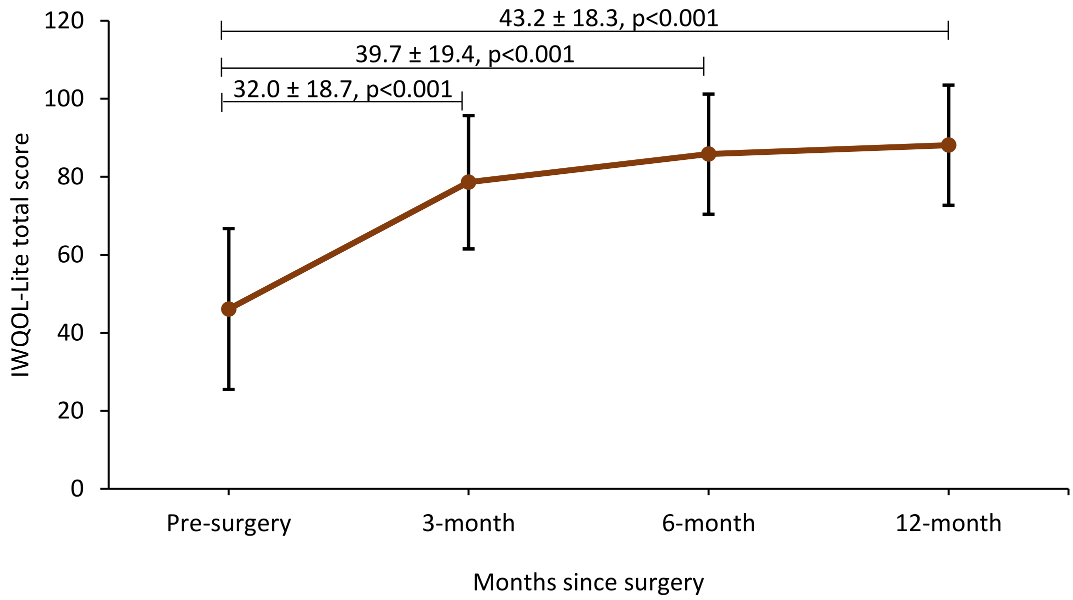


Figure 6. 4: Line graph illustrating the changes in the total IWQOL-Lite score in the first year following bariatric surgery. Error bars represent standard deviation.

All five subscales were also improved significantly at each time point following surgery, similar to the total IWQOL-Lite score, with the highest improvement reported of all domains at 12-month post-surgery. The highest score in the subscales at 12-month increased in the following order: self-esteem, sexual life, physical function, public distress and work (Figure 6.5).

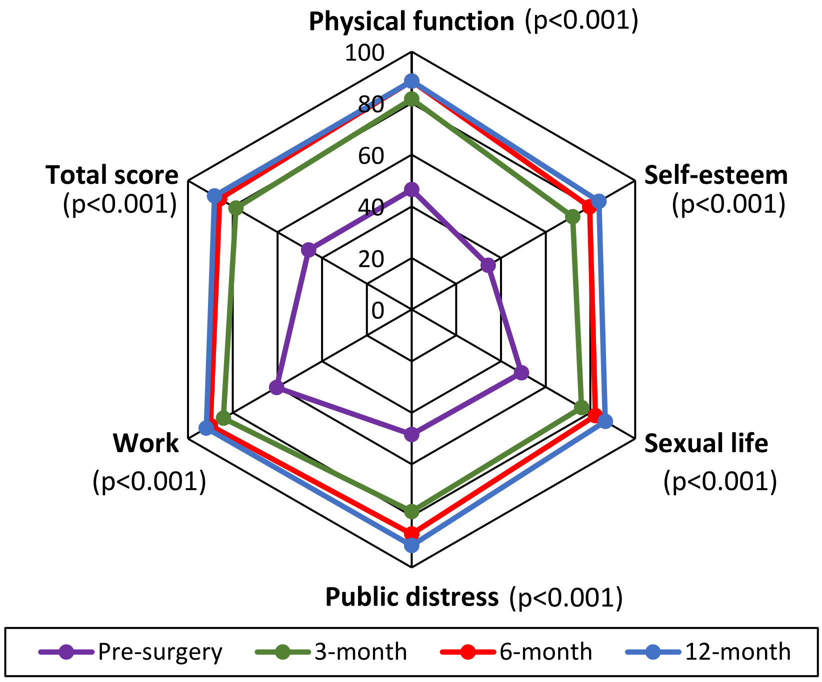


Figure 6. 5: Radar chart of the five subscales of the IWQOL-Lite in the first postoperative year.

Note: 100 represents the 'best' score and 0 represents the 'worst' score. Notice that the scores increase over time with the self-esteem scale being the most compromised component. P-value indicates the changes over time.

6.3.4 Factors associated with the post-surgery changes in EQ-5D-3L and IWQOL-Lite scores

We conducted a multivariate linear regression to identify factors associated with the post-surgery changes in EQ-5D-3L and IWQOL-Lite scores. This multivariate linear regression included the analysis of %WL, type of surgery, physical activity levels and sedentary behaviour, adjusting for age, gender, preoperative BMI, and baseline comorbidities status (Table 6.3). Higher %WL at 3 months post-surgery is associated with higher total scores and some of the subscales in IWQOL-Lite. Participants who had SG and OAGB reported higher EQ-VAS, total IWQOL-Lite and some of the subscales in IWQOL-Lite at 3- and 6-month post-surgery compared to participants who had RYGB. Whereas at 12-month post-surgery, higher time spent in MVPA was associated with higher scores of total EQ-5D-index, EQ-VAS, total IWQOL-Lite and some of the subscales in IWQOL-Lite (Table 6.3).

Table 6. 3: Multiple regression analysis adjusted for age, gender, baseline BMI and comorbidities. Data are expressed as regression coefficients (β).

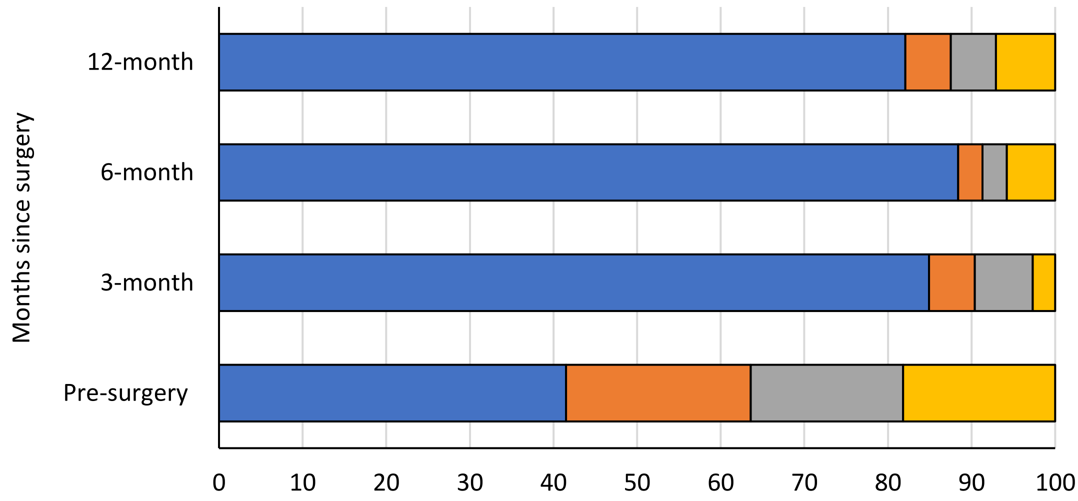
	%WL	Type of surgery[a]	SB	LPA	MVPA
3-month					
EQ-5D-index	0.01	0.08	0.00	-0.00	0.00
EQ-VAS	0.77	10.27	0.02	0.03	0.08
IWQOL-Lite total	1.82*	13.80**	0.02	0.05	0.01
Physical function	1.22**	13.46**	0.03	0.04	-0.02
Self-esteem	2.26*	11.24	0.04	0.11	0.01
Sexual life	1.9	24.25**	0.00	-0.02	0.04
Public distress	2.23**	7.94	0.04	0.03	0.21
Work	2.17	18.63** 23.32**,[b]	0.01	0.02	-0.11
6-month					
EQ-5D-index	-0.00	0.12	0.00	0.00	0.00
EQ-VAS	0.76	14.40*	0.04	0.05	0.03
IWQOL-Lite total	0.97	14.92**	-0.00	0.02	0.02
Physical function	0.63	16.84* 14.95**,[b]	0.01	0.02	-0.04
Self-esteem	1.51	11.54	-0.02	0.01	0.02
Sexual life	1.23	16.26	0.02	0.06	-0.06
Public distress	0.78	13.51	-0.02	0.00	0.11
Work	0.75	15.89** 18.35**,[b]	-0.00	0.02	0.12
12-month					
EQ-5D-index	0.00	-0.08	0.00	0.00	0.01*
EQ-VAS	0.16	3.73	0.04	0.07	0.30**
IWQOL-Lite total	0.39	6.12	0.04	0.04	0.34**
Physical function	0.28	3.89	0.07	0.06	0.36*
Self-esteem	0.49	4.47	0.03	0.04	0.37
Sexual life	0.29	13.15	0.06	0.09	0.58**
Public distress	0.45	3.99	0.05	0.03	0.36*
Work	0.32	10.87	0.00	0.04	0.15

Note: * indicates $p<0.01$, ** indicates $p<0.05$, [a] indicates RYGB versus SG and [b] indicates RYGB versus OAGB. IWQOL-Lite, Impact of Weight on Quality of Life-Lite; LPA, light physical activity; MVPA, moderate-to-vigorous physical activity; OAGB, one-anastomosis gastric bypass; RYGB, Roux-en-Y gastric bypass; SB, sedentary behaviour; SG, sleeve gastrectomy; VAS, visual analogue scale.

6.3.5 Impact of bariatric surgery on mental health assessed using BDI-II

The mean total BDI-II score improved significantly throughout the first postoperative period with the mean [95% CI] score improvement over time of -0.8 [-0.9 to -0.6], $p<0.001$. This therefore translated to significant improvements in both cognitive-affective and somatic subscales, -0.3 [-0.4 to -0.2] and -0.5 [-0.6 to -0.1], all $p<0.001$, respectively. The changes in BDI-II total score and the cognitive-affective and somatic subscales at each time point are shown in Table 6.1.

There was a significant decrease in the proportion of participants with moderate to severe depressive symptomatology at each time point post-surgery compared to the baseline pre-surgery. The proportion decreased from 36.4% at pre-surgery to 9.6% at 3-month post-surgery ($p<0.001$), to 8.7% at 6-month post-surgery ($p<0.05$) but increased slightly to 12.5% at 12-month post-surgery ($p<0.05$), although still below the pre-surgery proportion (Figure 6.6).



	Pre-surgery	3-month	6-month	12-month
None or minimal	41.5	84.9	88.4	82.1
Mild	22.1	5.5	2.9	5.4
Moderate	18.2	6.9	2.9	5.4
Severe	18.2	2.7	5.8	7.1

Figure 6. 6: Stacked bar chart illustrating the changes in the percentage of participants with none or minimal, mild, moderate and severe depressive symptomatology in the first year following bariatric surgery.

There was no significant difference in %WL at all time points post-surgery between participants with preoperative no or minimal to mild versus participants with moderate to severe depressive symptomatology. Although not statistically, participants with no or minimal to mild depressive symptomatology had higher %WL compared to participants with moderate to severe depressive symptomatology at 3-month (14.6 ± 3.9 versus 11.5 ± 2.4%, p=0.06) and 12-month post-surgery (25.3 ± 8.6 versus 21.1 ± 5.4%, p=0.21). In contrast, at 6-month post-surgery, participants with no or minimal to mild depressive symptomatology had significantly higher %WL compared to participants with moderate to severe depressive symptomatology (21.3 ± 5.2 versus 15.6 ± 2.7%, p=0.001). A further exploratory analysis showed that there were no significant associations between the magnitude of weight loss and the change in total BDI-II scores at 3- (β=-0.01; p=0.757), 6- (β=-0.07; p=0.293) and 12-month (β=-0.09; p=0.342) after surgery.

Following surgery, participants with no or minimal to mild depressive symptomatology had better HRQoL compared to their counterparts. Participants with moderate to severe depressive symptomatology had significant lower EQ-5D-index, EQ-VAS and IWQOL-Lite, total score and all of the individual subscales (Table 6.4).

Table 6. 4: The difference in HRQoL between participants with post-surgery no or minimal to mild depression and participants with moderate to severe depression assessed using EQ-5D-3L and IWQOL-Lite.

	No or minimal to mild depression	**Moderate to severe depression**	**p-value**
3-month	***n*=64**	***n*=7**	
EQ-5D-index	0.90 ± 0.15	0.63 ± 0.21	<0.001
EQ-VAS	80.0 ± 13.9	67.9 ± 15.0	0.03
IWQOL-Lite total	81.8 ± 14.2	49.2 ± 13.5	<0.001
Physical function	83.9 ± 14.1	61.0 ± 20.3	<0.001
Self-esteem	75.7 ± 18.8	37.7 ± 18.9	<0.001
Sexual life	79.5 ± 19.6	47.4 ± 23.9	<0.001
Public distress	82.1 ± 20.4	43.6 ± 19.1	<0.001
Work	88.5 ± 15.5	45.6 ± 27.4	<0.001
6-month	***n*=63**	***n*=6**	
EQ-5D-index	0.89 ± 0.18	0.67 ± 0.19	<0.01
EQ-VAS	82.7 ± 12.2	60.8 ± 10.2	<0.001
IWQOL-Lite total	88.7 ± 12.3	55.3 ± 10.7	<0.001
Physical function	89.7 ± 13.2	76.9 ± 17.0	<0.05
Self-esteem	84.0 ± 17.4	33.3 ± 11.2	<0.001
Sexual life	87.2 ± 17.3	38.6 ± 30.5	<0.001
Public distress	90.4 ± 14.7	50.8 ± 13.6	<0.001
Work	93.2 ± 12.6	56.3 ± 19.0	<0.001
12-month	***n*=49**	***n*=7**	
EQ-5D-index	0.89 ± 0.18	0.55 ± 0.34	<0.001
EQ-VAS	88.2 ± 10.7	70.0 ± 14.4	<0.001
IWQOL-Lite total	92.3 ± 10.4	58.7 ± 13.2	<0.001
Physical function	91.4 ± 10.9	69.2 ± 16.1	<0.001
Self-esteem	89.0 ± 16.8	47.4 ± 19.7	<0.001
Sexual life	93.1 ± 12.2	41.7 ± 33.0	<0.001
Public distress	95.6 ± 9.0	62.9 ± 12.2	<0.001
Work	96.4 ± 10.3	59.2 ± 23.9	<0.001

Note: BDI-II, Beck Depression Inventory-II; HRQoL, health-related quality of life; IWQOL-Lite, Impact of Weight on Quality of Life-Lite; *n*, number; VAS, visual analogue scale.

6.3.6 Correlation between EuroQol, IWQOL-Lite and BDI-II scores

The HRQoL assessed using EuroQol and IWQOL-Lite showed significant moderate to strong correlations both at pre- and post-surgery. Similarly, significant negative correlations were also observed between BDI-II scores and EuroQol as well as IWQOL-Lite both pre- and post-surgery (Table 6.5).

Table 6. 5: Correlation between EuroQol, IWQOL-Lite and BDI-II at all study time points analysed using Pearson's Correlation. Data are expressed as correlation coefficient.

	EQ-5D-index	EQ-VAS	BDI-II
Pre-surgery			
EQ-5D-index			-0.5*
EQ-VAS			-0.27**
IWQOL-Lite total	0.42*	0.54*	-0.67*
3-month			
EQ-5D-index			-0.6*
EQ-VAS			-0.42*
IWQOL-Lite total	0.54*	0.48*	-0.66*
6-month			
EQ-5D-index			-0.5*
EQ-VAS			-0.54*
IWQOL-Lite total	0.39*	0.57*	-0.73*
12-month			
EQ-5D-index			-0.55*
EQ-VAS			-0.62*
IWQOL-Lite total	0.59*	0.66*	-0.84*

Note: *indicates $p<0.001$ and **indicates $p<0.05$. BDI-II, Beck Depression Inventory-II; IWQOL-Lite, Impact of Weight on Quality of Life-Lite; VAS, visual analogue scale.

6.4 Discussion

This study aimed to assess the impact of bariatric surgery upon HRQoL and mental health. Additionally, this study also aimed to investigate whether the changes in these parameters were mediated by factors such as the weight loss magnitude, type of surgery undertaken, and time spent on physical activity levels and sedentary behaviour. From the present cohort, we found that HRQoL and mental health improved significantly in the first year post-surgery. The peak improvement in parameters assessed differed across instruments used, with the magnitude of improvement being highest in the first 3-month post-surgery. Importantly, %WL, type of surgery and time spent on MVPA were found to mediate the improvement in HRQoL depending upon the time point post-surgery. Furthermore, having moderate to severe depressive symptomatology 6 months after surgery was associated with less weight loss than those with no or minimal to mild depressive symptomatology.

Despite being simple and quick to use with high completion rates (Devlin and Brooks, 2017), limited studies have used the EQ-5D-3L questionnaire to assess the changes in HRQoL following bariatric surgery (Date *et al.*, 2013, Mar *et al.*, 2013, Ribaric *et al.*, 2013, Warkentin *et al.*, 2014). In the UK, as recommended by NICE, the EuroQol is the preferred HRQoL instrument for health economic evaluation (NICE, 2019). Prior to undergoing bariatric surgery, patients in the present cohort had an impaired HRQoL with a reported pre-surgery EQ-5D-index score of 0.68 ± 0.29, which was below the UK general practice reference group of patients with normal BMI, EQ-5D-index score of 0.80 ± 0.22 (Sach *et al*., 2007). Our findings corroborated with the previous studies, which also reported the pre-surgery EQ-5D-index scores that ranged between 0.56 to 0.69 (Mar *et al.*, 2013, Ribaric *et al.*, 2013, Warkentin *et al.*, 2014). Following bariatric surgery, the EQ-5D index score of the present cohort improved significantly to 0.85 ± 0.23 at 12-month post-surgery, slightly above the aforementioned reference UK range for patients with normal BMI. Also, the EQ-VAS score of 85.9% reported at 12-month post-surgery is also slightly higher than the UK adult general population mean score of 82.8%. (Kind *et al*., 1998). Although not at the same post-surgery time point, the EQ-5D-index reported in the present study is quite similar to the previous studies that reported a utility index of 0.85 ± 0.26 and 0.84 ± 0.21 at 2 and 3 years following bariatric surgery, respectively (Mar *et al.*, 2013, Ribaric *et al.*, 2013). As such, when assessed using the EQ-5D-index, bariatric surgery leads to a sustained short to medium term improvement in HRQoL.

Consistent with the study by Date *et al.*, we also found that both the pain/discomfort and anxiety/depression domains of EQ-5D improved significantly following surgery (Date *et al.*, 2013). However, we did not observe any significant improvement in the self-care domain as observed by Date *et al.*, instead, the mobility domain of the present cohort improved significantly post-surgery. This result agrees with our finding in Chapter 5, which shows that patients' functional capacity, assessed by using 6MWT and STS-test, improved significantly in the first postoperative period. The small variability between our findings and the study by Date *et al.* on the changes in some of the health dimensions might be explained by the 3-level version that is less sensitive to small changes and prone to have a ceiling effect (maximum score) compared to the new 5-level version. Hence, future studies should adopt the 5-level version as it has been recently validated in patients undergoing bariatric surgery (Fermont *et al.*, 2017).

IWQOL-Lite, on the other hand, is the most commonly used obesity-specific questionnaire to assess HRQoL in bariatric surgery (Kolotkin and Andersen, 2017). Not only does this questionnaire cover specific aspects that are particularly crucial in people living with obesity, such as body image and social stigma, but it is also more sensitive to small changes in QoL compared to the generic questionnaire (Kolotkin and Andersen, 2017). Prior to surgery, the lowest reported scale was for self-esteem and physical function, the latter has been discussed thoroughly in the previous chapter. Poor self-esteem often caused by body image dissatisfaction is very common among people seeking bariatric surgery, which is linked to poorer QoL (Hrabosky *et al.*, 2008). Furthermore, in the present cohort, higher pre-surgery BMI is associated with poorer physical function score, and it is also linked to a lower score for the public distress scale. Indeed, it has been previously reported that weight-related stigmatisation experienced by bariatric surgery candidates was associated with poorer QoL coupled with greater symptoms of depression (Sarwer *et al*., 2008a).

Following bariatric surgery, significant improvements were reported in all IWQOL-Lite scales that peaked at 12-month post-surgery which is consistent with the results from a systematic review (Raaijmakers *et al*., 2017). Despite a significant improvement in all scales, the score for self-esteem remained the lowest at all time points post-surgery. Whether this improvement is sustained over the long-term needs to be explored further as concerns regarding excess skin following substantial weight loss could impact upon body image; hence the overall self-esteem (Ivezaj and Grilo, 2018). Overall, 98.2% of participants achieved the MCID for IWQOL-Lite which is above and beyond the proportion of patients achieving MCIDs for EQ-5D-index and EQ-VAS, 67.9% and 83.9%, respectively. This larger post-surgery effect size produced by the obesity-specific questionnaire compared to the generic questionnaire is consistent with a conclusion made in a systematic review of reviews (Kolotkin and Andersen, 2017). Despite the difference in the effect size, the strong correlation between the IWQOL-Lite and EuroQol scores as observed in the present study has confirmed the reliability of EuroQol to assess the changes in generic HRQoL from pre- to post-bariatric surgery.

In the present cohort, several factors that mediated the improvement in HRQoL following bariatric surgery were identified, including %WL, type of surgery and time spent on MVPA. Higher %WL at 3-month post-surgery significantly corresponds to higher total IWQOL-Lite scores and some of its subscales (physical function, self-esteem, and public distress). This might be explained by the rapid weight loss magnitude in the earlier post-surgery period as this significant association did not sustain over time as the weight loss magnitude started to slow down beyond 3-month post-surgery. Conversely, Monpellier *et al*. reported an association between higher percentage total weight loss with better HRQoL at 15 and 24 months after RYGB (Monpellier *et al*., 2017). This contrast observation might be due to the difference in the metric used to report post-bariatric weight loss outcome.

To date, no published studies have reported the different HRQoL outcomes based on surgical procedures. In the present cohort, we found that SG and OAGB are superior to RYGB in relation to HRQoL at 3- and 6-month post-surgery. Lower complication rates in SG and OAGB compared to RYGB might have explained the differences although, in the present study, we did not collect additional data regarding post-surgery complications to further investigate the association (Husain *et al*., 2018, Magouliotis *et al*., 2019). Nevertheless, an earlier study has shown that patients experiencing post-bariatric complications reported lower HRQoL scores (Rea *et al*., 2007). Our preliminary results, however, should be interpreted with caution as this study is not powered to detect the difference in HRQoL between surgical procedures. There are currently two ongoing RCTs, with HRQoL as one of the study endpoints, the By-Band-Sleeve study (*n*=1351) and the Scandinavian BEST (Bypass Equipoise Sleeve Trial) (*n*=2100). These studies will further inform the impact of a different type of surgical procedures upon HRQoL outcomes (Rogers *et al*., 2017, Hedberg *et al*., 2019).

At 12-month post-surgery, we found a significant positive association between higher time spent in MVPA with a total score of IWQOL-Lite and its subscales (physical function, sexual life and public distress) as well as the EQ-5D-index and EQ-VAS scores. Our findings, therefore, support the results from an RCT (*n*=33) that found a high-volume post-bariatric exercise programme significantly improved physical function, self-esteem, sexual life and public distress of the IWQOL-Lite scales compared to the control group (Shah *et al*., 2011). Moreover, in another study involving 62 women undergoing RYGB, those meeting the 150 mins of MVPA/week recommendation and spending higher time in light physical activity and lower time in sedentary behaviour were associated with better HRQoL (Sellberg *et al*., 2019).

In a recent systematic review and meta-analysis of RCTs, it was concluded that bariatric surgery did not improve the mental health component of QoL (Szmulewicz *et al*., 2019). However, the authors have highlighted that the included studies did not use validated measures of mental health conditions, hence limiting its interpretation. In the present cohort, using the BDI-II questionnaire, a validated tool to characterise depressive symptomatology, we found that patients' mental health condition improved steadily, at least in the first 6-month post-surgery. At 12-month post-surgery, the mean BDI-II scores, and the post-surgery proportion of patients with moderate to severe depressive symptomatology showed a minimal increment although remained below the baseline values. This slow deteriorating pattern could be attributed to later postoperative issues that negatively affect mental health, such as complications requiring further treatments, dissatisfaction with weight loss, weight regain, excess skin and/or scarring, among others (Tindle *et al*., 2010). Our finding, therefore, further aids to the existing moderate-quality evidence from an earlier systematic review by Dawes *et al*. that concluded bariatric surgery is associated with lower rates of depression post-surgery (Dawes *et al*., 2016).

To date, there are inconsistent findings as to whether the preoperative mental health conditions have an impact upon postoperative weight loss outcomes (Dawes *et al*., 2016). In the present cohort, we found that the pre-surgery depressive symptomatology did not affect weight loss outcomes, which is in line with the findings from previous studies that used the same instrument to measure depressive levels (Odom *et al*., 2010, White *et al*., 2015). In contrast, we found that post-surgery moderate to severe depressive symptomatology, rather than the pre-surgery, was associated with lower %WL in the first postoperative period, with the difference appearing to be significant at 6-month post-surgery. In a previous study with a larger sample size (n=357) and longer duration, White *et al*. showed that post-surgery depressive symptoms are significantly associated with poorer weight loss outcomes at 6- and 12-month following surgery, although this association was not observed at 24 months post-surgery (White *et al*., 2015). We did not find any significant association between weight loss magnitude and improvement in the BDI-II score, contrasting to what has been previously reported (Dixon *et al*., 2003). Therefore, whether the association between post-surgery depression and weight loss is bidirectional remain inconclusive.

Another relevant finding observed is the link between post-surgery moderate and severe depression with poorer HRQoL. In addition, higher BDI-II scores at all time points post-surgery were significantly associated with lower HRQoL. This finding is in line with a study by Dixon *et al*. that reported high BDI-II scores correlated with poorer physical and mental QoL measures of the SF-36 questionnaire (Dixon *et al*., 2003). In another study evaluating the predictors of HRQoL changes in 154 patients undergoing RYGB and SG, higher pre-surgery depression severity was associated with lower post-surgery HRQoL score. Also, the changes in the BDI-II scores from pre- to post-surgery positively predicted HRQoL scores, assessed using the Short Form Health Survey-12 questionnaire (Peterhansel *et al*., 2017). Taken together, these findings underscore the importance of screening patients regularly for depression so that psychological support can be provided accordingly.

This study is not without limitations. During the COVID-19 pandemic, the lockdown may have impacted upon how patients perceived and felt about their health, physically and mentally. Therefore, the present results should be interpreted with caution. Also, that associations observed in the present study do not identify causation and do not describe the direction of the relationship.

6.5 Conclusions

In conclusion, the clinical effectiveness of bariatric surgery as reported in Chapters 4 and 5 corresponds very well with PRO as assessed using a combination of the generic and obesity-specific QoL assessment tools and mental health questionnaire. However, post-surgery improvement in HRQoL and mental health appeared to be variable with a small subset of participants are still experiencing issues in some components of the health dimensions such as pain/ discomfort, self-esteem, and anxiety/depression. Modifiable factors (such as engagement in MVPA) appeared to positively influence HRQoL. They should, therefore, be emphasised following surgery. Using the PRO assessment tools will enable the identification of health domains that need additional attention post-surgery. Enhancing post-surgery patient-centred care through targeted intervention will not only help to maximise the beneficial outcome of bariatric surgery but indirectly optimise resource allocation and utilisation.

Chapter 7

The impact of a combined nutritional-behavioural and supervised exercise intervention on weight loss and health outcomes following bariatric surgery: The BARI-LIFESTYLE randomised controlled trial[22]

7.1 Introduction

The results from the BARI-LIFESTYLE observational study as reported in Chapters 4, 5 and 6 have shown that bariatric surgery, as delivered in the UK healthcare setting, leads to significant weight loss, remission or improvement of comorbidities, improvement in physical function and strength as well as HRQoL and mental health. Unfortunately, the results have also revealed that 35.1% of patients experienced suboptimal weight loss, defined as weight loss less than 20% at 12-month post-surgery (Corcelles *et al*., 2016). Importantly, the rapid weight loss in the first 6-month post-

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[22]The work related to this chapter has been accepted for oral presentation for the best abstract session at the European Congress of Obesity 2022, Maastricht, The Netherlands, and available in Appendix 22.

surgery is also accompanied by the inevitable loss of fat-free mass with a significant declined in BMD observed at 12-month post-surgery. As described in Chapter 2, adhering to the post-bariatric lifestyle recommendations encompassing dietary intake, vitamin and mineral supplementation and physical activity is crucial in optimising weight loss and counteracting the aforementioned undesirable adverse outcomes. However, most patients find it difficult to adapt to the dramatic lifestyle changes required following surgery (Sheets *et al*., 2015, Hood *et al*., 2016, Coulman *et al*., 2020).

In the UK, the standard post-surgery care includes a few regular follow-ups with the bariatric team that mainly consists of the bariatric surgeon, dietitian, specialist nurse, and if indicated, the psychologist. However, the frequency of follow-up varies greatly across surgical centres (National Confidential Enquiry into Patient Outcome and Death, 2012). Some centres, albeit very rare, do provide support in a form of an exercise programme often run by the physiotherapist. In general, the frequency of follow-up is more in the first year than in the second postoperative year before patients are discharged to their general practitioner. Despite this, a recent qualitative study exploring patients' experiences of post-bariatric follow-up care from two UK bariatric centres found that patients expressed a sense of 'abandonment' and 'isolation' following surgery. They reported that the service was not set up to support them adequately with a lack of information and guidance about life following surgery (Coulman *et al*., 2020). Indeed, it has been previously reported that the lack of contact with the healthcare professionals following surgery is associated with poor outcomes (Endevelt *et al*., 2013).

The evidence regarding the benefits of engaging in physical activity following bariatric surgery is growing. Not only does performing regular physical activity aid in weight loss and maintenance, but it also helps in inducing further fat mass loss, mitigating BMD loss, and improving physical fitness (Coen and Goodpaster, 2016). However, our finding in Chapter 5 was that patients did not increase their physical activity and spent higher time in sedentary behaviour. In addition, despite a substantial weight loss, a small subset of patients still experienced functional limitations mainly caused by physical pain. This fact is supported further by the evidence from Chapter 6, which found that approximately 30% of patients still reported having some issues related to pain/ discomfort throughout the first postoperative year as assessed using the EQ-5D-3L questionnaire. As reported in a qualitative study, barriers such as fear of pain and/or injury continue to persist post-surgery which prevents patients to engage in physical activity (Zabatiero *et al*., 2018). In other qualitative studies, patients expressed the need for support from exercise professionals to provide them with tailored exercise prescriptions and help them manage their exercise behaviour after surgery (Peacock *et al.*, 2014, Wiklund *et al.*, 2014).

In view of the importance of adhering to the post-bariatric lifestyle recommendations coupled with the comprehensive support required by patients, a post-surgery lifestyle programme encompassing nutritional-behavioural and supervised exercise sessions is needed. However, implementing such programmes as part of a standard care post-surgery will incur additional costs to the NHS and hence its efficacy needs to be evaluated first in a real-world clinical setting. Furthermore, patients' views and acceptance of such service needs to be explored and taken into consideration. The need for research study in this area is in line with the recommendation by NICE (NICE, 2014a) and the recent two systematic reviews (Bellicha *et al*., 2021, Julien *et al*., 2021) to further evaluate the impact of a post-surgery lifestyle intervention programme as an adjunct therapy to bariatric surgery. Therefore, the objectives of this study are:

1. To compare the post-surgery %WL between people receiving standard care and people receiving standard care plus a lifestyle intervention programme at six

months after surgery, relative to baseline pre-surgery. This is the primary outcome of the BARI-LIFESTYLE trial.

2. To compare the post-surgery %WL between people receiving standard care and people receiving standard care plus a lifestyle intervention programme in the first year of surgery, relative to the baseline pre-surgery.
3. To compare between groups, the proportion of participants with suboptimal weight loss, defined as weight loss less than 20% at 12-month post-surgery (Corcelles *et al*., 2016).
4. To compare the changes in obesity-associated comorbidities (T2D, hyperlipidaemia, hypertension, OSA) at 12-month post-surgery between people receiving standard care and people receiving standard care plus a postoperative lifestyle intervention programme, relative to baseline pre-surgery.
5. To compare the changes in fat mass and fat-free mass at 3-, 6-, and 12-month post-surgery between people receiving standard care and people receiving standard care plus a post-surgery lifestyle intervention programme, relative to baseline pre-surgery.
6. To compare between groups, the proportion of participants with excessive fat-free mass loss, defined as fat-free mass loss exceeding 35% of total weight loss at 12-month post-surgery (Nuijten *et al*., 2020).
7. To compare the changes in BMD at 12-month post-surgery between people receiving standard care and people receiving standard care plus a post-surgery lifestyle intervention programme, relative to baseline pre-surgery.
8. To compare the changes in physical activity levels, percentage achieving 150 minutes of MVPA in a week and sedentary behaviour at 3-, 6-, and 12-month post-surgery between people receiving standard care and people receiving standard

care plus a postoperative lifestyle intervention programme, relative to baseline pre-surgery.

9. To compare the changes in physical function and strength at 3-, 6-, and 12-month post-surgery between people receiving standard care and people receiving standard care plus a postoperative lifestyle intervention programme, relative to baseline pre-surgery.
10. To compare the changes in HRQoL scores at 3-, 6-, and 12-month post-surgery between people receiving standard care and people receiving standard care plus a postoperative lifestyle intervention programme, relative to baseline pre-surgery.
11. To compare the changes in characteristics of attitude and symptoms of depression at 3-, 6-, and 12-month post-surgery between people receiving standard care and people receiving standard care plus a postoperative lifestyle intervention programme, relative to baseline pre-surgery.
12. To evaluate participants' views and acceptance of the lifestyle intervention programme assessed through a feedback form.

7.2 Materials and methods

The study design and setting, eligibility criteria, participant recruitment and data collection for BIA, DXA, objective physical activity and sedentary behaviour, physical function and strength, HRQoL and participants' feedback on the lifestyle intervention programme have been described in detail in Chapter 3. Throughout the nationwide lockdown between April to July 2020, all face-to-face assessments were suspended to comply with the restrictions, which led to several missing data for BIA, DXA, 6MWT, STS and HGS tests. Nevertheless, throughout this period, we posted the ActiGraph to participants' home address with the detailed instruction on how to wear the device. When the face-to-face assessment resumed, we were unable to do the 6MWT due to the 'one-way system' implemented to keep hospital COVID-safe. During the lockdown period, the body weight and HRQoL data were collected remotely via phone or video call by which participants reported their weight measured using their own body weight scale.

7.3 Statistical and data analyses

The statistical analysis plan of the primary and secondary outcomes has been previously described in Chapter 3. Bias owing to missing data were investigated by comparing the baseline characteristics of patients (age, gender, and body weight) with and without missing values for the primary outcome and adjusted accordingly. The estimation of coefficient is reported together with an associated 95% CI. Therefore, no mathematical correction was made for multiple comparisons. A p-value for a test of the null hypothesis that the mean difference is equal to zero against a two-sided alternative is reported using a significance level of 0.05.

Data from the feedback form on the tele-counselling and exercise sessions were presented in either frequency or proportion. Specific quotations from the free text boxes were extracted to support participants' rating on particular questions. Whereas for the overall feedback on the lifestyle programme, data collected from the free text boxes that have similar meanings were grouped into categories in order to generalise and explain broader concepts and ideas. The reviewed categories were then organised into themes. Specific quotations were extracted to illustrate the themes.

7.4 Results

7.4.1 Study participants

A total of 153 patients awaiting bariatric surgery from three NHS hospitals in London were enrolled in the trial and randomised on the day of surgery. Seventy-nine participants were randomised to receive the post-surgery standard care plus lifestyle intervention (intervention group) and 74 participants were randomised to receive the post-surgery standard care (control group). A summary of the flow of participants through the trial is depicted in Figure 7.1.

Baseline characteristics of the study groups are shown in Table 7.1. Of all participants randomised, 33 were males and 120 were females with the majority were White/ White British (58.2%), followed by Black/ Black British (22.8%), Asian/ Asian British (8.5%), other ethnicities backgrounds (5.9%) and mixed race (4.6%). On the day of surgery, the mean ± SD age was 44.2 ± 10.6 years, body weight was 118.0 ±19.1 kg and BMI was 42.4 ± 5.7 kg/m^2. No significant differences in body weight and BMI were seen between groups. However, participants in the intervention group were significantly taller than those in the control group, 1.68 ± 0.08 versus 1.65 ± 0.09 metre, p=0.03, respectively. In terms of educational background, 23.5% of the participants have GCSE/O or equivalent, 22.2% have A level or equivalent qualification and 43.8% were degree holders of which 15% completed a higher degree. The majority of the type of surgical procedures undertaken were SG (54.9%) followed by RYGB (28.8%) and OAGB (16.3%). Preoperative prevalence of comorbidities includes T2D (23.5%), hypertension (34%), hyperlipidaemia (18.3%) and OSA (28.1%). Most participants enrolled were from the main trial site, that is, UCLH. Other than height differences, other demographic characteristics showed no statistically significant difference between groups.

Retention rates for the intervention versus control groups were 91.1% versus 91.9%; p=0.87, 87.3% versus 87.8%; p=0.92 and 88.6% versus 74.3%; p=0.02 at 3-, 6-, and 12-month post-surgery, respectively. Throughout the trial period, seven participants withdrew due to pregnancy (*n*=4) and personal reasons (*n*=3). For the primary outcome analysis, a total of 44 participants in the intervention group and 47 participants in the control group that have available body weight data assessed using BIA were included in the ITT analysis. Whereas the remaining 30 participants with self-reported body weight collected remotely during the COVID-19 pandemic were included in a sensitivity analysis of the primary outcome analysis. Overall, the mean ± SD time intervals between the day of surgery to 3-, 6- and 12-month for all participants included in the analysis were 13.4 ± 1.3, 26.5 ± 1.4 and 52.4 ± 1.7 weeks, respectively. In addition, a sensitivity analysis showed that none of the baseline variables such as age, gender and body weight was related to the loss to follow-up at the primary outcome time point.

Of 79 participants allocated to the intervention group, three participants did not consent to receive the allocated lifestyle intervention, of which included in the ITT analysis. Two participants stated that they could not commit to the programme due to work demands and personal reasons and the third participant did not state any reason. Of all participants who consented to take part in the lifestyle programme, one participant could not be reached post-surgery by the research team hence did not receive the lifestyle programme which was later withdrawn from the trial. Therefore, a total of 75 participants received the allocated intervention. The mean number of tele-counselling sessions attended was 13 out of 17 sessions, by which 90.7% of participants completed more than half of the total session. Whereas for the supervised exercise session, 20 out of the 75 participants did not enrol in the programme. The common reasons stated were time commitments associated with family and work responsibilities, preferring to exercise on their own and inconvenience gym locations and exercise class schedules. During the COVID-19 pandemic, 16 participants were invited to complete the exercise sessions virtually and this is described in detail in Chapter 8. Overall, for the supervised exercise component, the mean number of attendance by each participant throughout the programme was 8 out of 12 classes, by which 76.4% of the enrolled participants completed more than half of the total exercise classes.

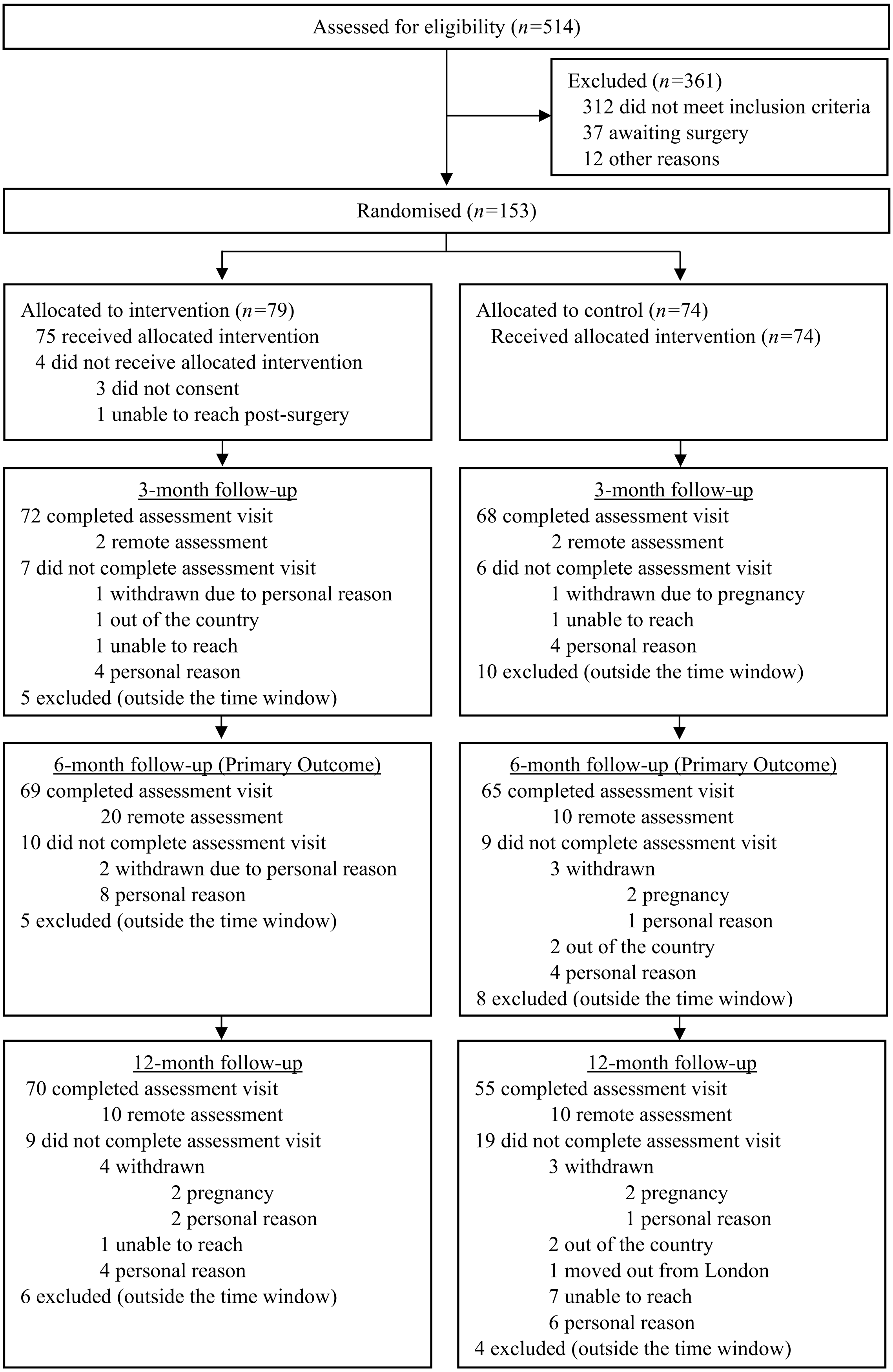


Figure 7. 1: Flow of participant enrolment, group allocation and follow-up.

Table 7. 1: Baseline characteristics of study participants

Participant characteristics	**All**	**Intervention**	**Control**	**p-value**
n	153	79	74	
Age (years)	44.2 ± 10.6	44.8 ± 10.8	43.6 ± 10.5	0.48
Gender, *n* (%)				
Male	33 (21.6)	20 (60.6)	13 (39.4)	0.24
Female	120 (78.4)	59 (49.2)	61 (50.8)	
Menopause, *n* (%)	29 (24.2)	15 (51.7)	14 (48.3)	0.83
Weight (kg)	118.0 ± 19.1	119.1 ± 18.2	116.8 ± 20.1	0.47
Height (m)	1.67 ± 0.09	1.68 ± 0.08	1.65 ± 0.09	0.03
BMI (kg/m^2)	42.4 ± 5.7	42.1 ± 5.8	42.7 ± 5.7	0.52
Type of Surgery, *n* (%)				
RYGB	44 (28.8)	24 (54.5)	20 (45.5)	
OAGB	25 (16.3)	13 (52)	12 (48)	0.89
SG	84 (54.9)	42 (50)	42 (50)	
Surgery Centre, *n* (%)				
UCLH	70 (45.7)	37 (52.9)	33 (47.1)	
Whittington	42 (27.5)	21 (50)	21 (50)	0.96
Homerton	41 (26.8)	21 (51.2)	20 (48.8)	
Ethnicity, *n* (%)				
White/ White British	89 (58.2)	43 (48.3)	46 (51.7)	
Mixed race	7 (4.6)	4 (57.1)	3 (42.9)	
Asian/ Asian British	13 (8.5)	7 (53.8)	6 (46.2)	0.84
Black/ Black British	35 (22.8)	19 (54.3)	16 (45.7)	
Other Ethnicity	9 (5.9)	6 (66.7)	3 (33.3)	
Education level, *n* (%)				
No qualification	9 (5.9)	6 (66.7)	3 (33.3)	
GCSE/O equivalent	36 (23.5)	14 (38.9)	22 (61.1)	
A level equivalent	34 (22.2)	16 (47.1)	18 (52.9)	0.24
University degree	44 (28.8)	24 (54.5)	20 (45.5)	
Higher degree	23 (15.0)	16 (69.6)	7 (30.4)	
Other	7 (4.6)	3 (42.9)	4 (57.1)	
Marital status, *n* (%)				
Single	51 (33.4)	23 (45.1)	28 (54.9)	
Married/lives with a partner/ civil partnership	79 (51.6)	45 (57)	34 (43)	0.59
Separated/ divorced	19 (12.4)	9 (47.4)	10 (52.6)	
Widow	4 (2.6)	2 (50)	2 (50)	
Employment status, *n* (%)				
Employed	106 (69.3)	55 (51.9)	51 (48.1)	
Unemployed	31 (20.2)	14 (45.2)	17 (54.8)	0.53
Others	16 (10.5)	10 (62.5)	6 (37.5)	
Smoking status, *n* (%)				
Current smoker	1 (0.7)	0	1 (100)	
Past smoker	71 (46.4)	38 (53.5)	33 (46.5)	0.55
Never	81 (52.9)	41 (50.6)	40 (49.4)	
Comorbidities, *n* (%)				
T2D	36 (23.5)	19 (52.8)	17 (47.2)	0.88
Hypertension	52 (34.0)	31 (59.6)	21 (40.4)	0.16
Hyperlipidaemia	28 (18.3)	12 (42.9)	16 (57.1)	0.30
OSA	43 (28.1)	27 (62.8)	16 (37.2)	0.08

Note: BMI, Body Mass Index; *n*, number; OAGB, one anastomosis gastric bypass; OSA, obstructive sleep apnoea; RYGB, Roux-en-Y gastric bypass; SG, sleeve gastrectomy; T2D, type 2 diabetes; UCLH, University College London Hospitals.

7.4.2 The impact of a lifestyle programme on weight loss

Table 7.2 presents the data for the primary outcome, which is the %WL difference between groups at 6-month post-surgery. The table also showed the weight loss data at 3-, and 12-month post-surgery. Overall, based on the data for the ITT analysis, participants in both groups experienced a mean weight loss of 16.6 kg at 3-month, 23.8 kg at 6-month and 29.7 kg at 12-month post-surgery. These correspond to a mean %WL of 14.0% at 3-month, 20.2% at 6-month and 25.1% at 12-month post-surgery. The ITT analysis revealed no significant difference in the primary outcome, the %WL at 6-month post-surgery between the intervention versus the control groups (19.6% versus 20.7%; MD=-1.0%; 95% CI, -3.4 to 1.4; p=0.39).

In a sensitivity analysis including the self-reported body weight data collected remotely during the COVID-19 pandemic, the %WL at 6-month post-surgery between the intervention versus control groups was 20.1% versus 20.8% (MD=-0.6%; 95% CI, -2.6 to 1.4; p=0.55), respectively, also showed no significant difference. A further per-protocol analysis that only included participants in the intervention group who completed more than 50% of both the tele-counselling and supervised exercise sessions that have available body weight data assessed using BIA (n=28) was also undertaken. The result showed no significant difference in %WL at 6-month post-surgery between the intervention versus control groups, (20.7% versus 20.7%; MD=0.1%; 95% CI, -2.6 to 2.9; p=0.94), respectively. Both groups also exhibited no significant differences in all body weight parameters at 3- and 12-month post-surgery in the ITT, sensitivity, and per-protocol analyses (Table 7.2). In the ITT analysis, no difference in the proportion of participants with suboptimal weight loss at 12-month post-surgery between the intervention and control groups, 29.6% versus 31.7%, p=0.83. Similar results were found in the sensitivity and per-protocol analysis.

Table 7. 2: Intention-to-treat analysis, sensitivity analysis and per-protocol analysis of the primary outcome (weight loss outcome at 6-month post-surgery) and weight loss outcomes at 3- and 12-month post-surgery between the intervention and the control groups.

Group allocation	**Intervention**			**Control**			**p-value**		
Study time point	**3-month**	**6-month**	**12-month**	**3-month**	**6-month**	**12-month**	**Group**	**Time**	**Group x Time**
Model 1: Intention-to-treat analysis using BIA weight									
n	65	44	54	56	47	41			
Weight (kg)	102.0 ± 16.1	97.3 ± 15.8	88.3 ± 15.2*	102.9 ± 18.6	92.0 ± 18.2	88.7 ± 19.2*	0.63	<0.001	0.43
BMI (kg/m^2)	36.1 ± 5.2	34.5 ± 4.6	31.2 ± 4.6*	37.5 ± 5.6	33.8 ± 5.2	32.0 ± 5.5*	0.39	<0.001	0.57
%WL	14.2 ± 3.5	19.6 ± 6.1	24.9 ± 9.4	13.8 ± 3.7	20.7 ± 5.5	25.3 ± 8.8	0.91	<0.001	0.64
Model 2: Sensitivity analysis using BIA, DXA and self-reported weights									
n	67	64	64	58	57	51			
Weight (kg)	102.2 ± 16.0	94.9 ± 15.0	89.7 ± 15.5*	102.3 ± 18.6	91.5 ± 17.2	88.3 ± 18.0*	0.66	<0.001	0.48
BMI (kg/m^2)	36.1 ± 5.1	33.4 ± 4.6	31.5 ± 4.7*	37.2 ± 5.7	33.6 ± 5.2	32.0 ± 5.4*	0.35	<0.001	0.52
%WL	14.2 ± 3.5	20.1 ± 5.6	24.4 ± 9.0	14.0 ± 3.8	20.8 ± 5.5	24.7 ± 8.5	0.92	<0.001	0.72
Model 3: Per-protocol analysis using BIA weight									
n	39	28	33	56	47	41			
Weight (kg)	99.6 ± 13.5	94.6 ± 13.8	84.6 ± 12.9*	102.9 ± 18.6	92.0 ± 18.2	88.7 ± 19.2*	0.08	<0.001	0.28
BMI (kg/m^2)	35.1 ± 4.8	33.5 ± 4.6	30.1 ± 4.2*	37.5 ± 5.6	33.8 ± 5.2	32.0 ± 5.5*	0.60	<0.001	0.80
%WL	14.9 ± 3.6	20.7 ± 6.2	27.0 ± 8.9	13.8 ± 3.7	20.7 ± 5.5	25.3 ± 8.8	0.30	<0.001	0.46

Note: *indicates p<0.001 within group difference overtime, relative to baseline pre-surgery value. BIA, bioelectrical impedance analyser; BMI, Body Mass Index; DXA, dual-energy X-ray absorptiometry; *n*, number; %WL, percentage weight loss.

7.4.3 The impact of a lifestyle programme on the changes in comorbidities

Table 7.3 shows the changes in comorbidities in both groups. No differences were observed in the proportion of patients achieving complete and partial remission of T2D, hypertension, hyperlipidaemia and OSA at 12-month post-surgery, all p>0.05. The per-protocol analysis also showed no significant difference in comorbidities status between groups.

Table 7. 3: Intention-to-treat analysis of the changes in comorbidities between the intervention and the control groups at 12-month post-surgery, relative to baseline pre-surgery.

Comorbidities	***n* (%)**		**p-value**
	Intervention	**Control**	
Type 2 Diabetes			
Comorbidities present at baseline	19 (24.1)	17 (23.0)	0.88
Complete remission	8 (44.4)	7 (46.6)	
Partial remission	1 (5.6)	1 (6.7)	
Improved	9 (50.0)	6 (40.0)	0.94
Unchanged	0	0	
Worsened	0	1 (6.7)	
Hypertension			
Comorbidities present at baseline	31 (39.2)	21 (28.4)	0.16
Remission	8 (26.6)	7 (38.9)	
Improved	15 (50.0)	7 (38.9)	0.59
Unchanged	5 (16.7)	4 (22.2)	
Worsened	2 (6.7)	0	
Hyperlipidaemia			
Comorbidities present at baseline	12 (15.2)	16 (21.6)	0.30
Remission	4 (28.6)	3 (21.4)	
Improved	8 (57.1)	9 (64.3)	0.85
Unchanged	2 (14.3)	2 (14.3)	
Worsened	0	0	
Obstructive Sleep Apnoea			
Comorbidities present at baseline	27 (34.2)	16 (21.6)	0.08
Remission	9 (40.9)	8 (53.3)	
Improved	0	0	0.75
Unchanged	13 (59.1)	7 (46.7)	
Worsened	0	0	

Note: *n*, number.

7.4.4 The impact of a lifestyle programme on the changes in body composition

Of 153 participants in the study, 78.4% have available and valid (collected within time window) BIA measurements at 3-month post-surgery, 58.8% at 6-month post-surgery and 62.1% at 12-month post-surgery. Whereas for DXA, 62.7% of participants have available repeated measurement at 12-month post-surgery. Assessments undertaken outside the time window were excluded from the analysis. No significant differences in the baseline body composition parameters measured by BIA and DXA between groups.

Table 7.4 shows the pre- to post-surgery changes in body composition between groups. Based on the BIA data, the ITT analysis showed a significant reduction of fat mass, body fat percentage and fat-free mass in the first-year of surgery. No difference was observed in the percentage fat mass loss between the intervention and control groups throughout the study period (MD=0.8%; 95% CI, -3.7 to 2.1; p=0.60). Similarly, no difference was observed in the percentage fat-free mass loss between the intervention and control groups in the first year of surgery (MD=-0.02%; 95% CI, -1.5 to 1.5; p=0.98). The per-protocol analysis also demonstrated no significant differences in all parameters between groups. In the ITT analysis, no difference in the proportion of participants with excessive fat-free mass loss at 12-month post-surgery between the intervention and control groups, 37.0% versus 26.8%, p=0.29. The per-protocol analysis also demonstrated no significant difference.

Based on the DXA data, the ITT analysis showed a significant reduction of fat mass, body fat percentage and fat-free mass in the first-year of surgery. No difference was observed in the percentage fat mass loss between the intervention and control groups at 12-month post-surgery (MD=0.6%; 95% CI, -5.6 to 6.8; p=0.84). Similarly, no difference was observed in the percentage fat-free mass loss between the intervention and control groups at 12-month post-surgery (MD=-0.4%; 95% CI, -3.0 to 2.2; p=0.74). The per-protocol analysis also demonstrated no significant differences in all parameters between groups. In the ITT analysis, no difference in the proportion of participants with excessive fat-free mass loss at 12-month post-surgery between the intervention and control groups, 61.1% versus 54.8%, p=0.53. The per-protocol analysis also demonstrated no significant difference.

Table 7. 4: Intention-to-treat analysis and per-protocol analysis of the changes in body composition between the intervention and the control groups in the first year of bariatric surgery.

Group allocation	Intervention				Control				Group difference, p-value		
Study time point	Pre-surgery	3-month	6-month	12-month	Pre-surgery	3-month	6-month	12-month	Group	Time	Group x Time
BIA: Intention-to-treat analysis											
n	79	64	44	54	74	56	46	41			
Fat mass (kg)	56.2 ± 15.0	43.9 ± 12.7	40.6 ± 11.5	32.5 ± 10.9*	56.8 ± 14.3	46.3 ± 13.7	38.6 ± 12.4	34.1 ± 13.4*	0.64	<0.001	0.85
Body fat (%)	45.3 ± 7.3	42.5 ± 7.7	41.3 ± 7.4	36.3 ± 8.3*	46.7 ± 6.6	44.4 ± 7.7	41.3 ± 6.9	37.6 ± 8.5*	0.23	<0.001	0.29
Fat-free mass (kg)	66.8 ± 10.7	58.2 ± 9.4	56.6 ± 9.2	55.8 ± 9.7*	63.9 ± 11.6	56.6 ± 9.7	53.3 ± 9.3	54.6 ± 10.5*	0.17	<0.001	0.12
BIA: Per-protocol analysis											
n	41	39	28	33	74	56	46	41			
Fat mass (kg)	55.6 ± 13.5	42.2 ± 12.1	39.5 ± 11.4	29.9 ± 10.3*	56.8 ± 14.3	46.3 ± 13.7	38.6 ± 12.4	34.1 ± 13.4*	0.14	<0.001	0.37
Body fat (%)	45.4 ± 7.5	41.9 ± 8.4	41.3 ± 7.8	34.8 ± 8.6*	46.7 ± 6.6	44.4 ± 7.7	41.3 ± 6.9	37.6 ± 8.5*	0.12	<0.001	0.25
Fat-free mass (kg)	65.9 ± 9.9	57.4 ± 8.7	55.1 ± 8.4	54.7 ± 9.0*	63.9 ± 11.6	56.6 ± 9.7	53.3 ± 9.3	54.6 ± 10.5*	0.80	<0.001	0.55
DXA: Intention-to-treat analysis											
n	79			54	73			42			
Fat mass (kg)	53.2 ± 12.8			31.4 ± 8.8*	53.2 ± 11.7			33.4 ± 11.2*	0.50		
Body fat (%)	42.8 ± 6.0			34.9 ± 6.6*	43.8 ± 5.6			36.7 ± 7.8*	0.56		
Fat-free mass (kg)	70.3 ± 11.0			57.8 ± 10.1*	68.1 ± 12.7			56.8 ± 11.3*	0.79		
DXA: Per-protocol analysis											
n	41			34	73			42			
Fat mass (kg)	52.4 ± 10.7			29.8 ± 8.4*	53.2 ± 11.7			33.4 ± 11.2*	0.21		
Body fat (%)	42.7 ± 5.8			34.4 ± 7.2*	43.8 ± 5.6			36.7 ± 7.8*	0.49		
Fat-free mass (kg)	69.9 ± 9.7			56.2 ± 9.0*	68.1 ± 12.7			56.8 ± 11.3*	0.16		

Note: *indicates p<0.001 within group difference overtime, relative to baseline pre-surgery. BIA, bioelectrical impedance analyser; DXA, dual-energy X-ray absorptiometry; *n*, number.

7.4.5 The impact of a lifestyle programme on the changes in bone mineral density

Table 7.5 shows the changes in BMD in both groups. No significant differences in the baseline BMD between groups. At 12-month post-surgery, participants experienced BMD loss at total hip, femoral neck and lumbar spine. No differences were observed on the percentage BMD loss between the intervention and control groups at total hip (-7.8% versus -8.9%; MD=1.0%; 95% CI, -0.7 to 2.7; p=0.24), femoral neck (-5.5% versus -6.1%; MD=0.5%; 95% CI, -2.4 to 3.3; p=0.77), lumbar spine (-3.6% versus -3.3%; MD=-0.4%; 95% CI, -2.0 to 1.3; p=0.65) and whole-body BMD (1.2% versus 0.2%; MD=1.0%; 95% CI, -0.2 to 2.3; p=0.11) in the first postoperative year. Per-protocol analysis also showed similar observations except for participants in the intervention group had significantly higher percentage change in whole-body BMD compared to the control group (1.6% versus 0.2%; MD=1.5%; 95% CI, 0.1 to 2.8; p=0.04).

Table 7. 5: Intention-to-treat analysis and per-protocol analysis of the changes in bone mineral density between the intervention and the control groups in the first year of bariatric surgery.

Group allocation	**Intervention**		**Control**		**Group difference, p-value**	
Study time point	**Pre-surgery**	**12-month**	**Pre-surgery**	**12-month**	**Pre-surgery**	**12-month**
BMD (g/cm²): Intention-to-treat analysis						
n	79	54	73	42		
Total hip	1.173 ± 0.141	1.084 ± 0.141*	1.133 ± 0.107	1.031 ± 0.120*	0.06	0.35
Femoral neck	0.950 ± 0.160	0.892 ± 0.162*	0.907 ± 0.120	0.840 ± 0.116*	0.07	0.43
Lumbar spine	1.158 ± 0.159	1.127 ± 0.173*	1.108 ± 0.148	1.088 ± 0.176*	0.05	0.55
Whole-body	1.196 ± 0.107	1.208 ± 0.113**	1.185 ± 0.099	1.191 ± 0.111	0.50	0.13
BMD (g/cm²): Per-protocol analysis						
n	41	34	73	42		
Total hip	1.155 ± 0.128	1.067 ± 0.133*	1.133 ± 0.107	1.031 ± 0.120*	0.38	0.45
Femoral neck	0.919 ± 0.139	0.870 ± 0.146*	0.906 ± 0.120	0.840 ± 0.116*	0.62	0.23
Lumbar spine	1.164 ± 0.175	1.120 ± 0.182*	1.108 ± 0.148	1.088 ± 0.176*	0.09	0.86
Whole body	1.177 ± 0.092	1.190 ± 0.102**	1.185 ± 0.099	1.191 ± 0.111	0.67	0.04

Note: *indicates p<0.001 and **indicates p<0.05 within group difference relative to baseline pre-surgery. DXA, dual-energy X-ray absorptiometry; *n*, number.

7.4.6 The impact of a lifestyle programme on the changes in physical activity levels and sedentary behaviour

Twenty participants without valid baseline accelerometer data were excluded from the analysis. Reasons for missing data at any time points are (i) ActiGraph device not returned, *n*=91, (ii) missed study visit, *n*=44, (iii) did not meet the minimum wear time requirement, *n*=29, and (iv) ActiGraph not provided due to device shortfall or participants refused to wear, *n*=5. The mean ActiGraph wear time period at baseline was six days with a mean daily wear time of 15 hours. At baseline, men spent a significantly higher time in sedentary behaviour and vigorous physical activity but less time in light physical activity compared to women, all $p<0.01$. No correlation was observed between age and BMI with physical activity levels of any intensity. Overall, prior to surgery, 63.4% of waking time was spent on sedentary behaviour, 32.1% on light physical activity and only 4.5% on MVPA. Nevertheless, a total of 82% of participants achieved the WHO physical activity guidelines of a total accumulated MVPA ≥150 min/week (WHO, 2020b). At baseline, the time spent in physical activity levels and sedentary behaviour were similar in both groups, all $p>0.05$. However, a higher proportion of participants in the control group achieved MVPA ≥150 min/week ($p=0.04$).

Table 7.6 shows the pre- to post-surgery changes in physical activity levels and sedentary behaviour in both groups. In the ITT analysis, only daily steps count improved significantly over time following surgery. No differences between groups were observed in any of the parameters in the first year of surgery. Of the total daily waking period, no significant differences were observed between groups on the proportions of time spent in sedentary behaviour, light physical activity and MVPA, at all study time points. However, the proportion of participants in the control group who achieved MVPA≥150 min/week reduced significantly post-surgery, relative to baseline pre-surgery ($p<0.05$).

The proportion of participants with improvement in the accumulated total physical activity and increased time spent on sedentary behaviour post-surgery, relative to baseline pre-surgery, did not differ between groups. Similarly, the proportion of participants achieving ≥10,000 steps/day post-surgery, relative to baseline pre-surgery, did not differ between groups. The per-protocol analysis yielded similar results as in the ITT analysis.

Table 7. 6: Intention-to-treat analysis and per-protocol analysis of the changes in physical activity levels and sedentary behaviour between the intervention and the control groups in the first year of bariatric surgery.

Physical Activity Levels and Sedentary Behaviour	Intervention				Control				p-value		
	Pre-surgery	3-month	6-month	12-month	Pre-surgery	3-month	6-month	12-month	Group	Time	Group x Time
Intention-to-treat analysis											
n	70	50	49	46	63	43	36	37			
Number of valid days	6.1 ± 0.8	6.2 ± 0.8	6.1 ± 1.0	6.4 ± 0.8	6.0 ± 1.0	6.4 ± 0.7	5.9 ± 1.0	6.3 ± 1.0	0.93	0.08	0.97
Wear time (hour/day)	15.5 ± 1.3	15.9 ± 1.1	15.6 ± 1.3	15.6 ± 1.2	15.7 ± 1.2	15.6 ± 1.1	15.4 ± 1.2	15.6 ± 1.0	0.89	0.21	0.91
Sedentary (min/day)	599.0 ± 98.5	606.3 ± 80.6	603.0 ± 118.1	595.5 ± 102.0	590.0 ± 74.4	585.5 ± 98.0	561.4 ± 114.2	570.2 ± 106.2	0.20	0.14	0.19
Light physical activity (min/day)	291.7 ± 84.6	302.3 ± 76.5	289.9 ± 87.3	298.2 ± 78.5	312.6 ± 67.5	308.6 ± 87.6	320.4 ± 89.9	327.0 ± 99.2	0.10	0.80	0.09
MVPA (min/day)	41.2 ± 26.6	43.8 ± 27.0	41.3 ± 26.7	43.6 ± 28.0	44.1 ± 24.5	41.3 ± 20.0	40.7 ± 20.7	40.0 ± 22.4	0.84	0.38	0.85
Steps/day	5414 ± 2502	6555 ± 2859	6069 ± 2966	6339 ± 2985	5768 ± 1773	6070 ± 2105	6412 ± 2503	6033 ± 2633	0.85	0.04	0.82
MVPA≥150 min/week (%)	75.7	80.0	73.5	80.4	88.9[†]	86.1	86.1	70.3[a]	0.12	0.14	0.13
Per-protocol analysis											
n	39	34	32	33	63	43	36	37			
Number of valid days	6.2 ± 0.7	6.2 ± 0.8	6.2 ± 1.0	6.5 ± 0.7	6.0 ± 1.0	6.4 ± 0.7	5.9 ± 1.0	6.3 ± 1.0	0.33	0.07	0.40
Wear time (hour/day)	15.8 ± 1.0	15.8 ± 1.2	15.7 ± 1.3	15.6 ± 1.1	15.7 ± 1.2	15.6 ± 1.1	15.4 ± 1.2	15.6 ± 1.0	0.41	0.09	0.35
Sedentary (min/day)	615.2 ± 93.1	608.7 ± 74.2	618.8 ± 99.7	590.5 ± 88.3	590.0 ± 74.4	585.5 ± 98.0	561.4 ± 114.2	570.2 ± 106.2	0.06	0.05	0.05
Light physical activity (min/day)	289.1 ± 73.7	291.5 ± 66.4	278.1 ± 74.4	296.8 ± 70.1	312.6 ± 67.5	308.6 ± 87.6	320.4 ± 89.9	327.0 ± 99.2	0.07	0.30	0.07
MVPA (min/day)	45.2 ± 29.4	48.0 ± 28.2	44.4 ± 27.5	46.6 ± 29.6	44.1 ± 24.5	41.3 ± 20.0	40.7 ± 20.7	40.0 ± 22.4	0.43	0.35	0.41
Steps/day	5690 ± 2465	6854 ± 2769	6395 ± 2974	6672 ± 3020	5768 ± 1773	6070 ± 2105	6412 ± 2503	6033 ± 2633	0.39	0.04	0.45
MVPA≥150 min/week (%)	79.5	82.4	78.1	84.9	88.9	86.1	86.1	70.3	0.48	0.13	0.54

Note: [†]indicates $p<0.05$ between groups at baseline pre-surgery. [a]denotes $p<0.05$ within group difference overtime, relative to baseline pre-surgery value. MVPA, moderate-to-vigorous physical activity; *n*, number.

7.4.7 The impact of a lifestyle programme on the changes in physical function and strength

At baseline, the mean 6MWT was 420.1 metres, with values ranging between 120 and 608 metres. This is equivalent to a walking pace of 1.17 metres/second. The mean post-test heart rate was 103.3 ± 18.6 beats/min. Whereas the median rating perceived exertion was ‘somewhat strong’. Younger participants walked a greater distance compared to their older counterparts ($p<0.01$). Men had a greater walking distance than women ($p<0.01$). Whereas pre-menopausal women had better walking capacity compared to their post-menopausal counterparts (420.8 ± 52.1 versus 386.5 ± 74.2 metres, $p<0.01$). Only 27.5% of participants were able to walk more than 450 metres. This reference cut-off point is based on the 6MWT walking distance ranges from 450 to 800 metres in healthy subjects aged 20 to 75 years old (Camarri *et al.*, 2006, Chetta *et al.*, 2006). Of all participants, 33.6% reported physical problems when performing the test with the frequency of complaint following this order: knee pain (n=16), back pain (n=12), hip pain (n=10), ankle pain (n=6), calf pain (n=3), dizziness (n=3) and chest pain (n=2).

Similar to 6MWT, younger participants completed the STS-test more quickly than their older counterparts ($p<0.01$). There was no difference in the time taken to complete the test between gender ($p=0.53$) and between pre- and post-menopausal women ($p=0.24$). At baseline, men had greater absolute and relative HGS compared to women, ([44.2 ± 9.9 versus 30.6 ± 6.7 kg, $p<0.001$] and [1.1 ± 0.3 versus 0.7 ± 0.2 strength/BMI, $p<0.001$]), respectively. Between pre- and post-menopausal women, no significant differences in absolute HGS (30.9 ± 6.5 versus 29.4 ± 7.4 kg, $p=0.43$, respectively) and relative HGS were observed (0.7 ± 0.2 versus 0.7 ± 0.2 strength/BMI, $p=0.34$, respectively). No significant differences in the baseline 6MWT, STS-test and HGS between groups.

Table 7.7 shows the pre- to post-surgery changes in physical function and strength in both groups. In the ITT analysis, significant improvements in 6MWT, post-6MWT heart rate and rating perceived exertion were seen following surgery. However, participants in the intervention group had significantly higher improvement in 6MWT in the first year post-surgery as opposed to the control group (MD=+19.6 metres; 95% CI, 0.9 to 38.2; p=0.04). In particular, a significantly higher proportion of participants in the intervention group were able to walk more than 450 metres at 6-month post-surgery compared to the control group, 85.1% versus 66.7%, p=0.03 (Figure 7.2). No differences were observed in the improvement of post-6MWT heart rate, rating perceived exertion and the proportion of participants with physical complaint between groups.

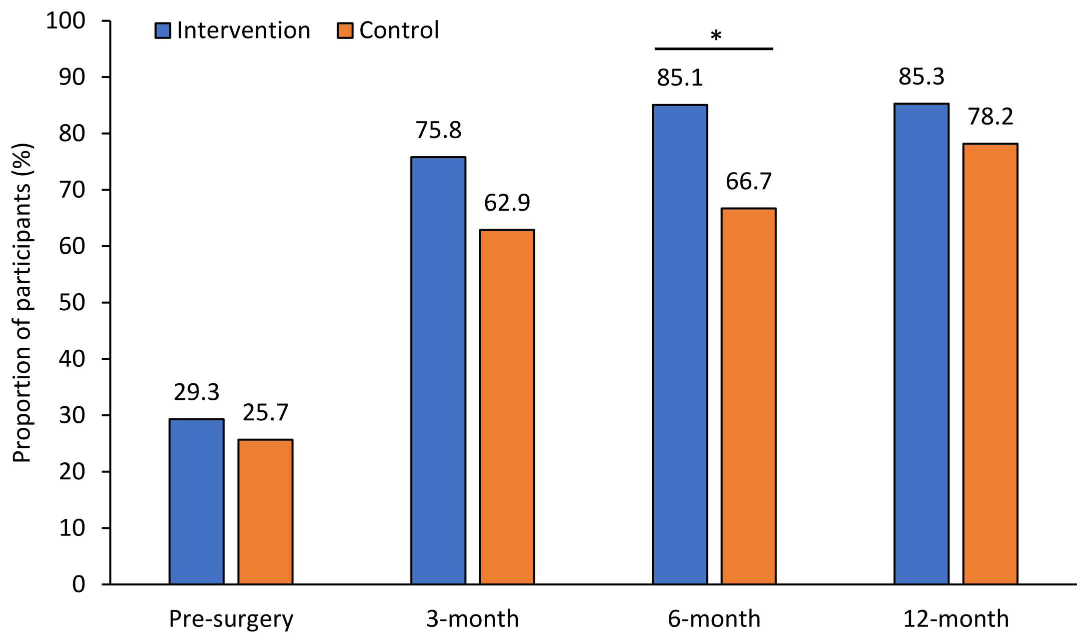
Significant improvements were also seen in the STS-test and relative HGS following surgery but did not reach statistically significant differences between groups. Participants in the intervention group were able to maintain the absolute HGS following surgery. However, participants in the control group experienced a significant reduction in the absolute HGS post-surgery, relative to baseline pre-surgery ($p<0.05$).

The per-protocol analysis revealed similar results as in the ITT analysis except for no difference in 6MWT between groups. Interestingly, participants in the intervention group had significantly higher relative HGS in the first year post-surgery as opposed to the control group (MD=+0.1 kg/BMI; 95% CI, 0.0 to 0.2; p=0.02).

Table 7. 7: Intention-to-treat analysis and per-protocol analysis of the changes in physical function and strength between the intervention and the control groups in the first year of bariatric surgery.

Physical function and strength	Intervention				Control				p-value		
	Pre-surgery	3-month	6-month	12-month	Pre-surgery	3-month	6-month	12-month	Group	Time	Group x Time
Intention-to-treat analysis											
n	78	69	48	34	74	63	55	25			
6MWT (m)	428.4 ± 64.7	492.5 ± 71.0	506.4 ± 70.1	530.3 ± 85.5[c]	411.4 ± 56.9	472.2 ± 60.0	482.9 ± 71.8	492.4 ± 52.7[c]	0.03	<0.001	0.04
Heart rate (beats/min)	103.8 ± 18.9	103.5 ± 17.7	98.4 ± 20.9	91.9 ± 17.9[c]	102.9 ± 18.4	101.5 ± 19.5	95.9 ± 21.0	84.6 ± 18.6[c]	0.35	<0.001	0.33
Borg's scale (0-10)*	4 (1, 7)	3 (1, 7)	2 (1, 9)	2 (1, 6)[c]	4 (1, 7)	3 (1, 6)	2 (1, 6)	1, (1, 6)[c]	0.99	<0.001	0.98
n	78	70	49	67	72	64	56	50			
STS-test (secs)	11.1 ± 5.6	9.5 ± 4.5	8.4 ± 2.9	7.8 ± 3.2[c]	10.5 ± 3.4	8.2 ± 2.0	8.3 ± 3.0	7.6 ± 2.4[c]	0.22	<0.001	0.16
n	79	70	49	67	74	65	52	50			
HGS-dominant (kg)	34.6 ± 9.3	34.4 ± 8.8	34.6 ± 7.1	34.4 ± 7.8	32.4 ± 9.3	32.7 ± 8.7	31.3 ± 6.9	31.7 ± 9.5[a]	0.11	0.06	0.11
Relative HGS (RHGS) (kg/BMI)	0.8 ± 0.3	1.0 ± 0.3	1.0 ± 0.3	1.1 ± 0.3[c]	0.7 ± 0.2	0.9 ± 0.3	0.9 ± 0.2	1.0 ± 0.4[c]	0.06	<0.001	0.09
Per-protocol analysis											
n	41	39	29	19	74	63	55	25			
6MWT (m)	419.0 ± 70.0	487.4 ± 80.1	498.6 ± 83.3	518.3 ± 106.8[c]	411.4 ± 56.9	472.2 ± 60.0	482.9 ± 71.8	492.4 ± 52.7[c]	0.19	<0.001	0.26
Heart rate (beats/min)	103.1 ± 17.1	103.7 ± 16.9	96.7 ± 18.1	92.2 ± 17.2[c]	102.9 ± 18.4	101.5 ± 19.5	95.9 ± 21.0	84.6 ± 18.6[c]	0.52	<0.001	0.47
Borg's scale (0-10)*	4 (1, 7)	4 (1, 6)	2 (1, 9)	1, (1, 6)[c]	4 (1, 7)	3 (1, 6)	2 (1, 6)	1, (1, 6)[c]	0.74	<0.001	0.78
n	41	39	30	40	72	64	56	50			
STS-test (secs)	11.6 ± 6.8	9.4 ± 5.0	8.6 ± 2.8	7.9 ± 3.2[c]	10.5 ± 3.4	8.2 ± 2.0	8.3 ± 3.0	7.6 ± 2.4[c]	0.30	<0.001	0.18
n	41	39	30	40	74	65	52	50			
HGS-dominant (kg)	36.2 ± 8.7[†]	35.2 ± 7.6	34.9 ± 6.8	34.1 ± 7.0[b]	32.4 ± 9.3[†]	32.7 ± 8.7	31.3 ± 6.9	31.7 ± 9.5[a]	0.06	<0.01	0.05
Relative HGS (RHGS) (kg/BMI)	0.9 ± 0.2[†]	1.0 ± 0.3	1.1 ± 0.3	1.2 ± 0.3[c]	0.7 ± 0.2[†]	0.9 ± 0.3	0.9 ± 0.2	1.0 ± 0.4[c]	<0.01	<0.001	0.02

Note: *indicates median and interquartile range. [†]indicates p<0.05 between groups at baseline pre-surgery. [a]denotes p<0.05, [b]denotes p<0.01 and [c]denotes p<0.001 within group difference overtime, relative to baseline pre-surgery value. 6MWT, 6-minute walk test; HGS, handgrip strength test; *n*, number; STS-test, sit-to-stand test; RHGS, relative handgrip strength.



Intervention (*n*)	78	69	48	34
Control (*n*)	74	63	55	25

Figure 7. 2: Proportion of participants achieved more than 450 metres walking distance in the 6MWT. *indicates p<0.05 between groups.

7.4.8 The impact of a lifestyle programme on the changes in health-related quality of life and mental health

The questionnaires completion rates were 91.5%, 89.5% and 81.7% at 3-, 6- and 12-month post-surgery, respectively. The mean baseline EQ-5D-index was 0.70 ± 0.26 and the mean baseline EQ-VAS was 60.7 ± 19.9%. Also, at baseline, only 31 (20.3%) participants had EQ-5D-index score of 1.0, where 1.0 represents perfect health and 0 represents death. Specifically, based on individual dimension of EQ-5D, the proportions of patients who reported having problems with pain/ discomfort were 66.6%, anxiety/ depression were 45.1%, mobility issues were 41.8%, problem performing usual activities such as work, study, housework, family or leisure activities were 37.3% and having issues with self-care were 10.5%. Participants with older age had significantly lower baseline

EQ-5D-index scores compared to their younger counterparts, $p<0.05$. No associations were observed between both the EQ-5D-index and EQ-VAS scores with baseline BMI. Both males and females reported similar scores in both parameters, $p>0.05$. No significant differences in the baseline EQ-5D-index and EQ-VAS scores between groups.

The mean baseline total score for IWQOL-Lite was 47.7 ± 20.0%, where 100 represents the 'best' score and 0 represents the 'worst' score. A total of 56.9% of participants had a total score below 50%. Specifically, based on the subscales of IWQOL-Lite, the lowest score was for the self-esteem scale, followed by physical function, public distress, sexual life, and work. Participants with higher baseline BMI was negatively associated with total IWQOL-Lite and its subscales (physical function, public distress, work) scores, all $p<0.05$. Furthermore, participants of advanced age had significantly lower baseline physical function scale scores than their younger counterparts, $p<0.05$. Both males and females reported similar scores in total IWQOL-Lite and all subscales, all $p>0.05$. No significant differences in the baseline total IWQOL-Lite score and all subscale scores between groups.

The mean baseline total score for BDI-II was 16.4 ± 11.1. A total of 42.5% of participants were categorised as having none or minimal depressive symptomatology, 22.8% having mild depressive symptomatology, 20.3% having moderate depressive symptomatology and 14.4% having severe depressive symptomatology. Age, baseline BMI and gender were not significantly related to the BDI-II total score, the cognitive-affective and the somatic subscales, all $p>0.05$. No difference in BMI was observed in participants with no or minimal to mild versus moderate to severe depressive symptomatology, $p>0.05$. Compared to participants with no or minimal to mild depressive symptomatology, participants with moderate to severe depressive symptomatology had significantly lower EQ-5D-index, EQ-VAS and total IWQOL-Lite and its subscales, all p<0.001. No significant differences in the baseline BDI-II total score, the cognitive-affective and the somatic subscales scores between groups.

Table 7.8 shows the pre- to post-surgery changes in HRQoL and mental health in both groups. In the ITT analysis, significant improvements in EQ-5D-index, EQ-VAS, IWQOL-Lite and BDI-II scores were seen following surgery. None of these improvements in HRQoL and mental health parameters reached a statistically significant difference between groups, in the first year of surgery. Similar improvements were seen in the five health dimensions of the EuroQol between the intervention and the control groups in the first year of bariatric surgery (Table 7.9).

No significant differences in the proportions of participants achieved the MCIDs for EQ-5D-index, EQ-VAS and IWQOL-Lite at all time points post-surgery between groups. Also, the proportion of participants with moderate to severe depressive symptomatology did not differ between groups at all time points post-surgery. The per-protocol analysis revealed similar results.

Table 7. 8: Intention-to-treat analysis and per-protocol analysis of the changes in HRQoL and mental health between the intervention and the control groups in the first year of bariatric surgery.

	Intervention				Control				p-value		
	Pre-surgery	**3-month**	**6-month**	**12-month**	**Pre-surgery**	**3-month**	**6-month**	**12-month**	**Group**	**Time**	**Group x Time**
Intention-to-treat analysis											
n	79	72	71	71	74	68	66	54			
EQ-5D-index	0.73 ± 0.23	0.83 ± 0.19	0.83 ± 0.23	0.83 ± 0.18[b]	0.68 ± 0.29	0.87 ± 0.18	0.88 ± 0.18	0.85 ± 0.23[b]	0.97	<0.001	0.87
EQ-VAS (%)	62.9 ± 20.3	74.8 ± 15.5	79.0 ± 15.2	83.5 ± 13.6[b]	58.4 ± 19.4	79.3 ± 14.2	80.8 ± 13.6	86.0 ± 12.8[b]	0.98	<0.001	0.82
IWQOL-Lite (%)	49.2 ± 19.4	72.5 ± 20.2	83.5 ± 17.6	88.1 ± 15.6[b]	46.1 ± 20.7	78.9 ± 17.1	86.1 ± 15.4	88.2 ± 15.6[b]	0.80	<0.001	0.51
Scales (%)											
Physical function	50.0 ± 21.7	76.0 ± 18.9	85.9 ± 15.7	90.2 ± 12.5[b]	46.5 ± 20.7	81.7 ± 16.1	88.8 ± 13.8	88.8 ± 13.7[b]	0.94	<0.001	0.59
Self-esteem	36.9 ± 27.1	65.6 ± 28.4	77.5 ± 24.0	81.9 ± 21.3[b]	34.7 ± 26.7	72.6 ± 20.8	80.1 ± 21.8	84.0 ± 22.3[b]	0.73	<0.001	0.48
Sexual life	52.0 ± 30.7	66.3 ± 27.7	78.1 ± 29.6	86.5 ± 23.1[b]	48.7 ± 31.2	76.2 ± 22.8	82.2 ± 24.3	86.5 ± 23.8[b]	0.66	<0.001	0.44
Public distress	49.9 ± 27.8	73.5 ± 25.5	85.4 ± 20.7	90.6 ± 18.5[b]	48.6 ± 27.9	78.8 ± 23.0	87.6 ± 18.2	91.7 ± 14.4[b]	0.75	<0.001	0.48
Work	64.8 ± 25.0	80.9 ± 21.9	90.6 ± 17.7	92.9 ± 16.9[b]	60.4 ± 27.9	84.8 ± 20.9	90.4 ± 16.0	91.7 ± 17.8[b]	0.66	<0.001	0.85
BDI-II (score)	16.1 ± 10.5	9.8 ± 9.0	8.0 ± 9.9	7.2 ± 7.5[b]	16.7 ± 11.7	7.2 ± 8.7	6.0 ± 8.1	7.3 ± 10.6[b]	0.67	<0.001	0.55
Scales (score)											
Cognitive-affective	5.8 ± 4.7	3.0 ± 3.9	2.5 ± 4.1	2.0 ± 3.0[b]	5.8 ± 4.7	2.0 ± 3.3	1.6 ± 3.2	2.2 ± 3.8[b]	0.59	<0.001	0.47
Somatic	10.2 ± 6.7	6.8 ± 5.6	5.5 ± 6.2	5.1 ± 5.0[b]	10.9 ± 7.7	5.2 ± 5.8	4.3 ± 5.4	5.1 ± 7.1[b]	0.75	<0.001	0.63
Per-protocol analysis											
n	41	40	41	41	74	68	66	54			
EQ-5D-index	0.70 ± 0.26	0.81 ± 0.20	0.82 ± 0.24	0.81 ± 0.20[a]	0.68 ± 0.29	0.87 ± 0.18	0.88 ± 0.18	0.85 ± 0.23[b]	0.62	<0.001	0.50
EQ-VAS (%)	61.4 ± 18.3	76.7 ± 13.0	79.3 ± 13.7	84.5 ± 11.9[b]	58.4 ± 19.4	79.3 ± 14.2	80.8 ± 13.6	86.0 ± 12.8[b]	0.71	<0.001	0.94
IWQOL-Lite (%)	47.9 ± 17.7	69.1 ± 20.4	82.4 ± 16.7	89.7 ± 11.6[b]	46.1 ± 20.7	78.9 ± 17.1	86.1 ± 15.4	88.2 ± 15.6[b]	0.72	<0.001	0.30

Scales (%)											
Physical function	48.2 ± 21.2	72.4 ± 19.1	84.3 ± 16.1	91.2 ± 10.1[b]	46.5 ± 20.7	81.7 ± 16.1	88.8 ± 13.8	88.8 ± 13.7[b]	0.69	<0.001	0.28
Self-esteem	37.4 ± 25.7	62.8 ± 25.5	74.6 ± 21.6	84.1 ± 16.6[b]	34.7 ± 26.7	72.6 ± 20.8	80.1 ± 21.8	84.0 ± 22.3[b]	0.79	<0.001	0.39
Sexual life	51.1 ± 29.5	62.5 ± 28.2	79.2 ± 27.3	85.2 ± 21.8[b]	48.7 ± 31.2	76.2 ± 22.8	82.2 ± 24.3	86.5 ± 23.8[b]	0.68	<0.001	0.33
Public distress	48.0 ± 26.5	70.0 ± 27.0	85.0 ± 20.6	93.9 ± 13.9[b]	48.6 ± 27.9	78.8 ± 23.0	87.6 ± 18.2	91.7 ± 14.4[b]	0.82	<0.001	0.40
Work	62.3 ± 25.0	76.7 ± 23.0	90.7 ± 16.1	94.4 ± 10.8[b]	60.4 ± 27.9	84.8 ± 20.9	90.4 ± 16.0	91.7 ± 17.8[b]	1.00	<0.001	0.63
BDI-II (score)	16.0 ± 10.1	10.8 ± 9.8	7.9 ± 10.0	7.2 ± 7.3[b]	16.7 ± 11.7	7.2 ± 8.7	6.0 ± 8.1	7.3 ± 10.6[b]	0.74	<0.001	0.54
Scales (score)											
Cognitive-affective	5.9 ± 4.3	3.4 ± 4.1	2.6 ± 3.9	2.1 ± 3.0[b]	5.8 ± 4.7	2.0 ± 3.3	1.6 ± 3.2	2.2 ± 3.8[b]	0.68	<0.001	0.49
Somatic	10.1 ± 6.7	7.3 ± 6.2	5.3 ± 6.5	5.1 ± 4.8[b]	10.9 ± 7.7	5.2 ± 5.8	4.3 ± 5.4	5.1 ± 7.1[b]	0.80	<0.001	0.60

Note: [a]denotes $p<0.01$ and [b]denotes $p<0.001$ within group difference overtime, relative to baseline pre-surgery value. BDI-II, Beck Depression Inventory-II; HRQoL, health-related quality of life; IWQOL-Lite, Impact of Weight on Quality of Life-Lite; VAS, visual analogue scale.

Table 7. 9: Intention-to-treat analysis of the changes in the proportions reporting levels within EQ-5D dimensions between the intervention and the control groups in the first year of bariatric surgery.

EQ-5D	Intervention				Control				Group difference, p-value			
	Pre-surgery *n*=79	**3-month** *n*=72	**6-month** *n*=71	**12-month** *n*=71	**Pre-surgery** *n*=74	**3-month** *n*=68	**6-month** *n*=66	**12-month** *n*=54	**Pre-surgery**	**3-month**	**6-month**	**12-month**
Mobility, *n* (%)									0.50	0.13	0.46	0.73
Level 1	48 (60.8)	58 (80.6)	63 (88.7)	62 (87.3)	41 (55.4)	61 (89.7)	61 (92.4)	46 (85.2)				
Level 2	31 (39.2)	14 (19.4)	8 (11.3)	9 (12.7)	7 (44.6)	7 (10.3)	5 (7.6)	8 (14.8)				
Level 3	0	0	0	0	0	0	0	0				
Self-care, *n* (%)									0.89	0.94	0.17	0.46
Level 1	71 (89.9)	69 (95.8)	69 (97.2)	68 (95.8)	66 (89.2)	65 (95.6)	66 (100)	53 (98.1)				
Level 2	8 (10.1)	3 (4.2)	2 (2.8)	3 (4.2)	8 (10.8)	3 (4.4)	0	1 (1.9)				
Level 3	0	0	0	0	0	0	0	0				
Usual activities, *n* (%)									0.41	0.91	0.15	0.34
Level 1	52 (65.8)	62 (86.1)	63 (88.7)	62 (87.3)	44 (59.5)	59 (86.8)	63 (95.5)	50 (92.6)				
Level 2	26 (32.9)	10 (13.9)	8 (11.3)	9 (12.7)	30 (40.5)	9 (13.2)	3 (4.5)	4 (7.4)				
Level 3	1 (1.3)	0	0	0	0	0	0	0				
Pain/ discomfort, *n* (%)									0.08	0.62	0.30	0.08
Level 1	24 (30.4)	38 (52.8)	38 (53.5)	38 (53.5)	24 (32.4)	41 (60.3)	44 (66.7)	35 (64.8)				
Level 2	52 (65.8)	32 (44.4)	31 (43.7)	33 (46.5)	40 (54.1)	26 (38.2)	20 (30.3)	17 (31.5)				
Level 3	3 (3.8)	2 (2.8)	2 (2.8)	0	10 (13.5)	1 (1.5)	2 (3.0)	2 (3.7)				
Anxiety/depression, *n* (%)									0.86	0.81	0.15	0.91
Level 1	43 (54.4)	54 (75.0)	49 (69.0)	46 (64.8)	41 (55.4)	54 (79.4)	48 (72.7)	37 (68.5)				
Level 2	33 (41.8)	17 (23.6)	18 (25.4)	22 (31.0)	29 (39.2)	13 (19.1)	18 (27.3)	15 (27.8)				
Level 3	3 (3.8)	1 (1.4)	4 (5.6)	3 (4.2)	4 (5.4)	1 (1.5)	0	2 (3.7)				

Note: EQ-5D, EuroQol 5 dimensions; *n*, number.

7.4.9 Adverse events

A total of 296 adverse events were recorded throughout the trial period of which 21 were categorised as serious adverse events. But none of the reported adverse events was related to either the tele-counselling or the supervised exercise interventions.

7.4.10 Participants' satisfaction towards the lifestyle intervention programme

A total of 63 participants that received the lifestyle intervention completed the feedback form at the end of the trial. The form was used to assess their satisfaction with the contents of the tele-counselling and supervised exercise sessions.

Feedback on the tele-counselling sessions

This section consists of eight questions related to the content of the tele-counselling. Overall, 96.8% of participants felt that the tele-counselling sessions were useful. For example, one participant viewed *'the tele-counselling was imperative to my success'*. Most participants reported that the sessions provided them with the opportunity for *'discussing diet and health tips'* as well as physical activity with their assigned tele-counsellor. Specifically, topics such as food portions, protein-rich food, meal-planning and preparation were useful to them. Some of the participants also opined that the sessions had offered them with *'coping mechanism'* associated with their eating habits post-surgery. For example, one participant wrote *'[Tele-counsellor name] was very interactive and was helpful at times when my appetite was not good, suggesting alternatives'*. Whereas other participants mentioned the sessions helped them *'dealing with food temptations'* and *'helped with snacking and hunger pangs'*. During the sessions, participants also had the opportunity to raise some common post-surgery issues that needed explanations and/ or solutions from the tele-counsellors such as constipation, nausea, and hair loss.

In the feedback form, participants were also asked about their feedback on the tele-counselling booklet provided including the diaries to self-report their food intake, step count, supplements intake, and body weight (Appendix 10). Of all participants, 65.1% were very satisfied, 23.8% were satisfied, 7.9% were neither satisfied nor unsatisfied and 3.2% were unsatisfied. Furthermore, in terms of how easy it was to use the booklet and diary, 60.3% rated as very easy, 28.6% rated as easy, 3.2% rated as neither easy nor difficult and 7.9% rated as difficult to use. Two participants further stated that the diary was *'…helpful to knowing what you actually eat'* and *'I could always refer back to them'*. In contrast, two participants described the diary was *'...too time consuming and inconvenient to fill'* and they *'…tend to forget to fill in the diaries'*. Other participants also expressed that the diary was *'a little confusing'* and had *'not enough space to write all foods'*. Therefore, as a solution, three participants suggested using smartphone applications or an online diary, which were perceived to be easier than the paper-based diary. Nevertheless, 74.6% were very satisfied, 15.9% were satisfied and 9.5% were neither satisfied nor unsatisfied with the amount of help provided by the research team on how to complete the diaries.

In terms of the 15 minutes length of each tele-counselling session, 84.1% of participants were satisfied. Whereas 14.3% of participants felt the call length was just 'about right' and only one participant felt the call length was too short. Of all participants, 92.1% did not find any difficulty to book the tele-counselling session with their tele-counsellor as the tele-counsellors *'…were so accommodating'*. Nevertheless, one participant found it challenging to have the session during working hours, *'...it all depends* *on if you are working and being allowed to speak with your tele-counsellor. It's all work permitted'*. Several participants suggested a few strategies to improve the tele-counselling sessions such as offering more frequent sessions during the maintenance phase between 6 to 12 months post-surgery as participants felt *'the last few months is the hardest as appetite comes back'*. Furthermore, some participants preferred to have the same tele-counsellor throughout the sessions and two participants suggested considering the use of video calls in future.

Feedback on the tailored supervised exercise programme

This section consists of ten questions related to the content of the tailored supervised exercise programme. Of 52 participants who completed this section in the feedback form, 98.1% of participants felt that the tailored supervised programme was useful. In general, most participants found that they *'enjoyed the choice and range of exercises'*. A large number of participants specifically enjoyed the resistance training that used the gym equipment, resistance bands and body weight. For example, one participant stated of enjoying *'learning how to use the exercise machines'*. Exercises such as leg press and weight training targeting the arms were the most commonly cited type of exercises they enjoyed the most. However, exercises such as press-ups, planks, lunges, sit-ups, squats and floor-related exercises were challenging. Some participants commented that their pre-existing comorbidities had limited their ability to perform certain exercises*, 'pre-existing injury delayed some exercise but did get easier'*. One participant mentioned how the exercise therapist helped tailor the exercise to their functional limitations*, 'I had shoulder problems but [therapist name] helped me adapt in real-time'*.

In terms of aerobic training, exercising on the treadmill and the stationary bicycle were among their favourites. Whereas cardio machines such as the climbmill and cross trainer were found to be challenging, *'the climbmill is difficult because of my osteoarthritis'*. One participant perceived that *'the use of cardio equipment alone was monotonous'* hence explained the reason why most participants enjoyed the resistance training more than the aerobic training. One other aspect that some participants viewed as enjoyable during the supervised exercise classes was the social aspect of it, *'the weekly group exercise was fun and interactive. Attending regularly give focus on the need and benefits of exercising'*. In terms of the 60 minutes length of each exercise class, 69.2% of participants were satisfied, 15.4% felt the length was just about right, 13.5% responded the length was too short and 1.9% perceived it as too long.

Another important component gathered from the feedback form was the quality and amount of time the exercise therapist dedicated to each participant. Overall, 96% of participants were satisfied with the quality and 92% were satisfied with the amount of time they received from the exercise therapist. On the contrary, the remaining participants commented, *'I hardly saw the therapist'* and *'would have liked longer'*. The participants highlighted that some of the qualities of the exercise therapists were professionalism, attentiveness, supportive and caring. The exercise therapist also '*knows our limits and pushed us every week'*. Indeed, an exercise routine that was not personalised to participants' fitness level was found to be demotivating. For example, one participant was not satisfied with the quality of exercise received from the therapist and commented on receiving *'…a generic basic exercise plan'*. In terms of the participants' feedback on the exercise booklet containing the weekly exercise log for 12 weeks (Appendix 11), 98% were satisfied with the material provided.

In terms of the exercise schedule and location, six participants found it hard to find a convenient slot. One of the participants mentioned, *“the only area I found a struggle was travelling to London each week”*. Therefore, for a future programme, participants suggested more options for gym location and time slots that included more evening and weekend sessions as ‘*…it’s difficult for people who work Mon-Fri’*. For the evening session, a time slightly later than 5:30 pm is more preferable. A total of seven participants suggested for the exercise programme to be extended longer than 3 months. For example, one participant commented *‘more sessions and perhaps on the session after 12-month post-surgery to keep you active’*.

Several themes were identified when participants were specifically asked whether the overall lifestyle intervention programme helped them cope with the lifestyle changes needed after bariatric surgery (Table 7.10). Participants perceived that the programme offered them ongoing support and guidance, helping them mentally and in all aspects of their weight loss journey. They felt that the support was always available whenever they had questions and needed answers. The programme has also helped participants to gain knowledge regarding diet and exercise following bariatric surgery. This has encouraged them to make a wise food selection and enabled insights into the types of exercise they were comfortable with. Many participants also highlighted how the programme assisted them coping with the challenges they faced following bariatric surgery not only in terms of diet and exercise but also on how to adjust themselves within society. In regard to the supervised exercise sessions, participants found the sessions have helped them to get into regular exercising that they *“...probably would not have started so quickly or intensely”*. It has boosted their confidence level and ‘*made exercise felt less scary’*. The programme also kept participants on track of their weight loss journey. Especially during the *‘bad months’*, the programme helped them to get back on track and refocus.

Overall, the majority of participants suggested for the programme to be offered to all people undergoing bariatric surgery. In addition, few participants proposed the programme to be extended beyond 12-month post-surgery to help maintain weight loss, *"I think that this programme should be given for a longer time to achieve better weight maintenance results"*.

Table 7. 10: Final overview of the BARI-LIFESTYLE intervention programme.

Themes	Examples
Constant support	*"I didn't feel that I was alone in the journey"(Female, 36)* *"Any worry or advice I needed, I was supported so much" (Female, 23)* *"Support mentally, should be given to all patients" (Female, 32)*
Diet and exercise knowledge	*"Without it, I would be clueless on what to eat or do in terms of exercise" (Male, 40)* *"Being aware of different exercises and movements which can be continued long term" (Male, 49)*
Coping with challenges	*"Fend off temptations. Cope with society and people in general" (Female, 31)* *"It helped me cope with all the changes" (Female, 44)*
Confidence to exercise	*"Gave you the confidence after the surgery to know what exercise was safe to do and to push yourself in a safe environment where you did not feel self-conscious about your loose skin" (Female, 42)* *"Helped me not to be afraid of exercise" (Female, 38)*
Keeping on the right track	*"Even if you are ultimately accountable for yourself, having [tele-counsellor and exercise therapist names] advice helped to stop me slipping too far in bad months" (Male, 42)* *"It has helped me watch out for the pitfalls and how to turn it around" (Female, 54)*

7.5 Discussion

The BARI-LIFESTYLE trial is the first UK multi-centre RCT aiming to evaluate the efficacy of a one-year combined nutritional-behavioural tele-counselling and supervised exercise programme in patients following bariatric surgery. Our findings showed that providing post-surgery support to patients in a form of 17 tele-counselling sessions combined with a 12-week tailored supervised exercise programme had no additional impact on weight loss in the first postoperative year compared to the control group receiving post-bariatric standard care. Nevertheless, secondary outcome analyses revealed that the lifestyle programme improved physical function. In a post-hoc analysis, participants who attended ≥ 50% of the programme exhibited a favourable impact on relative HGS and whole-body BMD. Overall, patients reported that enrolling in such a programme had benefited them in adapting to the lifestyle changes required following bariatric surgery.

At the time this trial was designed and funded, only three post-surgery nutritional behavioural RCTs (Swenson *et al.*, 2007, Nijamkin *et al.*, 2012, Sarwer *et al.*, 2012) and no supervised exercise RCTs were published that investigated the impact of such programmes on weight loss, delivered early in the first post-surgery year. Swenson *et al.* reported no significant difference in weight loss in the first post-surgery year between patients randomised to follow a low-fat diet (n=13) or a low-carbohydrate/ high-protein diet (n=19) through regular counselling (5 sessions) by dietitians from pre- to post-surgery (Swenson *et al.*, 2007). In a later pilot RCT, Sarwer *et al.* reported a provision of regular counselling (8 sessions) by dietitians in the first 4-month of surgery (n=41) showed no significant weight loss difference with those receiving standard care (n=43). Due to the poor attendance at the in-person counselling sessions, the initial study protocol was modified by offering the option of brief telephone interviews to participants who cannot attend the in-person counselling. At the end of the study, the mean number of sessions attended were 2.5 ± 2 with only 34% of the participants completed more than half of the sessions offered (Sarwer *et al*., 2012). Nijamkin *et al.*, on the other hand, found that patients (*n*=72) provided with a comprehensive nutrition education and behaviour modification intervention had better weight loss than patients (*n*=72) who were not offered the programme. The intervention components included six sessions of group-based lifestyle educational meetings, frequent contact via telephone calls, e-mail messages, and reminder messages from investigators and the option for additional individual counselling from healthcare professionals. During the study period, 31.3% of the participants opted to see the dietitian, 10.4% saw the psychologist and 61.1% visited their primary care physician or another healthcare professional (Nijamkin *et al*., 2012).

The distinctive design of the BARI-LIFESTYLE trial compared to the aforementioned RCTs was that we combined 17-session of nutritional-behavioural tele-counselling spread out over the first post-surgery year with a once-weekly tailored supervised exercise for 12 weeks commenced at 3-month post-surgery. The design of this lifestyle programme was based on the participants' feedback from our pilot feasibility study, where they preferred an individual over a group-based diet consultation (Jassil *et al*., 2015). In addition, the use of telephone counselling was to address the poor adherence towards the in-person counselling session as reported in the earlier pilot RCT (Sarwer *et al*., 2012). Whereas the supervised exercise programme was based on published systematic reviews of studies undertaken prior to 2015 which observed patients who spent higher time in physical activity were associated with better weight loss outcome (Livhits *et al.*, 2010, Egberts *et al.*, 2012), but most patients expressed the need for support to be physically active post-surgery (Peacock *et al*., 2014).

From 2015 onwards, a few more post-surgery nutritional-behavioural and supervised exercise RCTs have been published with weight loss as a primary outcome of interest. Ogden *et al*. undertook the first UK RCT assessing the efficacy of psychologist-led behavioural support from 2-week pre-surgery to 3-month post-surgery supporting participants in addressing psychological issues encompassing dietary control, self-esteem, coping and emotional eating (3 sessions). The programme, however, had no impact on weight loss as observed at 12-month post-surgery (*n*=82) compared to the standard care group (*n*=80) (Ogden *et al*., 2015). In the same year, Wild *et al*. also reported a one-year videoconferencing-based psychoeducational intervention focusing on diet and physical activity in a group setting (14 sessions) (*n*=58) showed no difference in weight loss compared to a group receiving standard care (*n*=56) (Wild *et al.*, 2015). Another psychologist-led group-based behavioural intervention programme focusing on dietary and physical activity adherence commenced at 7-month post-surgery (8 sessions) (*n*=24) also showed no impact on weight loss compared to patients in a standard care group (*n*=26) (Lent *et al*., 2019). Interestingly, one RCT has shown the benefit of providing participants (*n*=28) with mobile health (mHealth) applications (iPad© mini with the MyFitnessPal© apps) without additional inputs from the healthcare professionals in inducing a greater percentage of excess weight loss at 12- and 24-month post-surgery compared to the control group (*n*=28) (Mangieri *et al*., 2019). Two post-bariatric supervised exercise RCTs have been undertaken, to date, to evaluate the impact on weight loss outcome. A once-weekly supervised exercise programme delivered between 1 to 6 months following RYGB in patients randomised to the intervention group (*n*=66) did not lead to favourable weight loss compared to the control group (*n*=62) receiving six sessions of health education (Coen *et al*., 2015b). Similarly, patients (*n*=32) randomised to receive a twice-weekly supervised exercise session for 26 weeks delivered at a later postoperative period from 6 to 12 months post-RYGB did not enhance weight loss compared to those randomised to the control group (*n*=28) receiving standard care (Mundbjerg *et al*., 2018b).

The present study is the first evidence to show that combining both the nutritional-behavioural and tailored supervised exercise sessions in a single lifestyle intervention programme has no significant impact on weight loss in the first-year post-surgery. Two possible reasons might explain our findings. Bariatric surgery is a unique obesity treatment because of its potent physiologic effects in inducing a remarkable rapid weight loss in the first-year post-surgery. Therefore, a potential additive weight loss effect of any adjunctive interventions, regardless of the programmes' intensity, delivered during this period, as in the present study, might not be evident in the short-term. For example, in the exercise RCT by Mundbjerg *et al*., the difference in body weight between the intervention and the control groups was only significant at 24-month follow-up, which was not observed earlier at 12-month post-surgery follow-up (Mundbjerg *et al*., 2018b). Hence, a further data collection of the present RCT cohort is now warranted to explore the programme's efficacy on a longer-term weight loss outcome and weight loss maintenance. Secondly, some patients adapted very well to the post-surgery lifestyle changes and the additional support in the study might contribute very little or did not affect weight loss. Hence, it is highly likely that the impact of such intervention could only be apparent in patients who are at risk of poor weight loss. Taking for example, in a post-hoc analysis of an RCT by Wild *et al*., patients stratified based on the presence of clinically significant depressive symptoms at pre-surgery (*n*=29), who received the post-surgery lifestyle intervention, showed a trend towards greater weight loss compared to the matched control group (*n*=20) (Wild *et al*., 2015).

As reported in Chapter 4, patients with suboptimal weight loss at 12-month post-surgery can be identified as early as 3-month post-surgery through their low weight loss velocity. Emerging evidence has also shown that the early postprandial responses of gut hormones (including PYY, ghrelin, GLP-1, oxyntomodulin and glicentin) predict successful weight loss outcomes at 12 to 18 months post-surgery period (Papamargaritis and le Roux, 2021). Both methods, therefore, can be used to identify patients with higher risk of poor post-surgery weight loss and be offered with additional post-surgery lifestyle programmes. Such targeted intervention indirectly will allow for the NHS resources to be channelled to the right patients to optimise the health outcome of bariatric surgery.

In the analyses of the secondary outcomes, the lifestyle intervention programme promoted better improvement in physical function particularly in walking capacity in the first year of bariatric surgery. This finding is in line with the result from a previous small study (Castello *et al*., 2011). As reported earlier in Chapter 5, bariatric surgery led to a restoration of walking capacity as evidenced by a significant improvement in walking distance and the increased in the number of participants achieving ≥450 metres in the 6MWT. However, almost one-third of participants were still unable to reach the minimal cut-off points of normal walking distance following surgery which was mainly attributed to physical pain (knee and hip pain) and discomfort. Therefore, the present findings highlight the beneficial impact of providing tailored supervised exercise based on individual functional capacity to maximise improvement in physical function following bariatric surgery.

In a post-hoc analysis, participants who attended ≥ 50% of the programme exhibited greater relative HGS compared to the control group. Our findings, therefore, add to the earlier evidence demonstrating an adjunct exercise training following bariatric surgery prevented muscle strength loss (Daniels *et al*., 2018, Oppert *et al*., 2018, Gil *et al*., 2021). As shown in Chapter 5, fat-free mass was highly correlated with HGS hence an excessive loss of fat-free mass following bariatric surgery might negatively impact

HGS. Indeed, loss of muscle strength over the long term increases the risk of fall, loss of physical function and the ability to carry out activities of daily living hence negatively impacting QoL (Walowski *et al*., 2020). This is particularly important as the majority of people undergoing bariatric surgery in the UK are above the age of 30 (National Bariatric Surgery Registry, 2020), a point when muscle mass and strength started to decline involuntary. The rate of decline increases even further after the age of 60 (Volpi *et al*., 2004). Therefore, as patients who have undergone bariatric surgery get older, the risk associated with muscle mass and strength loss is likely to be higher. The present lifestyle programme, however, is unable to promote an attenuation of fat-free mass loss, similar to other studies (Daniels *et al*., 2018, Oppert *et al*., 2018). In contrast, a recent finding by Gil *et al*. demonstrated that three times per week of a combined aerobic and resistance training programme delivered for six months significantly counteracted the post-surgical loss of fat-free mass (Gil *et al*., 2021). This indicates that a higher dose of exercise intervention (higher frequency in a week with longer duration of exercise programme) is needed to achieve a favourable impact on fat-free mass.

The post-hoc analysis of participants who attended ≥ 50% of the programme also demonstrated a favourable impact on whole-body BMD. However, the present programme has no significant impact in mitigating loss of BMD at the femoral neck, total hip and lumbar spine which was in contrast with previous published RCTs (Murai *et al*., 2019, Diniz-Sousa *et al*., 2021). This could be explained by the difference in the intensity of the exercise programme across studies. The present study only involved a once-weekly exercise programme whereas the study by Murai *et al*. and Diniz-Sousa *et al*. involved three times per week of exercise sessions. Therefore, it is highly like that the impact of exercise training on the preservation of BMD may also appear to be in a dose-dependent manner. As previously discussed in Chapter 2 and demonstrated in Chapter 4, bariatric surgery leads to significant loss of BMD hence increasing fracture risk over the long term. Women are even at a higher fracture risk once they enter menopause, which represents more than 75% of patients undergoing bariatric surgery in the UK (National Bariatric Surgery Registry, 2020). Exercise programme following surgery incorporating resistance training is therefore essential to counteract the unintended loss of BMD and reduce fracture risk over the long term.

As reported in Chapter 5, physical activity levels and sedentary behaviour did not improve following bariatric surgery. The present adjunctive lifestyle intervention programme is also unable to promote better outcomes on the time spent on physical activity, similar to the other lifestyle programmes assessed previously (Oppert *et al*., 2018, Gil *et al*., 2021). No favourable impacts of the programme were also seen in HRQoL and mental health outcomes, which corroborated with the findings from previous RCTs (Wild *et al*., 2015, Mangieri *et al*., 2019). This could be explained by the profound impact of bariatric surgery in improving the HRQoL and mental health parameters in the first year of surgery. Therefore, further data collection is warranted to assess the impact of the programme over the long term.

Based upon the participants' feedback, the content of the current lifestyle programme was perceived to provide them with holistic support encompassing diet, exercise, social and psychological aspects with better accessibility. A recently published qualitative study had highlighted the need to investigate effective and acceptable follow-up care packages for patients undergoing bariatric surgery in the UK (Coulman *et al*., 2020), and the present study has provided some approaches that could be considered. Firstly, the high adherence rate of the tele-counselling session with an average attendance of 13 out of 17 sessions in the first-year post-surgery showed that delivering nutritional-behavioural consultation through a telephone call is feasible and acceptable. Secondly, to assist with the tele-counselling consultation, the use of mHealth apps for patients to keep track of their food intake, physical activity, nutritional supplementations and body weight should be considered as suggested by participants in the present study. This adoption could ensure a smooth delivery of remote teleconsultation whilst minimising patients' burden. Indeed, the use of mHealth has shown promise in promoting better weight loss following bariatric surgery (Mangieri *et al*., 2019). Thirdly, the use of video consultation has also been suggested by participants in the present study which has been previously utilised in The Bariatric Surgery and Education (BaSE) RCT (Wild *et al*., 2015). The COVID-19 pandemic has revolutionised telemedicine use in healthcare, including weight loss treatment, with videoconferencing being more advantageous in terms of the interpersonal connection associated with in-person care (Ufholz and Bhargava, 2021). Therefore, telemedicine should be utilised in future obesity treatment and more studies should explore how it can be effectively integrated into real-world clinical practice. This is also aligned with the NHS Long Term Plan to promote the use of technology in prevention, care and treatment to be mainstreamed across the NHS (National Health Service, 2019). Lastly, the tailored supervised exercise sessions helped in tackling the common barriers faced by patients to be physically active following surgery such as poor exercise knowledge and confidence level, fear of injury, physical limitation, and inadequate professional support (Peacock *et al.*, 2014, Wiklund *et al.*, 2014, Zabatiero *et al.*, 2018). Notwithstanding, the fact that 26.7% of participants allocated to the intervention group did not enrol in the exercise sessions, with only 76.4% of those enrolled completing more than half of the sessions, proved that accessibility remains a limiting factor. Indeed, barriers such as the geographical location of the exercise facility and travelling time were among the issues that affected attendance in a previous post-bariatric exercise RCT (Mundbjerg *et al*., 2018b). The COVID-19 pandemic has given us the opportunity to deliver the exercise session virtually and participants' views and experiences on the tele-exercise sessions are reported in the next chapter.

7.6 Conclusions

In conclusion, our findings add to the limited existing evidence that a provision of an intensive lifestyle intervention in the first year of bariatric surgery did not lead to an additive weight loss outcome. Nevertheless, the programme improves physical function and has a favourable impact on physical strength and whole-body BMD. Patient-reported outcomes support the beneficial aspects of such a programme in helping them adapt to the lifestyle changes after bariatric surgery. However, considering the cost of implementing this programme, it might not be feasible to offer it to all patients undergoing surgery. Therefore, in institutions with limited resources, the programme could be prioritised and targeted to patients at risk of poor weight loss.

Chapter 8

Patients' views and experiences of live supervised tele-exercise classes following bariatric surgery during the COVID-19 pandemic: The BARI-LIFESTYLE qualitative study[23]

8.1 Introduction

In March 2020, the UK government imposed a nationwide lockdown to contain the spread of COVID-19 (UK Government, 2020), which we now know had a negative impact on mental health and health-related behaviours such as physical activity, especially for people living with obesity (Brown *et al*., 2021). All research-related in-person activities were suspended to abide by the restrictions. As previously mentioned

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[23]The published version of this chapter is available in Appendix 23. JASSIL, F. C., RICHARDS, R., CARNEMOLLA, A., LEWIS, N., MONTAGUT-PINO, G., KINGETT, H., DOYLE, J., KIRK, A., BROWN, A., CHAIYASOOT, K., DEVALIA, K., PARMAR, C., & BATTERHAM, R. L. (2021). Patients' views and experiences of live supervised tele-exercise classes following bariatric surgery during the COVID-19 pandemic: The BARI-LIFESTYLE qualitative study. *Clinical obesity*, e12499. The work related to this chapter was also presented at the 12th British Obesity Metabolic Surgery Society (BOMSS) Annual Scientific Meeting 2021, Oxford UK.

in Chapter 3, in order to maintain the integrity of BARI- LIFESTYLE, the supervised exercise component was modified to be delivered remotely via Zoom, a cloud-based video conferencing service, (referred to hereafter as tele-exercise) (McDermott and Newman, 2020).

With the advancement in digital communication technology, health systems worldwide are looking to integrate online delivery of services to improve the overall efficiency and effectiveness of care (World Health Organization, 2016). The acceptability of such technology for patients is essential for the successful implementation and uptake of such services. To date, the use of telehealth to deliver exercise programmes in patients pre- and post-bariatric surgery is scarce (Coldebella *et al*., 2018). Therefore, further qualitative research that aim to evaluate participants' beliefs, attitudes, needs and situations towards tele-exercise is warranted, and one way of doing this is by using the person-based approach (Yardley *et al*., 2015). Indeed, a profound understanding of patients' perspective of tele-exercise would ensure optimal provision and overcome shortcomings and challenges encountered for future interventions to maximise efficacy and effectiveness. In view of this, the present study sought:

1. To explore experiences and views of patients who have undergone bariatric surgery on supervised tele-exercise classes.
2. To identify the barriers to, and limitations of such classes.
3. To identify points of intervention that could be targeted to optimise the delivery and safety of, and adherence to, a future tele-exercise programme.

8.2 Materials and Methods

8.2.1 Study design and participants

This qualitative study is an additional sub study of the BARI-LIFESTYLE trial as part of a protocol amendment resulted from COVID-19 pandemic. The use of semi-structured interviews as exploratory method provided a wealth of raw data that is particularly useful in assessing needs and informing the design for future interventions. Semi-structured interviews were selected to ensure that specific research questions were addressed, however participants retained the freedom to bring up other topics if they felt they were important to the study.

Data were analysed using thematic analysis, which involves identifying and making sense of patterns that emerge from qualitative data by organising them into meaningful themes (Braun *et al*., 2016). Because thematic analysis adopts an inductive approach, it is particularly useful when studying under researched areas where there is insufficient knowledge to apply meaningful theories or hypotheses a priori, which is the case in this present study of bariatric surgery patients' perspectives on tele-exercise.

By the time the UK government announced the stay-at-home order (UK Government, 2020), a total of 16 remaining participants in the intervention group were still actively participating in the gym exercise class. Of these, 13 participants agreed to complete the remaining exercise sessions remotely via Zoom (Zoom Video Communications, Inc. California, U.S.). Two months after the end of the tele-exercise classes, these 13 participants were invited to take part in qualitative interviews via phone call and/or email, or an invitation letter to those who could not be reached. Interested subjects were given a copy of the participants' information sheet for the qualitative study (Appendix 24), detailing what the study entails, and encouraged to contact the research team should they have further questions related to the study. To be eligible for inclusion, participants must have had attended at least three tele-exercise classes to ensure they could provide in-depth insights into the tele-exercise programme. Of all eligible participants approached, 12 participants agreed to be interviewed (Figure 8.1).

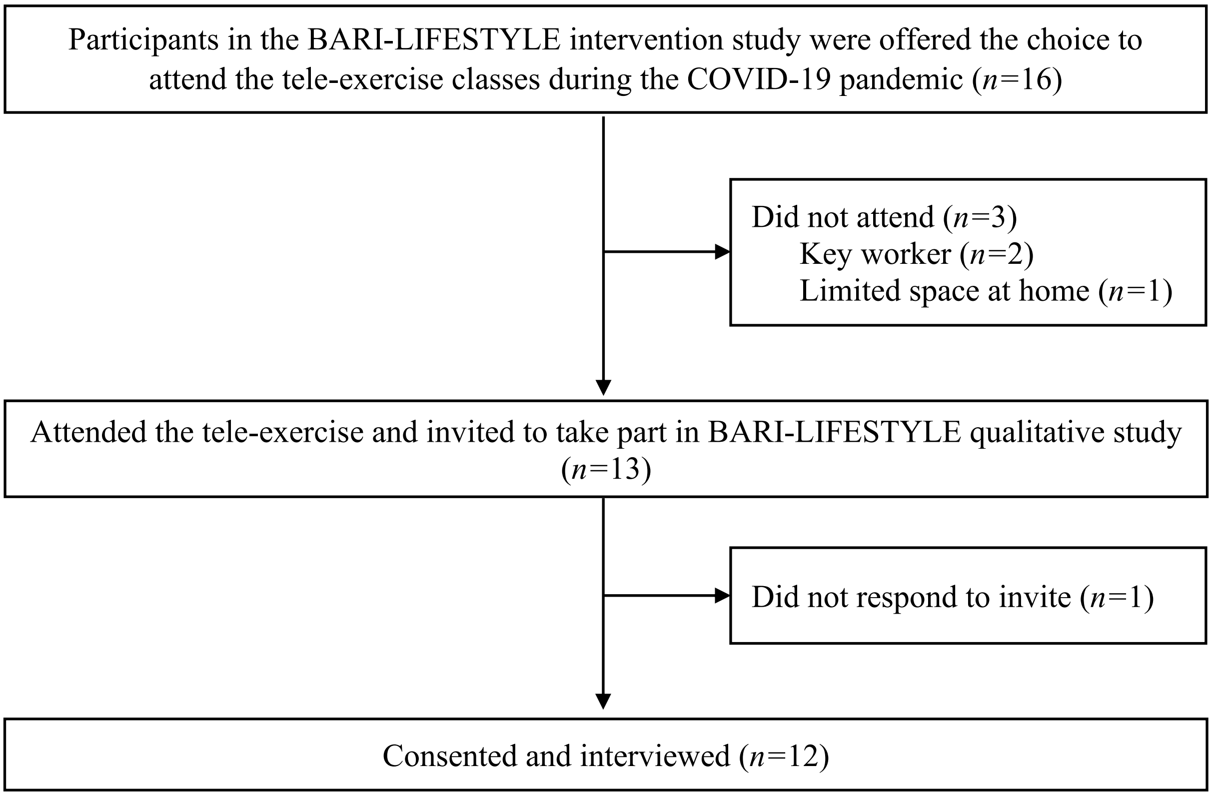

Figure 8. 1: Participant flow diagram.

8.2.2 Tele-exercise classes

Participants who were originally attending the in-person exercise classes were invited to attend one of the three tele-exercise classes, delivered via Zoom in a group format, each week (Tuesday at 10:30, Thursday at 17:30 and Saturday at 10:30). To assist the organisation of the classes, a group messaging app, WhatsApp (Facebook, Inc. California, U.S.) was set up. The tele-exercise class content was designed based on our experiences in a previous pilot feasibility study (Jassil *et al*., 2015). Each tele-exercise class lasted for 60 minutes, consisted of 10 minutes warmup, 40 minutes of a combined aerobic and resistance training, and 10 minutes of cool down. In all classes, the exercise therapists performed the exercises and interacted with participants in real-time. The warmup and cool down period involved gentle mobilising and muscle stretching, mimicking some yoga- and Pilates-style movements. The main exercise session consisted of aerobic training which involved a variety of exercises aimed to increase heart rate that was mixed up with resistance training targeting all major muscles.

The three types of resistance bands (PhysioRoom.com, UK) used in the classes were provided to participants during their first in-person exercise class pre-lockdown. The type of exercises using the resistance bands included exercises such as biceps curls, triceps extensions, overhead press, front and lateral raises, and reverse flies. The exercise therapist also used body weight to perform the resistance exercises such as squats, lunges, press ups and planks. The resistance exercises were performed in three sets with between eight to ten repetitions each. Exercise intensity was adjusted by increasing the pace and duration of the exercises, based on individual fitness and functional capacity as deemed necessary by the exercise therapist. A total of 45 classes were carried out throughout the lockdown period from April to July 2020. The overall attendance in each class ranged between two to six participants.

8.2.3 Topic guide

The interview topic guide was developed using the research questions and review of previous qualitative literature that explored the use of telehealth to deliver exercise programmes (Chen *et al.*, 2018, Lai *et al.*, 2020) and exercise interventions for patients who have undergone bariatric surgery (Gill *et al*., 2018, Zabatiero *et al*., 2018). Questions focused on exploring participants' overall experiences and views of the tele-exercise classes, including the use of technology, the content of the classes, the exercise therapist and supervision; identifying barriers and facilitators of participation, benefits and/or limitations of the classes; and identifying elements for future improvements of the classes (Table 8.1). The interview questions were tested and revised in the first three interviews to ensure participants were able to comprehend the questions. These three interviews were included in the analysis.

Table 8. 1: Semi-structured interview guide.

Main question	Probing questions
Can you share your experience on the tele-exercise that you took part during the COVID-19 pandemic?	• Were there any benefits of the tele-exercise? • Did it have impacts on your physical and mental wellbeing? • How was the scheduling and the length of each class? • Did the classes help you cope with the pandemic?
What do you think about the use of telecommunication technology to deliver the exercise programme?	• Can you comment on the installation process, the device you used and your internet connection? • Did you experience any technical issues or any other difficulties using this platform? • Did you have any privacy concerns using this platform? • What do you think about the video recording of the classes? • Can you comment on the number of participants in each class?
Can you share your view about the content of the tele-exercise classes? Did the classes meet your expectation?	• How was the intensity compared to the gym classes that you have attended?

	• Was there any aspect of exercise you liked most/least enjoy and easiest/hardest to do? What were they and why? • Do you have any suggestion on the type of exercise we should do more in the class? • How confident were you to perform the exercise remotely? Did you have any concern of getting yourself injured? • Do you think the resistance band we gave enough? Any other home-based exercise equipment you would like to suggest giving to participants? • Can you comment on the space at home to do the exercise? • Did you do any extra exercise on your own based on what you have learned in the classes?
Can you share about the level of supervision you received from the exercise therapist in the classes?	• Did you have the opportunity to give feedback about what you feel about each class? • If you have any concern for example injury, do you think that was being addressed? • Was it easy to communicate with the therapist throughout the tele-exercise classes?
Can you share if there are any enablers or any barriers that you faced in participating in the weekly classes?	• Any support you received from family members, the tele-exercise group or therapist that facilitated your attendance? • Any strategies or personal skills that you found helpful that enabled you to attend the classes? • For the classes that you were unable to attend, what were the reasons?
In the future, does tele-exercise could be an effective way to deliver the programme?	• From your experience in attending both the gym and tele-exercise classes, can you share the pros and cons of both programmes? • Any aspects of the exercise you continue doing beyond the study? Which one and to what extent?

	• What do you think of the tele-exercise to be included as part of standard care after bariatric surgery? • Any suggestions to improve the tele-exercise provision in future?

8.2.4 Data collection

The lead author, Friedrich Christie Jassil (FCJ) recruited and conducted 12 individual, in-depth, semi-structured interviews with participants, of which seven were conducted in-person, three by telephone, and two by video call using Zoom. All in-person interviews took place at UCLH. Written informed consent (Appendix 25) for participation in the study was obtained prior to the face-to-face interviews. Whereas for the telephone and video call interviews, the consent forms were either: (1) posted to the participants' home address and the signed consent forms were returned using a stamped addressed envelope provided or (2) emailed to the participants and the signed consent forms were emailed back, prior to the interviews undertaken. All interviews were audio recorded and anonymised by using the same unique PIN number assigned in the initial RCT, participants consented to the audio-recording when signing the consent form. Interviews were conducted between October to December 2020 with interviews lasting between 23 to 46 minutes (mean of 33 minutes). All interviews were transcribed verbatim and checked against the recordings for accuracy.

8.2.5 Data analysis

Transcripts were analysed using an inductive form of thematic analysis (Braun *et al.*, 2016) using Nvivo 12 (QSR International Pty Ltd., version 12, 2014) to provide a detailed and data driven account of participant's view and experiences. Given the limited knowledge of patients' views and experiences of live supervised tele-exercise classes following bariatric surgery, the aim of the current study was not to test a specific theory, but rather to take an inductive approach that identified points of particular salience in patients' own accounts of their experience. Reflexivity was maintained by keeping a research journal and by regular discussion among the researchers, FCJ and Rebecca Richards (RR), to help manage pre-assumptions and cross-check that the analysis was reflective of the data.

Initially, two researchers (FCJ and RR) independently read four transcripts to familiarise themselves with the data and coded the transcripts line-by-line. Both FCJ and RR met weekly to discuss their preliminary codes and refined them through an iterative process until a consensus was reached. Using this initial framework of codes, FCJ then continued coding the remaining transcripts. FCJ and RR continued to meet weekly to discuss new codes and refine them, until no more new codes were generated from the data. Next, FCJ and RR independently extracted the codes that shared similar ideas and concepts to represent broader level categories that held relevance to the research questions. Both FCJ and RR met to discuss their framework of categories and refined them through an iterative process until a consensus was reached. The reviewed categories were organised into potential themes or sub-themes. Next, the codes and themes were reviewed and refined to ensure that the themes demonstrated a valid, accurate, and coherent pattern. When all themes were finalised, the names of the themes were refined to check that they provided a valid account of the data that they represent. Specific quotations were extracted to illustrate the themes and subthemes. FCJ is a dietitian and involved in BARI-LIFESTYLE trial. RR is a health psychologist with training and experience in conducting and analysing qualitative interviews. RR was not involved in the wider BARI-LIFESTYLE trial.

8.3 Results

Participants' characteristics are presented in Table 8.2. Four overarching themes were generated from the data (Figure 8.2). Additional examples of quotations for themes and subthemes are also presented in Table 8.3.

Table 8. 2: Summary of participants' characteristics**.**

Participant characteristics	**Total samples, *n*=12**
Gender, *n* (%)	
Male	4 (33.3)
Female	8 (66.7)
Age (years), *n* (%)	
30-40	5 (41.7)
41-50	2 (16.7)
51-60	4 (33.3)
61-64	1 (8.3)
Mean (y)	46.3
Range (y)	(33-63)
Ethnicity, *n* (%)	
Asian or Asian British	3 (25)
Black or Black British	2 (16.7)
White or White British	7 (58.3)
Education level, *n* (%)	
No qualification	1 (8.3)
A level or equivalent	1 (8.3)
University degree	6 (50)
Higher degree	4 (33.3)
Employment status, *n* (%)	
Employed	9 (75)
Unemployed	1 (8.3)
Others	2 (16.7)
Study site, *n* (%)	
UCLH	6 (50)
Whittington	3 (25)
Homerton	3 (25)
Type of surgery, *n* (%)	
RYGB	4 (33.3)
SG	8 (66.7)
Exercise classes attended, *n* (%)	
Gym exercise (face-to-face)	
<50%	8 (66.7)
≥50%	4 (33.3)
Mean (day)	5
Range (day)	1-8
Tele-exercise (virtual)	
<50%	5 (41.7)
≥50%	7 (58.3)
Mean (day)	7
Range (day)	3-11

Notes: *n*, number; RYGB, Roux-en-Y gastric bypass; SG, Sleeve gastrectomy; UCLH, University College London Hospitals.

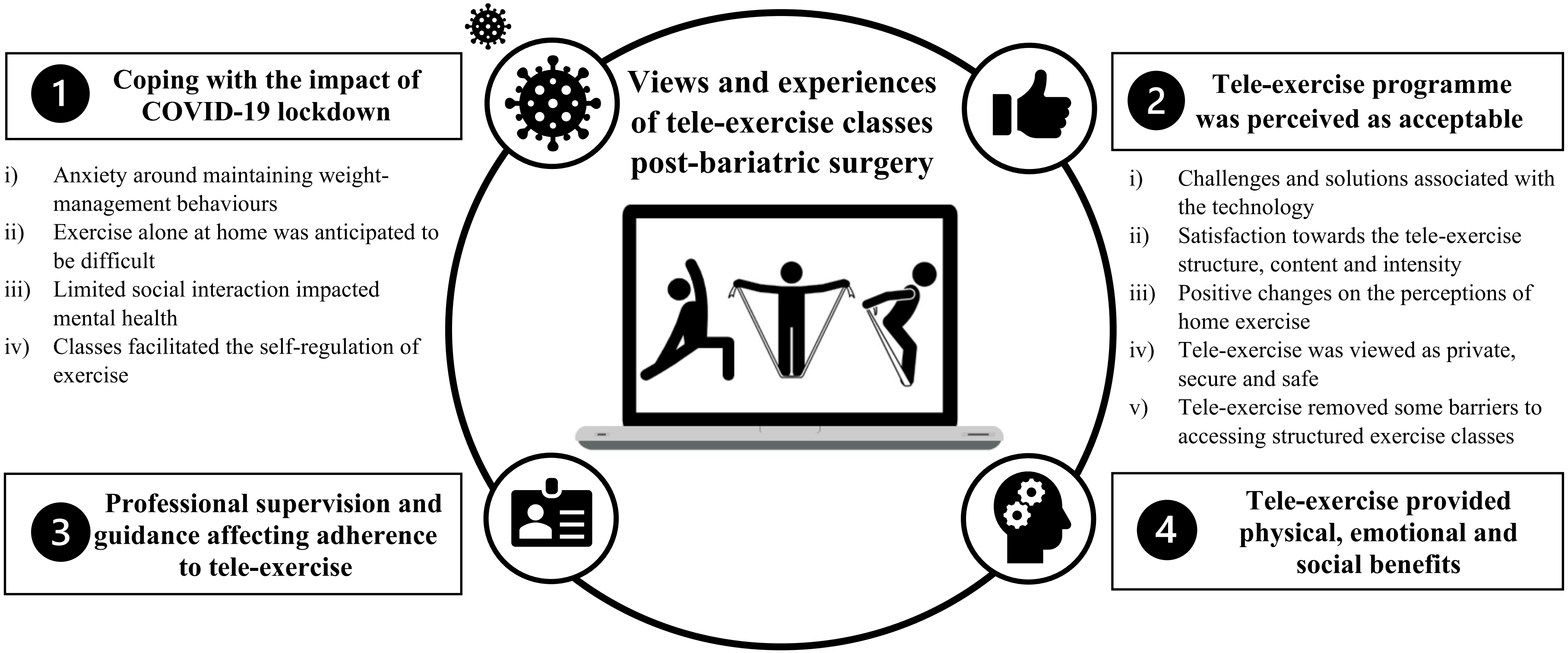

Figure 8. 2: Visual representation of themes and sub-themes.

Theme 1: Coping with the impact of COVID-19 lockdown

Most participants described how the COVID-19 pandemic had negatively impacted many aspects of their daily routines, which made it challenging to adhere to the post-bariatric surgery lifestyle recommendations. Being enrolled in the tele-exercise classes was perceived to have helped them to cope with the changes brought about by lockdown.

Sub-theme i): Anxiety around maintaining weight-management behaviours

Due to the restrictions imposed during lockdown, such as gym closures and changes in routines, some participants felt anxious about being able to maintain their weight-management behaviours, such as healthy eating and exercise, in line with their post-surgery recommendations. This led to a fear of weight regain.

> *"I thought when the gyms closed, that's it. I can't exercise, my diet is ruined. I'm going to gain a lot of weight." (P3, Male, 52)*

Sub-theme ii): Exercise alone at home was anticipated to be difficult

In addition, a few participants anticipated that having to exercise at home, alone, would have been difficult due to having no one to properly guide or monitor them. Furthermore, the lockdown appeared to negatively impact their motivation to stay physically active. As a result, these participants felt that having access to the tele-exercise classes provided them with the much-needed support to engage in physical activity and helped to increase their motivation to keep active during this challenging period.

> *"Having the class online really felt very supportive, motivating and very helpful in order to keep me on track exercising. I had the support because to do it on my own, without someone in real-time being there, I find more difficult." (P5, Male, 63)*

Sub-theme iii): Limited social interaction impacted mental health

Many participants described how the limited face-to-face social interaction during lockdown had also negatively impacted their mental health. The tele-exercise classes gave them something to look forward to and enabled them to interact with others, as well as expand their social networks, which appeared to help them cope with the social isolation caused by the pandemic.

> *"It helped with mental health when in lockdown. You had something to look forward to on a Saturday and you talk to other people and meet other people even though you weren't actually going out anywhere." (P6, Female, 48)*

Sub-theme iv): Classes facilitated the self-regulation of exercise

Several participants reported a loss of sense of control due to the many changes caused by the pandemic and the associated uncertainty. For example, they struggled to maintain their regular exercise routines. The tele-exercise classes appeared to facilitate the self-regulation of exercise by implementing a temporal and physical structure within participants' daily routines, as well as providing a source of accountability and motivation. Some participants described that having the tele-exercise classes booked in their schedule had held them accountable to their exercise routine and promoted commitment which may otherwise be difficult when exercising on their own.

> "*I find it very helpful to have it as a reference point in my diary rather than to say, okay tomorrow I will exercise, and then tomorrow finishes and I didn't exercise." (P5, Male, 63)*

Furthermore, the group-format of the classes created further accountability which was perceived to be an important factor that would help them to achieve better results over long term. Being part of a small group, as well as knowing the therapist was waiting in class, encouraged them to turn up to sessions for fear of embarrassment that their absence would have been noticed.

Theme 2: Tele-exercise programme was perceived as acceptable

All participants appreciated the invitation to tele-exercise classes and the majority reported having a positive experience. Participants found the tele-exercise schedule, content and intensity to be acceptable, and were satisfied with the privacy, security and safety of the technology and classes.

Sub-theme i): Challenges and solutions associated with the technology

None of the participants reported experiencing any major technical difficulties in setting up the Zoom software as the majority of participants had used Zoom during lockdown. Nevertheless, several minor issues were reported by a few participants, such as the difficulty to remember the ID and password hence causing them to enter the classes late and missed the earlier part of the exercise. Furthermore, a few participants mentioned the inconveniences when accessing the classes using a phone due to the small screen size. Some participants also experienced a problem with poor internet connection which led to audio and video lagging. This happened either due to having a low internet bandwidth or when trying to access the classes outdoors (e.g., the yard, balcony).

> *"When my internet speed gets slower, there was a bit of lagging, but that again improved because all I needed is to get my internet upgraded. It's inevitable. There will be some tuning issues when you first start using technology for things like this." (P4, Female, 42)*

Several practical solutions were suggested by a few participants to ensure a smooth conduct of the classes, such as having a device with larger screen (e.g., desktop, laptop, or tablet), a minimum internet bandwidth and instruction for them to follow.

Sub-theme ii): Satisfaction towards the tele-exercise structure, content and intensity

Almost all participants described how they particularly liked the structure of the tele-exercise classes, for example, how they included a warm-up and cool-down, and a variety of cardiovascular and resistance exercises at different levels of intensity. In addition, participants perceived the exercises to be challenging but enjoyable and felt they did more exercise in classes than they would have done alone at home.

> *"Most of the sessions really delivered within my expectation and were very pleasant but still work. There was the warmup and then the work which involved working on muscle strength with the bands targeting different parts of the body and also cardio. And then the ending which was stretching and relaxing. So, all in all, it was well structured." (P5, Male, 63)*

Physical fitness and ability varied between participants. As a result, a small number of participants felt that some of the exercise routines were not challenging enough. In contrast, one participant reported the exercises were too challenging as he didn't get enough rest time in between the routines.

> *"I think because you are doing it without a break, that's another issue because you are not 100% fit. Try to fit in so many activities within 60 minutes without a break, it's a bit too much." (P2, Male, 58)*

Based on the intensity of the tele-exercise classes and that participants felt fatigued at the end of classes, the length of the classes was considered to be *"just right" (P8, Female, 55)*. Nevertheless, a minority of participants felt that slightly shorter classes would have been sufficient, while one participant wanted longer than an hour due to increased energy at the end of the class.

When participants were specifically asked about their preferences between the tele-exercise and in-person exercise classes, the responses were mixed with almost half of them still preferring the in-person gym classes. This was mainly because they enjoyed working out in a gym environment, felt they had better supervision in terms of having someone watching over their techniques when using the gym equipment and valued the in-person social interaction with peers. It is also useful for people who have not used the gym as it helped them to be confident when exercising in the gym. Nevertheless, most participants believed the tele-exercise classes were comparable to in-person classes in terms of keeping them on track with physical activity and perceived that they would therefore be useful for patients who are unable to attend in-person classes. As a result, a few participants have suggested including both in-person and tele-exercise classes in future programmes as it may increase attendance.

> *"I think having a mix of both is a more effective way for the programme. It would definitely help when people couldn't attend a face-to-face session. That might also improve how much time people attend." (P4, Female, 42)*

Sub-theme iii): Positive changes on the perceptions of home exercise

Due to having no previous experience of home workouts delivered via technology, a few participants appeared to have preconceived expectations that home-based workouts would not be as effective as in-person workouts in a gym. However, after attending the tele-exercise classes, these participants were positively surprised by the level of exertion they experienced which they perceived to be as invigorating as the in-person exercises classes. Participation in the tele-exercise classes taught them that they do not need gym equipment, nor a large space at home, to have an effective workout. As a result, one participant commented how tele-exercise could be useful not just for lockdown but could be integrated into the post-surgery programme.

> *"I think it opened up the possibility that is something that does not necessarily only apply when you have a lockdown or social distancing. But it could be integrated in the programme at almost no additional cost to exercising in the gym." (P5, Male, 63)*

Sub-theme iv): Tele-exercise was viewed as private, secure and safe

One of the advantages of tele-exercise classes that was reported by a few participants was feeling less self-conscious and intimidated by their peers, compared to attending in-person classes at the gym. These participants did not feel they were being judged because of their physical limitations or feel they were in competition with others in the tele-exercise classes.

> *"When I was big, I lack a lot of confidence. So, I didn't like people to watch me do things. When I was doing it at home, I felt comfortable. Definitely more confident at home in your own environment. I think more people would want to do it that way." (P6, Female, 48)*

Although participants appeared aware of the privacy and security risks associated with using any type of virtual platform, they generally felt that the tele-exercise classes did not require any additional security above and beyond other activities that they have had previously performed on a virtual platform. Most participants were also familiar with Zoom software, which they believed to be fairly secure. However, two participants suggested that the use of a hospital-based virtual platform would reassure participants that their privacy is being well protected.

Participants also generally perceived the tele-exercise classes to be physically safe, as they did not feel pressured to do exercises that they deemed as unsuitable for themselves. Additionally, participants appreciated having the instructor therapist guiding their technique and providing alternative exercises when needed, in order to prevent injuries.

Sub-theme v): Tele-exercise removed some barriers to accessing structured exercise classes

The tele-exercise classes appeared to increase the accessibility of exercise by removing some of the barriers that are commonly associated when attending in-person gym classes, such as geographical accessibility of exercise facilities, travel time, parking issues and poor weather conditions. Furthermore, participants appreciated the range of tele-exercise classes offered, such as morning and evening options and weekdays and weekends, which also facilitated attendance. For example, two participants were able to join the tele-exercise from abroad. Several participants, however, suggested that the evening sessions could be moved to a later time to allow them to attend the classes after work.

> *"I have a long way to travel, it's two buses to get there and if the weather is bad, you really don't want to go out. But if you're doing the online, it doesn't matter what the weather is like, you can just get on and do it." (P6, Female, 48)*

Nevertheless, some barriers to attending the tele-exercise classes were reported by some participants, including busy work schedules, caring for family, competing priorities and illness or injury. In addition, a few participants reported that poor mental health had also led to reduced motivation for attendance on occasion.

> *"I injured my shoulder, and my daughter was sick, so not any other reasons behind that. I would love to attend but sometimes not everything is under your control, especially health wise and family related things." (P10, Female, 35)*

As a result, the majority of participants valued the recorded tele-exercise session as it enabled them to attend the class even if they had missed the live session. Additionally, they could repeat the class to remind themselves of the exercises, if needed. Even though there are existing exercise videos freely available online, some participants explained that the recording of the tele-exercise class was particularly valuable as it was specifically tailored to their needs as a post-bariatric surgery patient.

> *"You can redo it [from the recordings] when you want to or when you have time. You don't remember all the time, what exercise you've done. Because even if I want to repeat what I've done on Saturday, I don't remember all of them. That is the advantage of the tele-exercise." (P1, Female, 39)*

Theme 3: Professional supervision and guidance affecting adherence to tele-exercise

All participants valued the professional supervision and guidance from an exercise therapist, which appeared to increase participants' motivation to exercise and attend the tele-exercise classes. Most of the participants told of the challenges of being physically active following surgery, such as having poor exercise knowledge, fear of injury and poor motivation and confidence to exercise. Receiving prescriptive exercise from a professional, who was able to supervise and guide them, was therefore perceived as enabling and motivating. Furthermore, having a therapist who was aware and knowledgeable of their personal medical issues or injuries was perceived as important, as the exercises could specifically be tailored to meet their needs.

> *"I had someone that was a professional that knew about the fact that we all had surgery and so the types of exercises that were given to us was very specific and really tailored towards our own special needs at that particular time." (P4, Female, 42)*

Participants valued having a therapist who was attentive, able to communicate and give feedback whenever needed. This has helped them boost their level of confidence and motivation in the classes. Conversely, failure to address individualised needs proved to be off putting for participants. For example, one participant explained:

> *"I think the therapist should know each individual capability and what they are fit to do, so that you don't push anyone to a level where they can't do it." (P2, Male, 58)*

The class size was judged to be acceptable, as many participants felt that in a small class, the therapist would be able to better observe and provide personalised guidance and feedback. Participants believed that having too many attendees in each session would have negatively impacted the level of individual attention from the therapist, which may cause participants to be less inclined to attend.

Theme 4: Tele-exercise provided physical, emotional and social benefits

Overall, all participants reported to have experienced benefits from participating in the tele-exercise classes including physical, emotional and social benefits. In turn, these perceived benefits appeared to facilitate adherence to the classes and encouraged participants to continue engaging in physical activity beyond the research study. Among physical health benefits reported by the majority of participants are improved fitness, muscle strength, balance and weight loss. Furthermore, most participants believed that the tele-exercise classes had enhanced their overall psychological wellbeing. They enjoyed the good feeling they experienced after the classes. In particular, the classes helped to take their mind off of what was going on in their lives for that hour of the exercise.

A large number of participants stated that they felt supported, encouraged and motivated by being part of the group of people who had also had bariatric surgery around the same time as them. It opened up the opportunity to share and learn the experiences of others.

> *"Being able to interact with other people that are using the session, that was good because you could discuss each other journey so far and what they were struggling with or what they found it useful. And then a lot of them would actually share tips with each other on how they do exercise and overcome their challenges." (P4, Female, 42)*

Similarly, a good connection with the exercise therapist also appeared to motivate participants to continue with the classes. This camaraderie between participants and exercise therapist also appeared to facilitate their engagement in everyday physical activity by keeping everyone invested in a shared commitment towards reaching the same exercise goals. However, a small number of participants felt that the tele-exercise classes had less interaction in comparison to the in-person classes. In the tele-exercise classes, they only had the opportunity for brief interaction before and after the classes. Whereas in the gym classes, socialising in person with their exercise peers was perceived as more enjoyable.

Many participants claimed that participation in the tele-exercise classes had increased their confidence to exercise on their own. For example, some participants bought exercise equipment to add variability to their home exercise routines such as a trampoline, stepper, weights and exercise ball. They also incorporated the exercises learned from the classes into their regular exercise routines. In addition, two participants stated that the programme had prompted them to sign up to online exercise classes after the end of the research programme.

> *"I've now got online personal trainer who exercise with me. So, all the exercises that I started off with the therapist from our earlier tele-exercise sessions, I've now developing them even more and more with my personal trainer." (P12, Female, 55)*

Table 8. 3: Examples of quotations for themes and subthemes.

Themes	**Sub-themes**	**Examples**
Coping with the impact of COVID-19 lockdown	Anxiety around maintaining weight-management behaviours	*"Especially now we've got this second lockdown, finding that I'm going to struggle to find times to exercise or be motivated to exercise." (P4, Female, 42).*
	Exercise alone at home was anticipated to be difficult	*"For me, because of COVID and everything, I'll be exercising by myself at home. I don't like to exercise alone. I don't like it at all." (P10, Female, 35)*
	Limited social interaction impacted mental health	*"Especially at that point in the lockdown, you were told to go outside only if it's essentials. So, it [the tele-exercise] was an outlet, it stabilising mood, it kept you active. It provided a lot of help." (P7, Male, 33)*
	Classes facilitated the self-regulation of exercise	*"It was good to have a bit of a structure during the lockdown that having sort of diary appointments. It encouraged me to do more exercise and push myself harder during lockdown and have structure." (P9, Female, 37)* *"Sometimes when I didn't really feel like it, then I think sort of knowing that there was a small group who would be aware that I wasn't there, would encourage me to log on." (P9, Female, 37)*
Tele-exercise programme was perceived as acceptable	Challenges and solutions associated with the technology	*"We didn't have any issues getting linked to the Zoom. I think everyone is doing it now. I think it's quite easy and quite commonly used." (P2, Male, 58)* *"It was a little confusing about the passwords at first, but I mean it wasn't terribly complicated once you understand how to use Zoom." (P5, Male, 63)* *"It was hard for me because I suppose to watch the class from phone. But then I moved on to the laptop and much better." (P1, Female, 39)* *"I only have problems one time and it was when I was trying to do it outside the house, so the signal wasn't so good, but I wanted the bigger space to move." (P3, Male, 52)*

		"In the early days, my screen used to freeze, and I'd be thrown out and had to log back in. Once I changed over the amount of Internet that got into the house it was much better." (P12, Female, 55) *"Maybe send them an email about the 'how-to' guide just to make sure everyone is up to speed. Because that way, you can get straight into the session if there were no technical issues." (P7, Male, 33)*
	Satisfaction towards the tele-exercise structure, content and intensity	*"All the exercises were quite good. [The therapist] worked every kind of muscle, with the legs, hands, neck, back, shoulders. [The therapist] was multi choices as well, using bands, carpet [floor exercises], all the heavy things, and doing a lot of stretching. I think it was kind of including Pilates and yoga." (P1, Female, 39)* *"It was absolutely just right because there's only so much exercise that you could fit in that you can get everyone's participation. I'd say if you did it any longer, I think you'd lose people." (P8, Female, 55)* *"Even though I wanted more but 60 minutes I think is nice for everyone. If I would do it again, I will ask for more time because after 60 minutes, I have more energy." (P10, Female, 35)* *"I think the 60 minutes was fine. You got enough wear out and was ready to rest after the 60 minutes." (P6, Female, 48)* *"Especially like people who maybe haven't used the gym much or not for many years, I think it's an important aspect to do this sort of face-to-face and trying to get people in the gym and develop those healthy habits and give people confidence in the gym." (P9, Female, 37)* *"Ideally, a combination of the two [in-person and tele-exercise] would be the perfect thing. Perhaps the first session could be at least in person, to let the therapist*

		understand your level of exercise, your ability to exercise. And then, if you're not using weights, I just don't even see why you have to be in person. You can probably reach so many more people." (P3, Male, 52)
	Positive changes on the perceptions of home exercise	*"At first I was a little bit apprehensive because I've never done anything like that before. But after doing the first, I couldn't move. So, for the following sessions what I found was, yeah, I'm enjoying this." (P8, Female, 55)* *"Being able to get such a good full workout in the house changed my whole perspective on what was possible from home. [The therapist] showed me you can work out in kind of 'a small little box'." (P3, Male, 52)* *"Something about the gym is you don't learn a lot of the different kinds of ways to exercise various muscles because you do over-rely on the machine. So that's why I said about learning new exercise regimes from the Zoom sessions. It allows you to learn what you would do at the gym, how to do at home in a much simpler way." (P7, Male, 33)*
	Tele-exercise was viewed as private, secure and safe	*"I think it [tele-exercise] is definitely the way forward, especially as an individual who may feel self-conscious about yourself in the way that you look when you exercise. In that sense, it doesn't debilitate your confidence rather than a booster. It's brilliant". (P12, Female, 55)* *"I think, for what we were doing, the level of privacy is fine, and it included a password. I know there are some larger issues around Zoom, but I don't feel that we were doing something particularly private." (P11, Female, 39)* *"I think it would be better off if the hospitals or the NHS device something that they can use solely for patients, then that would be a good idea." (P8, Female, 55)* *"I was a little bit concerned with some of the exercises, but I think that the difference here is that I'm not forced to do them. So, where I found I knew already that*

		carrying out those core exercises, I would probably cause myself more injury or damage because of the medical conditions I previously had, then I would leave them out." (P4, Female, 42)
	Tele-exercise removed some barriers to accessing structured exercise classes	*"It [tele-exercise] made exercise very accessible to me. Of course, one of the big advantages of it is that I could take it abroad. I did the exercise class in [country name] and that was great." (P5, Male, 63)* *"I think, maybe for the evening, to move it till 6 pm, but I don't know if that works for everybody." (P9, Female, 37)* *"I'm a key worker, and during this lockdown, I went to work. And sometimes I was supposed to do overtime and stuff, and that was the reason I couldn't attend to all of it" (P1, Female, 39)* *"My own health was the biggest barrier and my stress level. They're particularly biggest barriers for me." (P11, Female, 39)* *"I would certainly make recordings available and find a clear way of formalising it. I'm aware that there are maybe copyright issues that need to be sorted, but I'm sure it's possible to sort that one out." (P5, Male, 63)*
Professional supervision and guidance affecting adherence to tele-exercise		*"You can tell that while exercising you were being watched and if you found it difficult, the therapist would say 'are you okay? If you can't do it this way, you can do it this way'. It was very good communication as well." (P3, Male, 52)* *"[The therapist] was a good listener. Whenever I asked something, [the therapist] will answer me directly and will give me options if the exercise was difficult to do. [The therapist] is amazing." (P10, Female, 35)*

		"I think a session will probably a maximum of eight. Anything bigger than that, I think I would have probably felt like less involved or less likely it was actually tailored towards my needs." (P4, Female, 42) *"I think if it was a lot much larger group then people might be less inclined to attend, but as it was a small group then it was very positive." (P9, Female, 37)* *"If you have too many, it becomes less personal and if you have too few, it can feel a bit off. Too many people, the therapist would have trouble spotting things like people's technique." (P7, Male, 33)*
Tele-exercise provided physical, emotional and social benefits		*"I did it once a week, but it has an amazing impact. My body has changed especially I'm losing a lot of weight very quick. That helped a lot." (P10, Female, 35)* *"Obviously it [the tele-exercise] helped with weight and build up muscle mass, and that because when you've had surgery you lose a lot of muscle mass." (P6, Female, 48)* *"It helped me keep fit and it took your mind off of what was going on for that hour of the exercise. You were due for an hour of what was going on around you." (P6, Female, 48)* *"Having that interaction with the therapist and meeting with the group on a weekly basis, you have something to look forward to. I found it was emotionally empowering as well as mentally." (P4, Female, 42)* *"It's very good and it's nice because you could see the other people, [the therapist], and they could see me too. You could have a chat with them so you can sort of connect and support each other." (P11, Female, 39)*

		"But I prefer the session in the hospital because I prefer socialising with others in person than via online, it's convenient to be in the gym." (P1, Female, 39) *"Now I have a personal trampoline, I have a personal stepper, I have weights, all these things so I can exercise in the house. It really changed my idea of what was possible." (P3, Male, 52)* *"The tele-exercise has increased my confidence to exercise by myself. I've incorporated press-ups, lunges, squats, and things into my running. It's not just about confidence, it's more about motivation and keeps going." (P9, Female, 37)*

8.4 Discussion

This is the first qualitative study to report patients' views and experiences of a home-based tele-exercise programme following bariatric surgery. Participants described how tele-exercise classes helped them to cope with the changes to their lives due to the COVID-19 pandemic including how it helped them in adhering to the lifestyle change required post-surgery. Participants found the tele-exercise schedule, content and intensity to be acceptable, and were satisfied with the privacy, security and safety of the technology and classes. Professional supervision and guidance from the exercise therapist were described as central to the tele-exercise provision. Importantly, participation in the tele-exercise provided physical, emotional and social benefits.

A recent survey of 800 patients pre- and post-bariatric surgery supports the current findings of the impact of COVID-19 on health behaviours and mental wellbeing, as 75% experienced an increased level of anxiety, 60% had decreased levels of physical activity and 30% experienced weight gain (Waledziak *et al.*, 2020). In fact, during the earlier period of the COVID-19 outbreak, seven weeks of lockdown led to 3.8 kg of weight gain with significantly lower weight gain observed in patients who reported performing regular exercise than those who were inactive, 1.1 versus 4.6 kg weight gain, respectively (de Luis *et al.*, 2021). These observations during the pandemic came to no surprise as physical inactivity and increased sedentary behaviour following bariatric surgery are associated with poor long term weight loss outcomes (Herman *et al.*, 2014).

Overall, participants in the present study reported positive views and experiences of the tele-exercise classes. The structure, content and intensity of the tele-exercise classes were perceived as equally acceptable and satisfactory as the in-person gym classes they attended prior to COVID-19 pandemic. Enjoyment and a positive experience of exercise have been shown to increase exercise adherence and motivation (Peacock *et al.*, 2014, Burgess *et al.*, 2017), which in the case of the present study, appeared to contribute to the changing perceptions of home-based exercise. In addition, some participants expressed better confidence level in the tele-exercise classes, compared to how they previously felt during in-person gym classes. It has been previously reported that self-consciousness about physical appearance when exercising in public spaces and exercise facilities did not disappear despite significant weight loss after bariatric surgery (Zabatiero *et al*., 2018), therefore tele-exercise classes may enable patients to overcome this barrier to exercise post-surgery.

The increased accessibility of tele-exercise compared to in-person classes overcome several barriers faced by patients to engage in physical activity such as lack of time, geographical accessibility of exercise facilities and poor weather, which is in line with findings from previous studies (Dikareva *et al.*, 2016, Gill *et al.*, 2018, Zabatiero *et al.*, 2018). An earlier feasibility study that evaluated an in-home supervised exercise programme via telehealth in patients awaiting bariatric surgery reported greater attendance compared to the in-hospital supervised exercise programme (95.8% versus 80.1%, respectively) (Baillot *et al*., 2017). In the present study, the problem associated with the access to the tele-exercise classes and technical setup of software were minimal. This is unsurprising as of 2020, 96% of households in the UK have internet access (Office for National Statistics, 2020). Additionally, 83% of participants in this study were from a higher educational background, with an age below 65 that was deemed to be technology savvy (Fischer *et al*., 2014).

People living with obesity generally experience a wide range of barriers to engaging in physical activity encompassing both internal barriers, which can be divided into physical (excess weight, poor fitness, health problems, injury) and psychological barriers (weight perception, low mood, lack of enjoyment and motivation/ willpower), and also external barriers (lack of time and knowledge, poor weather, competing demands) (McIntosh *et al*., 2016). Despite a significant weight loss following bariatric surgery, the majority of these barriers to exercise continue to persist (Zabatiero *et al*., 2018). Ongoing support from an exercise professional is therefore recommended particularly following bariatric surgery (Dikareva *et al*., 2016) and our data suggest that this was needed during the COVID-19 pandemic, which created further barriers to engaging in physical activity. In the present study, participants emphasised the important role of the exercise therapist both in providing an exercise programme tailored to their physical capacity and in supporting them to tackle psychological barriers. A study by Bergh *et al.* has recently highlighted the importance of interventions targeting patients' abilities to make plans, enhance self-efficacy and improve action control skills as they found a strong relationship between these self-regulation factors with both objective and self-reported physical activity after bariatric surgery (Bergh *et al*., 2017).

To date, a growing number of studies have attempted to elucidate the beneficial effects of exercise programmes following bariatric surgery in order to support a post-surgery exercise recommendation (Coen and Goodpaster, 2016). Although the effect of exercise post-bariatric specifically in enhancing weight loss remains inconclusive due to the paucity of high-quality studies (Carretero-Ruiz *et al*., 2019), several other positive outcomes were reported hence favoured recommendation, including preventing excessive loss of fat-free mass, enhancing physical and cardiorespiratory fitness, promoting better HRQoL, among other benefits (Pouwels *et al.*, 2015, Coen *et al.*, 2018). In the present study, participants perceived that the tele-exercise not only benefited them in terms of physical health but also their social and emotional wellbeing were improved. Notwithstanding, high-quality studies of tele-exercise following bariatric surgery that measure these reported outcomes using objective assessment tools are still needed to confirm these early findings.

Practical considerations for future implementation

To optimise the delivery of tele-exercise, several important aspects should be taken into consideration. Using a hospital-based virtual platform to deliver the tele-exercise would be a better option as this will assure participants of their privacy and safety being well-protected. Providing participants with clear written guidance such as login instruction will ensure a smooth process of the tele-exercise delivery. For a clear visual and access, ideally, participants would require a device with a larger screen (e.g., desktop, laptop, or tablet) and a minimum internet bandwidth required to access a virtual platform. To ensure tailored and personalised supervision, the class size should be limited ideally between five to eight participant per session. Furthermore, an initial in-person session with an exercise therapist prior to enrolment in tele-exercise is needed to assess participants' exercise capacity for tailored exercise prescription and building rapport. Recording the tele-exercise classes with availability to access this resource on demands were found to be useful but the copyright of the recordings should be taken into consideration. As per participants' suggestions, consider providing other simple and cheap exercise tools such as a yoga mat and exercise ball which were thought to be suitable and applicable for the tele-exercise. Finally, regarding the scheduling, a mix of weekdays and weekend options covering morning and evening classes would increase the likelihood of attendance. For the evening class, consider a later evening time to provide an opportunity for patients who are working in the daytime to get ready for the tele-exercise.

Strengths and limitations

The present study captured in-depth views and experiences of patients towards a tele-exercise intervention following bariatric surgery and included a varied sample of male and female participants, with a wide age range and diverse ethnic backgrounds. We assumed that a sample of 12 participants was deemed appropriate because of the early, exploratory nature of this study and the focus was to gain preliminary insights that were useful for the planning and development of future robust tele-exercise interventions. However, as the majority of participants in this study were highly educated and employed, the generalisability is somewhat limited. Digital exclusion, especially among patients from a lower socio-economic group, may impact the uptake of such programmes (Public Health England, 2020). In the current climate of the COVID-19 pandemic and associated restrictions, tele-exercise might be perceived positively, and as beneficial. Therefore, patients' perceptions towards tele-exercise delivered during a non-pandemic period should be further explored. In addition, the present study did not explore the views and experiences of the exercise therapists, which are important to consider when designing and implementing future tele-exercise interventions. Lastly, although the majority of participants perceived the tele-exercise to be as effective as the in-person classes, we recognise that a quantitative study that objectively compares both methods is required in order to support the present findings.

8.5 Conclusions

The COVID-19 pandemic has revolutionised the way healthcare is provided through telehealth. The present study suggests that tele-exercise, when implemented specifically in patients who have undergone bariatric surgery, is feasible and well-accepted, and potentially as effective and useful as in-person exercise classes. These preliminary findings have provided additional insights into much-needed evidence for the potential use of telehealth in the provision of care following bariatric surgery (Coldebella *et al*., 2018). In today's technologically advanced society, it is foreseeable that telehealth will eventually become a new norm for future health care. Therefore, it is timely and relevant now to undertake more robust research designs to investigate the efficacy and effectiveness of tele-exercise pre- and post-bariatric surgery. The research findings will be not only useful to face the present and future pandemics but can also be translated and integrated into the existing bariatric care pathway to optimise patient outcomes.

Chapter 9
Implications, conclusions, and future studies

9.1 Summary of the key findings

The research in this thesis has provided additional insights into the health benefits of bariatric surgery as delivered in the UK healthcare setting, using the one-year prospective longitudinal cohort of the BARI-LIFESTYLE observational study. In addition, the embedded RCT of a post-surgery lifestyle intervention within the observational cohort, as reported in Chapters 7 and 8, has addressed the need for such a programme to be tested in the NHS setting as recommended by NICE (NICE, 2014b).

The weight loss outcome data in the first year of bariatric surgery, as presented in **Chapter 4**, showed a mean %WL of 24.6% with a comparable weight loss across the type of procedures; RYGB (23.9%) OAGB (26.4%), and SG (24.4%). This durable weight loss was accompanied by a complete remission of T2D (43.8%), hypertension (40%), hyperlipidaemia (20%) and OSA (46.7%). However, weight loss was highly variable across individuals, with 35.1% of patients experiencing suboptimal weight loss. Both BIA and DXA that were used to measure body composition changes showed a strong linear correlation. As expected, the rapid weight loss achieved by participants following bariatric surgery was accompanied by the inevitable loss of fat-free mass that peaked at the first 6-month of surgery. In fact, the mean total weight loss of 31.8 kg at 12-month post-surgery accounted for 60.6% fat mass and 39.4% fat-free mass. And of all patients, more than 56.5% met the criteria for an excessive fat-free mass loss. BMD also declined significantly by 8.5% at total hip, 5.7% at femoral neck, 2.9% at lumbar spine and 0.1% for whole-body BMD. The degree of BMD loss was influenced by the different type of bariatric procedures undertaken and the weight loss magnitude.

In **Chapter 5**, we found that despite a significant weight loss produced by bariatric surgery, the time spent in any intensity of physical activity and sedentary behaviour did not change when assessed periodically in the first postoperative year. High sedentary behaviour was associated with lower %WL at 6-month post-surgery and lower fat mass loss at 3- and 12-month post-surgery. On the other hand, higher time spent on MVPA correlated with higher fat mass loss at 6-month post-surgery. The physical function, assessed through walking capacity and both functional relative upper and absolute lower extremities strength, improved significantly after surgery. Importantly, the findings from Chapter 5 suggested that maximising weight loss and fat mass loss can optimise the improvement in walking capacity and functional lower extremity strength. Whereas minimising loss of fat-free mass and whole-body BMD post-surgery lead to better preservation of upper extremity strength.

Chapter 6 focused on PRO, in particular on how patients' function or feel following bariatric surgery. Overall, our findings demonstrated that patients' HRQoL and mental health improved significantly in the first-year post-surgery. The peak improvement in parameters assessed differed across instruments used, with the magnitude of improvement being highest in the first 3-month post-surgery. Importantly, %WL, type of surgery and the time spent on MVPA were found to mediate the improvement in HRQoL depending upon the time point post-surgery. Furthermore, patients with moderate to severe depressive symptomatology at 6-month post-surgery had significantly less weight loss compared to those with no or minimal to mild depressive symptomatology.

Given the variability in the outcomes of bariatric surgery, **Chapter 7** sought to test a hypothesis as to whether providing additional support in a form of a lifestyle programme would maximise weight loss and health outcomes. This was the primary outcome measure of the multi-centre RCT, the BARI-LIFESTYLE intervention study. The findings showed that providing post-surgery support to patients in a form of 17 tele-counselling sessions combined with a 12-week of weekly tailored supervised exercise programme had no additional impact on weight loss in the first postoperative year compared to the control group receiving post-bariatric standard care. Nevertheless, the programme improves physical function and has a favourable impact on physical strength and whole-body BMD. Furthermore, patients reported that enrolling in such a programme had benefited them in adapting to the dramatic lifestyle changes required following bariatric surgery.

Chapter 8 of this thesis reported patient's views and experiences of live supervised tele-exercise classes that was delivered during the COVID-19 lockdown. Participants perceived that the tele-exercise classes were deemed acceptable and compared favourably to in-person exercise classes. They described how it enabled them to cope with the changes to their lives due to the COVID-19 pandemic including how it helped them in adhering to the lifestyle change required post-surgery. Participants found the tele-exercise schedule, content and intensity to be acceptable and were satisfied with the privacy, security and safety of the technology and classes. Professional supervision and guidance from the exercise therapist were described as central to the tele-exercise provision. Importantly, participation in the tele-exercise provided physical, emotional and social benefits.

9.2 The novelty of the present findings

As outlined in Chapter 1, bariatric surgery is underutilised in the UK, as evidenced by the low number of procedures undertaken annually compared to our European counterparts with a comparable obesity prevalence (Angrisani *et al*., 2018). One of the contributing factors is the paucity of published prospective UK studies on the outcome of bariatric surgery to support increased provision. In fact, a comprehensive literature review in Chapter 2 has revealed that the majority of the published evidence on the outcomes of bariatric surgery come from countries such as the United States, Brazil, and France where the number of procedures performed is among the highest worldwide. Our findings from the BARI-LIFESTYLE observational study, therefore, add to the limited evidence that bariatric surgery, as delivered in the UK healthcare setting, leads to substantial weight loss, remission or improvement of comorbidities, improvement in physical function and strength, and better HRQoL and mental health. Currently, there are two ongoing large prospective UK studies, the By-Band-Sleeve RCT (*n*=1341) and the SurgiCal Obesity Treatment Study (SCOTS) longitudinal study (*n*=445), that recruited participants undergoing bariatric surgery from various NHS hospitals in England and Scotland which will further expand upon our findings (Rogers *et al*., 2017, Mackenzie *et al*., 2021).

OAGB is a new bariatric procedure that is increasing in popularity due to being technically simpler than RYGB. However, there is still a lack of outcome data on OAGB in the literature. Our findings, in Chapter 4, further informed the impact of OAGB on weight loss and changes in body composition that comparable to RYGB and SG in the first postoperative year. Although there is already some evidence that weight loss is accompanied by a significant loss of fat-free mass (Haghighat *et al*., 2021), there is no standard reference range currently exist regarding the amount of fat-free mass loss considered safe following bariatric surgery. Our findings showed that 26.7% of patients experienced excessive fat-free mass loss at one-year post-surgery, which agree with the earlier findings reported by Nuijten *et al*. (Nuijten *et al*., 2020). Furthermore, there are limited validation studies to support the use of BIA to measure body composition in patients undergoing bariatric surgery (Savastano *et al.*, 2010, Faria *et al.*, 2014). The present study is the first to show a high correlation of body composition measurements between BIA (Tanita DC-430MAS; Tanita, Tokyo, Japan) and DXA. As reviewed in Chapter 2, it was still uncertain whether RYGB and SG affect BMD in a similar way. Our findings, therefore, add to the evidence that both RYGB and SG significantly reduced total hip and femoral neck BMD in a similar magnitude, but RYGB leads to a greater reduction in lumbar spine and whole-body BMD than SG. Importantly, our results on the impact of OAGB on BMD further expand the findings from the only published study to date by Luger *et al*. (Luger *et al*., 2018).

Another gap in the literature is the inconsistencies of findings on the impact of bariatric surgery on physical activity levels and sedentary behaviour. Data reported in Chapter 5 further support the evidence that physical activity levels and sedentary behaviour remain unchanged from pre- to post-surgery despite a significant weight loss (Berglind *et al*., 2015, Sellberg *et al*., 2019). Evidence is currently scarce regarding the link between time spent in objectively assessed physical activity levels and sedentary behaviour with weight loss and changes in body composition following bariatric surgery. Consistent with the recent finding by Nielsen *et al*., we also observed a link between higher time spent in MVPA with a larger reduction in fat mass at 6-month post-surgery (Nielsen *et al*., 2021). Another relevant novel finding that we identified, which has never been reported thus far, is the link between higher time spent on sedentary behaviour with less favourable outcomes on weight loss and fat mass loss. Therefore, our data suggest that replacing sedentary behaviour with any form of physical activity would promote better weight loss and fat mass loss post-surgery. Importantly, our data in Chapter 5 has demonstrated that bariatric surgery improved muscle quality (calculated as HGS divided by BMI), expanding the earlier finding by Alba *et al*. (Alba *et al*., 2019).

As highlighted in Chapter 2, one of the main reasons that limits the conclusions from a systematic review regarding the impact of bariatric surgery on HRQoL and mental health was the heterogeneity of questionnaires used to measure the outcome. To address this shortfall, we used the obesity-specific questionnaire together with a validated instrument to assess depressive symptomatology and found that HRQoL and mental health improved significantly in the first-year post-surgery. In particular, we were able to demonstrate the link between higher %WL, type of surgery and higher time spent on MVPA with better improvement in HRQoL. Also, the finding from Chapter 6 was the first to demonstrate the correlation between post-surgery moderate and severe depression with lesser %WL at 6-month post-surgery.

As extensively reviewed in Chapter 2, there is a paucity of high-quality studies investigating the efficacy of post-surgery lifestyle programmes to maximise weight loss outcome in the first year of bariatric surgery. The BARI-LIFESTYLE intervention study is the first study to show that combining both the nutritional-behavioural and tailored supervised exercise sessions in a single lifestyle intervention programme has no significant impact on weight loss in the first year post-surgery. Nevertheless, the programme improves physical function and has a favourable impact on physical strength and whole-body BMD. Furthermore, patient-reported outcomes support the beneficial aspects of such a programme in helping them adapt to the lifestyle changes after bariatric surgery. The outcome data from Chapter 7, addressed the need to investigate the efficacy and acceptable follow-up care packages for patients undergoing bariatric surgery in the UK (Coulman *et al*., 2020). Another novel finding of the present thesis is the in-depth exploration of patients' views and experiences of live supervised tele-exercise classes, as reported in Chapter 8. This is the first qualitative study to report the acceptability of an exercise programme delivered virtually following bariatric surgery, which now has a high potential to be adapted in future post-bariatric lifestyle programmes. Our findings, therefore, add to the limited evidence on the use of telehealth to deliver healthcare in patients undergoing bariatric surgery (Coldebella *et al*., 2018).

9.3 Implications of findings

The findings from this thesis have several implications to a wide range of groups including patients, healthcare professionals, the general public, policymakers, service commissioners and clinical decision-makers.

a. **Support increased provision of bariatric surgery in the UK.**

   The demand for publicly funded bariatric surgery in the UK is high, however, the capacity is limited by healthcare funding decisions (Welbourn *et al*., 2016). The outcome data of bariatric surgery from the BARI-LIFESTYLE observational study can assist policymakers, service commissioners and clinical decision-makers in making informed decisions to support the increased provision of bariatric surgery in the country.

b. Spread awareness regarding the health benefits of bariatric surgery.

Due to a strong weight bias and obesity stigma in the UK society, people living with obesity do not receive adequate health care (Flint, 2021). Furthermore, the stigma attached to bariatric surgery makes access to effective weight loss treatment difficult (Welbourn *et al.*, 2016, Phelan, 2018). Therefore, through various media platforms, the data from the BARI-LIFESTYLE observational study will be communicated to the general public to raise awareness regarding the health benefits of bariatric surgery.

c. Improve clinical practice guidelines for post-bariatric care.

Our findings suggest that patients who exhibited poor weight loss can be identified as early as 3-month post-surgery. In addition, post-surgery moderate to severe depression is also linked to poor weight loss. A higher depressive score is also associated with poorer HRQoL. Therefore, an early screening could allow identification of this subset of patients so that additional support such as the lifestyle programme can be targeted and offered.

As reported in Chapter 4, body composition assessment can provide further information regarding the quality of weight loss following bariatric surgery. Excessive fat-free mass loss, in particular, can be a sign of inadequate protein intake. Information about body composition can assist the bariatric MDT in providing individualised care for patients to maximise outcomes. However, the current clinical guidelines have no recommendation on routine body composition assessment (Mechanick et al., 2013b, Busetto et al., 2017). Therefore, we suggest body composition assessment be included as part of routine bariatric care and recommend the use of BIA. Whereas, due to the cost and limited accessibility, DXA scan can be indicated in patients with increased fracture risks such as in post-menopausal women and older patients.

d. Emphasise the importance of engaging in physical activity following bariatric surgery.

Higher time spent in sedentary behaviour is negatively associated with weight loss and fat mass loss. Therefore, replacing time spent in sedentary behaviour with any form of physical activity intensity must be emphasised following bariatric surgery, in line with the latest WHO physical activity guidelines (WHO, 2020b). Engaging in MVPA is even more beneficial in promoting further fat mass loss and better HRQoL. This is an important clinical message as patients often explain they do not find the need or will to engage in physical activity during the substantial weight loss period (Zabatiero *et al.*, 2018). Post-surgery physical function assessments, such as the walking test and the STS-test, can be applied to screen patients who are still suffering from functional limitations after bariatric surgery. Additional support provided by exercise professionals can then be targeted to this subset of patients to promote increased engagement in physical activity.

e. Support the provision of an adjunctive post-bariatric surgery lifestyle programme to maximise health outcomes of bariatric surgery.

The health outcomes of bariatric surgery vary markedly from person to person as demonstrated in the present observational study. Furthermore, excessive fat-free mass and BMD loss may have a negative impact over the long term. An adjunctive lifestyle programme could therefore be offered to patients following surgery to maximise outcomes. However, implementing such a programme on a large scale might not be feasible. Therefore, screening of patients who would need additional support post-surgery will allow for the programme to be targeted to patients who will benefit most.

f. Recommend telehealth as the way forward for the bariatric care service.

Nutritional-behavioural counselling delivered remotely via a telephone call is well-accepted based on the high adherence rate on the programme and how patients perceived it, as reported in Chapter 7. Furthermore, the remote supervised exercise classes delivered virtually via videoconferencing software was perceived as acceptable and beneficial through a qualitative analysis of patients' views and experiences in Chapter 8. Therefore, our findings highly recommend the use of telehealth to be adapted in the bariatric care service. This is in line with the NHS Long Term Plan to promote the use of technology in prevention, care and treatment to be mainstreamed across the NHS (National Health Service, 2019).

9.4 Strengths and limitations

The strength of the findings reported from the BARI-LIFESTYLE observational study is mainly on the methods used in assessing the outcomes measures. Both BIA and DXA (a reference gold standard) (Lee and Gallagher, 2008) were used to perform body composition analysis. The physical activity levels and sedentary behaviour, as reported in Chapter 5 were assessed objectively using an accelerometer as patients who have undergone bariatric surgery tend to over-report their physical activity levels when assessed using the conventional physical activity questionnaires (Herring *et al.*, 2016). Also, the present study used obesity-specific HRQoL questionnaire and validated instrument to assess depressive symptomatology that are very sensitive to detect minimal changes in the parameters measured. Another strength of the longitudinal study is a comprehensive assessment and data collection at four study time points in the first year of surgery, enabling an in-depth analysis of the outcome measures. The main strength of the BARI-LIFESTYLE intervention study is the use of a high-quality study design which was a two-arm, parallel-group, single-blinded, multi-centre RCT. The adherence rate of the tele-counselling sessions in the present study is also high (90.7%).

The research reported in this thesis is not without limitations. Due to the nature of the study, as commonly occurred in RCTs involving lifestyle intervention programmes (Younge *et al*., 2015), blinding the outcome assessors in this trial was deemed to be challenging. During the nationwide lockdown of the COVID-19 pandemic, all in-person follow-up assessments were carried out remotely hence throughout this period, outcomes data such as body composition and physical function were missing. The lockdown also may have impacted upon weight loss, physical activity levels and sedentary behaviour as well as HRQoL and mental health, so the present results should be interpreted with caution. Missing physical activity data was attributed to either participant did not meet the required wear time period, they did not return the device, or the returned device via mail did not reach our department. The unequal sample size that represented each type of bariatric procedure also limited the interpretation of our results. Another limitation of the RCT was that a total of 26.7% of participants randomised to the intervention group did not enrol in the exercise programme. Lastly, the use of the feedback form to assess the tele-counselling and the in-person exercise programme did not allow for an in-depth exploration of participants’ views and experiences.

9.5 Remaining work and future directions

There are several remaining analyses of the secondary outcome data of the BARI-LIFESTYLE observational study. The data regarding dietary intake collected from the food diary will further inform the relationship between calorie and macronutrient intake particularly dietary protein on weight loss and fat-free mass loss. Whereas the sleep data collected using the accelerometer will provide further insights into the impact of bariatric surgery on the changes in sleep quality. Furthermore, the healthcare resource utilisation and costs assessed using an adapted version of the CSRI will provide further information regarding the cost-effectiveness of bariatric surgery delivered in the UK healthcare setting. Whereas the cost-effectiveness analysis of the BARI-LIFESTYLE intervention study will provide further information for such a programme to be delivered in real-world clinical setting.

For future plans, long-term data collection from the present observational cohort will provide further insights into the impact of bariatric surgery beyond one-year post-surgery. Furthermore, collecting the long-term follow-up data from the intervention cohort will help answers whether delivering a lifestyle programme in the first postoperative year would have an impact upon long term weight loss maintenance as reported previously in an RCT (Mundbjerg *et al*., 2018b). To date, it remains inconclusive in regard to when is the best time to deliver the post-surgery lifestyle intervention programme (Bellicha *et al.*, 2021, Julien *et al.*, 2021). Therefore, future RCTs should randomise patients to receive the lifestyle programme at different time points post-surgery (e.g., lifestyle intervention during a substantial weight loss phase versus lifestyle intervention during the weight loss maintenance phase versus standard care) and assess outcomes. A reverse translational study should also be embedded in the future RCTs as it enables the researchers to further explain the expected and unexpected therapeutic outcomes of such programmes (Shakhnovich, 2018).

9.6 Concluding remarks

Obesity is a major public health challenge of the 21st century in the UK but access to effective weight loss treatments such as bariatric surgery is very limited. The lack of published UK prospective studies on the health outcomes of bariatric surgery leads to inadequate evidence to support the increased provision of such effective treatment in this country. The findings from the BARI-LIFESTYLE observational study, as reported in this thesis, therefore provided much-needed evidence on the beneficial impact of bariatric surgery in promoting substantial weight loss, remission or improvement of associated comorbidities, improvement in physical function and strength and better HRQoL and mental health. The dramatic lifestyle changes following bariatric surgery can be very challenging and difficulty in adapting to the post-surgery lifestyle recommendation can lead to poor outcomes. Although providing a lifestyle intervention programme as an adjunct therapy in the first year of surgery did not aid in weight loss, the programme led to an improvement in physical function and had a favourable impact on physical strength and whole-body BMD. Furthermore, patient-reported outcomes gathered from the BARI-LIFESTYLE intervention study support the beneficial impacts of such a programme in helping them adapt to life after bariatric surgery. Importantly, the present thesis further supports the use of telehealth as a method to deliver healthcare to patients following bariatric surgery.

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Appendices

Appendix No	Item
1	JASSIL, F. C. & BATTERHAM, R. L. 2021. Medical Complications of Obesity. *In:* WASS, J., ARLT, W. & SEMPLE, R. (eds.) *Oxford Textbook of Endocrinology and Diabetes.* Third ed.: Oxford University Press.
2	JASSIL *et al*. 2018. Protocol for a 1-year prospective, longitudinal cohort study of patients undergoing Roux-en-Y gastric bypass and sleeve gastrectomy: the BARI-LIFESTYLE observational study. BMJ Open, 8, e020659.
3	Research Ethics Committee (REC) approval letter
4	Health Research Authority (HRA) approval letter
5	Participant information sheet: The BARI-LIFESTYLE observational study
6	Consent form: The BARI-LIFESTYLE observational study
7	Participant information sheet: The BARI-LIFESTYLE intervention study
8	Consent form: The BARI-LIFESTYLE intervention study
9	Tele-counselling Manual
10	Tele-counselling Booklet
11	Exercise Booklet
12	Alcohol Use Disorders Identification Test-C (AUDIT-C) questionnaire
13	Activity Diary
14	Food Diary
15	3-Level EuroQol-5D (EQ-5D-3L)
16	Impact of Weight on Quality of Life-Lite (IWQOL-Lite)
17	Beck Depression Inventory-II (BDI-II)
18	Client Service Receipt Inventory (CSRI)
19	Feedback Form
20	JASSIL *et al.* (2022). Changes in accelerometer-measured physical activity levels and sedentary behaviour, physical function, and physical strength in the first year following bariatric surgery: the BARI-LIFESTYLE observational study.
21	JASSIL, F. C., BATTERHAM, R. L. & THE BARI-LIFESTYLE TEAM 2020. Health-related quality of life of patients awaiting bariatric surgery: A multi-centre observational study in the United Kingdom.
22	JASSIL *et al.* (2022). The impact of a combined nutritional-behavioural tele-counselling and supervised exercise intervention on weight loss and health outcomes following bariatric surgery: The BARI-LIFESTYLE randomised controlled trial.

23	JASSIL *et al*. (2021). Patients' views and experiences of live supervised tele-exercise classes following bariatric surgery during the COVID-19 pandemic: The BARI-LIFESTYLE qualitative study. Clinical obesity, e12499
24	Participant information sheet: The BARI-LIFESTYLE qualitative study
25	Consent form: The BARI-LIFESTYLE qualitative study