Changes in body composition over 5 years after Roux-en-Y Gastric Bypass and Sleeve Gastrectomy.

Bradley Matheson

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Abstract

Background and aim: Bariatric surgery produces extensive weight loss unrivalled by non-surgical obesity treatments. However, there is limited evidence comparing the effects of different procedures on body composition beyond the first year. Findings are often further limited by body composition assessment methods with unreliable or unproven validity in individuals with obesity.

This thesis aimed to compare changes in body composition over five years following two types of bariatric surgery: Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SG). Secondly, it aimed to assess the validity of bioimpedance techniques for measuring body composition in a population with obesity using dual-energy x-ray absorptiometry (DXA) as a reference standard.

Methods: This thesis analysed data collected from participants randomised to undergo either RYGB or SG. Data was collected two days before surgery, one year after surgery, and five years after surgery. Body composition was measured using DXA, single-frequency bioelectrical impedance analysis (SF-BIA) and multi-frequency bioimpedance analysis (MF-BIA). Assessment outcomes included body weight, fat-free mass, appendicular skeletal muscle mass, fat mass, visceral adipose tissue mass, and android adipose tissue mass.

Results: Body composition assessment information was available for 91 participants. Compared to the SG group at five years, the RYGB group had more significant reductions in body weight measured as percentage excess weight loss (%EWL) ($p<0.0001$), total body fat ($p<0.0001$), body fat percentage ($p=0.002$), android fat mass ($p<0.001$), and visceral fat mass ($p<0.001$), and a more significant increase in fat-free mass percentage ($p=0.003$). Fat mass and fat-free mass derived from five BIA equations were compared against DXA measurements. Bias ranged from -8.2% to 10.23% of DXA values, and Pearson correlation coefficients exceeded 0.94. However, the limits of agreement were large for all five equations.

Conclusions: Greater weight loss was achieved following RYGB due to greater initial weight loss and lower weight regain. Qualitative changes in body composition appear similar between the groups, and differences are likely associated with the extent of weight loss.

Factory BIA equations and equations extracted from pre-existing literature failed to estimate body composition in a population with obesity accurately. Without derivation and validation of specific equations for obesity, SF-BIA & MF-BIA applications remain limited by poor individual accuracy and large limits of agreement.

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Chapter 1. Introduction

1.1 Introduction to Obesity

Obesity is a chronic disease defined by excessive body fat that poses a risk to health (World Health Organisation, 2024). The distinction between the categorisation of overweight and obesity is made using body mass index (BMI) cutoffs of 25 kg/m^2 and 30 kg/m^2 (World Health Organisation, 2024). Despite mass recognition of the obesity epidemic, the prevalence of obesity continues to increase globally, with an estimated third of the world's population classified as overweight or obese (Chooi et al., 2019; GBD 2015 Obesity Collaborators et al., 2017). Obesity is a multisystem disease and a prominent risk factor for type 2 diabetes mellitus (T2DM), cardiovascular disease, and various types of cancer (Guh et al., 2009). Obesity is emerging as a major economic burden as increased BMI is correlated with reductions in productivity, early mortality, and higher per capita healthcare costs (Dee et al., 2014).

Strategies for treating obesity are as fundamentally simplistic as the origins of obesity itself. Fat deposition occurs during states of positive energy balance where energy intake exceeds energy expenditure (Hill, 2006). Therefore, treatment strategies address one or both components of the equation by increasing expenditure or decreasing caloric intake. Current non-surgical treatment strategies include dietary modification, physical activity, multi-faceted lifestyle modifications and pharmacotherapy (Blüher et al., 2023). However, non-surgical interventions consistently produce only modest reductions in body weight (Ruban et al., 2019). Behavioural modification and public health interventions contribute greatly to obesity prevention, but the efficacy of bariatric surgery for treating excessive adiposity is currently unrivalled. Increased acceptance of surgical interventions for treating obesity is reflected in the steadily increasing volume of bariatric procedures performed (Chousleb et al., 2019; Clapp et al., 2022).

1.2 Thesis Objectives

The number of bariatric surgeries performed in New Zealand has grown significantly in both public and private settings as a treatment for obesity. The sleeve gastrectomy (SG) and gastric bypass are the most common procedures and result in drastic changes in body composition. Both locally and internationally, the gastric sleeve has replaced the gastric bypass as the primary procedure. However, evidence supporting either procedure is limited. Previous comparative investigations are from unrandomised cohorts and infrequently extend beyond one year post-operatively. Therefore, the first objective of this thesis was to;

1) Compare body composition changes, including fat mass (FM), visceral adipose tissue (VAT), subcutaneous adipose tissue, fat-free mass (FFM) and appendicular skeletal muscle mass (ASMM) over 5 years following laparoscopic banded-Roux-en-Y gastric bypass (RYGB) and laparoscopic SG.

Despite the value of information obtained from body composition analysis to researchers and health professionals, it is infrequently utilised. Methodologies with sufficient evidence supporting their accuracy, such as dual-energy x-ray absorptiometry (DXA) and four-compartment models, are impractical for widespread use due to their low availability and higher costs. Bioimpedance devices offer an affordable and accessible method of assessing body composition. However, the validity of bioimpedance techniques is often contested. Therefore, the next objective of this thesis was to:

2) Compare the validity of two bioimpedance methods for assessing FM and FFM using DXA as the reference technique.

The accuracy of single-frequency bioelectrical impedance analysis (SF-BIA) and multifrequency bioelectrical impedance analysis (MF-BIA) is heavily dependent on the validity of the prediction equation used. Findings from frequently used equations, such as from large studies or those provided by manufacturers, should be cautiously interpreted. Prediction equations require validation in new populations due to inter-individual differences. The lack of population-specific equations is apparent in populations classified as overweight or obese. Bioimpedance techniques typically overestimate FFM and underestimate FM in these populations due to increased FFM hydration compared to normal-weight individuals. Generating an equation or validating existing equations for a population with obesity may improve the validity of SF-BIA in these cohorts. Therefore, the final objective of this thesis was to:

3) *Extract from the published literature SF-BIA equations featured in validation studies of populations classified as overweight/obese and those derived from populations classified as*

overweight/obese and compare body composition estimates generated by those equations with those from DXA in the current cohort of New Zealand bariatric patients.

1.3 Thesis Overview

Chapter 1 provides background information on the obesity epidemic and currently available treatment strategies.

Chapter 2 of this thesis is divided into two sections that review the current literature relating to body composition analysis methods and bariatric surgery outcomes. The first section covers different methodologies for assessing body composition and considers their application in a population with obesity. Section two reviews body composition outcomes following RYGB and SG. This section compares post-surgical changes in body weight, FM, FM distribution, FFM, skeletal muscle mass and T2DM management.

Chapter 3 describes the study methodology, including participant eligibility and recruitment, the study protocol, and descriptions of assessed outcomes. The techniques used for measuring body composition are also presented here.

Chapter 4 reports the results of this study.

Chapter 5 discusses the study results and compares them to pre-existing literature. The strengths and limitations of the study are discussed within the context of the study findings. Finally, recommendations for the application of the study findings and the direction of future research are discussed.

Chapter 2. Literature Review

2.1 Body Composition Assessment

Body composition refers to the components of body mass and their proportions (Müller et al., 2016). Body composition can be described using multi-compartment models ranging from elemental constitution at an atomic level to proportions of skeletal muscle and adipose tissue at the organ-tissue level (Müller et al., 2016). These models are the theoretical foundation for modern body composition analysis techniques. Body composition assessment techniques are utilised in clinical settings for the risk assessment of nutritional such as sarcopenia, obesity, and osteoporosis (Andreoli et al., 2016).

Body composition analysis methods can be classified as direct, indirect or criterion methods. Direct measures like isotope dilution and neutron activation and criterion methods like densitometry and DXA have represented 'gold standards' as they measure the body or its properties directly. However, these techniques are limited in clinical use as they require highly skilled operators and expensive equipment with low availability. In contrast, indirect methods see widespread clinical use as measurements are easy to obtain and require equipment that is affordable and readily available.

Indirect methods describe the relationship between proxy measures and body composition. Indirect methods such as BIA and anthropometry utilise regression equations derived from validation studies against direct or criterion methods to estimate body compartment components. Consequently, the precision of indirect methods is typically inferior and additional caution is required when applying equations beyond the original sample population.

2.1.1 Anthropometry

Anthropometric measurements are frequently used to describe body composition or body composition-related health risks. Anthropometric techniques are non-invasive, quick to obtain and use widely available equipment. Anthropometric measures commonly used to describe body composition include BMI and skinfold thickness (SFT) for total body fat (TBF), waist circumference for fat distribution, and mid-upper arm circumference (MUAC) for total muscle mass.

2.1.1.1 Body Mass Index

BMI is the most widely used anthropometric measure for assessing body fat. BMI is calculated by dividing a person's weight in kilograms by the square of their height in meters. BMI categorises

individuals by weight statuses that are associated with varying levels of disease risk (Table 1) (World Health Organisation, 2000). The primary limitation of BMI is that it is unable to distinguish between FM and FFM or quantify their distribution. The distribution of FM is of particular significance as central obesity is more strongly associated with mortality than BMI (Sahakyan et al., 2015).

Table 1. Classification of adults according to BMI.

Classification	BMI (kg/m^2)	Risk of comorbidities
Underweight	<18.5	Low*
Normal Range	18.5-24.99	Average
Overweight:	≥25	
Pre-obese	25-29.99	Increased
Obese Class I	30-34.99	Moderate
Obese Class II	35-39.99	Severe
Obese Class III	≥40	Very Severe

*Risk of other clinical problems is increased. BMI = Body mass index.

2.1.1.2 Waist Circumference

Waist circumference is an anthropometric measurement used as an indicator for intra-abdominal FM (Chan et al., 2003) and metabolic health risk (Darsini et al., 2020). Sex-specific thresholds of WC are used to categorise the risk of metabolic complications as either 'increased' or 'substantially increased' (Table 2)(World Health Organization, 2011). WC is strongly correlated with several health risks, such as type 2 diabetes mellitus, hypercholesterolemia, and hypertension (Darsini et al., 2020). Being able to describe body fat distribution patterns is the main advantage of using WC compared to BMI. However, waist circumference is better suited to describe disease risk than body composition compared to the array of quantitative body composition analysis (BCA) methods currently available.

Table 2. Sex-specific waist circumference and risk of metabolic complications associated with obesity in Caucasians.

Risk of metabolic complications	Waist Circumference (cm)	
	Men	Women
Increased	≥ 94	≥ 80
Substantially Increased	≥ 102	≥ 88

MUAC is an anthropometric measurement used in malnutrition screening as an alternative to BMI (Benítez Brito et al., 2016; Van Tonder et al., 2019). In addition to its practicality for bedside assessment, it is generally accepted that MUAC is influenced to a lesser degree by hydration status and conditions of fluid overload than weight-based measures (Modi et al., 2015; Todorovic et al., 2011) Therefore, MUAC may be more reliable than BMI for monitoring changes in nutritional status in disease states with altered hydration states, such as heart failure, kidney disease, and obesity (Cotter et al., 2008; Gonçalves et al., 2006; Waki et al., 1991). MUAC can also be used to calculate mid-arm muscle area (MAMA) and then estimate total body muscle mass (Heynsfield et al., 1982). This is of particular interest for use in immobile or critically ill patients as total muscle mass can be estimated from measures done at bedside (MUAC & triceps SFT).

2.1.1.4 Skinfold Thickness

SFT is an anthropometric measurement obtained by pinching the skin with specialised callipers (Durnin & Rahaman, 1967). SFT measures subcutaneous body fat and enables the estimation of TBF through previously validated prediction equations. The age and sex-specific equations developed by Durnin and Womersley may be the most widely used (Durnin & Womersley, 1974). The sum of SFT measurements at up to four sites is related to body density measures in healthy subjects obtained by hydrodensitometry. FM can then be calculated from body weight using the Siri equation (Siri, 1956). Like other anthropometric techniques, the accuracy and repeatability of skinfold measurements are dependent on operator experience and the use of standardised methodology (Lohman et al., 1988; Totosy de Zepetnek et al., 2021).

Despite ongoing refinement of equations for estimating FM from SFT, their accuracy proves highly inconsistent when compared to modern ‘gold standard’ techniques like DXA (Bacchi et al., 2017; Benito et al., 2019; López-Taylor et al., 2018; Truesdale et al., 2016). The inconsistent performance of SFT equations is likely attributable to differences between study populations and the population from which the equation was derived. FM estimations from SFT rely on the assumption that body fat distribution is uniform. However, body fat distribution is shown to differ across age, ethnicity, sex, and body type (Hattori et al., 1991). Additionally, standard callipers may be unable to accommodate larger skinfold thicknesses seen in subjects with obesity (Gray et al., 1990).

2.1.2 Bioimpedance

Bioimpedance techniques involve measuring the resistance of the body to a weak, alternating electrical current (Kyle et al., 2004a). Whole-body resistance is typically measured using a current applied between electrodes on the ankle and wrist. Resistance is influenced by body composition as tissues with a high water content, like muscle, conduct current well, and tissues with low water content, like fat and bone, are poor conductors. When expressed as height $(H)^2/R$, a derivative from the equation for the volume of a cylindrical conductor of electrolyte with resistance, R, a strong correlation is found with fluid volume measures from dilution experiments (Kushner, R. et al., 1992). However, modelling the body as a single cylinder or series of cylinders is a crude approximation. Therefore, regression equations based on the relationship between H^2/R and fluid volume include adjustments for factors such as weight, sex, and age (Kyle et al., 2004a). Different applications of the basic principles behind bioimpedance and the utilisation of various other assumptions have led to the distinction of three main bioimpedance techniques. These techniques are SF-BIA, MF-BIA, and Bioimpedance Spectroscopy (BIS).

2.1.2.1 Bioelectrical Impedance Analysis - Single Frequency

Early bioimpedance devices measured bodily resistance using a single frequency. This application is appropriately named SF-BIA and typically uses a 50 kHz frequency. Resistance measures from SF-BIA are used to estimate total body water (TBW) through regression equations developed from reference data such as isotope dilution experiments. FFM and FM estimates can be derived from TBW and body weight, as FFM is assumed to have constant hydration at ~73% (Pace & Rathbun, 1945; Wang, Z. et al., 2000). Alternatively, some regression equations may estimate FM or FFM directly from total body resistance. Equations derived for body composition assessment by SF-BIA are presented in reviews by Kyle et al. (2004) and Houtkooper et al. (1996).

SF-BIA is an attractive technique as devices are easily accessible, affordable, and relatively simple to operate. However, the assumptions present in the methodology of SF-BIA introduce significant barriers to clinical application. Firstly, the assumption that resistance values at a 50 kHz frequency are representative of both ICW and ECW may be invalid outside of healthy populations (De Lorenzo et al., 1997). Unlike at high frequencies, current at intermediate frequencies only propagates through a portion of the intracellular fluid (Matthie, J. et al., 1998). In healthy populations, the proportions of extra and intracellular water are tightly controlled, and both ECW and TBW can be estimated with relative precision (Kushner, Robert, 1992). However, notable inaccuracies are observed in populations prone to altered hydration states (Kyle et al., 2004b). Additionally, SF-BIA estimates of TBW correlate poorly with reference measures in individuals

with severe obesity (Bernhard et al., 2016). This effect is likely attributable to altered tissue distribution and the correlation between the ECF:ICF ratio and adiposity (Bernhard et al., 2016; Kyle et al., 2004a; Levitt et al., 2010). These findings highlight the need for caution when applying regression equations beyond the populations in which they were derived. Further work is required on developing and validating reference equations specific to disease states with altered hydration and excess adiposity.

Despite its limitations, there is a growing field of literature on the clinical applications of bioimpedance beyond volume estimations. One primary focus of such research is phase angle, the index of the ratio of reactance to resistance (Institute of Medicine & Committee on Military Nutrition Research, 1997). Phase angle is proposed as a marker for cellular integrity and health and is gaining attention in the prediction of nutritional status and disease outcomes (Rinaldi et al., 2019; Toso et al., 2000).

2.1.2.2 Bioelectrical Impedance Analysis - Multi-frequency

MF-BIA applies the same principles as SF-BIA, except resistance is measured at both low and high frequencies (Kyle et al., 2004a). Low frequencies are unable to overcome the capacitance of the cell membrane and, therefore, are only conducted through the extracellular space (Kyle et al., 2004a). In contrast, high-frequency currents may overcome the 'resistance' of the cell membrane and travel through both the extracellular and intracellular compartments (Kyle et al., 2004a). By applying both low and high-frequency currents, both TBW and the extracellular compartment can be determined. From this, ICW can also be calculated by subtracting ECW from TBW. Thus, unlike in SF-BIA, TBW estimation is not constrained by the assumption of a constant ECW: ICW ratio. Therefore, MF-BIA estimates may be less susceptible to changes in hydration status. The meta-analysis by Martinoli et al. (2003) found SF-BIA and BIS, but not MF-BIA, overestimated TBW in healthy adults, adults with obesity, and in chronic renal failure. The validity of MF-BIA, specifically in populations with obesity, has been reviewed by Becroft et al. (2019), who found that MF-BIA typically overestimates FFM and underestimates FM in these populations. Acceptable population-level concordance is observed, but large individual variability. This supports earlier conclusions that MF-BIA methodology lacks sufficient accuracy and reliability to assess body composition at the individual level in states of altered hydration (O'Brien et al., 2002).

2.1.2.3 Bioimpedance Spectroscopy

BIS fundamentally differs from SF-BIA and MF-BIA as it uses mathematical modelling to estimate volumes from resistances obtained across a spectrum of frequencies. A detailed description of the

principles and rationale behind these modelling methodologies is available in a review by De Lorenzo et al. (1997). The primary benefit of BIS is its application in individuals with altered hydration status. Firstly, through the application of very high frequencies, both ICF and ECF can be quantified (Matthie, James R., 2008). Therefore, unlike SF-BIA, assumptions of a normal hydration status are not required. BIS further individualises the estimation of fluid compartments by applying gender-specific resistivity constants derived from dilution experiments (De Lorenzo et al., 1997).

Despite more advanced methodology, validation studies for BIS also typically find large individual variability alongside good population-level agreement (Becroft et al., 2019; Earthman et al., 2007). Additionally, BIS consistently overestimates TBW and FFM in obesity (Cox-Reijven et al., 2002; Mager et al., 2008). Increased margins of error are attributed to the effect of adipose tissue on ICW-specific resistivity (Matthie, James R., 2008). Moissl et al. (2006) attempted to address this by introducing BMI into modelling equations as a marker for adiposity. This approach resulted in significantly more accurate estimations for all subjects, with more drastic effects at statistically extreme BMIs (Moissl et al., 2006). BIS methodology offers clear advantages over traditional BIA techniques, but further modifications to modelling approaches are required to improve its validity and usefulness in a clinical setting.

2.1.3 Direct Methods

2.1.3.1 Isotope Dilution

Isotope dilution is a technique for measuring TBW (and ECF). The underlying principle is that the quantity of tracer administered is the same before and after administration. Dilution procedures take fluid samples, such as blood, urine or saliva, before and after administering tracers such as deuterium (^{2}H) and oxygen-18 (^{18}O) into the body. TBW can be calculated using the tracer quantity, baseline concentration, and equilibrium concentration. FFM and FM are typically derived by assuming the hydration of FFM is constant at 73% (Pace & Rathbun, 1945; Wang, Z. et al., 2000). However, the proportion of water in FFM may be influenced by disease states, adiposity, and age (Hewitt et al., 1993; Levitt et al., 2010; Waki et al., 1991).

2.1.3.2 Total Body Counting

Total body counting or whole-body counting is a technique that measures high-energy gamma rays from naturally occurring radioactive potassium 40 in the body (Forbes et al., 1991). Potassium is found almost exclusively inside cell bodies and can, therefore, be used to estimate body cell mass (BCM). Using ratios identified in cadaver work from Forbes and colleagues, total body potassium

(TBK) can also be used to estimate FFM (Forbes et al., 1991). The validity of this assumption is challenged by consistent findings of lower mean potassium concentrations within FFM in other studies (Ellis, 2000). Additionally, small differences in TBK/FFM are exacerbated when FFM derived from TBK is used to estimate FM in a two-compartment model (Pierson Jr et al., 1991). This suggests TBK is better applied within multicompartmental models as a measure of BCM alongside other body composition analysis techniques.

2.1.3.3 Neutron Activation

Neutron activation analysis is a technique for measuring the elemental composition of the body (Ellis, 2000). When subjects are exposed to neutron radiation beams, energy is absorbed into nuclei and subsequently released as gamma rays. The energy characteristics and intensity can be used to identify the element and its quantity (with suitable calibration of the methodology). Using this technique, elements like nitrogen, calcium, carbon, and sodium can be measured (Ellis, 2000). Total body nitrogen can subsequently be used to estimate total body protein (Haas et al., 2007; Wang, J. et al., 1993). The distribution and proportions of chemical elements within the body can be used to estimate body composition in a four-compartment model. This is known as elemental partition analysis. Various methods for elemental partition analysis are described in a 1999 review by Kehayias & Valtueña. Neutron activation techniques have been used infrequently due to their high radiation exposure for subjects.

2.1.4 Criterion Methods

1.4.1 Hydrodensitometry

Hydrodensitometry, also known as underwater weighing, was historically considered the gold standard for body composition analysis. Hydrodensitometry involves submerging subjects underwater to estimate their body volume through fluid displacement (Katch et al., 1967). The measurement of body volume can be used with body mass and residual lung volume to calculate body density. Finally, body fat percentage can be derived using equations based on two-compartment models, such as those of Siri (1956) or Brozek (1963).

Air displacement plethysmography (ADP) is a modern alternative that also measures body density. The use of air displacement devices offers some advantages over hydrodensitometry, such as a reduced reliance on subject performance and the need for full immersion under water (Demerath et al., 2002; McCrory et al., 1995). However, both ADP and hydrodensitometry are scarcely used for subjects with obesity as the requirement for lightweight or tight swimwear may discourage and limit participation. Additionally, as FM has a lower density than FFM, subjects with obesity may require

counterweights to remain still or achieve full submersion for underwater weighing (Behnke et al., 1942).

1.4.2 Dual-Energy X-Ray Absorptiometry

DXA is a two-dimensional imaging technique used to estimate total and segmental FM, FFM, and bone mineral density (BMD) (Roubenoff et al., 1993). It is globally accepted as the gold standard for measuring bone mineral density and is considered an accurate measure of FM compared to other techniques (Guglielmi et al., 2016). The fundamental principle behind DXA involves measuring the attenuation of high and low-energy X-rays through the body. The degree of attenuation is dependent on the density and thickness of the tissue it passes through, as well as the energy level of the x-ray (Crabtree et al., 2007). This can be applied to a two-compartment model of the body to estimate bone mineral and soft tissue mass. Bone can be distinguished from soft tissue as its higher density results in greater attenuation (Bazzocchi et al., 2016). This principle can also be applied to a three-compartment model of bone mineral, FM and lean tissue mass. In tissue without bone, the ratio of attenuation between high and low-energy X-rays is found to be proportional to the fat content of the tissue (Laskey, 1996). Manufacturer-specific algorithms are then applied to estimate fat content in tissue where bone is present. By analysing areas of soft tissue with and without bone, FM and lean tissue mass can be differentiated (Toombs et al., 2012).

Like other techniques, DXA relies on assumptions around hydration and tissue density. These assumptions can vary between manufacturers, models and software, which leads to notable variability (Plank, 2005). DXA scans can be completed quickly, in 5-15 minutes and utilise very low doses of radiation (Crabtree et al., 2007). Additional technological developments have improved the practicality of DXA for subjects with obesity, as older devices were not suited for larger body sizes (Tataranni & Ravussin, 1995).

DXA is also less affordable and accessible than other techniques but offers the distinct advantage of enabling regional body composition assessment (Pietrobelli et al., 1996). However, high margins of error have been identified in areas containing minimal bone-free soft tissue, like the arm and thorax (Roubenoff et al., 1993). Validation studies against the gold standard four-compartment model indicate DXA may underestimate FM (Toombs et al., 2012). However, this finding is not consistent between studies. Unlike MRI (magnetic resonance imaging), DXA is unable to distinguish visceral and subcutaneous fat. Software attempts to enable this show strong correlations with CT (computed tomography) measurements but exhibit larger margins of error in subjects with obesity (Meredith-Jones et al., 2018; Taylor et al., 2021). DXA performs well at the group level when tracking changes

in body composition over time, but large intra-individual differences limit its individualised use (Toombs et al., 2012).

1.1.3.3 Magnetic Resonance Imaging

Whole-body MRI is considered the gold standard for body composition analysis as it accurately measures the quantity and distribution of both adipose tissue and skeletal muscle (Mitsiopoulos et al., 1998; Thomas et al., 2013). MRI uses radio waves and strong magnetic fields to generate images of the body's soft tissue (Machann et al., 2005). There are three approaches for assessing body composition in MRI images: single-slice, multi-slice, and whole-body (Hu et al., 2016). Multi-slice and whole-body approaches enable the direct quantification of visceral adipose tissue (VAT), a key component for assessing metabolic disease risk (Thomas et al., 2013).

Unlike other imaging techniques, CT and MRI do not utilise ionizing radiation. Therefore, MRI is preferred for whole-body assessments and in research settings. Despite this, the use of whole-body MRI is infrequent due to costly equipment, availability, and the difficulty of analysing three-dimensional images (Hu et al., 2016). MRI devices were also previously limited by gantry size or table weight capacity. However, the designs of newer imaging devices address these issues and make MRI more accessible for populations with obesity (Rothschild et al., 1991).

2.1.5 Comparison of DXA and Bioimpedance Techniques

DXA is traditionally accepted as the preferred method for body composition analysis due to its validation against the gold standard four-compartment model (Toombs et al., 2012). The complexity of four-compartment models makes them tedious and impractical for use in clinical settings or large studies. The affordability and accessibility of bioimpedance instruments provide an alluring alternative to DXA in these settings. However, there is limited evidence validating bioimpedance techniques against four-compartment models or DXA. Additionally, determining the validity of bioimpedance techniques is further complicated by variations between devices, equations, and measurement techniques. The high heterogeneity between studies often means meta-analysis is not possible. This limitation is exacerbated in clinical subpopulations like bariatric surgery patients as the available literature is further reduced. A summary of studies comparing body composition measures from BIA and DXA can be found in Table 3.

Conclusions on the validity of bioimpedance techniques must carefully consider the BMI of study populations. In a 2018 retrospective study of 3,655 individuals, Achamrah et al. compared body composition measures from DXA and SF-BIA at 50 Hz. Strong correlations between DXA and SF-BIA for both FM and FFM were observed at the population level alongside large limits of

agreement. For BMI ≥ 18.5 kg/m^2 and BMI < 40 kg/m^2, compared to DXA, SF-BIA overestimated FFM by 3.38-8.28 kg and underestimated FM by 2.51-5.67 kg. Interestingly, SF-BIA overestimated FFM by 5.87 kg in BMI ≥ 40 and underestimated FFM by 2.25 kg in BMI < 16 kg/m^2. Differences in FM and FFM between SF-BIA and DXA increased with BMI in patients between 18.5 and 25 kg/m^2, and ≥ 40 kg/m^2 (Achamrah et al., 2018). Two key conclusions can be drawn from these findings.

1) For BMI ≥ 18.5 kg/m^2 SF-BIA overestimates FFM and underestimates FM compared to DXA.

2) The validity of FM and FFM determination by SF-BIA is poor at the individual level.

These findings are in agreeance with other comparative studies of SF-BIA and DXA (Savastano et al., 2009; Widen et al., 2014). Findings from Savastano et al. are notable as measures of FM and FFM were compared at baseline, six months and twelve months following LAGB. The overestimation of FFM by SF-BIA was diminished at both follow-up time points and was attributed to the participants' weight loss. Investigations into MF-BIA have produced identical findings where FFM is overestimated, and FM is underestimated in participants classified as overweight and/or obese. Six studies identified in a systematic review by Becroft et al. (2019) reported that the inclusion of algorithmic adjustments for BMI and waist circumference improved the accuracy of FM and FFM by MF-BIA. However, no detailed information was provided on the adjustments made.

Table 3. *Summary of Studies comparing body composition measured by bioimpedance techniques to reference methods.*

Author (Study Design)	Study Population	BMI (kg/m^2)[1]	BCA Techniques	Bioimpedance methods compared to reference method:		Comments
				FFM	FM	
Achamrah et al., 2018 (Retrospective, Cohort)	Nutrition Unit Patients seen for malnutrition, obesity, or eating disorder. (n=3,655)	Analysis split into BMI ranges: < 18.5 (n=379) 18.5 - 25 (n=237) 25 - 30 (n=328) ≥ 30 (n=2,711)	MF-BIA & Whole body DXA	FFM strongly correlated irrespective of BMI (r=0.89, p<0.0001). In BMI <16 kg/m^2 underestimated FFM by 2.2kg. Overestimated FFM in 18.5≤BMI<25 kg/m^2 by 3.3 kg and in 25≤BMI<30 kg/m^2 by 7.1 kg.	FM strongly correlated irrespective of BMI (r=0.95, p<0.0001). In BMI <16 kg/m^2, overestimated FM by 2.5kg. Underestimated FM in 18.5≤BMI<25 kg/m^2 by 2.5 kg and in 25≤BMI<30 kg/m^2 by 5.6 kg.	MF-BIA device used only used 50kHz to calculate TBW. Large limits of agreement (LOA) were observed in all BMI groups. In patients with normal BMI or BMI ≤40 kg/m^2, differences between FFM and FM increased with BMI.
Ballesteros-Pomar et al., 2022 (Cross-sectional)	Severe obesity. (n=115)	46.1	MF-BIA & Whole body & segmental DXA	Determined by a proprietary equation, overestimated ALM by 7.3 kg. Equations by Sergi, Kyle and Yamada overestimated ALM by 2.8 kg, 4.1 kg, & 2.7 kg respectively.	Determined by proprietary equation, underestimated FM by 3.4 kg.	Large LOA observed for FM (14 kg). Across equations, larger LOA and bias compared to DXA was typically found in male subjects for ALM.
Berstad et al., 2012 (Prospective, Cohort)	Randomly sampled participants in a Norwegian sleep apnoea study. (n=93)	30.9	BIS & Whole body DXA	Overestimated FFM by 3.5 kg.	Underestimated FM by 3.5 kg. Underestimated BF% by 3.8%.	

Faria et al., 2014 (Cross-sectional)	Patients undergoing pre-operative treatment for bariatric surgery. (n=73)	40.2	MF-BIA & Whole body DXA	Overestimated FFM by 1.28 kg.	Underestimated FM by 2.05 kg.	Participants with body weights exceeding 120 kg were excluded due to the DXA device capacity. 89% of participants were female.
Savastano et al., 2009 (Prospective, Cohort)	Obese Women undergoing LAGB. (n=45)	42.1 at baseline.	SF-BIA @ 50 Hz & Whole Body DXA	FFM strongly correlated at T0 (r^2= 0.87), T6 (r^2=0.82), & T12 (r^2=0.99).	FM strongly correlated at T0 (r^2= 0.98), T6 (r^2=0.94), & T12 (r^2=0.99). BF% strongly correlated at T0 (r^2= 0.91), T6 (r^2=0.89), & T12 (r^2=0.98).	Correlation between SF-BIA & DXA for FM & FFM increased with weight loss.
Verdich et al., 2011 (Prospective, Cohort)	Obese women participating in the NUGENOB study. (n=131)	33.8 & 35.7. No mean BMI reported for the entire cohort.	MF-BIA & Whole body DXA (Two devices)	Overestimated FFM by 3.04 kg and 1.95 kg at baseline ($p<0.001$). Overestimated ΔFFM by 0.47 kg ($p<0.05$).	Underestimated FM by 3.17 kg and 0.98 kg at baseline ($p<0.001$ & $p<0.05$). Underestimated ΔFM by 0.38 kg (N.S)	Strong correlations were found between DXA and MF-BIA for FM & FFM at baseline and following weight loss. Wide LOA observed.
Widen et al., 2014 (Prospective, Cohort)	Bariatric Patients. (n=50)	44.1 at baseline	SF-BIA & a 3-compartment model consisting of D_20 dilution & Bod Pod.		BF% is highly correlated with the three-compartment model BF% at T0, T12, and weight loss. Underestimated BF% at T0 & T12 by 3.3% ($p<0.001$) & 1.66% ($p=0.03$).	SF-BIA used foot-to-foot electrodes. Large LOA observed for BF% (T0 19.3%, T12 19.1%, and total change 20.4%)

[1] Mean BMI of total study cohort unless stated otherwise. . Abbreviations: ALM = Appendicular Lean Mass; BCA = Body Composition Analysis; BF% = Body fat percentage; BIS = Bioimpedance spectroscopy; BMI = Body mass index; DXA = Dual-energy x-ray absorptiometry; FM = Fat mass; FFM = Fat-free mass; LOA = Limits of agreement; MF-BIA = multi-frequency bioelectrical impedance analysis; SF-BIA = Single-frequency bioelectrical impedance analysis.

2.2 Bariatric Surgery and Body Composition

2.2.1 Bariatric Surgery

The primary mechanisms of weight loss following bariatric surgery are malabsorption and restriction. Malabsorptive procedures like the jejunoileal bypass limit intestinal nutrient and caloric absorption through shortening or bypassing lengths of the small intestine. Alternatively, restrictive procedures such as gastric banding or the SG reduce caloric intake by invoking early satiety through reductions in stomach capacity. The RYGB and biliopancreatic diversion are examples of procedures with both restrictive and malabsorptive outcomes. The SG has replaced the gastric bypass as the most frequently performed procedure in New Zealand and internationally despite there being no clear consensus on procedure superiority (Garrett et al., 2020).

2.2.2 Sleeve Gastrectomy

The SG involves the resection of the stomach through stapling along an orogastric bougie. Approximately 75% of the stomach is removed along the greater curvature, with the resected stomach resembling a tubular sleeve (Huang et al., 2019). The SG was initially utilised for weight loss in 'super-obese' patients prior to a secondary procedure, usually a gastric bypass or biliopancreatic diversion with duodenal switch (BPD-DS) (Marceau et al., 1998). However, over time, SG has grown in popularity as a standalone procedure due to the procedure's relative ease of technique, low complication risk and low mortality rates (Gagner et al., 2013; Udelsman et al., 2019).

The alteration to the stomach's structure influences body weight and metabolic function through numerous factors. Being a restrictive technique, the primary weight loss mechanism of the SG is reduced oral food intake. Food intake is reduced following an SG due to reductions in stomach capacity and reductions in the appetite-stimulating hormone ghrelin (Huang et al., 2019). Ghrelin is produced in parietal cells found in the fundus and body of the stomach and previous studies have observed significant reductions in fasting ghrelin levels and suppression of post-prandial ghrelin production five years following SG (Bohdjalian et al., 2010; Karamanakos et al., 2008).

2.1.2 Roux-en-Y Gastric Bypass

The RYGB also involves segmentation of the stomach into an upper and lower portion through stapling. The upper portion of the stomach or gastric pouch acts similarly to the SG to reduce stomach capacity and limit food intake (Rubino et al., 2010). The gastric pouch is anastomosed to the jejunum, resulting in a bypassing of the distal stomach, duodenum, and proximal jejunum. This is known as the Roux-limb and typically measures 100 cm in length. The proximal jejunum is then anastomosed to the distal jejunum, which is known as the biliopancreatic limb. This results in food

bypassing the distal stomach, duodenum, and proximal jejunum (Rubino et al., 2010). The bypass reduces the capacity for nutrient absorption, further contributing to weight loss (Abdeen & Le Roux, 2015). Long-term considerations of RYGB include the management of nutrient deficiency risk and subsequent complications such as anaemia and osteoporosis (Abdeen & Le Roux, 2015).

2.2.3 Weight Loss

The effectiveness of bariatric surgery in producing weight loss is consistently upheld in the literature. A systematic review and meta-analysis of RCTs conducted in 2016 by Cheng et al. reported that surgical interventions resulted in greater weight loss than non-surgical approaches in RCTs with 1-year, 2-year and long-term (3-year or greater) follow-up durations (Cheng et al., 2016). The superiority of surgical procedures was maintained irrespective of surgery type, with greater weight loss observed following SG, RYGB, BPD and laparoscopic adjustable gastric banding (LAGB).

Weight loss after bariatric surgery is highly variable and influenced by factors such as the presence of comorbidities, pre-operative weight, and post-operative behaviours such as physical activity and dietary habits (Livhits et al., 2011). Estimating the degree of weight loss following bariatric surgery is limited by the lack of studies featuring follow-up durations greater than three years. In a 2021 review by van Rijswijk et al., the mean percentage total weight loss (%TWL) ranged from 27.5% to 32.3% for RYGB and 23.9% to 26.1% for SG (Van Rijswijk et al., 2021). The superiority of any specific procedure is currently not supported. However, currently, available comparative evidence of weight loss outcomes achieved from RYGB and SG favours RYGB. A 2021 meta-analysis by Uhe et al. included 20 studies comparing RYGB and SG and found RYGB resulted in greater %TWL at three months, six months, one year, two years, and five years post-surgery. RYGB also produced a greater percentage of effective weight loss (%EWL) than SG at 3-year and 5-year follow-ups (Uhe et al., 2022). However, it is worth noting that the use of non-standardised definitions of ideal body weight (IBW) and preoperative weight can generate significant variation in %EWL (Montero et al., 2011).

2.2.4 Fat Mass

Correlations between excessive adiposity, inflammation and ill health have been made for decades (Baumgartner et al., 1995; Vahdat et al., 2012). Clinical advancements in reducing metabolic disease risk have and will continue to target reductions in body FM alongside the preservation of FFM. Developments in bariatric surgery trends are guided by these two objectives.

Despite being referred to as weight loss surgery, the primary purpose of bariatric procedures is the reduction of body FM. The effect of SG and RYGB on changes in FM within the first year following surgery has been less extensively studied than total body mass (Table 4). Additionally, significant variability exists between studies by surgical specifications (such as SG bougie volume and RYGB limb length), methods of body composition analysis, and reported measures of body composition.

One prospective, non-randomised study by Otto et al. (2015) included 173 individuals and found that the group receiving RYGB had a lower body fat percentage (BF%) than SG after one year. However, the RYGB group had a lower preoperative BF% and no statistically significant difference was found when adjusted for BMI. Further studies by Kavanagh et al. (2019), Keidar et al. (2013), and Wells et al. (2015) also found no difference between the percentage change in FM between SG and RYGB. Notably, bioimpedance techniques or ADP were used to measure body composition within these studies. Comparisons utilising DXA to measure body composition are further limited. Guerrero-Perez et al. (2019) conducted a randomised study but only compared changes in FM, not BF% or percentage change in FM. Moize et al. (2013) also used whole-body DXA in a non-randomised study of 50 individuals and found no significant change in BF% one year post-surgery between RYGB and SG.

While high variability is observed in the extent of FM reduction twelve months following SG or RYGB, both procedures appear to produce similar reductions in FM percentage ranging from 10-25%. Like weight loss, FM reduction occurs continuously over the first twelve months following bariatric surgery, with the largest reductions occurring during the first 3-6 months. Trends in FM reduction beyond 12 months have been rarely investigated. One 2021 study by Ceriani et al. followed bariatric patients over five years, including 48 undergoing RYGB and 46 undergoing SG, with mean changes in FM being 33.6 kg and 26.6 kg, respectively. However, the study aimed to compare BPD and long common limb revision BPD to RYGB and SG. Thus, no statistical comparisons were made between the RYGB and SG groups. Further investigations into the effects of SG and RYGB on FM are required before drawing conclusions with any certainty.

2.2.5 Fat Mass Distribution

In addition to total body FM, the effect of bariatric surgery on FM distribution is of notable clinical importance. Investigations into body fat distribution have repeatedly found that high visceral FM contributes to increased metabolic disease risk independent of total FM or body weight (Kissebah et al., 1982; Lopes et al., 2016; Stefan, 2020). Most data available utilises single abdominal slices from MRI techniques to estimate VAT and subcutaneous adipose tissue (Korner et al., 2008). Few

studies have directly quantified the entirety of the sub-depots of adipose tissue before and after bariatric surgery.

Toro-Ramos et al. (2015) utilised whole-body MRI to quantify changes in FM and its distribution in the first 24 months following bariatric surgery. Significant reductions in total adipose tissue (TAT), subcutaneous adipose tissue (SAT), intramuscular adipose tissue (IMAT) and VAT occurred during the first 12 months following surgery (Toro-Ramos et al., 2015). No further significant changes were observed between 12- and 24 months post-surgery except in females. Reductions in both VAT and IMAT occurred despite no further significant reductions in body weight. Additionally, both male and female subcategories in the surgical group had similar VAT values to non-surgical controls after 24 months despite significantly higher body weight, TAT & SAT post-surgery (Toro-Ramos et al., 2015). This suggests that bariatric surgery may have targeted effects on VAT. This finding is supported by those of Schneider et al. (2016), where greater reductions in truncal fat were observed compared to leg fat in 42 individuals following LRYGB or SG.

Comparative investigations between surgery types are further scarce. Schneider et al. (2016) also compared changes in fat distribution between the two surgery types and found no differences in truncal or leg fat reduction. This contrasts with findings from Kayshap et al. (2013) where a greater absolute reduction in percent truncal fat was observed in RYGB compared to SG (16% vs 10% $p=0.04$) despite similar total weight loss. The utilisation of whole-body DXA is a key limitation of both studies, as adipose tissue sub-depots could not be quantified. One study by Kennegott et al. (2019) compared changes in adipose tissue quantified by whole-body MRI and found no differences in relative changes in VAT or SAT 12 months following RYGB and SG.

2.2.6 Fat-Free Mass

Lean mass or FFM losses typically comprise 20-30% of total weight loss in individuals classified as overweight or obese (Bradley et al., 2012; Magkos et al., 2016; Santanasto et al., 2011). Skeletal muscle represents the largest component of FFM, and in addition to generating contractile forces for movement, it plays important roles in metabolic function. Skeletal muscle is the primary site for insulin-mediated glucose absorption and largely determines resting energy expenditure (Baron et al., 1988; Zurlo et al., 1990). Low levels of skeletal muscle mass (SMM) are associated with impaired glucose homeostasis, osteoporosis, and increased mortality risk (Jang et al., 2020; Park & Yoon, 2013; Wang, Y. et al., 2023). Thus, the contribution of FFM to weight loss is a critical consideration when analysing weight loss interventions.

Trends in lean body mass (LBM), FFM, and SMM following bariatric surgery have been well documented. Strong correlations are observed between total weight loss and losses of LBM, FFM & SMM (Nuijten et al., 2022). Similar to FM, greater rates of lean tissue loss occur during the first three months, with more gradual losses occurring up to twelve months post-surgery. Pooled findings from a meta-analysis by Nujiten et al. (2022) found that 55% of LBM losses, 52% of FFM losses and 66% of SMM losses observed at twelve months occurred during the first three months following bariatric surgery. Additionally, of the eight studies identified that assessed LBM at 12 months and between 18-36 months, a mean loss of only 1.29 kg was found (Nuijten et al., 2022). This shows that lean tissue mass remains relatively stable beyond 12 months.

Comparisons of the effect on lean tissue of different types of bariatric surgery have rarely identified differences. In the previously mentioned meta-analysis by Nujiten et al. (2022), no differences were identified between procedures when comparing LBM, FFM and SMM relative to total weight loss. Comparative studies inconsistently report superior preservation of absolute LM following RYGB compared to SG (Davidson et al., 2018; Otto et al., 2015; Wells et al., 2015). However, in concordance with conclusions from pooled data, these effects are abolished when adjusting for differences in total weight loss or body composition at baseline.

Table 4. Summary of studies comparing body composition outcomes 1-year after SG and RYGB

Author (Study Design)	BCA technique	Sample size n(%F)	Variable	RYGB	SG	Comments
Guerrero-Perez et al., 2020 (Prospective, randomised)	Whole-body DXA	30 (60)	%TWL	35.3%	27.3%	The study was not powered to detect differences in FM or FFM between surgery groups.
			ΔFM	-19.6 kg	-11.6 kg	
			ΔLM	-9.6 kg	-6.1 kg	
Kavanagh et al., 2019 (Prospective, non-randomized)	ADP	66	TWL	27.9 kg	27.3 kg	No significant differences were identified between the surgery groups.
			%EWL	53.4%	47.2%	
			ΔFM	-23.3 kg (10.5%)	-23.3 kg (9.2%)	
			ΔLM	-4.6 kg (10.5%)	-3.9 kg (9.4%)	
Keidar et al., 2013 (Prospective, randomised)	BIA	37 (57)	%TWL	25.9%	28.4%	No significant differences were identified between the surgery groups.
			ΔFM	-23.9 kg (23.7%)	-24.9 kg (24.2%)	
			ΔFFM	-5.3 kg (6.9%)	-9.3 kg (9.1%)	
Moize et al., 2013 (Prospective, non-randomized)	Whole-body DXA	50 (82)	%TWL	32.1%	33.5%	No significant differences in weight loss or fat loss. %LM loss was greater in SG than RYGB after adjusting for baseline LM.
			ΔFM	-31.3 kg	-31.9 kg	
			ΔBF%	-15.2%	-13.5%	
			ΔLM	-6.2 kg	-9.3 kg	
Otto et al., 2015 (Prospective, non-randomized)	BIA	173 (71)	%TWL	31.7%	30.5%	No significant differences were found between the two groups after adjusting for baseline BMI. At baseline mean BMI was 45.6 kg/m^2 in RYGB (n=127) and 55.9 kg/m^2 in SG (n=46)
			%EWL	62.9%	52.3%	
			ΔFM	-30.2 kg	-37.6 kg	
			ΔBF%	-15.5%	1-2.1%	
			ΔLM	-9.7 kg	-14.7 kg	

Strain et al., 2009 (Prospective, non-randomized)	BIA	131 (73)	%EWL	70.4%	32.1%	Analysed data only included follow-up data from <12 months after surgery. Mean follow-up times were 19.1 ± 10.6 months in RYGB and 16.7 ± 5.6 months in SG. Few direct comparisons were made between the two groups. The analysis included ANCOVA for four groups: RYGB, SG, BPD-DS & AGB.
			ΔBF%	-20.9%	-17.7%	
			ΔLM	16.0%	9.1%	
Wells et al., 2015 (Retrospective, non-randomized)	BIA	53 (87)	ΔFM	-39.8 kg	-37.4 kg	Data was originally published in lbs. A Baseline difference in BMI between groups was reported. A larger increase in FFM% was observed in RYGB than in SG.
			ΔBF%	-7.7%	-4.9%	
			ΔFFM	- 6.3kg	-6.6 kg	
			ΔFFM%	17.1%	10.8%	

Reported values represent the reported group means. Sample sizes are expressed as n (Percentage of sample who are female). Sample sizes only include study participants allocated to RYGB or SG groups. Other surgical groups are not included in the reported value.
Abbreviations: ADP = Air displacement plethysmography; AGB = Adjustable gastric banding; BCA = Body Composition Analysis; BF% = Body fat percentage; BMI = Body mass index; BPD-DS = Biliopancreatic diversion with duodenal switch; DXA = Dual-energy x-ray absorptiometry; EWL = Excessive weight loss; FM = Fat mass; FFM = Fat-free mass; LM = Lean Mass; RYGB = Roux-en-Y gastric bypass; SG = Sleeve gastrectomy; TWL = Total weight loss.

Table 5. Summary of studies comparing body composition outcomes ≥3-years after SG and RYGB

Author (Study Design)	BCA technique	Sample size n(%F)	Variable	RYGB	SG	Comments
Ceriani et al., 2021 (Retrospective, non-randomized)	BIA	94 (85)	%EWL	81.7%	78.6%	No significant differences were found between the groups at 5-years.
			ΔFM	-33.6 kg	-26.6 kg	The retrospective analysis included RYGB patients since 2003 and SG patients since 2010. The study included BPD (2002) and BPD+LCL-R (2007) groups.
			ΔFFM	-11.2 kg	-9.8 kg	
Davidson et al., 2018 (Prospective, non-randomized)	3-Compartment model using Bod Pod & D_20 dilution. Whole-body MRI	69 (100)	TWL	41.8 kg	40.0 kg	The sample size was not consistent between the groups (RYGB: 58; SG: 11). An additional 14 males underwent RYGB. However, pooled data was not published.
			ΔFFM	-10.2 kg	-6.2 kg	BMI was higher, and FFM% was lower in the SG group than in RYGB at all time points.
			ΔFFM%	12.9%	8.7%	5-year data was only available in 62% of participants.
Yang et al., 2015 (Prospective, randomised)	Only body weight.	64 (66)	%TWL	31.0%	27.1%	A non-significant difference in baseline weight was present between the groups (p=0.055). However, height was greater in the RYGB group, and no difference in baseline BMI was detected.
			TWL	29.5 kg	24.3 kg	
			%EWL	92.3%	81.9%	At three years, %TWL, TWL and %EWL were significantly greater in RYGB than SG.
Zhang et al., 2014 (Prospective, randomised)	Only body weight.	64 (59)	%EWL	76.2%	63.2%	%EWL was significantly higher in RYGB than SG at 2-years, 3-years, 4-years, and 5-years.

Reported values represent the reported group means. Sample sizes are expressed as n (Percentage of sample who are female).

Abbreviations: BCA = Body Composition Analysis; BMI = Body mass index; BPD = Biliopancreatic diversion; BPD+LCL-R = Revisional long common limb biliopancreatic diversion; EWL = Excessive weight loss; FM = Fat mass; FFM = Fat-free mass; RYGB = Roux-en-Y gastric bypass; SG = Sleeve gastrectomy; TWL = Total weight loss.

2.2.7 Type 2 Diabetes Mellitus Remission

Body composition changes following bariatric surgery also have significant effects on metabolic health. Pooled data from a systematic review of RCTs found five-year T2DM resolution rates (HbA_{1C} below 6.0%) of 37.4% following RYGB and 27.5% following SG (Sharples & Mahawar, 2019). However, differences in T2DM resolution rates, improvement rates or HbA_{1C} levels at five years failed to reach statistical significance. While not statistically significant, differences in T2DM resolution rates may be explained by the greater %EWL achieved following RYGB in the included studies.

In a study of 60 subjects with uncontrolled T2DM, those receiving RYGB achieved greater weight loss and had significantly lower HbA_{1C} levels at 24 months post-surgery than those receiving SG or intensive medical therapy (Guerrero-Pérez et al., 2019). Additionally, 58% of SG patients and 80% of RYGB patients achieved T2DM remission (defined as an HbA_{1C} below 7.0% or 53 mmol/mol). Kashyap et al. (2013) also reported superior outcomes following RYGB compared to SG. Participants randomised to undergo RYGB had improvements in insulin sensitivity and beta cell function compared to the control group receiving intensive medical treatment (Kashyap et al., 2013). No improvements were found in the SG group. These differences were attributed to the greater reduction in truncal fat in the RYGB group. In contrast, Yang et al. (2015) found no difference in HbA_{1C} values three years after SG or RYGB despite greater weight loss occurring in the RYGB group. Interestingly, a greater reduction in HbA1c values was observed at 3 and 6 months in the RYGB group.

Analysis of T2DM remission outcomes at five years of 114 individuals from this trial cohort has been previously published (Murphy et al., 2022). Participants were randomly assigned to undergo RYGB or SG and were assessed at one year and five years post-operatively. T2DM remission was defined as an HbA_{1C} <6% or 42 mmol/mol. T2DM occurred at a greater rate following RYGB (47%) than SG (33%). Percentage weight loss was also greater in the RYGB group. Applying the definition of T2DM remission used by Guerrero-Pérez (2019) (HbA_{1C} <7.0%) produces similar remission rates of 70% in RYGB and 58% in SG (Murphy et al., 2022).

Currently, there is insufficient evidence to claim superior T2DM remission outcomes following one type of bariatric surgery. Despite this, potential physiological explanations are well established. Improvements in insulin sensitivity following bariatric surgery are primarily attributed to reductions in body weight and body FM. Further, markers of obesity, such as abdominal adiposity, have long been correlated with insulin sensitivity (Goodpaster et al., 1997). With the previously discussed evidence suggesting quantitative and qualitative differences in body composition outcomes

following bariatric surgery, further investigation into T2DM remission and diabetes-associated factors is warranted.

Chapter 3. Methods

3.1 Randomised Clinical Trial

3.1.1 Ethics and Trial Registration

This clinical trial (Murphy et al., 2016) is registered with the Australian New Zealand Clinical Trials Registry (ACTRN12611000751976). Ethics approval was obtained from the Northern Y Regional Ethics Committee (NTY/11/07/082).

3.1.2 Power Analysis

Power analysis was completed for the primary outcome of the study, T2DM remission. A minimum of 42 patients per arm was calculated to provide 80% power to detect a difference between the two groups using a two-sided alpha value of 0.05. After adjusting for an expected loss to follow-up rate of 20%, a minimum of 53 patients per arm was required (Murphy et al., 2022).

3.1.3 Patient eligibility and recruitment

Patients referred to the bariatric surgery program at North Shore Hospital aged 20-55 years, with a BMI of 35-65 kg/m^2 and a diagnosis of T2DM at least six months prior, were invited to attend an information evening for the study. Eligible participants were also required to be suitable for either surgical procedure and able to commit to long-term follow-up. Exclusion criteria included pregnancy, type 1 diabetes mellitus, chronic pancreatitis, oral steroid therapy, active smokers, previous bariatric or esophagogastric surgery, myocardial infarction or cerebrovascular events within the last six months, malignancy in the last five years and those with contraindications for general anaesthesia. Recruitment of participants began in September 2011 and was completed in October 2014. A total of 114 participants were recruited from a single centre (North Shore Hospital).

3.1.4 Study Design

The study was a single-centre, prospective, parallel, two-arm, randomised, double-blind, superiority trial. The trial protocol has been previously published (Murphy et al., 2016). The primary outcome assessed was the comparative rates of T2DM remission following RYGB or SG. Secondary outcomes included weight change, the resolution of comorbidities, peri- and post-operative complications, change in body composition, resting energy expenditure and bone density, and

quality of life. A sub-study was completed with additional outcomes related to T2DM remission, including food intake and satiety, as well as changes in gut hormones and gut bacteria.

Participants providing informed consent and with confirmed eligibility were placed on a very low-calorie diet (VLCD) two weeks prior to surgery. Two days prior to surgery, participants attended a pre-surgery appointment at the body composition laboratory at Auckland City Hospital. Baseline data obtained included height, weight, BMI, DXA, SF-BIA, MF-BIA and BIS measurements. Participants were invited to attend an identical appointment at one- and five-years post-surgery, where measurements were collected again. The methods used during these assessments are described in detail in section 3.3.

Participants were randomised to a surgery type on the day of surgery. Both the assessor and patient were blinded to the surgery they had received. All surgeries were performed under the direct supervision of an experienced bariatric surgeon at North Shore Hospital, Auckland, New Zealand. Further details on the procedures are provided in section 3.2.3.

3.2 Study Protocol

3.2.1 Very Low-Calorie Diet (VLCD)

All participants were prescribed a VLCD for two weeks preoperatively. This consisted of three daily servings of OPTIFAST (Nestlé, Vevey, Switzerland), each containing ~150 kCal plus vegetables.

3.2.2 Randomisation and Blinding

Participants were randomised to either LSG or SR-LRYGB through computer-generated random number codes (Minim, London) managed by an independent study member and included minimisation based on ethnicity (Māori, Pacific, NZ European/other), BMI category (35-44.9 kg/m^2, 45-54.9 kg/m^2 or 55-65 kg/m^2), age category (20-29, 30-39 or 40-55), duration of T2DM diagnosis (<5, 5-10 or >10 years), and the presence of insulin therapy.

Participant allocation was disclosed to the surgical team following the administration of general anaesthesia to the participant. Surgery allocation was not disclosed to participants, researchers or other clinicians throughout the study.

3.2.3 Surgical Procedures

Identical laparoscopic incisions were used during both surgical procedures to maintain blinding of participant surgery allocation.

3.2.3.1 Laparoscopic Sleeve Gastrectomy

Participants receiving the laparoscopic SG had a sleeve fashioned using a laparoscopic stapling device over a 36-Fr oro-gastric bougie starting 2 cm proximal to the pylorus.

3.2.3.2 Laparoscopic Silastic Ring Roux-en-Y Gastric Bypass

Participants receiving the laparoscopic RYGB had a lesser-curve based gastric pouch fashioned over a 32-Fr oro-gastric bougie, with a 100-cm antecolic Roux limb anastomosed by a hand-sewn single-layer gastrojejunostomy. Biliopancreatic limbs measured 50 cm. A 6.5 cm silastic ring was placed 2-3 cm above the gastrojejunostomy to prevent stomal dilation.

3.2.4 Post-Operative Management

Both groups received identical postoperative management and follow-up. All pharmacological agents for diabetes, hypertension and hyperlipidaemia were stopped at the time of surgery. Participants were reviewed by an endocrinologist at six weeks, nine months and annually for medication adjustments and monitoring of vascular complications. The endocrinologists remained blinded to which surgery participants had received. Glucose-lowering agents were restarted in participants whose postoperative capillary glucose exceeded 12 mmol/L. The protocol for medication adjustment was published with the study protocol (Murphy et al., 2022).

3.3 Outcome Measures

3.3.1 Anthropometry

3.3.1.1 Body Weight

Body weight was assessed two days prior to surgery following two weeks of VLCD and at one year and five years post-operatively. Weight was measured to the nearest 0.1 kg using digital scales (SECA, Chino, California, USA) at the University of Auckland's Body Composition Laboratory, Auckland City Hospital. The removal of shoes and any heavy clothing items was requested. Adjustment was made for estimated weight of clothing.

3.3.1.2 Height

Height was recorded to the nearest 0.5 cm at each of the three clinical assessments using a stadiometer. Without shoes, participants were asked to stand with their backs and heels against the stadiometer, with their heads in the Frankfort horizontal plane.

3.3.1.3 Anthropometric Derivatives

BMI was calculated for each time point as the participant's weight in kilograms divided by their height in meters squared.

$$BMI\ (kg/m^2) = \frac{Body\ Weight}{Height^2}$$

%EWL standardises weight loss against an 'ideal' body weight (IBW) at a BMI of 25 kg/m^2. %EWL was calculated at one year and five years following surgery using the following formula:

$$\%EWL = \frac{(Weight_{Baseline} - Weight_{Follow\ up})}{(Weight_{Baseline} - IBW)} x\ 100$$

3.3.2 Dual-energy X-ray Absorptiometry

DXA (iDXA, software V.15, GE-Lunar, Madison, Wisconsin, USA) was used to measure total FM, total lean soft tissue mass, total bone mineral content, and fat, lean soft tissue and bone mineral content of the limbs. ASMM was derived according to Heymsfield et al. (1990):

ASMM = limb lean soft tissue mass – 0.82 x limb bone mineral content

Total FFM was calculated as the sum of total lean mass and total bone mineral content. Regional analysis provided measures of abdominal fat and abdominal visceral fat, with the latter estimated using CoreScan™ software. Subcutaneous abdominal fat was calculated by subtracting abdominal visceral fat from total abdominal fat. Scans were performed with participants in the supine position. Where participants could not fit entirely within the scan area, the composition of the left arm was assumed to be that of the fully scanned right arm.

3.3.3 Bioimpedance Assessment

SF-BIA & MF-BIA measurements were carried out in the supine position immediately following the DXA scan.

3.3.3.1 Single-Frequency Bioimpedance Analysis

A four-terminal impedance analyser operating at 50 kHz and 800 mA was used to measure whole-body resistance (R) and reactance (Xc) following the manufacturer's instructions (Model BIA-101, RJL Systems, Clinton Township, MI, USA). Gel electrodes (#0525, Bodystat Ltd, UK) were placed on the dorsal surfaces of the right hand and right foot, at the distal metacarpals and metatarsals, respectively, and between distal prominences of the radius and the ulna at the wrist, and the medial

and lateral malleoli at the ankle. The measured values of R and Xc were entered into a computer program supplied by RJL systems, along with the participant's weight, height, age and sex, to provide estimates of TBF. FFM was calculated by subtracting TBF from body weight.

3.3.3.2 Multi-frequency Bioimpedance Analysis

R and Xc at 50 kHz and impedance values at 5, 50, 100 and 200 kHz were measured immediately following the single-frequency measurements using the four-terminal Quadscan 4000 (Bodystat Ltd, UK) multi-frequency analyser operating at 800 mA. The manufacturer's proprietary equations were used to obtain estimates of TBF based on the participant's weight, height, age, and sex. FFM was calculated by subtracting TBF from body weight. Data are presented as mean ± standard error of the mean unless stated otherwise.

3.4 Statistical Analysis

Repeated measures data were analysed using linear mixed models to compare changes over time between the groups. A significant group x time (operation x time) interaction effect indicated that the groups differed in their responses over time. A non-significant interaction indicated that the time profiles were similar for the two groups, i.e., the responses over time were essentially parallel to one another. Comparisons between groups for differences in variables of interest were conducted using Fisher's exact test for categorical data, Student's two-sample t-tests for normally distributed data and paired t-tests for within-group changes. Comparison results obtained by DXA and SF-BIA/MF-BIA equations were compared using scatter plots and the Bland-Altman approach (Bland & Altman, 1986), providing the bias with 95% confidence limits (limits of agreement) and the correlation coefficient indicated the extent of proportional bias. Pearson correlations and the concordance coefficient of Lin (1989) were determined for the scatter plots between DXA and BIA data. For FFM and FM, the accuracy of each BIA equation was calculated by the percentage of patients with a difference between BIA and DXA results within ±10% or ±5% of the data obtained by DXA. Statistical analysis was performed using Excel (Microsoft, Redmond, WA) or SAS release 9.4 (SAS Institute, Cary, NC). A p-value <0.05 was considered statistically significant.

Chapter 4. Results

4.1 Patient Characteristics

Body composition data were available at all three follow-up points for 91 of the 114 patients measured at baseline. Exclusion rates were similar between the surgery groups, with 10 RYGB (18%) and 13 SG (22%) patients being lost to follow-up, for a total of 20%. A further three patients were excluded from bioimpedance analysis due to missing either single-frequency or multi-frequency measurements at baseline. The demographics of participants included in the data analysis are shown in Table 6. The mean BMI of the SG group (40 kg/m^2) was slightly higher than in the RYGB group (38.9 kg/m^2). However, this was not statistically significant (p=0.37). DXA measurements of baseline body composition of the two groups are shown in Table 7. There were no significant differences in FM or fat-free variables between the groups.

Table 6. Baseline demographic characteristics

Parameter	RYGB (n=46)	SG (n=45)	P value
Age, years	46.8 ± 6.7	47.3 ± 6.1	0.74
Weight, kg	113.6 ± 19.5	115.4 ± 21.3	0.67
BMI, kg/m^2	38.9 ± 5.2	40.0 ± 6.0	0.37
Sex, n (%)			0.68
Male	20 (43.5)	22 (48.9)	
Female	26 (56.5)	23 (51.1)	
Ethnicity, n (%)			0.38
NZ European	27 (58.7)	31 (68.9)	
Māori	9 (19.6)	7 (15.6)	
Pacific	5 (10.9)	1 (2.2)	
Other	5 (10.9)	6 (13.3)	

Values are expressed as mean ± SD or as percentages. BMI = body mass index; RYGB = Roux-en-Y gastric bypass; SG = sleeve gastrectomy.

Table 7. Body weight and body composition measured by DXA at baseline, 1 year and 5 years.

	RYGB (n=46)	SG (n=45)	P value
BW (kg)			
Baseline	113.7 (±2.9)	115.5 (±3.2)	0.63
1-Year	81.8 (±2.6)	87.7 (±2.1)	0.12
5-Year	88.6 (±2.7)	101.4 (±2.4)	<0.001
%EWL			
1-Year	85.8 (±5.0)	65.9 (±3.2)	<0.001
5-Year	66.8 (±4.2)	32.4 (±2.7)	<0.0001
TBF (kg)			
Baseline	51.3 (±1.9)	52.2 (±2.1)	0.72
1-Year	25.3 (±1.5)	30.2 (±1.4)	0.037
5-Year	33.4 (±1.5)	43.3 (±1.6)	<0.0001
TBF%			
Baseline	45.0 (±1.1)	44.9 (±1.1)	0.93
1-Year	30.5 (±1.2)	34.4 (±1.3)	0.016
5-Year	37.6 (±1.1)	42.7 (±1.1)	0.002
FFM (kg)			
Baseline	62.5 (±1.9)	63.6 (±1.9)	0.68
1-Year	57.3 (±1.9)	58.2 (±1.8)	0.74
5-Year	55.6 (±1.9)	58.6 (±1.8)	0.26
FFM%			
Baseline	55.1 (±1.1)	55.3 (±1.1)	0.89
1-Year	70.5 (±1.3)	66.4 (±1.3)	0.017
5-Year	62.9 (±1.2)	57.9 (±1.1)	0.003
ASMM (kg)			
Baseline	26.0 (±0.9)	26.9 (±0.9)	0.51
1-Year	22.3 (±0.9)	23.0 (±0.8)	0.56
5-Year	21.8 (±0.9)	24.0 (±0.9)	0.095
ASMM%			
Baseline	22.8 (±0.5)	23.3 (±0.5)	0.59
1-Year	27.0 (±0.5)	26.2 (±0.6)	0.26
5-Year	24.5 (±0.6)	23.5 (±0.6)	0.20
AFAT (kg)			
Baseline	5.57 (±0.22)	5.70 (±0.25)	0.64
1-Year	2.34 (±0.17)	2.89 (±0.16)	0.05
5-Year	3.31 (±0.19)	4.49 (±0.18)	<0.001
VFAT (kg)			
Baseline	2.58 (±0.17)	2.59 (±0.16)	0.98
1-Year	0.91 (±0.07)	1.13 (±0.08)	0.20
5-Year	1.29 (±0.19)	1.98 (±0.12)	<0.001
VFAT:AFAT			
Baseline	47.1 (±2.6)	47.4 (±2.7)	0.93
1-Year	42.7 (±3.1)	41.3 (±2.7)	0.70
5-Year	39.2 (±2.5)	44.9 (±2.4)	0.12

Values are expressed as mean ± standard error of the mean. BW = body weight; %EWL = percentage excess weight loss; TBF = total body fat; FFM = fat-free mass; ASMM = appendicular skeletal muscle mass; AFAT = android fat; VFAT = visceral fat; VFAT:AFAT = (VFAT/AFAT)*100.

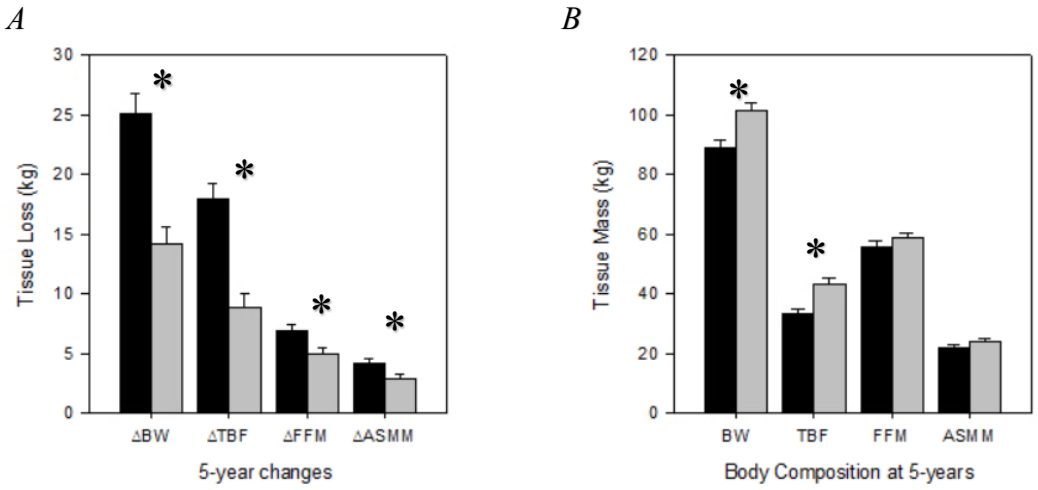


Figure 1. *(A) Total changes in body weight (BW), total body fat (TBF), fat-free mass (FFM), and appendicular skeletal muscle mass (ASMM) after five years for RYGB (■) and SG (■) patients. (B) Patient body composition at five years as measured by DXA for RYGB (■) and SG (■). * P<0.05 for the difference between the groups.*

4.2 Body Weight

Body weight (BW) decreased across the entire cohort from baseline to (T0) to 5-years (T2) and is shown in Table 8 and Figures 1 & 2A. Mixed model analysis detected a significant operation x time interaction (p<0.0001) and a statistically significant difference in BW at five years (mean difference: 12.79 kg, p=0.0009; Figures 1B & 2A). There was no significant difference in change in BW between the groups after one year (p=0.097). Between 1 and 5 years, weight regain was greater in the SG group than in the RYGB group (13.7 kg vs 6.8 kg, p<0.001) (p<0.001). At five years, the mean total weight loss in the RYGB group was 25.1 kg, compared to 14.1 kg in the SG group (p<0.0001).

Mixed model analysis also identified a significant operation x time interaction (p=0.0037) for %EWL, and differences in %EWL at one year (p=0.0005) and five years (p<0.0001) were seen (Figure 2B). In the RYGB group, %EWL was 85.8% at one year and 66.8% at five years. %EWL was significantly lower in the SG group at both time points, with %EWL of 65.9% at one year (p=0.001) and 32.4% at five years (p<0.0001).

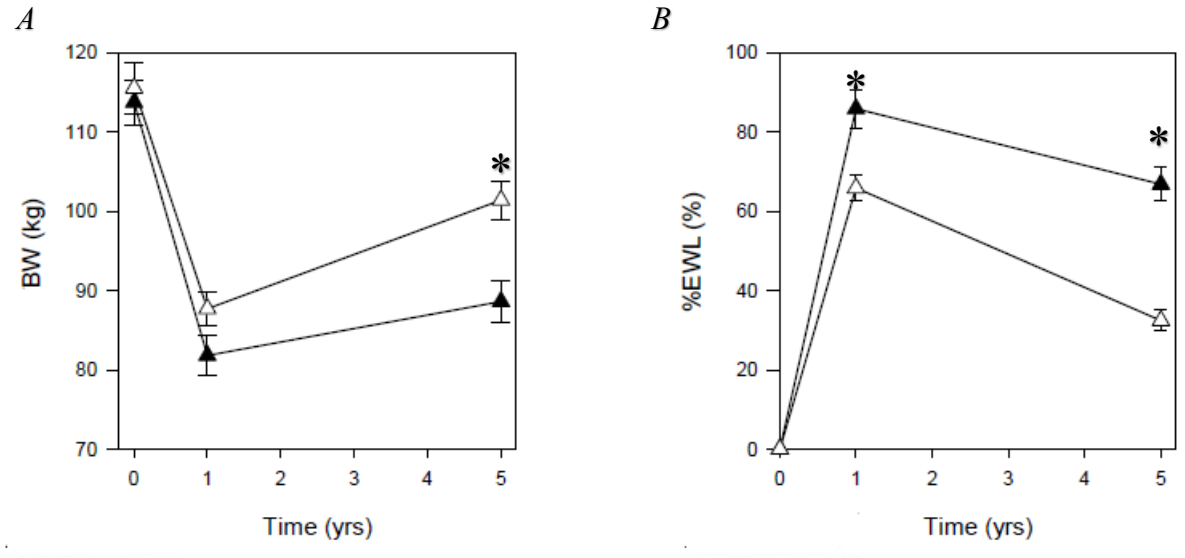


Figure 2. *(A) Body weight measured at baseline, one year and five years post-surgery for SG (Δ) and RYGB (▲). (B) Percentage excess weight loss at one year and five years post-surgery for SG (Δ) and RYGB (▲). %EWL was calculated as 100 * (Baseline Weight – Follow-up Weight)/(Baseline Weight – IBW).*

Table 8. Change in BW and %EWL over 5 years.

Parameter	**RYGB (n=46)**	**SG (n=45)**	**P value**
ΔBW (kg)			
1-year	-31.9 (±1.5)	-27.8 (±1.9)	0.097
5-year	-25.1 (±1.6)	-14.1 (±1.5)	<0.0001
Δ1-5 years	6.8 (±1.1)	13.7 (±1.6)	<0.001
%EWL (%)			
1-year	85. 8 (±5.0)	66.0 (±3.2)	0.001
5-year	66.8 (±4.2)	32.4 (±2.7)	<0.0001
Δ1-5 years	-18.9 (±3.3)	-33.3 (±3.6)	0.004

Values are expressed as mean ± standard error of the mean. ΔBW = Change in body weight; %EWL calculated as: [(initial weight − current weight) / (initial weight – ideal weight)] × 100.

4.3 Fat Mass

As shown in Table 9, a greater reduction of FM occurred in the RYGB group over five years. Mixed model analysis identified a significant operation x time effect across the groups ($p<0.001$; Figure 3). Change in TBF at five years was -17.9 kg (7.4%) following RYGB compared to -8.8 kg (2.2%) in the SG group (ΔTBF; $p<0.0001$, ΔTBF%; $p<0.0001$). Fat loss occurred rapidly after surgery with reductions in TBF of 26 kg for RYGB and 21.9 kg for SG after one year ($p=0.053$). Following the short-term loss of FM after one year, the SG group regained significantly more FM between 1 and 5 years than the RYGB group ($p= 0.003$). All within-group changes were highly significant ($p<0.0001$).

Mixed model analysis also identified significant operation x time effects for AFAT ($p<0.001$), VFAT ($p<0.001$), and VFAT:AFAT ($p=0.008$) (Figure 4). Changes in central FM followed the same pattern as observed for TBF and are shown in Table 9. Changes in AFAT and VFAT at five years in the RYGB arm were -2.3 kg and -1.3 kg, respectively. For SG, smaller losses of 1.2 kg of AFAT and 0.6 kg of VFAT were seen ($p<0.001$ for both). Initial losses of both AFAT and VFAT at one year were not statistically different between the groups. However, between 1-year and 5-year follow-ups, the SG group regained a greater amount of AFAT ($p=0.002$) and VFAT ($p<0.001$).

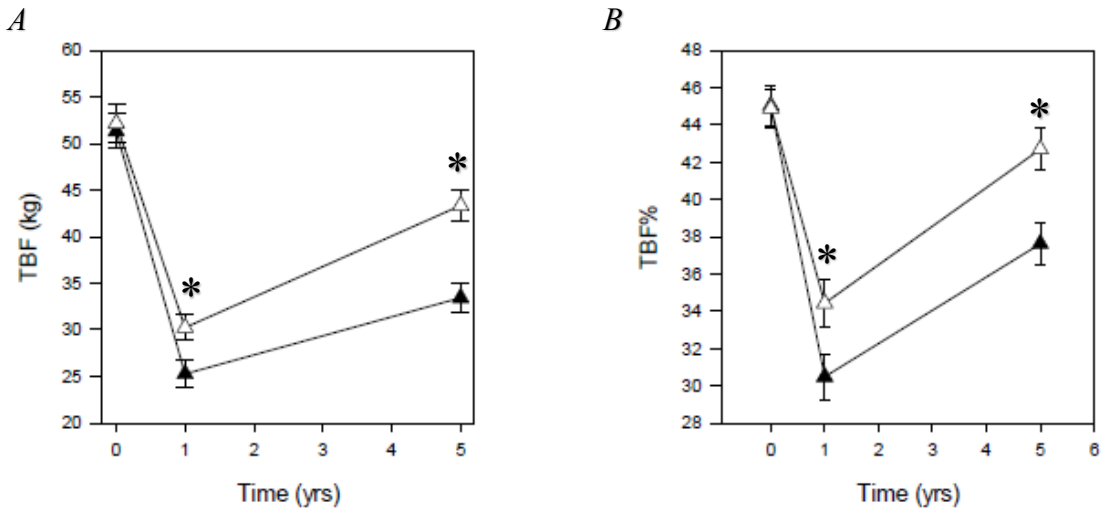


Figure 3. *(A) Total body fat measured by DXA at baseline, one year and five years post-surgery for SG (Δ) and RYGB (▲). (B) Total body fat % at baseline, one year, and five years post-surgery for SG (Δ) and RYGB (▲).*

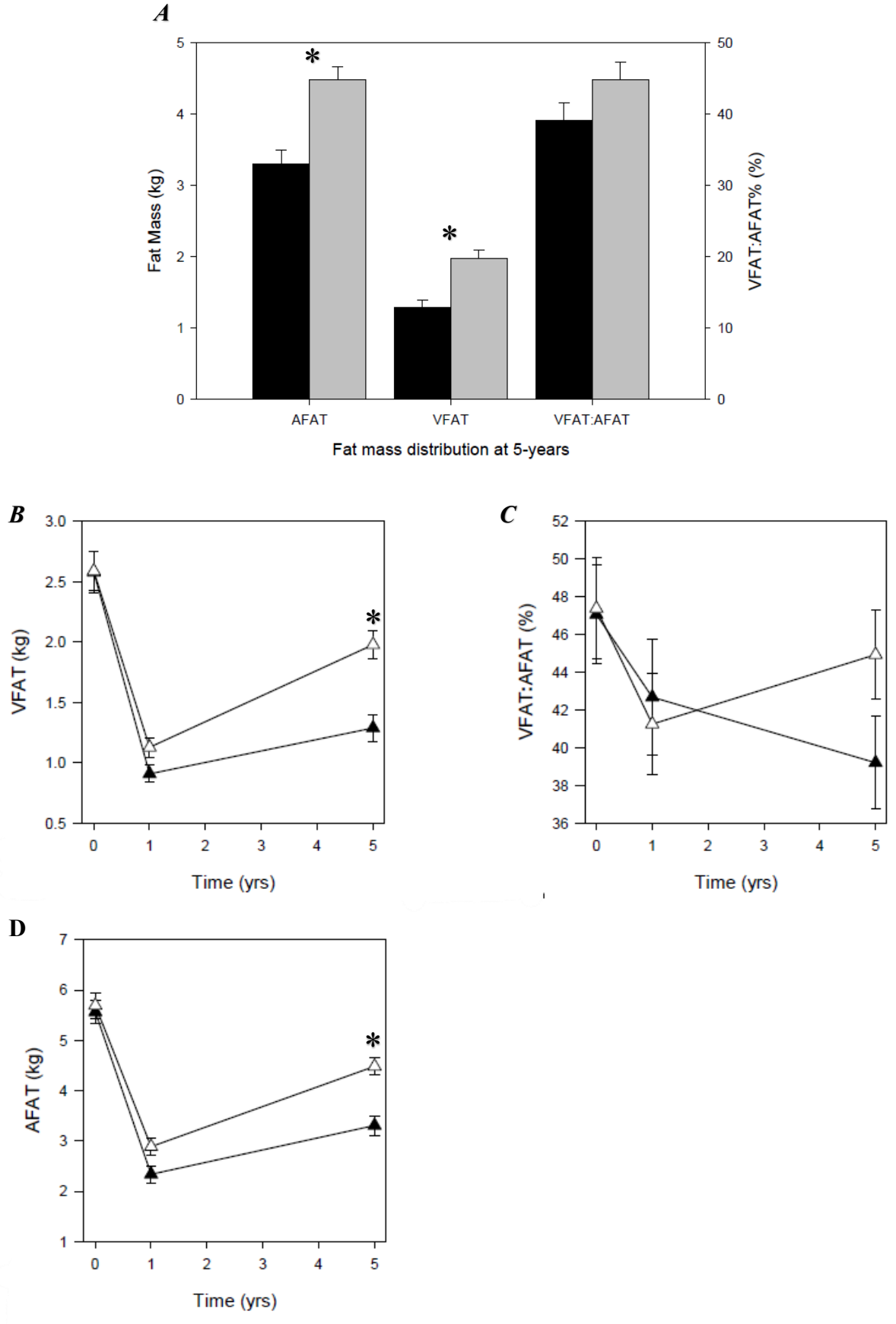


Figure 4. *(A) Patient central fat distribution at five years as measured by DXA for RYGB (■) and SG (■). (B) Visceral fat (VFAT) measured by DXA at baseline, one year and five years post-surgery for SG (Δ) and RYGB (▲). (C) Visceral fat as a percentage of android fat (AFAT) at baseline, one year, and five years post-surgery for SG (Δ) and RYGB (▲). (D) Android fat (AFAT) at baseline, one year, and five years post-surgery for SG (Δ) and RYGB (▲).*

Table 9. Changes in total body fat and central fat mass over 5 years

	RYGB (n=46)	SG (n=45)	P value
ΔTBF (kg)			
1-year	-26.0 (±1.4)	-21.9 (±1.6)	0.053
5-year	-17.9 (±1.4)	-8.8 (±1.2)	<0.0001
Δ*1-5 years*	8.2 (±0.9)	13.1 (±1.3)	<0.01
ΔTBF% (%)			
1-year	-14.5 (±0.9)	-10.5 (±0.8)	0.001
5-year	-7.4 (±0.7)	-2.2 (±0.5)	<0.0001
Δ*1-5 years*	7.1 (±0.8)	8.3 (±0.7)	0.30
ΔAFAT (kg)			
1-year	-3.23 (±0.16)	-2.81 (±0.19)	0.10
5-year	-2.26 (±0.15)	-1.22 (±0.15)	<0.0001
Δ*1-5 years*	0.97 (±0.11)	1.60 (±0.15)	<0.01
ΔVFAT (kg)			
1-year	-1.67 (±0.13)	-1.46 (±0.12)	0.23
5-year	-1.29 (±0.10)	-0.60 (±0.10)	<0.0001
Δ*1-5 years*	0.38 (±0.08)	0.85 (±0.10)	<0.001
ΔVFAT:AFAT (%)			
1-year	-4.38 (±2.33)	-6.13 (±1.28)	0.60
5-year	-7.86 (±1.10)	-2.46 (±1.22)	<0.01
Δ*1-5 years*	-3.48 (±2.36)	3.67 (±1.49)	<0.01

Values are expressed as mean ± standard error of the mean. P values derived from Student's t-test. TBF = total body fat, TBF% = body fat percentage, AFAT = android fat, VFAT = visceral fat, VFAT:AFAT = 100*(VFAT/AFAT).

4.4 Fat-Free Mass

Alongside reductions in TBF, both surgery groups had significant losses in FFM after five years, with reductions of 6.9 kg in RYGB (p<0.0001) and 5.0 kg in SG (p<0.0001), as shown in Table 10. Mixed model analysis confirmed significant operation x time interactions for FFM (p=0.0015), FFM% (p<0.001), ASMM (p=0.0012) and ASMM% (p=0.0027) (Figure 5).

Loss of FFM primarily occurred during the first year following surgery in both groups. However, a further gradual loss of 1.7 kg of FFM occurred beyond one year in the RYGB group, while the SG group had a minor increase in FFM of 0.4 kg. Despite greater losses of absolute FFM at five years, FFM% was higher in RYGB than SG (62.9% versus 57.9%; p=0.003). A greater increase in FFM% was seen at one year (p<0.001) and five years (p<0.0001) in RYGB than in SG (Table 10).

Trends in FFM were reflected in changes in ASMM. Both groups had similar absolute reductions in ASMM at one year (p=0.75) that equated to a greater increase in ASMM% in RYGB than SG

(p=0.003). Additionally, further loss of ASMM occurred between 1 and 5 years in the RYGB group (-0.5 kg) and not in the SG group (+0.9 kg). No significant differences were found between the groups for ASMM or ASMM% at five years (Table 7). ASMM trended towards significance (p=0.095), and analysis of changes over five years in ASMM and ASMM% showed significantly greater changes for RYGB (Table 10).

Table 10. Changes in fat-free mass and appendicular skeletal muscle mass over 5 years

	RYGB (n=46)	**SG (n=45)**	**P value**
ΔFFM (kg)			
1-year	-5.2 (±0.4)	-5.4 (±0.4)	0.73
5-year	-6.9 (±0.5)	-5.0 (±0.5)	<0.01
Δ*1-5 years*	-1.7 (±0.5)	0.4 (±0.4)	<0.001
ΔFFM% (%)			
1-year	15.4 (±0.9)	11.1 (±0.8)	<0.001
5-year	7.9 (±0.8)	2.6 (±0.5)	<0.0001
Δ*1-5 years*	-7.5 (±0.9)	-8.6 (±0.8)	0.39
ΔASMM (kg)			
1-year	-3.8 (±0.2)	-3.9 (±0.3)	0.75
5-year	-4.2 (±0.4	-2.9 (±0.3)	<0.01
Δ*1-5 years*	-0.5 (±0.3)	0.9 (±0.2)	0.001
ΔASMM% (%)			
1-year	4.2 (±0.3)	2.9 (±0.3)	<0.01
5-year	1.7 (±0.4)	0.3 (±0.2)	<0.01
Δ*1-5 years*	-2.5 (±0.3)	-2.6 (±0.3)	0.79

Values are expressed as mean ± standard error of the mean. P values derived from Student's t-test. FFM = fat-free mass. ASMM = appendicular skeletal muscle mass.

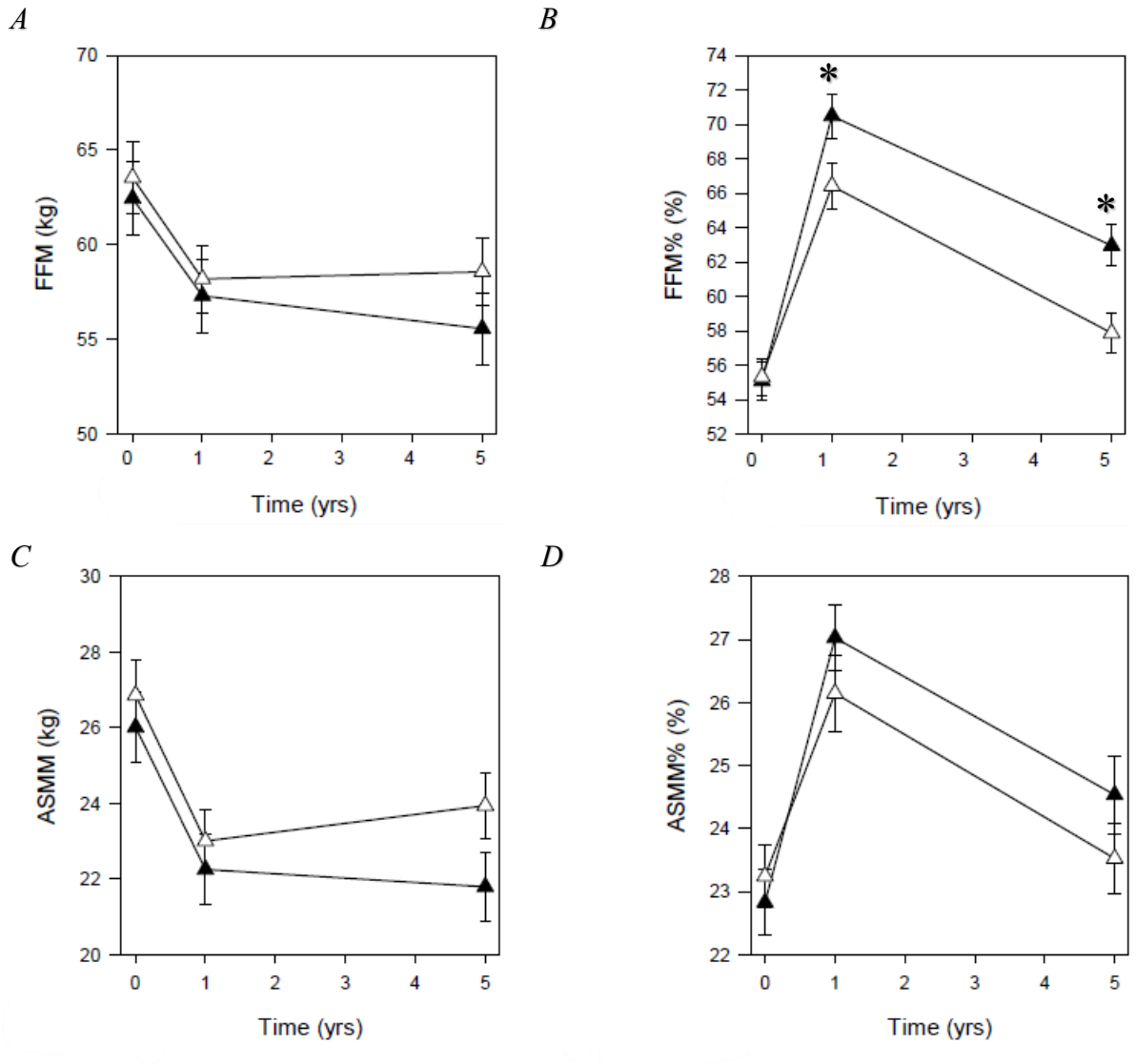


Figure 5. *Fat-free tissue measured by DXA at baseline, 1 year and 5 years for SG (Δ) and RYGB (▲). (A) Fat-free mass (FFM). (B) Fat-free mass as a percentage of body weight. (C) Appendicular skeletal muscle mass (ASMM). (D) Appendicular skeletal muscle mass as a percentage of body weight.*

4.5 Bioimpedance Equation Performance

A literature search was completed for pre-existing SF-BIA equations suitable for retrospective application to the study cohort. Three equations were selected for analysis (Table 11) in addition to factory equations from the single-frequency and multi-frequency devices utilised during data collection. Body composition at baseline was estimated for 88 participants with complete bioimpedance data. The surgery groups were combined for the bioimpedance analysis. Four equations calculated TBF, and one calculated FFM. TBF and FFM were subsequently derived for each equation using the assumption that TBF + FFM = BW.

Of the included equations, only one was derived from a population with obesity (Horie et al., 2008). The other equations of Deurenberg et al. (1991) and Roubenoff et al. (1997) have previously been applied to a population with obesity in a 2022 study (Coëffier et al., 2022). The Roubenoff equation was found to be the most accurate for predicting body composition in that study.

Table 11. Bioimpedance equations for body composition

Author	Population	Reference Method	Equation
Deurenberg et al., 1991	Healthy Subjects	Densitometry	$FFM = -12.44 + (0.34 * h^2/R_{50}) + (0.1534 * h) + (0.273 * Wt) - (0.127 * age) + (4.229 * sex)$
Horie et al., 2008	Bariatric Patients	Densitometry	$TBF = 23.25 + (0.13 * age) + Wt + (0.09 * R_{50}) – (0.80 * h)$
Roubenoff et al., 1997	Elderly People	DXA	$FFM = 5.741 + (0.4551 * h^2/R_{50}) + (0.1405 * Wt) + (0.0573 * X_{50}) + (6.2467 * sex)$

Values are expressed as mean ± standard error of the mean. P values derived from Student's t-test. FFM = fat-free mass. ASMM = appendicular skeletal muscle mass.

Comparative data between BIA and DXA-derived values for TBF and FFM are reported in Table 12 and Figure 6. Pearson correlation r was greater than 0.9 for all BIA equations for TBF. The lowest r was found in both factory equations (0.94) and the highest for the Deurenberg equation (0.98). The highest Lin concordance coefficient of 0.96 was also observed for the Deurenberg equation. The Deurenberg equation showed the smallest bias (-1.02 kg, -0.88%), and the Roubenoff equation had the largest bias (4.93 kg, 10.23%). Large biases were also seen for the BIA-101 and Quadscan 4000

devices. Only the Deurenberg equation surpassed an accuracy of 50% for a margin of ±5%. Large limits of agreement were observed for all equations, as shown in Bland-Altman plots (Figure 6) and Table 13. However, a strong proportional bias was evident for the Deurenberg equation with BIA overestimating TBF at TBF<50 kg with underestimation at higher TBF. Significant proportional biases were also seen for the Horie and BIA-101 equations.

Findings for FFM were similar to TBF. Pearson correlation r was equal to or greater than 0.95 in all equations. The Lin concordance coefficient ranged from 0.88 to 0.96. Accuracy was slightly higher for FFM as four equations exceeded 75% accuracy for a margin of ±10%. The Deurenberg equation had the lowest bias (0.88 kg, 1.47%). However, large limits of agreement were found for all five equations (Figure 6 and Table 13). No proportional bias was seen for the Deurenberg and Horie equations, while the others all showed significant proportional bias.

Table 12. *Fat mass and fat-free mass obtained by DXA and BIA equations.*

Method	**Fat mass (kg)**	**Fat-free mass (kg)**
DXA	51.8 ±1.4	62.6 ±1.3
Deurenberg equation	50.7 ±1.2	63.5 ±1.3
Horie equation	47.9 ±1.5	66.3 ±1.3
Roubenoff equation	56.7 ±1.4	57.6 ±1.2
RJL Systems BIA-101	47.8 ±1.2	66.4 ±1.6
Quadscan-4000	49.0 ±1.5	65.2 ±1.6

Values are expressed as mean ± standard error of the mean.

Table 13. Comparison of fat mass and fat-free mass obtained by DXA and BIA equations.

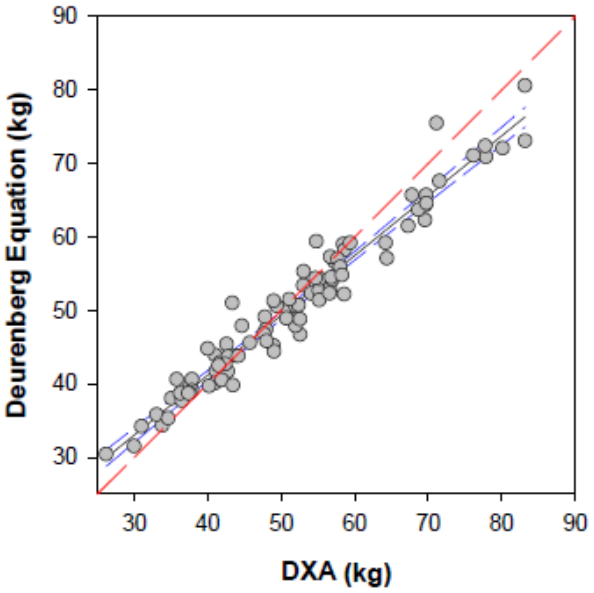
	Bias (kg)	95% CI (kg)	Bias (%)	Accuracy (%) ±5%	Accuracy (%) ±10%	Pearson r	Lin ρ
Fat mass							
Deurenberg et al.	-1.02	[-1.73; -0.30]	-0.88	54.6	87.5	0.98	0.96
Horie et al.	-3.83	[-4.65; -3.02]	-8.20	26.1	61.4	0.96	0.91
Roubenoff et al.	4.93	[4.31; 5.55]	10.23	17.1	56.8	0.97	0.89
RJL Systems BIA-101	-3.92	[-4.01; -2.93]	-6.76	33.0	59.1	0.94	0.90
Quadscan-4000	-2.72	[-3.73; -1.72]	-5.59	40.9	63.6	0.94	0.92
Fat-free mass							
Deurenberg et al.,	0.88	[0.15; 1.61]	1.47	63.6	92.1	0.96	0.96
Horie et al.	3.70	[2.92; 4.47]	6.21	35.2	77.3	0.96	0.92
Roubenoff et al	-5.06	[-5.66; -4.46]	-8.03	22.7	68.2	0.97	0.91
RJL Systems BIA-101	3.79	[2.79; 4.78]	5.78	43.2	76.1	0.95	0.88
Quadscan-4000	2.59	[1.61; 3.57]	3.78	45.5	81.8	0.95	0.92

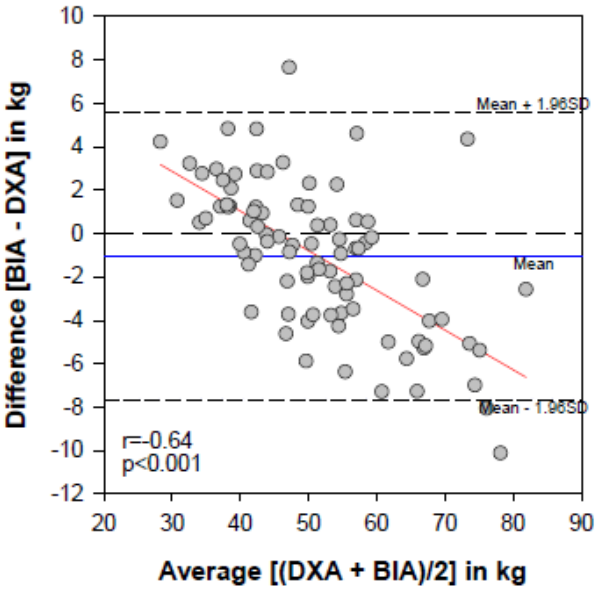
Bias was calculated as: BIA calculated value– DXA value. 95% CI, 95% confidence interval. Accuracy is the percentage of participants with bias values within ±5% or ±10% of DXA value.

A

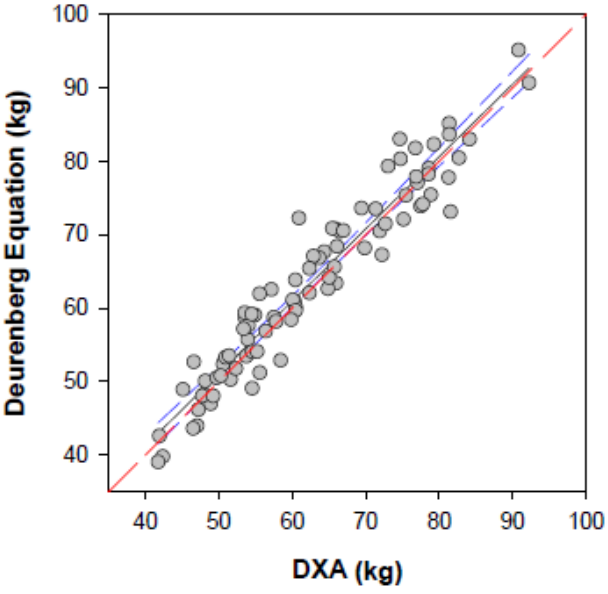
Deurenberg Equation

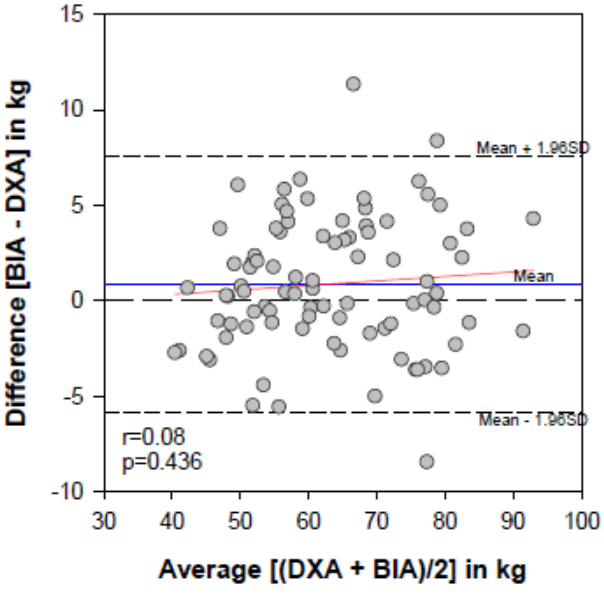
Fat Mass





Fat-Free Mass

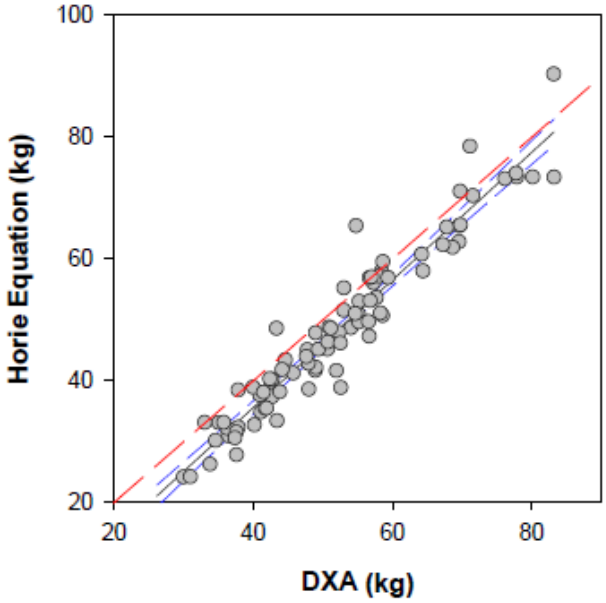


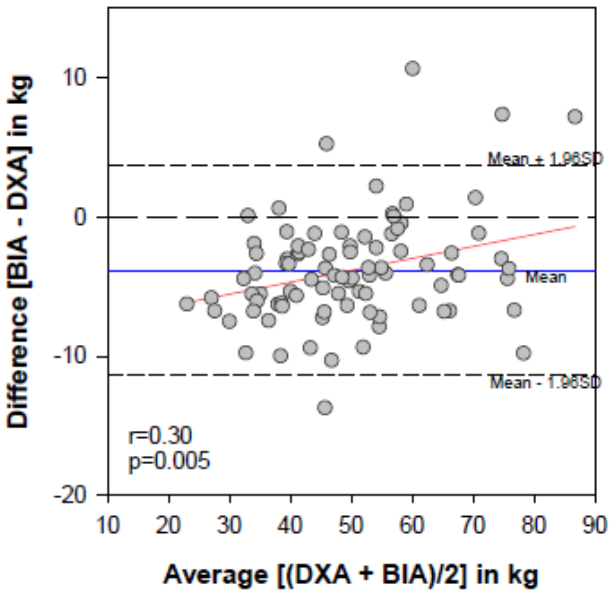


B

Horie Equation

Fat Mass





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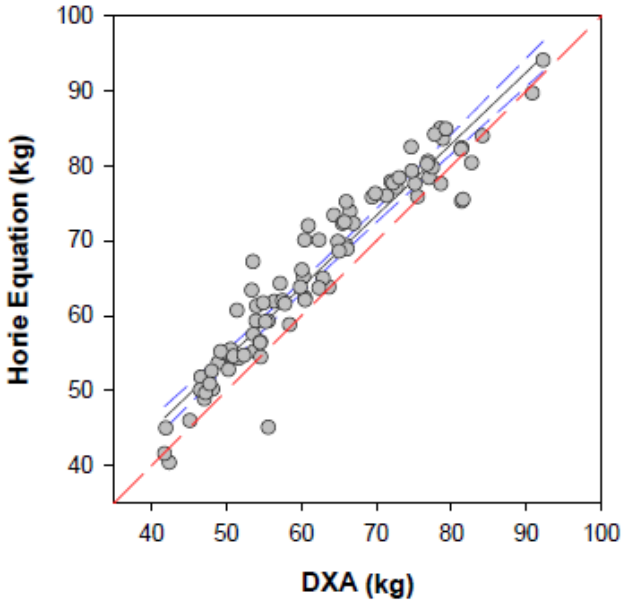
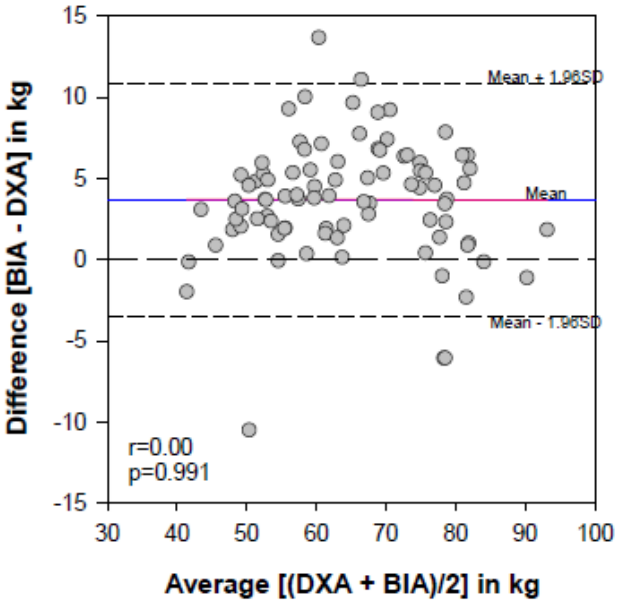
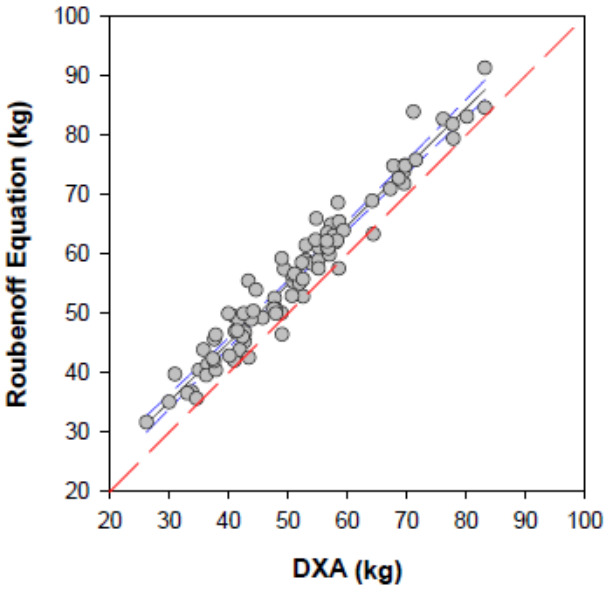


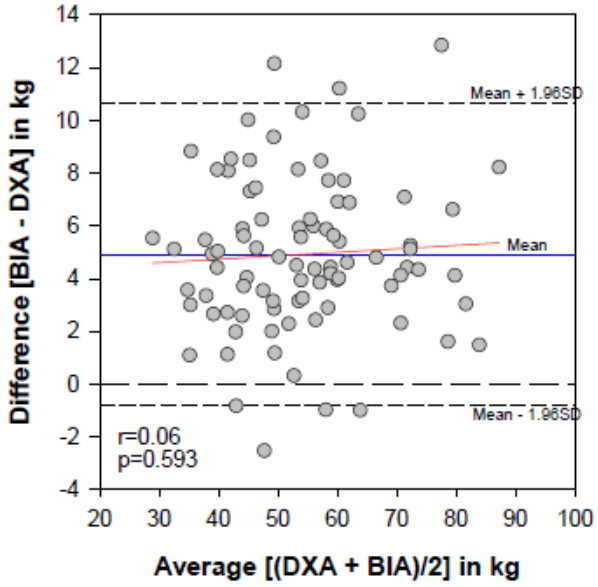


C

Roubenoff Equation

Fat Mass





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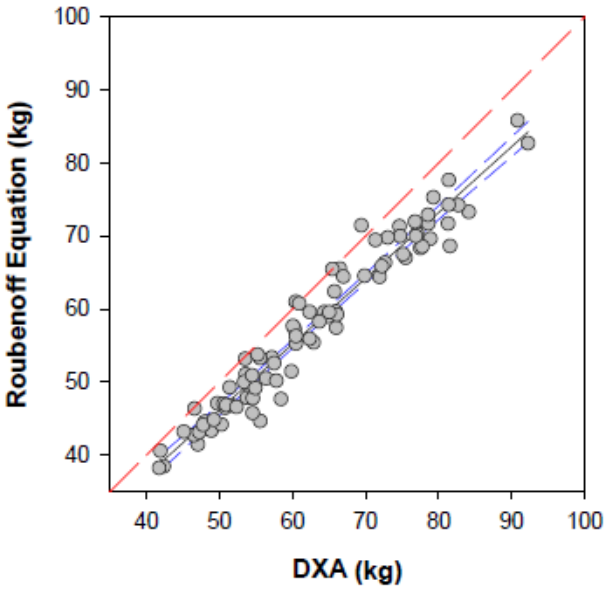
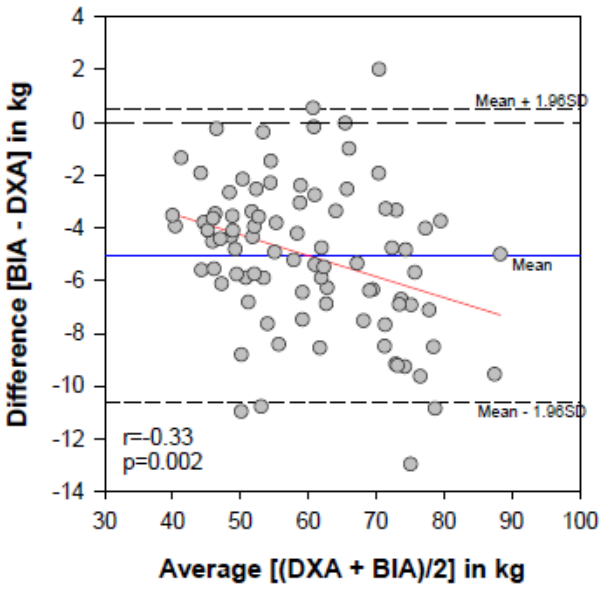
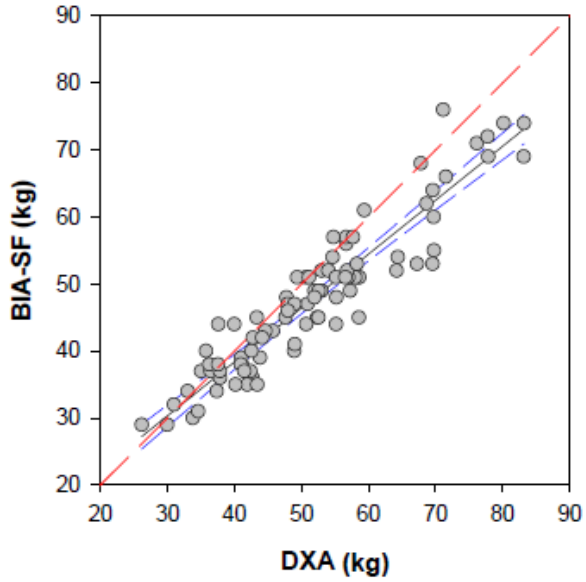


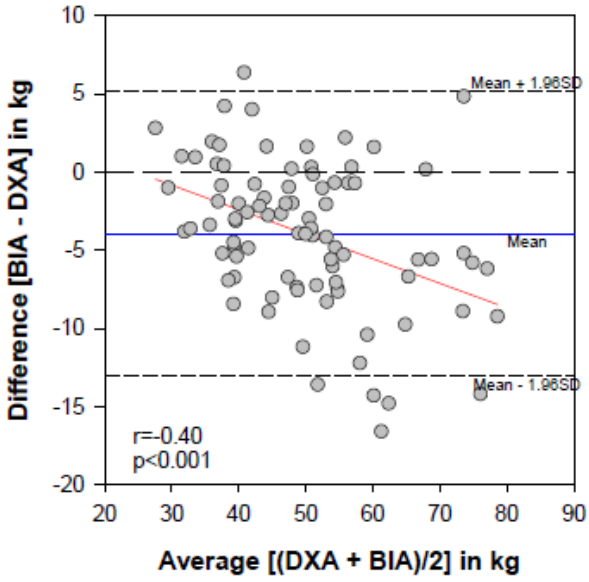


D

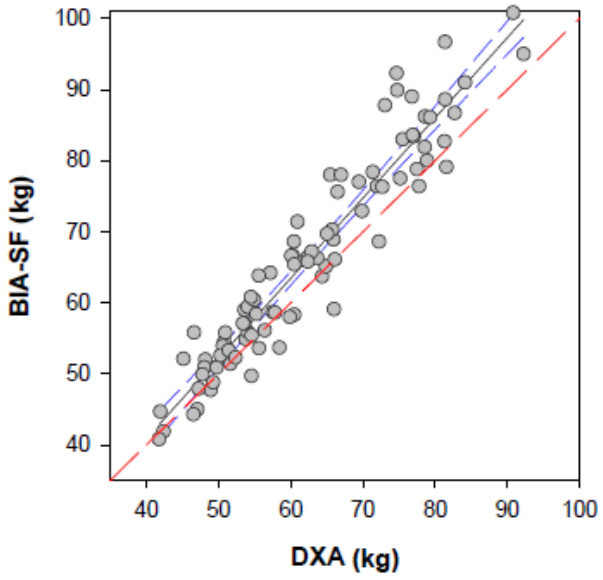
BIA-SF Factory Equation (RJL Systems Model BIA-101)

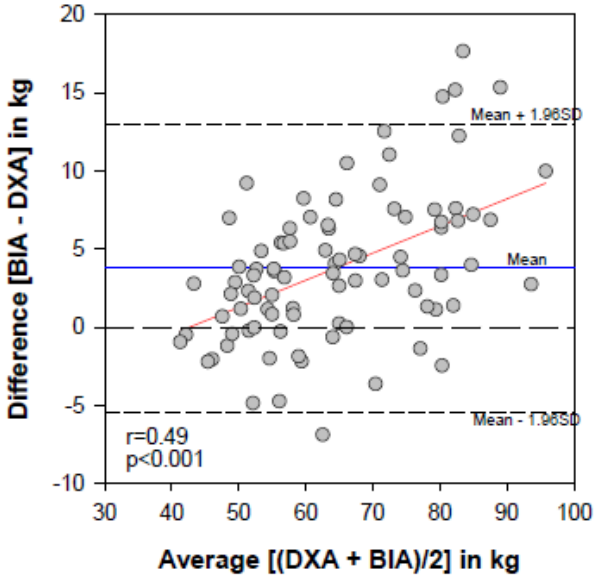
Fat Mass





Fat-Free Mass





E

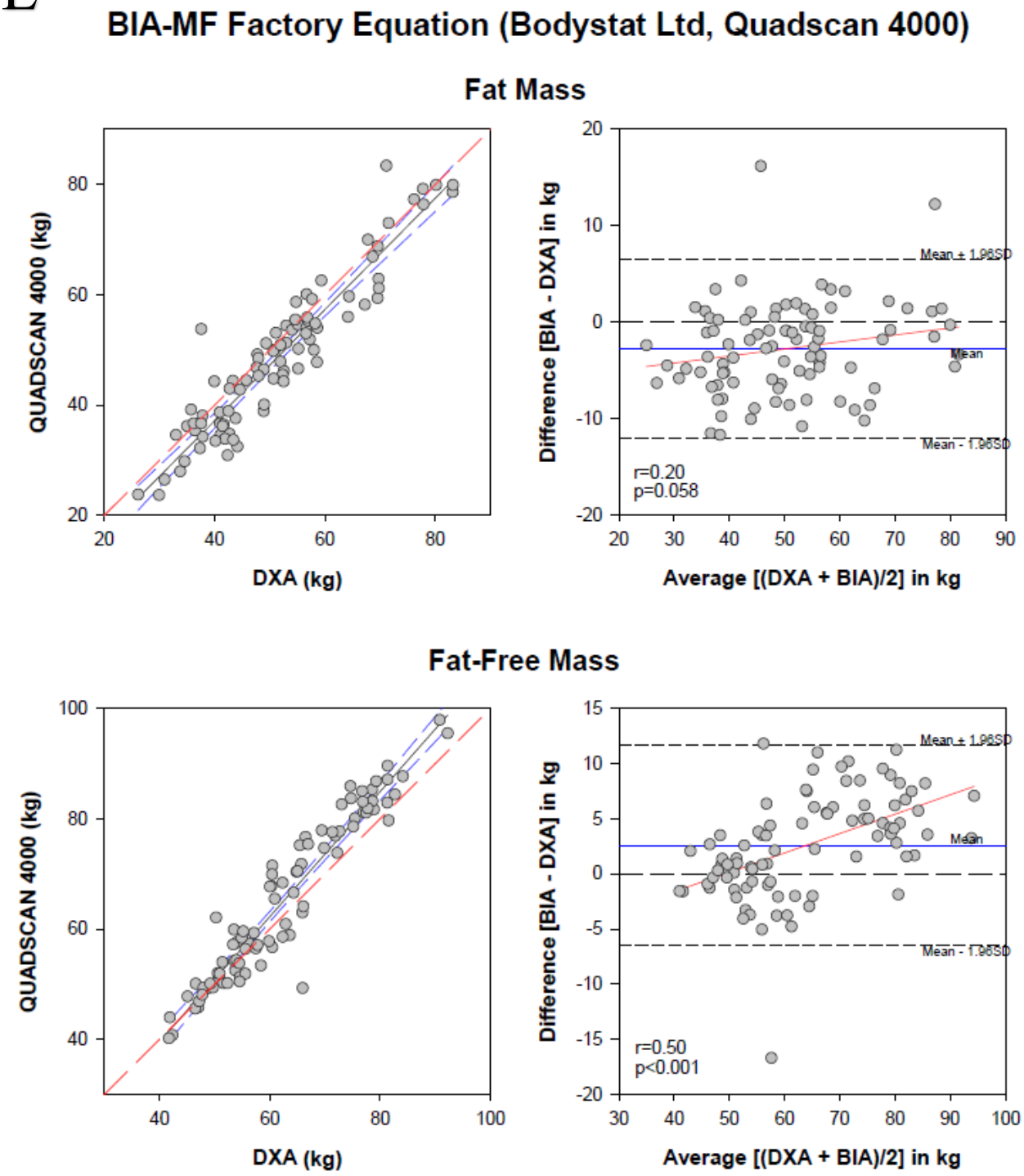


Figure 6. *Scatter graphs and Bland-Altman plots for the comparison of fat mass and fat-free mass measured by DXA and BIA-derived values from equations. On the left-hand graphs, regression lines are shown with 95% confidence limits for the mean (blue dashed lines) and the line of identity (red dashed line). On the Bland-Altman plots, regression lines are shown in red, along with Pearson correlation coefficients (r).*

Chapter 5. Discussion

Weight loss after bariatric surgery is known to be highly variable and dependent on factors such as pre-operative weight, the presence of comorbidities, and post-operative dietary habits (Livhits et al., 2011). Consideration of this variability is critical when assessing the currently available literature on bariatric surgery outcomes. The current evidence base is heavily informed by observational studies that are inherently susceptible to internal error due to their methodology. Furthermore, investigations into body composition outcomes beyond the initial twelve months post-surgery are scarce. To our knowledge, this is the first and only randomised control trial to use DXA to assess body composition outcomes five years after bariatric surgery. While some studies have investigated the long-term outcomes of bariatric surgery, these generally were observational in nature and lacked the use of gold-standard techniques for body composition analysis (Table 5). The follow-up duration, relatively large sample size, and use of DXA to assess body composition make this study novel.

5.1 Body Weight

Weight loss at one year measured as %EWL in RYGB (85.8%) and SG (65.9%) exceeded findings reported in studies by Otto et al. (2015) and Kavanagh et al. (2019). In a prospective, non-randomised study of 173 participants, Otto et al. (2015) found % an EWL of 62.9% in RYGB and 52.3% in SG. The observed difference in %EWL reported by Otto et al. may be a result of differences in baseline characteristics as %TWL was similar between studies. %TWL at one year was 28.2% (RYGB) and 23.3% (SG) within our cohort, and 31.7% (RYGB) and 30.4% (SG) in Otto et al. Therefore, discrepancies in %EWL may reflect differences in baseline BMI as group means were notably lower within our cohort (RYGB: 39.0±5.2 kg/m^2 and SG: 40±6.0 kg/m^2 compared to RYGB: 45.6±5.7 kg/m^2 and SG: 55.9±7.8 kg/m^2). Another prospective, non-randomised study of 66 individuals by Kavanagh et al. (2019) observed %EWL of 53.4% in RYGB and 47.2% in SG. Baseline body weight and TWL at one year were similar to those of our cohort. However, baseline BMI was not published, and weight loss was only reported as TWL and %EWL. Additionally, no standard deviations or other measure of error were included. Therefore, it is unclear if within-group differences in distribution as a result of the lack of randomisation contribute to explaining differences in %EWL.

%EWL at five years following RYGB (66.8%) was only slightly lower than in other long-duration studies. %EWL five years following RYGB was 76.2% in a prospective, randomised trial by Zhang et al. (2014) and 81.7% in a retrospective, non-randomized study by Ceriani et al. (2021). However,

the 32.4% %EWL in the SG group of our study is vastly inconsistent with the weight loss observed within SG cohorts in these two studies (Ceriani et al., 78.6%; Zhang et al., 62.35%). The disagreement between findings appears to develop throughout the study duration. In contrast with comparisons against shorter duration studies, %EWL of 65.9% was lower than observed by Zhang et al. (73.9%). This difference appears to have been confounded by notably greater weight regain between 1-year and 5-year measurements, with approximately half of the weight loss observed at one year being regained. This differs drastically from the current literature, with mean weight regain not typically exceeding 25% (King et al., 2020). The occurrence of excessive weight regain is further abnormal as its impact was isolated to the SG group. Excessive weight regain can be attributed to procedural failures but is more frequently a result of lifestyle factors such as inadequate physical activity and dysregulated eating (Noria et al., 2023).

Significant differences in weight loss were found between the two surgery groups at 1 and 5 years. Minor differences were identified at one year as weight loss was significant by %EWL and not by absolute weight despite similar baseline weights and BMIs. Differences in absolute weight loss and %EWL at five years were stark as weight regain between 1 and 5 years was significantly larger in the SG group. This suggests that weight loss following RYGB is better sustained than SG. Reported differences between weight loss outcomes at one year following RYGB and SG are often not statistically significant. No studies identified during the literature review process of this thesis reported differences in weight loss at one year that were not abolished by adjustment for differences in baseline characteristics (Table 4). In this context, the differences identified at one year appear abnormal. However, body composition changes are not isolated to the first-year post-bariatric surgery. Findings from studies with short follow-up durations are not necessarily reflective of the long-term outcomes.

The current literature extensively covers the immediate outcomes of bariatric surgery but fails to assess long-term changes. Pooled data by Uhe et al. (2021) and findings from long-term studies suggest that differences in weight loss and body composition may develop outside of the first 12 months (Yang et al., 2015; Zhang et al., 2014). Two randomised trials have reported on yearly body weight assessments following RYGB and SG. The study by Yang et al. (2015) monitored body weight in 64 individuals for three years and found differences in %TWL, TWL, and %EWL only after three years. Zhang et al. (2014) produced similar findings over five years in a sample of 64 individuals. Weight loss measured by %EWL was similar after one year but significantly greater

following RYGB at each yearly assessment between 2 and 5 years. Potential differences in weight loss at one year are likely marginal in comparison to the changes occurring beyond this point.

5.2 Fat-free mass

Few studies report relative changes in FFM following bariatric surgery. The pool of literature is further limited by non-standardized reporting methods. FFM and LBM are often mistakenly used interchangeably. Unlike FFM, LBM does not include bone mass (Müller et al., 2016). This thesis opted to report on FFM and %FFM as changes in bone mass following bariatric surgery correlate with changes in FFM and are unlikely to significantly contribute to changes in body weight (Brzozowska et al., 2013). A 2021 study retrospectively found no differences in change in FFM after five years between SG and RYGB patients (Ceriani et al., 2021). However, the study used BIA to determine FM and FFM. Despite appeals to its validity, bioimpedance techniques have not yet been shown to accurately measure body composition or its changes over time (Table 3).

Another 2018 study by Davidson et al. assessed body composition over five years using a 3-compartment model consisting of total body density (BodPod) and TBW (D_2O dilution). An additional subset of the study cohort underwent whole-body MRI to measure skeletal muscle mass. During the first year, the RYGB group had larger reductions in FFM and greater increases in FFM%. After five years, the FFM% in RYGB was higher than in SG. The study was non-randomised, and the RYGB group had a lower BMI and higher FFM% than the SG group at baseline. Additionally, the sample was unbalanced (RYGB; n=58, SG; n=11) and 5-year data was only available for 62% of recruited participants. Despite limitations in study methodology, trends in FFM observed by Davidson et al. are consistent with our observations. During the first year, both surgery groups have similar reductions in FFM alongside a larger increase in FFM% in RYGB. In both studies, FFM is maintained in SG between 1 and 5 years, while a mild decrease is observed in RYGB. Despite further loss in FFM, FFM% remained higher in RYGB than SG.

This trend emphasises the importance of including relative measures of body composition. Despite greater loss of FFM, increases in FFM% were significantly larger in RYGB than SG. FFM losses are known to strongly correlate with reductions in body weight. Therefore, differences in FFM between RYGB and SG are likely attributable to differences in weight loss and fat loss.

5.3 Fat Mass

Significant reductions in TBF were observed across the entire cohort during the first year. TBF and TBF% were lower in the RYGB arm at both one year and five years. Fat loss within the first year did not reach statistical significance (Table 9). However, reductions in TBF and TBF% were significantly greater at five years in the RYGB arm. Trends in FM were consistent with those observed in body weight and FFM as the SG group regained a greater amount of FM between one year and five years. Again, these findings are inconsistent with the pre-existing literature.

Studies by Kavanagh et al. (2019), Keidar et al. (2013), and Wells et al. (2015) all found no differences in the percentage change of FM between RYGB and SG after one year. One non-randomised trial reported a lower body fat percentage following RYGB, but this effect was abolished following adjustment for differences in baseline BMI (Otto et al., 2015). The previously mentioned studies by Ceriani et al. (2021) and Davidson et al. (2018) also found no differences in FM trends between RYGB and SG over five years.

5.4 Fat Mass Distribution

Changes in FM distribution are of particular importance due to the association between central obesity and metabolic disease (Kissebah et al., 1982; Lopes et al., 2016; Stefan, 2020). The effects of bariatric surgery on T2DM management in this study cohort have previously been published (Murphy et al., 2022). T2DM remission rates defined as an HbA_{1C} <6% or 42 mmol/mol were notably higher following RYGB than SG. The finding is not restricted to this cohort, as superior T2DM remission rates have been reported by other studies (Guerrero-Pérez et al., 2019; Kashyap et al., 2013). Differences in T2DM remission rates failed to reach significance in a systematic review by Sharples and Mahawar (2019), as resolution rates of 37.4% and 27.5% were found for RYGB and SG, respectively. Despite failing to reach significance, further investigation into the potential role of changes in central obesity is warranted. Correlations between abdominal adiposity and insulin sensitivity are well established but have not been investigated in the context of bariatric surgery (Goodpaster et al., 1997).

Android fat mass (AFAT) and visceral fat mass (VFAT) were lower in the RYGB group after five years. Analysis of the changes in central fat stores between assessment points reveals critical differences between one and five years. Reductions in both AFAT and VFAT after one year were similar between the groups. However, the SG regained significantly more AFAT and VFAT in five

years. Differences in weight regain appear as the primary contributor to differences after five years. This suggests that the potential beneficial effects of bariatric surgery on T2DM management may emerge over a longer time course.

5.5 Bioimpedance Equations

FM and FFM values measured by DXA were compared with values derived from four SF-BIA equations and one MF-BIA equation. Bias was small, ranging from -5.06 kg to 4.93 kg. Four equations showed bias that underestimated FM and overestimated FFM compared to DXA values. Only the Roubenoff equation overestimated FM and underestimated FFM. Investigations into bioimpedance methods consistently report the overestimation of FFM and underestimation of FM (Ballesteros-Pomar et al., 2022; Berstad et al., 2011; Faria et al., 2014; Verdich et al., 2011). In a study of women undergoing gastric banding, a strong correlation was found between values derived from SF-BIA and DXA. This correlation increased with weight loss, suggesting that the accuracy of SF-BIA is influenced negatively by body weight (Savastano et al., 2009). This is consistent with findings from Achamrah et al. (2018), where bias increased with BMI in participants with a BMI greater than 40 kg/m^2.

This highlights the need for specific equations developed for populations classified as overweight/obese. One of the equations included in the analysis was derived from a bariatric population (Horie et al., 2008). However, it had lower accuracy than the included factory equations. The performance of the Roubenoff equation was also inconsistent with previous findings. Following retrospective analysis, the Roubenoff equation was recommended for use in populations with obesity (Coëffier et al., 2022). The Roubenoff equation had a 5% accuracy of 53.1% for FFM and 34.8% for FM. However, in this study, the Roubenoff equation had the greatest bias and lowest accuracy for FM and FFM. Accuracy at 5% for the Roubenoff equation in this study was 22.7% for FFM and 17.1% for FM.

Despite the origins of a given equation, it must be validated in a population before considering its use. In this study cohort, the Deurenberg equation exhibited the lowest bias and highest accuracy for both FM and FFM. The correlation was high for all equations with Pearson coefficients above 0.94. However, large limits of agreement were found for all equations, which is evident in the Bland-Altman plots. This, alongside low accuracy, shows that SF-BIA and MF-BIA equations are not suitable for assessing body composition in individuals. SF-BIA and MF-BIA are appealing

alternatives for body composition assessment due to their non-invasive methodology and low costs. However, its validity in populations with obesity has not yet been proven.

Chapter 6. Conclusion

This study identified clear differences between body composition outcomes following RYGB and SG. These findings were mostly inconsistent with the results of other studies. RYGB produced favourable changes in body composition compared to SG. These findings challenge the consensus developed mostly from studies with follow-up durations of less than two years. Differences between the groups at five years were likely a product of minor short-term differences and more significant differences in long-term weight regain. To confirm the validity of these results, future randomised controlled trials with sufficiently long follow up periods are required.

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