Physical Activity for Optimising and Sustaining Long-term Bariatric Surgery Outcomes

By

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A Doctoral Thesis

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For my family

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In many respects this thesis was a cooperative venture and the final outcome would not have been possible without the valuable support and guidance of many people.

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Abstract

Obesity levels are increasing worldwide, and in the United Kingdom the prevalence of overweight and obesity is amongst the highest in the developed world. Obesity is associated with reduced physical function and health-related quality of life, as well as an increased risk of co-morbidities such as type 2 diabetes and hypertension. As a result of high levels of morbid obesity and a failure of conventional methods of weight loss, more people are resorting to invasive weight loss techniques such as bariatric surgery. Bariatric surgery combined with lifestyle modification is currently the most successful weight loss intervention for the treatment of obesity and its associated co-morbidities. However, weight regain is becoming more apparent, generally occurring between 12 and 24 months after surgery. Weight regain is generally attributed to the failure of individuals to adopt or maintain the necessary lifestyle changes. The most common factors leading to weight regain after bariatric surgery are insufficient exercise and returning to pre-operative eating behaviours. Increasing physical activity after surgery positively affects weight loss and physical function outcomes; therefore, adopting an active lifestyle is fundamental. This thesis combines three research studies which collectively provide evidence for understanding the importance of physical activity for optimising physical function and facilitating the prevention of weight regain. Study one is a systematic review and meta-analysis which assessed pre to post-operative changes in physical activity behaviour and physical function outcomes among obese adults receiving bariatric surgery. This demonstrates improvements in objective and self-reported activity and function by 12 months. Study two is an analysis of body mass, co-morbidity and physical function data from pre to post-bariatric surgery. This retrospective UK NHS dataset analysis aimed to identify if and when weight regain occurs, the proportion of co-morbidity resolution, and physical function patterns in patients after bariatric surgery. Weight loss patterns indicate weight stability from 12 to 24 months and weight regain 24 months post-surgery. Study three is a randomised controlled trial, The MOTION Study, which examined the effect of a 12 week exercise intervention on physical function and body composition in patients 12-24 months post-bariatric surgery. This trial also examined maintenance of effects at six months. Findings suggest that implementing exercise at the point of weight regain is effective, notably for improving physical function and body composition in this population. This thesis therefore contributes to advancing the understanding of the role of physical activity in enhancing long-term outcomes after bariatric surgery and to informing future post-operative bariatric care.

Key words: Obesity, bariatric surgery, physical activity, physical function, exercise, weight loss, weight regain.

Thesis Contribution

All work in this thesis was undertaken by the author under the supervision of Dr Clare Stevinson and Dr Patrice Carter. All aspects of the systematic review reported in chapter three were undertaken by the author. Secondary reviewing processes were undertaken by the two academic supervisors aforementioned. The observational data reported in chapter four was collected routinely by the bariatric surgery departments direct care team. The whole study was conducted by the author from the collaboration development to the study concept, to full manual data extraction and analysis. Chapter five reports a randomised controlled trial of which the initial idea was generated by the Leicester Loughborough Diet, Physical activity and Lifestyle Biomedical Research Unit. The author undertook all aspects of the study including study protocol and design development, all NHS ethics and institution approval processes, recruitment, assessments, gym session design and supervision and data analysis.

Publications related to this thesis

Journal articles

Herring, L.Y., Scott, A., & Wagstaff, C. (2014). The Efficacy of 12 Weeks Supervised Aerobic or Resistance Training for Obesity Management. *Clinical Obesity*, 4 (4): 220-227.

Herring, L.Y., Stevinson, Davies M. J., Biddle, S. J. H., Sutton, C., Bowrey, D., & Carter, P. (2015) Changes in physical activity behaviour and physical function after bariatric surgery: a systematic review and meta-analysis. *Obesity Reviews*. 2016; 17 (3): 250-261.

Conference presentations

Herring, L., Stevinson, C., Carter, P., Biddle, S. J. H., Sutton, C., Bowrey, D., Yates, T., & Davies M. J. The effect of 12 weeks exercise training on the psychological well-being of obese adults 12 to 24 months post-bariatric surgery. (ISBNPA, Edinburgh, UK, 2015).

Herring, L., Stevinson, C., Carter, P., Biddle, S. J. H., Sutton, C., Bowrey, D., Yates, T., & Davies M. J. Body composition, physical activity and physical function outcomes 12 to 24 months after bariatric surgery. (ACSM, San Diego, USA, 2015). Published abstract in Medicine & Science in Sport & Exercise (May 2015 – Volume 47 – Issue 5S – p 462-468).

Herring, L., Stevinson, C., Carter, P., Biddle, S. J. H., Sutton, C., Bowrey, D., Yates, T., & Davies M. J. The effect of bariatric surgery on self-reported physical function: a systematic review. (ISBNPA, San Diego, USA, 2014).

Herring, L., Stevinson, C., Carter, P., Biddle, S. J. H., Sutton, C., Bowrey, D., Yates, T., & Davies M. J. The Effect of Bariatric Surgery on Functional Walking Ability: a Systematic Review. (ACSM, Florida, USA, 2014). Published abstract in Medicine & Science in Sport & Exercise (May 2014 – Volume 46 – Issue 5S – p 168-176).

Herring, L., Scott, A., & Wagstaff, C. The Efficacy of 12 Weeks Supervised Aerobic or Resistance Training for Obesity Management. European College of Sports Science Conference (Barcelona, Spain, 2013).

Journal articles in preparation

Herring, LY., Stevinson, C., Carter, P., Biddle, S. J. H., Sutton, C., Bowrey, D., Yates, T., & Davies M. J. The effects of supervised exercise training 12-24 months after bariatric surgery on physical function and body composition: a randomised controlled trial.

Orme, M., Herring,LY., Esliger, D., Sherar, L., & Stevinson, C. Wear-time compliance and intensity classification between wrist and waist accelerometry in bariatric surgery patients.

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Abbreviations

APP	as per protocol
ASMBS	American Society for Metabolic and Bariatric Surgery
BMI	body mass index
CVD	cardiovascular disease
ECG	electrocardiogram
FM	fat mass
FFM	fat free mass
GB	gastric band
GORD	gastro-oesophageal reflux disease
HADS	Hospital Anxiety And Depression Scale
HbA1c	glycated haemoglobin
HDL	high density lipoproteins
HR max	maximum heart rate
HRQoL	health-related quality of life
IPAQ	International Physical Activity Questionnaire
ISWD	incremental shuttle walk distance
ISWT	incremental shuttle walk test
ITT	intention to treat
Kcal	kilocalories
LDL	low density lipoproteins
MDT	multidisciplinary team
MET	metabolic equivalents
MCID	minimal clinically importance difference
MCIPS	minimal clinically important points scores
MVPA	moderate to vigorous physical activity
NBSR	National Bariatric Surgery Registry
NICE	National Institute For Health And Care Excellence
NHS	National Health Service
PCOS	polycystic ovary syndrome
RCT	randomised control trial
RPE	rating of perceived exertion
RYGB	Roux-en-Y gastric bypass
SD	standard deviation
SERPA	Self-Efficacy to Regulate Physical Activity scale
SPPB	short physical performance battery
STS	seat to stand
TUG	timed up and go

T2DM	type 2 diabetes mellitus
VO_2	volume of oxygen
WHO	World Health Organisation
WHR	waist to hip ratio
1-RM	one repetition maximum
6MWT	six minute walk test
%EWL	percentage excess weight loss

Chapter One

Introduction

Chapter overview

This chapter firstly introduces obesity and its prevalence. It also provides an overview of the universal measurement of body shape and the obesity classifications which the population is categorised by. Furthermore, this chapter outlines the associated obesity related co-morbidities, the cost of obesity on the National Health Service (NHS) and introduces weight loss methods such as bariatric surgery. Finally, this chapter presents the aim of the research projects that underpin this thesis.

1.1 Introduction

According to the World Health Organisation (WHO) obesity prevalence worldwide has more than doubled since 1980[1]. Adult and childhood obesity incidence in the United Kingdom (UK) are among the highest in the developed world[2]. England's overweight and obesity prevalence accounts for around 62% of the adult population, of which 25% of adults are categorised as obese; this is a 10% increase since 1993[3, 4]. Class III obesity (body mass index [BMI] 40kg·m^2) currently affects 1.5 million adults in England, corresponding to 3.5% of the male population and 1.5% of the female populations[4].

The current universal body mass measurement is BMI which is a simple calculation derived from a height and weight measurement[5]. The BMI equation is body mass in kilograms (kg) divided by height in metres (m) squared [(2)] (BMI = kg / m^2)[5].

Table 1.1: The World Health Organisations (WHO) BMI classifications.

Classification	**BMI (kg·m^2)**	
	Principal cut-off points	**Additional cut-off points**
Underweight	**< 18.50**	**< 18.50**
Normal range	**18.50 – 24.99**	**18.50 – 22.99**
		23.00 – 24.99
Overweight	**≥ 25.00**	**≥ 25.00**
Pre-obese/at risk	25.00 – 29.99	25.00 – 27.49
		27.50 – 29.99
Obese	**≥ 30.00**	**≥ 30.00**
Obese class I	30.00 – 34.99	30.00 – 32.49
		32.50 – 34.99
Obese class II	35.00 – 39.99	35.00 – 37.49
		37.50 – 39.99
Obese class III	≥ 40.00	≥ 40.00

KEY: kg·m^2: kilogram per metre squared[5].

Such universal measurement allows calculation of national and international prevalence rates for each classification listed in Table 1.1 and is therefore comparable between nations[6]. BMI classifications are modified for Asian populations, because in general Asians have a greater body fat percentage at a given BMI classification than Caucasian counterparts[7, 8], see Table 1.2.

Table 1.2: The WHO's BMI classifications for Asian adults.

Classification	**BMI ($kg \cdot m^2$)**
	Asian population cut-off points
Underweight	**< 18.50**
Normal range	**18.50 – 22.99**
Overweight:	**≥ 23.00**
Pre-obese/ at risk	23.00 – 24.99
Obese class I	25.00 – 29.99
Obese class II	≥ 30.00

KEY: $kg \cdot m^2$: kilogram per metre squared[9].

Rising levels of obesity and morbid obesity have contributed to higher rates of cardio-metabolic complications and an increase in associated diseases[10]. Obesity also negatively impacts physical function. Activities such as housework, walking up stairs and transitioning from sitting to standing are limited in obese individuals due to musculoskeletal disorders and restricted mobility[11, 12]. Common obesity related diseases, co-morbidities and musculoskeletal disorders include diabetes mellitus (T2DM), cardiovascular diseases (CVD), hypertension, dyslipidaemia, arthritis, obstructive sleep apnoea and non-alcoholic fatty liver disease[13, 14]. Morbid obesity also negatively affects all domains of health-related quality of life (HRQoL), specifically domain areas of activity/mobility, symptoms, personal hygiene/clothing, emotions, social interactions, sexual life and eating behaviour[15].

The Department of Health reports that the NHS spends more than £5billion on the health problems associated with obesity and being overweight[16]. According to 'The Action on Obesity: Comprehensive Care for All' report, by the Royal College of Physicians published in January 2013, the current £5billion UK obesity cost is set to double by 2050 if the obesity epidemic is not addressed appropriately[2]. To reverse obesity and its negative associations, commercial weight loss

programmes are growing in popularity, although long term weight maintenance is questionable in such programmes[17]. More recently NHS multidisciplinary team (MDT) weight management services are being set up nationwide. The Royal College of Physicians highlight the importance of these MDT services[2]. Individuals lose on average 3% of their body mass when attending such lifestyle and weight management programmes. Unfortunately, for long term benefits it is suggested that more than 5% weight loss is necessary, and must be maintained for life[4]. This difficulty to optimise weight-loss through conventional methods and commercial weight-loss programmes highlights why there is a growing demand for more invasive weight loss techniques such as bariatric surgery procedures[4, 18].

Bariatric surgery, combined with long-term lifestyle modification, is currently the most effective and sustainable method of weight-loss[19]. Rates of weight loss and maintenance after surgery vary depending on the type of bariatric surgery performed and the lifestyle adaptations patients make and sustain[20, 21]. The Royal College of Physicians also recommend multidisciplinary support after surgery to optimise the concomitant lifestyle changes required; suggested advice includes nutritional, psychological, physical activity and exercise education[2]. If such advice is not available, or adhered to, post-operative weight regain is likely to occur[22]. Typically, post-operative weight regain becomes apparent between 12 and 24 months after bariatric surgery[23]. Due to the importance of dietary change after bariatric surgery, dietetic monitoring is the only discipline consistently offered nationwide for two years after surgery as part of NHS normal care. Psychology and physical activity support are not routinely available[24], however, post-operative weight loss can be influenced by individuals physical activity levels[14]. Higher levels of physical activity have been associated with additional weight loss[25, 26]. A meta-analysis established that physically active patients had a greater mean weight loss of 3.62kg than those who are physically inactive[25].

In order to minimise the likelihood of weight regain post-bariatric surgery, it is important to optimise patients' post-operative support. Similarly, to ensure bariatric surgery is sustainable as a life-long weight-loss method for morbid obesity, intervention post-surgery must be identified and implemented to facilitate the positive long-term outcomes associated with this invasive weight loss technique.

1.2 The aims of this thesis

The research described in this thesis aimed to increase the understanding of the role of physical activity in enhancing long-term outcomes of bariatric surgery. Three studies have been conducted to contribute to knowledge in the field. Chapter three describes a systematic review and meta-analysis which assessed pre to post-operative changes in physical activity behaviour and physical function outcomes among obese adults receiving bariatric surgery. Chapter four reports an analysis of body

mass, co-morbidity and physical function data from pre to post-bariatric surgery. This retrospective NHS dataset analysis aimed to identify if and when weight regain occurs, the proportion of co-morbidity resolution and physical function patterns in patients after bariatric surgery. Secondary to this, did demographic variables affect post-operative weight loss and physical function. Chapter five reports a randomised controlled trial (RCT) which examined the effect of a 12 week exercise intervention on physical fitness and body composition in patients 12-24 months post-bariatric surgery. Maintenance of effects at six months was also examined.

Chapter Two

Literature Review

Chapter overview

This chapter outlines existing literature which supports the thesis research rationale. It describes the effectiveness of different methods of obesity management, specifically bariatric surgery and its procedures. Furthermore, weight loss patterns as a result of bariatric surgery are discussed, in particular post-operative weight regain. The chapter also outlines the importance of post-operative physical activity for optimising post-surgery outcomes, specifically physical function, weight loss and co-morbidities. This leads to discussing the current post-operative exercise interventions that exist and their findings. Finally, this chapter highlights the key research gaps thus identifying areas of research needed to strengthen the current literature.

2.1 Recommendations for the management of overweight and obesity

The National Institute for Health and Care Excellence (NICE) have developed guidelines for managing overweight and obese adults within the NHS[27]. Due to the concerns over validity of BMI alone, these guidelines have incorporated both BMI and waist circumference. If co-morbidities are also present, individuals may have a greater risk at a lower BMI category; therefore this is also taken into consideration. Table 2.1 outlines the NHS guidelines for obese and overweight individuals.

Table 2.1: NICE guidelines for the management of overweight and obesity.

BMI classification	Waist circumference			Co-morbidities present
	Low (males ≤94cm; females ≤80cm)	**High** (males 94-102cm; females 80-88cm)	**Very high** (males ≥ 102cm; females ≥ 88cm)	
Overweight	General advice on healthy weight and lifestyle	Diet and physical activity	Diet and physical activity	Diet and physical activity; consider drugs
Obesity I	Diet and physical activity	Diet and physical activity	Diet and physical activity	Diet and physical activity; consider drugs
Obesity II	Diet and physical activity; consider drugs	Diet and physical activity; consider drugs	Diet and physical activity; consider drugs	Diet and physical activity; consider drugs; consider surgery
Obesity III	Diet and physical activity; consider drugs; consider surgery	Diet and physical activity; consider drugs; consider surgery	Diet and physical activity; consider drugs; consider surgery	Diet and physical activity; consider drugs; consider surgery

KEY:BMI: body mass index[27].

Typically lifestyle advice consists of advice from an individual's general practitioner[28]. Weight management referral typically entails undergoing a multidisciplinary team (MDT) service, comprising of dietary advice, psychological support and physical activity advice. This is usually offered through specialist tier 1 and tier 2 weight management services depending on the severity of obesity[29]. A systematic review comparing diet and exercise vs diet alone in obese adults shows that a combination of both results in significant and clinically meaningful initial weight loss compared to diet alone[30].

Drug therapy may be offered and involves prescribing medications such as Orlistat[31, 32]. Surgery is the most invasive weight loss intervention which involves reducing the size of the stomach through different methods[33].

2.2 Bariatric surgery

Bariatric surgery, otherwise known as weight loss surgery, is defined as the 'surgical removal of parts of the stomach and small intestines to induce weight loss[34]. Jejunoileal bypass was the first type of bariatric surgery performed in humans in the 1950s. This lead to complications such as inhibited absorption and digestion of important nutrients and was therefore stopped in the late 1970s[19]. Bariatric surgery was infrequent and focused on gastric restriction until the introduction of laparoscopic techniques in the 1990s[35]. This allowed surgery to be performed through a small incision, which decreases the risks of wound complications and pain commonly associated with earlier methods[19, 35, 36]. The NHS is the main public provider of this weight loss technique in England[37]. The type of bariatric surgery procedure performed is dependent on the bariatric surgery department's expertise, combined with the surgeon and patient preference. Laparoscopic adjustable gastric banding is currently the most common and least invasive bariatric surgery procedure worldwide[19]. The greatest percentage of weight change occurs with Roux-en-Y gastric bypass surgery[23]. There are different types of bariatric surgery procedures and adaptations, below are the three main surgical techniques currently used worldwide and in the UK[4, 19, 38].

2.2.1 Gastric Band

Laparoscopic adjustable gastric band is a restrictive type of bariatric surgery and a comparatively non-invasive procedure in which a pouch is created in the upper stomach due to the application of an adjustable silicone band. The band causes a narrowing between the upper stomach pouch and the main stomach, reducing food ingestion and reducing the feeling of hunger. The band can be adjusted through an under skin portal by injecting and removing saline and if complications occur it is relatively easy to remove the band[38]. Gastric banding accounts for 17.8% of bariatric surgery procedures and has decreased in popularity from 42.3% in 2008[4]. The average weight loss three years after gastric band surgery is 15.9%[39]. Figure 2.1 shows an illustration of the stomach and gastric band placement.

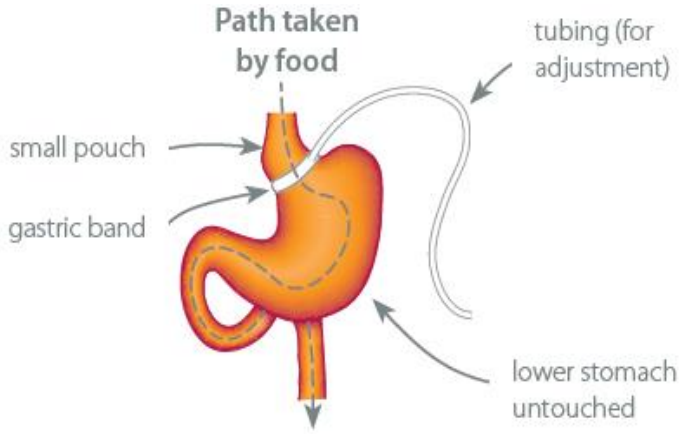


Figure 2.1: An illustration of the gastric band bariatric surgery procedure.
Reproduced with permission from Dendrite Clinical Systems and The UK National Bariatric Surgery Registry[4]

2.2.2 Sleeve Gastrectomy

Vertical sleeve gastrectomy is also a restrictive type of bariatric surgery which reduces the stomach by approximately 75%, which limits food intake and affects appetite[4]. The stomach is divided vertically; digestion and stomach function remain unaltered (Figure 2.2). This procedure cannot be reversed and often leads to Roux-en-Y gastric bypass or duodenal switch in severely obese patients, as a single stage procedure can be dangerous and technically challenging[38]. This bariatric surgery procedure accounts for 27.8% of procedures in the UK and has grown in use from 5.3% in 2008[4]. The average weight loss three years after sleeve gastrectomy has been reported as 21%[39].

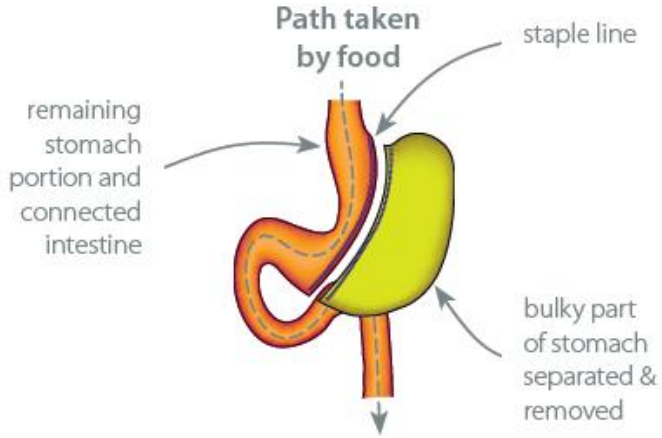


Figure 2.2: An illustration of the sleeve gastrectomy bariatric surgery procedure.
Reproduced with permission from Dendrite Clinical Systems and The UK National Bariatric Surgery Registry[4]

2.2.3 Roux-en-Y Gastric Bypass

Roux-en-Y gastric bypass is a combined malabsorptive and restrictive procedure and accounts for 46.6% of bariatric surgery procedures in the UK[4]. It is either an open or laparoscopic surgical procedure in which a small pouch of the stomach is created. This pouch remains attached to the oesophagus whilst being connected to a segment of the small intestine, bypassing the initial loop of the small intestine and the remaining stomach area[38] (Figure 2.3). The greatest percentage of weight loss occurs with Roux-en-Y gastric bypass surgery, this is on average 31.5%[23, 39].

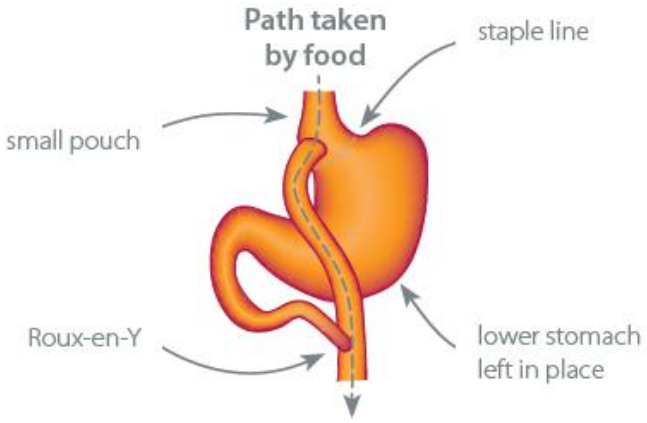


Figure 2.3: An illustration of the Roux-en-Y gastric bypass bariatric surgery.
Reproduced with permission from Dendrite Clinical Systems and The UK National Bariatric Surgery Registry[4]

2.3 The effectiveness of bariatric surgery, compared to conservative weight loss approaches

Typical non-surgical weight loss interventions include lifestyle advice provision, weight management referral, anti-obesity drug therapy and bariatric surgery referral[10]. The severity of obesity dictates the referral pathway. Comparisons between bariatric surgery and lifestyle interventions for morbid obesity have been undertaken to identify the most effective method for weight loss, the improvement of co-morbidities and optimising long term weight maintenance[40, 41]. Approximately 97% of morbidly obese patients cannot achieve durable weight loss (BMI of >35kg·m^2) through conventional methods of diet restriction and increased physical activity alone[42-44]. A systematic review and meta-analysis compared RCTs of bariatric surgery to non-surgical treatments. They found surgery results in greater weight loss (mean difference between groups of -26kg), greater improvements in quality of life and showed superior remission rates in T2DM (relative risk to achieve remission was 22.1 times higher than the non-surgical group)[45]. Martins *et al*[41] compared body mass, co-morbidities and health risk

factors of patients awaiting bariatric surgery who were given the option to undertake alternative treatment or remain on the waiting list. Treatments included one of three different lifestyle interventions; a residential intermittent programme, a commercial weight loss camp and a hospital outpatient programme. Results at one year revealed that bariatric surgery induced greater weight loss than the three conservative treatments (40kg versus 22kg); lifestyle interventions did still however reduce risk factors and body mass[41]. When comparing cardiovascular risk factors in gastric bypass patients versus individuals undergoing an intensive lifestyle intervention, short term follow-up reported T2DM and cardiovascular risk factors improved in both groups. Nevertheless, outcomes were more effectively reduced in those who underwent surgery (glycated haemoglobin [HbA1c], surgery -0.4% vs lifestyle -0.1%; triglycerides, surgery -0.9 mmol/l vs lifestyle -0.4 mmol/l)[40]. Another intensive lifestyle intervention was reported to be less effective than Roux-en-Y gastric bypass surgery for improving the prevalence and severity of obstructive sleep apnoea in morbidly obese individuals (apnoea hypopnea index, surgery -21.6 events/h vs lifestyle -8.8 events/h)[46]. Research on long term weight change and obesity related disease remission after obesity interventions is currently limited. A study by Sjöström *et al*[23] compared three different types of bariatric surgery to a conventionally treated control group and their weight patterns were followed post-operatively for 10 years. They showed a mean 1.6% increase in body mass in the conventionally treated group, with the three surgical groups mean body mass decreased between 13.2% and 25% 10 years post-surgery.

The literature although limited, indicates positive outcomes for both surgical and lifestyle interventions, however surgery induces greater weight loss and larger improvements in obesity related diseases and co-morbidities[40, 41, 46]. Lifestyle interventions are increasingly incorporated as an adjunct to bariatric surgery in the attempt to maximise long term success[20].

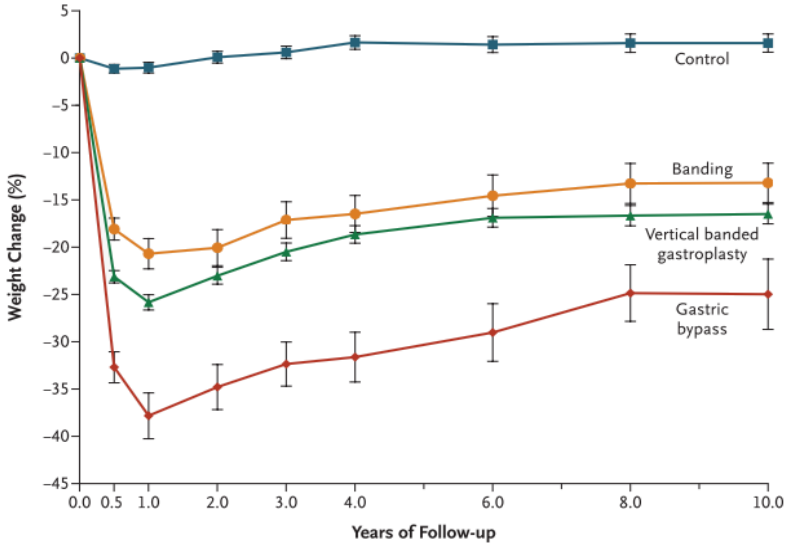
2.4 Bariatric surgery and co-morbidity resolution

Bariatric surgery aims to improve overall health by reversing and preventing obesity related co-morbidities as a result of weight loss[4]. A systematic review of 136 studies (22,094 patients) examined the impact of bariatric surgery on weight loss and four co-morbidities (T2DM, hypertension, hyperlipidaemia and obstructive sleep apnoea)[47]. Co-morbidity resolution or improvement occurred in 86% of people with T2DM, 70% of those with hyperlipidaemia, 79% of hypertensive patients, and eight percent of sleep apnoea sufferers, and the mean percentage excess weight loss (%EWL) was 61%. The UK national bariatric surgery registry (NBSR) report states that 50% of males and females with T2DM have resolution of diabetes within one year post-surgery[4]. Similar results were observed for hyperlipidaemia and obstructive sleep apnoea[4]. Research reports T2DM is one of the more costly co-morbidities associated with obesity and the resolution of T2DM alone (assuming 40% resolution) has found bariatric surgery to be cost-effective[48].

Weight regain increases the likelihood of obesity related co-morbidities returning[49]. A systematic review presents evidence for exercise prescription in the treatment of co-morbidities such as metabolic syndrome-related disorders, heart and pulmonary diseases, muscle, bone and joint diseases and cancer, depression and asthma[50]. A systematic review by Christensen *et al*[51] reported methods of weight management in knee osteoarthritis; the review supports exercise prescription, reported that arthritic pain was positively affected by weight loss induced by diet plus the addition of exercise[52]. This research could also support the addition of post-bariatric surgery exercise prescription in addition to usual care.

2.5 Weight-regain post-bariatric surgery

Research demonstrates that bariatric surgery is more successful than non-surgical interventions for weight loss and the treatment of morbid obesity[41]. Rates of weight loss and maintenance after bariatric surgery vary significantly in the literature; however, post-operative weight regain is increasingly apparent between 12-24 months post-bariatric surgery[20 23, 53]. The large scale Swedish Obesity Study by Sjöström *et al*[23] reported 10 year weight patterns for three different bariatric surgical procedures. Weight patterns changed at different rates dependant on the procedure undertaken, however, weight regain occurred at 12 to 24 months post-surgery in all surgery types (Figure 2.4). A 5-year prospective study by Magro *et al*[53] indicated that about half of the 782 patients assessed regained weight within 24 months post-operatively. Bariatric surgery is a tool that assists individuals with a new start towards a healthier life; surgery alone will not help weight loss and long term maintenance[54]. Weight regain is typically attributed to the inability to adopt or maintain the necessary changes in physical activity and dietary behaviour[22]. Richardson *et al*[54] report that decreased exercise and returning to pre-operative eating habits are the most common factors of weight regain. This can lead to changes in operative anatomy, such as an enlargement of the gastric pouch and/or gastrojejunostomy in Roux-en-Y gastric bypass patients[54, 55]. This stretching of the gastric pouch is caused by overeating and can lead to weight regain and sometimes revisional procedures[56, 57].



No. of Subjects									
Control	627	585	594	587	577	563	542	535	627
Banding	156	150	154	153	149	150	147	144	156
Vertical banded gastroplasty	451	438	438	438	429	417	412	401	451
Gastric bypass	34	34	34	34	33	32	32	29	34

Figure 2.4: Ten year body mass changes of participants from the Swedish Obesity Study and participant numbers.

Reproduced with permission from (Sjöström *et al*[23]), Copyright Massachusetts Medical Society.

On average individuals exhibit a large amount of weight loss in the first year after surgery regardless of the type of procedure undertaken[23]. Research suggests undertaking post-operative maintenance programmes as an adjunct helps prevent weight regain and aids optimisation of long term outcomes[58]. A study by Zalesin *et al*[59] reports that weight loss maintenance is very challenging and that behavioural components of dietary control, regular physical activity, and behaviour modification are essential. The study also concludes that multidisciplinary follow-up interventions are vital for the successful prevention of weight regain. Weight regain has been referred to as a warning sign and if caught in its early stages, is easier for a patient to get back on track[54].

The effectiveness of post-operative behavioural management for long term weight control was examined in a recent systematic review[60]. The behavioural management was delivered via lifestyle interventions or support groups. From 15 studies, 13 concluded that individuals who undertook post-operative behavioural interventions had a significantly greater weight loss compared to those receiving usual care or no intervention[60]. The Royal College of Physicians suggest that such MDT approaches should include specialist consultant physicians, surgeons, dieticians, nurses, psychologists and psychiatrists and exercise/physical activity professionals[2]. MDT services should address areas of advice such as the psychological aspects of behaviour change, dietetics and physical activity. MDT services in the UK, if provided, predominantly adopt an educational approach[2, 22, 45]. Patients regularly attribute poor outcomes to non-compliance with behavioural recommendations, and the main area of

non-compliance is exercise[61]. This supports other literature reporting that exercise education alone is insufficient for weight loss[62, 63], indicating that other methods of delivery should be explored to facilitate weight loss and long term weight maintenance.

There are currently no standardised guidelines in the UK to deliver such services, only advice for service provision is available[2]. This shows that pre and post-operative interventions are needed to enable the development of standardised guidelines for all bariatric surgery services to optimise long term surgical outcomes, such as weight loss, physical function and co-morbidity resolution.

2.6 Bariatric surgery combined with lifestyle intervention

Behavioural intervention research for bariatric surgery is currently limited but is a growing area of interest. It is necessary to identify whether pre or post-operative behavioural interventions, or both, optimise long term weight loss and co-morbidity resolution. A recent systematic review and meta-analysis of 11 studies has explored behavioural interventions for severe obesity before and/or after bariatric surgery[64]. The authors concluded that provision of behavioural interventions as an adjunct to bariatric surgery appear to improve post-operative weight loss outcomes, however, they point out that the results should be interpreted with caution due to the small number of trials, low methodological quality, and short duration of follow-ups[64]. Ogden *et al*[65] evaluated the impact of pre and post-operative psychological support. They found it had no impact on weight loss one year post-bariatric surgery and should be implemented at the point of weight regain.

2.6.1 Pre-operative lifestyle interventions on bariatric surgery outcomes

A prerequisite for consideration for bariatric surgery on the NHS in England, is that candidates must have fully engaged in a structured weight loss programme, but failed to maintain a clinically significant weight loss for the individuals needs[66]. In the United States health insurers have made it mandatory that all candidates undergo a medically supervised weight management programme before undergoing bariatric surgery[67]. Research on the success of these pre-operative weight management programmes is limited.

Parikh *et al*[67] conducted a pilot study to define the effect of a pre-operative medically supervised weight management programme to improve gastric banding outcomes. When comparing usual care to the intervention group no significant differences were found for weight or patient behaviour scores, including adherence, eating behaviour and activation. The only significant improvement as a result of the pre-operative medically supervised weight management programme was self-reported physical activity. Lier *et al*[68] studied pre-operative counselling on post-operative treatment adherence in 141 gastric bypass patients. An association was identified between weight loss and adherence to dietary and physical activity interventions, however, adherence varied dramatically in individuals one year

post-operatively. No post-operative benefit on weight loss, adherence to physical activity and dietary lifestyle changes occurred from pre-operative psychological counselling.

King & Bond's[69] review examined the importance of pre and post-operative physical activity counselling for bariatric surgery. They concluded that fitness, weight loss and body composition were all associated with increasing physical activity pre to post-operatively, with higher levels of physical activity after surgery. It has also been reported that inactive patients with sufficient support can become sufficiently active, and further improve surgical outcomes. Although patients self-report an increase in post-operative physical activity they do not meet the recommended physical activity guidelines. The authors suggest that the use of physical activity counselling strategies and exercise testing throughout all phases of patients care. This helps to meet the recommendations of 60/90 minutes of moderate to vigorous physical activity (MVPA) per day recommended for weight maintenance[69].

2.6.2 Post-operative lifestyle interventions on bariatric surgery outcomes

Randomised controlled trials (RCT) have more readily explored the effect of post-operative intervention on bariatric surgery outcomes, yet research in this area is still limited. The main aim of the available research is to look at incorporating lifestyle interventions as an attempt to aid holistic post-operative bariatric surgery success and the majority of interventions adopt an educational approach [20, 67, 68, 70, 71].

Nijamkin *et al*[71] recruited Hispanic Americans (n = 72) after gastric bypass surgery and implemented a nutrition and behaviour education intervention to explore the effect on weight loss and physical activity one year after surgery. They found a 16% greater excess weight loss in the intervention group compared to usual care at 12 months, with 82% of the intervention group reporting regular physical activity compared to 64% of controls[71].

A seven year multi-intervention treatment supporting lifestyle change was introduced by Steffen *et al*[70] with 388 patients post gastric band surgery. The intervention included dietary restriction, increasing physical activity, living with a band, and smoking cessation, in addition to attending sessions with an obesity specialist. BMI reduced by 28% at five years and remained stable with a mean excess weight loss of 61% at seven years. Metabolic syndrome was prevalent in 59.7% of patients pre-operatively compared with 13.3% at seven years, and this was completely reversed in those with a BMI reduction of >40%. Mortality rate as result of this MDT intervention decreased to 18 deaths per 10,000 in the current study, although there was no control group to allow comparisons[70].

A study by Papalazarou *et al*[20] included the use of a control group when evaluating the effect of a post-operative lifestyle intervention on female bariatric surgery patients. They also undertook

objective measures of physical activity, weight loss and dietary habits at 12, 24 and 36 months after vertical banded gastroplasty (where a band and staples are used to create a pouch). The intervention and control groups attended their dietetic appointments (normal care) with an additional 40 minute session at the end of these appointments for the intervention group (focusing on behaviour change techniques, overcoming barriers, body mass regulation through improving dietary and physical activity habits). The lifestyle group when compared to usual care displayed a significantly lower body mass at 12 (14kg), 24 (18.9kg) and 36 (18.3kg) months after surgery. Significant improvements were also seen for physical activity and diet.

The first review and meta-analysis to systematically examine studies looking at behavioural lifestyle interventions on weight loss post-bariatric surgery was undertaken by Rudolph and Hilburt[60] Fifteen studies met their inclusion criteria; out of these 15 studies 13 reported greater weight loss as a result of behavioural management interventions as opposed to those receiving no treatment or usual care. As this area of research is in its infancy, there is currently no specific structure or standardised guideline for behavioural programmes. The interventions in the current review differed not only in content, but in the delivery, with the educational sessions predominantly lead by dieticians or psychologists. As suggested by the author, another important factor to consider is at which point after surgery a behavioural intervention should be implemented, as the majority of research focuses on interventions directly after surgery. Follow-up contact between patient and professional post-operatively has been associated with increased weight loss. However, the current systematic review could not determine whether an increased weight loss was the result of follow-ups with a professional or due to the delivered intervention content. An area for future research includes focusing on individuals displaying either poor weight loss, or weight regain.

More recently Coen *et al*[72] conducted a RCT on 128 gastric bypass patients. Individuals were randomly allocated to either a semi-supervised moderate exercise protocol or a health education control. Both groups saw a significant reduction in body mass and fat mass (FM). Though, glucose effectiveness and cardiorespiratory fitness improved in the exercise group. This may therefore indicate that post-operative health education and exercise elicits similar improvements, with the exercise intervention displaying additional fitness benefits. More research is needed to determine the optimal and cost effective approach for long term weight management after surgery.

Research currently shows that the combination of bariatric surgery and post-operative lifestyle interventions positively affects weight loss and additional outcomes. Heterogeneity between intervention types and methods of delivery makes it difficult to determine an optimal post-operative behavioural intervention. Longer term follow-ups are needed to help determine the most successful post-operative lifestyle interventions. Pre-operative intervention research is relatively new so it cannot

conclusively be stated that it is not beneficial on post-operative weight loss outcomes, although this is currently indicated. It would be important to develop standardised bariatric surgery intervention guidelines and methods of delivery, alongside the most effective time point such interventions should be delivered.

2.7 Physical activity behaviour and bariatric surgery

Bariatric surgery patients' post-operative weight loss is associated with their physical activity levels[14, 73]. Associations have been identified between long term weight loss outcomes, high sitting time and MVPA in 303 patients following bariatric surgery (7±4 years)[74]. Self-reported participation in 150 minutes per week of MVPA has been shown to produce a significantly greater weight loss six and 12 months post gastric band surgery[75]. A large scale study by King *et al*[76] showed an increase in objectively measured physical activity at one year post-operatively as a result of bariatric surgery alone, however, patients still remained insufficiently active. Furthermore, by three years MVPA was no different to pre-operative levels[77]. This research indicates that regardless of the improvements noted at one year, physical activity and function performance after bariatric surgery is still significantly inferior to recommended weight-dependent activity reference values[76]. Therefore, exercise interventions initiated post-operatively could aid the promotion of sufficient activity levels further improving long term surgical body composition and functional outcomes.

2.7.1 Physical activity and post-operative weight loss

Three systematic reviews have been undertaken on physical activity and post-operative weight loss outcomes. Livitus *et al*[26] reviewed 13 studies from the years 1988 to 2009 which looked at exercise and its effect on body mass following bariatric surgery. Measurements of physical activity in these studies were predominately self-reported. Eleven of the thirteen included studies found that post-operative exercise positively affected weight loss 12-24 months after surgery. The authors were unable to establish a causal effect between exercise and weight loss due to the observational nature of the data, so it is unclear whether increased activity results in weight loss or weight loss causes this increase in physical activity. Jacobi *et al's*[73] systematic review also examined physical activity and weight loss after bariatric surgery. Twenty observational studies from 1990 to 2009 met the inclusion criteria. Similarly to Livitus *et al* [26], they found that physical activity was related to post-operative weight loss, and that self-reported physical activity measures indicate increased amounts of activity after surgery. Egberts *et al*[25] undertook the most recent systematic review titled "Does exercise improve weight loss after bariatric surgery?". Seventeen short term observational studies met the inclusion criteria and no RCT's of exercise interventions were found. In 15 studies the relationship between physical activity and weight loss was positively associated[25, 26, 73]. A limitation of all of these systematic reviews is the heterogeneity of physical activity measurements, the definition of exercise

and the absence of any exercise interventions. Nonetheless, all three reviews found a positive correlation between post-operative weight loss and physical activity.

Recent studies have measured pre and post-operative daily physical activity using objective measures such as pedometers and accelerometers[76, 78-80]. Of these four studies, two reported pre to 6-month total physical activity or MVPA, and two reported pre to 12 months post-operative MVPA. Liu *et al*[78] and Bond *et al*[79] found a decrease in physical activity when objectively measuring MVPA and total physical activity from pre to six months post-surgery. However, King *et al*[77] and Berglind *et al's*[80] research revealed a mean improvement in MVPA at 12 months post-operatively. Liu *et al*[78] suggests this reduction in physical activity could be a result of post-surgical metabolic adaptations to calorific restriction. A study by Josbeno *et al*[81] which assessed step count before and after surgery showed an improvement in daily step count at six months. Unfortunately, the intensity of activity cannot be determined when measuring step count; patients could therefore be undertaking more light activity than moderate-intensity activity six months after surgery. Based on the findings from all of these studies with objective measurements, physical activity appears to increase by 12 months post-surgery. However, it is likely a shift in the intensity of physical activity undertaken occurs six months post-operatively. Participants may, therefore undertake more light activity at earlier post-operative time points. Rigorous trials of exercise interventions using objective measurements are needed to increase the validity of current findings. Future pre and post-operative physical activity monitoring is necessary to confirm this relationship and to determine a universal exercise prescription (exercise frequency, intensity, time and type) to optimise post-operative outcomes[25, 26, 73].

2.7.2 Physical activity recommendations post-bariatric surgery

Current physical activity recommendations for the general adult population are at least 150 minutes of moderate intensity physical activity per week[82]. For additional health benefits (for example lowering blood pressure, a healthier BMI/ body composition, lowering rates of T2DM and coronary heart disease and increasing cardiorespiratory and muscular fitness), WHO recommend that adults should engage in 300 minutes of moderate intensity physical activity and include muscle strengthening exercises using major muscle groups on two or more days a week[82]. The American College of Sports Medicine[83] similarly recommend at least 60 minutes of moderate intensity exercise on five days per week, however, they specify this is to aid weight loss. Bond *et al*[79] found that pre-operatively 10% of patients met the guidelines of ≥150 minutes of MVPA per week, whereas six months post-operatively only 5% met these guidelines. At this point, exercise guidelines for post-bariatric surgery have not been established and the optimal frequency, intensity time and type of exercise are unknown. Some studies have provided preliminary data on this subject[84, 85]. A systematic review focusing on exercise following bariatric surgery by Livhits *et al*[26] reviewed 14 articles. The active post-operative patient

definition varied between studies. Although the active post-operative patient definition varied, in general a minimum of 30 minutes three times per week was required to be classed as an active post-operative patient.

Akkary *et al*[85] compared the exercise habits of successful (achieved a minimum of 80% excess weight loss one year post-operatively) Roux-en-Y gastric bypass patients to those of BMI matched, physically fit controls. No significant difference was found with regards to exercise frequency; both groups exercised between four and seven days a week for one to two hours in duration. However, 60% of the control and 80% of the operative group undertook more than 30 minutes of cardiovascular exercise on a typical day; this was statistically significant. Significantly more of the control group (86%) undertook weight training routinely compared to the operative group (50%). Thirty-four percent of the operative group undertook recreational sport, significantly less than the control (60%). The operative group typically climbed more than five flights of stairs a day significantly more than the control group. These results suggest that one to two hours of exercise should be completed on four to seven days of the week post-operatively, including a minimum of 30 minutes cardiovascular exercise combined with an active lifestyle.

Bond *et al*[86] undertook the first prospective study to identify a positive relationship between physical activity change and improved bariatric surgery outcomes. Physical activity was determined using the international physical activity questionnaire (IPAQ). An inactive individual was defined as <200 minutes of MVPA per week and an active individual was defined as ≥ 200 minutes of MVPA per week. Individuals classified as inactive pre-operatively and active one year post-operatively lost 6kg more than patients that remained inactive. No significant difference occurred when comparing to the active/ active group. Greater improvements were seen in inactive/active and active/active patients in HRQoL when compared to inactive/inactive patients. It is therefore proposed that the magnitude of change in physical activity from pre to post-surgery could be more important for increasing weight loss as a result of bariatric surgery. This research highlights the importance of physical activity for superior post-operative bariatric surgery outcomes; intervention research could aid the current uncertainty and help the development of physical activity guidelines.

2.7.3 Physical activity intervention research

Two trials reporting physical activity levels following post-operative exercise training are available[84, 87]. Shah *et al*[84] carried out the first RCT of a 12 week partially-supervised high-volume exercise programme involving 33 patients at least three months after surgery to aid in the prevention of weight regain. The exercise group were advised to expend ≥2000kcal/week in moderate intensity aerobic exercise (starting at 500kcal and increasing in 500kcal increments weekly), exercising a minimum of five days per week. During the last four weeks of the intervention 50% of the subjects were

undertaking ≥2000kcal/week of moderate intensity aerobic exercise and >80% were expending at least 1500kcal/week. The 7-day physical activity recall showed a significant improvement in the exercise group's time spent undertaking moderate intensity physical activity at six and twelve months, with no change in the control group. Step count also increased in the exercise group from ~4,500 steps to just under 10,000 steps/day, suggesting that the additional exercise did not negatively affect daily physical activity. Weight loss was similar between groups, however, the control group reported a 1.7 fold greater reduction in energy intake compared to the exercise group (593 kcal/day versus 358 kcal/day). Physical fitness expressed as VO_2 max relative to body mass also significantly improved in the exercise group. It is interesting to note that for some patients it took longer than 12 weeks to progress to the required level, and a high proportion discontinued the study (n = 9), indicating the challenging nature of the level of exercise for this population, even though individuals with a BMI ≥40kg·m^2 were excluded. Nonetheless, this study demonstrates that a high-volume moderate intensity exercise programme is achievable, and can lead to sustained improvements in moderate-intensity physical activity and daily step count. More research is required, to see if this type of exercise aids long term weight loss outcomes.

Zagarins *et al*[87] enrolled 46 patients on to a 12 week post-surgical exercise programme (two hour group session per week), and found the average frequency and duration of at home exercise increased from three 37.4 minute sessions to four 50.8 minute sessions weekly, there was no control group. The exercise intensity of group sessions increased from 3.5 METs (moderate walking) at baseline to 6.3 METs (very brisk walk or slow jog) by 12 weeks. The authors concluded that post-surgical exercise programmes are effective for improving exercise behaviours.

Although research is limited on physical activity levels as a result of post-operative exercise interventions, these studies indicate that an exercise intervention initiated post-operatively improves physical activity levels and physical fitness, and might facilitate improvement of long term body composition outcomes. In addition to physical activity increases, positive changes in physical function outcomes have also been reported following post-operative exercise interventions[72, 84, 87-92].

2.8 Physical function and bariatric surgery

As well as physical activity behaviour, functional performance as a result of weight loss initiated through bariatric surgery is an important outcome[93]. Improvements in physical function as a result of bariatric surgery help enhance individuals ability to perform activities of daily living (e.g. walking, stair climbing, getting in and out of a chair) which ultimately improves quality of life[94]. The UK NBSR report states that prior to surgery 70% of adults report poor functional status (stair climbing), one year after surgery this value decreased to less than 30%[4]. Several studies have assessed changes in self-reported functional status pre to post-surgery by using the physical function component from the

SF-36 questionnaire which measures domains of health-related quality of life. This research predominantly shows that patients report a significant improvement in physical function within six months and continue to report improvements one year post-surgery[95-99]. More recently research has incorporated objective measurement of physical function before and after bariatric surgery[100-103]. Walking performance is the most readily assessed measure of physical function, predominantly measured by treadmill tests and the six minute walk test (6MWT), all showing an improvement in function [81, 101, 102, 104-115]. Furthermore, absolute muscle strength has been shown to decrease with extreme weight loss induced by bariatric surgery, however, relative muscle strength improved from pre to post-surgery[102, 105, 116, 117]. It is apparent that physical function improves pre to post-bariatric surgery, although it is unclear if this is a direct consequence of weight loss or if physical activity is an essential contributor. Future research is recommended to help identify this relationship to aid in the development of post-bariatric surgery activity guidelines.

2.8.1 Observational physical function research

A large scale observational study by Wasmund *et al*[106] (n=153) supports the notion that physical function improves as a result of bariatric surgery. The authors investigated treadmill walking using a modified Bruce protocol before and two years after Roux-en-Y gastric bypass surgery. They reported patients walking duration; pre-operatively a mean duration of 917 seconds was reported with a mean improvement of 445 seconds reaching a faster speed and steeper incline two years after surgery.

Steele *et al*[94] undertook the first narrative review looking at the effect of bariatric surgery (any type) on physical functioning; 15 studies were identified. Nine observational studies reported established functional outcome measurements such as 6MWT, sit-to-stand (STS) test, timed up-and-go (TUG) test, with maximal and submaximal exercise testing reported in six studies. The authors concluded that physical functioning improves as a result of bariatric surgery. However, it is suggested that this may not be a result of absolute improvements in cardiorespiratory or muscle function; improvements could be attributed to improved efficiency in performing activities. Steele *et al*[94] therefore recommend future post-surgical intervention research focusing on physical function as such interventions are likely to be beneficial and should be introduced into routine care[94]. The authors also suggest distinguishing the relationship between weight loss and physical function.

A longitudinal study by Wilms *et al*[93] assessed changes in exercise performance and pulmonary function before and at least one year after surgery. Patients showed an improved anaerobic tolerance and performance capacity after weight loss; although this remained significantly lower than published weight-dependent reference values. Exercise intervention research would help distinguish the importance of physical activity levels after surgery to optimise physical function outcomes compared to reference values and positively contribute to HRQoL.

2.8.2 Physical function intervention research

Although few clinical trials exist, there are encouraging findings with respect to the benefits of post-surgical exercise on physical function[72, 87-92]. The time point at which to introduce an exercise programme is important to consider, for example, it is not clear whether it is more effective to initiate an exercise programme straight after, or several months after surgery[84, 89, 91].

Results of three RCTs indicate that an additional aerobic exercise programme after gastric banding surgery led to superior improvements in functional capacity over surgery alone, as assessed by the 6MWT[89, 91, 92]. Stegen *et al*[89] undertook a pilot study (n = 15) investigating the effect of a 12 week combined aerobic and resistance training programme in the first four months after gastric bypass surgery. The surgery group and combined surgery and exercise group had a range of measurements taken pre-operatively and repeated four months post-operatively. Both groups saw a similar decrease in total body mass, BMI, waist circumference, FM and fat free mass (FFM). Dynamic muscle strength increased in the training group and decreased in the untrained group, whilst static muscle strength decreased in both groups. Tests of physical function including the STS test and 6MWT distance improved significantly four months post-surgery in the exercise group alone. The authors therefore concluded that an exercise training programme undertaken in the first four months post-operatively is beneficial for improving physical function (muscle strength and functional capacity) in gastric bypass patients.

A similar randomised trial by Castello *et al*[91] initiated a 12 week aerobic exercise programme one month after gastric band surgery and compared it to routine care (control) four months post-surgery; the sample included 21 female patients. Interestingly, a significant improvement in the 6MWT distance also occurred in the exercise group alone, concurring with Stegen *et al's*[89] findings. There were also significant increases in all heart rate variability indexes and a decrease in diastolic blood pressure. Five of the six body circumferences were significantly lower in the training group at the four month assessment than the control. Body composition (e.g. total weight, FM, FFM and skin folds) improved significantly in both groups, however no inter-group differences were found. The authors therefore concluded that aerobic training for 12 weeks improved functional capacity in obese females four months after gastric bypass surgery. These studies outline the importance of exercise training post-bariatric surgery to optimise pre to post-operative physical activity, physical function and body composition.

Exercise interventions have also been initiated post-operatively with baseline data being collected upon commencing the exercise intervention. Although it is not stated, it can be assumed that Huck *et al*[88] recruited individuals for a resistance training study in the early post-operative stages as they were still attending follow-ups. This non-randomised study investigated the effects of resistance

training on fitness and functional strength after bariatric surgery. A significant improvement and inter-group difference was reported for flexibility, the STS test and functional strength when compared to non-exercising controls[88]. Body composition significantly improved with no differences occurring between the training and control groups. Another intervention investigated six months of semi supervised exercise versus health education on individuals one to three months after gastric bypass surgery[72]. Although the main focus was insulin sensitivity, body composition and VO_2 peak were also assessed. The authors found that body composition improved significantly within groups only and VO_2 peak was significantly higher in the exercise group showing increased cardiorespiratory fitness. Both studies again highlight greater improvements in patients undertaking supervised or semi-supervised exercise post-bariatric surgery compared to usual care.

The most recent post-operative exercise intervention has focused on a non-randomised intensive programme of road running for a 10 patient cohort one to three years post gastric bypass surgery[90]. The study's aim was to investigate a 10 month personalised training programme of three one hour sessions per week for possible benefits on weight loss maintenance, physical health and psychological health. Comparisons between the running group (n=7) and the self-selected control group (individuals who could not 'logistically' take part in the road running, n=10) revealed significant between group differences in BMI, waist circumference, fat percentage, VO_2 max and oxygen volume uptake versus work rate slope. By initiating a road running intervention between one and three years post gastric bypass surgery, greater improvements were shown in body composition and cardiopulmonary function than their matched controls. It must be noted that the inclusion criteria was restricted to individuals <50 years, <35 BMI, deemed 'fit for running' and who displayed a good level of compliance and motivation; therefore may not be representative of a large proportion of the bariatric population. However, this preliminary research highlights the need for physical activity interventions at the point of weight plateau/regain to combat the concern associated with the long term effectiveness of bariatric surgery outcomes.

All of the exercise intervention studies display positive physical function outcomes regardless of the time point at which they were initiated. Body composition improvements between groups only occurred in the study initiated between one and three years after the surgical procedure[90]. This could be due to the type and length of this exercise intervention; it could also be because weight loss initiated by the surgical procedure has slowed or stopped by 12 to 24 months[23]. It is therefore still unclear when such exercise training should be initiated and what type of exercise (e.g. aerobic, resistance or combined aerobic and resistance) training should be undertaken, and if this varies depending on the type of bariatric surgery. Further research is needed to ascertain this. It can be suggested that structured and supervised exercise should be included as part of usual care, although

further RCTs are needed for the development of specific physical activity guidelines for patients following bariatric surgery.

2.9 Key research gaps

It is apparent from the bariatric surgery literature that research on the relationships between physical activity, physical function and weight outcomes after bariatric surgery is in its infancy. More exercise interventions are needed at various stages pre and post-operatively to determine what is ideal for long term success. Post-bariatric surgery exercise guidelines need to be developed to prevent the growing occurrence of weight regain. The causal relationship as to whether increased activity results in weight loss or weight loss causes this increase in physical activity also needs to be established. Finally, it is necessary to distinguish whether weight loss initiated through surgery improves physical function, or is physical activity is an essential contributor. The current PhD research studies have been developed to strengthen the current literature and add additional information to ensure optimal long term outcomes.

Chapter Three

Changes in physical activity behaviour and physical function after bariatric surgery: a systematic review and meta-analysis

Chapter overview

This chapter reports a systematic review and meta-analysis of pre to post-operative changes in physical activity and physical function outcomes among obese adults undergoing bariatric surgery. The review reports 50 studies assessing changes in physical activity behaviour or physical function, at short (3-6 months) and longer-term (12 months) time points after bariatric surgery. Given the growing recognition of the important physical activity after bariatric surgery, this review makes a timely and original contribution to the literature. This is the first review to assess physical activity alongside physical function also employing a systematic approach with quantitative synthesis, to examine objective and self-reported measures. It is therefore able to provide a comprehensive and up-to-date review of the physical activity evidence for this population. This chapter concludes by recommending the need for large RCTs to fully understand the effects of physical activity on post-surgical outcomes.

Key findings

- Objective and self-reported physical activity improves by 12 months after bariatric surgery.
- Walking, musculoskeletal and self-reported physical function all improved by 12 months.
- No relationship was identified between changes in weight and physical function.
- Objectively measured MVPA decreases and step count increases at 3-6 months, indicating a shift towards a greater amount of lower intensity physical activity within the first six months after surgery.

Publications

The research described in this chapter is currently in press for the journal Obesity Reviews (2015).

The research described in this chapter was also presented at the International Society of Behavioral Nutrition and Physical Activity 13th annual meeting (ISBNPA, San Diego, USA, 2014).

3.1 Introduction

Bariatric surgery is an effective weight-loss intervention for morbidly obese patients, and also a successful treatment for co-morbidities such as T2DM[14]. A higher level of physical activity after surgery has been associated with additional weight loss [25, 26, 73]. There is currently limited information on patterns of physical activity in bariatric surgery patients. One review suggested that physical activity tended to increase after surgery, although considerable variation in results was observed [73]. This was partly attributed to the heterogeneity in measurement tools across the studies included, most of which relied on self-reported methods for assessing physical activity. It is notable that more recent studies[76, 77, 89] have included objective methods which may provide more accurate estimates of changes in physical activity.

In addition to weight loss, several studies have reported positive changes in physical function outcomes after surgery, such as cardiovascular endurance and muscular fitness[68, 76, 115-117].

These functional abilities are important for enabling individuals to carry out activities of daily living such as housework, childcare, lifting and carrying heavy objects, walking up hills or stairs. A recent narrative review suggested that physical function improves after bariatric surgery[94], but it remains unclear whether the improvements are a direct consequence of weight loss, or whether physical activity leads to superior outcomes, over and above the weight loss associated with surgery.

Given the rapidly-growing literature in physical activity for bariatric surgery patients, a comprehensive and up-to-date review of the evidence is due. This review, therefore, aims to assess pre to post-operative changes in physical activity behaviour and physical function outcomes among obese adults receiving bariatric surgery.

3.2 Methods

3.2.1 Eligibility criteria

Studies were included if they involved at least 10 adults (aged ≥18 years) undergoing weight-loss surgery, reported prospective assessments of physical activity or physical function pre-surgery and at three or more months post-surgery. Published and unpublished studies were eligible, and no language restrictions were imposed. Physical activity measures included self-reported and objective methods (e.g. accelerometer, pedometer). Measures of physical function included tests of cardiovascular endurance (e.g. treadmill/cycle ergometer stress tests, timed walking tests), musculoskeletal fitness (e.g. timed up-and go, 1-rep repetition maximum tests) and self-report (e.g. physical functioning scale of the Short-Form Health Survey; SF-36). Studies were excluded if they only reported measurements at one time point (i.e. only pre-surgery or only post-surgery), or only assessed anthropometric outcomes, gait biomechanics, cardiac or respiratory muscle function.

3.2.2 Search methods

The search strategy was developed for Medline with advice from an information specialist. The following electronic databases were searched from their respective inceptions: MEDLINE, SPORTDiscus, Cinahl, EMBASE, Cochrane Library, SCIRUS and OpenGrey (an unpublished literature source included to reduce publication bias[118]). Search terms included MeSH headings and key words based on bariatric surgery (e.g. bariatric surgery, gastric bypass, gastric band), physical activity/ physical function (e.g. exercise, physical activity, physical fitness, muscle strength) and were modified for each individual database. In addition to searching databases, the reference lists of all included papers and relevant review articles were scanned for further eligible studies[119]. The citation tracking service within Web of Science was also used for all papers meeting the review criteria in order to identify papers published subsequently that may be eligible for inclusion. Finally, five experts in the field of exercise and obesity were contacted to ask for any further published or unpublished studies. The experts selected were those authors whom had more than two studies that met the systematic review inclusion criteria. Studies were included up until July 2015.

3.2.3 Study selection

The titles and abstracts of all items identified through the electronic searches were screened for potential eligibility by the primary reviewer and a random 25% of items were screened independently by a second reviewer to check for consistency. A kappa score of 0.93 was achieved. Full versions were read by two reviewers (100% by the primary reviewer and 50% each by two further reviewers) who independently applied the selection criteria and recorded the decisions on a standardised form. The three reviewers met to discuss any disagreements to reach a consensus.

3.2.4 Data extraction

A data extraction form was developed and piloted. Details on study design, participants, outcome measures, and results were recorded. The primary researcher reviewed and extracted 100% of the data and two reviewers independently reviewed and extracted 50% each. Any disagreements regarding data extraction were discussed until consensus reached. In eight cases study authors were contacted in an attempt to obtain any missing information.

3.2.5 Data analysis

All included studies were summarised descriptively in tables. Meta-analyses were conducted using Review Manager version 5.3 for Windows, for outcomes where mean and standard deviation data were available, or could be obtained, from at least four studies. Post-surgery assessments mostly aligned with one of two time points: 3-6 months, and 12 months. In most studies, an increase in the outcome measure indicated an improvement. However, for outcomes where a reduction indicated an

improvement (e.g. walking speed), data were transposed for meta-analysis so that there was consistency in the direction of results. Standard error if reported was converted to standard deviation for meta-analysis purposes.

To allow for the use of different measures across studies for some outcomes, pre-post changes were calculated as a standardised mean difference (SMD) using Hedges' (adjusted) g, which includes a correction for sample size bias. Studies were combined using a random-effects model. Random-effects was used due to between study variation, and it is more conservative and allows for heterogeneity; this therefore minimises the likelihood of drawing the wrong conclusion. Statistical heterogeneity was assessed by the I^2 test[120].

3.3 Results

3.3.1 Study characteristics

After removing duplicates, 990 articles had been identified by the search; 50 studies met the inclusion criteria for the review and 26 papers reported data to be included in the meta-analysis (Figure 3.1).

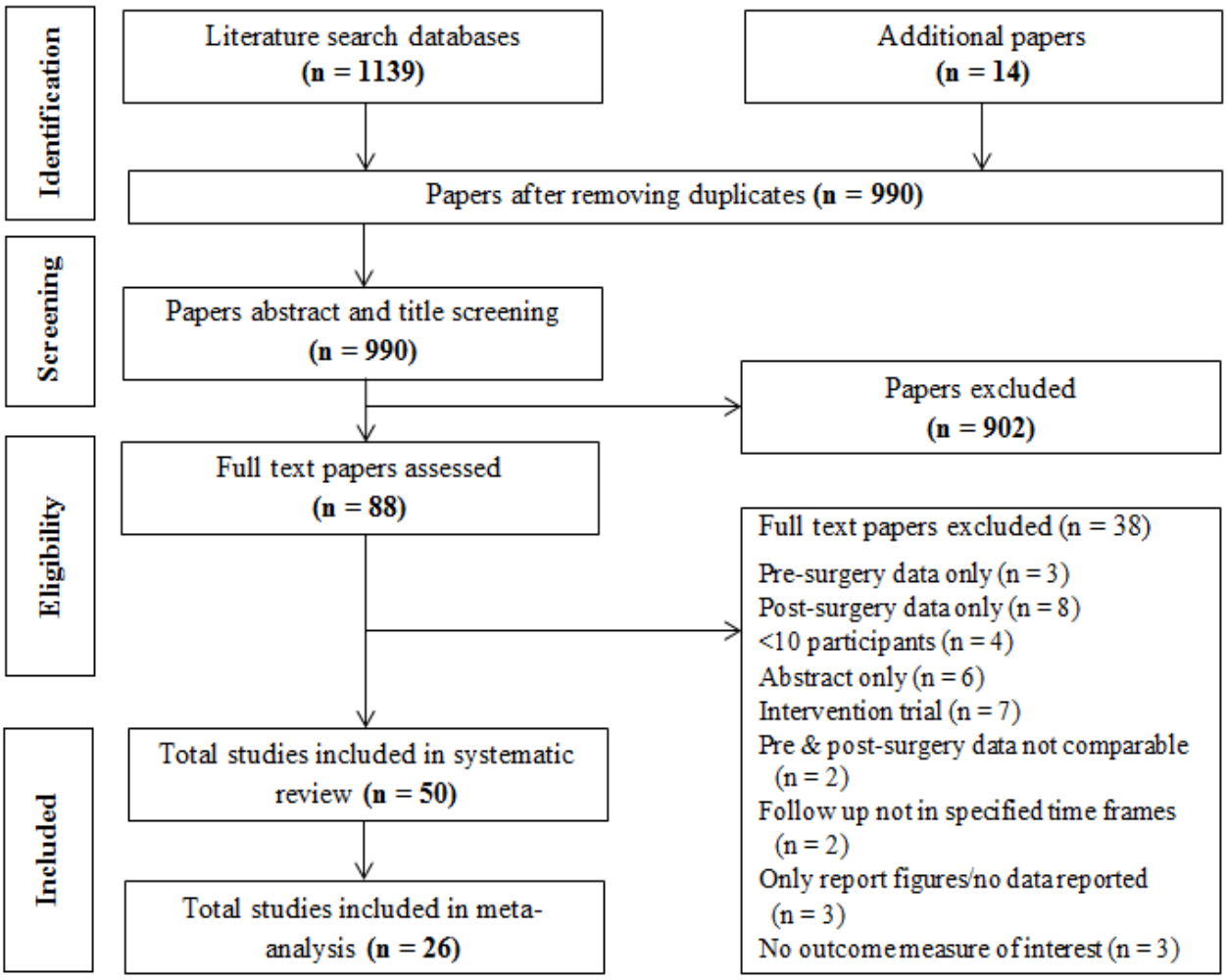


Figure 3.1: The systematic review search process.

The majority of studies were performed in the United States[76-79, 81, 86, 98, 99, 103, 104, 106, 108-110, 121-126], with five conducted in the Netherlands[127-131] and four in Brazil[102, 107, 114, 115]. The types of bariatric surgery received by participants varied between studies, but the two main surgery types were Roux-en-Y gastric bypass (29 studies)[78, 80, 81, 86, 95, 96, 98, 99, 101-109, 114, 115, 121-125, 128, 132-135] and gastric band (8 studies)[111, 112, 127, 129-131, 136, 137]. Fourteen studies reported a physical activity outcome[23, 77-80, 121, 122, 125, 129-131, 133, 135, 138], 30 reported a physical function outcome[93, 95-99, 102-104, 106-117, 123, 124, 126-128, 132, 134, 136, 139]and six reported both physical function and physical activity data[76, 81, 86, 101, 105, 137]. Included studies are described in Table 3.1 (physical activity outcomes) and Table 3.2 (physical function outcomes).

3.3.2 Physical activity outcomes

Seventeen studies employed self-reported measures of physical activity, with seven reporting increased activity at 3-6 months and 11 at 12 months (Table 3.1). All but one study[122] reported improvements in activity 12 months post-surgery. Two studies reported leisure time physical activity at both time points. Sjöström *et al* [23] reported from a study of 1845 participants that the proportion of individuals classified as active increased by 37.3% at 3-6 months, which was maintained at 12 months. Vatier *et al* [133] reported an improvement in leisure time physical activity of 10 minutes per week at 3-6 months, and a further improvement of eight minutes per week at 12 months. Seven studies used objective measures of physical activity (five used accelerometers and two used pedometers). Step count data indicated an average increase of between 1225-2749 daily steps[76, 81, 137], but accelerometer results suggested little change at either 3-6 months or 12 months[77-80].

3.3.3 Physical function outcomes

All studies assessing cardiovascular endurance outcomes reported improvements post-surgery (Table 3.2) These included 20 tests of walking performance (treadmill exercise test, fastest possible walking speed, walking speed, walking minutes per week, 6MWT, 4-metre walk time, walking energy expenditure)[81, 86, 97, 101-115, 126, 128]and two of cycle ergometer endurance[93, 139].

Table 3.1: Characteristics of all included studies with a pre and post-operative measures of physical activity.

Author, publication date (Reference)	Sample size analysed	Drop out	BMI	Surgery type	Measure of physical activity	Measurement units	Physical activity level pre-surgery	Physical activity level 3-6 month post-surgery	Physical activity level 12 month post-surgery	Improved outcome when compared to baseline
Self-Reported Physical Activity										
Boan *et al*., 2004[121]	40	Not stated	52.9	RYGB	Baseline questionnaire of activity	Kcal/week	239.8 ± 266.0	1230.3 ± 1092.0	N/A	Yes (990.5 Kcal/week)
Bond *et al*., 2008[86]	119	94	49.9	RYGB	International PA questionnaire – short form	min/week	170.2 ± 325.2	N/A	385.9 ± 458	Yes (215.7 min/week)
Bond *et al*., 2010[79]	20	6	50.1	RYGB, GB	Paffenbarger PA questionnaire	min/week	44.6 ± 80.8	212.3 ± 212.4	N/A	Yes (167.7 min/week)
Carrasco *et al*., 2007[135]	31	7	44	RYGB	Leisure time PA questionnaire	min/week	600 ± 878.4	1410 ± 1374	N/A	Yes (810 min/week)
Colles *et al*., 2008[137]	129	44	44.3	GB	Baecke PA questionnaire	Baecke total score	6.3 ± 1.2	N/A	7.3 ± 1.3	Yes (1.0 total score)
Das *et al*., 2003[122]	30	6	50.1	RYGB	Minnesota leisure time PA questionnaire	min/week	2205 ± 1540	N/A	1869 ± 91.7	No (336 min/week)
Josbeno *et al*., 2010[81]	18	2	46.9	RYGB	7 day PA recall	min/week	191.1 ± 228.2	231.7 ± 239.0	N/A	Yes (40.6 min/week)
King *et al*., 2012[76]	276	145	47	All	7 day PA diary (≥150 min/week)	Number of people	82 ± 29.7	N/A	127 ± 46	Yes (45 people)
Lyytinen *et al*., 2013[101]	16	2	45.1	RYGB	Leisure time PA scale	Point scale (1[low]-3 [high])	1.8 ± 0.7	2.0 ± 0.6	N/A	Yes (0.2 point scale)
Mathus-Vliegen *et al*., 2007[130]	44	6	50.7	GB	PA duration per week	Point scale (1[low]-5 [high] min categories)	2.2 ± 1.0	N/A	2.8± 1.0	Yes (0.6 point scale)
Mathus-Vliegen *et al*., 2004[129]	49	1	50.0	GB	PA scale Score	Point scale	5.5 ± 1.4	N/A	7.2 ± 2.3	Yes (1.7 point scale)
Rosenberger *et al*., 2010[125]	131	Not stated	51.8	RYGB	Proportion of people reporting no PA	%	37.4	N/A	7.6	Yes (29.8%)
Ruiz-Tovar *et al*., 2013[138]	50	Not stated	50.4	SG	Modifiable PA questionnaire	% of sample (sedentary, moderate & active)	45 (90%) sedentary; 4 (8%) moderate; 1 (2%) active	N/A	20 (40%) sedentary; 25 (50%) moderate; 5 (10%) active	Yes (42% moderately active, 8% active)
Sjöström *et al*., 2004[23]	1845	210	41.9	GB, RYGB, VBG	Proportion active during leisure time	%	54.7 (95% CI)	92.0 (95% CI)	92.0 (95% CI)	Yes (37.3%); Yes (37.3%)

Table 3.1: continued

Author, publication date (Reference)	Sample size analysed	Drop out	BMI	Surgery type	Measure of physical activity	Measurement units	Physical activity level pre-surgery	Physical activity level 3-6 month post-surgery	Physical activity level 12 month post-surgery	Improved outcome when compared to baseline
Vatier *et al*., 2012[133]	86	Not stated	48.1	RYGB	Leisure time PA questionnaire	min/week	80.0 ± 80.0	90.0 ± 80.0	108.0 ± 84.0	Yes (10); Yes (18 min/week)
Wouters *et al*., 2010[131]	42	59	47.0	GB	Baecke PA questionnaire	Sport index score	2.0 ± 0.6	N/A	2.5 ± 0.7	Yes (0.5 sport index score)
Wiklund *et al*., 2014[105]	29	10	42.0	RYGB	International PA questionnaire – short form	MET min/week	1231 ± 2001	N/A	2428 ± 2979	Yes (1197 MET min/week)
Objective Physical Activity										
Berglind *et al*., 2014[80]	56	Not stated	39.1	RYGB	Accelerometer	MVPA min/day	30.9 ± 17.7	N/A	32.1 ± 24.0	Yes (1.2 min/day)
Bond *et al*., 2010[79]	20	6	50.1	RYGB, GB	Accelerometer	MVPA min/week	41.3 ± 109.3	39.8 ± 71.3	N/A	No (1.5 min/week)
Colles *et al*., 2008[137]	129	44	44.3	GB	Pedometer	steps/day	6061.0 ± 2740.0	N/A	8716.0 ± 5348.0	Yes (2655 steps/day)
Josbeno *et al*., 2010[81]	11	2	46.9	RYGB	Pedometer	steps/day	4621.0 ± 3701.2	7370.0 ± 4240.0	N/A	Yes (2749 steps/day)
King *et al*., 2012[76]	310	145	47.0	All	StepWatch 3	steps/day	7563 (median)	N/A	8788 (median)	Yes (1225 steps/day)
King *et al*., 2015[77]	473	218	45.4	All	StepWatch 3	MVPA min/week	77.3 (median) (70.9-84.2)	N/A	106.0 (median) (97.8-116.4)	Yes (28.7 min/week)
Liu *et al*., 2012[78]	18	Not stated	44.6	RYGB	Accelerometer	All PA hours/day	11.1 ± 4.2	10.6 ± 2.5	N/A	No (0.5 hours/day)

KEY: RYGB: Roux-en Y gastric bypass; GB: gastric banding; VBG: vertical banded gastrectomy; PA: physical activity; min: minutes; Kcal: kilocalories; N/A - not applicable; CI: confidence interval.

Table 3.2: Characteristics of all included studies with a pre and post-operative measure of physical function.

Author, publication date (Reference)	Sample size analysed	Drop out	BMI	Surgery type	Measure of physical function	Measurement units	Physical function level Pre-surgery	Physical function level 3-6 month post-surgery	Physical function level 12 months post-surgery	Improved outcome when compared to baseline
Self-Reported Physical Function										
Bond *et al*., 2008[86]	119	94	49.9	RYGB	SF – 36	Physical function score	35.2 ± 10.6	N/A	51.9 ± 8.4	Yes (16.7 score)
Colles *et al*., 2008[137]	129	44	44.3	GB	SF – 36	Physical component score	37.2 ± 10.0	Not stated	49.2 ± 9.8	Yes (12 score)
Frezza *et al*., 2007[99]	40	51	46.55 (median)	RYGB	SF – 36	Physical function score	17 (range, 10-38)	26.5 (range 11-30)	26.5 (range 11-30)	Yes (9.5 score)
Gorin *et al*., 2009[123]	196	Not stated	47.2	RYGB	SF – 36	Physical function score	46.5	79.5	N/A	Yes (33.2 score)
Hooper *et al*., 2007[124]	48	6	51.0	RYGB	SF – 36	Physical function score	38.0 ± 19.0	N/A	74.0 ± 21.4	Yes (36 score)
Horchner *et al*., 1999[127]	39	Not stated	40.9	GB	SF – 36	Physical function score	72.7 ± 23.2	N/A	90.0 ± 14.3	Yes (17.3 score)
Huang *et al*., 2011[134]	40	Not stated	43.6	RYGB	SF – 36	Physical function score	57.3 ± 25.9	73.8 ± 22.6	N/A	Yes (16.5 score)
Iossi *et al*., 2013[98]	39	11	49.0	RYGB	SF – 36	Physical component score	30.1 ± 9.1	40.9 ± 9.5	45.9 ± 11.4	Yes (10.8); Yes (15.8 score)
Julia *et al*., 2013[96]	71	53	47.6	RYGB	SF – 36	Physical function score	38.9	49.9(mean change)	52.6 (mean change)	Yes (49.9); Yes (52.6 score)
Josbeno *et al*., 2010[81]	17	3	46.9	RYGB	Medical outcomes SF – 36	Physical function score	38.2 ± 23.6	89.7 ± 15.5	N/A	Yes (51.5 score)
King *et al*., 2012[76]	310	276	47.0	All	SF – 36	Physical function score	37.6 ± 10.7	N/A	50.7 ± 8.3	Yes (13.1 score)
Lyytinen *et al*., 2013[101]	16	2	44.0	RYGB	RAND – 36	Physical function score	58.5 ± 18	81.5 ± 25.6	N/A	Yes (23.0 score)
Nickel *et al*., 2005[136]	21	1	47.4	GB	SF – 36	Physical function score	37.8 ± 13.1	N/A	61.3 ± 17.2 (3 years)	Yes (23.5 score)
Ohrstrom *et al*., 2001[97]	11	6	41	VBG	SF – 36	Physical function score	46 ± 24	78 ± 23	88±17	Yes (32); Yes (42 score)
Sarwer *et al*., 2010[95]	200 (198, 147)	2 & 53	N/A	RYGB	SF – 36	Physical function score	34.2 ± 25.5	67.5 ± 23.9	74.0 ± 21.8	Yes (33.3); Yes (39.8 score)
Tompkins *et al*., 2013[109]	25	5	45.5	RYGB	SF – 36	Physical function score	34.4 ± 9.6	52.1 ± 8.6	N/A	Yes (11.5 score)

Table 3.2: continued

Author, publication date (Reference)	Sample size analysed	Drop out	BMI	Surgery type	Measure of physical function	Measurement units	Physical function level Pre-surgery	Physical function level 3-6 month post-surgery	Physical function level 12 months post-surgery	Improved outcome when compared to baseline
Vincent *et al*., 2012[126]	25	Not stated	47.0	RYGB, GB	SF – 36	Physical function score	32.1 ± 11.9	43.6 ± 11.2	N/A	Yes (17.17 score)
Wiklund *et al*., 2015[132]	70	Not stated	44.7	RYGB	Disability rating index	Total score	30.4	N/A	14.2 (18 months)	Yes (16.2 DRI score)
Objective Physical Function										
Ben-Dov *et al*., 2000[139]	19	21	43.3	VBG	Incremental maximal cycle test	watts	124.0 ± 30.5	N/A	127.0 ± 39.2	Yes (3.0 watts)
Bond *et al*., 2008[86]	119	94	49.9	RYGB	Walking	min/week	170.2 ± 325.0	N/A	385.9 ± 458.0	Yes (215.7 min/week)
Da Silva *et al*., 2013[102]	17	9	46.0	RYGB	6MWT	m	489.0 ± 14.0	536.0 ± 14.0	N/A	Yes (47 metres)
Da Silva *et al*., 2013[102]	17	9	46.0	RYGB	30% handgrip force	kgf	10.0 ± 0.7	9.0 ± 0.7	N/A	No (1kgf)
De Souza *et al*., 2010[114]	61	Not stated	49.4	RYGB	Treadmill exercise test	m	401.8 ± 139.0	513.4 ± 159.9	690.5 ± 76.2	Yes (111.6); Yes (288.7 metres)
De Souza *et al*., 2009[115]	49	8	51.1	RYGB	6MWT	m	381.9 ± 49.3	N/A	467.0 ± 40.3	Yes (85.1 metres)
Handrigan *et al*., 2010[117]	10	Not stated	49.1	DS	Lower limb maximal force	kg	74.4 ± 15.1	58.9 ± 11.8	50.4 ± 8.6	No (15.5kg); No (24.0kg)
Hortobagyi *et al*., 2010[128]	10	10	43.2	RYGB	Walking speed	step/min	121.0 ± 7.5	117.0 ± 8.2	119.0 ± 8.6	Yes (4.0); Yes (2.0 step/min)
Hue *et al*., 2010[116]	10	Not stated	50.2	DS	Lower limb maximal force	N	742.8 ± 131.3	N/A	493.9 ± 84.3	No (248.9 N)
Iossi *et al*., 2013[98]	39	11	49.0	RYGB	Timed get up and go	sec	12.6 ± 3.1	10.3 ± 2.4	9.6 ± 2.7	Yes (2.3); Yes (3.0 s)
Josbeno *et al*., 2010[81]	17	3	46.9	RYGB	6MWT	m	393 ± 62.1	446 ± 41.4	N/A	Yes (53 metres)
Josbeno *et al*., 2010[81]	18	2	46.9	RYGB	Short physical performance battery	SPPB score	11.2 ± 1.2	11.7 ± 0.6	N/A	Yes (0.5 SPPB score)
Kanopakis *et al*., 2001[113]	16	Not stated	49.0	VBG	Treadmill exercise test	s	675.0 ± 226.0	1007.0 ± 389.0	N/A	Yes (332 s)
Lyytinen *et al*., 2013[101]	16	2	44.0	RYGB	6MWT	m	500.7 ± 56.8	561.4 ± 50.6	N/A	Yes (60.7 metres)

Table 3.2: continued

Author, publication date (Reference)	Sample size analysed	Drop out	BMI	Surgery type	Measure of physical function	Measurement units	Physical function level Pre-surgery	Physical function level 3-6 month post-surgery	Physical function level 12 months post-surgery	Improved outcome when compared to baseline
Lyytinen *et al*., 2013[101]	16	2	44.0	RYGB	Timed up and go	s	7.4 ± 1.7	6.4 ± 0.9	N/A	Yes (1.1 s)
Maniscalo *et al*., 2006[111]	15	4	42.1	GB	6MWT	m	475.7	N/A	626.3	Yes (150.6 metres)
Maniscalo *et al*., 2007[112]	12	3	43.2	GB	6MWT	m	416.5 ± 67.1	N/A	615.2 ± 104.0	Yes (198.7 metres)
Miller *et al*., 2009[103]	18	6	53.0	RYGB	4 meter walk time	s	5.4 ± 3.3	4.2 ±2.4	3.9 ± 1.4	Yes (1.2); Yes (2.5 s)
Miller *et al*., 2009[103]	18	6	53.0	RYGB	Short physical performance battery score	SPPB score	9.1 ± 1.7	10.3 ± 2.1	11.1 ± 1.3	Yes (1.2); Yes (2.0 SPPB score)
Miller *et al*., 2009[103]	16	8	53.0	RYGB	Maximal torque	Nm	126.3 ± 7.2	111.7 ± 36.8	97.7 ± 31.6	No (14.6); No (28.6 Nm)
Ohrstrom *et al*., 2001[97]	11	6	41.0	VBG	Walking energy expenditure	$KJ.min^{-1}$	27.4 ± 4.9	19.3±3.3	19.1 ± 3.0	Yes (8.1); Yes (8.3 $KJ.min^{-1}$)
Seres *et al*., 2006[110]	31	Not stated	51.0	Not stated	Treadmill exercise test	min	13.8 ± 3.9	N/A	21.6 ± 4.3	Yes (7.8 minutes)
Tompkins *et al*., 2013[109]	25	5	45.5	RYGB	6MWT	m	414.1 ± 104.0	551.5 ± 101.2	N/A	Yes (137.4 metres)
Valezi *et al*., 2011[108]	43	1	35.9	RYGB	Treadmill exercise test	m	378.9 ± 126.5	N/A	595 ± 140.4	Yes (216.1 metres)
Vargas *et al*., 2013[107]	67	Not stated	50.5	RYGB	6MWT	m	405.3 ± 92.3	500.1 ± 111.6	N/A	Yes (94.8 metres)
Vargas *et al*., 2013[107]	67	Not stated	50.5	RYGB	Timed up and go	sec	10.0 ± 2.5	7.5 ± 1.4	N/A	Yes (2.5 s)
Vincent *et al*., 2012[126]	25	Not stated	47.0	RYGB, GB	Fastest possible walking speed	cm/ s	155.0 ± 26.0	162.0 ± 27.0	N/A	Yes (7 cm/ s)
Wasmund *et al*., 2011[106]	153	Not stated	47.0	RYGB	Treadmill exercise test	s	917.0 ± 358.0	N/A	1362 ± 322 (2 years)	Yes (445 s)
Wiklund *et al*., 2014[105]	37	10	42	RYGB	Peak grip force (Right & Left)	N	298 ± 102 (R) 295 ± 92 (L)	N/A	287 ± 62 (R) 276 ± 60 (L)	No (11 N) No (19 N)
Wiklund *et al*., 2014[105]	37	10	42	RYGB	6 MWD	m	532.0 ± 81.0	N/A	599.0 ± 70.5	Yes (67 metres)
Wilms *et al*., 2012[93]	18	Not stated	46.3	RYGB, Sleeve	Cycle exercise test	s	518.0 ± 127.3	N/A	549 ± 165.5 (27.7 months)	Yes (31 s)

Table 3.2: continued

Author, publication date (Reference)	Sample size analysed	Drop out	BMI	Surgery type	Measure of physical function	Measurement units	Physical function level Pre-surgery	Physical function level 3-6 month post-surgery	Physical function level 12 months post-surgery	Improved outcome when compared to baseline
Zavala *et al*., 1984[104]	13	Not stated	Not stated	RYGB	Treadmill exercise test	METs	4.6	3.8	N/A	Yes (0.8 METs)

KEY: RYGB: Roux-en Y gastric bypass; GB: gastric banding; VBG: vertical banded gastrectomy; DS: duodenal switch; PF: physical function; 6MWT: 6 minute walk test; MET: metabolic equivalent; KJ: Kilojoule; Nm: Newton metre; SPPB: short physical performance battery; kgf: kilogram force; m: metre; min: minute; s: second; cm: centimetre; N/A: Not applicable.

Of the 24 reported physical activity measurements, retention post-surgery was reported for 18 measurements and attrition ranged from one to 218; six did not report attrition. Of 50 physical function measurements recorded, the retention rate was reported in 34 studies, ranging from one to 276 and not reported for 16 studies. Thirty percent of the outcome measures recorded for either physical activity or physical function did not report study attrition; this could lead to uncertainty of outcomes. However, all outcome measures included in the meta-analysis were objective or validated measures of physical function.

Meta-analysis based on 11 studies showed an increase in walking performance at 3-6 months (SMD: 0.82; 95% CI: 0.57 to 1.06), with a heterogeneity score of I^2 =43% (Figure 3.2). At 12 months, analysis of nine studies also indicated increased performance (SMD: 1.53; 95% CI: 1.02 to 2.04: I^2 =83%) (Figure 3.3).

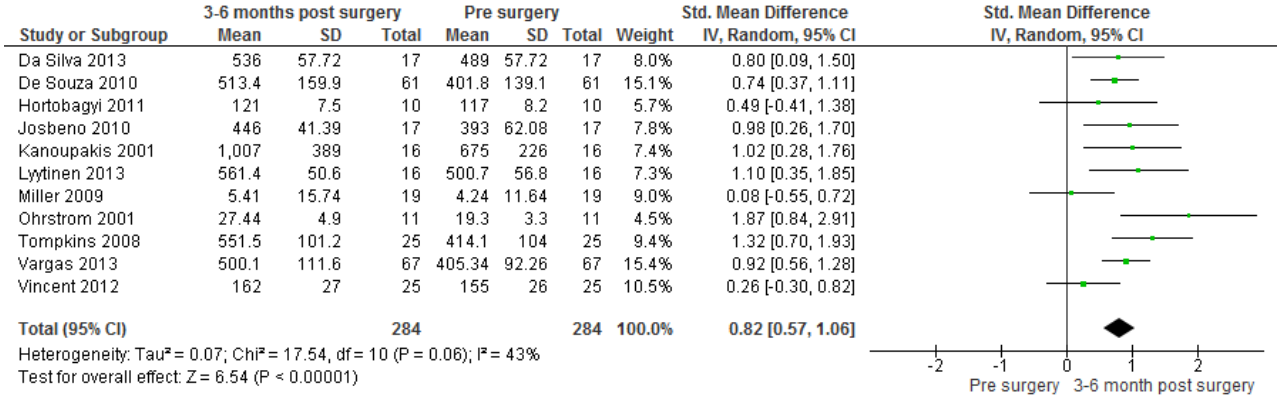


Figure 3.2: Meta-analyses of pre to post-operative walking ability at 3-6 months. Forest plots of random-effects meta-analyses of pre to post-operative objective functional walking ability.

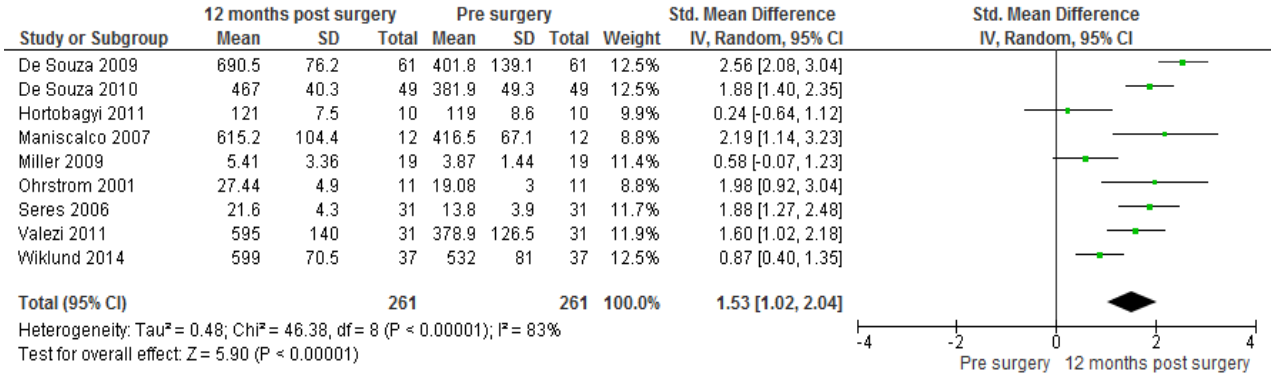


Figure 3.3: Meta-analyses of pre to post-operative walking ability at 12 months. Forest plots of random-effects meta-analyses of pre to post-operative objective functional walking ability.

Sub-sample analyses were carried out on the 6MWT, a test indicative of functional exercise capacity. At 3-6 months, based on five studies, an increase of 74.55 metres (95% CI: 46.9 to 102.2) was shown, with a heterogeneity score of 59%. From the three studies reporting 12 month data the increase was 184.36 metres (95% CI: 1.35 to 2.30).

There was no clear association between percentage weight change and percentage change in walking performance pre to 12 months post-bariatric surgery (Figure 3.4).

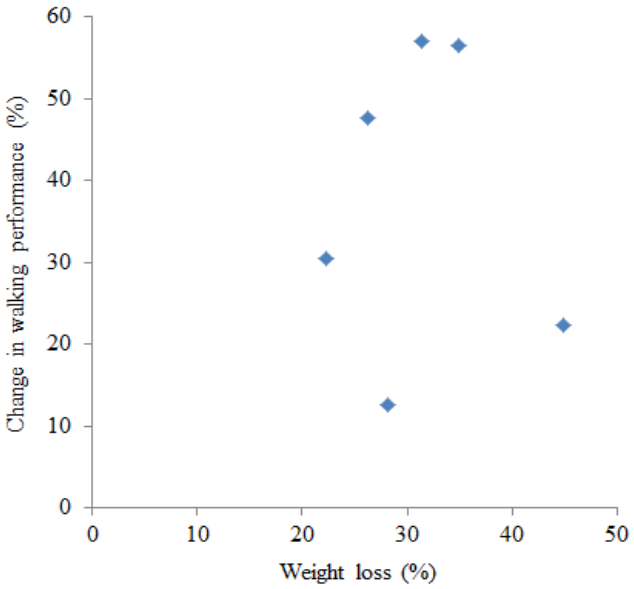


Figure 3.4: Percentage improvement in pre to 12 months post-operative walking performance versus weight loss.

Measures of musculoskeletal function were used in 10 studies. Table 2 displays the specific tests and indicates the direction of results. Meta-analysis demonstrated improvements 3-6 months post-surgery with a SMD of 1.51 (95% CI: 0.60 to 2.42; I^2 = 81%) (Figure 3.5). Only two studies examined musculoskeletal outcomes at 12 months with both showing improved outcomes[98, 103].

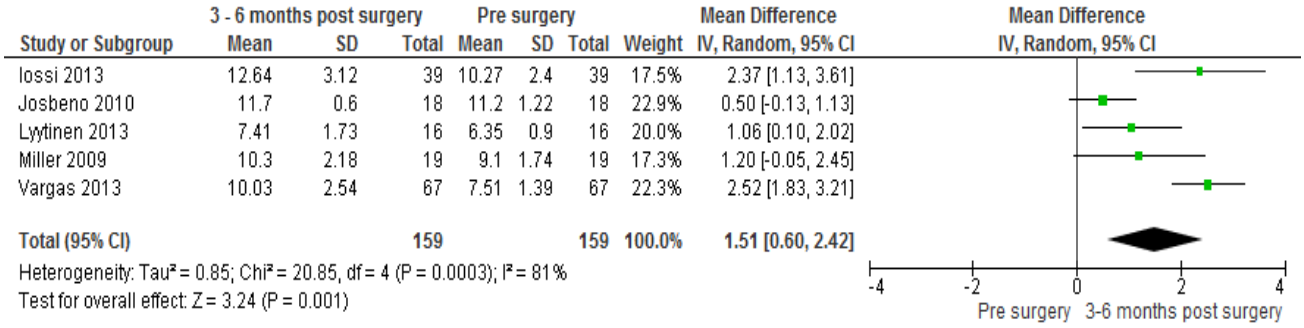


Figure 3.5: Meta-analyses of pre to post-operative musculoskeletal function at 3-6 months. Forest plots of random-effects meta-analyses of pre to post-operative objective musculoskeletal function.

Measures of absolute muscle strength/force/torque were reported in five studies with post-surgery assessment ranging from 3 to 12 months. All studies reported a reduction in absolute strength post-surgery, with pooled data indicating a SMD of -1.04 (95% CI: -1.76 to -0.33), and heterogeneity score of I^2 =77% (Figure 3.6).

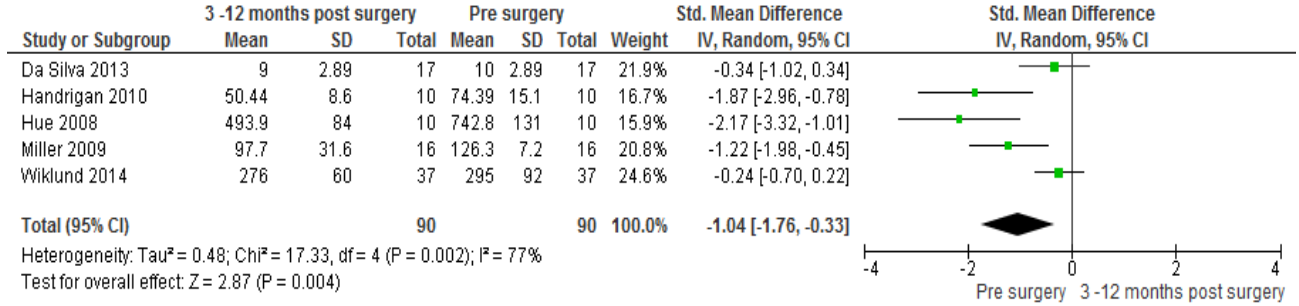


Figure 3.6: Meta-analyses of pre to post-operative muscle strength at 3-12 months. Forest plots of random-effects meta-analyses of pre to post-operative objective muscle strength.

Eighteen studies included self-reported physical function, 17 of which used the self-reported 36-item short-form health survey (SF-36) [76, 81, 86, 95-99, 101, 109, 123, 124, 126, 127, 134, 136, 137] for assessing physical function. All studies reported an increase in the physical function or physical component score post-surgery (Table 3.2). Mean SF-36 scores are recorded out of a maximum of 100. Meta-analysis of eight studies indicated a mean SF-36 score difference of 22.57 (95% CI: 14.92 to 30.21) and heterogeneity score of I^2 = 91% at 3-6 months (Figure 3.7).

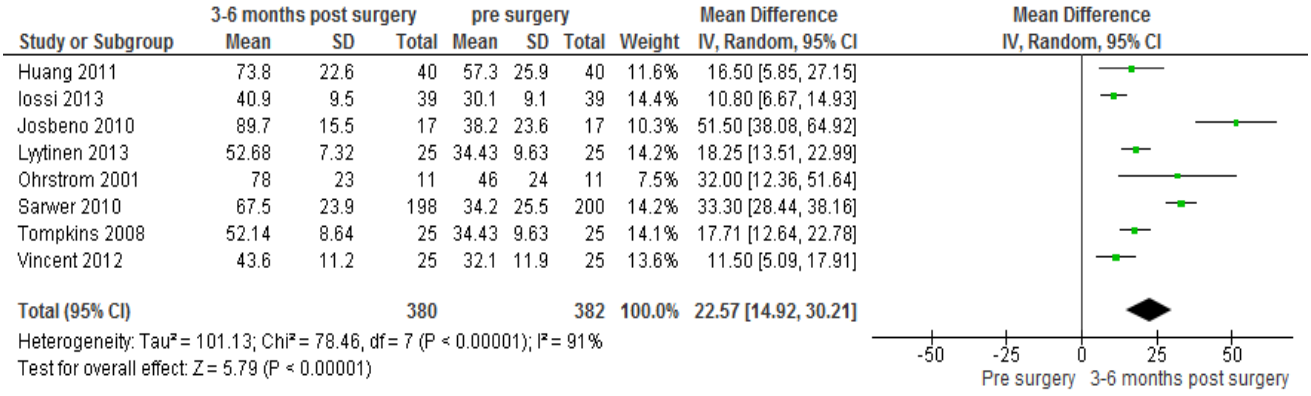


Figure 3.7: Meta-analyses of pre to post-operative SF-36 at 3-6 months. Forest plots of random-effects meta-analyses of pre to post-operative objective SF-36.

At 12 months, the mean SF-36 score difference from eight studies was 22.35 (95% CI: 16.6 to 28.10, I^2 = 95%). (Figure 3.8).

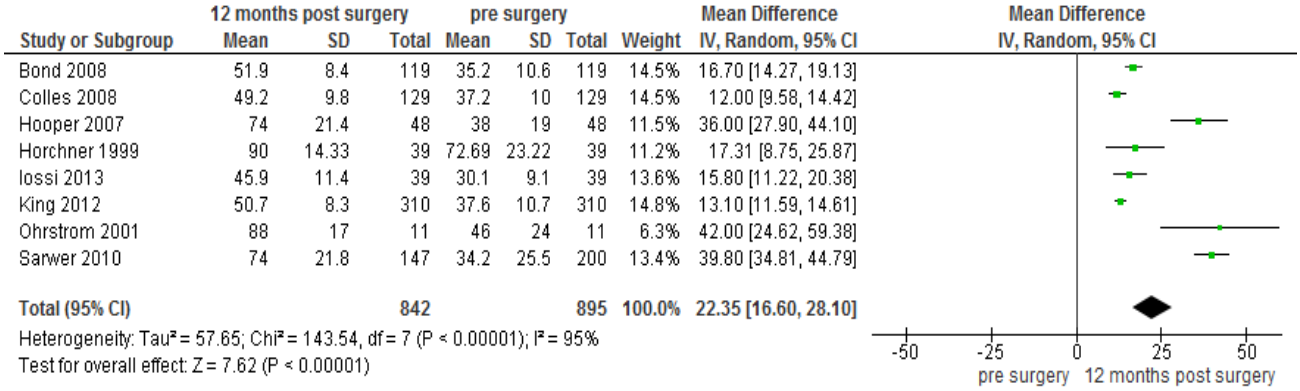


Figure 3.8: Meta-analyses of pre to post-operative SF-36 at 12 months. Forest plots of random-effects meta-analyses of pre to post-operative objective SF-36.

3.4 Discussion

This review indicates that physical activity is increased after bariatric surgery, as assessed by self-reported and objective measures. All cardiovascular and musculoskeletal measurements of physical function improved from pre to post-surgery, while absolute muscle strength measurements decreased. Meta-analyses of physical function suggest that self-reported physical function (SF-36), objective musculoskeletal, and walking function improved within six months of bariatric surgery and improved further by 12 months post-surgery.

3.4.1 Physical activity

Self-reported outcome measures consistently indicated increased physical activity post-surgery. However, the heterogeneity of measurement tools makes comparisons between studies difficult. The Leisure Time Physical Activity Questionnaire[140] was used in 3 studies, but a further 12 other tools were reported across the remaining 14 studies. These provide a range of outcome data based on minutes of activity[79, 81, 86, 105, 122, 133, 135], energy expenditure[121], points on a scale[101, 129, 130], questionnaire specific scoring[131, 137] or percentage of active participants[23, 125, 138]. Consistent use of a validated assessment tool across studies would allow meaningful comparisons of physical activity behaviour in this population.

When examined by length of follow-up, self-reported physical activity increased after surgery in all studies at 3-6 months, and in all except one study at 12 months. However, whether self-reported measures of physical activity concur with objectively measured physical activity in this population has been questioned[79].

In the current review, accelerometers and pedometers were utilised to obtain objective measurements in seven studies. Only one of three studies demonstrated an increase in physical activity based on step count from pre to 3-6 month follow-up[81], whereas all four studies showed increases at 12 months. The two studies indicating a decrease in physical activity at 3-6 months post-surgery were based on accelerometer data collected at exactly six months[78, 79]. However the type of physical activity differed (total physical activity[78] versus MVPA[79]). This reduction in physical activity could be a result of the post-surgical metabolic changes induced by calorific restriction[78]. The study reporting increased physical activity 3-6 months post-surgery found an increase of 2749 steps per day[81]. Step count does not provide an indication of the intensity of the activity undertaken; however, when taking in to consideration the reduction of MVPA and total physical activity, an increase in step count would suggest a shift in the intensity of physical activity being undertaken 3-6 months post-operatively. Participants may therefore undertake more light activity at earlier post-operative time points.

The improvement in self-reported physical activity from pre to 3-6 months, and the general reduction in objectively measured physical activity using accelerometers at the same post-operative time point is of interest. Results support previous research which has also demonstrated over-reporting of post-operative physical activity[79]. Over-reporting may represent a change in perceptions in the ease of performing activities, due to improved physical function resulting from weight loss. Further research is therefore needed to determine the reason for over-reporting post-operative physical activity in this population. This over-reporting of physical activity, if unintentional, could have a detrimental outcome on long-term weight maintenance. This review does, none the less, indicate that from pre to 12 months post-bariatric surgery both objective and self-reported physical activity increases.

Only two studies measured physical activity at both 3-6 months and 12 months post-surgery, both of which used self-reported tools[23, 133]. Sjöström *et al*[23] reported that the proportion of individuals that were self-categorised as active increased by 37% at 3-6 months and was maintained at 12 months after surgery, although their volume of physical activity cannot be determined. Vatier *et al*[133] reported an improvement in leisure time physical activity at both post-operative time points. Physical activity increased more in the first 3-6 months after bariatric surgery and then continued to improve at 12 months but at a slower rate, reflecting weight loss patterns observed in previous research[23]. Weight loss after bariatric surgery occurs rapidly in the first six months and slows towards 12 months with weight regain indicated at the 12 to 24 month time point[23].

The most recent study included in this review focused on objective MVPA assessed by accelerometry in a large sample. It suggested that 89.4% of post-surgery patients were still not sufficiently active by 12 months post-surgery[76], that is they were not meeting the guidelines of ≥150 minutes of moderate intensity physical activity weekly as recommended for the general adult population[82]. Step count data indicated that participants were classified as 'somewhat active'; that is, likely to be undertaking some volitional activities and/or occupational activity 12 months post-surgery[141]. Self-reported physical activity questionnaires predominantly focus on leisure time physical activity, making it difficult to determine intensity and enable comparisons to current physical activity guidelines. A large study by Colles *et al*[137] did however differentiate between physical activity domains showing leisure time and sport physical activity increased whereas work physical activity remained the same 12 months post-operatively. The variability of self-reported and objectively measured physical activity tools used in the different studies within this review makes it difficult to definitively state that physical activity guidelines are not met 12 months post-surgery. More research is therefore needed to determine if the increase in physical activity is sufficient. If not, interventions for increasing physical activity to recommended levels post-surgery should be explored.

3.4.2 Objective physical function

Extreme obesity drastically inhibits physical function, physical performance and increases disability[103]. The current meta-analyses displayed large improvements in walking outcomes at 3-6 months and even greater improvements at 12 months through bariatric surgery. As previously reported, walking speed slows as a result of obesity[101]. Therefore any post-operative improvements in walking speed would be likely attributed to weight loss which would mean the greatest improvements occurring within six months of surgery. Walking distance improvement appeared to be similar between post-surgery segments (pre to 3-6 months, 3-6 to 12 months) and functional walking distance patterns increased consistently to 12 months at a greater rate than either physical activity or weight loss. This suggests that walking improves as a result of weight loss, although it seems likely that physical activity is required for improvement to be maintained once the rate of weight loss plateaus. However, the 12 month pooled result should be interpreted with caution due to high heterogeneity.

Objective evaluation of fitness and functional exercise capacity in this population is regularly assessed by the 6MWT[115]. The mean improvements in all the studies which reported the 6MWT distance from pre to 3-6 months and pre to 12 months post-surgery were 75 meters and 184 meters respectively. A minimal clinically importance difference (MCID) for the 6MWT in bariatric surgery patients has not been established. However, for patients with chronic obstructive pulmonary disease, a change in the range of 54 to 80 metres has been estimated as clinically meaningful[142]. Based on these data, the improvement of 184 metres observed at 12 months in this analysis, is likely to be of sufficient magnitude to be clinically useful in this population.

Large increases in musculoskeletal function were recorded at 3-6 months, which can translate into mobility and strength improvements that facilitate activities of daily living. These might include housework, stair climbing, hill walking, lifting and carrying heavy objects[94, 103, 105]. Previous research has also found that obesity affects musculoskeletal function and movements of daily living such as transitioning from sitting to standing[103,101]. The small number of studies reporting 12 month outcomes meant meta-analysis was not possible. The two studies which did report 12 month data also reported 3-6 month data helping the understanding of post-surgery musculoskeletal function patterns. One study reported the timed ‘get up and go’ test which improved by 2.3 seconds by 3-6 months, and a further 0.7 seconds at 12 months[98]. This improvement is more than double the minimal detectable change of 1.14 seconds reported in the literature[143]. The second study reported the short physical performance battery score improvement of 1.2 points at 3-6 months and a further 0.8 points at 12 months[103]; this is double the score of 1.0 which represents a substantial meaningful change[144]. Both studies show the majority of improvement occurs by 3-6 months concurring with previous research[98]. The current review does show that musculoskeletal function continues to improve at least up until 12 months post-bariatric surgery.

With rapid weight loss, drastic FFM loss also occurs, typically between 33% and 50% [105,145].This supports the large reduction in absolute muscle strength indicated by the meta-analysis (SMD of -1.04). Muscle torque was the only absolute value reported at both post-operative time points showing a decrease of 15 newton metres by 3-6 months, and a twofold decrease by 12 months. FFM loss negatively affects resting metabolic rate, with this metabolic response occurring naturally to counter weight loss[146]. Exercise training post-bariatric surgery would be a useful intervention to optimise post-surgical weight loss and body composition outcomes[94, 147].

3.4.3 Self-reported physical function

All included studies reported improvements in self-reported physical function regardless of post-operative follow-up time frame. This suggests patients perceive an improvement in their day to day lifestyle activities and mobility after bariatric surgery. Studies reporting data from both post-operative time points reveal greater improvements in self-reported physical function by 3-6 months after surgery, with smaller improvements or maintenance from 3-6 to 12 months[97-99]. This suggests that the weight loss is directly responsible for functional improvements. However, it also reflects the patterns observed of post-operative physical activity although data assessing both post-operative time points is currently limited[133]. Minimal clinically important points scores (MCIPS) for the SF-36 have been identified between 10 (small) and 30 (large) in patients with chronic obstructive pulmonary disease[148]. The improvement of 18 points demonstrated at 12 months in the current analysis could therefore be tentatively interpreted as moderately important changes in perceived function.

3.4.4 Objective versus self-reported physical function

Objective and self-reported physical function measurements are not easily comparable because they do not assess the same outcome. Nevertheless when examining the post-operative improvements, physical function as assessed by the SF-36 as a component of health-related quality of life showed a similar mean improvement at both 3-6 and 12 months, whereas the objective measurement of the 6MWT more than doubled in improvement from 3-6 to 12 months. Objective musculoskeletal results also display larger improvements by 3-6 months with continued improvement by 12 months, albeit at a slower rate. Absolute muscle torque was the only absolute value reported at both post-operative time frames showing absolute muscle torque decreased consistently to 12 months. No obvious pattern was shown between objective and self-reported methods. This may suggest that self-reported assessments of physical function may over estimate improvements 3-6 months post-surgery, or under estimate improvements 12 months post-surgery, indicating the importance of objective measurement of physical function. It is important to acknowledge that both objective and self-reported physical function can be affected by an individual's co-morbidity status, for example musculoskeletal disorders

such as arthritis may limit physical functional ability[149]. However, the included studies did not report participant's co-morbidity status and therefore was not included in the current systematic review.

3.4.5 Physical function and weight loss

Positive changes in physical function outcomes and weight loss alone have been reported following bariatric surgery[76, 115-117]. Therefore the results of eight studies that provided data on the 6MWT and weight were plotted in Figure 3.4, concluding that the relationship between weight loss and walking performance is still unclear. Research also suggests that physical activity is associated with greater weight loss leading to improved physical function[94], however self-reported improvements in physical function from pre to post-surgery as a result of weight loss alone have also been reported[81]. A clear relationship between physical activity, physical function and weight loss is yet to be identified, since patterns have not been directly investigated. Objective physical activity, self-reported physical function and weight have been investigated in two studies[76, 137]. Similarly only two studies report objective physical function, self-reported physical activity and weight[101, 105] and only one study reports weight with both objective activity and function[81]. In addition to this, the absence of recognised tools to assess quality in these types of studies, retention rates were extracted and indicated predominantly high retention or was regularly not reported[150] This makes it difficult to draw conclusions about the relationship between post-operative outcomes, and more studies are needed that assess physical activity, physical function and weight loss so that post-operative activity guidelines can be developed to optimise individuals' outcomes.

One way to examine the importance of physical activity after surgery for optimising physical function and weight outcomes is through exercise interventions. Although few such clinical trials exist, there are encouraging findings in respect of the benefits of post-surgical exercise. Results of three randomised trials indicate that an additional aerobic exercise programme after gastric band surgery led to superior improvements in functional capacity over surgery alone[89, 91, 92] (as assessed by the 6MWT). A further trial investigated the effects of resistance training on fitness and functional strength after bariatric surgery, and reported improvements in the sit-to-stand test, VO_2 max and functional strength compared to non-exercising counterparts[88]. This research therefore suggests the importance of exercise training alongside dietary advice post-bariatric surgery to optimise physical activity, physical function , FM loss and preserve FFM.

3.4.6 Strengths and limitations

This systematic review is the first review and meta-analysis to the author's knowledge to examine both objective and self-reported physical activity and physical functions as a result of bariatric surgery. This is the first review to explore physical activity and physical function at both short and longer term

post-operative time points. This is also the first meta-analysis to examine objective and self-reported physical function at specific post-operative time points.

Limitations include the variability of self-reported and objective measures of physical activity. Although non validated measures were reported in studies, all outcomes in the meta-analysis were either objective or validated to minimise bias. The physical activity measurement heterogeneity makes it difficult to define study comparison. Due to the limited literature sources available, the review only reported 3-6 months and 12 months post-surgery. The co-morbidity status of individuals was not reported, this could affect participants physical function status and physical activity levels.

It is important for future research to follow up patients at later post-operative time frames to determine their physical activity levels and physical function status. Future research should also control for co-morbidity status to ensure the improvements shown are resulting from surgery alone. This review found no relationship between changes in weight and physical function. Future large scale trials are essential to help determine if weight loss alone improves physical function or whether physical activity is an essential contributor.

3.5 Conclusion

This systematic review of the evidence demonstrates that objective and self-reported physical activity improves by 12 months after bariatric surgery. A decrease in objectively measured MVPA and an increase in step count at 3-6 months, indicates a shift towards a greater amount of lower intensity physical activity within the first six months after surgery. Walking, musculoskeletal and self-reported physical function all improved by 12 months. No relationship was identified between changes in weight and physical function. However, based on promising results from pilot studies, larger trials are necessary to further understand the effects of physical activity on post-surgical outcomes.

Chapter Four

A retrospective cohort analysis of body mass, health, and functional outcomes after bariatric surgery

Chapter Overview

This chapter reports the results of a retrospective analysis of a cohort of 233 patients undergoing bariatric surgery at a large NHS hospital in England. The dataset was extracted from a national database the National Bariatric Surgery Registry (NBSR) and includes pre and post-operative measurements of body mass, stair climbing ability, and co-morbidities. The study aimed to identify if and when weight regain occurs, the proportion of co-morbidity resolution and physical function patterns in patients after bariatric surgery. The chapter concludes that body mass reduction, physical function and co-morbidity improvements occur through both gastric band and Roux-en-Y gastric bypass surgery, but weight regain is evident 24 months post-surgery.

Key findings

- Body weight, physical function and co-morbidities improved as a result of bariatric surgery.
- Weight loss patterns indicated weight regain occurs 24 months post-surgery.
- Resolution was indicated in all reported co-morbidities; sleep apnoea showed the highest rate of resolution.
- Gastric bypass led to greater weight loss than gastric band, supporting the recent shift towards gastric bypass procedures to optimise post-operative outcomes and cost-effectiveness for the National Health Service.

Publications

The research described in this chapter was presented at the 61st Annual Meeting of the American College of Sports Medicine (ACSM, Florida, USA, 2014).

4.1 Introduction

The number of bariatric surgery procedures undertaken for the treatment of obesity is increasing in line with rising obesity rates[4, 54]. The Health Survey for England data shows adult obesity (BMI ≥30 kg·m^2) increased from 15.4% in 1993 to 24.8% in 2012 whilst morbid obesity (BMI ≥40 kg·m^2) increased from 1.6% to 2.4% respectively[151]. Therefore approximately 1.5 million of England's adult population have a BMI of ≥40 kg·m^2[4]. Bariatric surgery aims to improve overall health by reversing or preventing obesity-related co-morbidities and contributing to HRQoL through weight loss[4, 96].

Current NICE guidelines are to consider patients for bariatric surgery if they have a BMI of ≥40 kg·m^2, a BMI of ≥35 kg·m^2 with co-morbidities, or a BMI of ≥35 kg·m^2 and unable to lose sufficient weight through conventional methods[152]. Since 2014 patients with T2DM are now also assessed for bariatric surgery; NICE updated the guidelines because of the associated cost benefit for the NHS from reducing the T2DM burden[24]. A systematic review by Picot *et al*[153] confirmed the clinical and cost-effectiveness of bariatric surgery for the treatment of moderate and severe obesity when compared to non-surgical alternatives. Further to this a systematic review by Warren *et al*[48] examined the effect of bariatric surgery on co-morbidity resolution. The authors reported an improvement or complete resolution of T2DM in 76.8% of patients with diabetes as a result of surgery. Obesity also negatively impacts HRQoL and an important component of HRQoL is physical function[154]. Essential activities of daily living, such as walking, stair climbing, and getting up from a chair are limited in obese individuals due to the high prevalence of musculoskeletal disorders related to excessive weight[12]. Research suggests that as a result of bariatric surgery, improvements in physical function are seen as early as three months post-operatively and continue to improve to 12 months[96].

It is increasingly apparent that many bariatric patients begin to regain weight between 12 and 24 months of surgery[41, 42]. Weight regain is believed to occur due to the patient's inability to adopt or maintain the necessary changes in physical activity and dietary behaviour[22]. A study by Zalesin *et al*[59] identified that multidisciplinary follow-up interventions are successful in preventing this weight regain. Research has suggested that post-bariatric surgery care is complicated and lifelong follow-up is fundamental for long-term success[54]. NICE guidelines highlight the importance of pre and post-surgery support including regular dietetic advice, co-morbidity management, pathology monitoring, psychology provision if needed, and physical activity advice[24]. Due to the absence of any UK data on physical function and weight patterns, this analysis was conducted to explore data collected through routine NHS care in an entire NHS bariatric surgery cohort to allow a detailed examination of long term outcomes.

The study reported in this chapter aimed to examine the pattern of changes in body weight, functional performance, co-morbidities and blood biomarkers up to four years post-bariatric surgery. Specific objectives were:

- To identify the stage at which weight loss peaks.
- To identify if weight regain is evident and at what stage
- To examine any differences in weight loss or weight regain between patients receiving different surgical procedures or different demographic sub-groups (gender, age).
- To examine changes in stair climbing ability as a marker of physical function.
- To examine resolution rates of eight co-morbidities (T2DM, hypertension, dyslipidaemia, sleep apnoea, asthma, arthritis, gastro oesophageal reflux disease and polycystic ovary syndrome [PCOS (females only)]) associated with obesity.
- To examine changes in two blood biomarkers (total cholesterol and non-fasting HbA1c).

4.2 Methods

4.2.1 Study design

A retrospective analysis was performed on pre and post-surgical outcome data from a sample of bariatric surgery patients. The sample had undergone bariatric surgery at the Royal Berkshire NHS Foundation Trust, one of the largest general hospital foundation trusts in England which provides medical services to half a million people[155]. The two main surgical procedures carried out at this NHS trust are Roux-en-Y gastric bypass and gastric banding; there are also small numbers of revisional gastric band procedures and gastric balloon placements. From September 2009 all bariatric surgery procedures undertaken at this hospital were stored on the NBSR national database. The NBSR is the largest database in the UK and Ireland for hospitals and clinics to record their pre and post-operative bariatric and metabolic surgery outcomes; it includes data for 136 institutions. Comprehensive reports are published based on the NBSR national data set to describe the national bariatric surgery outcomes for the UK and Ireland[4, 156].

All data are anonymised prior to being uploaded on the NBSR national database, hence the hospital's total sample of patients (n=233) were stored as numbered subjects to ensure patient confidentiality. Data for each of the 233 patients were extracted independently for this analysis.

4.2.2 Participants

All patients' who underwent any bariatric surgical procedure from September 2009 to May 2014 at the Royal Berkshire NHS Foundation Trust were included.

This hospital provides a pre-operative lifestyle intervention for their bariatric surgery patients as recommended in the NICE guidelines to prepare patients for surgery. The hospital also follows up patients regularly for two years after the surgical procedure[24]. Due to the nature of routine follow up data, the number of patients attending at each follow-up visit varied. The total number of follow-up appointments attended varied from none to ten. Since the numbers of patients attending each follow-up varied, an additional sub-sample analysis of the total sample was included. A 63 patient sub-sample who had undergone gastric banding and who had both pre-operative and 24 month post-operative follow-up data were explored separately. This was to detect changes in a complete patient sample at both pre and 24 months post-surgery to identify whether it reflects the total sample results (n=233).

4.2.3 Outcome measures

Extracted data included basic demographics (e.g. gender, ethnicity, age), the surgical procedure details (e.g. type of bariatric procedure, details of the procedure, equipment used, additional procedures and any complications) and pre and post-operative follow-up appointment data (anthropometric, co-morbidities and functional status).

Pathology reports were only obtained for the sub-sample (n=63). The sub-samples pathology reports were individually extracted. Of the 63 patients, blood results were available for 53 (43 females; 10 males) patients, although not all had complete data.

Anthropometric measurements

Body mass was measured using specialist weighing scales (Class III High Capacity Digital Scales with BMI, Alpine, UK) and stretch stature was measured using a portable stadiometer (Holtain, UK). Body mass and stretch stature were used to calculate BMI. The %EWL was calculated based on the following equation[4, 156]:

$$\frac{\text{Initial body mass (kg)} - \text{current body mass (kg)}}{\text{Initial body mass (kg)} - [25\ (\text{kg}\cdot\text{m}^2) \times \text{height}^2\ (\text{m}^2)]} \times 100$$

Measurements of physical function

Functional status was measured by patients' self-reported stair climbing ability. Stair climbing ability was recorded at every pre and post-operative assessment into one of four categories: chair/bed bound;

can climb half a flight of stairs; can climb one flight of stairs; and can climb at least three flights of stairs. Poor functional status is classified as the inability to climb more than one flight of stairs according to the NBSR report.

Co-morbidities

Pre and post-operative co-morbidity status was reported for T2DM, hypertension, dyslipidaemia, sleep apnoea, asthma, arthritis, gastro oesophageal reflux disease (GORD) and PCOS via diagnosis health care professionals. Depression, atherosclerosis, liver disease and risk factors for pulmonary embolus were only reported pre-operatively. All co-morbidity information was recorded by formal reassessment by the bariatric nurse and any additional information from the patients' medical notes. Typically, blood samples are obtained to coincide with follow-up appointments which inform co-morbidity status along with verbal reassessment of symptoms for co-morbidities such as GORD and arthritis.

Biochemical measurements

Venous blood sample results were obtained by the direct care team through pathology reports for full lipid profile (total cholesterol, high density lipoproteins [HDL], low density lipoproteins [LDL] and Triglycerides), total calcium and non-fasting HbA1c. These blood samples were obtained through routine care by qualified nursing staff using the standard NHS protocol for taking venous bloods.

4.2.4 Data analysis

Pre and post-operative follow-up information were reported in the database as dated follow-up appointments. Consequently for analysis, follow-up appointments were transformed to fit one of the standard follow-up time-points (1, 6, 12, 18, 24, 36 and 48 months). Any appointment dates that deviated from these standard time-points were aligned with the closest one.

A full dataset analysis of all available data was undertaken on body mass, %EWL, BMI, stair climbing ability and co-morbidities. Demographic grouping variables for this bariatric sample were compared to explore differences in the main outcomes (e.g. surgery type [band versus bypass], age group [≤40 years, 41-60 years, ≥60 years] and gender). Ethnicity was not analysed because of the limited variation in the sample and high percentage of Caucasians (91%).

As the number of patients attending at each follow-up varied, a sub-sample analysis was undertaken on 63 gastric band patients who had baseline and 24 month follow-up data available.

Data were extracted into Excel (Microsoft 2010, Washington, USA) then transferred into SPSS statistics software (IBM Corp, version 20, Armonk, NY, USA). Frequency statistics were performed

to screen for missing data and potential outliers. Since a large proportion of non-attendance occurred at follow-ups, data were not imputed.

Categorical data has been presented in figures and tables; gender associations were determined using chi-square tests and effect sizes (phi) were calculated (φ [small: 0.10; medium: 0.30 and large: 0.50]). Continuous data were checked for parametric assumptions and analysed using a one way ANOVA or paired sample t-test. A post hoc Scheffe test was used to determine where statistically significant differences occurred between groups (e.g. surgery type, gender and age). All data was analysed using SPSS statistics software (IBM Corp, version 20, Armonk, NY, USA).

4.3 Results

4.3.1 Participant characteristics

Total sample

Data from 233 male (24.0%) and female (76.0%) patients aged 45.2 ± 9.8 years with a mean pre-operative BMI of 49.7±6.7kg·m^2 were extracted from the national NBSR database. The total available data for all outcomes have been reported in tables and figures. It may be noted that the available data ranged from 24 to 233 patients at different post-operative follow-ups (e.g. body mass data varied from 231 patients on the day of surgery to 24 patients at 48 months post-surgery). Pre-operative characteristics are outlined in Table 4.1. Also included in Table 4.1 is the sum of co-morbidities. The 12 pre-operative co-morbidities included T2DM, hypertension, dyslipidaemia, atherosclerosis, sleep apnoea, asthma, risk of pulmonary embolus, arthritis, GORD, liver disease, PCOS (females only) and depression.

Sub-sample

The sub-sample (n=63) comprised both males (20.6%) and females (79.4%) with a mean age of 45.6 ± 8.9 and BMI of 49.5 ± 6.4kg·m^2. The sub-sample included only gastric band patients who had at least pre-operative and 24 month post-operative data. This allowed changes to be examined in a complete patient sample at both pre and post-surgery to ascertain whether it reflects the total sample. It must also be noted that the available data was less than 63 at the follow-up time points between the day of surgery to 24 months. For example body mass data existed for 63 patients on the day of surgery and 24 months post-surgery, but varied between six and 34 patients at the other follow-ups.

Table 4.1: Patient characteristics (n=233).

Characteristics	Total sample (n=233) Mean (SD) or Percent (number)	Sub-sample (n=63) Mean (SD) or Percent (number)
Age (years)	45.2 ± 9.8	45.6 ± 8.9
Height (cm)	167.4 ± 9.3	165.9 ± 8.4
Weight (kg)	139.7 ± 23.1	136.3 ± 22.0
BMI ($kg \cdot m^2$)	49.7 ± 6.7	49.5 ± 6.4
Gender (%)		
Male	24.0% (56)	20.6% (13)
Female	76.0% (177)	79.4% (50)
Ethnicity (%)		
Caucasian	91.0% (212)	92% (58)
Asian	0.4% (1)	N/A
Afro-Caribbean	3.0% (7)	4.8% (3)
African	0.4% (1)	N/A
Other	0.9% (2)	1.6% (1)
Not stated	10.0% (10)	1.6% (1)
Surgery type (%)		
RYGB	14.2% (33)	N/A
GB	81.1% (189)	98.4% (62)
Revisional GB	1.3% (3)	1.6% (1)
Gastric balloon	3.4% (8)	N/A
Source of funding (%)		
Publically funded	87.6% (204)	88.9% (56)
Privately funded	12.4% (29)	11.1% (7)
ASA grade (%)		
ASA I	7.7% (18)	9.5% (6)
ASA II	68.2% (159)	66.7% (42)
ASA III	23.2% (54)	23.8% (15)
ASA IV	0.9% (2)	N/A
Pre-operative co-morbidities		
0 to 3	45.5% (106)	42.9% (27)
4 to 6	47.6% (111)	49.2% (31)
7 to 9	6.9% (16)	7.9% (5)

KEY: ASA: American Society of Anesthesiologists (Physical Status classification system); m: males; f: females; GB: Gastric band; RYGB: Roux-en-Y gastric bypass; SD: standard deviation.

4.3.2 Body mass

Body mass, BMI and %EWL were obtained upon initial assessment, the day of surgery and at the respective follow-up time-points for the total sample. A significant decrease in body mass occurred from the initial assessment (139.9 ± 22.6kg) to the day of surgery (135.0 ± 21.9kg) ($t_{(230)}$ =-10.259; P<0.001). The total samples' body mass and BMI follow-up data are shown in Figure 4.1 and Figure 4.2. Secondary analysis of body mass variables for the 63 patient sub-sample who had recorded on the day of surgery and at 24 months post-surgery have also been reported.

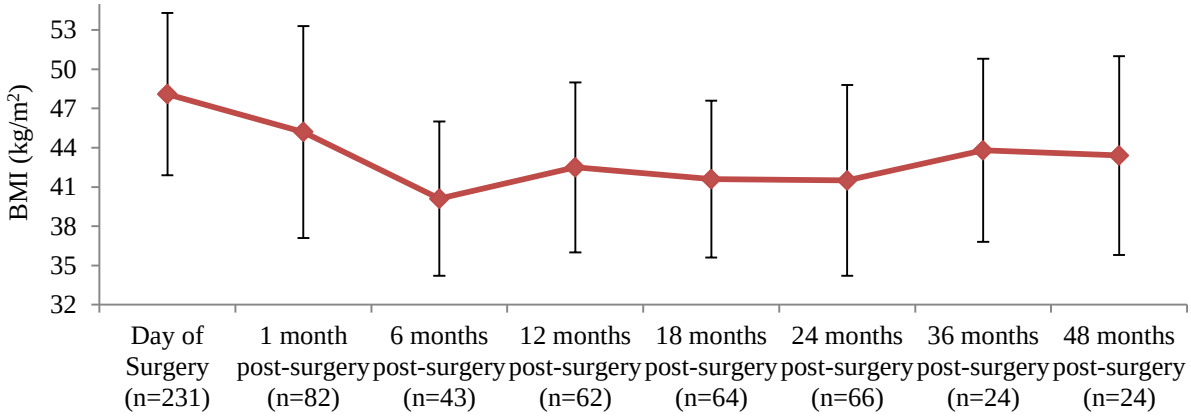


Figure 4.1: Change in mean BMI from the day of the bariatric procedure to 48 months post-surgery in the total sample. Data are reported as mean and SD.

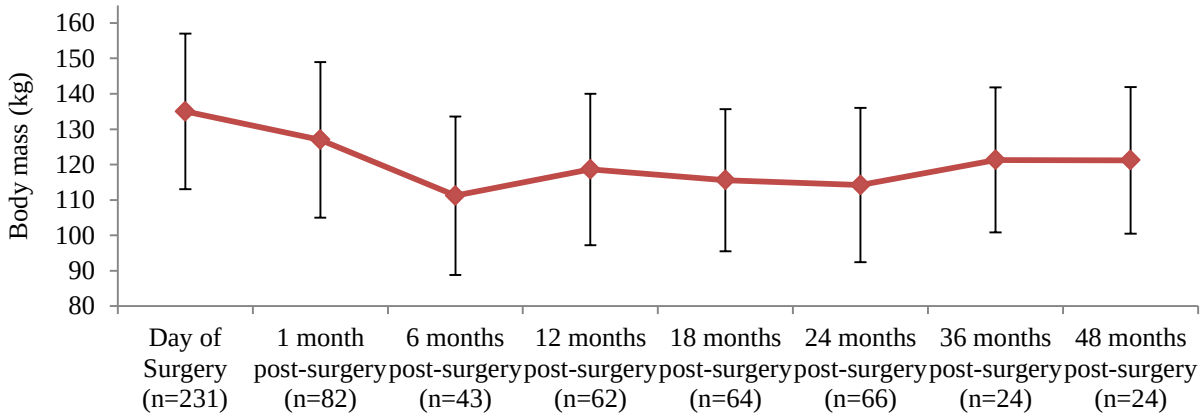


Figure 4.2: Change in body mass from the day of the bariatric procedure to 24 months post-surgery in the total sample. Data are reported as mean and SD.

In the total sample, a lowest BMI of 40.1kg.m^2 occurred at six months post-surgery and plateaued thereafter until 24 months (41.7kg.m^2) post-surgery. An overall decrease of 6.4 kg.m^2 is noted from the day of surgery to 24 months post-surgery. The sub-sample analyses on gastric band patients showed BMI decreased from 48.3 ± 6.2 kg·m^2 pre-surgery to 43.0 ± 6.2 kg·m^2 at 6-months, plateauing from 6 to 24 months where it peaked (41.7 kg·m^2). BMI increased from 24 to 48 months (46.9 kg·m^2). An overall 6.6 kg.m^2 decrease is noted from the day of surgery to 24 months post-surgery; this corresponds to a reduction in body mass of 17.9kg. From 24 to 48 months an increase in body mass was reported based on 10 patients. Overall both the total sample and the sub-sample showed weight regain at 24 months post-surgery. This is shown in the %EWL data presented in Figure 4.3 (total-sample) and Figure 4.4 (sub-sample).

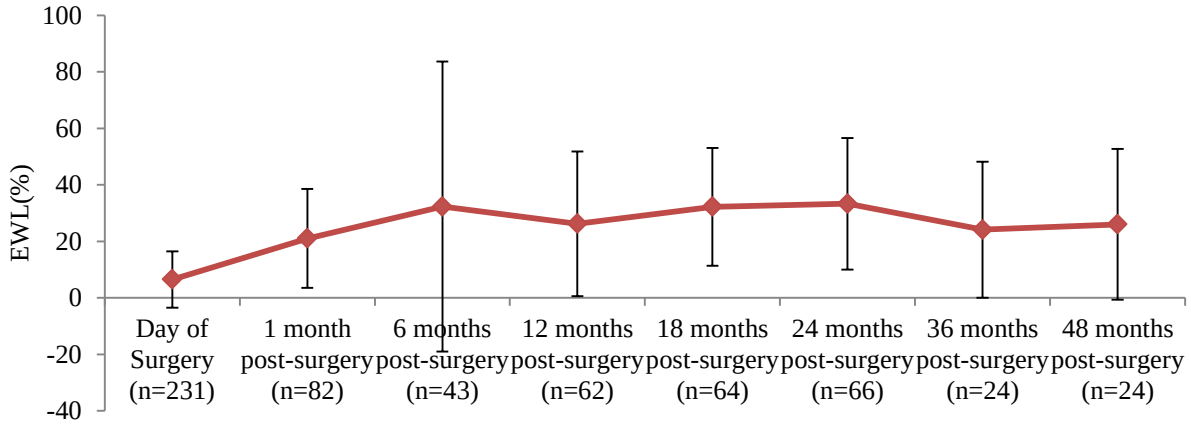


Figure 4.3: Change in %EWL from the day of the bariatric procedure to 24 months post-surgery in the total sample. Total sample data are reported as mean and SD.

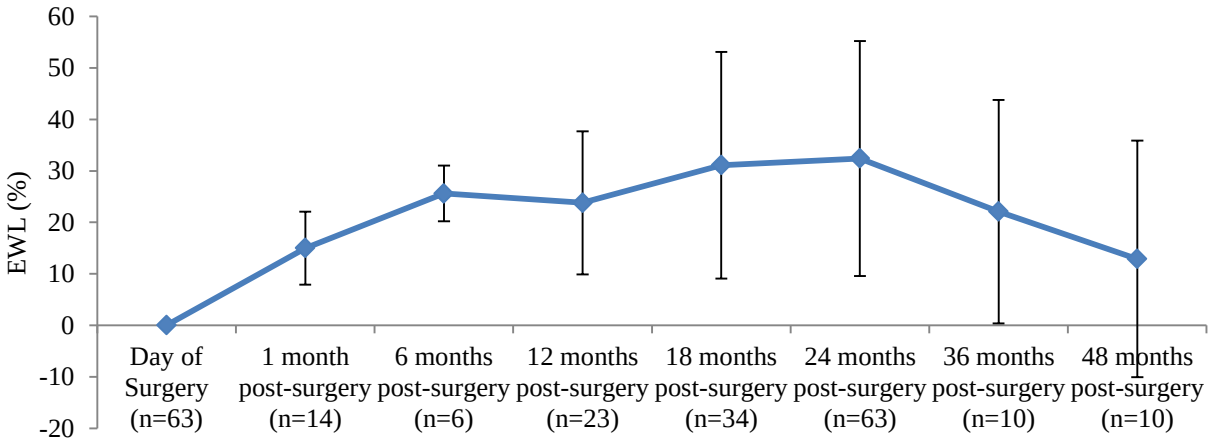


Figure 4.4: Change in %EWL from the day of the bariatric procedure to 24 months post-surgery in the sub-sample. Data are reported as mean and SD.

The total sample's %EWL pattern showed an increase from the day of surgery to six months (32.3%), although the large SD at six months demonstrates the variability in %EWL. The peak %EWL value was 33.3% at 24 months post-surgery, which decreased by 36 months (24.1%). Similarly, the sub-sample's %EWL improved rapidly from the day of surgery to six months post-surgery, although the 6-month assessment is only based on six patients. From six to 24 months post-surgery, %EWL plateaued varying by 8.6%. Peak %EWL occurred at 24 months with an improvement of 32.4% of excess weight lost since pre-surgery measurements. A reduction in %EWL was shown in those attending later follow-ups (n=10).

Gender comparisons of the total sample showed there was no significant difference between genders; mean BMI was 50.0 ± 6.9kg·m^2 and males 48.9 ± 5.8 kg·m^2. No difference occurred between genders in %EWL recorded at follow-up to 36 months or %EWL to date (%EWL based on last follow up attended). There was a significant difference between age categories in %EWL at 36 months post-surgery ($f_{(2, 23)} = 3.614$; $p= 0.045$). When exploring the sub-sample there was a significant difference between age categories in %EWL at 12 months post-surgery ($f_{(2, 23)} = 5.202$; $p= 0.015$). Patients ≤40 years (22.2 ± 7.5%) and 40-60 years (29.1 ± 12.1%) had a significantly greater %EWL than patients ≥60 years (-3.6 ± 8.41%); however, no differences existed at 24 months. No difference existed for gender where a sufficient number of males were available.

The total sample's %EWL was significantly different between Roux-en-Y gastric bypass and gastric banding procedures ($f_{(1, 218)} = 50.102$; $p<0.001$). A mean %EWL to date of 37.9 ± 31.1% in gastric bypass patients was significantly higher than 9.5 ± 19.0% in gastric band patients. Differences between gastric bypass and gastric band at follow-up can be seen in Table 4.2. No difference between gastric bypass and gastric banding existed for body mass, age and the sum of co-morbidities at initial consultation.

Table 4.2: Post-operative %EWL follow-up differences between Roux-en-Y gastric bypass and gastric band in the total sample.

Follow-up	Surgery type	Patient numbers	Mean ± SD (%)	df	f	p
1 month	RYGB	21	27.5 ± 10.3	(1,75)	3.526	0.064
	GB	55	19.2 ± 19.0			
6 month	RYGB	14	61.8 ± 21.2	(1,41)	51.404	< 0.001
	GB	28	28.3 ± 9.2			
12 month	RYGB	6	72.3 ± 14.7	(1,59)	57.612	< 0.001
	GB	54	23.6 ± 14.9			
18 month	RYGB	4	56.1 ± 11.0	(1,62)	5.944	0.018
	GB	59	31.0 ± 20.3			

KEY: RYGB: Roux-en-Y gastric bypass; GB: gastric band; df: degrees of freedom; f: f statistic; p: significance level

4.3.3 Physical function

Physical function was assessed by self-reported stair climbing ability. Figure 4.5 displays the percentage of individuals in the total sample in each category from pre to post-surgery. The proportion of patients in the total sample able to climb three flights of stairs increased from 25.8% at initial assessment to 75% at 18 months and showed slight decline at subsequent follow-ups. Similarly the number of individuals only able to climb one flight of stairs decreased from 61.8% at initial assessment to 18.3% at 18 months but increased at 24 to 48 months.

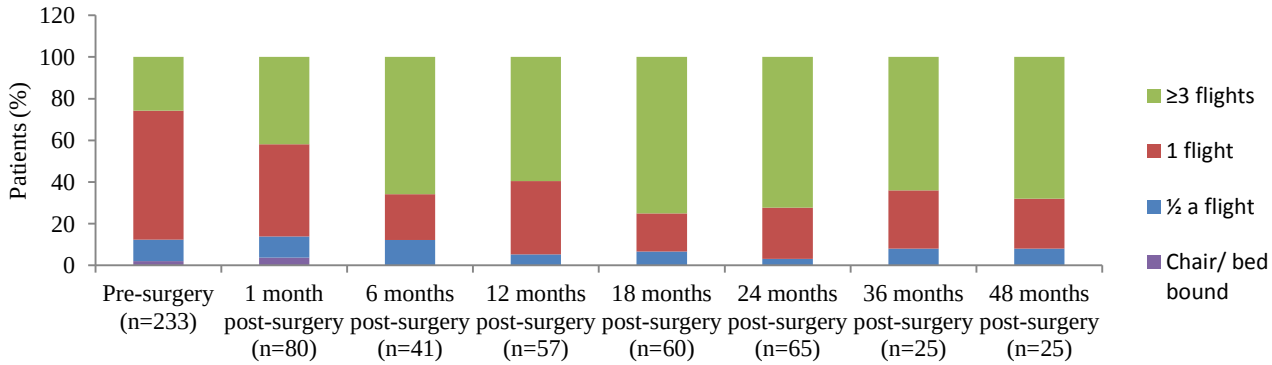


Figure 4.5: The percentage of patients in each stair climbing category across 48 months of follow up in the total sample.

Table 4.3 presents the proportion of sub-sample patients in each category of stair climbing ability across the follow-up period. The proportion of patients able to climb three flights of stairs increased from 22.2% at initial assessment to 72.7% at 18 months and showed a decline to 71.4% at 24 months.

Similarly the proportion of individuals with poor function decreased from 77.8% at their initial assessment to 27.3% at 18 months; however, an increase at 24 months is shown (28.6%). In a second analysis, the four categories have been collapsed into two groups: ≤1 flight, and ≥3 flights. This total samples data are displayed in Figure 4.6.

Table 4.3: The percentage of sub-sample patients (n=63) in each stair climbing ability category.

Functional stair climbing status	**Initial assessment (n=63)**	**12 month follow-up (n=21)**	**18 month follow-up (n=33)**	**24 month follow-up (n=63)**
½ a flight	15.9% (10)	4.8% (1)	9.1% (3)	3.2% (2)
1 flight	61.9% (39)	33.3% (7)	18.2% (6)	25.4% (16)
≥3 flights	22.2% (14)	61.9% (13)	72.7% (24)	71.4% (45)

KEY: n: number of patients.

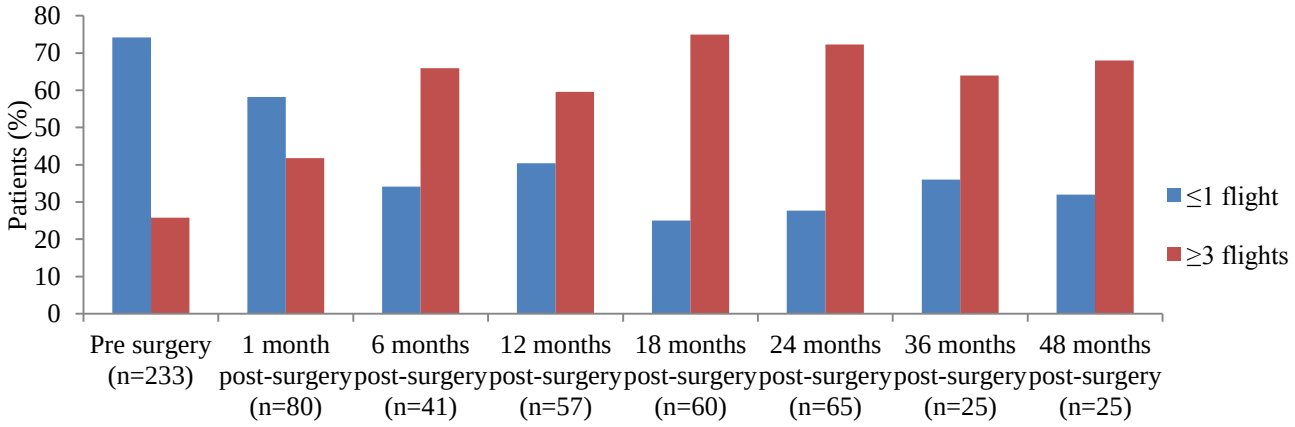


Figure 4.6: The percentage of patients able to climb at least one or at least three flights of stairs across 48 months of follow-up in the total sample.

4.3.4 Co-morbidities

Twelve co-morbidities were reported on the NBSR database pre-surgery. Of the 233 patients with data before surgery 14.9% had six to nine co-morbidities, 62.6% of patients had three to five and only 22.8% of patients had two or fewer. When examining prevalence of co-morbidities by age group (≤40 years, 41-60 years and ≥61 years), a significant difference was shown between patients ≤40 years and

41-60 years in the sum of co-morbidities upon initial consultation ($f_{(3, 232)} = 7.031$; $p = 0.001$). The mean sum of co-morbidities increased with age: patients ≤40 years (n=71) had 3.2 ± 1.5 co-morbidities, patients between 41-60 years (n=146) had 4.1 ± 1.7 and individuals ≥61years (n=16) had 4.3 ± 1.7. No gender or surgery type differences were found for the sum of pre-operative co-morbidities.

Of the 12 co-morbidities recorded before surgery, eight were followed up post-surgery. The percentage of patients that had co-morbidities pre and post-surgery are displayed in Table 4.4. Before surgery the most prevalent co-morbidities amongst the total patient cohort were arthritis (63.7%), sleep apnoea (39.9%), hypertension (38.2%), GORD (29.6%) and T2DM (27.6%). The most prevalent co-morbidity for males was sleep apnoea (58.9%) and for females it was arthritis (66.1%). Gender differences are reported and statistically significant associations are shown for arthritis, sleep apnoea, hypertension, T2DM, depression, dyslipidaemia and atherosclerosis, all showing a small to medium effect (Table 4.4). Male patients had a greater prevalence of sleep apnoea (25.0% higher), hypertension (18.0% higher), dyslipidaemia (14.5% higher), T2DM (12.6% higher) and atherosclerosis (10.7% higher) than females. For females, arthritis (21.5% higher), depression (17.7% higher) and GORD (12.7% higher) prevalence was higher than for males.

Table 4.4: Prevalence of co-morbidities pre-surgery and association with gender in the total sample.

Co-morbidities	Total sample (%) (n=233)	Male (%) (n=56)	Female (%) (n=177)	*p*	φ
Arthritis	63.7	44.6	66.1	0.006	0.183
Sleep apnoea	39.9	58.9	33.9	0.003	0.198
Hypertension	38.2	53.6	35.6	0.008	0.178
GORD	29.6	16.1	28.8	0.074	0.125
T2DM	27.6	37.5	24.9	0.025	0.148
Depression	23.5	8.9	26.6	0.007	0.182
Asthma	20.3	12.5	22.6	0.112	0.104
Dyslipidaemia	17.7	28.6	14.1	0.015	0.160
Pulmonary embolus risk	6.4	8.9	5.6	0.363	0.057
Liver disease	5.4	8.9	4	0.159	0.102
Atherosclerosis	2.6	10.7	0	<0.001	0.289
PCOS (female only)	N/A	N/A	12.4	N/A	N/A

KEY: GORD: gastro oesophageal reflux disease; T2DM: type 2 diabetes mellitus; PCOS: polycystic ovary syndrome; p: significance level; Φ (Phi) effect size.

When comparing pre-operative to post-operative co-morbidity data at each post-operative follow-up, resolution was indicated for a small percentage of patients at different time points (Table 4.5). The lowest percentage of patients with T2DM occurred at 18 month (indicating 7.6% resolution) however the lowest percentage of patients with sleep apnoea occurred at 48 months suggesting resolution in 27.9% of patients. Data are based on those who attended the assessments and these are not the same patients at each follow-up. Table 4.6 presents the proportion of patients whose co-morbidities resolved as a result of bariatric surgery. This also includes gender differences and number of days until resolution.

Table 4.5: The number, percentage and recorded data for co-morbidities pre and post-surgery in the total sample.

Co-morbidities	Pre-surgery (n=233)			1 month post-surgery (n=82)			6 months post-surgery (n=43)			12 months post-surgery (n=62)			18 months post-surgery (n=64)			24 months post-surgery (n=66)			36 months post-surgery (n=25)			48 months post-surgery (n=25)		
	%	n	rd	%	n	rd	%	n	rd	%	n	rd	%	n	rd	%	n	rd	%	n	rd	%	n	rd
T2DM	27.6	64	232	25.0	19	76	24.4	10	41	25.9	15	58	20.0	12	60	27.7	18	65	36.0	9	25	36	9	25
Hypertension	38.2	89	233	35.1	27	77	31.7	4	41	31.6	18	57	35.0	21	60	33.8	22	65	38.5	10	25	34.6	9	25
Dyslipidaemia	17.7	41	231	15.6	12	77	8.1	3	37	10.7	6	56	10.0	6	60	7.7	5	65	24.0	6	25	24	6	25
Sleep apnoea	39.9	93	233	41.8	33	79	29.3	12	41	33.3	19	57	23.3	14	60	29.2	19	65	16.0	4	25	12	3	25
Asthma	20.3	47	232	15.4	12	78	24.4	10	41	21.1	12	57	26.7	16	60	23.1	15	65	32.0	8	25	32	8	25
Arthritis	63.7	142	223	50.7	38	75	69.2	27	39	66.1	37	56	57.6	34	59	62.5	40	64	69.6	16	23	65.2	15	23
GORD	29.6	60	202	18.1	13	72	30.3	10	33	36.5	19	52	29.1	16	55	26.2	16	61	30.0	6	20	30	6	20
PCOS (Females only)	12.4	21	171	9.3	5	54	35.5	11	31	52.1	25	48	49.0	25	51	64.4	38	59	72.7	16	22	68.2	15	22

KEY: n: number of patients; rd: recorded data.

Table 4.6: Co-morbidity resolution for all patients with co-morbidities pre-surgery.

Co-morbidities	Total sample	Female	Male	Mean days for resolution
T2DM (n=65)	7 (11%)	3 (7%)	4 (19%)	415
Hypertension (n=93)	6 (7%)	6 (10%)	0 (0%)	308
Dyslipidaemia (n=41)	10 (23%)	6 (24%)	4 (25%)	599
Sleep apnoea (n=93)	30 (32%)	22 (37%)	8 (24%)	449
Arthritis (n=142)	20 (14%)	18 (15%)	2 (8%)	311
GORD (n=60)	14 (23%)	10 (20%)	4 (44%)	184

KEY: GORD: gastro oesophageal reflux disease; T2DM: type 2 diabetes mellitus.

In the sub-sample the most prevalent co-morbidities pre-surgery were arthritis (68.3%), sleep apnoea (46.0%), hypertension (33.3%) and T2DM (30.6%), thus matching the total sample. When exploring the co-morbidity associations with gender in the gastric band subsample only sleep apnoea (X^2 (1, n=63) =5.253, p=0.022) and atherosclerosis were significantly associated (X^2 (1, n=63) = 8.946, p=0.003). At 24 months, three of the most prevalent co-morbidities were reduced in frequency: arthritis by 5.7%, sleep apnoea by 14.9%, and T2DM by 3.2%; hypertension showed little change. The sub-sample's co-morbidity data are described in Table 4.7.

Table 4.7: Prevalence of co-morbidities pre-surgery and 24 months post-surgery in the sub-sample.

Co-morbidities	Pre-surgery			24 months post-surgery		
	%	n	Missing data	%	n	Missing data
T2DM	30.6	19	1	28.6	18	0
Hypertension	33.3	21	0	34.9	22	0
Dyslipidaemia	9.5	6	0	7.9	5	0
Sleep apnoea	46.0	29	0	28.6	18	0
Asthma	28.6	18	0	23.8	15	0
Arthritis	68.3	43	0	63.9	39	1
GORD	24.1	14	5	27.1	16	4

KEY: GORD: gastro oesophageal reflux disease; T2DM: type 2 diabetes mellitus; n: number of patients.

Biochemical results

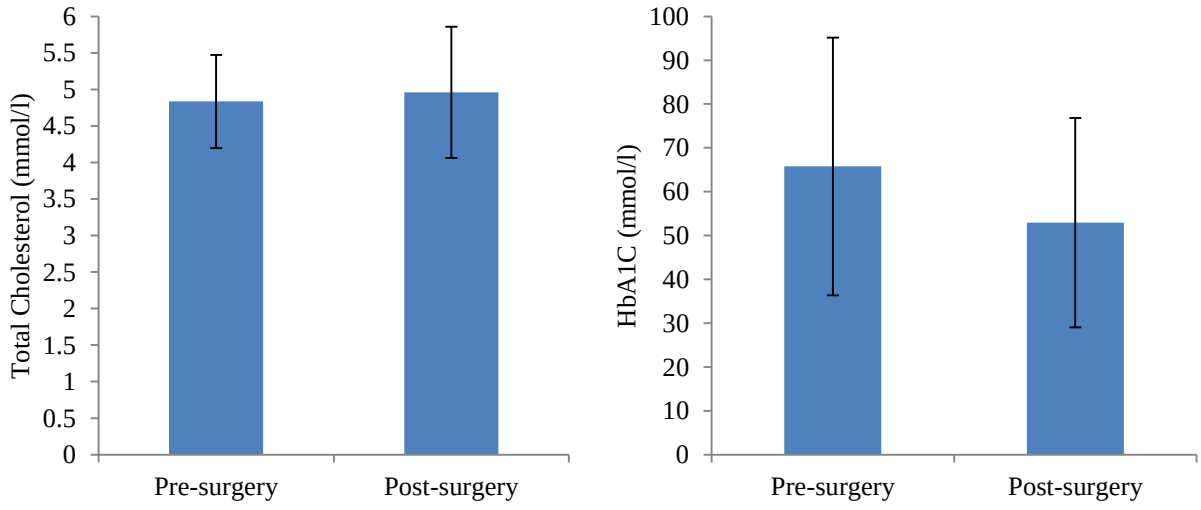
Available pathology results were obtained for the patients in the gastric band sub-sample. Of the 63 patients, blood results were available for 53 (43 females; 10 males), however not all had complete data. Mean pre-surgery values are presented in Table 4.8 along with normal values for comparison.

Table 4.8: Pre-operative blood results for the sub-sample.

Blood sample	**Pre-surgery mean ± SD**	**Normal values**[157-159]
HbA1c (%) (n=30)	7.1 ± 2.2	< 6.0
HbA1c (mmol/mol) (n=29)	53.0 ± 23.9	< 42.0
Total Calcium (mmol/l) (n=35)	2.3 ± 0.1	2.1 - 2.6
Cholesterol (mmol/l) (n=35)	4.8 ± 0.7	≤ 5
HDL (mmol/l) (n=11)	1.3 ± 0.2	> 1
LDL (mmol/l) (n=10)	2.4 ± 0.5	≤ 3
Triglycerides (mmol/l) (n=16)	1.7 ± 0.7	< 4

KEY: HDL: high density lipoproteins; LDL: low density lipoproteins.

Post-operative data were only available for total cholesterol (n = 20) and HbA1c (n = 14). Changes from baseline are shown in Figure 4.7(a) and Figure 4.7(b). No significant change in total cholesterol was observed (mean increase 0.13 mmol/l). The reduction in HbA1c was statistically significant (12.9 mmol/l; $t_{(13)} = 2.727$; $p = 0.017$).



a b

Figure 4.7: Pre and post-operative total cholesterol (a) and HbA1c (b) blood results for gastric band patients in the sub-sample. Results are displayed as mean and SD.

4.4 Discussion

Data were available from a consecutive cohort of 233 patients undergoing bariatric surgery within a five year period. Changes in weight, physical function, and co-morbidity prevalence over four years of follow-up were examined. Data from a sub-sample of 63 patients who received gastric banding surgery and who had data pre-surgery and at 24 months post-surgery were also included in a separate analysis, along with additional blood biomarker analyses.

4.4.1 Patient characteristics

Both males and females are referred for bariatric surgery however the percentage of females that undergo surgery is significantly greater than males. This is potentially attributed to females being more likely than men to identify their weight status accurately and seek professional help[160]. Of the 233 patient cohort 76% were female patients; this is similar to four large scale studies which report that females account for 73% to 81% of all bariatric surgery procedures[47, 161-163]. The mean BMI for this cohort was 50kg·m^2 and mean body mass was 140kg. Compared with the NBSR total dataset, based on 136 contributing institutions from the UK and Ireland[4], mean pre-operative BMI in the current sample was 1kg·m^2 lower and 2kg·m^2 greater in males and females respectively. The equivalent comparisons for body mass indicated that males were 1.4kg lighter, and females were 5.8kg heavier than the reported national average.

The mean age of the patients who underwent bariatric surgery at this NHS hospital from September 2009 to May 2014 was 45 years (16-71); this is similar to the literature[4]. Evidence shows that the mean age of individuals undergoing gastric procedures for weight loss increased from 1998 (40 years) to 2002 (42 years)[164]. A more recent systematic review of 100,100 patients who underwent bariatric surgery between 2002 to 2012 reported a mean age of 45 years[161]. This increase in age is likely attributed to the aging population. The type of bariatric surgery procedures patients undergo vary depending on the focus and speciality of the provider and the need of the patient[4, 24]. It is important to note that Roux-en-Y gastric bypass is a newer procedure at this hospital. Only 14% of the 233 patient sample had undergone this procedure compared to 81% who underwent gastric banding procedures. Previously, gastric band surgery was the universal procedure undertaken to facilitate weight loss due to its minimally invasive nature. Gastric banding was then overtaken by Roux-en-Y gastric bypass procedures, and more recently sleeve gastrectomy procedures are undertaken more frequently than gastric band surgery[4].

4.4.2 Weight loss

Prior to surgery weight loss is required to demonstrate that individuals are committed and can make the appropriate lifestyle adaptations needed for post-operative bariatric surgery success. Pre-operative

weight loss has also been associated with fewer complications after surgery[165, 166]. This particular hospital provides a multidisciplinary education program for morbid obesity that includes diet and physical activity advice which potential bariatric surgery candidates must undertake. This reflects this significant decrease in body mass from initial assessment to the day of surgery. Previous research has distinguished weight loss patterns and the degree of weight loss expected as a result of bariatric surgery, and more specifically for the different surgical procedures undertaken[4, 23]. The degree of weight loss differs per surgical procedure; the NBSR reports the degree of %EWL in order of Roux-en-Y gastric bypass (55-70%), sleeve gastrectomy (55-60%) and gastric banding (45-55%)[4]. The current analysis found no gender differences in mean %EWL. The peak %EWL in the current cohort was 33.3% occurring at 24 months after surgical intervention. A systematic review by Buchwald *et al*[47] found the mean %EWL based on 22,094 patients was 61.2% after bariatric surgery, however it is unclear at what time point this occurred. The cohort's mean %EWL pattern exhibited rapid weight loss from the day of surgery to six months post-operatively, weight loss then plateaued with %EWL peaking at 24 months; weight regain is indicated there after. This is in line with previous research indicating that weight regain occurs between 12 and 24 months post-bariatric surgery[23].

Roux-en-Y gastric bypass and gastric banding are the main procedures undertaken at this NHS hospital; it is well noted that %EWL differs depending on the surgical procedure performed[23, 47]. The %EWL has been reported in a large scale review as significantly lower after gastric banding than Roux-en-Y gastric bypass, hence reporting a mean %EWL of 47.5% in gastric band patients and 61.6% in Roux-en-Y gastric bypass patients[47]. A more recent systematic review by Puzziferri *et al*[167] analysed %EWL from 29 studies which had at least two years of follow-up data. They found that only 31% of gastric band patients lost more than 50% of their excess weight. When comparing gastric band and Roux-en-Y gastric bypass procedures, %EWL after gastric banding was 20.7% lower than the 65.7% reported in gastric bypass patients[167]. A significant difference was also identified in %EWL between gastric band and gastric bypass surgery in the current cohort. Differences were significant at six, 12, and 18 months post-surgery; gastric bypass group's 12-month mean %EWL was 72.3% compared to 23.6% post gastric banding surgery. The current results therefore agree with existing research, indicating that those who undergo Roux-en-Y gastric bypass have a significantly higher post-operative %EWL to those undergoing gastric banding. The total sample's %EWL was lower than the 61.2% reported in previous literature[47]. The NBSR's 2011-2012 report presents the average post-operative %EWL for the UK and Ireland by surgery type. At 12 months, gastric band patients' %EWL was 36-40% and Roux-en-Y gastric bypass patients' %EWL was 64-69%. The NBSR report therefore also shows greater %EWL after Roux-en-Y gastric bypass when compared to gastric banding procedures.

A comparison of one year post-operative %EWL induced by Roux-en-Y gastric bypass in the current cohort with data from the NBSR report indicates that the current cohort's result is above average, whereas %EWL through gastric banding procedures is below average. It is important to note that the sample sizes reported both for the current cohort and the NBSR dataset reduce at latter follow-up time points, and is not necessarily the same individuals through follow-up assessments[4, 156]. To see if any differences occurred when following up the same patient cohort, a sub-sample analysis was carried out on the current dataset.

Sub-sample

The sub-sample analysis examined 63 gastric band patients who had %EWL follow-up data at least 24 months post-operatively to see if results differed to the total sample. Similarly the sub-samples mean %EWL was 32.4% and peaked at 24 months post-surgery. All patients in the sub-sample had undergone gastric banding surgery alone. When comparing the sub-samples' %EWL to the mean %EWL for gastric band surgery results in the NBSR (43-50%), the results remained lower than average two years post-surgery. However, contrary to the research carried out by Sjostrom *et al*[23] which followed up a single sample to 10 years showing weight regain occurred one year after gastric band surgery, the NBSR report displays continued weight-loss three years after surgery[4].

4.4.3 Co-morbidities

Previous literature has reported the importance of bariatric surgery in the treatment of obesity related co-morbidities because long term resolution of such diseases is cost-effective for the NHS[168]. The NBSR report shows that 64% of patients undergoing bariatric surgery have more than three serious medical co-morbidities[4]. The current cohort showed 77% of patients presented three or more co-morbidities upon initial consultation and the older the patient the more co-morbidities were present. This highlights the importance of optimising and sustaining co-morbidity resolution and weight loss for this hospital. Both the 2009-1010 and 2011-2013 NBSR reports identify arthritis as the most common co-morbidity, and atherosclerosis, liver disease and PCOS being the least prevalent[4, 156]. The prevalence of co-morbidities varied by gender, with sleep apnoea, hypertension, T2DM, dyslipidaemia and atherosclerosis being significantly more common in men. Arthritis and depression were significantly more prevalent among female patients. The current cohort reflects the results by the NBSR report; the only notable difference was arthritis which was higher in the current cohort.

Co-morbidity resolution

Sleep apnoea was the most commonly resolved co-morbidity in this study population. At 12, 24 and 48 months, 33%, 24% and 12% of patients respectively had sleep apnoea compared with 40% at baseline. Schauer *et al*[169] found obstructive sleep apnoea resolved in 33% of patients which is similar

to that reported at 24 months in this cohort. A significant association between sleep apnoea and gender exists with a greater proportion of males having sleep apnoea than females. However, more females than males resolved sleep apnoea. Male and females both had a higher prevalence of sleep apnoea in the current sample compared with the NBSR reports' data[4]. The female resolution rate from the current cohort was similar to the females in the NBSR report, whereas male improvement was less.

A significant association has also been shown between T2DM and gender. Before surgery, 28% of the current cohort had T2DM; male prevalence was 13% greater than females. The percentage of patients with T2DM remained similar at follow-up, however post-operative resolution was shown in 7% and 19% of females and males respectively. The NBSR report shows T2DM is present in approximately 30% of the patients at baseline; this is reduced by 13% at 12 month with a further reduction of 2% at 24 month follow-ups. Schauer *et al*[169] reported resolution or improvements of T2DM in all of the post-bariatric surgery patients they evaluated, with total resolution accounting for 83% of Roux-en-Y gastric bypass patients. Buchwald *et al*[47] reported 77% experienced total resolution regardless of surgery type although mean resolution after gastric band surgery was 48%. It is however unclear at what post-operative time point resolution occurred. Resolution is dependent on pre-operative T2DM duration; the longer an individual has had T2DM the slower the rate of resolution[169]. It has been suggested that diabetes reversal is reliant on the improvement of skeletal muscle insulin sensitivity[170]. It is well known that weight loss initiated through bariatric surgery results in large improvements in insulin sensitivity, although this can be facilitated by implementing post-operative exercise[171, 172]. The data in the current study only shows percentage resolution, however analysis also demonstrated a significant improvement in post-operative HbA1c. HbA1c is a simple and reliable marker of insulin sensitivity[173] and this may therefore indicate that further individuals had improvements in glucose control in addition to those who experienced resolution of T2DM.

Dyslipidaemia was present in 18% of patients before undergoing bariatric surgery (29% of males and 14% of females). This reduced to 7% of the total sample 24 months after surgery. The NBSR report shows 24% of the bariatric surgery patients had dyslipidaemia pre-surgery reducing to approximately 12% at 12 months and 10% at 24 months post-surgery. The NBSR report shows that males and females both significantly improve dyslipidaemia rates between baseline to 12 and 24 months post-operatively. A large systematic review found lipid profile improved in 70% of patients post-surgery[47]. When looking at resolution in the current cohort, for the males and females that resolved, resolution occurred at a mean duration of 20 months. Fewer patients resolved in the current cohort compared to the NBSR report data[4], potentially due to the fact that less of the current cohort had dyslipidaemia pre-surgery. Research shows that weight loss induced by Roux-en-Y gastric bypass improves lipid profile and males reportedly show a superior lipid profile than females after surgery[174]. The current study found no statistically significant change in cholesterol from pre to post-surgery in the

individuals with available bloods. However, just under a quarter of patients with dyslipidaemia resolved as a result of bariatric surgery.

Arthritis was the most prevalent co-morbidity affecting 64% of patients at baseline; prevalence was higher in females (66%) than males (45%). The pattern of patients presenting arthritis at follow-up remained similar; 15% of females symptoms resolved as did 8% of males. Research suggests weight loss induced by bariatric surgery improves knee pain, physical function and stiffness associated with osteoarthritis[51, 175]. Weight loss induced by bariatric surgery has also shown lower disease activity and lowered medications in rheumatoid arthritis[176]. Improved physical activity has also been suggested to contribute towards these improvements in both osteoarthritis and rheumatoid arthritis[51, 176]. The NBSR report does not include arthritis follow-up after bariatric surgery, presumably because the likelihood of arthritis resolving is very low. However the symptoms associated with arthritis are likely to improve, depending on the severity of the arthritis[51]. The large proportion of patients with arthritis is likely to contribute alongside obesity to the high proportion of individuals with poor functional status before surgery in this cohort.

Sub-sample

The sub-sample results generally supported the overall findings. The three most common pre-operative co-morbidities in the gastric band sub-sample remained the same as for the total sample (arthritis, sleep apnoea and hypertension). When comparing their co-morbidities at baseline versus their co-morbidities at a 24 month follow-up, an improvement of ≥15% occurred for sleep apnoea, between 3% and 5% for arthritis, asthma and GORD, between 1% and 2% for T2DM and dyslipidaemia. The percentage of individuals presenting hypertension increased by 1.6%. Resolution of co-morbidities is less prevalent in individuals who have undergone gastric banding surgery because weight loss is less than is induced by other bariatric surgery techniques[177]. The NBSR report shows the main improvements in co-morbidity resolution occur in the first year after surgery with minimal improvements to 24 months[4]. In the total sample, mean resolution occurred within one year for hypertension, arthritis and GORD. Resolution for T2DM, dyslipidaemia and sleep apnoea occurred between one and two years, thus supporting that of the NBSR report.

4.4.4 Physical function

The importance of obesity's impact on physical function is often overlooked with the focus predominantly on weight loss and the resolution of obesity related diseases[94]. Physical function is compromised in obese individuals; the ability to undertake basic tasks of daily living such as walking, stair climbing and the transition from sitting to standing is impaired which negatively affects quality of life[94, 96]. The NBSR records self-reported stair climbing ability as an indicator of the patients'

physical function. Poor physical function is reported in approximately 72% of all patients in the UK and Ireland (NBSR report) undergoing bariatric surgery. Poor physical function is defined in the NBSR report as the inability to climb three flights of stairs or more without resting[4]. Poor pre-operative physical function in the current sample was evident in 74.2% of patients of which 2.1% were bed/chair bound, 10.3% could climb half a flight of stairs and 61.8% could only manage one flight of stairs. Excess body weight is likely to influence this because the higher an individual's BMI the more likely their physical function will be inhibited[4, 178]. The percentage of individuals in the current cohort with poor physical function was 2% more than the average reported in the NBSR report; this may reflect the cohorts slightly higher pre-operative mean BMI.

Follow-up data from the current cohort showed considerable improvements in functional stair climbing ability. Improvements were seen at the one month follow-up. At six months no individuals reported being chair/bed bound, and from the six month follow-up onwards, less than 40% of individuals were classified as having poor physical function. Previous literature has reported that improvements in physical function can be seen as early as three weeks after undergoing bariatric surgery[103]. The NBSR report states that 12 and 24 months after surgery, approximately 74% and 75% of patients had normal functional status respectively[4]. The total sample analysis showed the proportion of patients of normal functional status peaked at 18 months with 75% of patients being able to climb three flights of stairs or more. At 24 months post-surgery the proportion of patients able to climb ≥3 flights decreased by 3% and decreased further by 36 months to 8%.

A previous study investigating objective physical function (short physical performance battery) as a result of bariatric surgery reported a small improvement in physical function three weeks post-operatively. However, continued improvements occurred at three, six and 12 months post-operatively[103]. This supports the continued improvements shown to 12 months in the current cohort. However, no previous studies have monitored physical function beyond 24 months post-surgery, so it is unknown when these physical function improvements slow or decline. Overall the results in the current analysis concur with current literature and the post-operative data reported in the NBSR report.

Sub-sample

The sub-sample's physical function remained similar to the total sample; the percentage of patients with poor physical function reduced by 65% within 24 months. However, when comparing pre-operative functional status specifically in gastric band patients to the NBSR report, there is a clear difference, with an 18% higher prevalence of poor physical function in the study sub-sample. One explanation for this may be the relatively high prevalence of arthritis and higher BMI in female participants compared with NBSR report. Obesity is a risk factor for arthritis; individuals who have arthritis and are classified as overweight are reported as physically inactive and experience loss of physical function[179, 180].

4.4.5 Cost-effectiveness

Publically funded bariatric surgery procedures according to the NBSR report, account for 76% of all procedures[4]. In the current analysis, 88% of procedures were publically funded. Previous literature has reported the importance of bariatric surgery in the treatment of obesity related co-morbidities as long term resolution of such diseases confers a greater cost saving for the NHS[153]. Bariatric surgery is reportedly more cost effective than alternative non-surgical treatments and can potentially pay for itself within a few years by reducing medical costs[153, 181]. Both gastric band and Roux-en-Y gastric bypass have been found to be cost effective[177]. In a study looking at newly diagnosed patients with T2DM after gastric banding or gastric bypass surgery, bypass was reported as less costly than banding[177]. Bypass led to greater diabetes remission, larger weight loss and larger improvements in quality of life, indicating it could be the best surgical method to ensure cost-effectiveness long term[177]. This therefore highlights the importance of resolving disease permanently and sustaining and maintaining the positive outcomes associated with bariatric surgery to ensure cost-effectiveness. The lower than average resolution in the current cohort in the majority of co-morbidities explains the recent increase in Roux-en-Y gastric bypass procedures and decrease in gastric band procedures being undertaken at this hospital.

4.4.6 Advantages and disadvantages of secondary datasets

The main advantage of using this secondary dataset was the breadth of the routinely collected data available. An individual researcher could not typically collect routine NHS data representative of a full bariatric surgery sample. Alongside the main advantages of using such secondary datasets, it must be noted that there are also disadvantages. Over the years of data collection practices and the clinicians obtaining measurements could have changed. Weight, co-morbidity and functional status at the latter follow-ups could just reflect those still attending. The reasons for loss of patients to follow-up cannot be determined and could be attributed to different factors. Such factors could include patients believing they no longer need monitoring as they feel the surgery has been successful, individuals having difficulties post-operatively embarrassed to return or not understanding the importance of post-operative follow up appointments.

4.4.7 Strengths and limitations

The main strength of this study relates to the authenticity of the dataset, since it represents measurements taken during routine NHS care in an entire patient population. In contrast, many studies rely on recruiting a sample of participants that may not always be representative of the wider population. The wealth of data available over four years of follow-up enabled a detailed examination of the pattern of change in important clinical outcomes. In particular, the stages of weight loss, and

comorbidity resolution could be delineated, as well as the point of weight regain and functional decline. The study included the analysis of a patient subsample who attended both pre and 24 months post-surgery to support outcomes.

The limitations to this retrospective data analysis are that there are only two types of bariatric surgery undertaken at this NHS hospital, with Roux-en-Y gastric bypass being a newer procedure. This meant there were limited follow-up data for this surgical procedure. Follow-up appointments on the NBSR database were reported by date, hence were converted to follow-up time points for analysis. Dates that deviated from specified time points were aligned with the closest one for analysis purposes therefore this possibly could have affected the accuracy of follow-up patterns. The small number of patients at some follow-up assessments is also a limitation as it may show some bias in attendance, hence the inclusion of the sub-sample analysis. It must be noted that resolution of co-morbidities are recorded on the NBSR database based on follow-up attendance; firstly if patients did not attend their follow-up, resolution would not be noted. Further to this, as the data reported is based on disease status at the time of follow-up, it could give an indication of when the co-morbidities resolved rather than specific dates. Finally the measurement of physical function used is rudimentary, and relies on self-report.

4.5 Conclusion

The current retrospective cohort indicates improvements in body weight, physical function and co-morbidities as a result of bariatric surgery. Weight loss occurred regardless of the type of surgery undertaken, nonetheless weight loss patterns indicate weight regain by 24 months post-surgery. Resolution was indicated in all reported co-morbidities with sleep apnoea showing the highest rate of patient resolution. The greatest proportion of patients with normal physical function after surgery was indicated in the 233 patient cohort at 18 months; this proportion of patient's reduced thereafter. It is important that regardless of surgery type, the physical function improvements shown at 18 months are maintained and weight regain after 24 months is prevented. These results along with the literature therefore highlight the need for exercise interventions 12 to 24 months post-surgery to optimise these outcomes.

Chapter Five

The effects of supervised exercise training 12-24 months after bariatric surgery on physical function and body composition: a randomised controlled trial (The MOTION Study)

Chapter Overview

This chapter reports a randomised controlled trial assessing the effectiveness of a post-operative supervised and structured exercise intervention implemented at 12 to 24 months post-surgery: the typical point of weight regain. The intervention involved three supervised 60-minute combined aerobic and resistance training gym sessions per week for 12 weeks. Control group participants received their usual follow-up care. The main outcome was physical function assessed by the incremental shuttle walk test. Effects on strength, anthropometric, physical activity, cardiovascular, psychological, and biochemical outcomes were also examined. Assessments were performed at three months following the intervention, and repeated at six months to examine the maintenance of effects.

Key findings

- Functional walking ability in the exercise training group improved by a mean distance of 112.5 metres at three months, with a greater mean improvement of 143.3 metres at six months. The control group showed a significantly lower mean reduction of 32.5 metres at six months.
- The sit to stand test speed was quicker in the exercise group and slower in the control group at both three and six months, with inter-group differences of 4.0 seconds and 4.5 seconds respectively.
- The exercise training group lost weight whilst the control group gained weight showing a body mass difference of 3.4kg at three months, which further increased to 5.6kg at six months.
- The exercise training group had a low drop-out rate (8%), and high adherence to the exercise (95%).

Publications

The research described in this chapter was presented at the following two international conferences:

International Society of Behavioral Nutrition and Physical Activity 14th annual meeting (ISBNPA, Edinburgh, USA, 2015).
62nd Annual Meeting of the American College of Sports Medicine (ACSM, San Diego, USA, 2015).

5.1 Introduction

Bariatric surgery is an effective weight-loss intervention for morbidly obese patients and is successful in the treatment of obesity and its related diseases[14]. Surgery, combined with long-term lifestyle modification is the most effective and sustainable method of weight loss[19]. More research is emerging showing evidence of weight regain in patients after bariatric surgery, typically occurring between 12 and 24 months post-surgery[23, 53]. In addition to weight regain there is a tendency for physical function to decline around 18 months, this is supported by the retrospective cohort analysis described in chapter four. Weight regain increases the risk of physical function decline which negatively affects an individual's ability to undertake activities of daily living (e.g. walking, stair climbing)[94]. Weight regain also increases the likelihood of obesity related co-morbidities returning[49, 182]. This augments the importance of the Royal College of Physicians recommendations and NICE guidelines for tackling diet and physical activity behaviours[2, 24].

The Royal College of Physicians has stated that MDT services are needed nationwide after bariatric surgery to tackle severe and complex obesity[2]. The development of supervised and structured interventions increases the likelihood of long term behaviour maintenance[58, 69]. Post-operative lifestyle interventions that adopt a combined diet, exercise and behaviour modification approach have proven successful in aiding long-term weight maintainence and improving physical function[20, 81]. NICE also recommends that follow-up care after bariatric surgery should incorporate physical activity advice and support in a two year post-operative care package[24]. These recommendations are encouraging but little research exists to support these guidelines.

No quantifiable physical activity recommendations currently exist for the bariatric population. Physical activity post-surgery is associated with increased weight loss and improved physical function; currently limited information on post-operative exercise exists [14, 25, 26, 73, 81]. There are a limited number of exercise interventions in bariatric surgery patients, and these are mainly performed within the first three to four months post-operatively. A high volume exercise programme undertaken in post-operative individuals highlighted an improvement in self-reported physical function and a significant improvement in VO_2 max relative to body mass, when compared to the post-operative control group[84]. Stegen *et al*[89] identified that improvements in physical fitness (strength, aerobic and functional capacity) did not occur with surgery induced weight loss alone (control group). These studies indicate the value of introducing exercise in the early post-operative stages, but there remains a lack of research on the effect of intervening later when patients are susceptible to regain weight.

It is well established that during significant weight-loss, FFM loss occurs[183]. Structured exercise can ameliorate this reduction in FFM loss, improve cardiovascular function whilst contributing to optimal weight loss outcomes[25, 84]. This has been shown in exercise interventions initiated within the first three

or four months of surgery, however it does not prevent FFM loss[89]. A non-randomised 10 month running intervention by Marchesi *et al*[90] showed mean improvements in FFM as a result of exercise initiated at a later post-operative phase (one to three years after surgery). The mean improvement in FFM as a result of exercise suggests intervening after 12 months is beneficial. Anecdotal reports also suggest patients often feel unsupported at this time point, hence the importance of a trial implemented at the point of weight regain and physical function decline. All exercise trials initiated after bariatric surgery have shown promising results; however, there is a lack of follow-up after completion.

Therefore the aim of this study was to examine the effect of a structured and supervised exercise intervention on physical function and body composition in patients 12-24 months post-bariatric surgery. A secondary aim, to also assess the combined effect of a 12 week structured and supervised exercise intervention in addition to a generic discharge advice session on physical fitness and activity maintenance at 24 weeks.

5.2 Methods

5.2.1 Study design

A single-centre RCT with two parallel arms was performed. Adult patients who were 12-24 months post-bariatric surgery were randomised to either supervised exercise training for 12 weeks or to usual follow up care. Assessments were performed pre-intervention, post-intervention at 12 weeks, and after six months (Figure 5.1). Ethical approval was received from the West Midlands NHS research ethics committee (Reference: 13/WM/0445(Appendix 5.1).

5.2.2 Participants

This RCT recruited adult bariatric surgery patients 12 to 24 months after any type of bariatric surgery procedure, who remained overweight (BMI of $\geq$30kg·m^2 or$\geq$ 28kg·m^2 for south Asians[5, 9]) and were classified as inactive (self-report $\leq$150 minutes MVPA per week[82]). Participants completed a health assessment and treadmill exercise test (Balke protocol) before being deemed healthy to participate in moderate intensity exercise by an in house clinician. Volunteers with unstable diabetes, stage II hypertension, CVD, pulmonary disease, renal disease, orthopaedic limitations, motor neurone disease or who were chair bound were excluded. They were also excluded if their bariatric surgery procedure did not fall into the post-operative time frame between 12 and 24 months, if they were classified as physically active (self-report >2.5 hours per week)[82], if they were under the age of 18 years at the point of recruitment.

A sample size calculation suggested that a total of 28 participants were required to detect a difference of 50 metres in the incremental shuttle walk test (the main outcome) between the two groups at the 3-

month assessment point, with 80% power, and a two-sided 0.05 significance level, and a standard deviation of 45 metres. A difference of 50 metres is defined as clinically meaningful in a similar clinical population[184]. Sedgwick[185] states that 80% power is generally accepted and this was realistic when taking into consideration the difficulty in recruiting in this population. Power would have been higher if more patients were available for recruitment. In the absence of data from a bariatric surgery sample, these estimates were based on results of a published trial of an exercise intervention in a clinical population (men with prostate cancer)[186]. It was anticipated that the current sample would be predominantly female, and that this would be reflected in a slightly lower walking performance, and greater variability than observed in this study. Hence, it was reasonable to assume a smaller group difference, and a higher standard deviation. In order to allow for a 20% drop out rate, 34 participants was the recruitment target.

5.2.3 Recruitment and randomisation

Patients were recruited from post-operative bariatric surgery lists from the NHS University Hospitals of Leicester and Spire Leicester Private Hospital between January 2014 and January 2015. All patients who were within 12-24 months of their surgery date were sent invitation letters and reply slip signed by their surgeon, along with a participant information booklet (Appendix 5.2). Participants were asked to return a reply slip in a pre-paid stamped addressed envelope to express whether they would be interested in participating or not. This gave permission for the investigator to contact them to discuss taking part. To maximise recruitment three recruitment phases were undertaken; if no response was received from the first recruitment letter a second letter was sent. Furthermore, private patients from Spire in addition to NHS patients were included in recruitment. Upon the successful completion of consent, screening and the initial assessment, participants were randomly allocated into either the exercise or control group using random number sequencing in concealed brown envelopes. The algorithm for randomisation was designed by a statistician using the random permuted-block procedure (blocks of 4). The randomisation was performed by an independent researcher, who had no other involvement in the study, ensuring adequate allocation concealment; Figure 5.1.

5.2.4 Intervention

Exercise intervention

The exercise intervention incorporated three 60 minute gym sessions per week for 12 weeks. Twelve week exercise interventions in this population have previously demonstrated positive results, informing the decision to select 12 weeks for the exercise interventions duration[84, 87, 91]. Twelve week exercise rehabilitation has been included in government guidelines for other clinical populations. The current government national service framework for cardiac exercise rehabilitation suggests no less

than six weeks supervised exercise rehabilitation[187]. However, typically 12 weeks of exercise comprising of at least 3 exercise sessions per week with a minimum of 2 supervised is endorsed. The exercise programmes are individualised to meet patients' needs and should include one education session[187]. The MOTION studies gym sessions were hospital based and supervised by a qualified gym instructor with the appropriate immediate life support training; this was for safety protocol purposes for exercising an 'at risk' population. Previous research has reported that supervised exercise leads to improved long-term outcomes and adherence to a more active lifestyle[83]. The gym facility was small and dedicated specifically to research participants. Equipment available in this facility included treadmills, recumbent bikes, upright bikes, rowing ergometers, kettle bells, medicine balls, leg press machine, leg extension machine.

The gym sessions consisted of moderate intensity aerobic and resistance training; this included 5-10 minute aerobic warm up and cool down, 30-50 minute moderate intensity aerobic training and 5-10 minutes of resistance exercise. Moderate intensity aerobic exercise was expressed as a percentage of maximum heart rate; in the main exercise session this equated to between 64 and 77% (RPE 12-14)[83]. Moderate intensity for resistance exercise was expressed as 60% of the participants estimated one-repetition maximum (1-RM) which equated to approximately 10-12 repetitions[188]. Programmes were personalised, specifying durations, resistances, inclines, sets and repetitions. Any limiting factors such as hypertension, arthritis, Ménière's disease (disorder affecting hearing and balance), musculoskeletal restrictions and medications were taken into consideration when designing the programmes. Due to the large variation in patients' abilities, programmes were designed to meet the individuals' needs and progression expectation varied. However all patients worked at a moderate intensity and were also closely monitored throughout. Programme progressions for patients ranged from three to six programmes during the 12 weeks of training to ensure progressive overload. Exercise programme progression was based on heart rate to ensure patients were consistently working at moderate intensity. Blood pressure (pre and post), heart rate (pre, during and post) and attendance was monitored at each session throughout the intervention; patients could attend a possible 36 sessions.

Upon completion of the 12-week structured exercise training programme the participants received a standard lifestyle advice session lasting 30 to 60 minutes. This individualised advice session represented a typical discharge advice session given to patients in follow up care. Relevant topics such as physical activity maintenance, overcoming barriers and goal setting were discussed. In addition an optional maintenance exercise programme was provided (e.g. gym continuation). Finally, a diet information sheet was provided based on standard post-operative advice that the individuals were familiar with from their dietetics appointment (Appendix 5.8).

Control group

During the 12-week intervention period, participants in the control group continued with their usual follow up care. After their 12-week assessment the control group also received the discharge advice session lasting 30 to 60 minutes. This appointment discussed topics such as overcoming barriers, goal setting and physical activity maintenance. An optional example exercise programme and progression was offered (e.g. home based walking outside, gym or swimming). The standard diet information sheet was also provided. Figure 5.1 outlines when these sessions occurred.

5.2.5 Outcome measures

All measurements were taken at the pre-intervention assessment (baseline), post-intervention assessment (3-months) and at a three month follow-up assessment (6-months) to allow comparisons (Figure 5.1).

Physical function measurements

The primary measure of physical function was the ISWT. The ISWT reflects walking ability, an important measure of daily living in these patients. This involved patients walking consecutive 10-meter shuttles in time with an audible beep that became progressively faster, until they were no longer able to maintain that pace. The test has a total of 12 levels lasting one minute each (total distance 1020 metres). Patients performed a practice ISWT beforehand to minimise the influence of learning effects. Participants were asked to walk for as long as possible until reaching test termination criteria whilst the assessor recorded the total number of shuttles performed (Appendix 5.3)[189, 190]. The patient remained in the clinical area for at least 15 minutes following the test where measures of blood pressure, oxygen saturation, rating of perceived exertion (RPE Borg scale) and breathlessness (the modified Borg dyspnoea scale) were taken. Predicted peak VO_2 was calculated using the ISWT distance (ISWD) and body mass using the following equations: 3.1 + (0.038 x ISWD) = Peak VO_2 (mL/min/kg) and 257 + (0.038 x ISWD x body mass) = Peak VO_2 (mL/min)[191]. Although the ISWT is not validated in a bariatric surgery patient cohort, a systematic review has reported the ISWT as a valid and reliable test to assess maximal exercise capacity in clinical populations[192]. The ISWT has been validated against VO_2 max and VO_2 peak in clinical populations[192, 193]. A linear relationship is reported between functional capacity and the number of shuttles completed in a clinical population[193]. This test of physical function was selected as it reflects activities essential for daily living.

Left and right hand grip strength were measured using the Takei A5001 Analogue Hand Grip Dynamometer. Participants stood with their arms down by their sides with a slight bend at the elbow and were directed to squeeze the dynamometer with as much force as possible. A pause of 10-20 seconds occurred between repetitions; the protocol was repeated three times on both sides. The five

times STS test was used to measure functional lower limb muscle strength. Participants started seated with their arms folded across their chest, they were then instructed to stand up and sit down five times as quickly as they could upon the command of 'Go'. The testing chair remained at a consistent height throughout the intervention (47 cm).

Anthropometric measurements

Body composition outcomes (FM, FFM, body fat% and body mass) were measured using bioelectrical impedance (Tanita Scales BC-418-MA [Tanita Corporation, Japan]). A method which has been validated in obesity[194]. Although not as accurate as alternative methods such as dual-energy X-ray absorptiometry (DXA), bioelectrical impedance is shown to have high validity and reliability in normal to severe obesity[194]. Participants were instructed to stand bare footed on the metal foot plates whilst simultaneously holding onto the hand plates and remain still until the measurement was confirmed. Body mass and stretch stature were measured to calculate BMI. Other anthropometric measurements were obtained using the International Society for the Advancement of Kinanthropometry accredited methods ensuring consistency and were repeated for precision. Waist (approximately 1cm above the iliac crest) and hip (widest area around the gluteus maximus) circumferences were recorded and waist:hip ratio (WHR) was calculated. These measurements were included as an indicator of abdominal obesity[195].

Cardiovascular measurements

Cardiovascular measurements included blood pressure using the Omron M7 Digital Intellisense Upper Arm Cuff Blood Pressure Monitor (Omron Corporation, Kyoto, Japan). Patients were seated with their left arm supported whilst the measurement was taken. Blood pressure was taken three times; the first measurement was discarded and a mean of the following two measurements was reported[196].
Oxygen saturation and resting heart rate were measured using the Contec Full-Colour OLED USB Finger Pulse Oximeter & Heart Rate Monitor (CONTEC DTx Inc, Melbourne, FL, USA). The participant was instructed to sit down and when the participant was well rested the oxygen saturation and resting heart rate measurements were obtained.

Physical activity measurements

Objective physical activity was measured using the ActiGraph GT3X+ accelerometer (ActiGraph, Pensacola, FL, USA). The GT3X+ assessed accelerations in the vertical, anterio-posterior and medio-lateral axes. Participants wore the GT3X+ on an elastic waist belt and positioned it in line with the auxiliary line of the right iliac crest. Participants were instructed to wear the accelerometer for seven days from the moment they woke up until they went to bed at night, only removing it for water-based activities such as showering and swimming. This is a validated method of measuring physical activity

with high inter-instrument reliability (0.97 ICC; $p < 0.001$)[197, 198]. The Freedson adult 1998 cut points were used to determine physical activity intensity as they are currently the most widely used adult cut points [199]. The accelerometer measured stationary time which included standing and sitting (< 100 counts), light activity (100 to 1951), MVPA (>1951) and step count. Data were included if it showed four valid days; a valid day was wear time of 10 waking hours.

Self-reported physical activity was measured using the short form IPAQ (Appendix 5.4); a seven day recall measure to assess weekly physical activity and daily sitting time. To ascertain total weekly physical activity, the IPAQ questionnaire asks for the duration and intensity of different physical activities performed (vigorous, moderate and walking activities) and how many days per week such activity was executed. MET minutes per week were derived using the walking, moderate and vigorous MET values. The MET values of 3.3 (walking), 4.0 (moderate) and 8.0 (vigorous) METS were applied to each patient's reported durations. The IPAQ-short form is validated and has demonstrated fair to moderate associations with accelerometer measures[86, 200].

Biochemical measurements

Venous blood samples were obtained by a study nurse for cholesterol, HDL, LDL, triglycerides, cholesterol:HDL ratio and non-fasting HbA1c. The standard NHS protocol for taking venous bloods was followed. Samples were measured in the pathology laboratories of Leicester Hospitals NHS Trust, UK.

Psychological measurements

Psychological parameters measured included Self-Efficacy to Regulate Physical Activity (SERPA)[201] and the Hospital Anxiety and Depression Scale (HADS)[202, 203]. SERPA is an 18 item questionnaire which asks individuals to rate their degree of confidence to perform their exercise routine regularly on a scale from 0 to 100. The results are reported as an average out of 100 to reflect the individual's confidence (Appendix 5.5)[201]. HADS is a validated scale comprising of 14 statements of which seven relate to anxiety and seven relate to depression (Appendix 5.6)[204]. Each statement has an option of four responses scored from 0-3. Upon completion the scores selected are totalled and reported for anxiety and depression individually[204].

Dietary measurement

The 24 hour food recall was delivered via a structured interview; the investigator asked the participant to recall all foods and drinks they consumed the previous day whilst prompting for food quantities and portion sizes. All 24 hour food recalls were manually entered into and analysed using NetWisp Version 4.0 (Tinuviel Software, Warrington, UK) software to estimate total daily calorific intake on

kilocalories (Kcal) (Appendix 5.7). The 24 hour food recall is reported as a validated method of assessing calorie intake[205, 206].

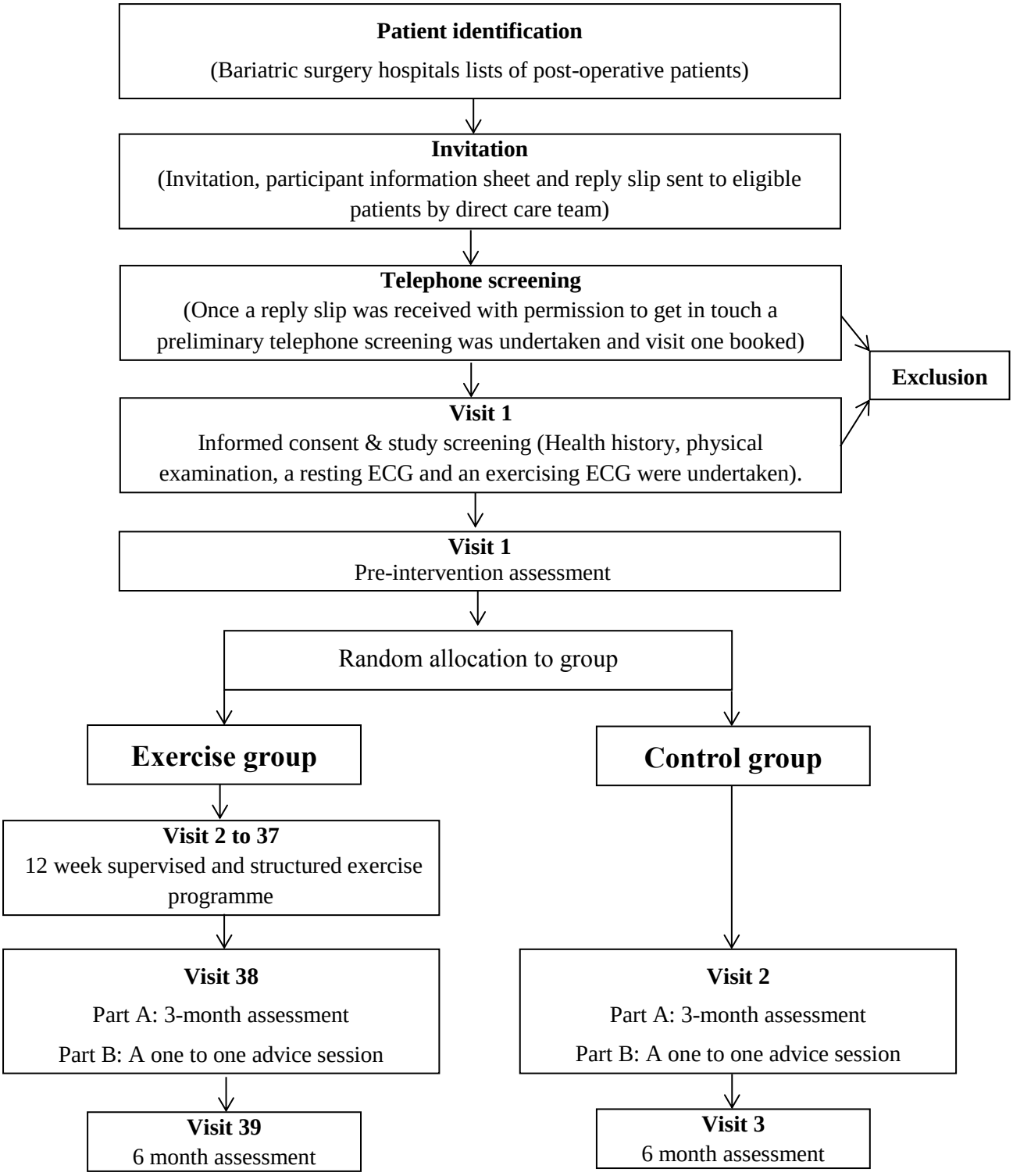


Figure 5.1: Study flow diagram.

5.2.6 Data analysis

Primary analysis used an intention to treat (ITT) protocol to include all participants who were randomised, using the last observation carried forward method for missing data[207]. For example, missing 3-month data was replaced with the value at baseline and missing 6-month data was replaced with the value at three months. This assumes that the people lost to follow up did not change their physical activity behaviour after they were lost; this is a reasonable assumption for the study population. If baseline data was missing, follow up data was not included in the analysis. Secondary analysis was as per protocol (APP); this analysis only analysed the outcome measurements available.

A descriptive exploratory analysis of all change data (baseline to 3-months and baseline to 6-months) was completed checking parametric assumptions using SPSS (IBM Corp, version 20, Armonk, NY, USA). The alpha level was set at $p \leq 0.05$ to indicate any significant differences between measures. Change differences between each arm were identified using an independent t-test. Change differences for objectively measured physical activity between each arm were determined using an ANCOVA controlling for accelerometer wear time respectively. The magnitude of an effect has been reported using the Cohen's d statistic. An effect size calculator (The Campbell Collaboration[208]) was used to compute means, SDs and sample size to determine the effect size. A small effect is classified as 0.2, a medium effect is 0.5 and a large effect is 0.8[209].

5.3 Results

5.3.1 Participant characteristics

Of 115 patients initially invited, 50% responded, 47 expressed interest and were screened for trial eligibility. Of the patients screened 49% were not eligible or changed their mind. When breaking down the rate of patients not eligible, 30% did not meet the study criteria for reasons such as a BMI of $<30 kg \cdot m^2$ (n=11), pregnant (n=1), <12 months post-bariatric surgery (n=1), or diagnosed and medically treated CVD (n=1). Exclusion on assessment accounted for 2% as a result of an abnormal exercising ECG. Two patients (4%) wanted to take part but had moved away from the area (too far to attend regularly). Finally 13% changed their mind after showing initial interest.

A total of 24 patients (21% of invited) met study criteria and consented to be randomised. Three discontinued before the end of the trial. (Figure 5.2). All 24 participants were included in the ITT analysis and APP sub analyses were based on the 21 completers (88% retention rate). The 24 randomised participants were aged 48.4 ± 8.9 years and had a mean pre-operative body mass of 136.3 ± 18.7 kg. Upon randomisation for The MOTION Study their mean body mass was 106.8 ± 16.7 kg; this is equivalent to a mean BMI of 39.0 ± 5.2 $kg \cdot m^2$. Of a possible 36 gym sessions, the exercise

group completers attended a mean of 34.2 ± 2.5 sessions; this accounted for 95% adherence. No adverse events or injuries were recorded throughout the exercise intervention.

Participants were randomly allocated to either the exercise group (males = 2; females = 10) or control group (males = 2; females = 10). Their mean post-operative status (the post-operative time point in months) in which they enrolled upon this study was 19.3 ± 5.4 months. Baseline data are presented as mean ± SD (Table 5.1).

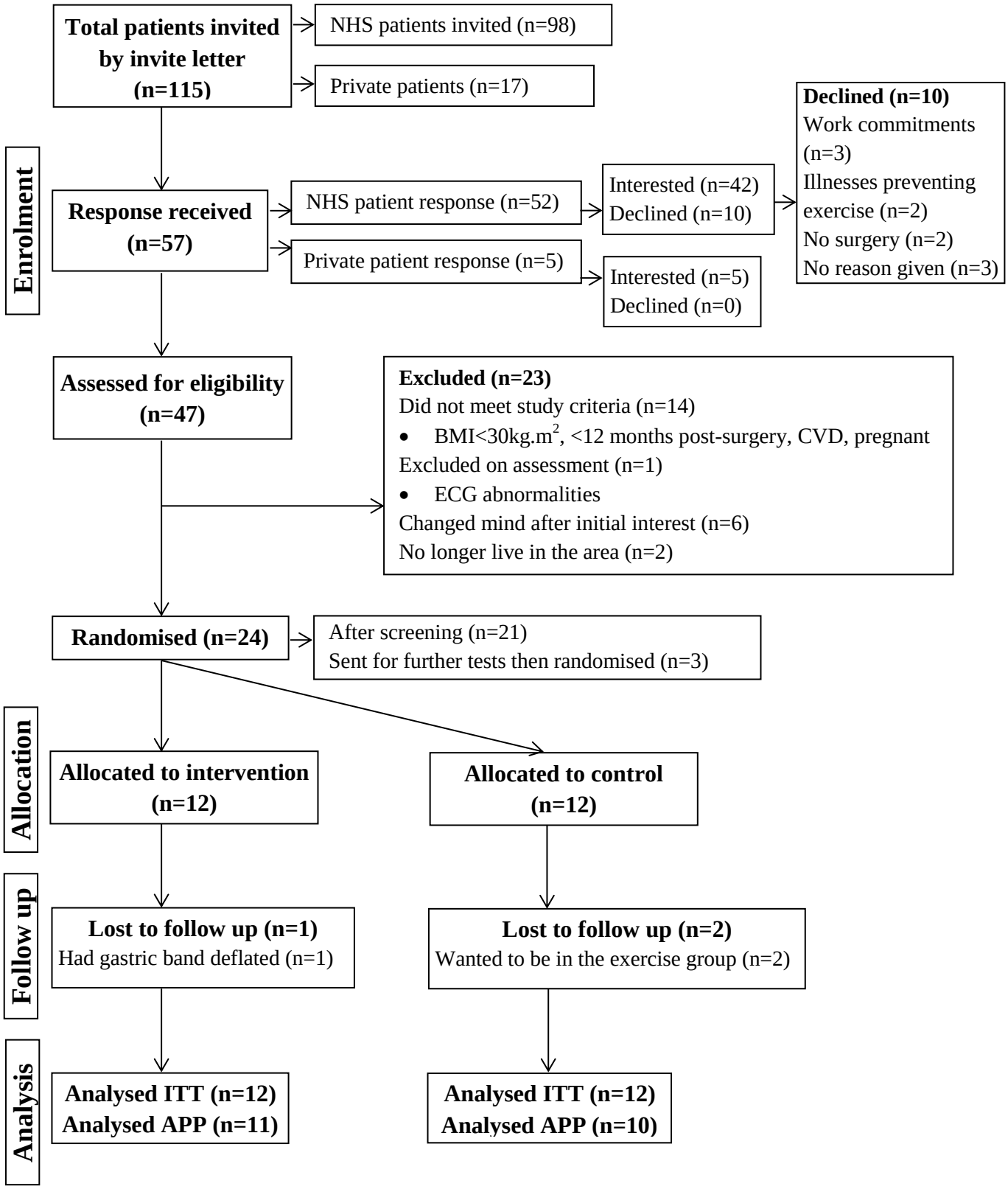


Figure 5.2: The CONSORT diagram showing the flow of participants through each stage of the randomised trial.

Table 5.1: Participants' baseline characteristics by arm.

Characteristic	Exercise Group	Control Group
Women	91.7 %	91.7 %
Men	8.3%	8.3%
Roux-en-Y gastric bypass	33%	33%
Sleeve gastrectomy	58%	67%
Gastric band	8%	N/A
Age (years)	44.3 ± 7.9	52.4 ± 8.1
Body Mass(kg)	106.5 ± 16.4	106.0 ± 17.5
Height (cm)	167.1 ± 7.1	163.8 ± 9.5
Body Mass Index (kg/m^2)	38.2 ± 6.1	39.4 ± 4.3
Body fat (%)	42.0 ± 7.3	45.2 ± 6.0
Fat Mass (kg)	45.2 ± 12.9	47.9 ± 10.0
Fat Free Mass (kg)	61.2 ± 9.3	58.1 ± 12.4
Systolic Blood Pressure (mmHg)	121.9 ± 16.4	120.4 ± 10.9
Diastolic Blood Pressure (mmHg)	80.8 ± 6.9	78.4 ± 7.7
Incremental Shuttle Walk Test (m)	325.0 ± 117.3	355.0 ± 80.6
Right Hand Grip Strength (kg)	27.5 ± 8.7	28.5 ± 9.6
Left Hand Grip Strength (kg)	27.6 ± 12.5	28.5 ± 9.6
Hip Circumference (cm)	131.0 ± 13.2	135.6 ± 11.5
Waist Circumference (cm)	118.2 ± 11.9	121.1 ± 12.3
Waist to Hip Ratio	0.9 ± 0.1	0.9 ± 0.1
Oxygen Saturation (%)	97.9 ± 0.8	97.3 ± 1.1
5 x Seat to Stand Test (sec)	13.7 ± 6.8	12.2 ± 2.9
Resting Heart Rate (beats per minute)	66.8 ± 9.2	76.0 ± 8.3
Total Cholesterol (mmol/L)	4.3 ± 0.8	4.5 ± 0.9
Triglycerides (mmol/L)	1.4 ± 0.4	1.6 ± 0.8

Table 5.1: Continued

Characteristic	Exercise Group	Control Group
Low Density Lipoproteins (mmol/L)	2.4 ± 0.7	2.3 ± 0.5
High Density Lipoproteins (mmol/L)	1.3 ± 0.2	1.5 ± 0.4
Cholesterol:HDL Ratio	3.5 ± 0.6	3.2 ± 0.8
HBA1c (%)	5.2 ± 0.2	5.6 ± 1.0
HBA1c (mmol/L)	33.2 ± 2.3	37.8 ± 10.5
Anxiety score	6.6 ± 4.6	5.5 ± 3.8
Depression score	2.4 ± 4.2	2.4 ± 3.3
SERPA score Average	50.4 ± 21.6	37.9 ± 23.5
IPAQ (MET-min/week)	3952.3 ± 4924.1	2059.6 ± 3070.2
Daily sitting time (min)	262.5 ± 134.8	310.0 ± 158.9
Calorific intake (kcal)	1713.6 ± 527.7	1559.8 ± 361.1
Stationary time (min/day)	559.6 ± 94.7	531.1 ± 131.4
Light activity (min/day)	304.5 ± 77.2	320.0 ± 91.2
MVPA (min/day)	28.3 ± 24.0	29.7 ±18.6
Step count (steps per day)	6379.4 ± 3316.0	5737.2 ± 1749.4

KEY: kg: kilograms; cm: centimetres; kg/m^2: kilograms per metre squared; mmHg: millimetres of mercury; mmol/L: millimole per litre; min: minutes; kcal: kilocalories; m: metres; N/A: not applicable

5.3.2 Physical function measurements

Table 5.2 displays the physical function change data between baseline and three and six months by intervention group. The functional measurements include the ISWT, grip strength, STS test and predicted peak VO_2.

Incremental shuttle walk test

The ITT analysis displayed a significant difference with a very large effect in the primary outcome (ISWT) between groups for baseline (exercise: 325.00 ± 117.28 m; control: 355.00 ± 80.62 m) to 3-month change ($t_{(22)}$= 5.820, p<0.001, d=2.38). The exercise training group showed a mean improvement of 112.50 ± 66.62 metres, and the control group had a mean reduction of -3.33 ± 17.75 metres.

A significant difference with a very large effect was also reported for between group change from baseline to six months ($t_{(22)}$= 5.289, p<0.001, d=2.16). The exercise group recorded an overall mean improvement of 143.33 ± 86.59 metres and the control group a reduction of -32.50 ± 75.93 metres. This resulted in a 6-month assessment ISWD of 468.3 ± 115.19 metres in the exercise group and 322.50 ± 102.26 among control participants (Figure 5.3 and Table 5.4).

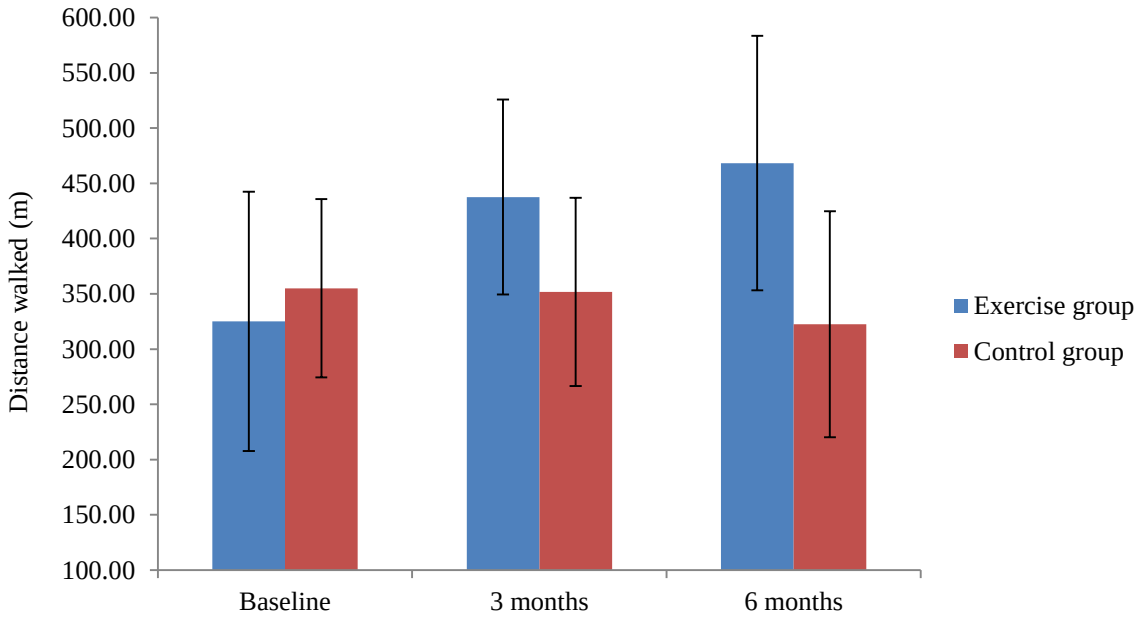


Figure 5.3: The ISWD in both the exercise training and control arms at baseline, three and six month assessments (ITT protocol).

Peak VO_2 calculated from body mass and the ISWD, improved progressively in the exercise group from baseline (1539.28 ± 440.49 mL/min) to six months (1822.22 ± 385.39 mL/min). The control

groups peak VO_2 decreased progressively, decreasing by 100.67 ± 318.61 mL/min at six months. Table 5.2 presents the change data and between group statistical analyses.

The APP data analysis indicated greater differences which favoured the intervention arm. APP results are presented in Appendix 5.9. A statistically significant difference in the ISWT between-group change from baseline (exercise 314.00 ± 117.00 m; control 350.00 ± 67.7 m) to three months (exercise 437.27 ± 92.53 m; control 346.00 ± 74.97 m) was reported ($t_{(19)}$= 6.447, p<0.001, d=2.82). The baseline to 6-month change data was also statistically greater in the exercise group ($t_{(18)}$= 5.411, p<0.001, d=2.43). The exercise group recorded a mean improvement of 156.4 ± 77.5 metres, leading to a 6-month assessment ISWD of 470.90 ± 120.5 metres. The control group reported a reduction of 39.0 ± 82.5 metres leading to a 6-month assessment ISWD of 297.8 ± 120.5 metres; Appendix 5.9 and Appendix 5.11.

Grip strength

Three month right hand grip strength change data was significantly higher in the exercise group than the control. A mean improvement of 2.45 ± 4.07kg compared to a mean reduction of 0.91 ± 3.25kg respectively ($t_{(22)}$=2.233, p=0.036, d=0.91) representing a large effect. The left hands 3-month mean grip strength improvement was slightly lower than the right (2.09 ± 4.98kg) in the exercise group, as was the reduction in the control group (0.58 ± 1.92kg) and there was no significant difference between groups.

At six months, no between group difference was identified for right hand grip strength as both groups showed a mean improvement (exercise 2.81 ± 3.72kg; control 0.82 ± 3.68). However, six month change showed a statistically significant difference in the left hands grip strength ($t_{(22)}$=2.755, p=0.012, d=1.13) representing a large effect. This was as a result of an improvement of 2.40 ± 3.01kg in the exercise group and reduction of 0.48 ± 2.00kg in the control group.

Sit to stand test

The STS duration, reported in Table 5.2, at three months improved in the exercise group by 3.81 ± 4.10 seconds and regressed in the control group by 0.21 ± 2.82 seconds. Therefore, exhibiting a statistically significant difference and large effect ($t_{(22)}$=-2.799, p=0.010, d=1.14) which further improved at six months. The exercise groups mean five times STS time at baseline was 13.69± 6.83 seconds, this improved by 4.22 ± 3.98 seconds at six months, whereas the control groups baseline STS time was 12.16 seconds this slowed by 0.23 ± 2.14 seconds ($t_{(22)}$=-3.411, p=0.003, d=1.39).

Table 5.2: Physical function changes between baseline and three and six months by intervention group.

Outcome Measures	Baseline		Baseline to 3-month change			Baseline to 6-month change		
	Exercise	Control	Exercise	Control	p-value	Exercise	Control	p-value
ISWT (m)	325.0 ± 117.3	355.0 ± 80.6	112.5 ± 66.6	-3.3 ± 17.8	<0.001	143.3 ± 86.6	-32.5 ± 75.9	<0.001
Right hand grip strength (kg)	27.6 ± 8.7	28.5 ± 9.6	2.5 ± 4.1	-0.9 ± 3.3	0.036	2.8 ± 3.7	0.8 ± 3.7	0.201
Left hand grip strength (kg)	27.6 ± 12.6	28.5 ± 9.6	2.1 ± 5.0	-0.6 ± 1.9	0.097	2.4 ± 3.0	-0.5 ± 2.0	0.012
5 x sit to stand test (sec)	13.7 ± 6.8	12.2 ± 2.9	-3.8 ± 4.1	0.2 ± 2.8	0.010	-4.2 ± 4.0	0.2 ± 2.1	0.003
Peak VO_2 (mL/min/kg)	15.5 ± 4.5	16.6 ± 3.1	4.3 ± 2.5	-0.1 ± 0.7	<0.001	5.5 ± 3.3	-1.2 ± 3.0	<0.001
Peak VO_2 (mL/min)	1539.3 ± 440.5	1669.6 ± 330.8	431.1 ± 308.5	4.4 ± 86.3	<0.001	546.3 ± 345.7	-100.7 ± 318.6	<0.001

ITT data are presented as mean ± SD.

KEY: ISWT: Incremental shuttle walk test; kg: kilograms; mL/min/kg: millilitres of oxygen per minute per kilogram of body weight; mL/min: millilitres of oxygen per minute; VO_2: volume of oxygen; m: metres; sec: seconds

5.3.3 Anthropometric measurements

Table 5.3 presents the anthropometric outcomes change data between baseline and three and six months by intervention group. Anthropometric measurements include body mass, BMI, FM, FFM, waist circumference, hip circumference and waist to hip ratio.

Body mass and BMI

Body mass decreased by a mean of 2.43 ± 3.35kg in the exercise training group from baseline to 3-months with a larger decrease of 2.70 ± 5.43kg by six months. Whereas the control group displayed an increase in body mass of 1.00 ± 1.40kg at three months and a larger increase of 2.93 ± 2.85kg at six months. Therefore, the exercise group change data was significantly different to the control group at both three months ($t_{(22)}$=-3.278, p=0.003, d=1.34) and six months ($t_{(22)}$=-3.179, p=0.004, d=1.30) exhibiting a large effect. As reflected by body mass, BMI also had significant between group improvements and a very large effect (Table 5.3).

Fat mass and fat free mass

Fat mass change also remained significantly different between groups with a large effect at both three months ($t_{(22)}$=-3.573, p=0.002, d=1.46) and six months ($t_{(22)}$=-2.843, p=0.009, d=1.16). The exercise group decreased (2.10 ± 2.58kg) and the control group increased (0.87 ± 1.27kg) in the first three months. By six months the control groups mean change increased further (2.12 ± 2.76kg) whereas the exercise groups mean change (1.93 ± 4.09kg) was maintained. No statistically signficant difference between groups was shown for FFM at three months, although FFM did reduce in the exercise group. At six months, FFM reduced further in the exercise training group (0.77 ± 1.67kg), although minimally, and increased in the control group (0.84 ± 1.81kg) showing a 1.61kg difference in FFM change from baseline to six months.

Waist and hip circumference

At three months the control groups mean waist circumference remained similar to baseline, whereas the exercise training groups 3-month waist circumference decreased by 7.53 ± 4.64cm, significantly smaller than the control group displaying a large effect ($t_{(22)}$=-1.605, p=0.123, d=1.80). The exercise groups mean waist circumference remained smaller than the control group at six months, although the mean reduction at six months (3.94 ± 9.14kg) was less than the change at three months.

Hip circumference again remained similar to baseline in the control group at three and six months. The exercise group showed a mean decrease of 6.30 ± 8.55kg from baseline to three months and 7.68 ± 12.50 cm at six months. This improvement meant there was a statistically significant difference of

large effect between the groups at three months ($t_{(22)}$=-2.396, p=0.026, d=0.98), but not at six months (Table 5.3).

Table 5.3: Anthropometric measurement changes between baseline and three and six months by intervention group.

Outcome Measures	Baseline		Baseline to 3-month change			Baseline to 6-month change		
	Exercise	Control	Exercise	Control	P-value	Exercise	Control	P-value
Body Mass (kg)	106.5 ± 16.4	106.0 ± 17.6	-2.4 ± 3.4	1.0 ± 1.4	0.003	-2.7 ± 5.4	2.9 ± 2.9	0.004
BMI (kg/m^2)	38.2 ± 6.1	39.4 ± 4.3	-0.9 ± 1.2	0.4 ± 0.5	0.003	-1.0 ± 2.0	1.0 ± 1.0	0.004
Body fat (%)	42.0 ± 7.3	45.2 ± 6.0	-1.0 ± 1.1	0.3 ± 0.9	0.004	-0.7 ± 1.5	0.6 ± 1.7	0.061
FM (kg)	45.2 ± 12.9	47.9 ± 10.0	-2.1 ± 2.6	0.9 ± 1.3	0.002	-1.9 ± 4.1	2.1 ± 2.8	0.009
FFM (kg)	61.2 ± 9.3	58.1 ± 12.4	-0.3 ± 1.4	0.2 ± 1.3	0.391	-0.8 ± 1.7	0.8 ± 1.8	0.034
Hip Circumference (cm)	131.0 ± 13.2	135.6 ± 11.5	-6.3 ± 8.6	-0.1 ± 2.5	0.026	-7.7 ± 12.5	-0.6 ± 2.1	0.067
Waist Circumference (cm)	118.2 ± 11.9	121.1 ± 12.3	-7.53 ± 4.6	-0.58 ± 2.9	<0.001	-3.9 ± 9.1	0.5 ± 3.0	0.123
Waist to Hip Ratio	0.9 ± 0.1	0.9 ± 0.1	-0.0 ± 0.1	0.0 ± 0.0	0.518	0.0 ± 0.2	0.0 ± 0.0	0.648

ITT data are presented as mean ± SD.

KEY: kg: kilograms; BMI: body mass index; %: percentage; FM: fat mass; FFM: fat free mass; cm: centimetres; kg/m^2: kilograms per metre squared.

5.3.4 Physical activity measurements

Table 5.4 displays the physical activity change data between baseline and three and six months by intervention group. The physical activity outcomes include stationary time, MVPA, light activity, step count, IPAQ daily sitting time and IPAQ total activity.

Objective physical activity

The exercise group's accelerometer data indicated an improvement in physical activity between baseline and three months in stationary time, light activity and MVPA. The control group's accelerometer data showed an improvement in stationary time, however time spent in light activity and MVPA reduced. The three month mean MVPA change in both groups was statistically significant and showed a large effect ($f_{(2,19)}$=4.788, p=0.043, d=0.98); no other between group significant differences occurred. From three to six months all objective parameters in both the exercise and control groups decreased. The six month changes in the exercise group's stationary time and MVPA showed improvements compared to baseline values. The control's baseline to 6-month change indicated that both light activity and MVPA levels were lower at six months than at baseline; no significant differences occurred between groups. Mean step count increased in the exercise group from baseline (6379 ± 3316 steps) to six months (by 243 ± 2358 steps). This was however 381 steps less than the mean improvement reported from baseline to three months. The control group improved throughout the six months, however no significant differences occurred between groups (Table 5.4).

Self-reported physical activity

Self-reported weekly activity was higher in the exercise group compared with the control group at all assessments. The exercise group's three month change for self-reported total weekly activity showed the greatest increase of 5429.42 ± 5882.49 MET-min/week, directly after finishing the exercise programme. At six months this dropped to an increase of 2743.75 ± 6991.51 MET-min/week showing a mean total of 6696.04 MET-min/week at six months. The control group's self-reported activity also increased from baseline to three months (by 3479.29 ± 7828.90 MET-min/week) and subsequently this also dropped to an increase of 941.42 ± 2994.92 MET-min/week showing a mean total of 3001.05 MET-min/week at six months. No significant differences existed between groups and no statistical differences were shown for self-reported sitting time (Table 5.4).

Table 5.4: Physical activity changes between baseline and three and six months by intervention group.

Outcome Measures	Baseline		Baseline to 3-month change			Baseline to 6-month change		
	Exercise	Control	Exercise	Control	p-value	Exercise	Control	p-value
Objective measure								
Stationary time (min/day)	559.6 ± 94.7	531.1 ± 131.4	-38.3 ± 100.0	-13.0 ± 69.2	0.562	-15.5 ± 89.4	-5.6 ± 79.5	0.905
Light activity (min/day)	304.5 ± 77.3	320.1 ± 91.2	0.6 ± 64.0	-4.0 ± 105.3	0.798	-25.6 ± 46.4	-14.8 ± 87.7	0.795
MVPA (min/day)	28.3 ± 24.0	29.7 ± 18.7	10.5 ± 9.2	-1.5 ± 14.5	0.043	7.5 ± 19.8	-3.4 ± 16.2	0.161
Step count (steps per day)	6379.4 ± 3316.0	5737.2 ± 1749.4	624.2 ± 1349.6	489.6 ± 1884.6	0.854	242.7 ± 2358.1	530.4 ± 2300.2	0.787
Self-reported measure								
IPAQ daily sitting time (min)	262.5 ± 134.9	310.0 ± 158.9	-10.0 ± 125.6	17.5 ± 169.0	0.655	67.5 ± 153.0	52.5 ± 156.7	0.815
IPAQ total activity (MET-min/week)	3952.3 ± 4924.1	2059.6 ± 3070.2	5429.4 ± 5882.5	3479.3 ± 7828.9	0.498	2743.8 ± 6991.5	941.4 ± 2994.9	0.421

ITT data are presented as mean ± SD.

KEY: MVPA: moderate to vigorous physical activity; min/day: minutes per day; IPAQ: international physical activity questionnaire; min: minutes; min/week: minutes per week; MET; metabolic equivalents.

5.3.5 Cardiovascular measurements

Table 5.5 presents the cardiovascular and biochemical measurement change data between baseline and three and six months by intervention group. Cardiovascular measurements include blood pressure, oxygen saturation and resting heart rate. Biochemical measurements include HbA1c, cholesterol, LDL, HDL, Cholesterol:HDL Ratio and Triglycerides.

Blood pressure

Systolic blood pressure was similar in both groups at baseline and showed a significant difference between groups at three ($t_{(22)}$=-2.738, p=0.012, d=1.12) and six months($t_{(22)}$=-2.738, p=0.012, d=1.12), both showing a large effect. Change in diastolic blood pressure also favoured the exercise group after three ($t_{(22)}$=-3.523, p=0.002, d=1.44) and six months ($t_{(22)}$=-3.836, p=0.001, d=1.57) again showing a large effect (Table 5.5).

Resting heart rate

Resting heart rate decreased from baseline to three months in the exercise (11.25 ± 9.04 bpm) and the control (2.83 ± 7.52bpm) groups. The mean change significantly differed between groups by 8.42 bpm with a large effect ($t_{(22)}$=-2.480, p=0.021, d=1.01). The mean change from baseline to six months was lower in the exercise group (5.00 ± 8.79bpm) and greater in the control group (3.42 ± 9.29bpm) which reduced the mean change to 1.58 bpm, and no statistical significance occurred (Table 5.5).

Biochemical results

Mean non-fasting HbA1c results increased in both groups at three and six months (Table 5.5). Analysis of the full lipid profile components exhibited no statistically significant differences between the control and exercise groups. The exercise training group exhibited an improvement in all parameters at three months. The control group's total cholesterol, LDL, triglycerides and cholesterol:HDL ratio all declined. By six months, values in the control group had declined further for total cholesterol, LDL, triglycerides and cholesterol:HDL ratio, yet HDL remained similar throughout. At six months the exercise group's lipid profile remained improved from baseline in all but total cholesterol. The mean improvements at six months were less than the change exhibited from baseline to three months (Table 5.5).

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Table 5.5: Changes in cardiovascular measurements and biochemical result between baseline and three and six months by intervention group.

Outcome Measures	Baseline		Baseline to 3-month change			Baseline to 6-month change		
	Exercise	Control	Exercise	Control	p-value	Exercise	Control	P-value
Cardiovascular measures								
Systolic Blood Pressure (mmHg)	121.9 ± 16.4	120.4 ± 10.9	-7.4 ± 11.2	3.7 ± 8.4	0.012	-6.9 ± 9.2	0.4 ± 6.7	0.036
Diastolic Blood Pressure (mmHg)	80.8 ± 6.9	78.4 ± 7.7	-5.3 ± 5.6	3.3 ± 6.2	0.002	-5.2 ± 5.6	2.7 ± 4.3	0.001
Oxygen Saturation (%)	97.9 ± 0.8	97.3 ± 1.1	0.6 ± 0.8	0.0 ± 1.0	0.138	0.4 ± 0.8	-0.2 ± 1.1	0.154
Resting Heart Rate (bpm)	66.8 ± 9.2	76.0 ± 8.3	-11.3 ± 9.0	-2.8 ± 7.5	0.021	-5.0 ± 8.8	-3.4 ± 9.3	0.672
Biochemical results								
Total Cholesterol (mmol/L)	4.3 ± 0.8	4.5 ± 0.9	-0.1 ± 0.6	0.1 ± 0.5	0.372	0.0 ± 0.5	0.1 ± 0.4	0.719
Triglycerides (mmol/L)	1.4 ± 0.4	1.6 ± 0.8	-0.2 ± 0.3	0.0 ± 0.8	0.388	-0.1 ± 0.4	0.1 ± 0.7	0.433
LDL (mmol/L)	2.4 ± 0.8	2.3 ± 0.5	-0.1 ± 0.6	0.1 ± 0.4	0.284	-0.0 ± 0.5	0.2 ± 0.5	0.245
HDL (mmol/L)	1.3 ± 0.2	1.5 ± 0.5	0.1 ± 0.2	0.0 ± 0.2	0.258	0.1 ± 0.3	0.0 ± 0.2	0.381
Cholesterol:HDL Ratio	3.5 ± 0.6	3.2 ± 0.8	-0.3 ± 0.5	0.1 ± 0.4	0.034	-0.1 ± 0.6	0.1 ± 0.4	0.243
HBA1c (%)	5.2 ± 0.2	5.6 ± 1.0	0.0 ± 0.1	0.1 ± 0.2	0.133	0.1 ± 0.2	0.2 ± 0.2	0.307
HBA1c (mmol/L)	33.2 ± 2.3	37.8 ± 10.5	0.1 ± 1.4	0.9 ± 1.6	0.189	1.6 ± 2.7	2.2 ± 2.0	0.551

ITT data are presented as mean ± SD.

KEY: mmHg: millimetres of mercury; %: percentage; bpm: beats per minute; mmol/L: millimoles per litre; HDL: high density lipoproteins; LDL: low density lipoproteins; HBA1c: glycated haemoglobin.

5.3.6 Psychological measurements

Table 5.6 displays the psychological measurement change data between baseline and three and six months by intervention group. Psychological measurements include SERPA and HADS.

The exercise group's self-efficacy was highest at three months showing a mean increase of 20.44 ± 18.90 points whereas the control group remained the same -0.42 ± 7.91 points, showing a statistically significant difference with a large effect between groups ($t_{(22)}$=3.527, p=0.002, d=1.44). When focusing on baseline to six month mean change, the exercise group sustained an increase from baseline, however this was lower than the 3-month change (6.05 ± 23.32 points). The control group also displayed a mean improvement of 9.04 ± 17.06 points at six months. There was no significant difference between the groups in the self-efficacy change at six months.

Anxiety and depression reduced in the exercise group at three months, yet both increased from three to six months. The mean anxiety score at six months does, however, remain -0.75 ± 3.33 lower than baseline, whereas the mean depression score at six months was 0.33 ± 3.60 higher than baseline. Anxiety also decreases at three months in the control group, however, baseline to six month change shows an increase 0.75 ± 4.39. Depression increases at both assessments in the control group, increasing from 2.42 ± 4.19 to 4.33 ± 5.12.

5.3.7 Dietary measurement

Table 5.6 displays the dietary measurement change data between baseline and three and six months by intervention group. The dietary measurement included is the 24 hour food recall.

Diet was assessed through the 24-hour food recall to check whether calorific intake differed between groups. Analysis confirmed no significant change differences occurred between groups at three or six months, (Table 5.6). The exercise group's baseline mean daily calorific intake was 1713.58 ± 527.70 kcal and the control groups was 1559.83 ± 361.08 kcal. At three months the exercise groups mean daily calorific intake was 1809.75 ± 620.93kcal and the controls was 1297.33 ± 325.77 kcal changing to 1504.42 ± 475.08kcal and 1712.25 ± 427.26 kcal at six months respectively.

Table 5.6: Dietary and psychological measurement changes between baseline and three and six months by intervention group.

Outcome Measures	Baseline		Baseline to 3-month change			Baseline to 6-month change		
	Exercise	Control	Exercise	Control	p-value	Exercise	Control	p-value
Psychological measurements								
Anxiety score	6.6 ± 4.6	5.5 ± 3.8	-1.3 ± 2.9	-0.7 ± 2.9	0.629	-0.8 ± 3.3	0.8 ± 4.4	0.356
Depression score	2.4 ± 4.2	2.4 ± 3.3	-0.6 ± 3.0	1.0 ± 3.3	0.228	0.3 ± 3.6	1.9 ± 5.9	0.433
SERPA score average	50.4 ± 21.7	37.9 ± 23.5	20.4 ± 18.9	-0.4 ± 7.9	0.002	6.1 ± 23.3	9.0 ± 17.1	0.724
Dietary measurement								
Calorific intake (kcal)	1713.6 ± 527.7	1559.8 ± 361.1	96.2 ± 889.9	-262.5 ± 376.1	0.212	-209.2 ± 478.5	152.4 ± 560.7	0.103

ITT data are presented as mean ± SD.

KEY: SERPA: self-efficacy to regulate physical activity; kcal: kilocalories

5.4 Discussion

The implementation of exercise after bariatric surgery is suggested to help maintain and optimise post-operative outcomes. Previous research in this population has reported that increasing physical activity in bariatric surgery patients improves physical function and weight loss maintenance[69]. This is the first RCT to initiate supervised and structured exercise initiated at a later post-operative time-frame when weight regain is more likely. The main findings were significant improvements in physical function, anthropometric, cardiovascular, psychological, and physical activity outcomes in patients directly after 12 weeks of exercise training compared with the control arm. After a further 3-month follow up period, the intervention group had maintained an advantage over the control participants in physical function, anthropometric, and cardiovascular outcomes.

5.4.1 Physical function

Physical functioning relates to the ability to perform basic activities of daily living such as walking, stair climbing, and transitioning from sitting to standing. These functional abilities are often limited in obese individuals, leading to reductions in HRQoL[94, 154, 210]. Hence exercise training that improves physical function is important.

The increase in the mean ISWD for the exercise group after six months was 143 metres. Minimal clinically important improvements for the ISWT in bariatric surgery patients have not been established. However, for patients with chronic obstructive pulmonary disease, two levels of improvement have been recognised; in terms of perceived exercise tolerance, a minimal clinically important improvement of 47.5 metres is reported, and additional benefits are reported at improvements of 78.7 metres[184]. The exercise group's improved distance of 143 metres is more than three times the minimally clinical value and nearly double the ISWD reported for additional benefits. Hence, notwithstanding the different clinical population being studied, the improvements resulting from the intervention can reasonably be regarded as clinically meaningful. Multiple factors could have contributed to this increased walking capability. Not only does the nature of the ISWT make it difficult to distinguish specific factors, the population being tested and the design of the exercise intervention undertaken also contribute. Factors might include a combination of improvements in mobility, aerobic fitness, weight loss, physical activity, self-efficacy/motivation, muscle strength and endurance.

This increased walking distance and speed in the exercise group indicate improvements in aerobic fitness[72, 88, 89]. The ISWT is a valid field based test of functional capacity as it strongly relates to VO_2 max and the ISWD reportedly correlates with peak VO_2[191, 211, 212]. Braun[213] states cardiovascular fitness is developed and maintained when performing exercise 60 to 90% of maximum heart rate, a

minimum of three times per week, between 20 and 60 minutes in duration. It is therefore likely that participants undertaking three 60-minute moderate intensity gym sessions weekly would show fitness improvements. In the current RCT, blood pressure and resting heart rate improvements favouring the exercise group could also indicate enhanced fitness[213]. The exercise training groups mean reduction in body mass will have likely positively affected the ISWT. A continual improvement in body mass was identified from baseline to six months, whilst the control group's increased body mass would have likely contributed to their reduced walking ability. The control group's body mass increased at every assessment from baseline. The mean 5.6kg difference between groups at six months was statistically significant and combined with improved fitness and mobility is likely to have contributed to the 179 metre ISWD difference between groups[102]. Although walking improves as a result of undertaking supervised aerobic exercise of three sessions per week for 12 weeks in the early stages post surgery, no significant differences were identified between the intervention and control groups[89, 91, 92]. These findings suggest that an exercise intervention initiated after peak weight loss is more beneficial for improving functional walking ability than an early post-operative intervention.

Increased self-efficacy may have contributed to both groups walking performance. A meta-analysis by Moritz *et al*[214] reviewed 45 studies and concluded that a significant relationship exists between self-efficacy and sports performance. In the current RCT, the mean baseline self-efficacy score was 12.5 points higher in the exercise group. This between group difference increased significantly favouring the exercise group at three months after gym training (33.4 points greater), reflecting the three month ISWT performance. The self-efficacy difference between groups reduced markedly at six months to 9.5 points. At six months the control group's self-efficacy improved which may be attributed to the advice session, whereas the training group's self-efficacy decreased possibly due to the loss of one-to-one support from the exercise instructor at the completion of the supervised gym sessions. Nonetheless, self-efficacy remained higher than baseline levels. Literature suggests that individuals who perceive they are making progress are more likely to want to improve and are motivated to do so than those lacking perceived progress[215]. Consequently, improved ISWD could be partly attributed to higher self-efficacy, and reduction in ISWD could be attributed to lower self–efficacy and motivation. This could be reflected in the current study, specifically the reduced ISWD seen in the control group, as most participants did verbally express disappointment when not randomly allocated to the exercise group. If self-efficacy in the exercise group had also remained significantly higher than the control group at six months, one could confidently suggest self-efficacy and motivation contributed to an improved ISWD in this cohort. However, self-efficacy reduced from three to six months in the exercise group whilst ISWD improved. Although self-efficacy and motivation could be contributing factors, improvement in physical function parameters is likely the biggest contributor.

Leg muscle strength has been shown to be associated with walking[216]. An objective measurement indicative of functional lower limb muscle strength and mobility is the five times STS test[217]. In this study, the STS test duration increased slightly from baseline to six months in the control group (baseline 12.2 to 12.4 seconds) and reduced throughout assessments from 13.7 to 9.5 seconds in the exercise group. The STS test was therefore performed 4.2 seconds faster at six[218] months than at baseline in the exercise group and when comparing that to a MICD of 1.7 seconds the degree of progress is apparent. Huck *et al*[88] reported a 44% improvement in the STS from baseline to directly after 12 weeks of resistance training. The current cohort displayed a 28% improvement directly after 12 weeks of combined aerobic and resistance training, which when followed up three months later had improved to 31%. This suggests that resistance training may be superior for increasing lower limb strength than a combined training programme.

Grip strength, another indicator of muscle strength and function focusing on the upper body, reported a continual right and left hand grip strength increase from baseline to six month assessments in the exercise group[219]. Grip strength has been shown to improve as a result of exercise training (combined aerobic and resistance training[89] or resistance training[88] only) in exercise interventions initiated in the first four months after bariatric surgery. However, no statistically significant changes are reported between exercise training and control groups[88, 89]. As well as grip strength, Stegen *et al*[89] reported that likewise the STS and 6MWT did not significantly differ between groups after undergoing combined aerobic and resistance training initiated in the first four months post-surgery. This might suggest that an exercise intervention initiated 12 to 24 months after surgery may be more beneficial than in the early post-operative phase.

It is clear that multiple factors contribute to physical function parameters (ISWT, STS test and grip strength). These functional outcome measures exhibit similar progression patterns in the exercise group. The largest mean improvements in the exercise group occur from baseline to three months and slower improvements are demonstrated from three to six months. This is supported by previous research which reports that the ISWD is strongly correlated with the STS test and grip strength, both indicators of muscle strength[220, 221]. It is therefore likely that improvements in muscle strength will have contributed to the improved ISWD. The ITT analysis is more conservative than the APP analysis which indicates greater improvements (Appendix 5.9). The results of The MOTION Study therefore suggests that significant improvements in functional capacity and absolute upper and lower body muscle strength occur when undertaking supervised and structured exercise. It must be noted that incremental improvements are observed through the three assessments; this shows progressions continued after the supervised gym phase was completed. Due to the known relationship between obesity and reduced physical function, a change in weight loss could have augmented these positive

outcomes and is likely to be accountable in combination with reduced self-efficacy for the reduced ISWD in the control group.

5.4.2 Body composition

The patients that enrolled in this RCT were a mean of 19.3 months post-bariatric surgery; they were therefore within the 12 to 24 months where weight regain most commonly occurs[23]. Most of the participants self-reported that they were either weight stable or gaining body mass upon commencing the trial. Despite physical activity being an important method for optimising surgical outcomes, it can sometimes lead to a compensatory response of increased calorific intake[222, 223]. The American Society for Metabolic and Bariatric Surgery (ASMBS) has reported that exercise changes body composition, increasing FFM which can result in slower body mass loss. They also report the frequency and intensity of exercise may affect metabolic rate resulting in weight loss plateaus[223]. As a result of this, and of previous exercise intervention research, post-surgery[72, 88, 89, 91, 92], body mass loss was not expected in this trial; the intervention aimed to facilitate the prevention of weight regain.

Body mass in the exercise group decreased progressively at every assessment. Conversely to this, the control group's body mass increased leading to a statistically significant 6-month mean body mass change of 5.4kg between groups from baseline. A 10-month running intervention initiated at a similar post-operative time point (1-3 years after bariatric surgery) also showed a significant difference in body mass after surgery in the intervention group compared with controls. This 10-month running intervention by Marchesi *et al*[90] reported a mean loss of 2.2kg·m^2 in the intervention participants (n=7), while, a mean reduction of 0.92kg·m^2 (2.43kg) was observed in the current exercise group directly after 12 weeks of moderate intensity gym based training. By considering the nature of the running intervention, overall improvements and between group-differences were more likely in that study. Firstly, they expected participants to perform 30 minutes of continuous running after the three months introductory phase; there was no randomisation so participants chose to take part in either the running or control group. It is notable that running is a higher impact exercise and participants were excluded if they were over 50 years or had a BMI of more than 35kg·m^2. This could inform the design of future studies initiated 12 months after bariatric surgery.

In obese populations, it has been reported that undertaking supervised exercise elicits greater FM reductions than non-supervised exercise[224]. In the current intervention FM was significantly different between groups after 12 weeks exercise training and after maintenance. The exercise group's FM decreased as a result of the intervention and remained similar at six months; the control group's FM increased at every assessment, leading to a mean difference of 4.1kg between groups. Post-operative exercise intervention literature suggests that FM does not differ significantly between arms when exercise is initiated in the early post-operative stages[72, 84, 87-89, 91, 92]. Marchesi *et al's*[90] running

intervention introduced at one year post-surgery, led to a 2.2kg reduction in FM after 10 months, although this was not significantly different to the control arm. Notably, a similar FM reduction of 2.1kg was observed in the MOTION Study despite the shorter duration (12 weeks) and lower intensity (moderate) of the intervention, while the control group had a slight increase in FM.

Conversely to FM, FFM decreased in the intervention arm and increased in the control group; this is not surprising because of the body mass gained in the control group. Typically, when patients undergo bariatric surgery, rapid weight loss occurs losing both FM and FFM which negatively impacts basal metabolic rate[105, 122]. FFM loss typically accounts for between 33% and 50% of total body mass loss [105,145]. Exercise interventions implemented during the period of rapid weight loss initiated by bariatric surgery have not found any significant differences in FFM between exercise training and usual care through the addition of exercise. Some interventions have attributed this to the type of exercise undertaken (aerobic)[91]. However, similar interventions initiated at an early post-operative time point which looked at resistance training alone[88] and combined aerobic and resistance training[89] have reported no significant differences in FFM between groups. Loss of FFM in The MOTION Study at the end of the 12 week exercise intervention amounted to 13% (0.32kg) of the total body mass reduction. This is lower than observed in the trials initiated earlier (23-39%)[88, 89, 91]. The MOTION Study did find an improvement in strength in the exercise group regardless of the small FFM reduction. Furthermore, despite body mass and FFM reducing further at the 6-month assessment in the current RCT (FFM equating to 28% (0.77kg) of the reduction in body mass), grip strength and the STS test continued to improve. This suggests that other factors may be affecting strength. Reductions in FFM with strength increases has previously been attributed to neurological factors such as enhanced firing frequency and spinal reflexes which occur during the early stages of a training programme[89]. The continued body mass loss after completing the 12 weeks of exercise could be attributed to a reduction in calorific intake of approximately 300kcal, as shown from the 24 hour food recall from three to six months in the exercise group. Overall body mass loss was predominantly FM loss and the small reductions in FFM did not affect the continual improvements in functional outcomes.

Improvements in abdominal fat are reported as a result of exercise-induced weight loss in obese individuals[225]. The significantly lower waist circumference in the exercise group compared with the control group could indicate a significantly lower amount of abdominal fat directly after supervised aerobic and resistance training (8.1cm between group difference). Waist circumference remained lower than baseline at 6-months however the difference between groups reduced to a mean of 4.45cm. Hip circumference change from baseline was significantly different between groups at three and six months. There are difficulties associated with obtaining waist circumference in this population. Due to abdominal aprons and excess skin it is difficult to find the iliac crest and the lower border of the costal

margin[226]. Therefore, to ensure this waist and hip circumferences accuracy the measurement was repeated two or three times. A reduction in abdominal fat is a fair assumption based on previous combined aerobic and resistance training programmes for obesity reportedly decreasing abdominal and visceral fat[227].

None of the previous interventions that have been implemented within the first four months of surgery (during the period of rapid body mass loss) have identified any body composition differences between their intervention and control groups[72, 84, 88, 89, 91, 228, 229]. Only the running intervention by Marchesi *et al*[90], which was initiated one year after surgery (the point of body mass peaks/ regains), displayed between group differences in body composition. The MOTION Study therefore confirms body composition changes are more effective when initiating an exercise intervention at 12 months post-surgery. To check that the significant differences between the two groups in the current RCT were not influenced by calorific intake, a 24 hour food recall was undertaken at every assessment. No statistically significant differences were identified between groups, therefore suggesting that the improvements seen in the exercise group are a result of the intervention undertaken. It can therefore be confidently concluded that this is the first exercise intervention and RCT initiated 12 to 24 months after bariatric surgery which as a result shows significant between group differences in body mass in combination with other outcomes.

5.4.3 Physical activity

Increased physical activity in bariatric surgery patients leads to improved physical fitness and superior weight loss maintenance[69]. This is the first exercise intervention in bariatric surgery patients to objectively measure physical activity. The exercise group recorded positive changes from baseline to six months in stationary time, MVPA and step count. This equated to 108.4 minutes less stationary time weekly, 52.4 minutes more MVPA weekly and 242.7 more steps per day; no change was shown for light activity. Physical activity in the control group reduced to six months, stationary time decreased at three months and remained less than baseline levels and step count improved progressively from baseline to six months.

In the exercise group directly after completion of the gym training, improvements were recorded in all activity parameters including self-reported activity and sitting time. Shah *et al's*[84] participants at the end of their 12 week exercise intervention also self-reported a mean increase in moderate intensity physical activity but not in light activity. Moderate intensity physical activity is important because activity guidelines are based on moderate intensity (≥150 minutes weekly[82]) and moderate intensity exercise is currently recommended for exercise interventions in obese populations for retention and motivation purposes[230]. King *et al*[77] reported objectively measured MVPA on 473 participants before, one, two and three years after bariatric surgery. MVPA increased as a result of surgery yet remained

more than 35 minutes a week below the recommended levels for the general adult population. The MOTION Study participants had relatively high levels at baseline (198 min/week) but still improved as a result of the exercise training. The greatest improvements were seen in the exercise group at three months; from three to six months all objective and self-reported parameters reduced and only light activity was lower than baseline levels. After completion of the supervised element, physical activity maintenance may have been difficult; this is potentially why all activity parameters in the exercise group reduced from three to six months. Participants from the exercise arm reported that it was harder to motivate themselves without the instructor there. This has also been identified in previous exercise training research which found motivation predicts exercise behaviour after a RCT[231]. One participant stated that the local gyms were too expensive so they undertook alternative forms of physical activity such as swimming which meant gradually building fitness for a different activity. Expense has also been identified as affecting exercise maintenance after reduced price (free in this case) gym fees[232]. Others reported that it was difficult to continue the three 60-minute sessions per week, so set alternative goals. Although physical activity reduced in the exercise group from three to six months, everything apart from light activity remained superior to baseline values. This suggests participants may have compensated for their increased MVPA by reducing their light activity. Shah *et al's*[84] participants at the end of their 12 week partially supervised exercise intervention showed that moderate physical activity increased by 40 minutes and simultaneously a 40 minute decrease in light activity; this shows a shift in physical activity intensity.

It is important to acknowledge the levels of weekly MVPA in both groups at baseline. Previous research suggested that 89.4% of patients were not sufficiently active 12 months post-surgery (not meeting the MVPA guidelines of ≥150 minutes weekly)[76, 82]. Another study shows MVPA is not significantly different from one to three years, however a mean reduction in MVPA after 24 months is shown[71]. At baseline and after 6-months in the study both groups were performing more MVPA than the general adult physical activity guidelines (baseline: control +58.0 minutes, exercise +48.2 minutes; 6-months: control +34.4 minutes, exercise +108.3 minutes per week). Berglind *et al*[80] reported that their 56 patient cohort at 12 months undertook a mean of 32.1 minutes of MVPA daily after RYGB surgery without intervention; they were also therefore classified as active 12 months post-surgery. The ASMBS, The Obesity Society and the American Association of Clinical Endocrinologists jointly recommend that for a healthy post-operative lifestyle at least 30 minutes of activity per day should be undertaken. This guideline is suggested to achieve optimal body mass and body composition after bariatric surgery[233]. At both 3 and 6-months the exercise group were performing more than 30 minutes of MVPA per day whereas the control performed less MVPA. This could help explain the control group's increase and the exercise group's decrease in body mass.

5.4.4 Health Related outcomes

Biochemical blood measures of non-fasting HbA1c and lipid profile were obtained; the mean values reported at the three time points all fell within the 'normal' ranges[234, 235]. Only the cholesterol:HDL ratio displayed a statistically significant difference between groups after the exercise intervention. However, triglycerides, LDL and HDL mean lipid profile results all favoured the exercise training group at both assessments. In contrast, the control group increased from their baseline levels to the top end of the normal ranges after six months. It should be noted that the changes in both groups were small and not statistically significant so it can be concluded that there was no significant effect. Other exercise interventions in this population have also reported positive results for LDL, HDL, triglycerides and insulin sensitivity in their sample with only a significant difference between groups for insulin sensitivity[72].

Mean blood pressure decreased as a result of exercise, and the control group remained higher than baseline showing a significant difference between groups. At 6-months, the control group's blood pressure had remained level (121/81mmHg), whilst the exercise group had improved to within the healthy range (115/75mmHg) indicating that the exercise intervention contributed to lowering risk of heart disease and stroke[236].

Anxiety and depression have been reported to improve by six to ten months post-operatively as a result of undergoing bariatric surgery[237]. The mean reported anxiety and depression scores for both groups were below the threshold on the HADS, and therefore classed as normal. At baseline only three participants presented with mild to moderate depression and five presented mild to severe anxiety. It is likely that initiating a programme one year after the operative procedure, anxiety and depression changes are likely to have already occurred[237].

5.4.5 Intervention

There are many difficulties associated with increasing exercise in this population. Moderate intensity exercise interventions gradually building from realistic levels as perceived by the patient, are suggested to help prevent drop out and aid the overall exercise intervention success in obese populations[230]. This is especially important in those with low-self efficacy and limited exercise familiarity[230]. As a clinical exercise intervention, the intervention was not underpinned by a formal theoretical framework. The exercise intervention for The MOTION Study was designed based on participants' performance during the maximal treadmill exercise test during initial screening. The exercise programme was therefore designed specifically for that individual to reflect his/her ability. Due to the lack of post-operative guidelines for this population, patient's were closely monitored to ensure gradual but continual progression through the 12 weeks of gym training[88]. Participant exercise

sessions were therefore supervised to monitor appropriate exercise levels to ensure progressive overload to facilitate improvements[238]. Individuals completed between three and six ability-dependant gym progressions which were designed and progressed based on their heart rate (most completed five to six) throughout the supervised training to ensure progression. Such improvements were shown for both aerobic exercises (performing longer durations at greater resistance, speeds and inclines) and resistance exercises (performing similar sets and repetitions at a progressively higher mass). No adverse events or injuries were recorded throughout the exercise intervention. Although the intervention was a combination of aerobic and resistance exercise, there was a predominant focus on aerobic exercise in the gym training sessions. A combined programme provides more variation and therefore helps maintain motivation. Although not directly comparable, when looking at the three weekly 60 minute gym sessions compared to a similar intervention in the same population comprising of 75 minute sessions, between group differences in function and body composition were only found in the current cohort[89]. This suggests that 60-minute sessions are sufficient for a 12-week combined aerobic and resistance training intervention performed three times per week.

Significant reductions in body mass and fat mass have been reported under the supervision of a qualified exercise specialist compared with non-supervised exercise in an earlier trial[224]. This supervised approach provided regular professional support, ongoing counselling and an increased knowledge and understanding of the exercise which all positively contributes to self-belief and self-confidence. Participants verbally expressed a lack of knowledge; not knowing what exercise will help them, what exercise is dangerous for them, not knowing where to start and most importantly what their bodies can cope with. This reflects the self-efficacy scores reported in the exercise group; the baseline levels were low and increased significantly directly after the completion of the exercise intervention. Self-efficacy did however decrease between the three and six month assessments; this is likely attributed to the removal of the supervision element although self-efficacy remained higher than baseline levels. This intervention show that the generic discharge advice session, combined with an example exercise programme and a diet sheet was insufficient for improving physical function and preventing weight regain in the control group. Previous research has found that in a morbidly obese population exercise education alone is insufficient for preventing declines in health related fitness[63].

Adherence to the protocol was higher than expected; the sample size calculation was based on a 20% drop out rate because of the nature of the population involved. In total 92% completed the training programme; the one participant who did not complete the gym training withdrew because she had her gastric band deflated (due to discomfort). The control group saw a higher drop-out rate with 83% completing the six months; the two participants who withdrew from this group reported it was because they were not randomised to the exercise group. The running intervention initiated at a similar post-operative time point only reported a 70% retention rate in the intervention group despite

participants volunteering to be in the running intervention[90]. The drop-outs in the running intervention attributed it to motivational reasons; suggesting that running may not be a suitable form of activity for everyone in this population.

Huck *et al*[88] reported high adherence for their 12 week resistance training intervention (84% adherence). In The MOTION Study, of a possible 36 gym sessions, the exercise group completers attended a mean of 34 sessions; this accounted for 95% adherence. This high adherence rate is likely to reflect the nature of the training sessions and training environment. Participants also reported that they felt this opportunity had come at the right time as they have less post-operative support at this stage after surgery. The low drop-out rate, high attendance and positive participant feedback shows the patients need for such an exercise intervention and the acceptability of this approach.

5.4.6 Strengths and limitations

To maximise recruitment in this post-operative bariatric surgery cohort three phases of recruitment occurred throughout the trial period to capture the patients 12 to 24 months post-surgery. Due to the limited amount of NHS patients available private patients were later recruited. Unfortunately the recruitment process relied on letter responses. To ensure this method was as effective as possible letters were sent a second time if the reply-slip was not returned within a month. Despite a thorough identification and screening process, the recruited sample was slightly smaller than intended, contributing to some minor differences between intervention and control arms at baseline. However, none of these were statistically significant, and analysis of change data indicated large and significant inter-group differences in the primary outcome measure (ISWT), and many other outcomes. A further limitation could be that some outcome measures have not been validated in a bariatric surgery population. The recruited sample was predominantly female, with only four men randomised. However, this reflects the gender bias in the characteristics of bariatric surgery patients [at a ratio of 3:1[47]]. The variability in outcome measures at the 6-month assessment could have been influenced by individual's type of activity and/or diet between the three and six month assessment. No measure of activity or diet was used between the assessments; this should be noted as it could influence findings.

The strengths of The MOTION Study include its rigorous design; this is the first RCT initiated at the point of weight regain. It is also the first intervention to report follow-up results three months after completion of the exercise intervention. The study obtained dietary information to allow controlling for diet. As there were no significant differences between groups, the improvements appear to be attributable to the exercise intervention alone. Finally in comparison to previous research, The MOTION Study reports low drop-out rates and high gym session attendance thus showing marked adherence.

5.4.7 Future research directions

Exercise intervention research after bariatric surgery is still in its infancy. This RCT has provided a foundation for future research for the use of physical activity to optimise long term post-bariatric surgery outcomes. Suggested future research includes larger scale RCTs to confirm the current findings. It would be of interest to follow up exercise interventions long-term to determine maintenance from such a programme. Also including all post-operative patients deemed healthy to exercise, rather than limiting those able to take part based on BMI, could be beneficial. If the current RCT included those individuals also classified as overweight, 11 more patients who expressed an interest would have been invited for screening. A large-scale RCT is necessary to study the combination of pre and post-operative counselling targeting physical activity behaviour change before initiating supervised exercise. Such supervised exercise should be initiated at the point of weight regain or when weight loss slows and include regular longer term follow-ups after completion. Ultimately, to determine if this combination of exercise and physical activity counselling is feasible and advantageous in optimising long term outcomes.

Future research exploring the cost effectiveness of such intervention and the feasibility of incorporating it into normal care is necessary. It is important to develop translational research in this population to ultimately be incorporated into usual care or inform current care packages.

5.5 Conclusion

The findings from The MOTION Study suggest that the implementation of a supervised exercise intervention at the point of weight regain is effective for improving physical function and body composition in this population. The MOTION Study has shown many positive outcomes as a result of exercise, notably the improvement in the primary outcome measure the ISWT. Functional walking ability showed a very large improvement directly after exercise and a further improvement when followed up. Since physical activity declined after the end of the supervised intervention, patients may need ongoing support to develop independence, to sustain these improvements in physical activity.

Chapter Six

Overall discussion

Chapter Overview

This final chapter closes the thesis by giving an overview of the findings from the three studies. Current physical activity guidelines and recommendations for bariatric surgery patients are discussed. The chapter also links the current literature, suggestions from national organisations and the thesis findings to build recommendations for physical activity and its clinical application. This ultimately aims to inform the direction for future research and post-operative bariatric support.

The primary aim of this research was to increase the understanding of the relationship between physical activity and long term outcomes for patients undergoing bariatric surgery. Three studies have been conducted to contribute to the existing literature and create a foundation for future research in this field. It is hoped that the results from this thesis will provide solid evidence of the benefits of physical activity for bariatric patients and therefore influence the design and implementation of future post-operative care, and ultimately improve bariatric patient's quality of life and health.

6.1 Thesis overview

Study one was a systematic review of the literature to examine changes in physical activity and physical function resulting from bariatric surgery. Study two represented a retrospective analysis of a UK patient cohort to identify the point of weight regain and associated functional and health outcomes. Study three was a RCT of supervised and structured moderate intensity gym based exercise for bariatric surgery patients who remained obese following surgery. This intervention aimed to improve physical function and facilitate weight maintenance. The main outcomes from each study of the research project are summarised below, followed by a collective discussion that combines these results to formulate an overarching recommendation.

Study one: Changes in physical activity behaviour and physical function after bariatric surgery: a systematic review and meta-analysis.

It is generally accepted that weight loss and physical activity increase as a result of bariatric surgery. The first piece of research that makes up this thesis, a systematic review and meta-analysis, aimed to identify the effect of bariatric surgery on both physical activity and physical function outcomes among obese adults. Physical function reflects ability to perform basic activities of daily living such as walking, stair climbing and transitioning from sitting to standing[94], and is often impaired in obese individuals. Improving physical function directly contributes to the improvement of HRQoL and wellbeing[94]. Results from the systematic review demonstrated improvements by 12 months in objective and self-reported physical activity and physical function. Objectively measured MVPA and an increase in step count at 3-6 months indicated that greater levels of lower intensity physical activity were carried out in the early post-operative stages of surgery. No relationship was identified between changes in weight and physical function. Trials with larger numbers of individuals are necessary to further understand the effects of physical activity on post-surgical outcomes.

Study two: A retrospective cohort analysis of body mass, health, and functional outcomes after bariatric surgery

Studies report that weight regain occurs between 12 and 24 months after bariatric surgery; this is based on research undertaken outside the UK. Study two, a retrospective cohort data analysis, aimed to identify if and when weight regain occurs, whether co-morbidities resolve and if physical function

improves in a UK NHS patient cohort following bariatric surgery. Data from this cohort demonstrates improvements in body mass, physical function and co-morbidities (e.g. sleep apnoea, dyslipidaemia and GORD) as a result of bariatric surgery. Superior outcomes observed following gastric bypass compared to gastric banding surgery. Weight loss patterns indicate rapid weight loss to six months weight stability (+/- 5kg[239]) from 12 to 24 months and weight regain 24 months post-surgery. This suggests a physical activity intervention may be beneficial if introduced 12 to 24 months after bariatric surgery, to aid weight loss maintenance and prevent further weight regain.

Study three: The effects of supervised exercise training 12-24 months after bariatric surgery on physical function and body composition: a randomised controlled trial (The MOTION Study).

Research on physical activity and bariatric surgery is in its infancy[69]. Few physical activity interventions exist in the bariatric population and currently no published exercise interventions are available in the UK. The aim of the RCT was to examine the effect of a 12 week supervised and structured gym based moderate intensity exercise intervention on physical function and body composition in patients 12-24 months post-bariatric surgery. A secondary aim was to examine the maintenance of the effects at six months (three months after the end of the intervention). At 12 weeks, improvements in the exercise intervention group were observed for body composition, walking function, functional lower limb muscle strength, grip strength, MVPA, blood pressure, resting heart rate, cholesterol:HDL ratio and self-efficacy. Three months later significant differences favouring the exercise intervention group remained for body composition, walking performance, functional lower limb muscle strength, grip strength, blood pressure. This research suggests that the addition of a moderate intensity supervised and structured exercise intervention 12-24 months after surgery is beneficial for bariatric surgery patients. To the best of our knowledge this is the first exercise intervention in this population to be undertaken in the UK, and the first RCT to initiate an exercise intervention at the point of weight regain.

6.2 Current recommendations

As research evolves, the importance of physical activity for optimising bariatric surgery outcomes is gaining greater recognition[26, 240]. Although currently there are no official guidelines relating to physical activity for bariatric surgery patients, the accumulating body of evidence supports the argument that development of formal recommendations are required.

It is important to develop international guidelines for physical activiy for individuals undergoing bariatric surgery. There are currently no specific requirements in the UK to provide physical activity within the delivery of post-bariatric surgery care. There is however, increasing encouragement to service providers to incorporate physical activity advice in their services[2]. The Royal College of Physicians identifies the need for the development of standardised guidelines for all bariatric surgery

services to optimise long term surgical outcomes. Regarding physical activity, the Royal College of Physicians acknowledge the importance of physical activity advice within multidisciplinary care, and state that it should be incorporated. However, no quantifiable guidelines of physical activity are suggested. NICE guidelines recommend that follow-up care after bariatric surgery should incorporate physical activity advice and support in a two year post-operative care package[24]. Yet again, no quantifiable physical activity recommendations are suggested for this population. NICE does suggest that health professionals 'advise people who have been obese and have lost weight that they may need to do 60–90 minutes of moderate intensity activity a day to avoid regaining weight'. This is referring to general weight loss, not specifically for bariatric surgery patients[24]. The National Obesity Observatory does not mention physical activity in their 'bariatric surgery for obesity' guidance document[38]. The NBSR recommendations suggests that lifestyle advice provided in the bariatric surgery weight assessment and management clinic should include access to a physical activity programmes, individually tailored to each patient to promote health and fitness[4]. The NBSR report, based on Livhits *et al's*[26] systematic review of exercise following bariatric surgery, recommends that after discharge from bariatric surgery services, bariatric physicians and GPs should arrange supervised physical activity which is individually tailored to each patient[4]. To the authors knowledge, no research on physical activity interventions have been undertaken in the UK; with most interventions having been undertaken in the USA[72, 84, 87, 88].

Although standardised guidelines have not been developed, organisations in the USA have more specific guidance than the UK. King & Bond[69] summarise current physical activity guidelines recommended for bariatric surgery. The ASMBS and American Heart Association recommend mild pre-operative exercise of 20 minutes per day, on three to four days per week prior to surgery, in order to improve cardio respiratory fitness and enhance post-operative recovery. Additionally the ASMBS recommends including aerobic and light resistance training. Post-operative recommendations of at least 30 minutes per day are jointly recommended by the ASMBS, The Obesity Society and the American Association of Clinical Endocrinologists to achieve optimal body mass and body composition. The expert panel on weight loss recommends low to moderate intensity exercise to increase pre and post-operative physical activity. Similar to the UK recommendations for those who have previously lost weight, recommendations for overweight and obese adults suggest that to control body mass, more physical activity is needed. A dose response relationship has been reported by Donnelly *et al*[241] between physical activity and both weight loss and weight loss maintenance.

6.3 Recommendations for physical activity and clinical application

Although physical activity intervention research for bariatric surgery is in its infancy, it is well accepted that physical activity positively affects bariatric surgery outcomes. Based on current

literature and the additional knowledge this thesis contributes, physical activity recommendations, such as an intervention of structured exercise, should be integrated into routine care for patients undergoing bariatric surgery. Introducing routine pre and post-operative physical activity counselling with the aim of increasing physical activity to target levels is recommended for weight maintenance[69]. In addition, a supervised and structured moderate intensity exercise programme (combined aerobic and resistance training sessions three days per week for 12 weeks) at 12 months, with the aim of improving physical function and the facilitation of weight loss and maintenance of physical activity. This should be offered at the typical point of weight regain.

Exercise interventions which have been initiated in the early post-operative stages have demonstrated numerous positive outcomes, yet none of these interventions have established differences in body composition when comparing the intervention and control groups[72, 84, 88, 89]. The MOTION Study and one other exercise intervention initiated after 12 months are the only trials identified that report body composition improvements between the exercise and control groups[90]. These data support the call for an exercise intervention at 12 months after surgery: the point of peak weight loss[23]. It is important to incorporate physical activity counselling which target current guidelines, as studies report that patients may remain insufficiently active a year after surgery[76]. Even if guidelines are being met, supervised and structured moderate intensity exercise has still proven to be beneficial. Patients in the MOTION Study were performing a mean of 29 MVPA minutes daily and still benefited from supervised and structured moderate intensity aerobic exercise.

Low cost objective measures of physical function such as the ISWT and STS test should also be incorporated into routine clinical practice (pre and post-operative follow up assessments). These are simple patient-centred measurements to monitor functional progress alongside weight loss and are accurate field based tests of functional capacity and functional muscle strength respectively[191, 220, 221]. Both the ISWT and STS tests are important predictors of physical function and therefore HRQoL[191, 221]. This is important as it reflects improvements and deteriorations in HRQoL are associated with the magnitude of weight loss and weight regain[242].

It would be beneficial for the UK to develop standardised guidelines for the delivery of bariatric surgery services which incorporate supervised and structured physical activity. Current national recomendations need to recognise that exercise advice alone is insufficient for improving health related fitness parameters for optimising bariatric surgery outcomes[2].

6.4 Recommendations for future research

Priorities for future research are evident from the outcomes of the research in this thesis. There is a need for more physical activity interventions, specifically large scale studies and RCTs to ultimately inform physical activity guidance in this population. Future research suggestions include:

1. A large scale physical activity monitoring study which assesses pre and post-operative activity (at the typical standard follow-up timeframes). This would help identify necessary physical activity levels in this population to optimise health outcomes. This information will inform RCTs and physical activity guidelines.
2. A large-scale randomised clinical trial to examine the combination of pre and post-operative counselling before initiating a structured and supervised exercise at the point when weight loss slows or weight regains. This should be coupled with regular longer term follow-ups to determine if this combination is feasible and advantageous in optimising long term outcomes.
3. A RCT initiated approximately 10 months post-operatively to identify whether intervening when weight loss slows is more beneficial than intervening at the point of weight regain. Further RCTs should look at the intensity and type of exercise performed on multiple health related fitness parameters and biochemical indicators of obesity related diseases.

6.5 Conclusion

It can be concluded that the findings from this thesis support the implementation of physical activity intervention at the point of reported weight regain to further improve physical function. Findings revealed that 12 weeks of supervised and structured moderate intensity gym training, comprising one hour of aerobic and resistance training three times per week, led to large functional improvements and additional improvements in body composition. The low drop-out rate, high attendance and positive participant feedback in the The MOTION Study emphasises the patient need for such a physical activity program. It is recognised that increased physical activity aids bariatric surgery success, however research is still in its infancy. This information has provided a foundation for future research in the use of physical activity to optimise long term post-bariatric surgery outcomes.

References

1. World Health Organisation (WHO). Obesity and overweight: WHO; 2015 [Date; cited 2013 7 September]. Available from: http://www.who.int/mediacentre/factsheets/fs311/en/.

2. Royal College of Physicians (RCP). Action on Obesity: Comprehensive care for all. London: RCP, 2013.

3. Public Health England. Adult weight data factsheet. Public Health England, 2014.

4. Welbourne R, Small P, Finlay I, Sareela A, Somers S, Mahawar K, *et al*. The NBSR National Bariatric Surgery Registry of The British Obesity & Metabiolic Surgery Society - Second Registry Report. Oxfordshire, England: 2014.

5. World Health Organisation (WHO). BMI classification 2006 [Date; cited 2013 19 June]. Available from: http://apps.who.int/bmi/index.jsp?introPage=intro_3.html.

6. James PT, Leach R, Kalamara E, Shayeghi M. The worldwide obesity epidemic. *Obesity Research*. 2001; 9(4):228-233.

7. Weisell RC. Body mass index as an indicator of obesity. *Asia Pacific Journal of Clinical Nutrition*. 2002; 11(8):681–684.

8. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *The Lancet*. 363(9403):157-163.

9. World Health Organisation (WHO). The Asia-Pacific perspective. Redefining obesity and its treatment Australia: Health communications Australia; 2000 [Date; cited 2013 19 June]. Available from: http://www.wpro.who.int/nutrition/documents/Redefining_obesity/en/.

10. Vinciguerra F, Baratta R, Farina MG, Tita P, Padova G, Vigneri R, *et al*. Very severely obese patients have a high prevalence of type 2 diabetes mellitus and cardiovascular disease. *Acta Diabetologica* 2013; 50(3):443-449.

11. Sainio P, Martelin T, Koskinen S, Heliövaara M. Educational differences in mobility: the contribution of physical workload, obesity, smoking and chronic conditions. *Journal of Epidemiology and Community Health*. 2007; 61(5):401-408.

12. Capodaglio P, Castelnuovo G, Brunani A, Vismara L, Villa V, Capodaglio EM. Functional limitations and occupational issues in obesity: a review. *International Journal of Occupational Safety and Ergonomics*. 2010; 16(4):507-523.

13. Nguyen T, Lau DC. The obesity epidemic and its impact on hypertension. *The Canadian Journal of Cardiology*. 2012; 28(3):326-333.

14. Colquitt JL, Picot J, Loveman E, Clegg AJ. Surgery for obesity. *Cochrane Database of Systematic Reviews*. 2009; 15(2):1-243.

15. Duval K, Marceau P, Lescelleur O, Hould FS, Marceau S, Biron S, *et al.* Health-related quality of life in morbid obesity. *Obesity Surgery*. 2006; 16(5):574-579.

16. Department of Health (DOH). Facts and figures on obesity London: Department of Health; 2010 [Date; cited 2012 July]. Available from: http://www.dh.gov.uk/health/2012/04/obesityfacts/.

17. Truby H, Bonham M. What makes a weight loss programme successful? *British Medical Journal*. 2011; 343: 1-2.

18. Steinbrook R. Surgery for severe obesity. *The New England Journal of Medicine* 2004; 350(11):1075-1079.

19. Madura JA, Dibaise JK. Quick fix or long-term cure? Pros and cons of bariatric surgery. *F1000 Medicine Reports*. 2012; 4(19):1-9.

20. Papalazarou A, Yannakoulia M, Kavouras SA, Komesidou V, Dimitriadis G, Papakonstantinou A, *et al.* Lifestyle intervention favorably affects weight loss and maintenance following obesity surgery. *Obesity*. 2010; 18(7):1348-1353.

21. Jassil FC, Manning S, Lewis N, Steinmo S, Kingett H, Lough F, *et al.* Feasibility and Impact of a Combined Supervised Exercise and Nutritional-Behavioral Intervention following Bariatric Surgery: A Pilot Study. *Journal of Obesity*. 2015; 2015:1-12.

22. Odom J, Zalesin KC, Washington TL, Miller WW, Hakmeh B, Zaremba DL, *et al.* Behavioral Predictors of Weight Regain after Bariatric Surgery. *Obesity Surgery*. 2010; 20(3):349-356.

23. Sjöström L, Lindroos AK, Peltonen M, Torgerson J, Bouchard C, Carlsson B, *et al.* Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. *The New England Journal of Medicine*. 2004; 351(26):2683-2693.

24. National Institute for Health and Care Excelence (NICE). Obesity: identification, assessment and management of overweight and obesity in children, young people and adults. 2014 [Date; cited 2015 11 May]. NICE clinical guideline 189:[Available from: https://www.nice.org.uk/guidance/cg189/resources/guidance-obesity-identification-assessment-and-management-of-overweight-and-obesity-in-children-young-people-and-adults-pdf.

25. Egberts K, Brown WA, Brennan L, O'Brien PE. Does exercise improve weight loss after bariatric surgery? A systematic review. *Obesity Surgery*. 2012; 22(2):335-341.

26. Livhits M, Mercado C, Yermilov I, Parikh JA, Dutson E, Mehran A, *et al.* Exercise following bariatric surgery: systematic review. *Obesity Surgery*. 2010; 20(5):657-665.

27. National collaborating centre for primary care and the centre for public health excellence at NICE. Obesity: Guidance on the prevention, identification, assessment and management of overweight and obesity in adults and children. Quick reference guide 2 [Internet]. 2006 2 July; 1. Available from: http://publications.nice.org.uk/obesity-cg43/guidance#public-health-recommendations.

28. Booth A, Nowson C. Patient recall of receiving lifestyle advice for overweight and hypertension from their General Practitioner. *BioMed Central Family Practice*. 2010; 11(1):1-7.

29. Morrison DS, Boyle S, Morrison C, Allardice G, Greenlaw N, Forde L. Evaluation of the first phase of a specialist weight management programme in the UK National Health Service: prospective cohort study. *Public Health Nutrition*. 2012; 15(1):28-38.

30. Curioni CC, Lourenco PM. Long-term weight loss after diet and exercise: a systematic review. *International Journal of Obesity and Related Metabolic Disorders*. 2005; 29(10):1168-1174.

31. Yanovski SZ, Yanovski JA. Long-term drug treatment for obesity: a systematic and clinical review. *The Journal of the American Medical Association*. 2014; 311(1):74-86.

32. Booth HP, Prevost AT, Gulliford MC. Access to weight reduction interventions for overweight and obese patients in UK primary care: population-based cohort study. *British Medical Journal Open*. 2015; 5(1):1-7.

33. Maggard MA, Shugarman LR, Suttorp M, Maglione M, Sugerman HJ, Livingston EH, *et al.* Meta-Analysis: Surgical Treatment of Obesity. *Annals of Internal Medicine*. 2005; 142(7):547-559.

34. Oxford Dictionaries. Definition of bariatric surgery 2013 [Date; cited 2013 4 July]. Available from: http://oxforddictionaries.com/definition/american_english/bariatric-surgery.

35. Prachand VN. The evolution of minimally invasive bariatric surgery. *World Journal of Surgery*. 2011; 35(7):1464-1468.

36. Nguyen NT, Goldman C, Rosenquist CJ, Arango A, Cole CJ, Lee SJ, *et al.* Laparoscopic versus open gastric bypass: a randomized study of outcomes, quality of life, and costs. *Annals of Surgery*. 2001; 234(3):279-291.

37. Ratcliffe D, Ali R, Ellison N, Khatun M, Poole J, Coffey C. Bariatric psychology in the UK National Health Service: input across the patient pathway. *BioMed Central Obesity*. 2014; 1(20):1-7.

38. Dent M, Chrisopoulos S, Mulhall C, Ridler C. Bariatric surgery for obesity. Oxford: National Obesity Observatory, 2010 20 June.

39. Obesity Action Coalition. Bariatric Surgery (Severe Obesity) 2015 [Date; cited 2015 October 2015]. Available from: http://www.obesityaction.org/obesity-treatments/bariatric-surgery.

40. Hofso D, Nordstrand N, Johnson LK, Karlsen TI, Hager H, Jenssen T, *et al.* Obesity-related cardiovascular risk factors after weight loss: a clinical trial comparing gastric bypass surgery and intensive lifestyle intervention. *European Journal of Endocrinology* 2010; 163(5):735-745.

41. Martins C, Strommen M, Stavne OA, Nossum R, Marvik R, Kulseng B. Bariatric surgery versus lifestyle interventions for morbid obesity-changes in body weight, risk factors and comorbidities at 1 year. *Obesity Surgery*. 2011; 21(7):841-849.

42. Brolin RE. Bariatric surgery and long-term control of morbid obesity. *The Journal of the American Medical Association*. 2002; 288(22):2793-2796.

43. Cummings DE, Overduin J, Foster-Schubert KE. Gastric bypass for obesity: mechanisms of weight loss and diabetes resolution. *The Journal of Clinical Endocrinology and Metabolism*. 2004; 89(6):2608-2615.

44. Jakicic JM. The effect of physical activity on body weight. *Obesity*. 2009; 17(3):34-38.

45. Gloy VL, Briel M, Bhatt DL, Kashyap SR, Schauer PR, Mingrone G, *et al.* Bariatric surgery versus non-surgical treatment for obesity: a systematic review and meta-analysis of randomised controlled trials. *British Medical Journal*. 2013; 347:1-16.

46. Fredheim JM, Rollheim J, Sandbu R, Hofso D, Omland T, Roislien J, *et al.* Obstructive sleep apnea after weight loss: a clinical trial comparing gastric bypass and intensive lifestyle intervention. *Journal of Clinical Sleep Medicine*. 2013; 9(5):427-432.

47. Buchwald H, Avidor Y, Braunwald E, et al. Bariatric surgery: A systematic review and meta-analysis. *The Journal of the American Medical Association*. 2004; 292(14):1724-1737.

48. Warren JA, Ewing JA, Hale AL, Blackhurst DW, Bour ES, Scott JD. Cost-effectiveness of Bariatric Surgery: Increasing the Economic Viability of the Most Effective Treatment for Type II Diabetes Mellitus. *The American Surgeon*. 2015; 81(8):807-811.

49. Hensrud DD, Weinsier RL, Darnell BE, Hunter GR. Relationship of co-morbidities of obesity to weight loss and four-year weight maintenance/rebound. *Obesity Research*. 1995; 3(2):217-222.

50. Pedersen BK, Saltin B. Evidence for prescribing exercise as therapy in chronic disease. *Scandinavian Journal of Medicine & Science in Sports*. 2006; 16(1):3-63.

51. Christensen R, Bartels E, Astrup A, Bliddal H. Effect of weight reduction in obese patients diagnosed with knee osteoarthritis: a systematic review and meta-analysis. *Annals of the Rheumatic Diseases*. 2007; 66(4):433-439.

52. Messier SP, Loeser RF, Miller GD, Morgan TM, Rejeski WJ, Sevick MA, *et al.* Exercise and dietary weight loss in overweight and obese older adults with knee osteoarthritis: the Arthritis, Diet, and Activity Promotion Trial. *Arthritis Rheum*. 2004; 50(5):1501-1510.

53. Magro DO, Geloneze B, Delfini R, Pareja BC, Callejas F, Pareja JC. Long-term weight regain after gastric bypass: a 5-year prospective study. *Obesity Surgery*. 2008; 18(6):648-651.

54. Richardson WS, Plaisance AM, Periou L, Buquoi J, Tillery D. Long-term Management of Patients After Weight Loss Surgery. *The Ochsner Journal*. 2009; 9(3):154-159.

55. Heneghan HM, Yimcharoen P, Brethauer SA, Kroh M, Chand B. Influence of pouch and stoma size on weight loss after gastric bypass. *Surgery for Obesity and Related Diseases*. 2012; 8(4):408-415.

56. Mason E, Scott D, Doherty C, Cullen J, Rodriguez E, Maher J, *et al.* Vertical Banded Gastroplasty in the Severely Obese under Age Twenty-One. *Obesity Surgery*. 1995; 5(1):23-33.

57. Sarwer DB, Wadden TA, Fabricatore AN. Psychosocial and Behavioral Aspects of Bariatric Surgery. *Obesity Research*. 2005; 13(4):639-648.

58. Wing RR, Tate DF, Gorin AA, Raynor HA, Fava JL. A self-regulation program for maintenance of weight loss. *New England Journal of Medicine*. 2006; 355(15):1563-1571.

59. Zalesin KC, Franklin BA, Miller WM, Nori Janosz KE, Veri S, Odom J, *et al.* Preventing Weight Regain After Bariatric Surgery: An Overview of Lifestyle and Psychosocial Modulators. *American Journal of Lifestyle Medicine*. 2010; 4(113):1-8.

60. Rudolph A, Hilbert A. Post-operative behavioural management in bariatric surgery: a systematic review and meta-analysis of randomized controlled trials. *Obesity Reviews*. 2013; 14(4):292-302.

61. Elkins G, Whitfield P, Marcus J, Symmonds R, Rodriguez J, Cook T. Noncompliance with Behavioral Recommendations Following Bariatric Surgery. *Obesity Surgery*. 2005; 15(4):546-551.

62. Pavlou KN, Krey S, Steffee WP. Exercise as an adjunct to weight loss and maintenance in moderately obese subjects. *The American Journal of Clinical Nutrition*. 1989; 49(5):1115-1123.

63. Herring LY, Wagstaff C, Scott A. The efficacy of 12 weeks supervised exercise in obesity management. *Clinical Obesity*. 2014; 4(4):220-227.

64. Stewart F, Avenell A. Behavioural Interventions for Severe Obesity Before and/or After Bariatric Surgery: a Systematic Review and Meta-analysis. *Obesity Surgery*. 2015:1-12.

65. Ogden J, Hollywood A, Pring C. The impact of psychological support on weight loss post weight loss surgery: a randomised control trial. *Obesity Surgery*. 2015; 25(3):500-505.

66. NHS Commissioning Board. Clinical Commissioning Policy: Complex and Specialised Obesity Surgery 2013 September 2015.

67. Parikh M, Dasari M, McMacken M, Ren C, Fielding G, Ogedegbe G. Does a preoperative medically supervised weight loss program improve bariatric surgery outcomes? A pilot randomized study. *Surgical Endoscopy*. 2012; 26(3):853-861.

68. Lier HO, Biringer E, Stubhaug B, Tangen T. The impact of preoperative counseling on postoperative treatment adherence in bariatric surgery patients: a randomized controlled trial. *Patient Education and Counseling*. 2012; 87(3):336-342.

69. King WC, Bond DS. The Importance of Preoperative and Postoperative Physical Activity Counseling in Bariatric Surgery. *Exercise and Sport Sciences Reviews*. 2013; 41(1):26-35.

70. Steffen R, Potoczna N, Bieri N, Horber FF. Successful multi-intervention treatment of severe obesity: a 7-year prospective study with 96% follow-up. *Obesity Surgery*. 2009; 19(1):3-12.

71. Nijamkin MP, Campa A, Sosa J, Baum M, Himburg S, Johnson P. Comprehensive Nutrition and Lifestyle Education Improves Weight Loss and Physical Activity in Hispanic Americans

Following Gastric Bypass Surgery: A Randomized Controlled Trial. *Journal of the Academy of Nutrition and Dietetics*. 2012; 112(3):382-390.

72. Coen PM, Tanner CJ, Helbling NL, Dubis GS, Hames KC, Xie H, *et al.* Clinical trial demonstrates exercise following bariatric surgery improves insulin sensitivity. *The Journal of Clinical Investigation*. 2015; 125(1):248-257.

73. Jacobi D, Ciangura C, Couet C, Oppert JM. Physical activity and weight loss following bariatric surgery. *Obesity Reviews*. 2011; 12(5):366-377.

74. Herman K, Carver T, Christou N, Andersen R. Keeping the Weight Off: Physical Activity, Sitting Time, and Weight Loss Maintenance in Bariatric Surgery Patients 2 to 16 Years Postsurgery. *Obesity Surgery*. 2014; 24(7):1064-1072.

75. Evans RK, Bond DS, Wolfe LG, Meador JG, Herrick JE, Kellum JM, *et al.* Participation in 150 min/wk of moderate or higher intensity physical activity yields greater weight loss after gastric bypass surgery. *Surgery for Obesity and Related Diseases*. 2007; 3(5):526-530.

76. King WC, Hsu JY, Belle SH, Courcoulas AP, Eid GM, Flum DR, *et al.* Pre- to postoperative changes in physical activity: report from the longitudinal assessment of bariatric surgery-2 (LABS-2). *Surgery for Obesity and Related Diseases*. 2012; 8(5):522-532.

77. King WC, Chen JY, Bond DS, Belle SH, Courcoulas AP, Patterson EJ, *et al.* Objective assessment of changes in physical activity and sedentary behavior: Pre- through 3 years post-bariatric surgery. *Obesity* 2015; 23(6):1143-1150.

78. Liu X, Lagoy A, Discenza I, Papineau G, Lewis E, Braden G, *et al.* Metabolic and neuroendocrine responses to Roux-en-Y gastric bypass. I: energy balance, metabolic changes, and fat loss. *The Journal of Clinical Endocrinology and Metabolism*. 2012; 97(8):1440-1450.

79. Bond DS, Jakicic JM, Unick JL, Vithiananthan S, Pohl D, Roye GD, *et al.* Pre- to postoperative physical activity changes in bariatric surgery patients: self report vs. objective measures. *Obesity* 2010; 18(12):2395-2397.

80. Berglind D, Willmer M, Eriksson U, Thorell A, Sundbom M, Udden J, *et al.* Longitudinal Assessment of Physical Activity in Women Undergoing Roux-en-Y Gastric Bypass. *Obesity Surgery*. 2014; 25(1):119-125.

81. Josbeno DA, Jakicic JM, Hergenroeder A, Eid GM. Physical activity and physical function changes in obese individuals after gastric bypass surgery. *Surgery for Obesity and Related Diseases*. 2010; 6(4):361-366.

82. World Health Organisation (WHO). Global Strategy on Diet, Physical Activity and Health WHO; 2015 [Date; cited 2015 11 May]. Available from: http://www.who.int/dietphysicalactivity/factsheet_adults/en/.

83. American College of Sports Medicine (ACSM). ACSM's Resource Manual for Guidelines for Exercise Testing and Prescription. Sixth ed. Baltimore, USA: Lippincott Williams & Wilkins 2010.

84. Shah M, Snell PG, Rao S, Adams-Huet B, Quittner C, Livingston EH, *et al.* High-volume exercise program in obese bariatric surgery patients: a randomized, controlled trial. *Obesity*. 2011; 19(9):1826-1834.

85. Akkary E, Cramer T, Chaar O, Rajput K, Yu S, Dziura J, *et al.* Survey of the Effective Exercise Habits of the Formerly Obese. *Journal of the Society of Laparoendoscopic Surgeons*. 2010; 14(1):106-114.

86. Bond DS, Phelan S, Wolfe LG, Evans RK, Meador JG, Kellum JM, *et al.* Becoming physically active after bariatric surgery is associated with improved weight loss and health-related quality of life. *Obesity* 2008; 17(1):78-83.

87. Zagarins SE, Allen NA, Skinner SS, Kemper AJ, Welch G. Improved exercise behaviors associated with a comprehensive structured exercise program following bariatric surgery. *Bariatric Nursing and Surgical Patient Care*. 2011; 6(2):85-90.

88. Huck CJ. Effects of Supervised Resistance Training on Fitness And Functional Strength in Patients Succeeding Bariatric Surgery. *Journal of Strength and Conditioning Research*. 2014; 29(3):589-595.

89. Stegen S, Derave W, Calders P, Van Laethem C, Pattyn P. Physical fitness in morbidly obese patients: effect of gastric bypass surgery and exercise training. *Obesity Surgery*. 2011; 21(1):61-70.

90. Marchesi F, De Sario G, Reggiani V, Tartamella F, Giammaresi A, Cecchini S, *et al.* Road Running After Gastric Bypass for Morbid Obesity: Rationale and Results of a New Protocol. *Obesity Surgery*. 2015; 25(7):1162-1170.

91. Castello V, Simões RP, Bassi D, Catai AM, Arena R, Borghi-Silva A. Impact of Aerobic Exercise Training on Heart Rate Variability and Functional Capacity in Obese Women After Gastric Bypass Surgery. *Obesity Surgery*. 2010; 21(11):1739-1749.

92. Castello V, Simões PR, Beltrame T, Bassi D, Maria Catai A, Arena R, *et al.* Effects of aerobic exercise training on variability and heart rate kinetic during submaximal exercise after gastric bypass surgery - a randomized controlled trial. *Disability and Rehabilitation*. 2013; 35(4):334-342.

93. Wilms B, Ernst B, Thurnheer M, Weisser B, Schultes B. Differential Changes in Exercise Performance After Massive Weight Loss Induced by Bariatric Surgery. *Obesity Surgery*. 2012; 23(3):365-371.

94. Steele T, Cuthbertson DJ, Wilding JP. Impact of bariatric surgery on physical functioning in obese adults. *Obesity Reviews*. 2015; 16(3):248-258.

95. Sarwer DB, Wadden TA, Moore RH, Eisenberg MH, Raper SE, Williams NN. Changes in Quality of Life and Body Image Following Gastric Bypass Surgery. *Surgery for Obesity and Related Diseases: Official Journal of the American Society for Bariatric Surgery*. 2010; 6(6):608-614.

96. Julia C, Ciangura C, Capuron L, Bouillot JL, Basdevant A, Poitou C, *et al.* Quality of life after Roux-en-Y gastric bypass and changes in body mass index and obesity-related comorbidities. *Diabetes & Metabolism*. 2013; 39(2):148-154.

97. Ohrström M, Hedenbro J, Ekelund M. Energy expenditure during treadmill walking before and after vertical banded gastroplasty: a one-year follow-up study in 11 obese women. *The European Journal of Surgery*. 2001; 167(11):845-850.

98. Iossi MF, Konstantakos EK, Teel DD, 2nd, Sherwood RJ, Laughlin RT, Coffey MJ, *et al.* Musculoskeletal function following bariatric surgery. *Obesity* 2012; 21(6):1104-1110.

99. Frezza EE, Shebani KO, Wachtel MS. Laparoscopic gastric bypass for morbid obesity decreases bodily pain, improves physical functioning, and mental and general health in women. *Journal of Laparoendoscopic and Advanced Surgical Techniques*. 2007; 17(4):440-447.

100. Wiklund M, Olsén MF, Willén C. Physical activity as viewed by adults with severe obesity, awaiting gastric bypass surgery. *Physiotherapy Research International*. 2011; 16(3):179-186.

101. Lyytinen T, Liikavainio T, Paakkonen M, Gylling H, Arokoski JP. Physical function and properties of quadriceps femoris muscle after bariatric surgery and subsequent weight loss. *Journal of Musculoskeletal and Neuronal Interactions*. 2013; 13(3):291-300.

102. da Silva RP, Martinez D, Faria CC, de Carli LA, de Souza WI, Meinhardt NG, *et al.* Improvement of exercise capacity and peripheral metaboreflex after bariatric surgery. *Obesity Surgery*. 2013; 23(11):1835-1841.

103. Miller GD, Nicklas BJ, You T, Fernandez A. Physical function improvements after laparoscopic Roux-en-Y gastric bypass surgery. *Surgery for Obesity and Related Diseases*. 2009; 5(5):530-537.

104. Zavala DC, Printen KJ. Basal and exercise tests on morbidly obese patients before and after gastric bypass. *Surgery*. 1984; 95(2):221-229.

105. Wiklund M, Monika F, O., Torsten O, Asa C. Physical Fitness and Physical Activity in Swedish Women before and one Year after Roux-en-Y Gastric Bypass Surgery. *The Open Obesity Journal*. 2014; 6(1):38-43.

106. Wasmund SL, Owan T, Yanowitz FG, Adams TD, Hunt SC, Hamdan MH, *et al.* Improved heart rate recovery after marked weight loss induced by gastric bypass surgery: two-year follow up in the Utah Obesity Study. *Heart Rhythm*. 2011; 8(1):84-90.

107. Vargas CB, Picolli F, Dani C, Padoin AV, Mottin CC. Functioning of obese individuals in pre- and postoperative periods of bariatric surgery. *Obesity Surgery*. 2013; 23(10):1590-1595.

108. Valezi AC, Machado VH. Morphofunctional evaluation of the heart of obese patients before and after bariatric surgery. *Obesity Surgery*. 2011; 21(11):1693-1697.

109. Tompkins J, Bosch PR, Chenowith R, Tiede JL, Swain JM. Changes in functional walking distance and health-related quality of life after gastric bypass surgery. *Physical Therapy*. 2008; 88(8):928-935.

110. Serés L, Lopez-Ayerbe J, Coll R, Rodriguez O, Vila J, Formiguera X, *et al.* Increased exercise capacity after surgically induced weight loss in morbid obesity. *Obesity* 2006; 14(2):273-279.

111. Maniscalco M, Zedda A, Giardiello C, Faraone S, Cerbone MR, Cristiano S, *et al.* Effect of bariatric surgery on the six-minute walk test in severe uncomplicated obesity. *Obesity Surgery*. 2006; 16(7):836-841.

112. Maniscalco M, Arciello A, Zedda A, Faraone S, Verde R, Giardiello C, *et al.* Right ventricular performance in severe obesity. Effect of weight loss. *European Journal of Clinical Investigation*. 2007; 37(4):270-275.

113. Kanoupakis E, Michaloudis D, Fraidakis O, Parthenakis F, Vardas P, Melissas J. Left ventricular function and cardiopulmonary performance following surgical treatment of morbid obesity. *Obesity Surgery*. 2001; 11(5):552-558.

114. de Souza SAF, Faintuch J, Sant'anna AF. Effect of weight loss on aerobic capacity in patients with severe obesity before and after bariatric surgery. *Obesity Surgery*. 2010; 20(7):871-875.

115. de Souza SAF, Faintuch J, Fabris SM, Nampo FK, Luz C, Fabio TL, *et al.* Six-minute walk test: functional capacity of severely obese before and after bariatric surgery. *Surgery for Obesity and Related Diseases*. 2009; 5(5):540-543.

116. Hue O, Berrigan F, Simoneau M, Marcotte J, Marceau P, Marceau S, *et al.* Muscle force and force control after weight loss in obese and morbidly obese men. *Obesity Surgery*. 2008; 18(9):1112-1118.

117. Handrigan G, Hue O, Simoneau M, Corbeil P, Marceau P, Marceau S, *et al.* Weight loss and muscular strength affect static balance control. *International Journal of Obesity*. 2010; 34(5):936-942.

118. Higgins J, Green S. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011] 2011. Available from: www.cochrane-handbook.org.

119. Horsley T, Dingwall O, Sampson M. Checking reference lists to find additional studies for systematic reviews. *The Cochrane Database of Systematic Reviews*. 2011; 10(8):1-27.

120. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *British Medical Journal*. 2003; 327(7414):557-560.

121. Boan J, Kolotkin RL, Westman EC, McMahon RL, Grant JP. Binge eating, quality of life and physical activity improve after Roux-en-Y gastric bypass for morbid obesity. *Obesity Surgery*. 2004; 14(3):341-348.

122. Das SK, Roberts SB, McCrory MA, Hsu LKG, Shikora SA, Kehayias JJ, *et al.* Long-term changes in energy expenditure and body composition after massive weight loss induced by gastric bypass surgery. *American Journal of Clinical Nutrition*. 2003; 78(1):22-30.

123. Gorin AA, Raftopoulos I. Effect of mood and eating disorders on the short-term outcome of laparoscopic Roux-en-Y gastric bypass. *Obesity Surgery*. 2009; 19(12):1685-1690.

124. Hooper MM, Stellato TA, Hallowell PT, Seitz BA, Moskowitz RW. Musculoskeletal findings in obese subjects before and after weight loss following bariatric surgery. *International Journal of Obesity* 2007; 31(1):114-120.

125. Rosenberger PH, Henderson KE, White MA, Masheb RM, Grilo CM. Physical activity in gastric bypass patients: associations with weight loss and psychosocial functioning at 12-month follow-up. *Obesity Surgery*. 2011; 21(10):1564-1569.

126. Vincent HK, Ben-David K, Conrad BP, Lamb KM, Seay AN, Vincent KR. Rapid changes in gait, musculoskeletal pain, and quality of life after bariatric surgery. *Surgery for Obesity and Related Diseases*. 2012; 8(3):346-354.

127. Hörchner R, Tuinebreijer W. Improvement of physical functioning of morbidly obese patients who have undergone a Lap-Band operation: one-year study. *Obesity Surgery*. 1999; 9(4):399-402.

128. Hortobágyi T, Herring C, Pories WJ, Rider P, Devita P. Massive weight loss-induced mechanical plasticity in obese gait. *Journal of Applied Physiology* 2011; 111(5):1391-1399.

129. Mathus-Vliegen EM, de Weerd S, de Wit LT. Health-related quality-of-life in patients with morbid obesity after gastric banding for surgically induced weight loss. *Surgery*. 2004; 135(5):489-497.

130. Mathus-Vliegen EM, Wit LT. Health-related quality of life after gastric banding. *The British Journal of Surgery*. 2007; 94(4):457-465.

131. Wouters EJ, Larsen JK, Zijlstra H, van Ramshorst B, Geenen R. Physical Activity After Surgery for Severe Obesity: the Role of Exercise Cognitions. *Obesity Surgery*. 2011; 21(12):1894-1899.

132. Wiklund M, Olsén M, F. Physical Function and Health Related Quality of Life Before and 18 Months after Bariatric Surgery. *The Open Obesity Journal*. 2015; 7(1):12-16.

133. Vatier C, Henegar C, Ciangura C, Poitou-Bernert C, Bouillot J-L, Basdevant A, *et al.* Dynamic relations between sedentary behavior, physical activity, and body composition after bariatric surgery. *Obesity Surgery*. 2012; 22(8):1251-1256.

134. Huang C-Y, Hsu M-C, Pan K-C, Huang C-K, Chi S-C. Early health status and health-related quality of life after laparoscopic gastric bypass surgery in morbidly obese patients. *Bariatric Nursing and Surgical Patient Care*. 2011; 6(4):193-200.

135. Carrasco F, Papapietro K, Csendes A, Salazar G, Echenique C, Lisboa C, *et al.* Changes in resting energy expenditure and body composition after weight loss following Roux-en-Y gastric bypass. *Obesity Surgery*. 2007; 17(5):608-616.

136. Nickel C, Widermann C, Harms D, Leiberich PL, Tritt K, Kettler C, *et al.* Patients with extreme obesity: change in mental symptoms three years after gastric banding. *International Journal of Psychiatry In Medicine*. 2005; 35(2):109-122.

137. Colles SL, Dixon JB, O'Brien PE. Hunger control and regular physical activity facilitate weight loss after laparoscopic adjustable gastric banding. *Obesity Surgery*. 2008; 18(7):833-840.

138. Ruiz-Tovar J, Zubiaga L, Llavero C, Diez M, Arroyo A, Calpena R. Serum cholesterol by morbidly obese patients after laparoscopic sleeve gastrectomy and additional physical activity. *Obesity Surgery*. 2014; 24(3):385-389.

139. Ben-Dov I, Grossman E, Stein A, Shachor D, Gaides M. Marked weight reduction lowers resting and exercise blood pressure in morbidly obese subjects. *American Journal of Hypertension*. 2000; 13(3):251-255.

140. Taylor HL, Jacobs DR, Jr., Schucker B, Knudsen J, Leon AS, Debacker G. A questionnaire for the assessment of leisure time physical activities. *Journal of Chronic Diseases* 1978; 31(12):741-755.

141. Tudor-Locke C, Bassett DR, Jr. How many steps/day are enough? Preliminary pedometer indices for public health. *Sports Medicine*. 2004; 34(1):1-8.

142. Wise RA, Brown CD. Minimal clinically important differences in the six-minute walk test and the incremental shuttle walking test. *Journal of Chronic Obstructive Pulmonary Disease*. 2005; 2(1):125-129.

143. Alghadir A, Anwer S, Brismee JM. The reliability and minimal detectable change of Timed Up and Go test in individuals with grade 1 - 3 knee osteoarthritis. *BioMed Central Musculoskeletal Disorders* 2015; 16(1):174-181.

144. Perera S, Mody SH, Woodman RC, Studenski SA. Meaningful change and responsiveness in common physical performance measures in older adults. *Journal of the American Geriatrics Society* 2006; 54(5):743-749.

145. O'Brien PE, McPhail T, Chaston TB, Dixon JB. Systematic review of medium-term weight loss after bariatric operations. *Obesity Surgery*. 2006; 16(8):1032-1040.

146. Johannsen DL, Knuth ND, Huizenga R, Rood JC, Ravussin E, Hall KD. Metabolic Slowing with Massive Weight Loss despite Preservation of Fat-Free Mass. *The Journal of Clinical Endocrinology and Metabolism*. 2012; 97(7):2489-2496.

147. Shada AL, Hallowell PT, Schirmer BD, Smith PW. Aerobic exercise is associated with improved weight loss after laparoscopic adjustable gastric banding. *Obesity Surgery*. 2013; 23(5):608-612.

148. Wyrwich KW, Fihn SD, Tierney WM, Kroenke K, Babu AN, Wolinsky FD. Clinically important changes in health-related quality of life for patients with chronic obstructive pulmonary disease: an expert consensus panel report. *Journal of General Internal Medicine* 2003; 18(3):196-202.

149. Arokoski MH, Haara M, Helminen HJ, Arokoski JP. Physical function in men with and without hip osteoarthritis. *Archives of Physical Medicine and Rehabilitation*. 2004; 85(4):574-581.

150. Sanderson S, Tatt ID, Higgins JP. Tools for assessing quality and susceptibility to bias in observational studies in epidemiology: a systematic review and annotated bibliography. *International Journal of Epidemiology*. 2007; 36(3):666-676.

151. The Health Survey for England - 2012 trend tables [Internet]. Health and Social Care Information Centre. 2013 [cited October 2015]. Available from: http://www.hscic.gov.uk/catalogue/PUB13219.

152. National Institute for Health and Care Excelence (NICE). Implantation of a duodenal–jejunal bypass sleeve for managing obesity 2013. Available from: http://www.nice.org.uk/guidance/ipg471/resources/guidance-implantation-of-a-duodenaljejunal-bypass-sleeve-for-managing-obesity-pdf.

153. Picot J, Jones J, Colquitt JL, Gospodarevskaya E, Loveman E, Baxter L, *et al.* The clinical effectiveness and cost-effectiveness of bariatric (weight loss) surgery for obesity: a systematic review and economic evaluation. *Health Technology Assessment*. 2009; 13(41): 215-357.

154. Foster SA, Hambright DS, Antoci V, Greene ME, Malchau H, Kwon YM. Effects of Obesity on Health Related Quality of Life Following Total Hip Arthroplasty. *The Journal of Arthroplasty*. 2015; 30(9):1551-1554.

155. Royal Berkshire NHS Foundation Trust. Annual Report and Financial Statements for the period 1 April 2014 - 31 March 2015. 2015.

156. Welbourne R, Fiennes A, Walton P, Kingsman R. The NBSR National Bariatric Surgery Registry First Registry Report to March 2010. Oxfordshire, England: 2011.

157. British Heart Foundation. High cholesterol 2015 [Date; cited 2015 27 October]. Available from: https://www.bhf.org.uk/heart-health/risk-factors/high-cholesterol.

158. Cancer Research UK. Your body and calcium 2014 [Date; cited 2015 27 October]. Available from: http://www.cancerresearchuk.org/about-cancer/coping-with-cancer/coping-physically/calcium/your-body-and-calcium.

159. Diabetes. Guide to HbA1c 2015 [Date; cited 2015 27 October]. Available from: http://www.diabetes.co.uk/what-is-hba1c.html.

160. Kuchler F, Variyam JN. Mistakes were made: misperception as a barrier to reducing overweight. *International Journal of Obesity and Related Metabolic Disorders*. 2003; 27(7):856-861.

161. Chang S, Stoll CT, Song J, Varela J, Eagon CJ, Colditz GA. The effectiveness and risks of bariatric surgery: An updated systematic review and meta-analysis, 2003-2012. *The Journal of the American Medical Association Surgery*. 2014; 149(3):275-287.

162. O'Brien PE, MacDonald L, Anderson M, Brennan L, Brown WA. Long-term outcomes after bariatric surgery: fifteen-year follow-up of adjustable gastric banding and a systematic review of the bariatric surgical literature. *Annals of Surgery*. 2013; 257(1):87-94.

163. Fuchs HF, Broderick RC, Harnsberger CR, Chang DC, Sandler BJ, Jacobsen GR, *et al.* Benefits of bariatric surgery do not reach obese men. *Journal of Laparoendoscopic and Advanced Surgical Techniques Part A*. 2015; 25(3):196-201.

164. Santry HP, Gillen DL, Lauderdale DS. TRends in bariatric surgical procedures. *The Journal of the American Medical Association*. 2005; 294(15):1909-1917.

165. Benotti PN, Still CD, Wood GC, Akmal Y, King H, El Arousy H, *et al.* Preoperative weight loss before bariatric surgery. *Archives of Surgery*. 2009; 144(12):1150-1155.

166. Gerber P, Anderin C, Thorell A. Weight loss prior to bariatric surgery: an updated review of the literature. *Scandinavian Journal of Surgery : SJS : Official Organ for the Finnish Surgical Society and the Scandinavian Surgical Society*. 2015; 104(1):33-39.

167. Puzziferri N, Roshek TB, Iii, Mayo HG, Gallagher R, Belle SH, *et al.* Long-term follow-up after bariatric surgery: A systematic review. *The Journal of the American Medical Association*. 2014; 312(9):934-942.

168. Sampalis JS, Liberman M, Auger S, Christou NV. The impact of weight reduction surgery on health-care costs in morbidly obese patients. *Obesity Surgery*. 2004; 14(7):939-947.

169. Schauer PR, Burguera B, Ikramuddin S, Cottam D, Gourash W, Hamad G, *et al.* Effect of laparoscopic Roux-en Y gastric bypass on type 2 diabetes mellitus. *Annals of Surgery*. 2003; 238(4):465-484.

170. Rosa G, Mingrone G, Manco M, Euthine V, Gniuli D, Calvani R, *et al.* Molecular mechanisms of diabetes reversibility after bariatric surgery. *International Journal of Obesity*. 2007; 31(9):1429-1436.

171. Schernthaner G, Morton JM. Bariatric surgery in patients with morbid obesity and type 2 diabetes. *Diabetes Care*. 2008; 31(2):297-302.

172. Coen PM, Menshikova EV, Distefano G, Zheng D, Tanner CJ, Standley RA, *et al.* Exercise and Weight Loss Improve Muscle Mitochondrial Respiration, Lipid Partitioning, and Insulin Sensitivity After Gastric Bypass Surgery. *Diabetes*. 2015; 64(11):3737-3750.

173. Borai A, Livingstone C, Abdelaal F, Bawazeer A, Keti V, Ferns G. The relationship between glycosylated haemoglobin (HbA1c) and measures of insulin resistance across a range of glucose tolerance. *Scandinavian Journal of Clinical and Laboratory Investigation*. 2011; 71(2):168-172.

174. Garcia-Marirrodriga I, Amaya-Romero C, Ruiz-Diaz GP, Fernandez S, Ballesta-Lopez C, Pou JM, *et al.* Evolution of lipid profiles after bariatric surgery. *Obesity Surgery*. 2012; 22(4):609-616.

175. Groen VA, van de Graaf VA, Scholtes VA, Sprague S, van Wagensveld BA, Poolman RW. Effects of bariatric surgery for knee complaints in (morbidly) obese adult patients: a systematic review. *Obesity Reviews*. 2015; 16(2):161-170.

176. Sparks JA, Halperin F, Karlson JC, Karlson EW, Bermas BL. Impact of bariatric surgery on patients with rheumatoid arthritis. *Arthritis Care and Research*. 2015; 67(12):1619-1626.

177. Hoerger TJ, Zhang P, Segel JE, Kahn HS, Barker LE, Couper S. Cost-effectiveness of bariatric surgery for severely obese adults with diabetes. *Diabetes Care*. 2010; 33(9):1933-1939.

178. Schoffman DE, Wilcox S, Baruth M. Association of Body Mass Index with Physical Function and Health-Related Quality of Life in Adults with Arthritis. *Arthritis*. 2013; 2013:1-10.

179. Porth C. Pathophysiology: Concepts of Altered Health States. Philadelphia: Lippincott 1998.

180. Mehrotra C, Chudy N, Thomas V. Obesity and physical inactivity among Wisconsin adults with arthritis. *Wisconsin Medical Society: Official Publication of the State Medical Society of Wisconsin*. 2003; 102(7):24-28.

181. Brethauer SA, Chand B, Schauer PR. Risks and benefits of bariatric surgery: current evidence. *Cleveland Clinic Journal of Medicine*. 2006; 73(11):993-1007.

182. Shah M, Simha V, Garg A. Long-Term Impact of Bariatric Surgery on Body Weight, Comorbidities, and Nutritional Status. *The Journal of Clinical Endocrinology and Metabolism*. 2006; 91(11):4223-4231.

183. Chaston TB, Dixon JB, O'Brien PE. Changes in fat-free mass during significant weight loss: a systematic review. *International Journal of Obesity*. 2007; 31(5):743-750.

184. Singh SJ, Jones PW, Evans R, Morgan MD. Minimum clinically important improvement for the incremental shuttle walking test. *Thorax*. 2008; 63(9):775-777.

185. Sedgwick P. The importance of statistical power. *British Medical Journal*. 2013; 347.

186. Windsor PM, Nicol KF, Potter J. A randomized, controlled trial of aerobic exercise for treatment-related fatigue in men receiving radical external beam radiotherapy for localized prostate carcinoma. *Cancer*. 2004; 101(3):550-557.

187. Department of Health. National Service Framework for Coronary Heart Disease Modern Standards & Service Models London: Crown; 2000.

188. Okay DM, Jackson PV, Marcinkiewicz M, Papino MN. Exercise and obesity. *Primary Care*. 2009; 36(2):379-393.

189. Lewis ME, Newall C, Townend JN, Hill SL, Bonser RS. Incremental shuttle walk test in the assessment of patients for heart transplantation. *Heart*. 2001; 86(2):183-187.

190. Revill SM, Morgan MD, Singh SJ, Williams J, Hardman AE. The endurance shuttle walk: a new field test for the assessment of endurance capacity in chronic obstructive pulmonary disease. *Thorax*. 1999; 54(3):213-222.

191. Dourado VZ, Guerra RL, Tanni SE, Antunes LC, Godoy I. Reference values for the incremental shuttle walk test in healthy subjects: from the walk distance to physiological responses. *The Brazilian Journal of Pulmonology and International Databases*. 2013; 39(2):190-197.

192. Parreira V, Janaudis-Ferreira T, Evans R, Mathur S, Goldstein RS, Brooks D. Measurement Properties of the Incremental Shuttle Walk Test: A Systematic Review. *Chest*. 2014; 145(6):1357-1369.

193. MacSween A, Brydson G, Creed G, Capell HA. A Preliminary Validation of the 10-metre Incremental Shuttle Walk Test as a Measure of Aerobic Capacity in Women with Rheumatoid Arthritis. *Physiotherapy*. 87(1):38-44.

194. Kushner RF, Kunigk A, Alspaugh M, Andronis PT, Leitch CA, Schoeller DA. Validation of bioelectrical-impedance analysis as a measurement of change in body composition in obesity. *Am J Clin Nutr*. 1990; 52(2):219-223.

195. Harvard T.H. Chan School of Public Health. Waist Size Matters 2015 [Date; cited 2015 29 November]. Available from: http://www.hsph.harvard.edu/obesity-prevention-source/obesity-definition/abdominal-obesity/.

196. Blood Pressure Asscoiation. What is normal blood pressure? 2008 [Date; cited 2015 20 November]. Available from: http://www.bloodpressureuk.org/BloodPressureandyou/Thebasics/Whatisnormal.

197. Santos-Lozano A, Marin PJ, Torres-Luque G, Ruiz JR, Lucia A, Garatachea N. Technical variability of the GT3X accelerometer. *Medical Engineering and Physics*. 2012; 34(6):787-790.

198. Atkin AJ, Gorely T, Clemes SA, Yates T, Edwardson C, Brage S, *et al*. Methods of Measurement in epidemiology: sedentary Behaviour. *International Journal of Epidemiology*. 2012; 41(5):1460-1471.

199. Freedson PS, Melanson E, Sirard J. Calibration of the Computer Science and Applications, Inc. accelerometer. *Medicine and Science in Sports and Exercise*. 1998; 30(5):777-781.

200. Wolin KY, Heil DP, Askew S, Matthews CE, Bennett GG. Validation of the International Physical Activity Questionnaire-Short Among Blacks. *Journal of Physical Activity and Health*. 2008; 5(5):746-760.

201. Bandura A. Self-Efficacy Beliefs of Adolescents Information Age Publishing, Inc 2006.

202. Ryan R, Frederick C, Lepes D, Rubio N, Sheldon K. Intrinsic motivation and exercise adherence. *International Journal of Sport Psychology*. 1997; 28(4):335-354.

203. Snaith R. The Hospital Anxiety And Depression Scale. *Health and Quality of Life Outcomes*. 2003; 29(1):1-4.

204. Herrmann C. International experiences with the Hospital Anxiety and Depression Scale--a review of validation data and clinical results. *Journal of Psychosomatic Research*. 1997; 42(1):17-41.

205. Gersovitz M, Madden JP, Smiciklas-Wright H. Validity of the 24-hr. dietary recall and seven-day record for group comparisons. *Journal of the American Dietetic Association*. 1978; 73(1):48-55.

206. Cade J, Thompson R, Burley V, Warm D. Development, validation and utilisation of food-frequency questionnaires - a review. *Public Health Nutrition*. 2002; 5(4):567-587.

207. Streiner D, Geddes J. Intention to treat analysis in clinical trials when there are missing data. *Evidence Based Mental Health*. 2001; 4(3):70-71.

208. Wilson DB. Practical Meta-Analysis Effect Size Calculator: The Campbell Collaboration; [Date; cited 2015 21 November]. Available from: http://www.campbellcollaboration.org/resources/effect_size_input.php.

209. Field A, editor. Discovering Statistics Using SPSS (Introducing Statistical Methods). 3rd ed. London: SAGE Publications LTD 2009.

210. Doll HA, Petersen SE, Stewart-Brown SL. Obesity and physical and emotional well-being: associations between body mass index, chronic illness, and the physical and mental components of the SF-36 questionnaire. *Obesity Research*. 2000; 8(2):160-170.

211. Singh SJ, Morgan MD, Hardman AE, Rowe C, Bardsley PA. Comparison of oxygen uptake during a conventional treadmill test and the shuttle walking test in chronic airflow limitation. *The European Respiratory Journal*. 1994; 7(11):2016-2020.

212. Pulz C, Diniz RV, Alves ANF, Tebexreni AS, Carvalho AC, de Paola ÂAV, *et al.* Incremental shuttle and six-minute walking tests in the assessment of functional capacity in chronic heart failure. *The Canadian Journal of Cardiology*. 2008; 24(2):131-135.

213. Braun LT. Exercise physiology and cardiovascular fitness. *The Nursing Clinics of North America*. 1991; 26(1):135-147.

214. Moritz SE, Feltz DL, Fahrbach KR, Mack DE. The relation of self-efficacy measures to sport performance: a meta-analytic review. *Research Quarterly for Exercise and Sport*. 2000; 71(3):280-294.

215. Schunk DH. Self-efficacy, motivation, and performance. *Journal of Applied Sport Psychology*. 1995; 7(2):112-137.

216. Hulens M, Vansant G, Claessens AL, Lysens R, Muls E. Predictors of 6-minute walk test results in lean, obese and morbidly obese women. *Scandinavian Journal of Medicine and Science in Sports*. 2003; 13(2):98-105.

217. Whitney SL, Wrisley DM, Marchetti GF, Gee MA, Redfern MS, Furman JM. Clinical Measurement of Sit-to-Stand Performance in People With Balance Disorders: Validity of Data for the Five-Times-Sit-to-Stand Test. *Physical Therapy*. 2005; 85(10):1034-1045.

218. Jones SE, Kon SS, Canavan JL, Patel MS, Clark AL, Nolan CM, *et al.* The five-repetition sit-to-stand test as a functional outcome measure in COPD. *Thorax*. 2013; 68(11):1015-1020.

219. Roberts HC, Denison HJ, Martin HJ, Patel HP, Syddall H, Cooper C, *et al.* A review of the measurement of grip strength in clinical and epidemiological studies: towards a standardised approach. *Age Ageing*. 2011; 40(4):423-429.

220. Subasi S, Inal-Ince D, Calik E, Vardar-Yagli N, Saglam M, Erdem F, *et al.* Clinical determinants of incremental shuttle walk test in bronchiectasis. *European Respiratory Journal*. 2013; 42(57):P5066.

221. Ozalevli S, Ozden A, Itil O, Akkoclu A. Comparison of the Sit-to-Stand Test with 6min walk test in patients with chronic obstructive pulmonary disease. *Respiratory Medicine*. 2007; 101(2):286-293.

222. Miller WC, Koceja DM, Hamilton EJ. A meta-analysis of the past 25 years of weight loss research using diet, exercise or diet plus exercise intervention. *International Journal of Obesity and Related Metabolic Disorders*. 1997; 21(10):941-947.

223. American Society of Metabolic and Bariatric Surgery. ASMBS Public and Professional Education Committee Bariatric Surgery: Postoperative Concerns. 2008.

224. Nicolai SP, Kruidenier LM, Leffers P, Hardeman R, Hidding A, Teijink JA. Supervised exercise versus non-supervised exercise for reducing weight in obese adults. *The Journal of Sports Medicine and Physical Fitness*. 2009; 49(1):85-90.

225. Mayo MJ, Grantham JR, Balasekaran G. Exercise-induced weight loss preferentially reduces abdominal fat. *Medicine and Science in Sports and Exercise*. 2003; 35(2):207-213.

226. National Obesity Forum. Waist circumference 2006 [Date; cited 2015 19 November]. Available from: http://www.nationalobesityforum.org.uk/index.php/healthcare-professionals/assessment-mainmenu-168/171-waist-circumference.html.

227. Sarsan A, Ardic F, Ozgen M, Topuz O, Sermez Y. The effects of aerobic and resistance exercises in obese women. *Clinical Rehabilitation*. 2006; 20(9):773-782.

228. Lanza IR. Enhancing the Metabolic Benefits of Bariatric Surgery: Tipping the Scales With Exercise. *Diabetes*. 2015; 64(11):3656-3658.

229. Doucet É, King N, Levine JA, Ross R. Update on Exercise and Weight Control. *Journal of Obesity*. 2011; 2011:1-3.

230. De Feo P. Is high-intensity exercise better than moderate-intensity exercise for weight loss? *Nutrition, Metabolism and Cardiovascular Diseases*. 2013; 23(11):1037-1042.

231. Courneya KS, Friedenreich CM, Reid RD, Gelmon K, Mackey JR, Ladha AB, *et al.* Predictors of follow-up exercise behavior 6 months after a randomized trial of exercise training during breast cancer chemotherapy. *Breast Cancer Research and Treatment*. 2009; 114(1):179-187.

232. Moore G, Moore L, Murphy S. Facilitating adherence to physical activity: exercise professionals' experiences of the National Exercise Referral Scheme in Wales. a qualitative study. *BioMed Central Public Health*. 2011; 11(1):1-12.

233. Mechanick JI, Kushner RF, Sugerman HJ, Gonzalez-Campoy JM, Collazo-Clavell ML, Spitz AF, *et al.* American Association of Clinical Endocrinologists, The Obesity Society, and American Society for Metabolic & Bariatric Surgery medical guidelines for clinical practice for the perioperative nutritional, metabolic, and nonsurgical support of the bariatric surgery patient. *Obesity*. 2009; 17(1):3-72.

234. Mayo Clinic Staff. Tests and Procedures Cholesterol test 2014 [Date; cited 2015 20 November]. Available from: http://www.mayoclinic.org/tests-procedures/cholesterol-test/basics/results/prc-20013282.

235. Mayo Clinic Staff. Tests and Procedures A1C test 2013 [Date; cited 2015 20 November]. Available from: http://www.mayoclinic.org/tests-procedures/a1c-test/basics/results/prc-20012585.

236. British Heart Foundation. High blood pressure 2015 [Date; cited 2015 11 November]. Available from: https://www.bhf.org.uk/heart-health/risk-factors/high-blood-pressure.

237. Tae B, Pelaggi ER, Moreira JG, Waisberg J, de Matos LL, D'Elia G. Impact of bariatric surgery on depression and anxiety symptons, bulimic behaviors and quality of life. *Revista do Colegio Brasileiro de Cirurgioes*. 2014; 41(3):155-160.

238. Latham N, Liu C-j. Strength training in older adults: The benefits for osteoarthritis. *Clinics in Geriatric Medicine*. 2010; 26(3):445-459.

239. Kaleta D, Kwasniewska M, Bednarek-Gejo A, Dziankowska-Zaborszczyk E, Jegier A, Kostka T, *et al*. Body weight change and health outcomes in middle-aged men--a prospective study results. *Przegl Lek*. 2005; 62(3):18-22.

240. Coen PM, Goodpaster BH. A role for exercise after bariatric surgery? *Diabetes, Obesity and Metabolism*. 2015.

241. Donnelly JE, Blair SN, Jakicic JM, Manore MM, Rankin JW, Smith BK. American College of Sports Medicine Position Stand. Appropriate physical activity intervention strategies for weight loss and prevention of weight regain for adults. *Medicine and Science in Sports and Exercise*. 2009; 41(2):459-471.

242. Karlsson J, Taft C, Ryden A, Sjostrom L, Sullivan M. Ten-year trends in health-related quality of life after surgical and conventional treatment for severe obesity: the SOS intervention study. *International Journal of Obesity*. 2007; 31(8):1248-1261.

Appendices

Appendix 2.1: Systematic review search strategy

Bariatric surgery

1. (MH "Bariatric Surgery+") (12,332)
2. AB "bariatric surg*" OR TI "bariatric surg*" (5,201)
3. AB "antiobesity surg*" OR TI "antiobesity surg*" (18)
4. AB ("anti£obesity surg*" or "anti#obesity surg*") OR TI ("anti£obesity surg*" or "anti#obesity surg*") (28)
5. AB "Obesity surg*" OR TI "Obesity surg*" (503)
6. AB (Gastroplasty or gastro£gastostomy or gastro#gastostomy or "gastric bypass" or "gastric surg*" or "restrict* surg*") OR TI (Gastroplasty or gastro£gastostomy or gastro#gastostomy or "gastric bypass" or "gastric surg*" or "restrict* surg*") (7,616)
7. (MH "Gastric Bypass") (4,417)
8. AB "Gastric Bypass" OR TI "Gastric Bypass" (4,701)
9. (MH "Jejunoileal Bypass") (540)
10. AB "Jejunoileal Bypass" OR TI "Jejunoileal Bypass" (773)
11. AB ("Jejuno#ileal Bypass" or "Jejuno£ileal Bypass") OR TI ("Jejuno#ileal Bypass" or "Jejuno£ileal Bypass") (956)
12. AB "Metabolic surg*" OR TI "Metabolic surg*" (117)
13. AB "gastrointestinal surg*" OR TI "gastrointestinal surg*" (1,515)
14. AB "gastrointestinal diver*" OR TI "gastrointestinal diver*" (19)
15. (MH "Biliopancreatic Diversion") (710)
16. AB "Biliopancreatic Diversion" OR TI "Biliopancreatic Diversion" (604)
17. AB ("Bilio#pancreatic Diversion" or "Bilio£pancreatic Diversion") OR TI ("Bilio#pancreatic Diversion" or "Bilio£pancreatic Diversion") (645)
18. AB ("Bilio#pancreatic bypass" or "Bilio£pancreatic bypass") OR TI ("Bilio#pancreatic bypass" or "Bilio£pancreatic bypass") (62)
19. AB "Gastric band*" OR TI "Gastric band*" (2,171)
20. AB "Silicon band*" OR TI "Silicon band*" (23)
21. AB "Biliopancreatic bypass" OR TI "Biliopancreatic bypass" (50)
22. (MH "Gastroenterostomy+") (7,152)
23. AB "Gastroenterostomy" OR TI "Gastroenterostomy" (711)
24. AB "Gastrectomy" OR TI "Gastrectomy" (15,704)
25. AB "Gastroplasty" OR TI "Gastroplasty" (1,468)
26. AB LAGB OR TI LAGB (598)
27. AB "stomach stap*" OR TI "stomach stap*" (9)
28. AB "lap* band*" OR TI "lap* band*" (276)
29. AB ("lap-band*" or "lap#and*" or "lap£band*") OR TI ("lap-band*" or "lap#and*" or "lap£band*") (386)
30. AB "malabsorptive surg*" OR TI "malabsorptive surg*" (22)
31. AB "malabsorptive procedure*" OR TI "malabsorptive procedure*" (91)
32. AB "mason* procedure*" OR TI "mason* procedure*" (19)
33. AB ("Roux-en-Y" or "Roux£en£Y" or "Roux#en#Y") OR TI ("Roux-en-Y" or "Roux£en£Y" or "Roux#en#Y") (5,023)
34. AB "anastomosis Roux-en-Y" OR TI "anastomosis Roux-en-Y" (8)
35. AB "duodenal switch*" OR TI "duodenal switch*" (374)
36. AB "restrict* surg*" OR TI "restrict* surg*" (172)
37. (S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36) (38,360)

Physical activity/ exercise and physical function

38. (MH "Exercise+") (98,038)
39. AB (Exercise* or "physic* activ*" or exert* or "physic* fit*" or sport*) OR TI (Exercise* or "physic* activ*" or exert* or "physic* fit*" or sport*) (392,105)
40. AB (Walk* or Jog* or swim*) OR TI (Walk* or Jog* or swim*) (85,055)
41. AB ("weight lift*" or "strength train*" or "resistance train*" or "circuit weight train*" or "aerob* train*") OR TI ("weight lift*" or "strength train*" or "resistance train*" or "circuit weight train*" or "aerob* train*") (7,293)
42. (MH "Physical Exertion") (51,460)
43. (MH "Physical Education and Training+") (12,857)
44. (MH "Physical Fitness") (20,203)
45. AB ("Physical* Fit*" or "Physical*-Fit*" or "Physical*#Fit*" or "Physical*£Fit*" or "physical* func*" or "function* capac*") OR TI ("Physical* Fit*" or "Physical*-Fit*" or "Physical*#Fit*" or "Physical*£Fit*" or "physical* func*" or "function* capac*") (24,203)
46. AB sport* OR TI sport* (36,971)
47. (MH "Sedentary Lifestyle") (1,554)
48. AB ("Sedent* Lifestyle" or "sedent* behav*") OR TI ("Sedent* Lifestyle" or "sedent* behav*") (2,820)
49. AB Active* OR TI Active* (641,465)
50. AB "motor activ*" or “exercise* test*” OR TI "motor activ*" or “exercise* test*” (29,786)
51. AB ("musculoskeletal fit*" or "aerobic fit*") OR TI ("musculoskeletal fit*" or "aerobic fit*") (1,580)
52. AB ("phyisical* behav*" or "physical* train*") OR TI ("phyisical* behav*" or "physical* train*") (4,323)
53. AB ("cardio* fit*" or "cardio* endurance") OR TI ("cardio* fit*" or "cardio* endurance") (2,712)
54. (MH “Muscle Strength+”) (14,193)
55. (S38 OR S39 OR S40 OR S41 OR S42 OR S43 OR S44 OR S45 OR S46 OR S47 OR S48 OR S49 OR S50 OR S51 OR S52 OR S53 OR S54) (1,154,157)
56. S37 AND S55 (1,339)

Methodological terms

57. S37 AND S55 **Limiters** - Publication Type: Clinical Trial, Clinical Trial, Phase III, Clinical Trial, Phase IV, Comparative Study, Controlled Clinical Trial, Evaluation Studies, Multicenter Study, Randomized Controlled Trial, Twin Study, Validation Studies (222)
58. (MH "Cohort Studies+") (1,210,613)
59. (MH "Randomized Controlled Trials as Topic+") (82,664)
60. (MH "Prospective Studies") (327,650)
61. (MH "Evaluation Studies as Topic+") (932,284)
62. (MH "Follow-Up Studies") (454,819)
63. AB (control* or prospectiv* or volunteer*or placebo* or random*) OR TI (control* or prospectiv* or volunteer*or placebo* or random*) (2,923,853)
64. (S58 OR S59 OR S60 OR S61 OR S62 OR S63) (4,366,851)
65. S56 AND S64 (584)
66. S57 OR S65 (507)
67. S57 OR S65 **Limiters** - Human; Age Related: Young Adult: 19-24 years, Adult: 19-44 years, Middle Aged: 45-64 years, Middle Aged + Aged: 45 + years, Aged: 65+ years, Aged, 80 and over, All Adult: 19+ years (343)

Appendix 5.1: The MOTION Study's NHS Ethical Approval.

University Hospitals of Leicester NHS
NHS Trust

DIRECTORATE OF RESEARCH & DEVELOPMENT

Director: **Professor N Brunskill**
Assistant Director: **Dr David Hetmanski**
R&D Manager: **Carolyn Maloney**

Research & Development Office
Leicester General Hospital
Gwendolen Road
Leicester
LE5 4PW

Direct Dial: (0116) 258 8351
Fax No: (0116) 258 4226

21 January 2014

Prof Melanie Davies
Leicester Diabetes Unit
The University of Leicester
Leicester Diabetes Centre, Leicester General Hospital
Leicester
LE5 4PW

Dear Prof Davies,

Ref: **UHL 120659**
Title: **The effect of implementing a 12 week supervised exercise programme 12 to 24 months post bariatric surgery on physical function and physical activity maintenance.**
Project Status: **Approved**
End Date: **01/12/2014**

I am pleased to confirm that with effect from the date of this letter, the above study has Trust Research & Development permission to commence at University Hospitals of Leicester NHS Trust. The research must be conducted in line with the Protocol and fulfil any contractual obligations agreed with the Sponsor. If you identify any issues during the course of your research that are likely to affect these obligations you must contact the R&D Office.

In order for the UHL Trust to comply with targets set by the Department of Health through the 'Plan for Growth', there is an expectation that the first patient will be recruited within 30 days of the date of this letter. If there is likely to be a problem achieving this target, please contact the office as soon as possible. You will be asked to provide the date of the first patient recruited in due course. In addition, the Title, REC Reference number, local target recruitment and actual recruitment for this study will be published on a quarterly basis on the UHL Trust external website.

All documents received by this office have been reviewed and form part of the approval. The documents received and approved are as follows:

Document Title	Version	Date	REC Approval
REC Favourable opinion letter	N/A	27/11/13	N/A
REC letter-conditions met.	N/A	10/12/13	N/A
GP/Consultant Information Sheets-Baseline	1	24/07/13	10/12/13
Participant baseline results letter	1	24/07/13	10/12/13
Participant 3 month results letter	1	24/07/13	10/12/13
Participant 6 month results letter	1	24/07/13	10/12/13
GP Letter-3 months	1	24/07/13	10/12/13
GP Letter-6 months	1	24/07/13	10/12/13

Version 11, 16/10/2012

Hospital Anxiety and Depression Score Sheet	1	24/07/13	10/12/13
24 Hour Dietary Recall Sheet	1	24/07/13	10/12/13
Example Exercise Programme Card	1	24/07/13	10/12/13
Exercise Intensity Card	1	24/07/13	10/12/13
Letter of Invitation	2	27/11/13	10/12/13
Participant Consent Form	2	27/11/13	10/12/13
Participant Information Sheet	2	27/11/13	10/12/13
Protocol	1	24/07/13	10/12/13
Questionnaire: Internal Physical Activity Questionnaire (Oct 2002)	1	Oct 2002	10/12/13
Questionnaire: Self Efficacy to Regulate Exercise/Physical Activity	1	24/07/13	10/12/13

Please be aware that any changes to these documents after approval may constitute an amendment. The process of approval for amendments should be followed. Failure to do so may invalidate the approval of the study at this trust.

Undertaking research in the NHS comes with a range of regulatory responsibilities. Please ensure that you and your research team are familiar with, and understand the roles and responsibilities both collectively and individually.

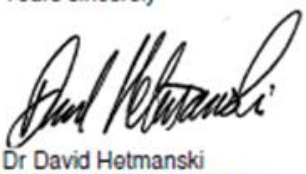
Documents listing the roles and responsibilities for all individuals involved in research can be found on the R&D pages of the Public Website. It is important that you familiarise yourself with the Standard Operating Procedures, Policies and all other relevant documents which can be located by visiting www.leicestershospitals.nhs.uk/aboutus/education-and-research

The R&D Office is keen to support and facilitate research where ever possible. If you have any questions regarding this or other research you wish to undertake in the Trust, please contact this office. Our contact details are provided on the attached sheet.

This study has been reviewed and processed by the Leicestershire, Northamptonshire & Rutland Comprehensive Local Research Network (LNR CLRN) using the Coordinated System for gaining Trust Permission (CSP). If you require any further information on the approval of this study please contact the LNR CLRN office on 0116 258 6185 making reference to the CSP number which is located at the top of this letter.

We wish you every success with your research.

Yours sincerely



Dr David Hetmanski
Assistant Director R&D

Encs: .R&D Office Contact Information

Appendix 5.2: The MOTION Study's Participant Information Sheet

NIHR Leicester-Loughborough
Diet, Lifestyle and Physical Activity
Biomedical Research Unit

MOTION STUDY

The Motion Study
an Exercise Programme

Participant Information Sheet

Version 3, 06/06/2014

Leicester-Loughborough
Diet, Lifestyle and Physical Activity
Biomedical Research Unit

Investigators

The investigators of the current study are all part of the Leicester-Loughborough Diet, Lifestyle and Physical Activity Biomedical Research Unit. They are based at the University of Leicester diabetes research department, the University Hospitals of Leicester NHS trust and the school of sport, exercise and health sciences at Loughborough University. The team are outlined below;

Professor Melanie Davies (Principal investigator)

Louisa Herring (Lead researcher)

Dr Clare Stevinson

Dr Patrice Carter

Professor Stuart Biddle

Dr David Bowrey

Dr Christopher Sutton

Dr Tom Yates

Dr Danielle Bodicoat

Leicester-Loughborough
Diet, Lifestyle and Physical Activity
Biomedical Research Unit

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Leicester-Loughborough
Diet, Lifestyle and Physical Activity
Biomedical Research Unit

The Motion Study – An Exercise Programme

This is your invitation to take part in our study called The Motion Study – An Exercise Programme. Before you decide if you want to take part in the study, it is important that you understand why we are doing the study. Please take the time to carefully read this information leaflet. It may help to talk about it with your friends and family. If there is anything you do not understand or want more information about, please contact one of the research team members and we will be happy to speak to you. Our contact details are on the back page of this leaflet.

What is the purpose of this research study?

Worldwide more and more people are becoming morbidly obese (extremely overweight). Obese people are more likely to suffer from health problems such as type 2 diabetes, heart disease, non-alcoholic fatty liver disease, problems with sleep and some cancers compared to people with a healthy weight. Obesity can also reduce how long people live.

Bariatric surgery is a successful way for obese people to lose weight. However some studies show that after surgery, some people put weight back on. Not everyone puts the same amount of weight back on after surgery. Increasing exercise and physical activity after bariatric surgery can improve weight loss and make daily activities easier; for example walking, house work and playing with children/ grandchildren. This study will offer a 12 week structured and supervised hospital gym based exercise programme at a time where patients often start putting weight back on after weight loss surgery. This study aims to improve movement and physical wellbeing whilst preventing weight regain. The study is being carried out as part of a University PhD research project.

Why have I been invited to take part?

You have been invited to take part in the study because you are over 18 years of age and you have had a bariatric surgery procedure at Leicester Royal Infirmary between 8 and 24 months ago.

Do I have to take part in the study?

No, it is entirely your own decision to take part in the study. If you do decide to take part now but change your mind later, you can stop taking part whenever you want. You don't have to give any reason if you do not want to take part and it will not affect your usual care.

If you do decide to take part in the study you will be asked to sign a consent form. You will keep one copy of this and we will keep another.

If I choose to take part: what will I have to do?

You will need to come to Leicester General Hospital (visit 1) to see the nurse and lead researcher. This does not mean that you are obliged to take part in the study. During this visit you will have time to ask any questions you may want to ask. If you do decide to take part in the study you will be asked to sign a consent form and your GP will be told that you are taking part. If you agree, we will also send a copy of your consent form to your GP.

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Visit 1

Visit 1 is also known as the eligibility and pre intervention assessment. On this visit you will meet the lead researcher and will have an appointment with the nurse. The nurse will do the following:

- Take a full medical history
- Carry out a physical examination
- Take your blood pressure
- Take a resting electrocardiogram (ECG)
- Carry out an exercise electrocardiogram (ECG)

All these will be carried out at Leicester general hospital. Once you are cleared and deemed able to participate in the study by the nurse, the **pre intervention assessment** below will be undertaken.

Pre intervention assessment

A walking test:

- You will be asked to walk 10 meters around two cones a number of times. You will be instructed by an audio tape and also by the researcher to make sure you understand. You will walk around the 10 metre course turning at the cones when the tape beeps. These beeps get closer together as you go up the levels. The researcher will accompany you for the first level to help and then stand midway between the two markers, giving encouragement for the rest of the test. A triple beep indicates the next level has been reached. The aim of the test is to walk for as long as possible. However participants are advised to stop the test when they cannot go any further or any unusual discomfort is experienced. This test is to give an idea of your current activity levels.

A grip strength test:

- The grip strength test involves squeezing a monitor in your hand to measure your grip.

A seat to stand test:

- This test times how long it takes for you to stand up and sit down 5 times in a row.

Body measures:

- Height, weight, body fat, waist circumference, and hip circumference using scales and a tape measure.

Cardiovascular measures:

- Blood pressure, resting heart rate and oxygen saturation using a finger clip.

Diet:

- A 24 hour food recall involves the lead researcher discussing the food you ate and what you drank in the last 24 hours.

Medications:

- We will need you to bring in a current copy of your prescription.

Blood test:

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Diet, Lifestyle and Physical Activity
Biomedical Research Unit

- We will take a blood sample to measure blood sugar and blood fats.

The following questionnaires will be completed:

- An anxiety and depression questionnaire and an activity questionnaire.

Daily activity:

- You will also be asked to wear an activity monitor for one week after your assessment. This will involve wearing a waist and/ or wrist band whichever is most comfortable for you. This equipment is not waterproof so you must remove it when you are in the bath/shower or swimming etc. We will show you how to wear the monitors and will provide you with a stamped addressed envelope for you to return it after 1 week.

The study procedure

After visit 1 you will be randomly assigned to **one** of two groups. This is a bit like tossing a coin to decide which group that you are going to go in. **You or the researcher cannot choose which group you are allocated into.**

Exercise group

If you are randomly allocated for the exercise group you will undertake a 12 week moderate intensity exercise programme. Moderate exercise will make you breathe a little harder and feel a little warmer but you will still be able to hold a conversation. You will attend three 60 minute sessions a week at Leicester General Hospitals diabetes centre gym (this gym is not open to the public). Session times will be as flexible as possible to help you attend as many gym sessions as possible. Exercises will start in their most simple form (very basic techniques) and progress depending on your personal ability. All gym sessions will be supervised. You will be given an exercise programme card which will tell you what exercises to do, for how long and how hard you need to work. The exercise sessions will be performed at a moderate intensity so nothing too strenuous.

After 12 weeks we will repeat the measurements taken at visit 1. This is your 3 month assessment.

After the 3 month assessment you will have an advice session (30 minutes). During this session we will talk about keeping active, goal setting and overcoming barriers. An optional exercise programme of your choice will be offered (e.g. home based, walking outside, gym or swimming) and a diet information sheet will also be provided.

Control group

If you are randomly selected for the control group you will return 12 weeks after your pre intervention assessment so we can repeat the test from visit 1. At this assessment you will be required to submit a record of any structured exercise you have undertaken since your first assessment (e.g. 12/11/2013 – 20minutes swim).

After this 3 month assessment you will receive a 30 minute individual advice session. During this session we will discuss relevant topics (e.g. physical activity and maintenance, overcoming barriers goal setting). You will be offered a personalised exercise programme of your choice to undertake in your own time for the next three months. This can be an exercise programme for home, the gym, walking or swimming it is your choice. A diet information sheet will also be provided.

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Final visit

At 6 months we will ask you to come in for a final visit to repeat the measurements taken at visit 1.

Will there be any adverse effects from any measurements or the exercise?

During any physical activity there is always an increased risk of a heart event or injury. For those without any underlying heart disease, the risks to health are very low. These risks are also lowered because you will be exercising at medium level. There is no vigorous exercise in this study so the risk to health during any prescribed physical activity is minimal. There will be a qualified gym instructor developing and supervising the programmes.

All other measurements are carried out by qualified individuals. A fully qualified nurse from the research team will carry out the blood test to ensure any pain should is kept to a minimum. Some people experience minor discomfort and slight bruising from blood tests.

What if I am harmed by the study?

We do not expect any harm will come to you as a result of taking part in the study. If you are harmed due to negligence, you may have grounds for legal action but you may have to pay for it as there are no special compensation arrangements for this study. If you wish to make a complaint or have any concerns about any aspect of the way you have been approached or treated during the course of the study, the normal National Health Services Complaints procedures are available to you. If you want to make a complaint please contact the Patient Advice and Liaison Service:

Patient Advice and Liaison Service
University Hospitals of Leicester
Gwendolen House
Gwendolen Road,
Leicester
LE5 4QF

Tel: 0808 1788337

Will I benefit from taking part?

You will all (control & exercise group) benefit from a free personalised exercise programme from a trained specialist. You will also receive a free advice session, maintenance exercise programme and diet information. The exercise group will receive free gym sessions at the Leicester General Hospital for 12 weeks.

Both groups will also receive information on your general fitness levels. You will also add to evidence-based exercise information that may improve the treatment for people with obesity and post bariatric surgery aftercare.

Will the exercise sessions or advice session cost me anything?

It is free. You will not be charged for any of the sessions or personalised programmes developed for you during the study.

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Will my taking part in the study be kept confidential?

Yes. We will follow ethical and legal practice in accordance with the Data Protection Act (1998). All information about you will be handled in confidence unless you disclose that you, or someone else, are in immediate danger of serious harm. Access to identifiable data such as your name and address will be limited to selected members of the research team and to auditors for the purpose of monitoring the quality of the research study. No personal details will be included in the analysis, publications or reports. All information collected during the study will be identified by a unique code so that you cannot be identified from it. All data will be kept on secure computer servers and in locked filing cabinets at the University Hospitals of Leicester.

What will be done with the results of the study?

When the study is finished we will send everyone who has taken part and given us their permission to do so a short report. We will present our results at conferences and write articles for scientific journals. Identifiable data will not be included in any of these reports.

Who has reviewed this study?

All research which takes part with NHS patients, NHS staff, uses NHS medical records or takes place on NHS premises must be approved by an NHS Research Ethics Committee before it can start. This study has been approved by West Midlands – Edgbaston REC.

Ethical approval does not guarantee you will not come to any harm if you take part in the study. Approval means that the committee believe your rights will be respected and any risks are kept to a minimum. Approval from the committee means that they think we have given you enough information to let you make an informed decision to take part in the study or not.

Who has funded this study?

This study is funded by The NIHR Leicester-Loughborough Diet, Lifestyle and Physical Activity Biomedical Research Unit which is a partnership between University Hospitals of Leicester NHS Trust, Loughborough University and the University of Leicester.

Will I get any payment for taking part?

No, you will not receive any payment for taking part in the study. You can claim up to £10 for travel expenses for each appointment that you come to as part of the study. Please bring your ticket or receipt with you.

What happens when the research study stops?

When the research study stops you will be advised to continue your activity whether it be home based, swimming, walking, gym based etc. Services to aid physical activity maintenance will be advised such as Leicester City Councils Active Lifestyle Scheme which is 'designed to help those who have medical conditions/physical ailments that could benefit from physical activity, the opportunity to exercise under the guidance of qualified exercise professionals'.

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Is there anything else I need to know?

You should know that any study may need to be checked by a regulatory body. This is to check we are carrying out the study properly. This does not happen to every study, but if it does the regulatory body may need to access your medical notes.

How can I find out more?

The study team members will be happy to answer any questions you might have and give you any more information. The person to contact is:

Louisa Herring

PhD Research Student
Physical Activity, Lifestyle and Bariatric Surgery

Address;
Sir John Beckwith Building
Physical Activity and Public Health Research Group
School of Sport, Exercise and Health Sciences
Loughborough University,
Leicestershire,
LE11 3TU

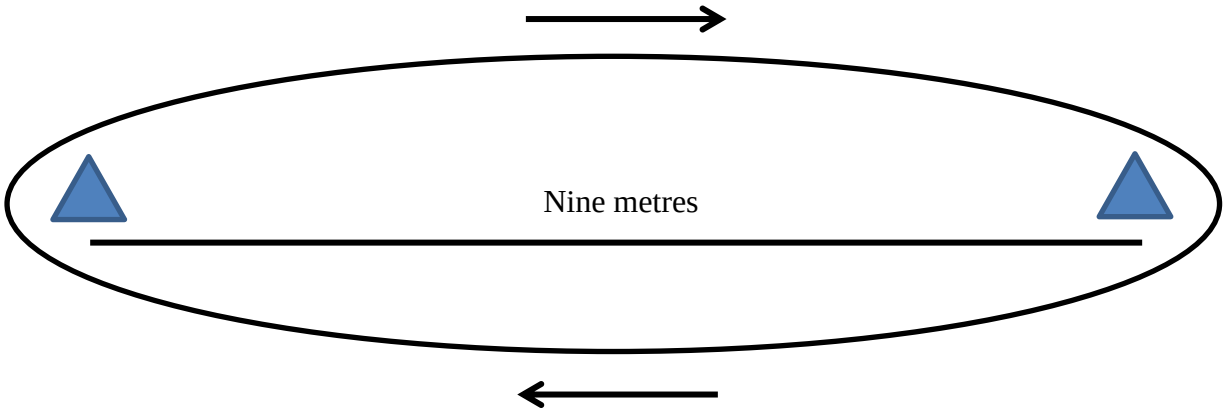
Tel. +44 (0) 1509 226452

Email: l.herring@lboro.ac.uk

Thank you for taking the time to read this information sheet, we look forward to hearing from you.

Appendix 5.3: The ISWT Termination Criteria and Record Sheet

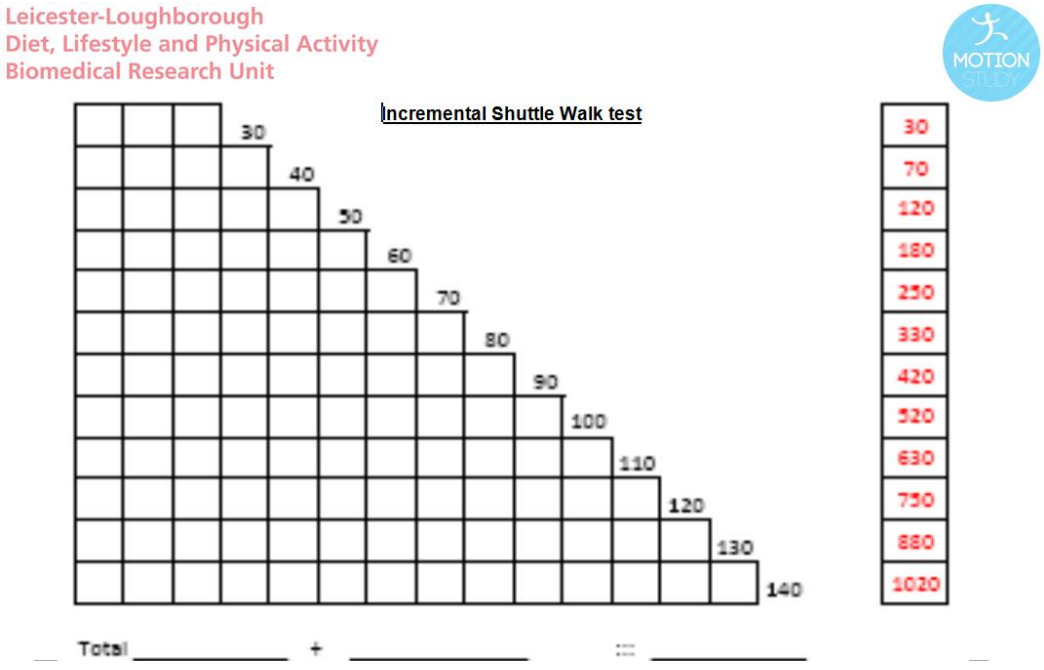
The ISWT termination criteria.



The ISWT ends if any one of the following occur:

- The patient is **more than** 0.5 m away from the cone when the beep sounds (allow one lap to catch up).
- The patient reports that they are too breathless to continue.
- The patient reaches 85% of predicted maximum heart rate
- The patient exhibits any of the following signs and symptoms:
- Chest pain that is suspicious of / for angina.
- Evolving mental confusion or lack of coordination.
- Evolving light-headedness.
- Intolerable dyspnoea.
- Leg cramps or extreme leg muscle fatigue.
- Persistent $SpO_2 \leq 85\%$.
- Any other clinically warranted reason.

The shuttles were recorded on the record sheet below and tallied up upon completion.



Appendix 5.4: The IPAQ Short Form Questionnaire

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE (August 2002)

SHORT LAST 7 DAYS SELF-ADMINISTERED FORMAT

FOR USE WITH YOUNG AND MIDDLE-AGED ADULTS (15-69 years)

The International Physical Activity Questionnaires (IPAQ) comprises a set of 4 questionnaires. Long (5 activity domains asked independently) and short (4 generic items) versions for use by either telephone or self-administered methods are available. The purpose of the questionnaires is to provide common instruments that can be used to obtain internationally comparable data on health–related physical activity.

Background on IPAQ

The development of an international measure for physical activity commenced in Geneva in 1998 and was followed by extensive reliability and validity testing undertaken across 12 countries (14 sites) during 2000. The final results suggest that these measures have acceptable measurement properties for use in many settings and in different languages, and are suitable for national population-based prevalence studies of participation in physical activity.

Using IPAQ

Use of the IPAQ instruments for monitoring and research purposes is encouraged. It is recommended that no changes be made to the order or wording of the questions as this will affect the psychometric properties of the instruments.

Translation from English and Cultural Adaptation

Translation from English is supported to facilitate worldwide use of IPAQ. Information on the availability of IPAQ in different languages can be obtained at www.ipaq.ki.se. If a new translation is undertaken we highly recommend using the prescribed back translation methods available on the IPAQ website. If possible please consider making your translated version of IPAQ available to others by contributing it to the IPAQ website. Further details on translation and cultural adaptation can be downloaded from the website.

Further Developments of IPAQ

International collaboration on IPAQ is on-going and an ***International Physical Activity Prevalence Study*** is in progress. For further information see the IPAQ website.

More Information

More detailed information on the IPAQ process and the research methods used in the development of IPAQ instruments is available at www.ipaq.ki.se and Booth, M.L. (2000). *Assessment of Physical Activity: An International Perspective*. Research Quarterly for Exercise and Sport, 71 (2): s114-20. Other scientific publications and presentations on the use of IPAQ are summarized on the website.

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE

We are interested in finding out about the kinds of physical activities that people do as part of their everyday lives. The questions will ask you about the time you spent being physically active in the **last 7 days**. Please answer each question even if you do not consider yourself to be an active person. Please think about the activities you do at work, as part of your house and yard work, to get from place to place, and in your spare time for recreation, exercise or sport.

Think about all the **vigorous** activities that you did in the **last 7 days**. **Vigorous** physical activities refer to activities that take hard physical effort and make you breathe much harder than normal. Think *only* about those physical activities that you did for at least 10 minutes at a time.

1. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, digging, aerobics, or fast bicycling?

   _____ **days per week**

   ☐ No vigorous physical activities → ***Skip to question 3***

2. How much time did you usually spend doing **vigorous** physical activities on one of those days?

   _____ **hours per day**

   _____ **minutes per day**

   ☐ Don't know/Not sure

Think about all the **moderate** activities that you did in the **last 7 days**. **Moderate** activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal. Think only about those physical activities that you did for at least 10 minutes at a time.

3. During the **last 7 days**, on how many days did you do **moderate** physical activities like carrying light loads, bicycling at a regular pace, or doubles tennis? Do not include walking.

   _____ **days per week**

   ☐ No moderate physical activities → ***Skip to question 5***

4. How much time did you usually spend doing **moderate** physical activities on one of those days?

_____ **hours per day**

_____ **minutes per day**

☐ Don't know/Not sure

Think about the time you spent **walking** in the **last 7 days**. This includes at work and at home, walking to travel from place to place, and any other walking that you have done solely for recreation, sport, exercise, or leisure.

5. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time?

_____ **days per week**

☐ No walking → ***Skip to question 7***

6. How much time did you usually spend **walking** on one of those days?

_____ **hours per day**

_____ **minutes per day**

☐ Don't know/Not sure

The last question is about the time you spent **sitting** on weekdays during the **last 7 days**. Include time spent at work, at home, while doing course work and during leisure time. This may include time spent sitting at a desk, visiting friends, reading, or sitting or lying down to watch television.

7. During the **last 7 days**, how much time did you spend **sitting** on a **week day**?

_____ **hours per day**

_____ **minutes per day**

☐ Don't know/Not sure

This is the end of the questionnaire, thank you for participating.

Appendix 5.5: The Self-Efficacy to Regulate Physical Activity Questionnaire

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Diet, Lifestyle and Physical Activity
Biomedical Research Unit

MOTION STUDY

Self-Efficacy to Regulate Exercise/ Physical Activity

A number of situations are described below that can make it hard to stick to an exercise routine. Please rate in each of the blanks in the column how certain you are that you can get yourself to perform your exercise routine regularly (three or more times a week).

Rate your degree of confidence by recording a number from 0 to 100 using the scale given below:

0	10	20	30	40	50	60	70	80	90	100
Cannot do at all					Moderately can do				Highly certain can do	

	Confidence (0-100)
When I am feeling tired	_____
When I am feeling under pressure from work	_____
During bad weather	_____
After recovering from an injury that caused me to stop exercising	_____
During or after experiencing personal problems	_____
When I am feeling depressed	_____
When I am feeling anxious	_____
After recovering from an illness that caused me to stop exercising	_____
When I feel physical discomfort when I exercise	_____
After a vacation	_____
When I have too much work to do at home	_____
When visitors are present	_____
When there are other interesting things to do	_____
If I don't reach my exercise goals	_____
Without support from my family or friends	_____
During a vacation	_____
When I have other time commitments	_____
After experiencing family problems	_____

Appendix 5.6: Hospital Anxiety and Depression Scale

Hospital Anxiety and Depression Score (HADS)

This questionnaire helps your physician to know how you are feeling. Read every sentence. Place an "X" on the answer that best describes how you have been feeling during the LAST WEEK. You do not have to think too much to answer. In this questionnaire, spontaneous answers are more important

A	**I feel tense or 'wound up':**	
	Most of the time	3
	A lot of the time	2
	From time to time (occ.)	1
	Not at all	0
D	**I still enjoy the things I used to enjoy:**	
	Definitely as much	0
	Not quite as much	1
	Only a little	2
	Hardly at all	3
A	**I get a sort of frightened feeling as if something awful is about to happen:**	
	Very definitely and quite badly	3
	Yes, but not too badly	2
	A little, but it doesn't worry me	1
	Not at all	0
D	**I can laugh and see the funny side of things:**	
	As much as I always could	0
	Not quite so much now	1
	Definitely not so much now	2
	Not at all	3
A	**Worrying thoughts go through my mind:**	
	A great deal of the time	3
	A lot of the time	2
	From time to time, but not often	1
	Only occasionally	0
D	**I feel cheerful:**	
	Not at all	3
	Not often	2
	Sometimes	1
	Most of the time	0
A	**I can sit at ease and feel relaxed:**	
	Definitely	0
	Usually	1
	Not often	2
	Not at all	3

D	**I feel as if I am slowed down:**	
	Nearly all the time	3
	Very often	2
	Sometimes	1
	Not at all	0
A	**I get a sort of frightened feeling like "butterflies" in the stomach:**	
	Not at all	0
	Occasionally	1
	Quite often	2
	Very often	3
D	**I have lost interest in my appearance:**	
	Definitely	3
	I don't take as much care as I should	2
	I may not take quite as much care	1
	I take just as much care	0
A	**I feel restless as I have to be on the move:**	
	Very much indeed	3
	Quite a lot	2
	Not very much	1
	Not at all	0
D	**I look forward with enjoyment to things:**	
	As much as I ever did	0
	Rather less than I used to	1
	Definitely less than I used to	2
	Hardly at all	3
A	**I get sudden feelings of panic:**	
	Very often indeed	3
	Quite often	2
	Not very often	1
	Not at all	0
D	**I can enjoy a good book or radio/TV program:**	
	Often	0
	Sometimes	1
	Not often	2
	Very seldom	3

Appendix 5.7: The MOTION Studies 24 Hour Dietary Recall Template

Leicester-Loughborough
Diet, Lifestyle and Physical Activity
Biomedical Research Unit

24 Hour Dietary Recall

Study: **Study ID:**

	Food	Drinks
Breakfast		
Mid-morning		
Lunch		
Afternoon		
Dinner		
Super		
Snacks		
Notes		

NB.
Use simple language
Use open ended questions
Ensure to obtain a record of everything eaten over the previous day from waking to retiring
Provide a full description and indication of amount

Appendix 5.8: The MOTION Study's Diet Advice Sheet

Leicester-Loughborough
Diet, Lifestyle and Physical Activity
Biomedical Research Unit

Diet Tips: The Motion Study

Making changes to lifestyle is very hard. Well done, you have already made many good changes to your diet and activity levels. Keeping going with these changes can be challenging because lots of things can get in the way of what you want to do. This leaflet has been put together to try and to support you to keep going.

Try not to reward doing exercise with food. It can undo all the good work that you have done. Instead, try to reward yourself with other things such as a relaxing bath, a magazine or something that else that you enjoy doing.

Feeling thirsty can often be mistaken for hunger. Try to drink plenty of water or other low calorie drinks regularly throughout the day. Remember to drink extra water when you are being more active to avoid getting dehydrated.

It is very easy to return to eating more calories than you need after surgery. Here are some suggestions that have worked for other people:

- Eat little and often e.g. every 2-3 hours
- Eat 3 small balanced meals a day. Serve meals on a 15cm teaplate.
- Eat breakfast. Studies show if you eat a breakfast you are more likely to keep to a healthier weight
- Choose snacks that are 50 calories or less. (e.g. small piece of fruit, a cheese triangle, 2 rice crackers, sugar free jelly pots, handful of cherry tomatoes)
- Avoid high calorie sweet and savoury snacks such as pastries, biscuits and crisps
- Avoid high calorie drinks such as smoothies, sugary squashes, milkshakes
- Choose lower calorie food and drinks where possible e.g. sugar free squashes, yogurts containing maximum 50-80 calories
- Remember that drier and textured foods take longer to eat and keep you satisfied for longer (eg. roast meat instead of minced or casseroled meat, grilled fish instead of fish in sauce)
- Plan your meals and snacks (eg. take suitable snacks to work) so you are less likely to eat something convenient, high in calories and low in nutrition

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- Avoid shopping when you are hungry
- Try to be aware if you are eating for emotional reasons. It is easy to return to using food as a way of dealing with stress or unhappiness, even after surgery.
- When eating, take small mouthfuls of food (half a teaspoon), chew at least 20 times and enjoy the taste.
- Wait 20 seconds before taking another bite. If you can feel food sitting in your stomach pouch, stop eating.
- Concentrate on what you are eating at mealtimes. Try to avoid eating whilst watching television or doing other activities which distract you.
- Keep a food diary to help you understand where you overeat and why, and work out what to do next. You can record:
    - The times you are eating
    - What you are eating
    - How much you are eating
    - The time it took to eat your meal
    - How you are feeling at the time you are eating. For example, are you feeling you happy, sad, cross, bored?
- Monitor your activity. People who monitor their activity are more likely to keep active. You could use a diary, a pedometer, or a phone app to monitor this.
- Ask for support from family, friends and colleagues if you need it.

As a general reminder, after surgery:

- Do keep taking your vitamin and mineral supplements
- Do attend all your appointments after surgery
- If you cannot attend, please contact the Dietitian to give an update on your progress instead.

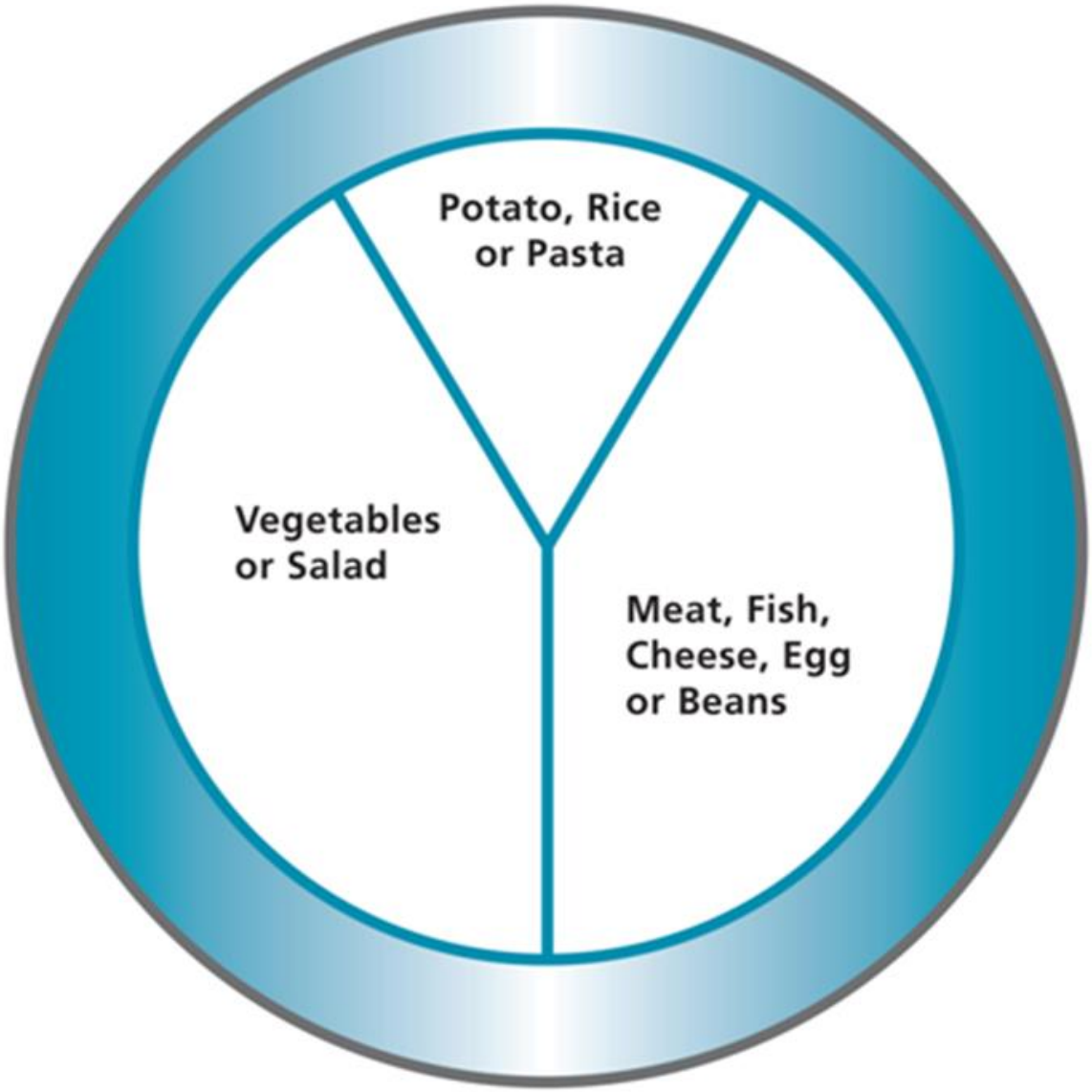
If you need any advice please contact your Dietitian
Jane Calow, Specialist Dietitian Bariatric Surgery:

Telephone number - 0116 258 6865
Email address - jane.calow@uhl-tr.nhs.uk

The Motion Study Version 1, 15/05/2014 Diet advise sheet

Leicester-Loughborough
Diet, Lifestyle and Physical Activity
Biomedical Research Unit

Your plate after surgery



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Appendix 5.9: All APP outcome measure change data between baseline and three and six months by intervention group.

Outcome Measures	Baseline		Baseline to 3-month change			Baseline to 6-month change		
	Exercise	Control	Exercise	Control	p-value	Exercise	Control	p-value
Body composition								
Body Mass (kg)	107.5 ± 16.8	107.9 ± 17.8	-2.7 ± 3.4	1.2 ± 1.5	0.004	-3.0 ± 5.6	3.5 ± 2.8	0.004
Body Mass Index (kg·m^2)	38.4 ± 6.4	39.6 ± 3.8	-1.0 ± 1.3	0.4 ± 0.5	0.003	-1.1 ± 2.1	1.2 ± 0.9	0.004
Body fat (%)	41.9 ± 7.7	44.8 ± 5.8	-1.1 ± 1.1	0.4 ± 1.0	0.005	-0.8 ± 1.6	0.7 ± 1.8	0.062
Fat Mass (kg)	45.6 ± 13.5	48.2 ± 9.4	-2.3 ± 2.6	1.0 ± 1.3	0.002	-2.1 ± 4.3	2.5 ± 2.8	0.009
Fat Free Mass (kg)	61.9 ± 9.5	59.7 ± 13.0	-0.4 ± 1.4	0.2 ± 1.4	0.402	-0.8 ± 1.7	1.0 ± 2.0	0.033
Hip Circumference (cm)	131.5 ± 13.7	135.6 ± 10.9	-6.9 ± 8.7	-0.2 ± 2.8	0.031	-8.4 ± 12.9	-0.8 ± 2.2	0.081
Waist Circumference (cm)	119.3 ± 11.9	121.7 ± 12.3	-8.2 ± 4.2	-0.7 ± 3.2	<0.001	-4.3 ± 9.5	0.6 ± 3.3	0.137
Waist to Hip Ratio	0.9 ± 0.1	0.9 ± 0.1	-0.0 ± 0.1	0.0 ± 0.0	0.456	0.0 ± 0.2	0.0 ± 0.0	0.678
Physical function								
ISWT (metres)	314.6 ± 117.0	350.0 ± 67.7	122.7 ± 59.2	-4.0 ± 19.6	<0.001	156.4 ± 77.5	-42.2 ± 86.6	<0.001
Right Hand Grip Strength (kg)	27.5 ± 9.1	29.1 ± 10.5	2.7 ± 4.2	-1.1 ± 3.6	0.040	3.1 ± 3.8	1.0 ± 4.1	0.239
Left Hand Grip Strength (kg)	27.7 ± 13.2	29.1 ± 10.4	2.3 ± 5.2	-0.7 ± 2.1	0.107	2.6 ± 3.1	-0.6 ± 2.2	0.014
5 x Seat to Stand Test (sec)	13.7 ± 7.2	12.5 ± 3.0	-4.2 ± 4.1	0.3 ± 3.1	0.013	-4.6 ± 3.9	0.3 ± 2.4	0.003
Cardiovascular measures								
Systolic Blood Pressure (mmHg)	121.2 ± 17.0	121.8 ± 11.4	-8.1 ± 11.5	4.4 ± 9.1	0.013	-7.6 ± 9.3	0.5 ± 7.4	0.043

Appendix 5.9: continued

Outcome Measures	Baseline		Baseline to 3-month change			Baseline to 6-month change		
	Exercise	Control	Exercise	Control	p-value	Exercise	Control	p-value
Diastolic Blood Pressure (mmHg)	80.0 ± 6.7	76.9 ± 7.2	-5.7 ± 5.6	3.9 ± 6.7	0.002	-5.6 ± 5.6	3.2 ± 4.6	0.001
Oxygen Saturation (%)	98.1 ± 0.5	97.4 ± 1.2	0.6 ± 0.8	0.0 ± 1.2	0.157	0.5 ± 0.8	-0.2 ± 1.2	0.164
Resting Heart Rate (bpm)	67.0 ± 9.6	76.7 ± 8.8	-12.3 ± 8.7	-3.4 ± 8.2	0.027	-5.5 ± 9.1	-4.1 ± 10.1	0.750
Biochemical results								
Total Cholesterol (mmol/L)	4.3 ± 0.8	4.5 ± 0.8	-0.1 ± 0.7	0.1 ± 0.5	0.374	0.0 ± 0.5	0.1 ± 0.5	0.634
Triglycerides (mmol/L)	1.3 ± 0.4	1.5 ± 0.9	-0.2 ± 0.3	0.0 ± 0.8	0.406	-0.1 ± 0.4	0.1 ± 0.9	0.462
LDL (mmol/L)	2.4 ± 0.8	2.3 ± 0.4	-0.1 ± 0.6	0.1 ± 0.4	0.288	-0.0 ± 0.6	0.2 ± 0.5	0.335
HDL (mmol/L)	1.3 ± 0.2	1.5 ± 0.5	0.1 ± 0.2	0.0 ± 0.2	0.283	0.1 ± 0.3	0.0 ± 0.2	0.492
Cholesterol:HDL Ratio	3.5 ± 0.6	3.2 ± 0.9	-0.3 ± 0.5	0.2 ± 0.5	0.037	-0.2 ± 0.6	0.1 ± 0.4	0.324
HBA1c (%)	5.2 ± 0.2	5.7 ± 1.1	0.0 ± 0.1	0.1 ± 0.2	0.113	0.1 ± 0.2	0.2 ± 0.2	0.203
HBA1c (mmol/L)	32.8 ± 2.1	38.9 ± 11.2	0.1 ± 1.5	1.1 ± 1.7	0.162	1.7 ± 2.8	2.6 ± 1.8	0.414
Physical activity								
Stationary time (min/day)	567.0 ± 96.5	569.8 ± 65.8	-42.1 ± 104.5	-14.6 ± 73.7	0.571	-17.0 ± 94.0	-6.3 ± 84.9	0.904
Light a Appendix 5.9: continued	81.5	300.7 ± 74.9	0.6 ±67.4	-4.5 ± 112.5	0.804	-28.1 ± 48.1	-16.7 ± 93.6	0.802
MVPA (min/day)	30.1 ± 24.5	26.7 ± 17.4	11.5 ± 9.0	-1.7 ± 15.5	0.043	8.2 ± 20.8	-3.8 ± 17.3	0.165
Step count (steps per day)	6474.2 ± 3494.9	5480.7 ± 1679.6	686.6 ± 1405.8	550.8 ± 2005.1	0.868	267.0 ± 2484.2	596.7 ± 2449.8	0.782
IPAQ (MET-min/week)	4308.6 ± 4999.6	1533.6 ± 2501.1	5923.0 ± 5903.2	4175.2 ± 8466.6	0.587	2993.2 ± 7276.5	1129.7 ± 3275.1	0.467

Appendix 5.9: continued

Outcome Measures	Baseline		Baseline to 3-month change			Baseline to 6-month change		
	Exercise	Control	Exercise	Control	p-value	Exercise	Control	p-value
Daily sitting time (min)	248.2 ± 131.5	354.0 ± 131.0	-10.9 ± 131.6	21.0 ± 186.6	0.653	73.6 ± 159.0	63.0 ± 171.1	0.884
Psychological questionnaires								
Anxiety score	6.9 ± 4.7	5.3 ± 4.2	-1.4 ± 3.0	-0.8 ± 3.2	0.683	-0.8 ± 3.5	0.9 ± 4.8	0.359
Depression score	2.6 ± 4.3	2.1 ± 3.5	-0.6 ± 3.1	1.2 ± 3.6	0.224	0.4 ± 3.8	2.3 ± 6.4	0.403
Total SERPA score	920.9 ± 402.4	668.5 ± 445.1	377.7 ± 327.0	-29.5 ± 166.8	0.002	91.8 ± 444.2	205.5 ± 324.9	0.515
SERPA score Average	51.6 ± 22.3	37.7 ± 25.0	22.3 ± 18.6	-0.5 ± 8.8	0.002	6.6 ± 24.4	10.8 ± 18.3	0.664
Dietary intake								
Calorific intake (kcal/wk)	1723.2 ± 552.4	1593.7 ± 367.7	-5.8 ± 902.5	-278.1 ± 416.9	0.281	-274.6 ± 452.4	228.9 ± 612.6	0.103

APP data are presented as mean ±SD

KEY: kg: kilograms; cm: centimetres; kg/m^2: kilograms per metre squared; mmHg: millimetres of mercury; bpm: beats per minute; mmol/L: millimole per litre; min: minutes; sec: second; MET; metabolic equivalence kcal: kilocalories

Appendix 5.10: The MOTION Study's mean absolute results by arm at baseline, three and six months (ITT).

Outcome Measures	Baseline		3-month assessment		6-month assessment	
	Exercise	Control	Exercise	Control	Exercise	Control
Body composition						
Body Mass(kg)	106.5 ± 16.4	106.0 ± 17.5	104.0 ± 15.7	107.0 ± 17.8	103.8 ± 14.3	108.9 ± 19.4
Body Mass Index (kg·m^2)	38.2 ± 6.1	39.4 ± 4.3	37.3 ± 5.7	39.8 ± 4.3	37.2 ± 5.1	40.4 ± 4.6
Body fat (%)	42.0 ± 7.3	45.2 ± 6.0	41.0 ± 7.2	45.6 ± 6.1	41.3 ± 7.4	45.8 ± 6.3
Fat Mass (kg)	45.2 ± 12.9	47.9 ± 10.0	43.1 ± 12.3	48.8 ± 10.6	43.3 ± 11.7	50.1 ± 11.6
Fat Free Mass (kg)	61.2 ± 9.3	58.1 ± 12.4	60.9 ± 8.9	58.2 ± 12.0	60.5 ± 8.9	58.9 ± 12.6
Hip Circumference (cm)	131.0 ± 13.2	135.6 ± 11.5	124.7 ± 13.5	135.4 ± 12.4	123.3 ± 11.9	134.9 ±11.9
Waist Circumference (cm)	118.2 ± 11.9	121.1 ± 12.3	110.7 ± 11.2	120.6 ± 12.1	114.3 ± 14.0	121.6 ± 12.8
Waist to Hip Ratio	0.9 ± 0.1	0.9 ± 0.1	0.9 ± 0.1	0.9 ± 0.1	0.9 ± 0.1	0.9 ±0.1
Physical function						
ISWT (metres)	325.0 ± 117.3	355.0 ± 80.6	437.5 ± 88.2	351.7 ± 85.3	468.3 ± 115.2	322.5 ± 102.3
Right Hand Grip Strength (kg)	27.5 ± 8.7	28.5 ± 9.6	30.0 ± 7.9	27.6 ± 9.0	30.4 ± 10.3	29.3 ± 8.4
Left Hand Grip Strength (kg)	27.6 ± 12.5	28.5 ± 9.6	29.7 ± 9.6	27.9 ± 9.4	30.0 ± 12.3	28.0 ± 8.1
5 x Seat to Stand Test (sec)	13.7 ± 6.8	12.2 ± 2.9	9.9 ± 3.7	12.4 ± 4.4	9.5 ±3.8	12.4 ± 2.6
Cardiovascular measures						
Systolic Blood Pressure (mmHg)	121.9 ± 16.4	120.4 ± 10.9	114.5 ± 10.5	124.1 ± 13.2	115.0 ± 11.2	120.8 ± 9.7

Appendix 5.10: continued

Outcome Measures	Baseline		3-month assessment		6-month assessment	
	Exercise	Control	Exercise	Control	Exercise	Control
Diastolic Blood Pressure (mmHg)	80.8 ± 6.9	78.4 ± 7.7	75.5 ± 6.9	81.7 ± 8.4	75.6 ± 8.7	81.1 ± 6.1
Oxygen Saturation (%)	97.9 ± 0.8	97.3 ± 1.1	98.5 ± 0.9	97.3 ± 1.0	98.3 ± 0.9	97.1 ±0.9
Resting Heart Rate (bpm)	66.8 ± 9.2	76.0 ± 8.3	55.5 ± 7.9	73.2 ± 6.5	61.8 ± 8.2	72.6 ± 7.1
			Biochemical results			
Total Cholesterol (mmol/L)	4.3 ± 0.8	4.5 ± 0.9	4.2 ± 0.7	4.6 ± 0.8	4.3 ± 0.7	4.6 ± 1.0
Triglycerides (mmol/L)	1.4 ± 0.4	1.6 ± 0.8	1.2 ± 0.4	1.6 ± 0.8	1.3 ± 0.4	1.7 ± 1.3
LDL (mmol/L)	2.4 ± 0.7	2.3 ± 0.5	2.3 ± 0.6	2.4 ± 0.5	2.4 ± 0.6	2.5 ±0.7
HDL (mmol/L)	1.3 ± 0.2	1.5 ± 0.4	1.4 ± 0.3	1.5 ± 0.5	1.4 ± 0.3	1.5 ±0.5
Cholesterol:HDL Ratio	3.5 ± 0.6	3.2 ± 0.8	3.2 ± 0.6	3.3 ± 0.9	3.3 ± 0.7	3.3 ± 1.0
HBA1c (%)	5.2 ± 0.2	5.6 ± 1.0	5.2 ± 0.3	5.7 ± 1.1	5.3 ± 0.4	5.8 ± 1.1
HBA1c (mmol/L)	33.2 ± 2.3	37.8 ± 10.5	33.3 ± 2.9	38.7 ± 11.7	34.8 ± 4.5	39.9 ± 11.6
			Physical activity			
IPAQ (MET-min/week)	3952.3 ± 4924.1	2059.6 ± 3070.2	9318.7 ± 8513.6	5538.9 ± 10020.5	6696.0 ± 6805.6	3001.0 ± 3480.6
Daily sitting time (min)	262.5 ± 134.8	310.0 ± 158.9	252.5 ± 152.1	327.5 ± 181.1	330.0 ± 149.7	362.5 ± 208.4
Stationary time (min/day)	559.6 ± 94.7	531.1 ± 131.4	521.3 ± 56.1	518.0 ± 146.7	544.0 ± 105.8	525.4 ± 150.7
Light activity (min/day)	304.5 ± 77.3	320.1 ± 91.2	305.0 ± 50.7	316.1 ± 88.9	274.4 ± 105.8	305.3 ± 93.4
MVPA (min/day)	28.31 ±24.0	29.7 ± 18.6	38.8 ± 23.4	28.2 ± 19.3	36.9 ± 18.8	26.3 ± 16.7

Appendix 5.10: continued

Outcome Measures	Baseline		3-month assessment		6-month assessment	
	Exercise	**Control**	**Exercise**	**Control**	**Exercise**	**Control**
Step count (steps per day)	6379.4 ± 3316.0	5737.2 ± 1749.4	7003.6 ± 2476.2	6226.8 ± 2603.1	6742.7 ± 2942.4	6267.5 ± 2595.8
			Psychological questionnaires			
Anxiety score	6.6 ± 4.6	5.5 ± 3.8	5.3 ± 4.1	4.8 ± 4.4	5.8 ± 4.8	6.3 ±6.2
Depression score	2.4 ± 4.2	2.4 ± 3.3	1.8 ± 2.0	3.4 ± 2.6	2.8 ± 3.4	4.3 ±5.1
SERPA score Average	50.4 ± 21.6	37.9 ± 23.5	70.8 ± 24.1	37.5 ± 24.5	56.4 ± 22.4	46.9 ±25.5
			Dietary intake			
Calorific intake (kcal/week)	1713.6 ± 527.7	1559.8 ± 361.1	1809.8 ± 620.9	1297.3 ± 325.8	1504.4 ± 475.1	1712.3 ± 427.3

ITT data are presented as mean ±SD

KEY: kg: kilograms; cm: centimetres; kg/m^2: kilograms per metre squared; sec: second; mmHg: millimetres of mercury; bpm: beats per minute; mmol/L: millimole per litre; min: minutes

Appendix 5.11: The MOTION Study's mean absolute results by arm at baseline, three and six months (APP).

Outcome Measures	Baseline		3-month assessment		6-month assessment	
	Exercise	Control	Exercise	Control	Exercise	Control
Body composition						
Body Mass(kg)	107.5 ± 16.8	107.9 ± 17.8	104.8 ± 16.3	109.1 ± 17.9	104.5 ± 14.8	111.4 ± 19.5
Body Mass Index (kg·m^2)	38.4 ± 6.4	39.6 ± 3.8	37.9 ± 6.0	40.0 ± 3.7	37.3 ± 5.3	40.8 ± 4.0
Body fat (%)	41.9 ± 7.7	44.8 ± 5.8	40.8 ± 7.5	45.2 ± 6.0	41.2 ± 7.7	45.5 ± 6.2
Fat Mass (kg)	45.6 ± 13.5	48.2 ± 9.4	43.3 ± 12.8	49.3 ± 10.2	43.5 ± 12.3	50.8 ± 11.3
Fat Free Mass (kg)	61.9 ± 9.5	59.7 ± 13.0	61.5 ± 9.1	59.9 ± 12.6	61.1 ± 9.1	60.7 ± 13.1
Hip Circumference (cm)	131.5 ± 13.7	135.6 ± 10.9	124.6 ± 14.2	135.4 ± 12.0	123.1 ± 12.5	134.8 ± 11.4
Waist Circumference (cm)	119.3 ± 11.9	121.7 ± 12.3	111.0 ± 11.7	121.0 ± 12.1	115.0 ± 14.4	122.3 ± 12.9
Waist to Hip Ratio	0.9 ± 0.1	0.9 ± 0.1	0.9 ± 0.1	0.9 ± 0.1	0.9 ± 0.2	0.91 ± 0.1
Physical function						
ISWT (metres)	314.6 ± 117.0	350.0 ± 67.7	437.3 ± 92.5	346.0 ± 74.0	470.9 ± 120.5	297.8 ± 88.4
Right Hand Grip Strength (kg)	27.5 ± 9.1	29.1 ± 10.5	30.1 ± 8.3	28.0 ± 9.9	30.5 ± 10.8	30.1 ± 9.1
Left Hand Grip Strength (kg)	27.7 ± 13.2	29.1 ± 10.4	30.0 ± 10.0	28.4 ± 10.3	30.4 ± 12.8	28.6 ± 8.8
5 x Seat to Stand Test (sec)	13.7 ± 7.2	12.5 ± 3.0	9.6 ± 3.7	12.7 ± 4.7	9.1 ± 3.8	12.7 ± 2.6
Cardiovascular measures						
Systolic Blood Pressure (mmHg)	121.2 ± 17.0	121.8 ± 11.4	113.1 ± 9.8	126.2 ± 13.5	113.6 ± 10.6	122.3 ± 10.0

Appendix 5.11: continued

Outcome Measures	Baseline		3-month assessment		6-month assessment	
	Exercise	Control	Exercise	Control	Exercise	Control
Diastolic Blood Pressure (mmHg)	80.00 ± 6.74	76.9 ± 7.2	74.3 ± 5.7	80.8 ± 8.7	74.4 ± 7.9	80.1 ± 5.8
Oxygen Saturation (%)	98.09 ± 0.54	97.4 ± 1.2	98.7 ± 0.5	97.4 ± 1.0	98.6 ± 0.5	97.2 ± 0.9
Resting Heart Rate (bpm)	67.0 ± 9.6	76.7 ± 8.8	54.7 ± 7.8	73.3 ± 7.0	61.6 ± 8.6	72.6 ± 7.7
			Biochemical results			
Total Cholesterol (mmol/L)	4.3 ± 0.8	4.5 ± 0.8	4.2 ± 0.7	4.7 ± 0.8	4.3 ± 0.8	4.8 ± 0.9
Triglycerides (mmol/L)	1.3 ± 0.4	1.5 ± 0.9	1.1 ± 0.2	1.6 ± 0.9	1.2 ± 0.3	1.7 ± 1.5
LDL (mmol/L)	2.4 ± 0.8	2.3 ± 0.4	2.3 ± 0.6	2.4 ± 0.5	2.4 ± 0.6	2.5 ± 0.6
HDL (mmol/L)	1.3 ± 0.2	1.5 ± 0.5	1.4 ± 0.3	1.5 ± 0.5	1.4 ± 0.4	1.6 ± 0.5
Cholesterol:HDL Ratio	3.5 ± 0.6	3.2 ± 0.9	3.2 ± 0.6	3.4 ± 1.0	3.3 ± 0.7	3.2 ± 1.0
HBA1c (%)	5.2 ± 0.2	5.7 ± 1.1	5.2 ± 0.3	5.8 ± 1.1	5.3 ± 0.4	6.0 ± 1.1
HBA1c (mmol/L)	32.8 ± 2.1	38.9 ± 11.2	32.9 ± 2.8	40.0 ± 12.4	34.6 ± 4.7	41.5 ± 12.2
			Physical activity			
Anxiety score	6.9 ± 4.7	5.3 ± 4.2	5.6 ± 4.3	4.5 ± 4.8	6.1 ± 5.0	6.2 ± 6.9
Depression score	2.6 ± 4.3	2.1 ± 3.5	2.0 ± 2.0	3.3 ± 2.8	3.0 ± 3.4	4.4 ± 5.6
SERPA score Average	51.6 ± 22.3	37.7 ± 25.0	73.9 ± 22.7	37.2 ± 26.1	58.2 ± 22.7	48.6 ± 26.9
			Psychological questionnaires			
IPAQ (MET-min/week)	4308.6 ± 4999.6	1533.6 ± 2501.1	10231.6 ± 8378.2	5708.8 ± 10913.8	7301.8 ± 6790.0	2663.3 ± 3259.8

Appendix 5.11: continued

Outcome Measures	Baseline		3-month assessment		6-month assessment	
	Exercise	Control	Exercise	Control	Exercise	Control
Daily sitting time (min)	248.2 ±131.5	354.0 ± 131.0	237.3 ± 149.7	375.0 ± 155.7	321.8 ± 154.2	417.0 ± 180.3
Stationary time (min/day)	567.0 ± 96.5	569.8 ± 65.8	524.8 ± 57.8	555.1 ± 102.3	550.5 ± 110.1	563.4 ± 105.5
Light activity (min/day)	302.7 ± 81.5	300.7 ± 74.9	303.3 ± 53.1	296.2 ± 70.3	269.2 ± 68.0	284.0 ± 72.8
MVPA (min/day)	30.1 ± 24.5	26.7 ± 17.4	41.6 ± 22.6	25.1 ± 17.9	39.8 ± 17.4	22.9 ± 14.1
Step count (steps per day)	6474.2 ± 3494.9	5480.7 ±1679.6	7160.8 ± 2551.7	6031.4 ± 2711.4	6888.3 ± 3082.5	6077.3 ± 2707.1
			Dietary intake			
Calorific intake (kcal/week)	1723.2 ± 552.4	1593.7 ± 367.7	1750.9 ± 615.1	1278.7 ± 333.0	1490.5 ± 495.7	1776.6 ± 423.1

ITT data are presented as mean ±SD

KEY: kg: kilograms; cm: centimetres; kg/m^2: kilograms per metre squared; sec: second; mmHg: millimetres of mercury; bpm: beats per minute; mmol/L: millimole per litre; min: minutes; MET; metabolic equivalence kcal: kilocalories

Appendix 5.12: The MOTION Study's estimated marginal means for physical activity (ITT).

	Physical activity intensity	Group	Mean	95% Confidence interval		
				Std Error	Lower Bound	Upper bound
Baseline to 3-month change	Sedentary	Exercise	-36.310	23.683	-86.277	13.658
		Control	-15.435	26.187	-70.684	39.814
	Light	Exercise	2.486	22.846	-45.714	50.686
		Control	-6.371	25.260	-59.666	46.923
	MVPA	Exercise	10.520	3.682	2.751	18.290
		Control	-1.500	4.072	-10.091	7.090
Baseline to 6-month change	Sedentary	Exercise	-12.800	21.661	-58.501	32.900
		Control	-8.903	23.952	-59.437	41.632
	Light	Exercise	-24.225	19.649	-65.679	17.203
		Control	-16.476	21.727	-62.316	29.363
	MVPA	Exercise	7.842	5.319	-3.380	19.064
		Control	-3.802	5.881	-16.211	8.606

Appendix 5.13: The MOTION Study's estimated marginal means for physical activity (APP)

	Physical activity intensity	Group	Mean	95% Confidence interval		
				Std Error	Lower Bound	Upper bound
Baseline to 3-month change	Sedentary	Exercise	-40.096	26.356	-96.272	16.081
		Control	-17.170	29.472	-79.988	45.647
	Light	Exercise	2.624	25.476	-51.676	56.924
		Control	-7.029	28.487	-67.748	53.690
	MVPA	Exercise	11.579	4.006	3.041	20.118
		Control	-1.697	4.479	-11.245	7.851
Baseline to 6-month change	Sedentary	Exercise	-14.261	24.169	-65.775	37.253
		Control	-9.790	27.027	-67.397	47.818
	Light	Exercise	-26.778	21.889	-73.433	19.877
		Control	-18.373	24.478	-70.546	33.801
	MVPA	Exercise	8.613	5.872	-3.902	21.129
		Control	-4.261	6.566	-18.257	9.734

Appendix 5.14: The CONSORT 2010 checklist.

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	71
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	72 + 73
	2b	Specific objectives or hypotheses	73
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	73 + 74
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	N/A
Participants	4a	Eligibility criteria for participants	73
	4b	Settings and locations where the data were collected	74
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	74 - 76
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	76 - 78
	6b	Any changes to trial outcomes after the trial commenced, with reasons	N/A
Sample size	7a	How sample size was determined	73 + 74
	7b	When applicable, explanation of any interim analyses and stopping guidelines	N/A
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	74
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	74
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	74
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	74
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	N/A N/A
	11b	If relevant, description of the similarity of interventions	N/A
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	80
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	80
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	82
	13b	For each group, losses and exclusions after randomisation, together with reasons	82
Recruitment	14a	Dates defining the periods of recruitment and follow-up	74
	14b	Why the trial ended or was stopped	
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	83 + 84
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	85 - 96
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	85 - 96
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	85 - 96
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	N/A
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	81
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	106
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	107
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	97 - 107
Other information			
Registration	23	Registration number and name of trial registry	ISRCTN17240262
Protocol	24	Where the full trial protocol can be accessed, if available	Vi
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	Vi

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.