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**Prevalence and Impact of Chronic Oedema
in a Population of Obese Patients
Prior to and Following Bariatric Surgery**

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**Dissertation submitted to the University of Nottingham
for the degree of Master of Research.**

February 2018

Abstract

Background

Chronic oedema (persistent swelling) is a common, often unreported, condition, which can have severe social and psychological implications for individuals and their families. Oedema can be especially problematic for obese patients, who often struggle with: immobility, co-morbidities, and the inability to lose weight.

Aims

The main aims of the study presented in this dissertation were two-fold: to determine the prevalence and impact of chronic oedema on health-related quality of life in a population of obese patients (Stage 1) and, to assess the impact of bariatric (weight loss) surgery on chronic oedema (Stage 2).

Methods

The study was based at the Royal Derby Hospital. Stage 1 participants were newly-referred patients to the weight-management clinical pathway. Stage 2 participants were patients who would soon be having bariatric surgery. Participants (both stages) were assessed for chronic oedema using the pitting test (primarily) and Stemmer's sign techniques. The pitting test was the gold standard test for assessing whether or not oedema was present. Quality of life questionnaires were completed by these participants to assess: anxiety, depression, impact of oedema, physical function, energy, pain and mobility. Fluid measurement techniques were used: to measure the overall fluid in the limb (using bioimpedance) and the amount of fluid in the tissue at specific points (using the tissue dielectric constant). For Stage 2, a perometer was used to measure lower limb volume. Stage 2 participants were assessed before and after surgery to determine if their oedema had improved.

Results

In Stage 1, 31 patients were recruited and 19 of these had oedema, giving a prevalence of 61.3%. However, the questionnaires indicated that the quality of life of participants with oedema did not differ significantly from those without oedema. The bioimpedance resistance at zero and infinite frequencies (R_{zero} and R_{infinity}) for participants with oedema were significantly different to those without oedema. The tissue dielectric constant data highlighted the presence of more oedema at the foot, ankle and below the knee sites.

In Stage 2, 21 patients were recruited and eleven of these had oedema, giving a prevalence of 52.4%. The quality of life, physical health, energy and pain of participants with oedema were significantly different to those without oedema. When comparing limb volumes of participants with and without oedema for Stage 2 (before surgery), there were no significant differences between them. R_{zero} and R_{infinity} data for those with oedema were significantly different to those without oedema. The only statistically significant tissue dielectric constant site was the right foot. Due to the size of the post-operative dataset, further post-operative assessments are required to fully assess the impact of bariatric surgery on chronic oedema.

Conclusions

This study indicates that the prevalence of chronic oedema is high among obese patients. However, biased recruitment and a small sample size limited data collection (especially data collected post-operatively in Stage 2), highlighting the limitations of recruiting in this population of patients. These issues will be addressed to allow future research to confirm the prevalence of chronic oedema in this population and to determine whether chronic oedema is impacted as a result of bariatric surgery.

Acknowledgements

I would firstly like to thank God for His faithfulness and for bringing me through this journey.

The clinical teams in the bariatric and pre-operative clinics have been wonderful. I would like to give a special mention to Carol Green and Manjit Nagra who have played key roles in the recruitment process. I could not have done this without them.

I have truly appreciated the invaluable help of Katie Riches in training me in lymphoedema assessment and giving me study advice. I am grateful for her patience in bearing with my stream of questions!

Thank you to all of the participants who took the time to contribute to my study. It has been a privilege meeting and getting to know them.

I have been blessed to have three supervisors who have guided me with the study: Professor Vaughan Keeley, Professor Christine Moffatt and Dr. Lorraine Pinnington. I am truly grateful for all of their advice, expertise, patience and support.

I would like to thank Andrea Venn for guiding me through the statistical side of the study. She has been wonderfully helpful.

Finally, I would like to thank my family for their continuing love and support.

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List of Abbreviations

BBS study	By-Band-Sleeve study
BCTRL	Breast Cancer Treatment-Related Lymphoedema
BMI	Body Mass Index
BNP	B-Type Natriuretic Peptide Test
CLLO	Chronic Lower Limb Oedema
CO	Chronic Oedema
CRF	Case Report Form
DLT	Decongestive Lymphoedema Therapy
DVT	Deep Vein Thrombosis
ECF	Extracellular Fluid
EQ-5D	EuroQOL-5 Dimensions
FBC	Full Blood Count Test
GAD-7	Generalised Anxiety Disorder 7-Item Scale
GCP	Good Clinical Practice
HbA1c	Glycated Haemoglobin Test
HQoL	Health-related Quality of Life
HSE	Health Survey for England
ISL	International Society of Lymphology
MLL	Massive Localised Lymphoedema
NHS	National Health Service
LFT	Liver Function/Aspartate Aminotransferase Test
LIMPRINT	Lymphoedema IMPact and PRevalence INTERNATIONAL study
LLS	Lymphoedema-Like Swelling
LYMQOL	Lymphoedema Quality of Life
NCO	Not Chronic Oedema
OIL	Obesity-Induced Lymphoedema
OSA	Obstructive Sleep Apnoea
PHQ-9	Patient Health Questionnaire – 9
R&D	Research and Development department
R_i	Resistance at infinite frequency
R_o	Resistance at 0 frequency
RDH	Royal Derby Hospital
RL	Role Limitations
SF-36	36-Item Short Form Health Survey
TDC	Tissue Dielectric Constant
TFT	Thyroid Function Test
UE	Urea and Electrolytes Test
WBA	Whole Body Analysis

CHAPTER 1: INTRODUCTION

1.1 Study background

Chronic oedema is a common, often unreported, condition, which can be harmful to patients both physically and psychologically. Although oedema can be managed through compression treatment, it can cause severe difficulties for some individuals, such as those who are obese. The research study presented in this dissertation will assess the prevalence and impact of oedema on health-related quality of life in an obese population. Furthermore, the research will assess the impact that bariatric surgery has on oedema.

This chapter will introduce the topics of chronic oedema and obesity. A literature review will follow, of research that has been carried out to date in the field. Specifically, studies of the prevalence of oedema in the obese/bariatric population and studies of the impact of bariatric surgery on oedema will be appraised. Finally, the plan of this dissertation with the aims of the study will be described.

1.2 Chronic oedema

Chronic oedema is defined as persistent swelling, which has been present for three months or more (Moffatt et al., 2003). Although it can affect any part of the body, it is most commonly found in the upper and lower limbs. Oedema may be caused by: the lymphatic system not functioning properly, being immobile, or chronic venous disease. (Moffatt et al., 2003; Todd, 2013) The condition affects approximately four in 1,000 people within health services, but it is often unreported due to misdiagnosis or lack of awareness (Moffatt and Pinnington, 2012). It can have severe social and psychological consequences beyond physical impairment which can place an emotional toll on patients and their families (Todd, 2013).

Although chronic oedema is a long term condition and is currently incurable, it can be managed by a combination of physical treatments which comprise decongestive lymphoedema therapy (DLT). DLT includes: wearing compression bandaging (or garments) and exercising to encourage functioning of the lymphatic system, and good skin care to reduce the risk of infection. (Lymphoedema Framework, 2006) However, for some patients, such as those who are obese, these methods can be difficult to apply.

1.3 Obesity

Whilst chronic oedema is a commonly unreported condition, obesity is a steadily growing and well recognised epidemic. According to the Health & Social Care Information Centre (2016), the prevalence of obesity in England has increased from 15% in 1993 to 26% in 2014. Not only does it cause immobility, but it is damaging to health and has the potential to cause a number of co-morbidities, such as: cardiovascular disease, hypertension and type 2 diabetes. Unfortunately, people who are obese often struggle to lose weight (or to maintain weight loss) due, for example, to their inability to exercise.

Treating obese patients with DLT does not seem to have a long-lasting impact on their oedema unless they have also lost weight (Lymphoedema Network Northern Ireland, 2011). Oedema treatment options are often limited for people who are overweight. Furthermore, cardiovascular disease is a common co-morbidity for obese patients (GBD 2013 Obesity Collaboration et al., 2014), which limits the ability to use compression garments as this puts pressure on the heart. As lymphoedema services struggle to treat this population effectively, it is not cost-effective to continue treatment until weight loss has occurred. (Rankin, 2015)

1.4 Bariatric surgery

For those who have not been able to maintain a sustained improvement in body weight with diet, exercise or medication, bariatric (weight loss) surgery can be considered. The aim of this surgery is to help patients lose weight by reducing the size of the stomach with or without bypassing the early part of the intestine, thereby reducing food storage capacity. It is becoming increasingly common for patients to choose this route. The UK National Bariatric Surgery Registry (NBSR Data Committee, 2010 & 2014) recorded 7,045 bariatric operations in 2009 and 2010 (mean of 3,523 operations each year) increasing to 18,283 bariatric operations in 2011-2013 (mean of 6,094 operations each year). Most operations result in patients maintaining weight loss for long periods of time and obesity-related co-morbidities (such as diabetes and hypertension) improving (Buchwald et al., 2004).

The research study presented in this dissertation was conducted in the East Midlands Bariatric & Metabolic Institute at the Royal Derby Hospital (RDH). Bariatric surgery at this hospital is offered to patients with a body mass index (BMI) of 40 and to those with a BMI of 35 if obesity-related co-

morbidities are present. All patients need to have attempted to lose weight by non-surgical methods in the past. Surgery aims to help patients lose weight through a number of techniques, including: laparoscopic gastric bypass, insertion of gastric bands and sleeve gastrectomies. (Derby Teaching Hospitals, 2016) Whilst it is also hoped that co-morbidities (whether obesity-related or not), will be improved or eliminated, the outcomes of surgery vary (Atiyeh & Ibrahim, 2012).

1.5 Introduction to literature reviews

First, studies are presented which explain how obesity and chronic oedema are associated (section 1.7). Next, two important articles are discussed that indicate a BMI threshold above which lymphoedema occurs (section 1.8). Prevalence studies of oedema in the obese/bariatric population are summarised (section 1.9) and the impact that bariatric surgery has on oedema is investigated (section 1.10). Finally, a separate literature review was undertaken to examine health-related quality of life (HQoL) amongst patients with lymphoedema and obesity (section 1.11).

The results from both reviews are evaluated to identify gaps in the research literature (section 1.12) and a plan of the study is presented to illustrate how this dissertation provides answers to the questions posed (section 1.12.1).

1.6 Literature search strategy

For the first literature review, a journal article search was carried out in the Cochrane Library, Medline (Citations and Ovid Medline 1946 to present) and Scopus databases (Figure 1.1). As the Cochrane Library search only produced a small number of journal articles, two further (more detailed) strategies were initiated to retrieve all relevant articles. The search strategy for the Medline database encompassed different categories within the general search terms of oedema, obesity and bariatric surgery. Two searches were run in the Scopus database to ensure that no relevant articles were missed.

The search results were screened to distinguish relevant from irrelevant material (Figure 1.2). The population consisted of patients who were both obese and had oedema. Articles were included to highlight: an association between obesity and oedema, prevalences of oedema in the obese/bariatric population and the impact of bariatric surgery on oedema. Articles were excluded for several reasons, including: duplicate articles, those not

published in English and, articles not directly relevant to the subject topics or research aims. Upon review of relevant studies, twenty were excluded (Appendices: A1.1, A1.2 and A1.3) due to methodological flaws [including: poor oedema classification and low sample size (n=<50 when this was the main reason)].

Figure 1.1 Database search strategies

The following search strategies were used in the corresponding databases (Cochrane Library, Medline and Scopus) to find relevant research articles.

Search Date	Cochrane Library Search Strategy
18/03/2016	Chronic oedema OR chronic edema OR oedema OR edema AND obesity OR obese AND bariatric surgery
30/03/2016	("chronic oedema" OR "chronic edema") AND (bariatric OR weight loss surgery) or (oedema OR edema) AND (bariatric OR weight loss surgery)
04/04/2016	("chronic oedema" OR "chronic edema") AND (bariatric OR "weight loss surgery") or (oedema OR edema) AND (bariatric OR "weight loss surgery")
Search Date	Medline Search Strategy
14/01/2017	[(exp Edema/ or exp Lymphedema/ or Cellulitis/ or "chronic oedema".mp.) OR (exp Lymphedema/ or *Skin/ or exp Edema/ or "chronic edema".mp.)] AND [(bariatric surgery.mp or exp Obesity/ or exp Bariatric Surgery/ or *Gastroplasty/ or *Gastric Balloon/ or exp Obesity, Morbid/) OR (exp Obesity, Morbid/ or exp Obesity/ or exp Weight Loss/ or weight loss surgery.mp. or exp Bariatric Surgery/ or exp Gastric Bypass/)]
Search Date	Scopus Search Strategy
08/11/2016	chronic oedema OR chronic edema OR oedema OR edema AND obesity OR obese AND bariatric surgery
06/12/2016	("chronic oedema" OR "chronic edema" OR oedema OR edema) AND (bariatric OR weight loss surgery)

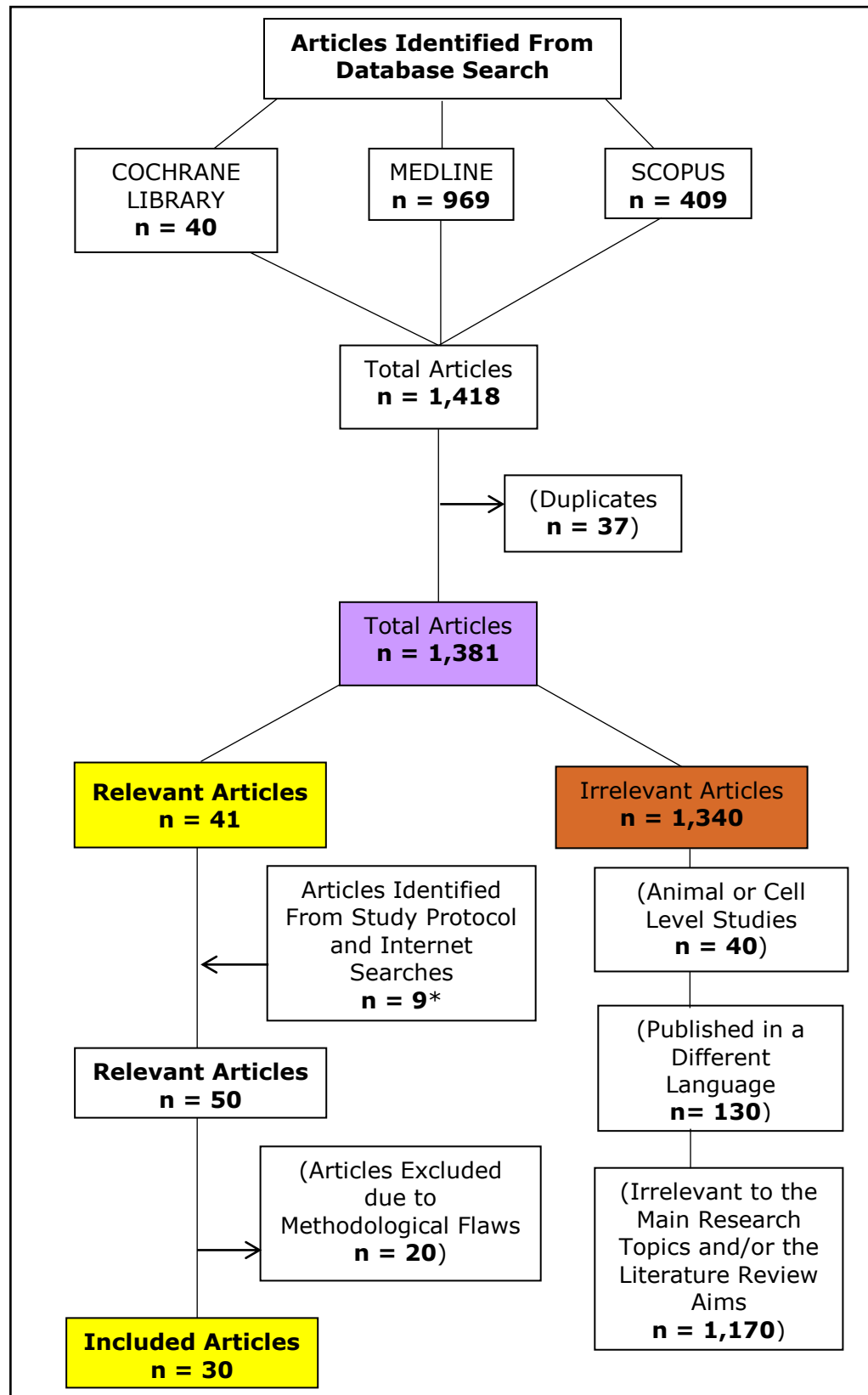


Figure 1.2 Article analysis

This flow diagram represents how the database articles were categorised into relevant and irrelevant articles, including details of the irrelevant article categories. *These articles were not found in the database searches due to the articles being conference abstracts and, found through internet searches and reference lists, etc.

1.7 Association between obesity and oedema

The following studies were reviewed which highlight the different ways that obesity and oedema are associated:

DiSipio et al. (2013) carried out a systematic review of breast cancer treatment-related lymphoedema (BCTRL) prevalence articles. They concluded that obese patients who are treated for breast cancer are more likely to develop arm lymphoedema, than those who are not obese, in at least 75% of the reviewed studies.

Maclellan et al. (2016) supported this conclusion by highlighting the association between BMI and massive localised lymphoedema (MLL). This was achieved by determining the association between MLL and obesity-induced lymphoedema (OIL). MLL is a large mass of lymphoedema occurring in obese patients, usually affecting the thigh (Farshid and Weiss, 1998). The 82 obese patients recruited from the lymphoedema programme (17 cases, 65 controls) were all assessed with lymphoscintigraphy to evaluate lower limb lymphatic function. All participants were found to have lymphatic dysfunction, defined by an absence of the technetium Tc-99m sulphur colloid uptake by the inguinal lymph node after 45 minutes. The cases (median BMI of 66kg/m²) had both MLL and OIL. The controls (median BMI of 36kg/m²) did not have MLL but 17% had OIL. There was a 213 times greater risk of developing MLL if the patients' (with OIL) BMI was greater than 56kg/m², as opposed to patients who had BMIs lower than (or equal to) 56kg/m². Not only was there a significant association between BMI and MLL, but: as the BMI of the patients increased, so did the risk of developing MLL.

This matched the conclusions of magnetic resonance imaging studies by Genu et al. (2013), Shi et al. (2003) and, West and West (2015). They determined that severity of oedema increased with patients' weight and, that BMI was associated significantly with the presence and extent of oedema.

Although being obese can lead to the development of oedema, a study by Shaw, Mortimer and Judd (2007) gives hope. The authors randomised 21 women with BCTRL into two groups that received weight loss education, one through dietary means and the other through healthy eating advice. Changes in arm volumes were assessed by manual circumferential measurements. After 12 weeks, the healthy eating group showed no improvement in weight or oedema. However, the dietary group had a

significant reduction in arm volume compared to the control group: 10% excess volume reduction compared to 0% and 349ml reduction compared to 11ml. They had also lost 3.3kg in weight (compared to 0kg). Although oedema changes were only analysed through arm volume changes, the results of the dietary group indicate that arm lymphoedema can be improved by losing weight.

1.8 Lymphoedema-associated BMI threshold

In this section, studies are reviewed that demonstrate an association between BMI and impaired lymphatic function (and consequently oedema):

In 2012, Greene, Grant and Slavin performed an insightful study which suggested lower limb lymphoedema could be caused by obesity and, hypothesised a BMI threshold associated with lymphoedema. Using lymphoscintigraphy, they discovered that: of 15 obese patients, those with a BMI less than 54kg/m² had normal lymphatic function (n=10). However, those with a BMI greater than 59kg/m² had lymphoedema (n=5). This indicated a BMI threshold for lymphoedema.

Greene et al. followed up this study in 2015. The authors assessed 51 obese patients, with a BMI greater than 30kg/m², for the presence of lymphoedema, using lymphoscintigraphy scans. Before lymphoscintigraphy, patients were split into two groups: group 1 consisted of patients who were at their maximum BMI (n=33) and group 2 patients had lost weight through diets or bariatric surgery (n=18). Abnormal lymphatic function was defined as: the radiolabelled colloid (used in the scan) taking longer than 45 minutes to travel through the lymphatic channels, a backflow of lymphatic fluid, and/or the presence of tortuous lymphatic channels with the fluid using alternate pathways than normal to function.

In group 1, nine patients with a BMI higher than 60kg/m² had lymphoedema (with an abnormal lymphatic function), whereas those with a BMI lower than 50kg/m² had a normal lymphatic function (n=20). Of the four patients with BMIs between 50 and 60kg/m², two had normal and two had abnormal lymphatic function, indicating a BMI threshold at which lymphatic dysfunction begins. Greene et al. (2015) also suggest that this lymphatic dysfunction may be irreversible. The patients in group 2 with a mean BMI of 78.6kg/m² reduced to 56.1kg/m² and higher maximum BMI history (maximum range of 44.3-85.4kg/m² reduced to 30.0-53.1kg/m²) had abnormal lymphatic function (n=nine). Those with a normal lymphatic

function (n=nine) had a mean BMI of 63.1kg/m² reduced to 41.6 kg/m² and a lower BMI history (maximum range of 60.4-105.6kg/m² reduced to 43.9-73.3kg/m²). This implies that patients with higher BMIs are more prone to having abnormal lymphatic function.

Although important, this study had a number of limitations. The study was carried out retrospectively by reviewing past results therefore the presence of lymphoedema was not confirmed through physical examination. Furthermore, the lymphoscintigraphy scans were not carried out before weight loss. Therefore, Greene et al. (2015) could not determine if weight loss improved lymphoedema or not. Finally, recruitment was biased as only patients from the authors' lymphoedema programme were recruited; therefore they may not have been representative of the wider population.

1.9 Prevalence of oedema in obese patients

The literature review established that there was a wide array of prevalence studies (Table 1.1). They have been split into two groups: those with a prevalence of oedema in an obese population and those with a prevalence of obesity in an oedematous population. Each group of studies will be discussed in order of prevalence (from lowest to highest). The methods of oedema assessment and any limitations will also be pointed out.

Table 1.1 Prevalence of oedema in obese patients

Study	Number of Participants	Prevalence (%)
Prevalence of oedema in an obese population		
Pittaluga and Chastanet (2012)	324	1.5
LABS Writing Group et al. (2008)	101	4.6
Inge et al. (2013)	1502	6.2
Lecerf, Reitz and de Chasteigner (2003)	18,102	24.3
Ridner et al. (2011)	59	28.8
O'Malley et al. (2015)	324	33.0
Rouzier et al. (2003)	137	37.2
Valensi et al. (2000)	51	51.0
Fife and Carter (2008)	15,000	74.0
Prevalence of obesity in an oedematous population		
Van der Molen and Tóth (1974)	733	10.0
L'Hermitte et al. (2003)	197	21.8
Wilkins, Swain and Cooke (2014)	> 1590	23.9
Meeske et al. (2009)	120	25.0
Wang and Keast (2016)	314	45.2
	326	45.7
Moffatt and Pinnington (2012)	371	69.0
Swenson et al. (2009)	92	69.0

1.9.1 Prevalence of oedema in an obese population

Firstly, a retrospective study by Pittaluga and Chastanet (2012) reviewed all varicose vein surgery records, searching particularly for lymphatic complications. Out of 324 obese patients, only four had lymphoedema (1.5%). For those who had a BMI greater than 30kg/m², this increased the likelihood of developing lymphoedema by 14.7. However, as the prevalence was only determined by reviewing medical notes, oedema may not have been reported consistently, which could have influenced the prevalence.

The LABS Writing Group et al. (2008) assessed the relationship between the BMI, demographic characteristics and co-morbidities of 2,559 patients having bariatric surgery. They were assessed through interviews and physical evaluation. After the first 359 participants were assessed, the co-morbidity 'venous oedema with ulcerations' was added to the assessment. Of the remaining 2,200 participants, 101 participants (4.6%) had venous oedema with ulcerations (with a BMI range of 40 to >60kg/m²). Compared

to those with a lower BMI of $40 < 50 \text{ kg/m}^2$, participants who had a higher BMI were more likely to: have more co-morbidities (including veno-thromboembolism and venous oedema with ulcerations) and have a history of venous oedema.

Another study by Inge et al. (2013) reported a low prevalence (6.2%) and investigated whether being obese at a young age meant that health risks were increased in severely obese adults. Out of 1,502 study participants who were assessed with a median BMI of 46 kg/m^2 (range of 34 to 94 kg/m^2), 93 (6.2%) had venous oedema (undefined). Compared with healthy adolescent adults, those with class 1 adolescent obesity increased the risk for venous oedema by 202%. Compared with adults who had a healthy weight at aged 18, those who were class 2 or 3 obesity at age 18 had a 435% greater risk of developing venous oedema in their lower limbs with skin manifestations. For each decade after aged 18, participants had an increased risk of venous oedema.

Lecerf, Reitz and de Chasteigner (2003) assessed 18,102 patients (mean BMI of 34.6 kg/m^2) for lower limb oedema and other disorders (hypertension, type 2 diabetes, etc.). There was a prevalence of 24.3% for oedema. However the presence of oedema was assessed using a closed questionnaire, which increased the likelihood of: mild or non-pitting oedema being missed and the estimate of prevalence being lowered. (The questionnaires were completed by general practitioners so participants may have been assessed. However, the abstract was unclear on this point and the full article was unavailable.)

Ridner et al. (2011) conducted a study to determine how BMI and obesity influence the development of BCTRL. There were 138 patients receiving treatment for breast cancer who were recruited from the same or nearby cancer centres. Out of 59 obese participants ($\text{BMI} \geq 30 \text{ kg/m}^2$), 17 had lymphoedema (28.8%).

Arm volumes were measured using a perometer, which measures the size and shape of a limb. Lymphoedema was classified as 200ml or 10% increase in arm volume on the side where the breast cancer was treated (as long as the other arm had stayed the same, which was measured by the perometer).

Lymphoedema breast cancer questionnaires were completed by the participants to self-report their symptoms (swelling and heaviness were important). There were 79 participants who had BMIs $< 30 \text{ kg/m}^2$ before

breast cancer treatment. After treatment, 14 of these increased their BMI to $\geq 30\text{kg/m}^2$, and 3 of the 14 had lymphoedema.

Their baseline BMI was strong and associated significantly with lymphoedema. Breast cancer participants who had BMIs $\geq 30\text{kg/m}^2$ at the time of treatment were about 3.6 times more likely to develop BCTRL six months or more after being diagnosed than participants who had a BMI less than 30kg/m^2 .

O'Malley et al. (2015) investigated the relationship between 'lymphoedema-like swelling' (LLS) and the physical function of 324 severely obese participants with a mean BMI of 51.6kg/m^2 . Out of all the participants, 33% had LLS. The participants' symptoms included: leg (shin) skin changes, feeling that their lower limbs were swollen towards the end of the day and feeling that their lower limbs were tight or heavy (Tomás Ahern, personal communication).

Rouzier et al. (2003) reviewed 194 patients with cancer of the vulva (who had had at least one lymph node dissection) to analyse their complications. Out of 137 obese patients, 51 had lymphoedema (37.2%). Lymphoedema was defined as: needing manual lymph drainage, requiring compression for longer than 6 months after the surgery or both.

Valensi et al. (2000) investigated extracellular fluid in overweight and lean women with swelling (called: 'swelling syndrome' in this article). Extracellular fluid was measured using the bioimpedance technique. Of the 51 women with swelling, 26 were overweight with a BMI of 32.8kg/m^2 (51%). The authors concluded that swelling was related to: an increase in extracellular fluid in both the overweight and lean women, and an increase in extracellular fluid when the overweight women were sitting down. However, the article did not explain clearly how the participants were recruited, so they may not have been recruited from the same population.

Fife and Carter (2008, p. 45) reported a "74% crude prevalence of lymphoedema in morbidly obese patients" (BMI of greater than 40kg/m^2). This was based on data from the Intellicure Research Consortium, a database of about 15,000 anonymised medical records from different wound centres in 18 American states. This study is limited because the prevalence was based on medical records, so consistent physical assessment of lymphoedema cannot be relied upon.

1.9.2 Prevalence of obesity in an oedematous population

A study by Van der Molen and Toth (1974) gave a lymphoedema prevalence of 10% in morbidly obese patients and 15% in moderately obese patients in a sample of 733 lymphoedema patients, recruited over 20 years. However, as with Inge et al. (2013), it was unclear how the lymphoedema was diagnosed.

A French study by L'Hermitte et al. (2003) investigated the factors involved with women who had lymphatic dysfunction and reported that they currently had swelling (however, this may not have been pitting oedema). Of 197 women recruited with swelling (mainly in the lower limbs and ankles), 43 were obese (21.8%). This study was limited because details of how participants were recruited and the methods used to assess/diagnose oedema were unclear.

Another large study by Wilkins, Swain and Cooke (2014) discussed the LOROS Hospice in Leicester (LOROS: Leicestershire Organisation for the Relief of Suffering). Out of more than 1,590 primary lymphoedema patients (article was unclear), more than 380 (23.9%) were obese (with a BMI of $\geq 40\text{kg/m}^2$).

In a study by Meeske et al. (2009), 494 white and black women with breast cancer were recruited, 120 of which reported lymphoedema. Only 30 of these were obese (25%). As the participants' BMI increased, their risk of developing arm lymphoedema grew stronger. The risk of obese women developing arm lymphoedema was 2.5 times greater than lean women. This study was limited because lymphoedema was 'determined' through interviews and self-reported data, rather than through clinical assessment. Furthermore, all participants were recruited as a result of being participants of a previous breast cancer study [Marchbanks et al. (2002) or Meeske et al. (2004)] therefore participants were probably not representative of the population.

Out of 314 patients diagnosed with secondary lymphoedema (defined as: oedema lasting more than three months, skin changes and oedema not improving with lower limb elevation) attending a wound clinic, 142 were obese (45.2%) (Wang and Keast, 2016). In the same clinic, 149 out of 326 lymphoedema patients were obese (45.7%).

In a chronic oedema prevalence study conducted by Moffatt and Pinnington (2012), 371 patients from the Royal Derby Lymphoedema service were recruited with a mean BMI of 35.3kg/m^2 . Sixty-nine percent of these

participants were obese and, from that 69%, 25% were morbidly obese (BMI of $>40\text{kg/m}^2$). However, this was only a sample of patients from the lymphoedema service and BMIs were not available for all who were identified to have chronic oedema (688 participants), so the prevalence of oedema in obese participants may have been greater.

Finally, Swenson et al. (2009) assessed two groups of 94 breast cancer patients (control and lymphoedema groups) to identify lymphoedema risk factors. The authors determined that the lymphoedema participants were more likely to be overweight (BMI $\geq 25\text{kg/m}^2$) than the controls. Out of the 94 lymphoedema participants, 65 (69%) were overweight. However, 47 from the control group (50%) were also overweight. This may be due to the participants being recruited from 5 different lymphoedema clinics in America, meaning that the participants would have had different characteristics and been part of different populations. Furthermore, the BMI of both the control and lymphoedema groups were calculated through self-reports of height and weight when patients were recruited, therefore these figures may be inaccurate.

1.10 Impact of bariatric surgery on oedema

Five studies were retrieved in this review regarding the impact of bariatric surgery (Table 1.2). The first four are group studies where patients were assessed before and after surgery. The final study is an important case-report study, focusing on the impact of high BMI on oedema before surgery.

Table 1.2 Summary of studies/case-report retrieved concerning the impact of bariatric surgery

Authors	Oedema Assessment Methods	Number of Participants	Post-Surgery Results
Khan et al. (2012)	Unspecified	10	Lymphoedema patients lost more weight than control patients, but no information about lymphoedema changes was provided.
Frigg et al. (2004)	Unspecified standard protocol and clinical examination	185	One year after surgery, oedema had disappeared for 51% of patients and improved for 30%.
Ratnasingham et al. (2011)	Unspecified	16	First surgery: mean excess lower limb volume decreased by 37% and excess body weight loss decreased by 27%. Second surgery: excess lower limb volume loss of 43-61% and excess body weight loss of 51-62%.
Sugerman et al. (2000)	Pitting Test	64	Oedema resolved in all but four out of 64 patients.
Greene, Grant and Maclellan (2015)	Unspecified	Case-report	BMI decreased from 80kg/m ² to 36, but there was no lymphatic function improvement.

Firstly, a study by Khan et al. (2012) analysed the effects of intra-gastric balloon insertion on obesity-associated lymphoedema, in super-obese patients. A small sample of participants with and without lymphoedema (10 participants each) were assessed before and after surgery. After surgery, those with lymphoedema had lost more weight than the control group. However, no specific information was provided regarding changes in lymphoedema.

Similarly, Frigg et al. (2004) investigated the effects of weight loss through laparoscopic adjustable silicone gastric banding on different co-morbidities, including oedema. In this research, 295 patients were recruited with a mean body weight of 125kg and a BMI of 45kg/m². Pre-operative prevalence of peripheral oedema (evaluated according to an unspecified standard protocol and clinical examination) was 63% (185 participants).

After surgery, oedema improvement was assessed by comparing the pre-operative and post-operative assessments. The data were analysed by: ANOVA analysis, the Least-Significant-Difference test and the Kruskal-Wallis test. Improvement in oedema after surgery was independent of the amount of weight loss (Table 1.3). For one patient with pre-operative oedema, the oedema grew worse temporarily and one non-oedematous patient developed oedema for a short time, even though they both had lost weight.

Table 1.3 Post-operative oedema improvement over 4 years

Time	Oedema Disappeared	Oedema Improved
After 1 year	51% of patients	30% of patients
After 2 years	67% of patients	14% of patients
After 3 years	79% of patients	8% of patients
After 4 years	71% of patients	7% of patients

The authors investigated the relationship between reduction of oedema and amount of weight loss. Although oedema had improved with weight loss, they concluded that there was no statistically significant relationship between reduction of oedema and weight loss.

Ratnasingham et al. (2011) assessed 16 patients with lymphoedema and a mean BMI of 73.9kg/m² before and after they had bariatric surgery to determine the effects on their lymphoedema. There were two stages to the surgery: firstly intra-gastric balloons were inserted, then after 6 months, the balloons were removed and a sleeve gastrectomy was performed. After the first surgery, the mean excess lower limb volume was reduced by 37% with an excess body weight loss of 27%. However, it is unclear how these variables were measured. Therefore, it remains uncertain whether the volume reduction was via fluid loss, fat loss or both. At the time the abstract was published, only 8 patients had completed the second surgery, which had resulted in an excess lower limb volume loss of 43 to 61% and an excess body weight loss of 51-62%. Furthermore, the surgery improved the patients' HqoL. However, this study was limited by its short follow-up period and the lack of any definite lymphoedema improvement following either surgery.

Sugerman et al. (2000) conducted a study to investigate the effects of weight loss through gastric bypass surgery on severe venous stasis disease in morbidly obese patients. This study is the first discussed in this review

to use a standardised assessment of oedema: the pitting test. There were 64 patients recruited, with a mean BMI of $61 \pm 12\text{kg/m}^2$ and a mean weight of $179 \pm 39\text{kg}$. All participants had pretibial pitting oedema. At 3.9 ± 4 years after surgery, participants had lost 55% of excess weight (62kg), reducing their BMI to 40kg/m^2 . The pretibial pitting oedema had resolved in all but four of the participants after one to 3.9 ± 4 years (article was unclear) after surgery. This study indicated the importance of weight loss for control of oedema however the final study described below demonstrates that weight loss may not be enough to improve oedema.

A case-report by Greene, Grant and Maclellan (2015) showed the impact of weight loss, initiated by bariatric surgery, on lymphoedema. The report gave information about a 46 year-old lady with bilateral shin swelling and a BMI of 80kg/m^2 . She had no other risk factors related to lymphoedema. Lymphoscintigraphy showed impaired lymphatic function bilaterally, consistent with a lymphoedema diagnosis. This was indicated by the Tc-99m filtered sulphur colloid (used in the lymphoscintigram) being delayed in travelling to the inguinal nodes 45 minutes following administration. The patient was referred to a bariatric weight loss service and had a sleeve gastrectomy. After 18 months, although her BMI had fallen to 36kg/m^2 , lymphoscintigraphy showed no improvement in lymphatic function. Normally, weight loss would cause the oedema to improve, but, as Greene et al. (2015) indicated: if a person's BMI is too high (80kg/m^2 in this case), losing weight will not help to improve the lymphatic system, causing oedema to continue.

1.11 Quality of life review

In this section, the HQoL of patients with lymphoedema and patients with obesity (with and without bariatric surgery) will be reviewed. The search strategy for this review consisted of a general internet search for systematic reviews under the topics of: HQoL of patients with lymphoedema and obesity.

HQoL is defined by the World Health Organisation Quality of Life Group (1993) as how a person views their life: in relation to their culture and values; and in light of their concerns, expectations, ambitions and standards. This is affected by their physical and mental health, independence, social relationships and association with important aspects of their environment.

HQoL highlights the different domains of health and how clinical factors affect patients. As clinicians may not evaluate HQoL effectively, self-report questionnaires are an important resource. HQoL questionnaires enable patients to describe how they feel, rather than simply relying on a clinical diagnosis. They should be used in clinical decision-making to affect how care is given and help the patients to express their views. (Franks, Moffatt, Morgan, 2007)

HQoL can be measured through generic questionnaires, such as the SF-36 (36-Item Short Form Health Survey), and disease-specific questionnaires, such as LYMQOL (Lymphoedema Quality of Life), or a combination of both. Generic questionnaires are valuable for gaining an overall HQoL score, especially in the absence of disease-specific questionnaires. However, they may not be specific enough to assess a person's HQoL accurately with regard to a particular disease or condition (lymphoedema, obesity, etc.). For example, the SF-36 questionnaire may not be sensitive enough to assess the negative emotions and mental distress brought on by having lymphoedema (Fu et al., 2013). Disease-specific questionnaires enable patients to describe the impact of a disease on different aspects of their life. However, even in disease-specific questionnaires, it may be difficult for patients to separate pain/discomfort that arises from lymphoedema or from other sources such as arthritis. Therefore, combinations of generic and disease-specific questionnaires are valuable.

1.11.1 Patients with lymphoedema

Based on the rigorous reviews of Armer et al. (2013), Burckhardt et al. (2014), Cemal et al. (2013), Morgan, Franks and Moffatt (2005), Pereira de Godoy et al. (2002) and Pusic et al. (2013), patients with lymphoedema have a lower HQoL than those without lymphoedema, physically, mentally and socially. Although Fu et al. (2013) reported that there were no significant differences emotionally and psychologically between those with and without lymphoedema, those with lymphoedema were found to have lower social well-being (relating to body image and appearance).

Qualitative studies have highlighted the negative psychological and social impact that patients experience as a result of developing lymphoedema (including emotional disturbance, negative self-identity, marginalisation and social isolation). It has been noted that patients can be given insufficient information about lymphoedema and clinicians may lack sensitivity. Patients with breast cancer-related lymphoedema were annoyed

that they were not given sufficient warning that lymphoedema can occur following treatment. They shared their fear and frustration, how they experienced difficulty receiving treatment and support, and how having lymphoedema caused them to have to change their everyday lives at work and home. (Fu et al., 2013; Morgan, Franks & Moffatt, 2005)

HQoL can be used as an outcome measure of the quality and impact of treatment and care (Franks, Moffatt, Morgan, 2007). Two studies have shown that when patients are treated with DLT, their mental and physical HQoL improved (especially if they were active) and their lymphoedema was reduced. Compression bandaging also improved their HQoL. (Cemal et al., 2013; Pusic et al., 2013)

There are a number of lymphoedema-specific assessment tools available however many have not been validated extensively. The Freiburg Life Quality Assessment-1 for upper and lower limb lymphoedema has good validity and reliability, assessing physical, social and emotional well-being (Augustin et al., 2005). The Lymphoedema Functioning, Disability and Health Questionnaire for arm lymphoedema assesses mobility and, physical and mental HQoL. It is valid and reliable, but its ability to test change over time has not been assessed. Furthermore, the English version of the questionnaire needs validating. (Devoogdt et al., 2011) The Lymphoedema Life Impact Scale is valid and reliable, assessing functional, psychosocial and physical lymphoedema-related impairments (Weiss and Daniel, 2015). The LYMQOL questionnaire for upper and lower limb lymphoedema assesses function, appearance, symptoms, mood and overall HQoL. It has been validated for clinical assessment use and as an outcome measure. (Keeley et al., 2010) The Lymphoedema Quality of Life Inventory assesses physical, psychosocial and practical aspects of life. It has been validated but the final version has not been reviewed by a patient expert group. This indicates that questionnaire validation studies are not always subject to quality control. (Klernäs et al., 2015) Finally, the Upper Limb Lymphoedema-27 questionnaire assesses functional, psychological and social effects of upper limb lymphoedema (Launois and Alliot, 2000). According to Pusic et al. (2013), it has good validity, reliability, and responsiveness.

Comparing HQoL across different studies can be difficult due to: the usage of different definitions of lymphoedema, and different generic and lymphoedema-specific questionnaires (Fu et al., 2013; Morgan, Franks & Moffatt, 2005). Furthermore, if patients have lymphoedema and another

condition (arthritis, cancer, etc.), the disease-specific questionnaires may not be suitable to assess the HQoL of patients with both conditions (Cemal et al., 2013).

The low HQoL that patients with lymphoedema can suffer from highlights the need for dedicated lymphoedema services, providing support to these vulnerable patients (Barlow et al., 2014; Burckhardt et al., 2014). Also, most lymphoedema research is focused on breast cancer-related (arm) lymphoedema, highlighting the need for high quality lower limb lymphoedema studies.

1.11.2 Patients with obesity

Reviews by Fontaine and Barofsky (2001) and, Kolotkin, Meter and Williams (2001) report that obese patients have a significantly impaired HQoL. This can be improved by losing weight but, as noted in section 1.3, this is not always easy for obese patients, which may lead them to consider having bariatric surgery.

The reviews by Andersen et al. (2015), Clegg et al. (2003), Driscoll et al. (2016), Gloy et al. (2013) and Lindekilde et al. (2015) report that bariatric surgery improves HQoL: physically, mentally and socially. Andersen et al. (2015) reported that: surgery led to improved HQoL, as long as patients maintained weight loss and experienced no side-effects. However, HQoL scores were still lower compared to those for comparison groups in the general population, indicating the long-term effects of obesity.

A number of obesity-specific HQoL instruments were highlighted by the review studies above. Similar to the lymphoedema-specific questionnaires, they were not all validated fully. These include: Impact of Weight on Quality of Life (Kolotkin et al., 1995), which is validated but there was only a short interval between testing questionnaire reliability (Kolotkin et al., 2001); Obesity-related Problems scale (Karlsson et al., 2003), which assesses the effects of obesity on psychosocial functioning, but is not convergently or discriminantly validated (Kolotkin et al. 2001); and Obesity-Related Well-Being Scale (Mannucci et al., 1999), which assesses HQoL and is validated, but only physically correlated with BMI (not mentally) (Kolotkin et al. 2001). The results of generic and disease-specific questionnaires have different implications, so the specific questionnaire must be considered when judging the scale of effect in HQoL change following bariatric surgery. Using both generic and disease-specific

questionnaires would allow HQoL to be analysed comprehensively (Lindekilde et al., 2015).

Limitations in assessing HQoL included: HQoL was not always reported in the different studies, many studies used invalid HQoL questionnaires, not all questionnaires were comparable across studies and only a few studies focused on patient HQoL more than five years following bariatric surgery (Clegg et al., 2003; Gloy et al., 2013; Driscoll et al., 2016).

1.12 Summary of literature reviews

The literature reviews explored: the association between obesity and chronic oedema, the prevalence of oedema in the obese population, the impact of bariatric surgery on oedema and, the HQoL of patients with lymphoedema and obesity.

The first literature review indicated that there is a greater likelihood of obese patients developing oedema than those who are not obese. Severity of oedema corresponds with BMI and increases with weight. Greene et al. (2012 and 2015) presented evidence of a lymphoedema-causing BMI threshold between 50 and 60kg/m², and that a high BMI may result in irreversible damage to the lymphatic system, even after weight loss.

Although several prevalence studies have been uncovered (from 1.5% in 324 participants to 74% in 15,000 participants), several evidence gaps remain. Firstly, almost half of these studies consisted of a small sample size or utilised an unclear recruitment method. Secondly, most articles were unclear in their definition of swelling/oedema and the presence of oedema was determined by self-reporting methods alone, both of which are not reliable. Finally, only four studies focused specifically on an obese/bariatric population [Inge et al. (2013); Lecerf et al. (2003); O'Malley et al. (2015); Fife & Carter (2008)]. Of these prevalences, the study by Lecerf et al. (2003) is questionable because oedema was only assessed through a closed questionnaire. The other prevalences were 6%, 33% and 74%, respectively. The wide variation in these estimates raises questions about their accuracy.

Five studies were reviewed that reported changes in oedema after bariatric surgery. The methods of assessing oedema and the post-surgery results were varied. Only Sugerman et al. (2000) gave a definitive assessment method (pitting test), the other studies were not specific. Although mainly Frigg et al. (2004) and Sugerman et al. (2000), the studies' results point to oedema improvement following bariatric surgery. However, the case-report

by Greene et al. (2015) highlighted the danger of having a high BMI that could cause irreversible damage to the lymphatic system.

The second literature review highlighted the negative impact that lymphoedema and obesity can have on HQoL. It raises the issue of obese patients having oedema, which may decrease HQoL even further. Surprisingly, in the first literature review, only Ratnasingham et al. (2011) mentioned the patients' HQoL, which improved following bariatric surgery. This indicates the need for further research of patients with oedema and obesity.

In order to clarify the prevalence of chronic oedema in an obese/bariatric population, the effects of bariatric surgery on oedema and the impact of oedema on the HQoL of this population, further research is needed. The study described in this dissertation provided: a prevalence study for chronic oedema in a bariatric population, a definitive method of recruitment and, a clear oedema definition and assessment (before and after bariatric surgery).

1.12.1 Aims of the study

The primary aims were: to determine the prevalence and impact of chronic oedema on HQoL in a population of bariatric patients and, to assess the impact of bariatric surgery on chronic oedema. A secondary aim was to test fluid measurements, bioimpedance and tissue dielectric constant (TDC) techniques, to see which is more effective at confirming the presence or absence of oedema. Finally, the clinical practice aim was: to improve the treatment and care pathway for obese patients with chronic oedema. The next two chapters will discuss the methods used in the study.

CHAPTER 2: STAGE 1 METHODS

2.1 Introduction

The study presented in this dissertation was conducted in two parallel stages, Stage 1 and Stage 2. The methods used in Stage 1 are described below and the methods adopted in Stage 2 are described in Chapter 3. The main aims of Stage 1 were: to determine the prevalence and impact of chronic oedema on HqoL and, to assess which of the fluid measurement techniques (bioimpedance or TDC) were more effective at determining the presence of oedema.

2.2 Preparatory phase

Prior to the study commencing, the researcher was trained in the clinical assessment techniques outlined in section 2.11. She observed lymphoedema clinics to improve her understanding of assessment techniques such as: the pitting and Stemmer's sign tests and, how to identify the various skin changes associated with oedema. She also assessed a sample of patients under observation to ensure the techniques were applied correctly.

The researcher attended: an 'Introduction to Good Clinical Practice (GCP)' workshop, which outlined the standards of conduct required when conducting clinical research, and induction training at RDH.

2.3 Patient and public involvement

As recommended by the National Institute for Health Research (INVOLVE, 2012), patient representatives from the Queen's Medical Centre lymphoedema patient support group were approached during the study design phase to provide feedback on the purpose and methods of the proposed study. This consultation provided perspectives from patients on the study as a whole and an assurance that the roles expected of prospective participants were reasonable. One patient representative also reviewed and provided feedback on all patient-facing study documents to ensure they were appropriate and written in an understandable form. Small typographical alterations were made where needed.

2.4 Approval of study documents

All study documents were approved by the University of Nottingham, Derby Teaching Hospitals NHS Foundation Trust and Liverpool Central Research Ethics Committee. The study was carried out in accordance with the

guidelines of the Declaration of Helsinki and the principles of GCP ICH E6 and EN540 standards. Patients were recruited during a five-month period, commencing August 2016.

2.5 Study sample

Participants taking part in Stage 1 were all newly-referred patients to the Tier 3 (weight-management) clinical pathway. The study took place in the bariatric clinic of RDH, located in the surgical outpatients department. All participants were assessed at their first clinic appointment whilst waiting to see one or more members of the bariatric team and/or at the end of their appointment.

As stated in section 1.4, each new Tier 3 patient (and therefore each participant) had a BMI of at least 40, or 35 with obesity-related co-morbidities, and had previously tried to lose weight. In general, each patient is seen by a bariatric nurse, a physician and a dietitian. They are also seen by a clinical psychologist if they score highly on the GAD-7 (Generalised Anxiety Disorder 7-item Scale) and PHQ-9 (Patient Health Questionnaire – 9) questionnaires, which measure anxiety and depression.

2.6 Identification of prospective participants

All patients, who were newly-referred to the Tier 3 clinical pathway of the bariatric service, were given or sent information about the study (invitation letters and participant information sheets, A2.1 and A2.2) with the aim of recruiting a consecutive sample of patients to avoid recruitment bias. (Figure 2.1 provides a review of the recruitment process.) General information about the study, including information about oedema and the purpose of the study, was made available through posters displayed in the waiting area and clinic rooms (A2.3).

2.7 Informed consent

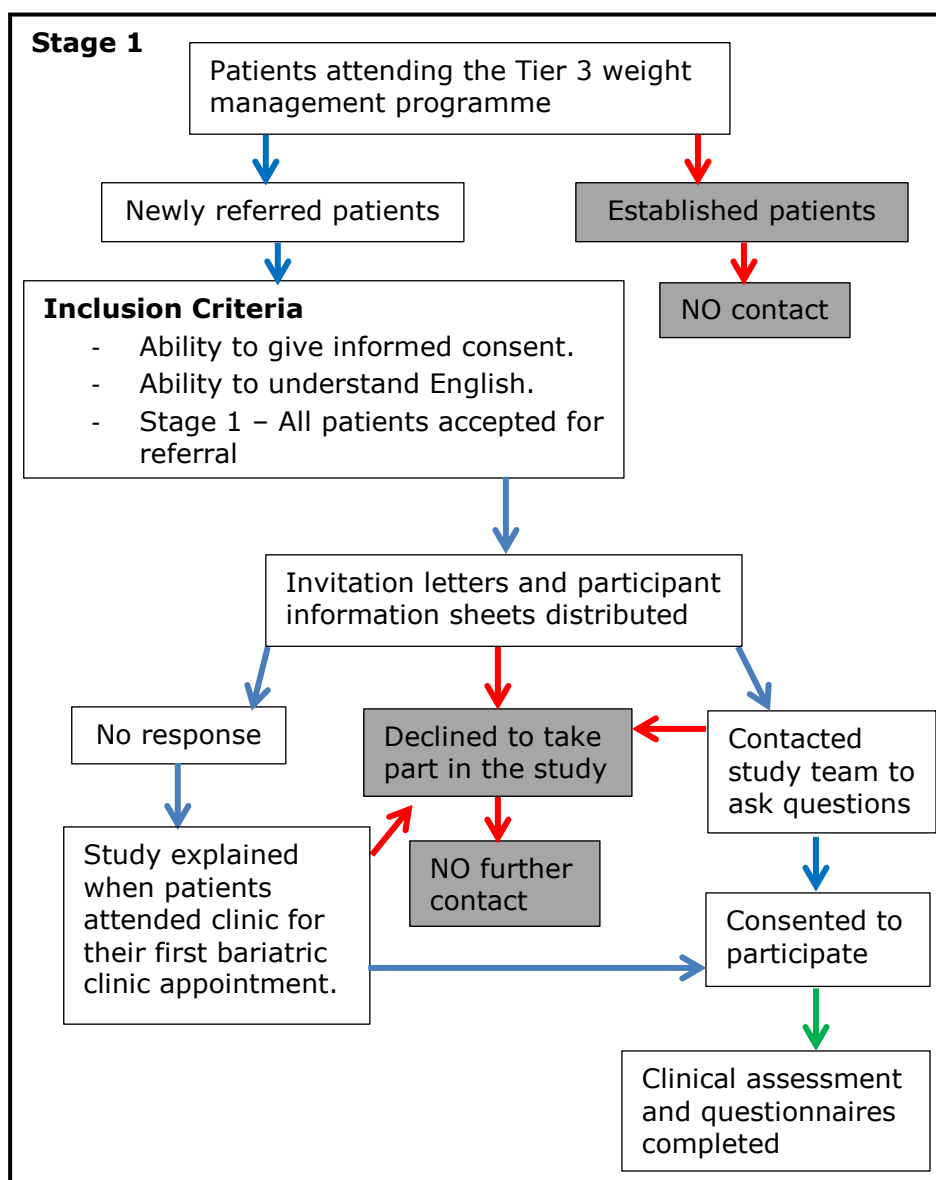
When patients attended the first clinic appointment, the study was explained verbally by the researcher and an opportunity was given to ask questions. Patients were reassured that participation in the study was entirely voluntary. Patients who agreed to take part were invited to sign a study/photographic consent form (A2.4). One copy was kept by the participant, one by the study team and a third was retained in the medical record.

For each participant, the researcher sent a letter (A2.5) and participant information sheet to the GP. The letter gave information about Stage 1 and advised that the patient had taken part.

2.8 Inclusion and exclusion criteria

All participants were adults who had the capacity to give informed consent to take part in the study. As one of the study questionnaires, the lymphoedema-specific LYMQOL, had not been validated in other languages, recruitment was limited to patients who could understand English.

Figure 2.1: Summary of Stage 1 recruitment process



2.9 Data collection

All data were recorded on case-report forms (CRFs), one for each participant (A2.6). A screening log was also kept, recording how many new

patients were provided with study information. Out of this number, the following information was recorded, how many: were recruited, declined to participate or could not be assessed as the researcher was occupied assessing others.

2.10 Data protection

All members of the study team protected the rights of the study participants to informed consent and privacy, adhering to the Data Protection Act, 1998. All confidential data and study documents were held securely in a locked room and computer-held data were password-protected. Participant information, both personal and medical, was considered confidential. Access was limited to the study staff and relevant regulatory authorities.

In order to keep data confidential, each participant was assigned a unique study number, written on their respective CRF and questionnaires. The researcher made a separate confidential document, consisting of: the participant's name, date of birth, NHS number and participant study number, in order to keep a record of all study participants. This also ensured that the participants could be contacted after the assessments if necessary, to answer any queries and to forward the study results if requested. Only the study team had access to this file and accessed it when appropriate.

When the study is completed (planned end date: January 2019), the University of Nottingham will archive the data and study documents at secure archive facilities. The Chief Investigator or his nominee will maintain all of the study documents and records. These will be retained for at least seven years.

2.11 Methods of assessment

The study assessment methods consisted of: a clinical history, a clinical assessment and, completion of generic and oedema-specific HQoL questionnaires. The participants were assessed once and each assessment lasted 50-60 minutes. This section describes these methods and explains why they were selected.

2.11.1 Clinical history

The researcher examined the clinical records of each participant to obtain blood test results, medical history and medication lists. Blood test results

were recorded to see if there were underlying medical causes for any oedema present (Table 2.1). The medical history, medication and mobility sections were recorded in order to help determine their impact on oedema. The study team were especially interested in conditions which may cause oedema. These included: history of cellulitis, heart failure, hypertension and obstructive sleep apnoea. Furthermore, the study team searched for medications that could exacerbate oedema, including: calcium channel blockers and medications for hypertension.

Table 2.1: Blood test result analysis

The blood tests analysed by the study team are listed below with the reasons for analyses listed.

Blood Test	Reason for Analysis
Haemoglobin levels of the Full Blood Count test (FBC)	To test for anaemia
Glycated Haemoglobin Test (HbA1c)	To test for diabetes
Albumin (ALB)	To test the function of the liver
Thyroid Function Test (TFT)	To test thyroid-stimulating hormone function
Estimated Glomerular Filtration Rate (EGFR)	To test kidney function
B-Type Natriuretic Peptide Test (BNP)	To test heart function

Oedema-related questions (concerning: oedema, history of cellulitis, skin conditions and wounds) were recorded in order to understand the impact of some of the secondary implications of oedema. Questionnaires used in a related study, entitled 'LIMPRINT' (Lymphoedema IMPact and PRevalence INTernational), were also incorporated, namely: the 'Core Tool' (A2.7) and 'Details of Swelling Tool' (A2.8). These questionnaires were chosen because they had been used previously in comparable studies.

2.11.2 Clinical assessment

This section describes the clinical assessment methods:

a) Presence or absence of oedema

The purpose of the clinical assessment was to determine the presence and extent of chronic oedema and skin integrity. In summary, the assessment involved: an inspection of lower limb and abdominal skin to note the presence of oedema and/or skin condition. Presence of oedema was assessed using the 'pitting test' (primarily) and 'Stemmer's sign' techniques. The skin was assessed at the following reproducible areas: dorsum of the feet, ankles, lower limbs (below and above the knee) and the abdomen. The pitting test was the gold standard test for assessing whether or not oedema was present. Although useful for identifying toe oedema, the Stemmer's sign technique was mainly used to determine the type and underlying cause of the oedema.

The pitting test (Dai et al., 2015) involves pressing firmly on the skin with the thumb and/or fingers, then monitoring how long it takes for the skin to rise to a normal level. If it is rapid, it is likely that no oedema is present at that site. If the pressure leaves an indentation in the skin and requires a few seconds to recover, this indicates oedema. A participant was classified as having oedema only when they had pitting oedema.

For the Stemmer's sign test (Stemmer, 1999), the skin is pinched at the proximal end of the second toe. If it is not possible to pinch and lift the skin, this is a positive Stemmer's sign, which normally indicates oedema in the toes. A negative result occurs when the skin can be pinched and indicates toe oedema is absent (although the possibility of feet and/or lower limb oedema remains). An equivocal Stemmer's sign is reported when it is not clear whether the skin can be pinched.

Photographs were taken at each oedema site, but these were not used as substitutes for clinical assessment. One supervisor (a clinical lymphoedema specialist) reviewed the photographs to approve the researcher's assessment. He compared the clinical assessment with the photographs, visually checking for the presence of swelling and thereby providing quality control. The findings were all confirmed but a few high TDC results amongst participants who were not thought to have oedema were queried. In these cases, the data were not changed but notes were added to the file to indicate that oedema may be present (see results of participants 024 and 042 in A4.18).

b) Fluid measurements

Fluid measurements were obtained using both bioimpedance and TDC techniques, in order to determine which was more effective at detecting the presence of oedema. Although these techniques have been used previously in lymphoedema research, they have not been used to detect oedema in obese patients.

A bioimpedance machine was used to measure the total fluid present in each upper and lower limb. Measurements were taken by passing an extremely small electrical current (similar to the strength of a watch battery) through the body, using wrist and ankle electrodes. These measured the resistance of the flow of electricity at different frequencies of the current. R_{zero} (R_0) is the resistance at 0 frequency and solely measures fluid (extracellular fluid). R_{infinity} (R_i) measures the resistance at infinite frequency, measuring everything in the limb (bone, cells, fatty tissue, fluid, etc.). The lower the resistance value, the higher the level of extracellular fluid (and oedema).

As well as resistance measurements, whole body analysis (WBA) data were calculated from the participants' age, gender, height and weight: total body water (TBW), extracellular fluid (ECF), intracellular fluid (ICF), fat free mass (FFM), fat mass (FM) and BMI.

In contrast to bioimpedance, the TDC approach is a more focused technique, which measures the presence of tissue water in the dermis layer of the skin. An ultra high-frequency electromagnetic wave is transmitted via a hand-held probe which is placed onto the skin (Nuutinen et al., 2004). As it is a dielectric constant, TDC values are not defined by units. The TDC approach was chosen because it is easy to use.

In this study, TDC was used to measure different points of lower limb and abdominal wall oedema. The probe measured the top 2.5mm layer of skin. This area is thicker with fluid when oedema is present and is the depth commonly used in clinical practice and lymphoedema research. Higher readings indicate more fluid is present at the measurement site.

2.11.3 Quality of life

Aspects of HqoL were assessed by questionnaires: EQ-5D (EuroQOL-5 Dimensions), LYMQOL, SF-36, GAD-7 and PHQ-9.

The EQ-5D, LYMQOL and SF-36 questionnaires are used extensively in lymphoedema trials. They were completed to enable comparisons to be made with other studies.

The EQ-5D questionnaire (A2.9) is a quality of life health index, providing a general health score for each participant. The LYMQOL questionnaire (A2.10) is a lymphoedema-specific HQoL instrument. It was used to assess oedema in upper and lower limbs and, the impact of oedema on everyday life. LYMQOL is split into: function, appearance, symptoms and mood (these are scored using the range of 1.0 to 4.0, meaning that the oedema had no impact to a lot of impact), and HQoL (ranging from 1.0 to 10.0).

The SF-36 questionnaire (A2.11) is a measure of physical health. It was chosen because it is a generic and easy-to-use questionnaire, and covers many of the domains affecting people with chronic oedema. It has been shown to be sensitive to change (Hemingway et al., 1997) and has been used in previous studies (Mosconi et al., 2002 and Lazovich et al., 2009).

Using both oedema-specific and generic (EQ-5D and SF-36) questionnaires was a powerful combination. One problem with solely using generic questionnaires is that they may not be sensitive enough to assess changes in a particular condition because they are designed to assess HQoL across a variety of conditions. However, condition-specific questionnaires should be more sensitive to change because they have been designed with specific patient groups in mind. (Jones et al., 2002)

Anxiety and depression were examined by the GAD-7 and PHQ-9 questionnaires (A2.12 and A2.13). These were chosen because they are short and easy to complete. Patients complete these routinely when attending clinic, therefore, these data were extracted from the medical records.

2.12 Recruitment alterations

During the early stages of data collection, it became clear that recruitment was quite slow and could be biased; therefore, a number of methods were employed to facilitate recruitment.

Firstly, two rather than three fluid measurements (using the TDC) were taken for each site. Where possible, some data were gathered whilst patients were waiting for a member of the bariatric team to become available. Finally, when time was limited, some details were confirmed subsequently by phone.

2.13 Statistical analyses

Descriptive statistics in Microsoft Excel were used to analyse characteristics of the participants and, to determine the severity and cause of oedema. The blood test results, co-morbidities and medications were also analysed to search for associations with oedema. As the study included a heterogeneous sample, the SF-36 questionnaire scores were compared with a normative dataset (consisting of adults aged 16 and above living in private houses) from the Health Survey for England (HSE) 1996 (Joint Health Surveys Unit, 1996).

For each of the questionnaires and fluid measurements, histograms showing the distribution of data were analysed. The normalcy of data was checked by comparing the means and medians, and by calculating the quotient of the statistics and standard errors of skewness and kurtosis scores. For normally distributed data, means and standard deviations of data were calculated. T-tests were calculated to determine whether the mean values of participants with and without oedema were statistically different to each other (alternate hypothesis) or not (null hypothesis).

Positively skewed data were transformed by using natural log, square root and/or reciprocal data; negatively skewed data were transformed by using squared and/or cubed data. T-tests were calculated using these data. When the data were still skewed, non-parametric Mann-Whitney U tests were calculated. Medians and interquartile ranges were calculated for skewed data.

Bioimpedance resistance (R_0 and R_i) values were analysed to provide two sets of ratios. The first ratio compared the ECF in the oedema lower limb with the control upper limb (R_0 upper limb/ R_0 lower limb). [ECF is inversely proportional to resistance (Ward, 2009).] This allowed the study team to determine if the resistance values of the control upper limb were different to those of the lower limb.

Secondly, the data were analysed to provide a ratio (focusing on the ECF compared to all of the tissue components) of the affected lower limb over the control arm, $[(R_i/R_0 \text{ lower limb})/(R_i/R_0 \text{ upper limb})]$. This enabled the study team to determine how much fluid resistance (therefore oedema) was present.

SPSS and Stata software were also used to: analyse data from the pitting test to determine the proportion (with 95% confidence intervals) of participants with oedema and to run independent-sample t-tests. The t-

tests were calculated to address questions about the impact of oedema on everyday life. They assessed whether mean/median values of participants with and without oedema were statistically different in the following sections: HQoL scores, fluid measurements of the upper and lower limbs (bioimpedance) and, fluid measurements at specific sites (TDC). Based on these results, the fluid measurements were analysed to determine whether the bioimpedance and TDC data could be used to define chronic oedema and which was more effective.

Statistical corrections were not applied artificially because this could change the significance (p) value of the t-tests (Perneger, 1998). Instead, caution was used in the interpretation of the results, especially the significant results.

2.14 Data checks

The CRFs and all source documents were available at all times for the supervisors and relevant regulatory authorities to review as necessary. A clinical supervisor reviewed each completed CRF, clarifying issues that the researcher raised.

2.15 Management of missing data

Although data were collected in a diligent manner, on occasions data were missing due to clinic disorganisation or participant error. At the start of recruitment, questions were omitted inadvertently; therefore this was taken into consideration when scoring them. Subsequently, questionnaires were always checked before participants left the clinic, providing an opportunity to complete any missed questions. Missing CRF or questionnaire data were highlighted upon data entry, allowing valid conclusions to be reached and statistical tests to be run accurately.

2.16 Summary

The main aim of Stage 1 was to determine the prevalence and impact of chronic oedema in a population of bariatric patients. Patients were recruited, consented and assessed at their first bariatric clinic appointment by the researcher. The assessment included: testing for the presence of oedema, measuring fluid levels of the body and completing HQoL questionnaires. The data were analysed to produce an account of the prevalence and impact of chronic oedema in a population sample of bariatric patients. The next chapter will describe methods used in Stage 2 of the study.

CHAPTER 3: STAGE 2 METHODS

3.1 Introduction

Stage 2 of the study took place in parallel with Stage 1 however a separate group of patients were recruited. Stage 2 was designed to establish the practicality of undertaking a definitive study into the impact of bariatric surgery on oedema, assessing for post-operative changes in oedema. As in Stage 1 (section 2.1), the prevalence and impact of chronic oedema on HQoL was assessed. The bioimpedance and TDC techniques were analysed to determine their effectiveness of confirming: the presence of oedema; whether they could be used to measure post-operative reduction in oedema; and whether weight changes that occur post-surgery were attributable to fluid loss, fat loss or both. In addition, a device for measuring limb volume, a perometer, was used to test the hypothesis that bariatric surgery and consequential weight loss will result in reduced oedema (Shaw et al., 2007). This chapter is structured in a similar manner to the previous chapter, and describes the recruitment and assessment methods adopted in Stage 2.

3.2 Preparatory phase and study approval

Preparations for Stage 2 were carried out as described for Stage 1 (section 2.2) however, training was also undertaken in the use of the perometer. The same steps were taken to obtain study approval as discussed previously (sections 2.3 and 2.4).

3.3 Duration of Stage 2

Participants were recruited to Stage 2 over a four-month period. It was important that patients were assessed as close as possible to their bariatric surgery date. They were assessed therefore at their pre-operative (usually one to two weeks before surgery) and six-week post-operative appointments. (Due to time limitations, it was not possible to assess all participants post-operatively before the data collection period came to an end.) Data collection commenced in September 2016 and ended in January 2017.

3.4 By-Band-Sleeve study

Patients were being recruited to another study [entitled the "By-Band-Sleeve" (BBS) study] at the same time as Stage 2 (section 5.4.1b). In order to distribute recruitment to both studies and to avoid patient fatigue,

patients were only recruited to the chronic oedema study if they were allocated to the observational control arm of the BBS study or if they were not taking part.

3.5 Identification of prospective participants

The pre-operative clinic receptionist sent out study invitation letters and participant information sheets (A3.1 and A3.2) to patients prior to the appointment date. The participant information sheet and letter for the GP (A3.3) were forwarded to the GP of each patient who agreed to take part.

3.6 Study population setting

Patients who were recruited had been scheduled for bariatric surgery. The study took place in the pre-operative and bariatric clinics of the Tier 4 weight management service provided by RDH, located in the surgical outpatients department.

A screening log was kept in which a record was made of all patients provided with study information and, out of that group, the number of: eligible patients, recruited participants, and patients that declined to take part (Figure 3.1). This enabled the study team to evaluate the ease with which this group of patients could be recruited. Furthermore, the log gave useful information about recruitment and the ease with which a larger prevalence study could be undertaken. As recruitment was restricted by the BBS study, a record was also made of how many randomised BBS patients had pre-operative appointments during the study recruitment period, impacting the total sample size.

3.7 Inclusion and exclusion criteria

The participant inclusion and exclusion criteria for Stage 2 were the same as those outlined for Stage 1 (section 2.8), with two exceptions. Firstly, all participants had completed the Tier 3 pre-surgery pathway and had been referred for bariatric surgery. Secondly, participants who were taking part in the interventional arm of the BBS study were excluded from taking part in the study.

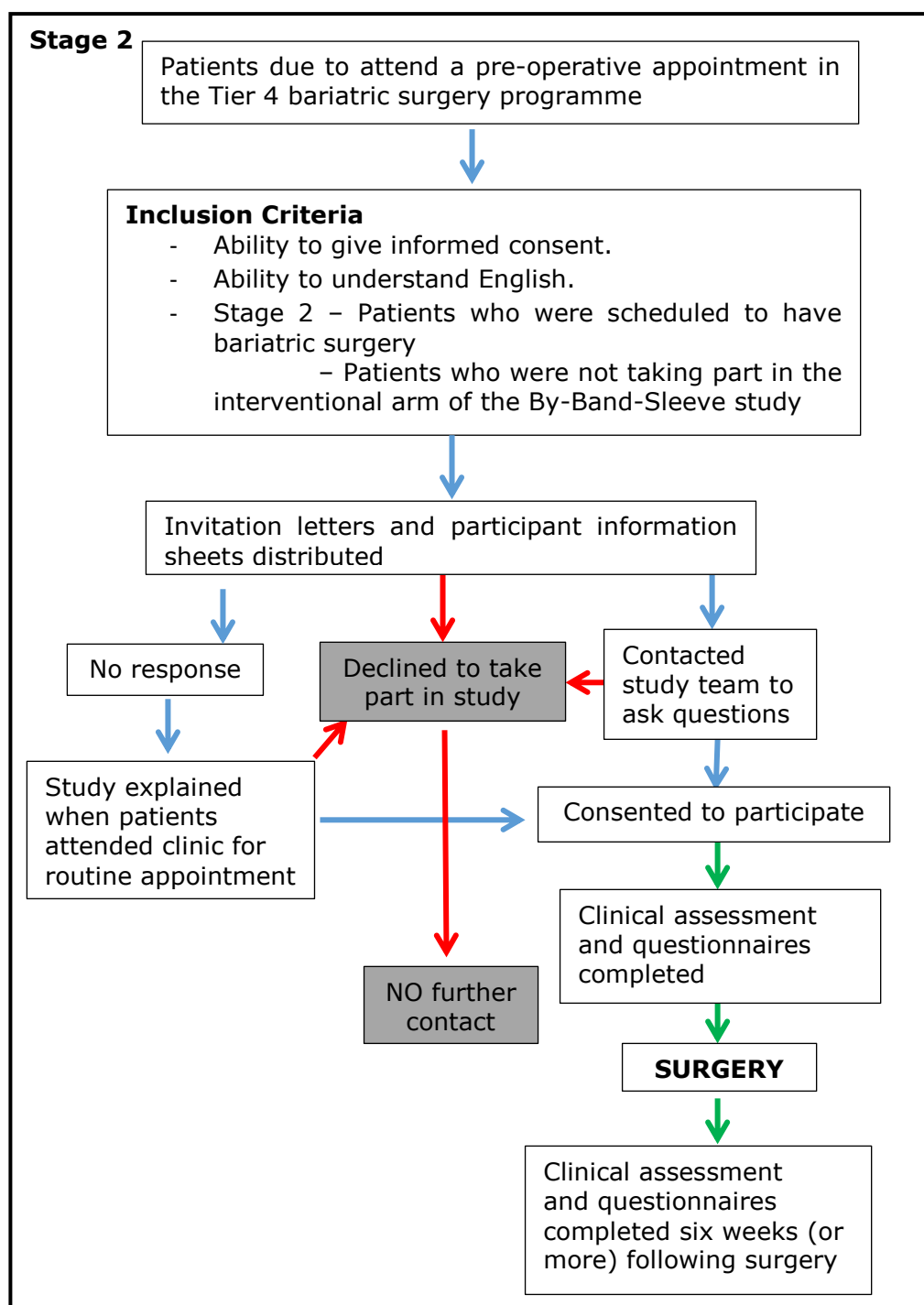


Figure 3.1: Summary of Stage 2 recruitment process

3.8 Data collection and protection

The same data collection and protection procedures were followed in Stage 2 pre-operative assessments (A3.4) as those outlined previously for Stage 1 (sections 2.9 and 2.10). The post-operative assessments were identical, but they also recorded any changes in: co-morbidities, complications and oedema (such as limb volume or oedema site) (A3.5). The data were checked for errors and any missing data were managed in the same way as for Stage 1 (section 2.14).

The number of recruited patients and the number of patients who declined or who failed to complete their follow-up appointment were analysed. This has aided the study team with knowing how to calculate the sample size and design study recruitment for future studies (section 5.6).

3.9 Methods of assessment

Pre-operative data collection was similar to Stage 1 (section 2.11). Participants who had oedema were assessed following surgery to monitor changes in oedema and, participants without oedema were followed up to help ascertain the efficacy and relative benefits of bioimpedance and TDC techniques at determining the contribution of fluid reduction to weight loss.

3.9.1 Clinical assessment

Participants were asked the same questions as Stage 1 and were also asked about the type of bariatric surgery planned. The clinical assessment was identical except for the inclusion of the perometer. This measured lower limb size and shape by moving the perometer frame up and down them to produce a 2D image. (Two measurements were taken and combined to form an average value.) This information was transferred into circumference measurements to create limb volumes. Any differences in limb volume were recorded at the follow-up appointments. The perometer was chosen because it is a quick technique that involves less 'operator error' than other methods.

Fluid measurements (bioimpedance and TDC techniques) were also used before and after surgery. This allowed the researcher to assess differences in fluid levels and, consequently, any changes in oedema after bariatric surgery. Any changes in medical history or medications were recorded during post-operative assessments. This helped to determine whether these factors contributed to the level of oedema present or any changes in oedema severity.

Photographs were taken of each oedema site at both pre-operative and post-operative assessments. This enabled any changes in oedema following surgery to be monitored.

Only one blood test result was collected during post-operative assessments, namely: 'glycated haemoglobin level'. This helped to assess whether or not the participants' diabetes status had improved. (However, no blood test results were available for the participants assessed post-operatively before data collection for the dissertation ended.)

3.9.2 Questionnaires

As in Stage 1, participants completed EQ-5D, GAD-7, LYMQOL, PHQ-9 and SF-36 questionnaires. The SF-36 data were compared with HSE population normative data.

3.10 Statistical analysis

Statistical analyses were carried out in a similar manner to Stage 1 (section 2.13):

Descriptive statistics were used to: analyse the characteristics of the participants, investigate the cause of oedema and, to make comparisons between pre-operative and post-operative data. BMIs and medications were analysed and compared before and after surgery to determine any changes. Questions concerning the presence/severity of oedema were also compared to determine the impact of weight loss on chronic oedema.

As with Stage 1, a proportion with 95% confidence intervals was obtained to determine the prevalence of chronic oedema in this population. Post-operative changes in oedema were ascertained: using the pitting test to determine if oedema was still present following surgery and, through limb and fluid volumes to assess changes over time. As section 1.10 indicated, changes in limb volume in obese patients may arise as a result of fat loss, fluid loss or both. Therefore, the limb volume measurements were analysed with the fluid measurements.

3.11 Summary

The main aim of Stage 2 was to determine the impact of bariatric surgery on chronic oedema. This was achieved by recruiting and assessing bariatric patients at their pre-operative appointment and assessing them after surgery. Each assessment consisted of: testing for the presence of oedema, limb volume measurements, measuring the levels of fluid in the body and the completion of HQoL questionnaires. The data were analysed to determine: the prevalence and impact of chronic oedema on HQoL, the impact of weight loss on oedema and how limb/fluid volumes changed following surgery. Data derived from both Stage 1 and 2 of the study are reported in the next chapter.

CHAPTER 4: RESULTS

4.1 Introduction

Data derived from both stages of the study are described in this chapter. The prevalence of chronic oedema will be presented in a sample of bariatric patients. The values of several clinical and HQoL parameters are summarised and any differences between participants with and without oedema identified. Additionally, data from Stage 2, both before and after surgery, will be analysed to compare differences as a result of bariatric surgery.

4.2 Stage 1

This section will describe the results obtained from Stage 1.

4.2.1 Prevalence of chronic oedema

During this stage, 31 patients were recruited from the Tier 3 bariatric service of RDH (see Figure 4.1 for more details). The prevalence of oedema in this population of patients was 61.3% (95% confidence intervals: 42.4-77.3%) with 19 out of the 31 participants having oedema.

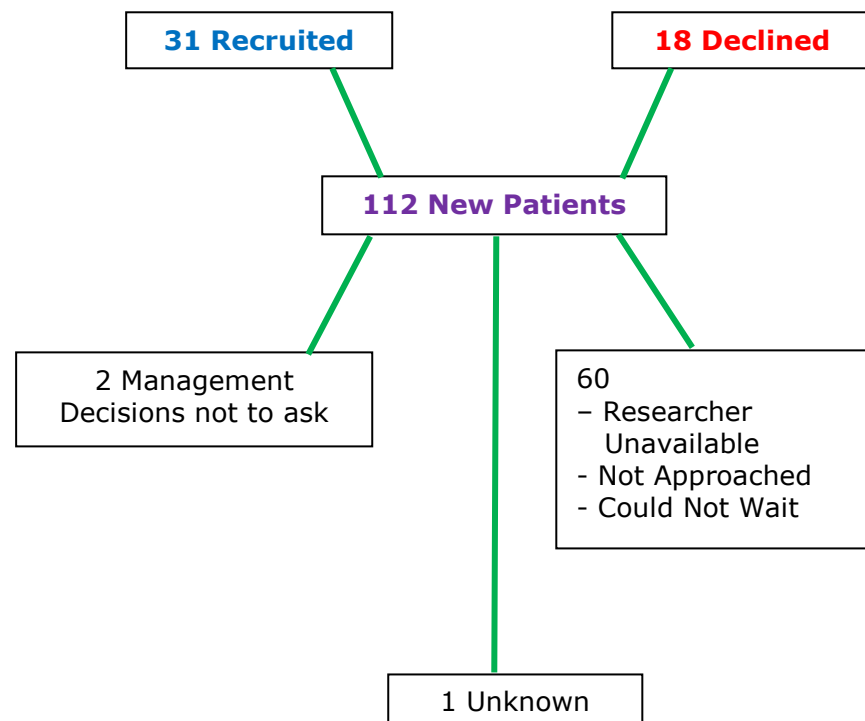


Figure 4.1: Screening log for Stage 1

General participant characteristics and information about skin conditions/conditions which commonly affect those who suffer with oedema were recorded (A4.1, A4.2 and A4.3). Table 4.1 provides a comparison between participants with and without oedema, highlighting that those with oedema had (compared to those without oedema): higher age group, higher weight range, presence of positive Stemmer's signs and skin conditions, and histories of cellulitis. Furthermore, the majority of participants with oedema were in the 50-60kg/m² BMI category (highlighted in Table 4.2).

Table 4.1: Comparison of characteristics and conditions between participants with and without oedema

(CO: chronic oedema, NCO: no chronic oedema)

Characteristics	Summary (CO)	Summary (NCO)
Age	Ranged from 35-64 (mean: 51.2)	Ranged from 23-55 (mean: 36.5)
Gender	8 Males : 11 Females	3 Males : 9 Females
Weight (kg)	Ranged from 106-236 (mean: 151.4)	Ranged from 101.2-160.4 (mean: 135.0)
BMI (kg/m²)	Ranged from 43.7-63.5 (mean: 52.5)	Ranged from 40.6-57.3 (mean: 48.9)
Condition	Summary (CO)	Summary (NCO)
Stemmer's Sign (SS)	11: both feet negative SS, 4: both positive SS, 3: 1 foot negative SS and 1 foot positive, 1: equivocal SS	11: both feet negative SS, 1: equivocal SS
Skin Conditions (Location)	10 participants with skin conditions (1 unanswered) - 8: both shins, - 1: 1 shin	1 participant with skin conditions (2 unanswered) - 1: shins and thighs
Skin Conditions (Type)	5: chronic lipodermatosclerosis, 3: dry skin, 2: eczema, 1: haemosiderin staining, 1: lymphangiectasia, 1: varicose eczema	1: healed bite and anxiety scratch marks
Cellulitis	8: Yes, 11: No	All: No

Table 4.2: BMI classification – Stage 1

The number of Stage 1 participants and those with oedema are identified next to their appropriate BMI class.

[BMI Classification reported by: (World Health Organization, 2004)]

BMI Classification		Stage 1 BMIs	Oedema
40-50 obesity kg/m ²	Class 3 (severe)	12	5
>50 kg/m ²	Superobesity	19	14
50-60 kg/m ²		18	13
>60 kg/m ²		1	1

4.2.2 Severity of oedema

For most of the 19 participants with oedema, they only had mild pitting oedema which improved after having their lower limbs elevated [International Society of Lymphology (ISL) Stage 1] (Table 4.3 and A4.4). There were only three participants who had severe oedema (ISL Stage 2). These had chronic lipodermatosclerosis (where the skin thickens, discolours and severely indents, potentially causing the shins to become inverted champagne bottle shapes) (Figure 4.2) or lymphangiectasia (where the lymph vessels are dilated, so blister-like bumps may appear on the skin) (Lymphoedema Framework, 2006).

Table 4.3: Summary of oedema characteristics

Characteristic	Summary
Location of Oedema	Most participants: both feet and shins. Other locations: both lower arms, right wrist, and both ankles. One participant: left foot, both shins (with possible oedema in both thighs and abdomen).
Tissues in Swollen Area	18: soft, 1: hard.
ISL Stage	16: Stage 1, 3: Stage 2.

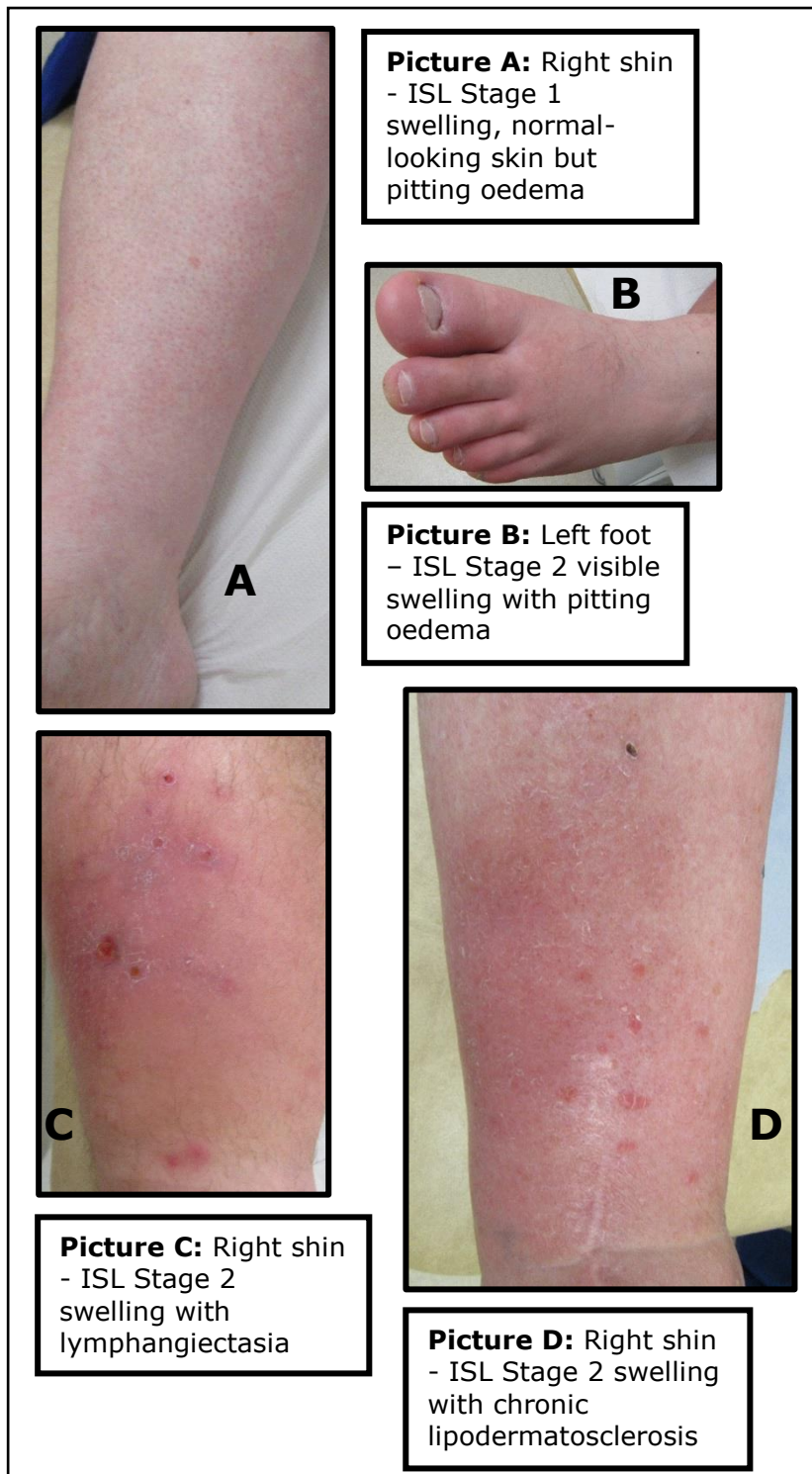


Figure 4.2: Range of oedema and skin conditions

4.2.3 Potential contributors of oedema

As well as determining the prevalence of oedema, it was important to endeavour to discover what had caused the oedema. A comparison indicated that Amlodipine, Atorvastatin and Pregabalin were common medications for participants with and without oedema (Table 4.4, A4.5 and A4.6). Routine blood test results showed that there was no evidence that

anaemia, diabetes, hypoalbuminaemia, thyroid dysfunction, renal failure or heart failure contributed to the oedema (see A4.7 for detailed information).

Table 4.4: Comparison of potential oedema-contributors between participants with and without oedema

Potential Oedema Contributors	Summary (CO)	Summary (NCO)
Co-Morbidities	Accident, Cardiac Disease, Immobility, Knee Surgery, Venous Disease	Ankle Surgery
Medications	Amlodipine (10mg), Atorvastatin (10mg, 20mg), Bumetanide (2mg), Pregabalin (150mg)	Amlodipine, Atorvastatin (80mg), Pregabalin (150mg)
Hormone Treatments	Proven (10mg)	Cerelle Pill, Contraceptive implant, Fluoxetine

4.2.4 Impact of oedema

The impact of oedema on HQoL was determined by running statistical tests on the scores from the EQ-5D (A4.8), GAD-7 (A4.9), PHQ-9 (A4.9), LYMQOL (A4.10) and SF-36 (A4.11) questionnaires. Participants with and without oedema were compared.

a) EQ-5D (Euroqol), GAD-7 and PHQ-9 data

As the individual sections of the EQ-5D questionnaire were used to calculate the Euroqol score, only the Euroqol values were statistically tested using the statistical programme, SPSS. The high significance values (>0.05) for EQ-5D, GAD-7 and PHQ-9 indicated that there were no statistically significant differences between those with and without oedema (null hypotheses) (A4.12).

b) LYMQOL data

T-tests could not be run on LYMQOL data as only participants with oedema were invited to complete this questionnaire (A4.13). Means/medians of the LYMQOL (lower limb) data were calculated to provide an evaluation of the impact of oedema on the participants' function (2.18: medium impact), appearance (2.38: medium), symptoms (1.70: low), mood (1.75: low) and HQoL (5.50: medium). (Upper limb data were not statistically analysed due to low sample size.)

c) SF-36 data

The SF-36 data for each of the sections produced high values (>0.05), indicating no significant differences between those with and without oedema (A4.14). Upon evaluation of the data, the following sections had lower mean/median HQoL values for those with oedema: physical functioning (35.00 compared to 53.33 for those without oedema), RL physical health (36.11 to 45.83), RL emotional problems (33.30 to 50.00) and pain (34.17 to 53.33). The emotional well-being section had a higher median HQoL value for those with oedema (76.00 to 56.00).

Upon comparison of SF-36 scores with HSE normative data, mean values of those with and without oedema were consistently different (to each other and the population norms) in the physical functioning, pain and general health sections (Table 4.5 and A4.15). However, the participant numbers within the individual age groups were very small, so these differences may not be reliable.

Table 4.5: Comparison of SF-36 scores and normative data

The means of study SF-36 questionnaire scores were compared with normative data from HSE 1996 (HSE Population Norm). Comparisons between participants with and without oedema have been made.

	Male 35-44			
	Study Mean (n=4)	Study Mean (n=2, CO)	Study Mean (n=2, NCO)	HSE Population Norm
Physical Functioning	51.3	27.5	75.0	91
Role Limitations due to Physical Health	37.5	25.0	50.0	89
Role Limitations due to Emotional Problems	50.0	50.0	50.0	89
Energy/Fatigue	27.5	22.5	32.5	66
Emotional Well Being (Mental Health in HSE Population Norm file)	49.0	46.0	52.0	77
Social Functioning	50.0	50.0	50.0	88
Pain	47.5	33.8	61.3	82
General Health	45.0	32.5	57.5	73
	Male 45-54			
	Study Mean (n=3)	Study Mean (n=2, CO)	Study Mean (n=1, NCO)	HSE Population Norm
Physical Functioning	61.7	50.0	85.0	87
Role Limitations due to Physical Health	50.0	50.0	50.0	84
Role Limitations due to Emotional Problems	55.5	66.7	33.3	86
Energy/Fatigue	25.0	25.0	25.0	66
Emotional Well Being (Mental Health in HSE Population Norm file)	64.0	56.0	80.0	77
Social Functioning	66.7	50.0	100.0	87
Pain	67.5	51.3	100.0	78
General Health	46.7	35.0	70.0	69
	Female 45-54			
	Study Mean (n=8)	Study Mean (n=6, CO)	Study Mean (n=2, NCO)	HSE Population Norm
Physical Functioning	42.5	48.3	25.0	82
Role Limitations due to Physical Health	43.8	45.8	37.5	80
Role Limitations due to Emotional Problems	66.7	61.1	83.4	84
Energy/Fatigue	36.9	35.0	42.5	60
Emotional Well Being (Mental Health in HSE Population Norm file)	76.5	78.7	70.0	74
Social Functioning	65.6	66.7	62.5	85
Pain	40.6	37.1	51.3	74
General Health	45.6	49.2	35.0	70

	Female 55-64			
	Study Mean (n=4)	Study Mean (n=3, CO)	Study Mean (n=1, NCO)	HSE Population Norm
Physical Functioning	11.3	6.7	25.0	72
Role Limitations due to Physical Health	6.3	0	25.0	72
Role Limitations due to Emotional Problems	8.3	0	33.3	81
Energy/Fatigue	31.3	26.7	45.0	60
Emotional Well Being (Mental Health in HSE Population Norm file)	61.0	72.0	28.0	73
Social Functioning	25.0	29.2	12.5	83
Pain	8.1	10.8	0	69
General Health	35.0	41.7	15.0	65

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4.2.5 Definition of oedema

The following section will describe results from the statistical tests on the fluid measurement techniques, namely: bioimpedance (A4.16 and A4.17) and TDC (A4.18).

a) Fluid measurement (whole limb)

T-tests for each WBA dataset (A4.19 and A4.20) produced non-significant results so participants with and without oedema were not significantly different from each other (A4.21 and A4.22). Table 4.6 compares the participants, highlighting the similarities between the right and left mean values.

Table 4.6: Comparison of WBA mean values between participants with and without oedema
(CLLO: chronic lower limb oedema)

		CLLO lower limbs (n: 28)	Non-CLLO lower limbs (n: 20)	p value
		Mean	Mean	
TBW (litres)	R	53.86	48.18	0.336
	L	53.32	48.52	0.600
ECF (litres)	R	30.73	25.73	0.068
	L	30.64	25.81	0.092
ICF (litres)	R	23.13	22.45	0.800
	L	22.68	22.71	0.852
FFM (kg)	R	73.59	65.82	0.336
	L	72.85	66.29	0.600
FM (kg)	R	76.84	72.44	0.720
	L	77.58	71.97	0.542
BMI (kg/m ²)		52.90	49.65	0.193

Upon statistically comparing those with and without oedema, both the R_0 upper/lower limb and $(R_i/R_0 \text{ lower limb}) / (R_i/R_0 \text{ upper limb})$ ratios were significantly different (A4.23). Table 4.7 highlights clear differences between those with and without oedema, indicating higher values (thus higher level of fluid) for those with oedema.

Table 4.7: Comparison of resistance ratios between participants with and without oedema

		CLLO lower limbs (n: 30)		Non-CLLO lower limbs (n: 24)	
		Values	Ratio	Values	Ratio
R	R zero upper limb	231.59	1.40	261.83	1.17
	R zero lower limb	164.93		222.91	
p value		0.019			
L	R zero upper limb	255.72	1.57	260.08	1.18
	R zero lower limb	162.66		221.31	
p value		0.003			
R	R infinity/R zero lower limb	0.767	1.17	0.723	1.02
	R infinity/R zero upper limb	0.653		0.708	
p value		0.027			
L	R infinity/R zero lower limb	0.767	1.10	0.717	1.01
	R infinity/R zero upper limb	0.697		0.707	
p value		0.005			

b) Fluid measurement (specific sites)

After independent t-tests were run, fluid measurement data from the sites below knee (except for left ankle) were significant (≤ 0.05) so alternate hypotheses of participants with and without oedema being statistically significantly different were accepted (Table 4.8 and A4.24).

Table 4.8: Comparison of fluid measurement site mean values between participants with and without oedema
(Yellow: significant (≤ 0.05) result)

		CLLO lower limbs (n: 28)	Non-CLLO lower limbs (n: 20)	p value
		Mean	Mean	
Foot	R	42.91	37.39	0.042
	L	42.00	37.69	0.054
Ankle	R	34.99	30.37	0.044
	L	35.56	30.48	0.062
Below Knee	R	38.52	31.24	0.003
	L	39.71	33.51	0.014
Above Knee	R	31.24	29.06	0.142
	L	30.50	29.24	0.294
Below Groin	R	29.71	28.13	0.675
	L	30.06	28.80	0.673
Abdominal Wall	R	34.79	31.21	0.705
	L	34.54	32.09	0.512

4.3 Stage 2

As participants for this stage were seen before and after bariatric surgery, the following sections include both pre-operative and post-operative data. Only five participants were assessed after surgery. However, the study will be continuing after the dissertation is completed, so this will allow participants to be reviewed further at their follow-up appointments. Two participants were withdrawn from the study due to physical inability to have bariatric surgery and withdrawal of consent (A4.25) however, their pre-operative data were still included.

4.3.1 Prevalence of chronic oedema

When patients were approached at their pre-operative appointments before bariatric surgery, 21 consented to take part (Figure 4.3). Seven patients on the interventional arm of the BBS study had their pre-operative appointments during the Stage 2 recruitment period so were not asked to take part in the study. If these patients had been recruited, this would have totalled the recruitment number to 28.

The prevalence of oedema in Stage 2 was 52.4% (95% confidence intervals: 30.2%-73.7%) with eleven out of the 21 participants having oedema (compared to Stage 1's prevalence of 61.3% with 19 of 31 having oedema).

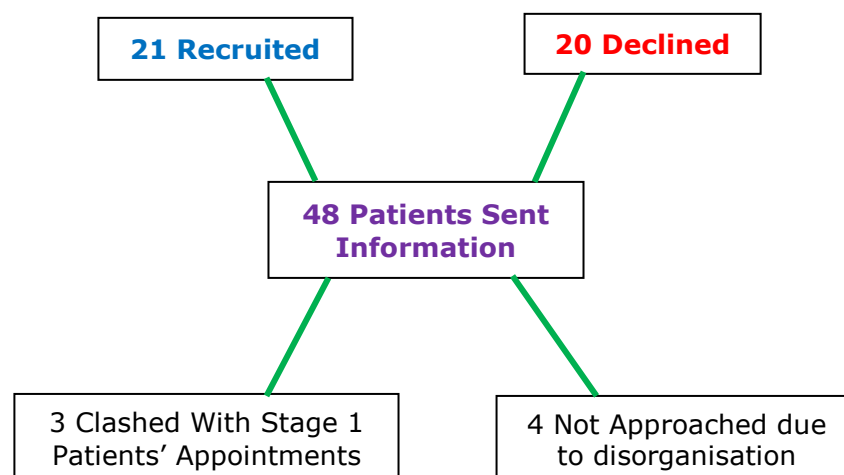


Figure 4.3: Screening log for Stage 2

As with Stage 1, general characteristics of participants and oedema-related conditions were recorded (A4.26, A4.27 and A4.28). Table 4.9 highlights a higher age group, mean weight and BMI and, the presence of positive Stemmer's signs and skin conditions among participants with oedema. These prominent factors were the same for Stage 1 participants with

oedema. However, Stage 2 participants had similar histories of cellulitis (only 1 with oedema and 1 without), as opposed to Stage 1 where 9 participants with oedema had histories of cellulitis.

Table 4.9: Comparison of Stage 2 baseline characteristics and conditions between participants with and without oedema

Characteristics	Summary (CO)	Summary (NCO)
Age	Ranged from 43-74 (mean: 55.9)	Ranged from 27-61 (mean: 48.6)
Gender	3 Males : 8 Females	3 Males : 7 Females
Weight (kg)	Ranged from 125.6-174.2 (mean: 140.3)	Ranged from 96.3-183.3 (mean: 128.6)
BMI (kg/m²)	Ranged from 41.0-61.0 (mean: 51.1)	Ranged from 38.1-61.4 (mean: 45.4)
Condition	Summary (CO)	Summary (NCO)
Stemmer's Sign (SS)	4: both feet negative SS, 4: both positive SS, 2: 1 foot negative SS and 1 foot positive, 1: equivocal SS	9: both feet negative SS, 1: equivocal SS
Skin Conditions (Location)	7 participants with skin conditions - 5: both lower legs, - 2: 1 lower leg	No participants had skin conditions
Skin Conditions (Type)	4: chronic lipodermatosclerosis, 2: discolourisation/ darkened skin, 1: chronic inflammation, 1: dry skin, 1: eczema	

Table 4.10 identifies which BMI category Stage 2 participants were classified into before and after surgery. As with Stage 1, most participants in the 50-60kg/m² BMI category had oedema. However, after surgery, all participants with oedema were in the 40-50kg/m² BMI category.

Table 4.10: BMI classification – Stage 2

The number of Stage 2 participants and those who had oedema are identified next to their appropriate BMI class.

BMI Classification		Stage 2 BMI (Before Surgery)	Oedema
40-50 obesity kg/m ²	Class 3 (severe)	13	5
>50 kg/m ²	Superobesity	8	6
50-60 kg/m ²		6	5
>60 kg/m ²		2	1
BMI Classification		Stage 2 BMI (After Surgery)	Oedema
35-39.9 kg/m ²	Class 2 obesity	2	0
40-50 obesity kg/m ²	Class 3 (severe)	3	3

4.3.2 Severity of oedema

As with Stage 1, most Stage 2 participants with oedema had mild pitting oedema (ISL Stage 1) in their feet and shins (Table 4.11 and A4.29). Those with ISL Stage 2 swelling had skin conditions (chronic lipodermatosclerosis or chronic inflammation, highlighted in Figure 4.4).

Table 4.11: Summary of oedema characteristics

Characteristic	Summary
Location of Oedema	Most participants: both feet and shins. Other locations: toes, ankles, hands.
Tissues in Swollen Area	10: soft, 1: hard
Significant Shape Distortion	1 participant
ISL Stage	7: Stage 1, 4: Stage 2

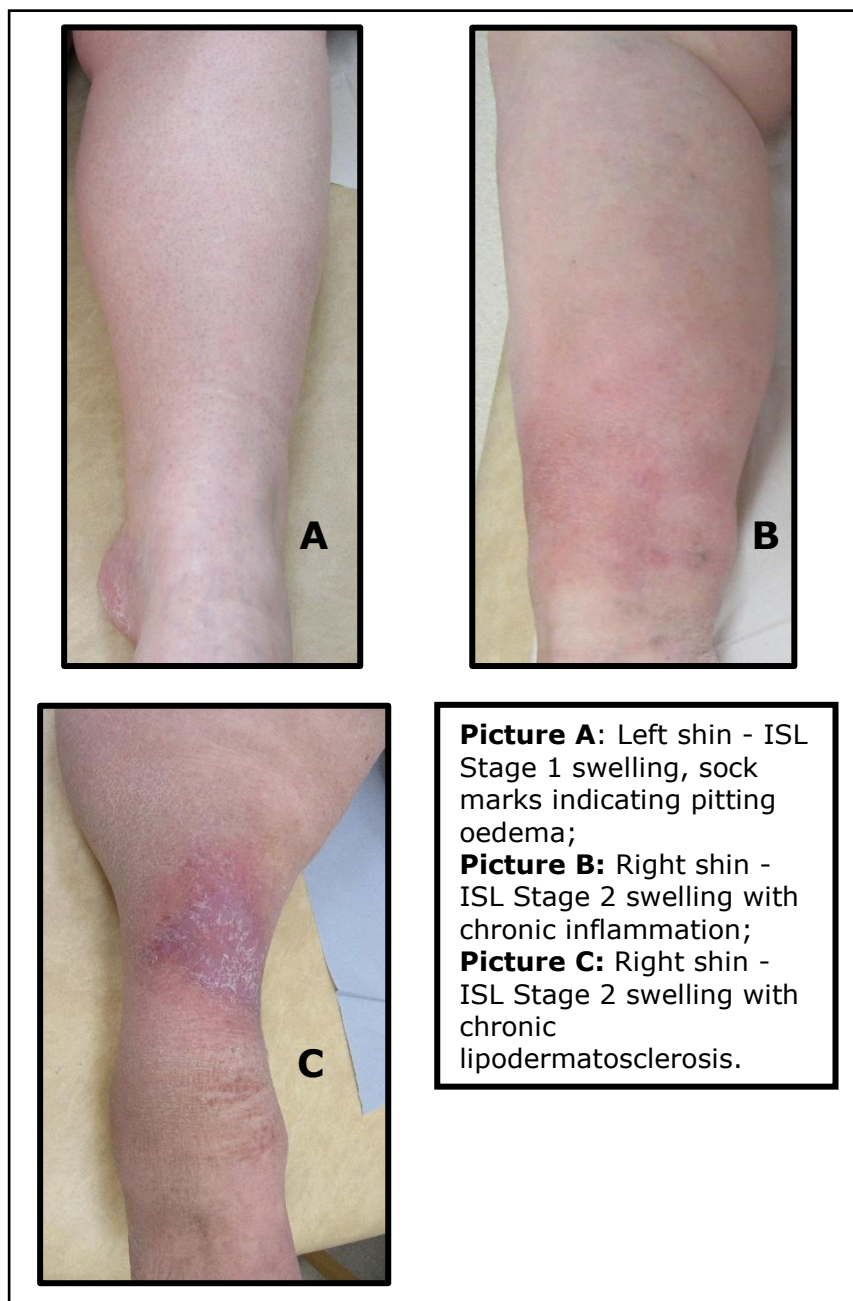


Figure 4.4: Range of oedema and skin conditions

4.3.3 Potential contributors of oedema

It was especially important in Stage 2 to record co-morbidities and other factors that may have caused pre-surgery oedema in order to provide insight to any changes in the presence or extent of post-surgery oedema. Table 4.12 highlights co-morbidities in participants with oedema and similarities in medication intake between participants (A4.30 and A4.31). As with Stage 1, routine blood test results showed that there was no evidence of medical conditions (like diabetes or renal failure) contributing to the oedema (see A4.32 for detailed information).

Table 4.12: Comparison of potential oedema-contributors between participants with and without oedema

Potential Oedema Contributors	Summary (CO)	Summary (NCO)
Co-Morbidities	Immobility, Primary lymphoedema, Venous Disease	
Medications	Amlodipine (10mg), Atorvastatin (40mg), Indapamide (1.5mg, 2.5mg)	Amlodipine (5mg, 10mg), Atorvastatin (10mg, 20mg), Indapamide (1.5mg)
Hormone Treatments		Norethisterone - 5mg (as per cycle)

4.3.4 Impact of bariatric surgery

The main aim of Stage 2 was to determine the impact of weight loss (in the form of bariatric surgery) on chronic oedema. At the time of dissertation recruitment ending, only five Stage 2 participants had been seen at their follow-up appointments.

Of these participants, three had oedema at their first assessment. This had not changed when they were assessed after surgery (A4.33). However, there were slight improvements in two of the participants with oedema (lack of toes' swelling, tissue softening and negative Stemmer's sign). Furthermore, a participant without assessed oedema, who normally had swelling due to venous insufficiency, reported an absence of swelling and decreased use of support stockings.

The participants' mean weight had improved from 130.2kg to 117.84kg. Their BMI had improved from 46.22kg/m² to 42.02kg/m². (Table 4.13 and A4.34)

Table 4.13: Summary of weight and BMI post-operative changes

Participant ID Number	Pre-Op Weight (kg)	Post-Op Weight (kg)
012 (CO)	128.2	116.2
016 (CO)	126.3	117.2
020 (CO)	130.0	118.4
027 (NCO)	131.6	116.6
028 (NCO)	134.0	120.8
Participant ID Number	Pre-Op BMI (kg/m²)	Post-Op BMI (kg/m²)
012 (CO)	45.90	42.20
016 (CO)	50.00	46.30
020 (CO)	52.80	48.00
027 (NCO)	43.00	38.00
028 (NCO)	39.37	35.60

4.3.5 Impact of oedema

Impact of oedema on the HQoL of Stage 2 participants was determined with the same statistical tests and analyses as Stage 1.

a) EQ-5D (Euroqol), GAD-7 and PHQ-9 data

Unlike Stage 1, the Euroqol significance value of 0.040 indicated a significant difference between those with and without oedema (A4.35 and A4.37). However, as with Stage 1, the values for GAD-7 and PHQ-9 were high and did not show a significant difference between participants (A4.36 and A4.37).

b) LYMQOL

Means/medians of LYMQOL (lower limb) data were calculated to provide an evaluation of the impact of oedema on participants' function (2.70: medium impact), appearance (3.60: high), symptoms (1.61: low), mood (1.50: low) and HQoL (5.50: medium) (A4.38 and A4.39). Upon comparison with Stage 1, the Stage 2 results indicated the same impact on HQoL (except for the impact on the participants' appearance: high value of 3.60 in Stage 2 as opposed to medium impact of 2.38 in Stage 1).

c) SF-36

Unlike Stage 1, the following sections indicated significant differences between participants with and without oedema: physical health (0.048), energy/fatigue (0.028) and pain (0.015) (A4.40 and A4.41). Comparing those with and without oedema, those with oedema had lower mean/median HQoL values in the physical functioning (20.00 to 65.00),

physical health (25.00 to 87.50), energy/fatigue (32.73 to 56.00), emotional well-being (67.64 to 70.80), social functioning (54.55 to 76.25), pain (35.46 to 69.50) and general health compared to 1 year ago (56.82 to 70.00) sections. The general health section had a higher mean HQoL value for those with oedema (56.82 to 53.00).

Table 4.14 compares study participants' SF-36 scores and HSE 1996 normative data. Comparing participants with and without oedema, mean values were consistently different in the pain and general health (matching Stage 1 data), and RL physical health sections (A4.42). As with Stage 1, although most of these values were different to the population normality values, participant numbers were very low.

Table 4.14: Comparison of baseline SF-36 scores and HSE normative data for participants with and without oedema

	Female 35-44			
	Study Mean (n=2)	Study Mean (n=1, CO)	Study Mean (n=1, NCO)	HSE Population Norm
Physical Functioning	90.0	85.0	95.0	87
Role Limitations due to Physical Health	62.5	25.0	100.0	84
Role Limitations due to Emotional Problems	100.0	100.0	100.0	85
Energy/Fatigue	52.5	30.0	75.0	61
Emotional Well Being (Mental Health in HSE Population Norm file)	96.0	92.0	100.0	73
Social Functioning	87.5	75.0	100.0	86
Pain	66.3	32.5	100.0	78
General Health	67.5	70.0	65.0	73
	Male 45-54			
	Study Mean (n=4)	Study Mean (n=1, CO)	Study Mean (n=3, NCO)	HSE Population Norm
Physical Functioning	32.5	25.0	35.0	87
Role Limitations due to Physical Health	43.8	0.0	58.3	84
Role Limitations due to Emotional Problems	58.3	100.0	44.4	86
Energy/Fatigue	46.3	55.0	43.3	66
Emotional Well Being (Mental Health in HSE Population Norm file)	62.0	76.0	57.3	77
Social Functioning	62.5	62.5	62.5	87
Pain	58.8	45.0	63.3	78
General Health	55.0	80.0	46.7	69

	Female 45-54			
	Study Mean (n=5)	Study Mean (n=2, CO)	Study Mean (n=2, NCO)	HSE Population Norm
Physical Functioning	55.0	17.5	70.0	82
Role Limitations due to Physical Health	65.0	25.0	87.5	80
Role Limitations due to Emotional Problems	80.0	50.0	100.0	84
Energy/Fatigue	62.0	35.0	77.5	60
Emotional Well Being (Mental Health in HSE Population Norm file)	80.8	70.0	82.0	74
Social Functioning	82.5	56.3	100.0	85
Pain	56.0	16.3	73.8	74
General Health	69.0	57.5	72.5	70
	Female 55-64			
	Study Mean (n=7)	Study Mean (n=5, CO)	Study Mean (n=2, NCO)	HSE Population Norm
Physical Functioning	17.1	20.0	10.0	72
Role Limitations due to Physical Health	28.6	25.0	37.5	72
Role Limitations due to Emotional Problems	57.1	60.0	50.0	81
Energy/Fatigue	24.3	23.0	27.5	64
Emotional Well Being (Mental Health in HSE Population Norm file)	57.1	62.4	44.0	73
Social Functioning	39.3	40.0	37.5	83
Pain	32.1	31.5	33.8	69
General Health	38.6	48.0	15.0	65

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4.3.6 Definition of oedema

The following section will discuss the results of limb volume and fluid measurement techniques, namely: the perometer (A4.43), bioimpedance (A4.44 and A4.45) and TDC (A4.46).

a) Limb volume

T-tests comparing the limb volumes of participants with and without oedema showed no significant difference (A4.47). The mean differences between those with and without oedema (right: 393.77 and left: 471.02) were similar.

Pre-operative and post-operative measurements were compared to calculate the percentage change (Table 4.15, A4.43 and A4.44). Each participant had decreased lower limb volume, with percentage changes ranging from 0.82 to 9.02%. Participant 012 was excluded from limb volume analysis because she was wearing lymphoedema bandage stockings after surgery, producing inaccurate measurements.

Table 4.15: Comparison of limb volume data (pre- and post-operatively)

Negative percentage change values highlight decreases in means.

Participant ID Number	Right Lower Limb Mean (mls)	Post-Op: Right Lower Limb Mean (mls)	Percentage Change (%)
016 (CO)	7292.5	7111.5	-2.48
020 (CO)	9638.0	9147.5	-5.09
027 (NCO)	8451.0	7892.0	-6.61
028 (NCO)	8371.5	7616.0	-9.02
Participant ID Number	Left Lower Limb Mean (mls)	Post-Op: Left Lower Limb Mean (mls)	Percentage Change (%)
016 (CO)	7828.0	7764.0	-0.82
020 (CO)	8916.0	8792.0	-1.39
027 (NCO)	8391.5	7824.0	-6.76
028 (NCO)	8256.5	7538.0	-8.70

Figures 4.5 and 4.6 highlight changes from the pre-operative to the post-operative assessment. Each of the participants' BMIs and lower limb means decreased, however participant 016's left lower limb mean only showed a small decrease.

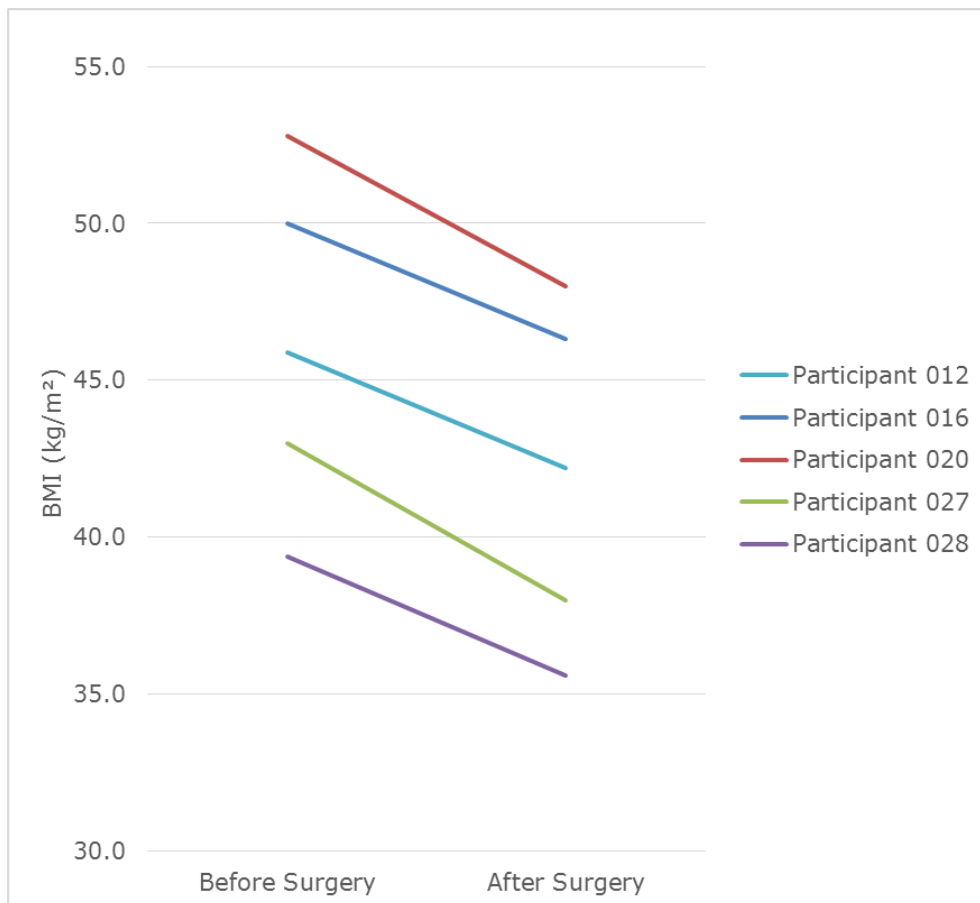


Figure 4.5: Comparison of BMI (before and after surgery)

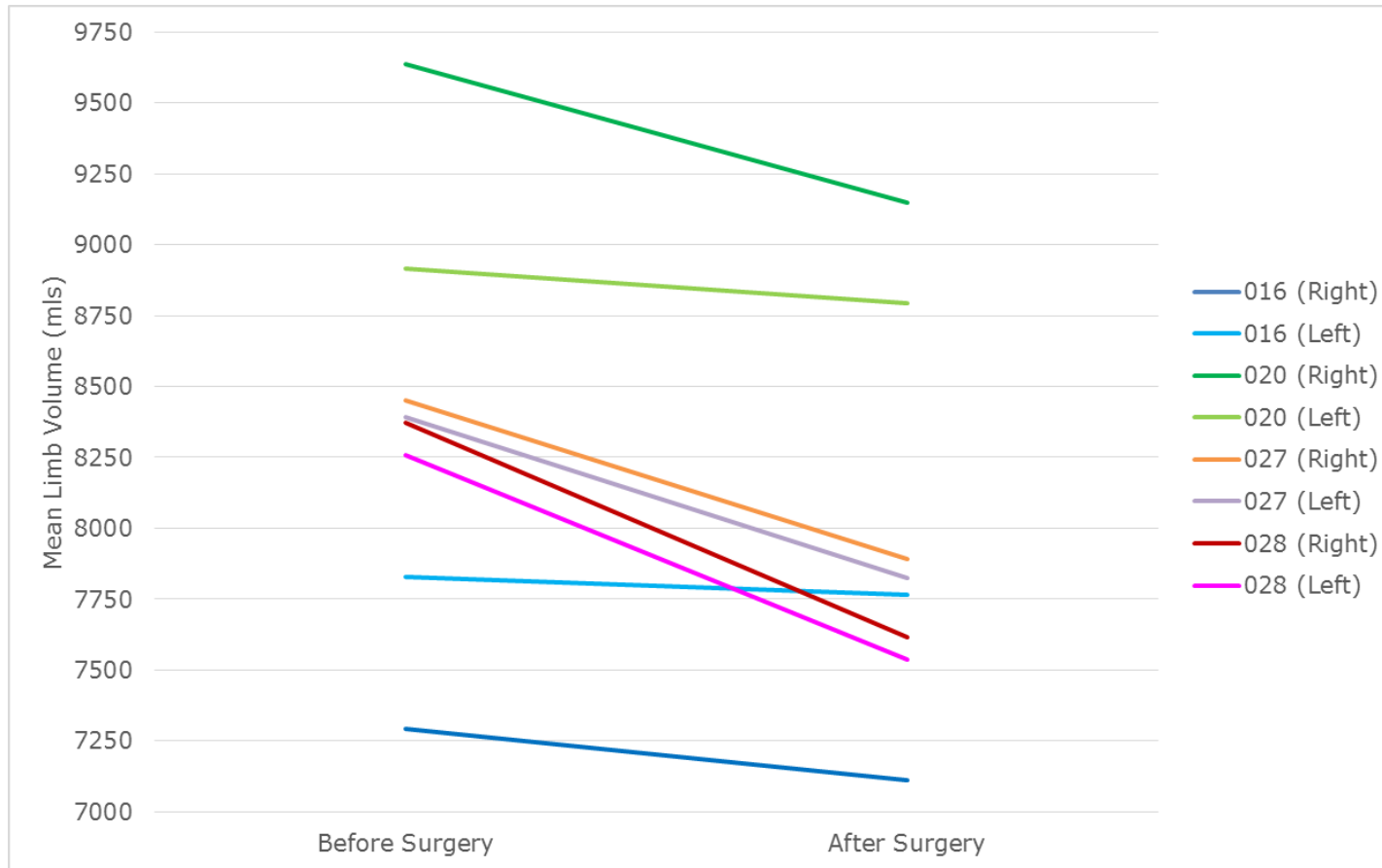


Figure 4.6: Comparison of limb volume data (before and after surgery)

a) Fluid measurement (whole limb)

Each significance value of the WBA datasets (A4.49 and A4.50) was greater than 0.05, so participants with and without oedema were not statistically different from each other (Table 4.16, A4.51).

Table 4.16: Comparison of WBA mean values between participants with and without oedema

		CLLO lower limbs (n: 18)	Non-CLLO lower limbs (n: 20)	p value
		Mean	Mean	
TBW (litres)	R	46.56	46.10	0.848
	L	46.16	45.71	0.908
ECF (litres)	R	25.77	25.57	0.898
	L	25.61	25.68	0.963
ICF (litres)	R	20.80	20.53	0.929
	L	20.54	20.03	0.857
FFM (kg)	R	63.61	62.98	0.848
	L	63.05	62.45	0.909
FM (kg)	R	74.50	65.60	0.220
	L	75.06	66.13	0.227
BMI (kg/m ²)		50.27	45.48	0.144

Statistical tests for the post-operative results were not presented due to the low sample size (A4.52 and A4.53). However, comparing the means of the before and after surgery data, the pre-operative data were higher than the post-operative data, suggesting a decrease in total fluid (therefore oedema) after surgery for these participants (A4.49 & A4.50 and A4.54).

The right R_0 ratios in those with and without oedema were the only significantly different ratios, $p=0.013$ (A4.55). Table 4.17 highlights similarities between right (R_i/R_0 lower limb)/(R_i/R_0 upper limb) ratio values for participants with and without oedema. Furthermore, unlike Stage 1, the right (1.04) and left (0.89) ratios at this infinite frequency for participants with oedema were different to each other. Finally, the R_{zero} values of those with and without oedema were clearly different to each other.

Table 4.17: Comparison of resistance ratios between participants with and without oedema

		CLLO lower limbs (n: 18)		Non-CLLO lower limbs (n: 20)	
		Values	Ratio	Values	Ratio
R	R zero upper limb	287.99	1.44	259.23	1.10
	R zero lower limb	200.13		234.64	
p value		0.013			
L	R zero upper limb	284.98	1.42	265.61	1.16
	R zero lower limb	201.34		229.42	
p value		0.073			
R	R infinity/R zero lower limb	0.748	1.04	0.717	1.01
	R infinity/R zero upper limb	0.719		0.708	
p value		0.504			
L	R infinity/R zero lower limb	0.639	0.89	0.723	1.02
	R infinity/R zero upper limb	0.721		0.711	
p value		0.566			

Comparison of post-operative resistance values between those with and without oedema highlighted: clear differences in the R_{zero} ratios and similar $R_{infinity}/R_{zero}$ values (A4.52 and A4.53). Furthermore, similar to pre-operative data, R_{zero} and $R_{infinity}/R_{zero}$ values were different for those with oedema and similar for those without oedema.

b) Fluid measurement (specific sites)

Data from the right foot measurement site produced a significant result of 0.031, however the other sites were not statistically significant (Table 4.18 and A4.56).

Table 4.18: Comparison of fluid measurement site mean values between participants with and without oedema

		CLLO lower limbs (n: 20)	Non-CLLO lower limbs (n: 20)	p value
		Mean	Mean	
Foot	R	42.33	37.19	0.031
	L	42.22	38.11	0.097
Ankle	R	30.10	28.32	0.496
	L	32.43	29.25	0.790
Below Knee	R	35.59	33.08	0.216
	L	33.82	35.05	0.882
Above Knee	R	29.97	29.17	0.577
	L	29.30	29.87	0.855
Below Groin	R	28.11	30.68	0.395
	L	28.63	29.12	0.407
Abdominal Wall	R	32.92	31.32	0.591
	L	32.38	31.47	0.351

Comparing the means of the before and after surgery data, each of the after surgery data for the measurement sites (except the left below groin site) were higher than the pre-operative data, indicating an increase in fluid (therefore oedema) after surgery for these participants (A4.57).

4.4 Summary

Results from Stage 1 highlighted an oedema prevalence of 61.3%, with 19 of 31 participants having oedema; Stage 2 indicated an oedema prevalence of 52.4%, with eleven of 21 participants having oedema. For both Stage 1 and Stage 2 pre-operative participants, the majority of those with oedema were in the 50-60kg/m² BMI category and had mild pitting oedema. Potential contributors included: immobility, venous disease and a variety of medications.

Most of the Stage 1 questionnaires indicated that the HQoL of participants with oedema did not differ significantly from those without oedema, with the LYMQOL questionnaire reporting the low to medium impact of oedema. In Stage 2, the EQ-5D and SF-36 questionnaires highlighted that the HQoL, physical health, energy and pain of participants with oedema were significantly different to those without oedema. The LYMQOL questionnaire confirmed the Stage 1 results, but indicated a high oedema impact on the participants' appearance.

Bioimpedance resistance ratios for Stage 1 confirmed that participants with oedema had a higher level of ECF than those without oedema. Furthermore, TDC data showed the greater amount of oedema in the sites below the knee. For Stage 2, although there were significant results (right R_{zero} bioimpedance ratio and TDC right foot measurement site), these were not conclusive. These results and the small post-operative sample size highlight the need for further research with more participants.

CHAPTER 5: DISCUSSION

5.1 Introduction

The main aims of this study were: to determine the prevalence and impact of chronic oedema on HQoL in a population of bariatric patients (Stage 1) and to assess the impact of bariatric surgery on chronic oedema (Stage 2). In this chapter, the study results will be discussed based on these aims.

The prevalence and impact of chronic oedema in both stages will be discussed. The prevalences will be compared with an important study by Greene et al. (2015). Differences in participants' HQoL and, how limb volume and fluid measurements can be used to define chronic oedema will be analysed. Finally, the study as a whole, future research and clinical implications will be discussed.

5.2 Study limitations

Both stages of the study were limited by small sample sizes (especially Stage 2 after surgery), which reduced the statistical power of the tests. Furthermore, sections of the results (like the fluid measurement data) were limited by multiple testing. This meant that the significant/non-significant results were vulnerable to Type 1 (false positive) and Type 2 (false negative) statistical errors. Therefore, for the study results (sections 5.3 and 5.4), further research with a larger group of participants is needed to confirm/reject the significant differences between participants with and without oedema. A larger sample of participants would have probably yielded narrower confidence intervals, giving a greater confidence of the prevalence. Section 5.6 explores how the results can be further applied.

5.3 Analysis of results – Stage 1

The following section analyses the results from Stage 1 of the study.

5.3.1 Prevalence of chronic oedema

Out of the 31 recruited Tier 3 patients, 19 were identified with oedema, giving a high prevalence of 61.3%. However, the corresponding confidence intervals gave a fairly wide 95% confidence that the true prevalence was between 42.4% and 77.3%. Several recruitment issues and limitations hindered a greater confidence from being achieved.

a) Recruitment limitations

Although the bariatric team and researcher aimed to recruit as many study participants as possible, this was not always possible:

Firstly, the researcher found that assessments took longer than planned. This was due to a combination of: time taken talking with patients, sometimes having to wait for patients to complete the questionnaires before she could complete the assessment, and occasional delays or problems with the bioimpedance and TDC equipment.

Secondly, fitting in with the clinic's schedule meant that it was not possible to see all new patients who attended the clinic. The structure of which patients she would see was not always well-organised due to the busyness of the clinic. Furthermore, the number of patients who could actually take part in the study was limited due to: the study assessment time, the waiting time that the patients encountered during the clinic appointment, and how long they could stay in short stay hospital car parks without incurring a fine.

Finally, the way that the clinics were structured also affected recruitment numbers. At the start of recruitment, there were normally four patients each hour rotating between the bariatric staff, sometimes having more new patients than follow-up patients in the clinic time. The researcher saw the patients after their appointments had finished. This meant that it was impossible to see each new patient without asking them to wait one or two hours, especially if their appointments were booked close together.

After two months of recruitment, the clinic system changed to having appointments every 10-15 minutes. This meant that more patients were seen in the clinic but it did not increase recruitment as the researcher still saw the patients after their appointments.

b) Change of recruitment

After almost three months of recruitment, participant numbers were lower than anticipated, causing the study team to alter the recruitment system. Where possible, instead of waiting until after the patients' appointments, the researcher started to complete half of the assessment whilst the patient was waiting to see one or more members of the bariatric team. The rest of the assessment was completed after the patient's appointment had finished. This greatly helped recruitment organisation and meant that some patients were willing to take part due to the assessment being in two parts, whereas they would have declined due to time issues before.

c) Analysis

Nevertheless, all of the limitations above resulted in a biased sample of recruited patients. The original aim was to recruit eight patients each week. However, only two to three patients were recruited per week, depending on how many new patients attended their appointments. Patients that were likely to consent to take part were: those who had oedema and those who did not need to leave quickly (not having to work that day, no concern of car parking, etc.).

Based on the total number of patients asked to take part in the study (112), the low number of participants (31) must have impacted the prevalence of oedema. Even with a small sample size, the study has shown that recruitment is an issue in this population of patients and in the bariatric clinic environment. Any future research needs to have a consecutive recruitment to provide a higher number of participants in a non-biased sample size. The aim would be to have an efficient recruitment method in the clinic regarding talking with patients and fitting in the assessments with the clinic schedule.

5.3.2 Impact of chronic oedema

The range of results in the LYMQOL questionnaire indicated that the presence of oedema impacted the participants in varying degrees, from not at all (1.0) to a lot (4.0) (Table 5.1). The following factors should be taken into account: the participants' gender and age groups (section 5.3.4), awareness of their oedema, severity of oedema and understanding of the questionnaire. Furthermore, it should be noted that three participants with oedema were taking Furosemide, a diuretic medication sometimes used to treat oedema. For the two participants that completed LYMQOL (the third left before study assessment completion), the scores indicated the high impact of oedema on their lives, especially: function, appearance and HQoL. In this instance, the participants had high oedema impact already however, being treated with diuretics may mask (or reduce) the presence of oedema, so this needs to be recognised when analysing impact of oedema.

Table 5.1 Summary of LYMQOL data

Upper Limb Groups	Range (n=2)
Function	1.0 to 2.8
Appearance	1.4 to 3.6
Symptoms	1.3 to 1.8
Mood	2.0 to 2.2
Overall Quality of Life	2.0 to 7.0
Lower Limb Groups	Range (n=18)
Function	1.0 to 4.0 (2.18)
Appearance	1.0 to 4.0 (2.38)
Symptoms	1.0 to 4.0 (1.70)
Mood	1.0 to 4.0 (1.75)
Overall Quality of Life	0 to 10.0 (5.50)

The only participant recorded to be unaware of her oedema produced high scores, both in the HQoL (9 out of 10) and in the impact sections (no impact). This may imply that the participants who were not aware of their oedema, as well as those whose oedema did not affect them, were likely to have high scores (as long as they did not associate any bodily pain with the oedema). Future research should include a record of the participants' awareness of the oedema in order to test this link to the oedema impact scores.

As stated in section 4.2.2, most Stage 1 participants had mild, pitting oedema, with only three having severe ISL Stage 2 oedema. However, eight participants still produced low scores, indicating that their oedema had a high impact on their HQoL. Even among the three participants with ISL Stage 2 swelling, the responses were varied: One participant had medium HQoL (6.0) with high function (3.0) and appearance (3.3) impact, and medium symptoms (2.4) and mood (1.8) impact. The second participant left before completing the assessment, but the third participant scored low impact (1.0-1.7) and high HQoL (8.0) scores. However, their different personalities, co-morbidities, and the first participant's limited mobility should be taken into account.

a) Causal analysis

The literature review in Chapter 1 provided evidence that obesity can have a damaging impact on the lymphatic system, leaving the body vulnerable to developing lymphoedema (MacLellan et al., 2016). However, several co-

morbidities, hormones and medications may have caused (or intensified) the oedema (Table 4.4):

Firstly, depending on the dose taken, a combination of (or specific) hormones and/or medications can cause oedema, including calcium channel blockers like Amlodipine (Keeley, 2008 and 2012). Patients taking Amlodipine can develop oedema due to arteriolar vasodilation (Keeley, 2008). Furthermore, taking Atorvastatin can lead to an uncommon (up to 1 in 100) side effect of oedema, especially ankle oedema (The electronic Medicines Compendium, 2016). (Other statins can cause oedema but it is most common in Atorvastatin.) Eleven of the oedema participants were taking these hormones/medications.

Lack of mobility (of which four oedema participants suffered) may have impacted the lymphatic system in being unable to function properly, causing oedema to develop. Furthermore, having a positive Stemmer's sign with oedema (which applied to four participants) indicates a lymphatic component to the development of oedema. Of the four participants, three had histories of cellulitis, one had chronic lipodermatosclerosis and one had lymphangiectasia.

Finally, five of the participants' oedema may have been caused by venous disease: venous flow dysfunction initiating skin changes (like chronic lipodermatosclerosis) and, in severe cases, lymphatic dysfunction (Lymphoedema Framework, 2006). As previously stated, one participant had both positive Stemmer's sign and chronic lipodermatosclerosis, indicating both a lymphatic and venous component to their oedema.

Two of the participants with ISL Stage 2 swelling had mobility issues, venous disease and were taking potential oedema-causing medications (including Amlodipine). These may not have been the cause of oedema but they were certainly not beneficial and probably exacerbated the oedema. The third participant with Stage 2 swelling did not appear to have any co-morbidities or medications that would have caused/affected the oedema, pointing to obesity being the main cause.

However, four participants were taking potential oedema-causing medications of: Amlodipine, Atorvastatin, Fluoxetine and Pregabalin, but they did not have oedema. Keeley (2008) indicates that: not only are a combination of factors sometimes required to cause oedema to develop, but the frequencies of oedema development increase with medication dosage. Amlodipine has a frequency of 1.8 to 10.8% with increasing

dosage from 2.5mg to 10mg. Pregabalin has a 5-12% frequency, depending on the dosage taken. Future research will allow analysis of participants with oedema to determine causal factors and compare these factors with participants without oedema.

5.3.3 Study comparison with research article

As discussed in section 1.8, Greene et al. (2015) performed a study that analysed the relationship between BMI and the presence of oedema, hypothesising that there is a BMI threshold between 50 and 60kg/m² where lymphatic dysfunction begins. Their study had two groups. Group 1 is most similar to the study's Stage 1, as the Group 1 participants were at their maximum BMI when scanned with the lymphoscintigram, therefore they will be discussed in this section. Group 2 will be discussed with the results of the study's Stage 2 (section 5.4.3). Table 5.2 highlights the correlation between an abnormal lymphoscintigram result and an increase in BMI. Table 5.3 compares the Group 1 core data of Greene et al. (2015) with the study data from Stage 1, highlighting the differences between them, especially the BMI ranges.

Table 5.2 Summary of Greene et al. (2015) results (Group 1)

Greene et al. (2015) Lymphoscintigram Result	BMI (kg/m²)	Number of Group 1 Participants
Normal	<50	20
Normal / Abnormal	50-60	2 / 2
Abnormal	>60	9

Table 5.3 Comparison of both studies

Group 1 (Greene et al., 2015)	Stage 1 (Study)
33 participants	31 participants
BMI: 30-83.3kg/m ²	BMI: 40.8-63.5kg/m ²
2009-2014	2016-2017
Referred to authors' lymphoedema program at Harvard Medical School	Referred to Tier 3 bariatric clinic at RDH

The main difference between the two studies is that five out of twelve participants in the 'normal' BMI range had oedema (Table 5.4). Based on Greene et al. (2015), they should have had a normal lymphatic function and no oedema. Presence of oedema may have been due to: immobility, bilateral knee replacement (surgery possibly affecting the lymphatic system) and potential oedema-causing medications (Atorvastatin and Proven) (Table 5.5).

Table 5.4 Comparison of study with lymphoscintigram values

The BMI values highlighted by Greene et al. (2015) lymphoscintigram results and the results of the study presented in this dissertation were compared.

Greene et al. (2015) Values	Stage 1 Participants
Normal (40-50kg/m ²)	5 out of 12 - Oedema
Abnormal/Normal (50-60kg/m ²)	13 out of 18 - Oedema
Abnormal (>60kg/m ²)	1 out of 1 - Oedema

Table 5.5 Analysis of participants with oedema and 'normal' BMI range (Greene et al., 2015)

Participant ID Number	Oedema Location	Co-morbidities
018	Both shins	Just obesity
023	Both feet and shins	Immobility & Swelling areas sometimes painful
032	Both shins	Atorvastatin medication, Bilateral knee replacement & Immobility
049	Both shins	Atorvastatin & Proven medication
051	Both ankles and shins	Atorvastatin medication

The results of Stage 1 cast doubt over Greene et al. (2015)'s potential threshold, suggesting that oedema is not limited to a specific BMI range. Future research with more participants would provide clarification.

5.3.4 Comparison of quality of life

According to the t-test results of EQ-5D, GAD-7, PHQ-9 and SF-36 data, HQoL of participants with oedema was not significantly different from participants without oedema even though there were visible differences between the means/medians of participants with and without oedema. The wide 95% confidence intervals provided uncertainty in knowing what the true differences were.

The questionnaires also had individual limitations. The EQ-5D questionnaire is not oedema-specific and has a limited number of options. However, it was still a valuable questionnaire for assessing the HQoL of participants. The GAD-7 and PHQ-9 questionnaires were both limited in that their questions covered the previous two weeks, therefore not allowing the participants to give general health answers, but they were a quick way of achieving anxiety and depression scores for each participant.

The SF-36 questionnaire is not a disease-specific tool, so important subtle issues may have been missed. Furthermore, as the SF-36 questionnaire is generic, it is limited by ceiling (highest score) and floor (lowest score)

effects. For the participants ($n=3$) who answered with the highest score of 100 (overall or in the individual sections), this indicates a healthy HQoL, however there is no way of measuring any positive changes that may occur over time. In the same way, the participants ($n=3$) who answered with the lowest score of 0 (overall or individual sections) indicated a poor HQoL and the questionnaire has no way of measuring any further deterioration that may occur.

As presented in Table 4.5, most of the study SF-36 scores were lower than the population normality scores, seeming to indicate that the study population was less healthy than the normal population. However, the means and participant numbers for each of the age groups were much smaller than the population normality means and participant numbers, so the scores were not comparable. Future research will provide a wider variety of participants and better comparisons between the population normality mean values.

5.3.5 Defining chronic oedema

The following section will discuss fluid measurement methods used for defining the presence of chronic oedema in Stage 1. Their efficacy will be discussed in section 5.5.

a) Fluid measurement (whole limb)

There were two sets of data tested for significance: whole body analysis and $R_{\text{zero}}/R_{\text{infinity}}$ data:

For the WBA data, there were no significant differences. This was surprising as the components of the WBA dataset should have indicated a clear difference. For those with oedema: an increase in total body water, extracellular fluid and fat free mass would have depicted an increase in oedema, especially extracellular fluid as this solely measures the fluid in the limb. The intracellular fluid and fat mass values were expected to be higher in those without oedema, which would have indicated less fluid present. A non-significant BMI result indicated that the BMIs of participants with and without oedema were similar however this may have been due to the small sample size.

The second set of tests concerned the resistance at 0 frequency (R_{zero}), which solely measured ECF, and resistance at infinite frequency (R_{infinity}), which measured everything in the limb (extracellular and intracellular fluid,

cells, fatty tissues, bone, etc.). Participants with and without oedema for all R_{zero} and R_{infinity} data were significantly different to each other.

The R_{zero} upper limb/lower limb ratios for those with oedema were higher than those without oedema. ECF is proportional to $1/R_{\text{zero}}$ (Ward, 2009), therefore this indicates the presence of more ECF (and thus oedema) present in those with oedema.

The $[(R_{\text{infinity}}/R_{\text{zero}} \text{ lower limb}) / (R_{\text{infinity}}/R_{\text{zero}} \text{ upper limb})]$ ratios were also higher in participants with oedema. ECF/ICF is proportional to $R_{\text{infinity}}/R_{\text{zero}}$ (Ward et al., 2011), therefore the higher ratios indicate a higher ratio of ECF to total volume compared to those without oedema. As the extracellular fluid (and thus the oedema) increased, the impedance values decreased (Rockson, 2007).

However, although the values of participants with oedema were highest, the $R_{\text{infinity}}/R_{\text{zero}}$ ratios of those with and without oedema were similar. This suggests a similar level of ECF (oedema) and matches the WBA data for those without oedema in being similar to those with oedema. Therefore, although the R_{zero} and R_{infinity} data of participants with and without oedema were significantly different, this may have occurred by chance, due to the low sample size and multiple testing.

Future research should investigate R_{zero} and $R_{\text{infinity}}/R_{\text{zero}}$ ratios. There was a clear difference between them, especially in the participants with oedema.

b) Fluid measurement (specific sites)

As the TDC machine measures how much fluid is present in the tissues at specific sites (Mayrovitz, Weingrad and Lopez, 2015), it was important to compare participants with and without oedema for differences. The TDC values in participants with oedema were visually higher than those without, especially at the three sites below the knee, indicating the presence of a greater amount of fluid at these sites. Furthermore, they were significantly different from each other at these sites (except for the left ankle site, which may have been non-significant due to 'operator error'; see section 5.5). This fits with the assessment of the presence/absence of oedema for the participants as most had feet and shin oedema (with only one participant potentially having thigh and abdomen oedema). However, the small sample size and increased chance of significance due to multiple testing need to be taken into account.

5.4 Analysis of results - Stage 2

The following section analyses the results from Stage 2 of the study.

5.4.1 Prevalence of chronic oedema

Of the 21 recruited patients of Stage 2, eleven were identified to have oedema, giving a prevalence of 52.4%, roughly half the population. As with Stage 1, the confidence intervals gave a wide 95% confidence, indicating the true prevalence was between 30.2% and 73.7%.

a) Recruitment limitations

Most of the recruitment limitations for Stage 1 also affected Stage 2 (delays with equipment, car parking restrictions, etc.). There were also clashes with the pre-operative and bariatric clinics. Not only would some of the Stage 2 patients have appointments at the same time as the Stage 1 clinic but the Stage 2 patients would sometimes have both: an appointment with the pre-operative clinic plus a group bariatric clinic appointment. This often meant that it was either not possible to see Stage 2 patients (as the researcher was busy seeing Stage 1 patients) or they were not willing to see the researcher due to their double appointments. Finally, due to a lengthy study approval process, dissertation recruitment had been shortened, which meant that only a few Stage 2 follow-ups were able to be included in the dissertation. Although recruitment for Stage 2 was more reliable consecutively, running parallel to Stage 1 caused recruitment issues, providing valuable information for future research practicalities.

b) By-Band-Sleeve study co-operation

When the study was first being planned, the study team were advised that the BBS study would be taking place in the bariatric clinic at the same time as the chronic oedema study.

Before the study could be submitted for approval, changes needed to be made to Stage 2, in consideration of the BBS study. Initially, it was not thought that the studies would have an impact on each other or that the two studies running at the same time would be a problem. This was due to the patients being seen in different clinics and different questionnaires being used.

However, when the BBS study team were contacted to learn more about their study protocol, they were concerned about the patients being invited

to take part in both studies. Due to the amount of time each study assessment would take, they did not want the patients to have to choose between taking part in one study or the other. Therefore, it was decided that the chronic oedema study team would only approach BBS patients who were in the observation arm or who had declined/were ineligible to take part in the BBS study, and this proved to be a good solution.

As alterations needed to be made so that the study teams could work together and assess the same patients, the patient representatives (section 2.3) should have been further involved. Ideally, they should have been asked whether, if they were given the choice, they would have taken part in both studies or just the BBS study. This would have allowed the study team to gain an assessment of the patients' feelings on being asked to take part in both studies. The study team would also have had an approximate idea of how many patients would have taken part in both studies and how many would have declined to take part in the chronic oedema study. However, as the preparation and approval of the study documents took longer than anticipated, it was not practical to seek more patient representative feedback due to the time needed for representatives to respond.

5.4.2 Impact of chronic oedema

Upon analysis, Stage 2 LYMQOL results were similar to Stage 1 (Table 5.6). The answers which the participants gave indicated that oedema impacted them in varying degrees. Six of the eleven oedema participants (three of which had ISL Stage 2 oedema) answered with low scores, signifying a high impact on their HQoL. However, the fourth participant with ISL Stage 2 oedema answered with high scores, ranging from 1.0 to 2.0, signifying that the oedema had a low impact. Three participants with oedema were taking Furosemide and Bendroflumethiazide diuretic medications. Their LYMQOL scores indicated that oedema had medium to high impact on their lives. Future research will allow greater comparisons between the presence of oedema and impact on HQoL.

Table 5.6 Summary of baseline LYMQOL data

Upper Limb Groups	Range (n=3)
Function	1.2 to 2.7 (1.80)
Appearance	2.4 to 3.4 (3.00)
Symptoms	1.8 to 2.5 (2.03)
Mood	1.5 to 2.0 (1.73)
Overall Quality of Life	3.0 to 7.0 (5.00)
Lower Limb Groups	Range (n=11)
Function	1.0 to 4.0 (2.70)
Appearance	1.6 to 4.0 (3.60)
Symptoms	1.0 to 3.4 (2.16)
Mood	1.0 to 2.3 (1.50)
Overall Quality of Life	0 to 8.0 (5.50)

a) Causal analysis

As stated in section 5.3.2a, along with obesity, a variety of factors can contribute to the development of oedema (Keeley, 2008 and 2012):

Four participants had positive Stemmer's signs which would suggest a lymphatic component to their oedema. However, three of these had chronic lipodermatosclerosis which also suggests a venous component.

The ISL Stage 2 participants suffered from combinations of: immobility, venous disease and potential oedema-causing medications (Atorvastatin and Indapamide). As with Stage 1, these may not have been the cause of the oedema, but they would have impacted and aggravated the lymphatic system, encouraging the development of oedema.

However, five participants were taking potential oedema-causing medications of: Amlodipine, Atorvastatin, Indapamide and Norethisterone, but they did not have oedema. Again, the participants were probably not taking a high enough dose to cause oedema to develop. Furthermore, diuretics may have masked the presence of oedema in three of the participants. Future research will provide further links between the presence of oedema and lymphatic/venous components, and allow further investigation into multiple factorial causes.

b) Impact of weight loss on chronic oedema

The aim of Stage 2 was to assess the impact of bariatric surgery on chronic oedema, whether weight loss improved chronic oedema. Due to the lack of post-operative data, further research is needed to fulfil this aim. At the time of dissertation recruitment ending, the three Stage 2 participants with

pre-operative oedema still had oedema. There are several possible reasons for this. Firstly, as they were only assessed at their first follow-up appointment (7-14 weeks after surgery), enough time and weight loss may not have occurred for oedema to improve. Furthermore, as their oedema had been present for five to greater than ten years and two of the participants had ISL Stage 2 oedema, it would logically take longer for the lymphatic system to recover and improve following weight loss. Finally, one participant may have had primary lymphoedema. This condition is thought to be caused by an inherited, genetic-based abnormality affecting the lymphatic system (Lymphoedema Framework, 2006). As she was unique among the participants in this, it will be fascinating to see whether/how weight loss over the follow-up appointments improves her oedema.

5.4.3 Study comparison with research article

The study by Greene et al. (2015) had two groups. Group 1 was discussed in section 5.3.3. Group 2 had lost weight through diets or bariatric surgery so they will be compared with Stage 2 of the study presented in this dissertation. As with Group 1, comparison between Group 2's lymphoscintigram results and BMI range highlighted the association between a dysfunctional lymphatic system and an increased BMI (Table 5.7). Table 5.8 indicates the differences between the participants of the two studies.

Table 5.7 Summary of Greene et al. (2015) results (Group 2)

Greene et al. (2015)		Group 2	
Lymphoscintigram Result	BMI (kg/m ²)	Lymphoscintigram Result	BMI (kg/m ²)
Normal	<50	Normal (n=9)	41.6 (30.0-53.1)
Normal / Abnormal	50-60		
Abnormal	>60	Abnormal (n=9)	56.1 (43.9-73.3)

Table 5.8 Comparison of both studies

Group 2 (Greene et al., 2015)	Stage 2 (Study)
18 participants	21 participants
BMI: 30-73.3kg/m ²	BMI: 38.1-61.4kg/m ²
2009-2014	2016-2017
Referred to authors' lymphoedema program at Harvard Medical School	Referred for bariatric surgery at RDH

Upon analysis, there were five participants with oedema and BMIs between 40 and 50kg/m², who should have had normal-functioning lymphatic systems according to Greene et al. (2015) (Table 5.9). Intriguingly, three

of these five had ISL Stage 2 oedema, highlighting a potential flaw in Greene et al. (2015)'s hypothetical normal/abnormal BMI values. If these participants had had oedema due to co-morbidities, this could potentially be accepted. It is possible that the oedema developed or was exacerbated by the participants' immobility and/or taking potential oedema-causing medication (Indapamide) and having venous disease (Table 5.10). Nevertheless, as ISL Stage 2 oedema is more severe, this cannot fit into the category of a normal lymphatic system.

Table 5.9 Comparison of study with lymphoscintigram values

The BMI values highlighted by Greene et al. (2015) lymphoscintigram results and the results of the study presented in this dissertation were compared.

Greene et al. (2015) Values	Stage 2 Participants
Normal (40-50kg/m ²)	5 out of 13 - Oedema
Abnormal/Normal (50-60kg/m ²)	5 out of 6 - Oedema
Abnormal (>60kg/m ²)	1 out of 2 - Oedema

Table 5.10 Analysis of participants with oedema and 'normal' BMI range (Greene et al., 2015)

Participant ID Number	ISL Stage	Oedema Location	Co-morbidities
009	1	Both feet and shins, right hand	Immobility & Venous Disease
012	2	Left and right: toes and feet	Immobility
016	2	Both shins	Immobility
036	1	Both shins	Just obesity
045	2	Both: feet, ankles, and shins	Indapamide medication

Furthermore, one participant in the abnormal BMI range of >60kg/m² did not have oedema or any oedema-related conditions. He had: negative Stemmer's signs, no skin conditions and no history of cellulitis, even though he was taking the potential oedema-causing medication of Atorvastatin. However, he was taking the diuretic Furosemide which suggests that he may have had oedema in the past and this may have masked any oedema present when the researcher assessed him.

The results of Stage 1 and 2 dispute the hypothesis by Greene et al. (2015) of a lymphoedema-associated BMI threshold between 50 and 60kg/m². This confirms the need for further research to compare the presence of oedema and BMI levels.

5.4.4 Comparison of quality of life

Unlike Stage 1 (which had no significant questionnaire results), the results of the EQ-5D and, SF-36 sections of RL: physical health, energy/fatigue and pain were significant. This indicates that the HQoL, physical health, energy, and pain of participants with oedema were significantly different to those without oedema. A visual comparison confirmed that those with oedema had worse scores. However, the multiple testing, that was required to test the significance of SF-36 sections, increased the chance of achieving significant results. Also, the presence of wide confidence intervals throughout the t-test results provides uncertainty in the mean/median differences between participants with and without oedema.

Unlike the SF-36 population normality scores of Stage 1, some of Stage 2's mean values were similar to the normative data and therefore of similar health to the corresponding population. However, the same issues of Stage 1 still apply in that: the study means were much smaller than the population means and the SF-36 questionnaire is still limited by ceiling and floor effects. The latter issue is especially relevant as the participants have been/will be followed up, therefore high scores cannot measure positive changes and low scores cannot measure any deterioration that may occur over time. Future research will provide a wider variety of participants to compare with the population means.

5.4.5 Defining chronic oedema

The following section will discuss limb volume and fluid measurement techniques used for defining the presence of chronic oedema in Stage 2.

a) Limb volume

When comparing limb volume values of participants with and without oedema for Stage 2 (before surgery), there were no significant differences (A4.48). As the perometer does not distinguish between fat, fluids or muscle mass, this was not surprising. The perometer measures limb volume and shape, so it is an indirect way of measuring oedema (Stanton, Badger and Sitzia, 2000). Although participant numbers were low, lack of significance and similar mean differences emphasise limitations of limb volume measurements and the need for fluid measurement techniques.

An aim of the perometer was to determine if bariatric surgery and the consequent weight changes result in reduced oedema. Further research is needed due to the lack of post-operative data. However, both participants who had oedema before surgery had decreased post-operative limb volumes, confirming weight changes. Furthermore, although the pitting test still indicated the presence of oedema, oedema had improved in two of the participants (section 4.3.4).

b) Fluid measurement (whole limb) - before surgery

As with Stage 1, participants with and without oedema for Stage 2 WBA data were not significantly different. Comparing the two stages, most Stage 2 values were even less significant than Stage 1, ranging from 0.963 to 0.144 compared to 0.852 to 0.068. This suggests that the pre-surgery groups were even more similar than Stage 1, as most participants had lost weight in preparation for surgery.

The right R_{zero} data for participants with and without oedema were significantly different. Also, the R_{zero} ratios for those with oedema were higher than those without oedema, indicating more ECF (and thus oedema) present. The right $[(R_{infinity}/R_{zero} \text{ lower limb}) / (R_{infinity}/R_{zero} \text{ upper limb})]$ ratio was also higher for those with oedema, indicating a higher ratio of ECF to total volume compared to those without oedema. However, the left ratio for participants with oedema was lower (0.89) than for those without oedema (1.02). This may have been impacted by arm dominance as 25 of 28 participants were right-handed.

Also, as with Stage 1, the $R_{\text{infinity}}/R_{\text{zero}}$ ratios for participants with and without oedema were similar, which matches the WBA data. Future research will allow a greater comparison to be drawn between Stage 1 and Stage 2 pre-operative participants.

Although (as with Stage 1) there were clear differences between the R_{zero} and R_{infinity} data, the R_{infinity} ratios were similar for those with and without oedema (especially the right set of values). Both of these aspects need to be investigated and analysed further, especially regarding continued use of both resistance tests in the future.

c) Fluid measurement (whole limb) – after surgery

The WBA post-operative dataset gave lower mean values than before surgery. This suggests that: even by their first post-operative appointment, as the participants lost weight, their total fluid also decreased. Further research will analyse the level of total fluid needed to decrease before oedema is no longer present.

The post-operative dataset indicated that the R_{zero} ratios for those with oedema were much higher than those without oedema. This highlighted the presence of more ECF and oedema in participants with oedema. Furthermore, the $R_{\text{infinity}}/R_{\text{zero}}$ ratios for participants with and without oedema were similar. Future research will encompass data from further appointments (not solely the 6-week post-operative appointment) and enable bigger comparisons between participants with and without oedema.

d) Fluid measurement (specific sites)

Unlike Stage 1, the only statistically significant measurement site was the right foot (0.031). However, due to low sample size and multiple testing, it is likely that this occurred by chance, especially as this was the only significant result. The low sample size may be a cause of mostly non-significant results, however the measurements of those with and without oedema were quite similar compared with Stage 1, indicating similar amounts of fluid being present. As the results are visually and significantly different from Stage 1's results, this seems to point to weight loss leading to less fluid being present (most participants' values were lower in Stage 2).

Upon comparison of the fluid measurements before and after surgery: most of the post-operative values were higher than the pre-operative values, indicating an increase in oedema after surgery. Further research

would provide postoperative data at the follow-up appointments and allow comparisons between pre- and post-operative values to highlight changes in significant measurement sites.

5.5 Analysis of bioimpedance and TDC

An aim of both Stage 1 and 2 was to determine how effective the bioimpedance and TDC techniques were at assessing for chronic oedema. For Stage 2, they were also utilised to test their use in differentiating between fat and fluid changes following weight loss. Although having only five follow-up participants does not allow for this specific aim, current results from the study point to weight loss being due to fat loss (because of the increase of post-operative fluid measurement values).

In order to determine the effectiveness of the bioimpedance and TDC techniques, both their results and practicalities will be analysed. A sole comparison between fluid measurement statistical data and oedema assessment would not have been reliable due to low participant numbers and multiple testing reducing the statistical accuracy (increasing the chance of the statistical tests being significant). Stage 2 post-operative results will be excluded from this analysis due to the very low sample size.

When looking at the results, the TDC values were easier and more logical to analyse as a higher value indicated a higher degree of fluid (and oedema). The bioimpedance values were more complicated as there were different factors involved. (The WBA data will not be discussed as they consisted of body composition data which was not expected to match the clinical assessment.) In Stage 1, the $R_{\text{zero}}/R_{\text{infinity}}$ data seemed to match the presence/absence of oedema assessment. The TDC data matched the oedema sites and showed increased fluid in those with oedema. The $R_{\text{zero}}/R_{\text{infinity}}$ data for Stage 2 matched the oedema assessment, but the TDC data did not. However, this may have indicated pre-surgery similarities between the participants. Overall, the bioimpedance technique confirmed the presence of oedema and the TDC measurements confirmed the individual oedema sites.

Using the mean TDC values from Jensen et al. (2012), six Stage 1 participants without oedema had higher-than-normal values, suggesting the presence of oedema. Two of these had already been highlighted by the clinical supervisor upon review of photographs and participant data in the CRFs. Seven Stage 2 participants without oedema also had high values.

Four of these had past swelling (or current swelling but not recognised upon assessment by the researcher). This highlights the value of using a fluid measurement technique along with the physical assessment tests (pitting test, Stemmer's sign).

Practically, although the TDC was easier and quicker to take measurements with than the bioimpedance, accuracy was sometimes affected by 'operator error'. Different areas on the lower limbs and abdomen sometimes produced different readings even if they were millimetres apart from each other (when the probe was pressing on a bone, etc.). Furthermore, if the participant needed to remain sitting up, the measurement points were different for the upper body values. The bioimpedance machine took longer to set up and there were more variables involved with taking measurements. Participants were required to lie on their backs with their arms at their sides for five to ten minutes. Although the researcher always encouraged participants to remain in this position, in some instances, this was not always possible. Once set up, the machine produced the measurements, so the values were more reliable. However, errors may have been produced by the gap between wrist/ankle electrodes being too close or far away from each other. Future research will include analysis of data with mentioned limitations to decide whether measurements were affected and should be excluded.

5.6 Analysis of the study

Although the aims of determining the prevalence and impact of chronic oedema on HQoL in a bariatric population were accomplished, results were limited by the low sample size. The study was limited by biased recruitment in Stage 1, low participant numbers in both stages and the BBS study taking place at the same time. Furthermore, only five participants had been followed up after surgery before dissertation recruitment ended. These factors limited the reliability of statistical analyses.

An aim of Stage 2 was to establish the practicality of undertaking a study into the impact of bariatric surgery on oedema. The low sample of follow-up participants meant that it was not possible to fully determine the impact of bariatric surgery however the study did provide practical information with study results and recruitment limitations, valuable for future research.

a) Study continuation

Upon completion of this dissertation, recruitment for Stage 1 and 2 will be continuing as part of the overall study. Stage 2 participants will continue to be followed up for a year or more after their surgeries in order to achieve the aim of assessing the impact of bariatric surgery on chronic oedema. The duration of the follow-up was based on the weight reduction pattern after the different bariatric surgeries. One year after gastric bypass and sleeve gastrectomy surgery, the weight reduction reaches a plateau (losing 70% and 60% of excess weight, respectively) (NBSR Data Committee, 2014). For the gastric band, the weight loss does not plateau until two to three years after surgery. However, by one year, their weight loss consists of about 40% of excess weight (with the next weight plateau being about 50%), so 80% of their final weight loss occurs in the first year. Thus, for these three main surgeries, there should be significant weight loss (and therefore potential change in oedema) after one year post-surgery.

b) Future research

The aim of this study was to determine the prevalence and impact of chronic oedema in the bariatric population, and to assess the impact of bariatric surgery on oedema. The study assessment methodology, sample size calculation and results have been (and will continue to be) analysed.

Based on this study, the following questions have emerged which need further research to explore:

How can the discussed recruitment limitations be overcome to confirm prevalence of chronic oedema in the bariatric population? Are the post-operative data from participants with and without oedema significantly different (does bariatric surgery improve chronic oedema)? Finally, do different bariatric surgeries impact oedema differently? For example, in the study so far, each of the five post-operative participants had sleeve gastrectomy surgery. A larger study would allow analysis of whether weight loss through a specific type of bariatric surgery was more instrumental in improving oedema.

c) Effects on clinical practice

The clinical practice aim of the study was: to improve the treatment and care pathway for obese patients with chronic oedema. From the results of this study (high oedema prevalence), clinical staff need to be reminded/trained how common oedema and associated skin conditions are

in obese patients and, that they are treatable. They need to be aware of how to assess oedema (through the pitting test) in order that treatment for oedema can be started quickly and properly. Furthermore, they need to recognise the preventable impact that immobility, medication and obesity can have on the lymphatic system.

5.7 Summary

Although both stages of the study were limited in their recruitment and statistical analyses, the study determined that chronic oedema is prevalent in the bariatric population and that it impacts the HQoL of patients in varying degrees. The overall results of Stage 1 indicated a statistical difference between participants with and without oedema in the Tier 3 population. However, the results of Stage 2 demonstrated the similarities between the participants just before surgery, highlighting the possibility of weight loss leading to less fluid being present. Further research and clinical training are needed to determine the impact of bariatric surgery on oedema and to raise awareness of oedema in the bariatric population.

CHAPTER 6: CONCLUSIONS

This study was established to determine the prevalence and impact of chronic oedema in a population of bariatric patients at RDH. Fluid measurement techniques (bioimpedance and TDC) were tested to determine their effectiveness of assessing oedema. Bariatric patients before and after surgery were also assessed to determine the impact of bariatric surgery on oedema.

The literature review highlighted that obese patients have a greater likelihood of developing oedema than non-obese patients. The review uncovered prevalence studies from 1.5% in 324 participants (Pittaluga and Chastanet, 2012) to 74% in 15,000 participants (Fife and Carter, 2008). However, the variety of prevalences, assessment methods and oedema definitions pointed to the need for further research (Stage 1). Bariatric surgery studies were reviewed that reported changes in oedema following surgery. But the assessment methods and different post-operative results demonstrated the need for a study with clear methods to confirm the effects of oedema after surgery (Stage 2).

Both Stage 1 and 2 determined high prevalences of chronic oedema in the bariatric population. The participants' HqoL was impacted in varying degrees by the oedema, with most having mild pitting oedema, potentially caused by: immobility, medications (including Amlodipine and Atorvastatin), obesity and venous disease. Fluid measurement techniques at Stage 1 were effective in highlighting the high level of fluid present in participants with oedema, especially at the sites below the knee. However, the results of Stage 2 suggested that the weight loss before surgery had led to the presence of less fluid, causing the participants with and without oedema to be similar. Further research is needed to determine the impact of bariatric surgery on oedema.

This study has indicated the prevalence and impact of oedema in a bariatric population. Study data have highlighted important research questions and clinical implications. These will be analysed to form a foundation for future studies, exploring the relationship between bariatric surgery, weight loss and chronic oedema.

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APPENDICES

A1: Excluded literature review studies

A1.1: List of excluded studies presenting the association between obesity and oedema

Study Name	Authors	Exclusion Information
Edematous obstructive sleep apnea patients have low normal serum albumin levels.	Blankfield, Ahmed and Zyzanski (2006)	Low number of participants due to exclusion criteria
Obesity is a risk factor for developing postoperative lymphedema in breast cancer patients.	Helyer et al. (2010)	Odds were discussed instead of numbers of participants
Health correlates of overweight and obesity in adults aged 50 years and over: results from the Survey of Health, Ageing and Retirement in Europe (SHARE).	Peytremann-Bridevaux & Santos-Eggimann (2008)	Reliance on patients' opinions of whether or not they had oedema
Randomized controlled trial comparing a low-fat diet with a weight-reduction diet in breast cancer-related lymphedema.	Shaw, Mortimer and Judd (2007)	Arm volume differences were not measured following weight reduction
Lymphedema development following breast cancer surgery with full axillary resection.	van der Veen et al. (2004)	Poor oedema classification
Arm edema in conservatively managed breast cancer: obesity is a major predictive factor.	Werner et al. (1991)	Unclear/unreliable data capture

A1.2: List of excluded prevalence studies

Study Name	Authors	Exclusion Information
On the importance of pedal edema in hemodialysis patients.	Agarwal, Andersen and Pratt (2008)	Low number of participants
Bilateral leg edema, pulmonary hypertension, and obstructive sleep apnea.	Blankfield and Zyzanski (2002)	Low number of participants; convenience sample of patients were enrolled, therefore not a true sample of the population
Bilateral leg edema, obesity, pulmonary hypertension, and obstructive sleep apnea.	Blankfield et al. (2000)	Low number of participants
The frequency of lymphedema in an adult spina bifida population.	Garcia & Dicianno (2011)	Low number of participants, uncertainty of how the data had been collected
Laparoscopic roux-en-y gastric bypass in the "megaobese".	Kreitz & Rovito (2003)	Low number of participants
Localized lymphedema (elephantiasis): a case series and review of the literature.	Lu et al. (2008)	Low number of participants

Study Name	Authors	Exclusion Information
Delayed onset of lactogenesis among first-time mothers is related to maternal obesity and factors associated with ineffective breastfeeding.	Nommsen-Rivers et al. (2010)	Low number of participants, not possible to separate obese from overweight
Adult patients with Prader-Willi syndrome: clinical characteristics, life circumstances and growth hormone secretion.	Partsch et al. (2000)	Low number of participants, lipolymphoedema was not specified
Verrucous localized lymphedema of genital areas: clinicopathologic report of 18 cases of this rare entity.	Plaza et al. (2014)	Low number of participants
The incidence and risk factors for occurrence of arm lymphedema after treatment of breast cancer.	Rebegea et al. (2015)	Low number of participants; the article looked at different risk factors, of which arm lymphoedema was only one factor
Postmastectomy lymphedema.	Rydell, Jennings and Smith (1958)	Unreliable data capture, low number of participants

A1.3: List of excluded studies presenting oedema changes after bariatric surgery

Study Name	Authors	Exclusion Information
Anesthesia for a patient with morbid obesity using dexmedetomidine without narcotics.	Hofer et al. (2005)	Case study, no details of oedema diagnosis, no clinical assessment after surgery to confirm lymphoedema improvement
Impact of bariatric surgery on quality of life, functional capacity, and symptoms in patients with heart failure.	Miranda et al. (2013)	Small sample size; unbalanced control and bariatric surgery groups; non-BMI comparable groups; lower limb oedema measured using a Likert scale
Impact of bariatric surgery on cardiovascular and musculoskeletal morbidity.	Sampalis, Sampalis and Christou (2006)	Unbalanced case-control groups, low case sample size, no post-surgery numbers, unknown oedema definition

A2: Study forms (Stage 1)

A2.1: Invitation letter (Stage 1)

Dear

I am writing to invite you to consider taking part in a study that is being carried out by the University of Nottingham in collaboration with the Royal Derby Hospital weight management clinic. If you agree to participate in this study, information would be collected when you come to hospital for your clinic appointment. The aim of this study is to establish how common swollen legs (known as chronic oedema) are amongst people with weight problems and how the swelling affects everyday life.

We would like you to consider taking part in this study even if you feel you do NOT have any swelling.

The enclosed information sheet explains more about why we are doing this research and what would be involved if you agreed to participate. When you attend hospital for your clinic appointment, a member of the study team will check if you would like to take part. Although we hope that people will agree to take part in the study, please be assured that there is no obligation to do so and that your decision will not affect your usual clinical care.

If you have any questions about the study please do not hesitate to contact Miss Amy Newman or Dr Vaughan Keeley, two members of the study team, if you have any questions

**Contact Number
Removed for
Security Reasons**

Yours sincerely,

**Mr Paul Leeder
Consultant Surgeon**

A2.2: Information sheet (Stage 1)

Participant Information Sheet
(Final Version 2: date 11th July 2016)

Title of Study: Prevalence and Impact of Chronic Oedema in a Population of Patients Prior to and Following Bariatric Surgery

Name of Researchers: Amy Newman, Dr. Vaughan Keeley,
Professor Christine Moffatt, Dr. Lorraine Pinnington

We would like to invite you to take part in a research study. Before you decide if you would like to take part, we would like you to understand why the research is being done and what it would involve for you. A member of the team will go through the information sheet with you and answer any questions you have. Talk to others about the study if you wish. Please ask us if there is anything that is not clear or if you would like more information. Thank you for reading this.

What is the purpose of the study?

Persistent leg swelling (chronic leg oedema) is quite a common condition. It can cause a number of problems including infections (known as cellulitis) in the swollen area and ulceration. Our experience suggests it is particularly common in people with weight problems but this has not been studied in detail before. We are therefore carrying out a study to measure how common it is in people with weight problems and how it affects their everyday life.

Why have I been invited?

You are being invited to take part because you are attending a weight-loss programme at Royal Derby Hospital. We are hoping to invite 180 patients to take part in this study.

We would like you to take part even if you feel you do not have swelling. This will allow us to confirm the percentage of people who do and who do not have swelling.

Do I have to take part?

It is up to you to decide whether or not you wish to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. This would not affect your legal rights.

What will happen to me if I take part?

If you agree to take part, you will only be assessed ONCE, which will take place when you come to hospital for your visit to the weight loss programme, and we expect this will take 40 minutes. This assessment will involve completing up to 3 questionnaires and a clinical assessment which will check if you have swelling or not.

- **Questionnaires**

If swelling is not found to be present, we will ask you to complete 2 questionnaires; if swelling is found to be present, we will ask you to complete 3 questionnaires. The questionnaires concern quality of life and mobility. They will be important to the study as they will provide information about the impact of the swelling (if present) on everyday life.

- **Clinical assessment**

The clinical assessment is to identify the presence of the swelling and its degree in each of the affected area(s). It will consist of a clinical examination of your legs and abdomen to look for swelling and changes in your skin associated with this. We will take several measurements of your legs and abdomen to assess the size, shape, and the amount of fluid in the tissues. The sections below describe the tests and techniques used to obtain this information. None of the tests should cause you any pain or discomfort and you can still take part in the project if you are unable to have one or more of the tests undertaken. Most can be done with you sitting in a chair or on an examination couch.

- **Bioimpedance**

We will use two different tests to assess the fluid changes in your legs. The first test measures total fluid within the whole leg and is called bioimpedance. [If you have a pacemaker (or any other active implanted medical devices), are undergoing external defibrillation, or are pregnant, you will not undertake this part of the assessment.] This test passes an extremely small electrical current through your body and measures the resistance to the flow of this current. You will not feel anything when the measurement is carried out as the current is very small, similar to the strength of a watch battery. If you are able to, we will undertake this test with you lying down on the examination couch or sitting in a chair. Small stickers will be placed on your hands and feet and clips attached to these.

- **Moisture Meter**

The second test uses a device (called a moisture meter) that measures fluid levels at different points. In order to record these fluid levels, a probe will be placed against the skin on your feet, lower legs and thighs. If you have swelling in your legs we would expect these readings to be higher than in people without swelling.

Details of your height, weight, blood test results, current medications, and other conditions will also be recorded.

You will be asked if a photograph can be taken of any sites where swelling is present. If you give consent for this, your identity will remain anonymous.

Expenses and payments

The assessments will be carried out when you attend hospital for your clinic appointment and will therefore not involve any extra travel. For this reason, we will not pay expenses.

What are the possible disadvantages and risks of taking part?

There are no expected disadvantages or risks to taking part in this study.

What are the possible benefits of taking part?

One benefit to taking part is that we may find that you have swelling and, if you wish, you could then ask your GP to refer you to the lymphoedema service for treatment.

The information we get from this study should help future patients in that the results are likely to lead to improvements in the treatment pathway for patients with weight problems who have swelling.

What happens when the research study stops?

When the study stops, patients will be provided with a summary of the results if they request it.

What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions. The researchers' contact details are given at the end of this information sheet. If you remain unhappy and wish to complain formally, you can do this by contacting PALS – Freephone: 0800 783 7691; Office: 01332 785 156; Email: dhft.contactpals@nhs.net.

Will my taking part in the study be kept confidential?

We will follow ethical and legal practice and all information about you will be handled in confidence.

If you join the study, some parts of your medical records and the data collected for the study will be looked at by authorised persons from the University of Nottingham who are organising the research. They may also be looked at by authorised people to check that the study is being carried out correctly. All will have a duty of confidentiality to you as a research participant and we will do our best to meet this duty.

All information which is collected about you during the course of the research will be kept **strictly confidential**, stored in a secure and locked office, and on a password-protected database. Any information about you which leaves the hospital will have your name and address removed (anonymised) and a unique code will be used so that you cannot be recognised from it.

Your contact details will be kept for up to 3 years after the end of the study so that we are able to contact you in case any queries arise. All other data (research data) will be kept securely for 7 years. After this time, your data will be disposed of securely. During this time, your identity will remain confidential, only members of the research team will have access to your contact details.

Although what you say in the assessment is confidential, should you disclose anything to us which we feel puts you or anyone else at any risk, we may feel it necessary to report this to the appropriate persons.

What will happen if I don't want to carry on with the study?

Your participation is voluntary and you are free to withdraw at any time, without giving any reason, and without your legal rights being affected. If you withdraw then the information collected so far cannot be erased and this information may still be used in the project analysis.

Involvement of the General Practitioner/Family doctor (GP)

Your GP will be notified of your participation by the study team, unless you ask us not to inform him/her.

What will happen to the results of the research study?

The study results will be presented at national and international conferences and also published in peer-reviewed journals. The findings will be used locally to support the development of an integrated bariatric/chronic oedema service. In addition, the work will be written up for a Masters thesis. The culmination of this work will form a research strategy for this patient group. Participants will not be identified in the Masters thesis or any publications.

Who is organising and funding the research?

This research is being organised by the University of Nottingham and, is being partially funded by the University of Nottingham and partially funded by the Masters research student.

Who has reviewed the study?

All research in the NHS is looked at by independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given a favourable opinion by the Liverpool Central Research Ethics Committee (Study IRAS ID: 198766).

**Contact Information Removed
for Security Reasons**

A2.3: Poster

This poster (in larger print) was placed in the waiting area and clinic rooms of the bariatric clinic to aid recruitment.

RESEARCH ON LEG SWELLING IN PEOPLE WITH A WEIGHT PROBLEM – PLEASE HELP US WITH THIS.

Persistent leg swelling (chronic leg oedema) is quite a common condition, which can cause a number of problems including a tendency to infections (cellulitis) in the swollen area and ulceration. Our experience suggests it is particularly common in people with weight problems but this has not been studied in detail before.

We are therefore carrying out a research study to measure how common it is in people with weight problems and how it affects their everyday life. We will also seek to determine whether the swelling improves after weight loss surgery, as our experience suggests that it does.

You may be invited to take part in this study. If so, you will be given/sent an invitation letter and a participant information sheet which explains more about why we are doing this project and about participant involvement.

We would like as many people as possible to take part in the study **even if you do NOT think you have swelling**.

However, if you decide not to take part, please be assured that this will not affect your usual clinical care.

If you have any questions about the study, please contact:

**Contact Information Removed
for Security Reasons**

A2.4: Consent form
(Smaller font and size to original)

CONSENT FORM
(Final Version 3) (11thJul16)

Title of Study: Prevalence and Impact of Chronic Oedema in a Population of Patients Prior to and Following Bariatric Surgery

REC ref: 16/NW/0340; IRAS ID: 198766

Name of Researchers: Amy Newman, Dr. Vaughan Keeley,
Professor Christine Moffatt, Dr. Lorraine
Pinnington

Name of Participant: **Please initial box**

1. I confirm that I have read and understand the information sheet (final version 2, dated 11th July 2016) for the above study and have had the opportunity to ask questions. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, and without my medical care or legal rights being affected. I understand that should I withdraw then the information collected so far cannot be erased and that this information may still be used in the project analysis. ☐
3. I understand that relevant sections of my medical notes and data collected in the study may be looked at by authorised individuals from the University of Nottingham, the research group and regulatory authorities where it is relevant to my taking part in this study. I give permission for these individuals to have access to these records and to collect, store, analyse and publish information obtained from my participation in this study. I understand that my identity and all personal details will be kept confidential. ☐
4. I give consent for a photograph(s) to be taken of sites where swelling is present. I understand that my identity will remain anonymous. Such photographs could be included in research publications or at educational events in an anonymised form. ☐
5. I understand my GP will be notified that I am participating in this study. ☐
6. I understand that the information collected about me may be used to support other research in the future. If so, this would only be shared anonymously with other researchers. ☐
7. I agree to take part in the above study. ☐

Name of Participant	Date	Signature
Name of Person taking consent	Date	Signature

3 copies: 1 for participant, 1 for the project notes and 1 for the medical notes

A2.5: Letter sent to GP (Stage 1)

GP Address:

Amy Newman
Division of Medical Sciences and
Graduate Entry Medicine
School of Medicine
University of Nottingham
Royal Derby Hospital
Uttoxeter Road
Derby
DE22 3DT

Date:

Title of Study: Prevalence and impact of chronic oedema in a population of patients prior to and following bariatric surgery

Name of Researchers: Amy Newman (Masters research student),
Dr. Vaughan Keeley (Chief Investigator)

Dear Dr.

Your patient date of birth (...../...../.....) has recently agreed to participate in a study that is hosted by the East-Midlands Bariatric & Metabolic Institute (EMBMI). The purpose of this study is to assess the prevalence of chronic oedema among obese patients attending a Tier 3 conservative management of weight loss programme at Royal Derby Hospital and to determine the impact of chronic oedema on everyday life. I have enclosed a participant information sheet about the study.

If the patient is found to have oedema, he/she may talk to you about seeking a formal referral to the lymphoedema clinic for treatment. We aim to publish the results once the study is complete, however, if you would like details of any interim results, please do not hesitate to ask.

Yours Sincerely,

Amy Newman

**Contact Information Removed
for Security Reasons**

A2.6: Case report form (Stage 1)
(Smaller font and size to original)

CASE REPORT FORM

**STUDY TITLE: Prevalence and Impact of Chronic Oedema in a
Population of Patients Prior to and Following Bariatric Surgery
(STAGE 1)**

R&D Reference Number:

Participant Study ID No

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Date of Assessment (dd/mm/yyyy): / /.....

Type of Facility: Out-Patient

CRF Final Version 1 (23rdMar16)

Demographics

Age:

Gender: ☐ **M**=Male, **F**=Female

Weight: Kg Height m BMI: Kg/m²

Level of Obesity (circle one): Under weight / Normal weight / Obese / Morbidly obese

Lower Body Mobility (circle one): Bed bound / Chair bound / Walks with aid / Walks unaided

Upper Body Mobility (circle one): Full range of movement / Limited range of movement / No function

Relevant medical history - precipitating factors:

Arthritis: Yes ☐ No ☐

If yes, provide details:

Diabetes: Yes ☐ No ☐

If yes, provide details:

Heart disease: Yes ☐ No ☐

If yes, provide details:

Hypertension: Yes ☐ No ☐

If yes, provide details:

Liver disease: Yes ☐ No ☐

If yes, provide details:

Neurological disorder: Yes ☐ No ☐

If yes, provide details:

Obstructive sleep apnoea: Yes ☐ No ☐

If yes, provide details:

Peripheral arterial disease: Yes ☐ No ☐

If yes, provide details:

Renal disease: Yes ☐ No ☐

If yes, provide details:

Other co-morbidities/complications (of obesity/oedema) Yes ☐ No ☐

If yes, provide details:

Other co-morbidities/complications (of obesity/oedema) Yes ☐ No ☐

If yes, provide details:

Blood tests results **Date:** N/A ☐

FBC (full blood count) – specifically haemoglobin level:

HbA1c (glycated haemoglobin):

LFT (liver function test)/AST (aspartate aminotransferase) – specifically albumin level (LFT):

TFT (thyroid function test) – specifically TSH (thyroid-stimulating hormone):

UE (urea & electrolytes) – specifically EGFR (estimated glomerular filtration rate):

BNP (B-type natriuretic peptide) test: YES/NO

If yes, provide result:

List of current medications:

Consent given for taking photograph(s): YES/NO

If yes: Details of area to be photographed:.....

.....

Date:

Presence and Classification of Swelling/Oedema

1. Does the patient have any swelling? Yes / No (circle one)
(If no, skip to question 12)
2. Does the area of swelling pit? Yes / No
2a. **If the swelling does pit**, please detail site(s) where pitting oedema is present (circle all that apply):
L toes / L foot / L lower leg / L upper leg / L buttocks / L abdomen
R toes / R foot / R lower leg / R upper leg / R buttocks / R abdomen
Vulva / Scrotum / Penis
Other
3. Are the tissues in the swollen area predominantly: Soft / Hard / N/A
4. Is there significant shape distortion in the affected limb?
Yes / No / N/A
5. If it **is** lymphoedema: Primary / Secondary
6. If it **is not** primary lymphoedema, is the swelling due to:
Cancer / Non Cancer / N/A
6a. **If Cancer** (circle all that apply): Treatment related / Metastatic
lymphatic obstruction / N/A
If **Non Cancer**: Venous / Immobility / Obesity / Lymphatic Filariasis /
Other
7. What is the severity of the swelling (ISL Severity Staging)?
ISL stage
ISL stage I – This represents early onset of the condition where there is accumulation of tissue that subsides with limb elevation. The oedema may be pitting at this stage.
ISL stage II - Limb elevation alone rarely reduces swelling and pitting is manifest.
ISL stage III - The tissue is hard (fibrotic) and pitting is absent.
Skin changes such as thickening, hyperpigmentation, increased skin folds, fat deposits and warty overgrowths develop.

8. Estimate the duration of the swelling/oedema:

<6 months / 6 months – 1 year / 1-2 years / 2-5 years /
5-10 years / >10 years

9. Has the patient been told the reason for the swelling/oedema? Yes / No

Skin Condition

10. Stemmers sign: Left Foot (circle only one): Positive / Negative

/ Equivocal

Right Foot (circle only one): Positive / Negative

/ Equivocal

11. Skin Conditions: Yes / No If yes, where?

11a. If yes, what type of skin conditions: (circle all that apply)

Eczema / Varicose eczema / Chronic lipodermatosclerosis /

Other (Specify)

12. History of Deep Vein Thrombosis (DVT)? Yes / No

12a. If yes, please detail site(s) and date(s) of DVT diagnosis (date:):

.....

Wound Assessment

13. Does the patient have a wound? Yes / No

(If no, skip to question 18)

14. Does the patient have a pressure ulcer? Yes / No

15. Does the patient have a leg/foot ulcer? Yes / No

16. Does the patient have an acute/surgical wound? Yes / No

17. What is the location of the wound(s) (circle all that apply):

Abdomen / Back / Hips / Upper leg / Groin

Lower leg/ankle / Foot / Other

PRECIPITATING FACTORS

18. Has the patient ever had cellulitis? Yes / No

(If no, skip to question 19)

18a. If **yes**: how many times

18b. In the past year, has the patient had cellulitis in the affected areas due to

the swelling? Yes / No If **yes**, how many times

- 18c. In the past year, has the patient been admitted to hospital as a result of cellulitis? Yes / No If **yes**, how many times
19. Is the participant currently receiving treatment for oedema? Yes / No
- 19a. If **yes**, are they receiving compression? Yes / No
20. In the patient's opinion, is the swelling controlled? Yes / No
/ Don't know

21. **Bioimpedance:** N/A ☐

	Yes	No	N/A
Contraindications: Does the participant have / Is the participant....			
• Any active implanted medical devices? (such as a pacemaker or defibrillator)			
• Undergoing external defibrillation?			
• Pregnant?			

If the answer to any of the 3 questions above is Yes, DO NOT undertake bioimpedance measurements

Please identify if the participant is / has:

	Yes	No	NA
• Currently menstruating, just finished or just prior to menstruation?			
• Currently taking Hormone treatments? If yes, specify drug name, dose and frequency:			
• Caffeine within the last 2 hours: If yes, provide details:			
• Has known renal impairment? If yes, provide details:			
• Has known cardiac failure? If yes, provide details:			
• Currently taking diuretics? If yes, specify drug name, dose and frequency:			
• Has artificial limbs? If yes, provide details:			
• Completed excessive exercise within the last two hours? If yes, provide details:			

• Consumed alcohol within the last 12 hours? If yes, provide details:			
• Any metal plates / pins insitu etc? If yes, provide details:			

22. Arm Dominance: Left / Right

23. Leg Dominance: Left / Right

24. In which leg(s) does the patient have swelling: Neither / Right /
Left / Both Legs

25. Bioimpedance Readings

	File number	Rzero	Rinf	Rinf ÷ Rzero
Whole body analysis (RIGHT) - 1				
Whole body analysis (RIGHT) - 2				
Right Arm - 1				
Right Arm - 2				
Right Leg - 1				
Right Leg - 2				
Whole body analysis (LEFT) - 1				
Whole body analysis (LEFT) - 2				
Left Arm - 1				
Left Arm - 2				
Left Leg - 1				
Left Leg - 2				

26. **Tissue Dielectric Constant (MoistureMeterD)** – Tick if N/A ☐

Site	Right Mmt 1	Right Mmt 2	Right Mmt 3	Left Mmt 1	Left Mmt 2	Left Mmt 3
Dorsum of the central part of the foot						
Posterior to the medial malleolus						
7cm from bottom of patella (along midline)						
7cm from the top of patella (along midline)						
7cm below inguinal crease (along midline)						
Abdominal wall						

Has the participant completed the EQ-5D questionnaire? Yes / No

Questionnaire Score:

If no, please provide reason

Has the participant completed the GAD-7 and PHQ-9 questionnaires?

Yes / No

Questionnaire Scores:

If no, please provide reason

Has the participant completed the LYMOL questionnaire? Yes / No

Questionnaire Score:

If no, please provide reason

Has the participant completed the SF-36 questionnaire? Yes / No

Questionnaire Score:

If no, please provide reason

END OF STUDY

Did the patient complete the study according to the protocol?

1 = Yes **0** = No

☐

All dates in **DD/MMM/YYYY** format

Date of patient's Completion of study: __ / __ / __

Tick if N/A

☐

Date of patient's Withdrawal from the study: __ / __ / __

Tick if N/A

☐

Primary reason for Withdrawal

☐

1 Adverse Event

2 Protocol Violation

3 Withdrawal of Consent

4 Death

5 Loss to follow up

6 Other, please specify

7 N/A

A2.7: LIMPRINT core tool

(Smaller font and size to original, adapted for dissertation margins)

Core Tool**Date:**

Day		Month		Year	

Site Number

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Patient Number

----------------------	----------------------	----------------------	----------------------	----------------------	----------------------

1. Facility Number

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Type of Facility (check one)

- | | |
|---|---|
| ☐ General practitioner | ☐ Nursing home |
| ☐ Community nursing / Home care service | ☐ Elderly care residential home |
| ☐ Acute hospital (check type of patient) | ☐ Specialist Lymphoedema service |
| ☐ In-patient | ☐ Other (specify) - _____ |
| ☐ Out-patient | |

2. Demographics**Gender:** ☐ Male ☐ Female**Age:** **3. Level of Obesity** (check one)

- ☐ Under weight ☐ Normal weight ☐ Obese ☐ Morbidly obese

4. Mobility**Lower body** (check one)

- ☐ Bed bound
☐ Chair bound
☐ Walks with aid
☐ Walks unaided

Upper body (check one)

- ☐ Full range of movement
☐ Limited range of movement
☐ No function

5. Relevant Co-morbidities (check all that apply)

- | | |
|--|--|
| ☐ Diabetes Mellitus | ☐ Heart failure / Ischaemic heart disease |
| ☐ Neurological disorder | ☐ Peripheral arterial disease |

6. Classification of Lymphoedema (check one)

- ☐ Primary ☐ Secondary

If Secondary, swelling due to: ☐ Cancer ☐ Non Cancer
 (check one and fill out appropriate section below)

If Cancer: (check all that apply)

- ☐ Treatment related
☐ Metastatic lymphatic obstruction

If Non Cancer: (check all that apply)

- ☐ Venous ☐ Immobility ☐ Obesity ☐ Lymphatic Filariasis
☐ Other (specify) _____

7. Lymphoedema History (check one)					
Estimate the duration of the lymphoedema:					
☐ <6 months	☐ 6 months – 1 year	☐ 1-2 years	☐ 2-5 years		
☐ 5-10 years	☐ >10 years				
8. Cellulitis					
Has the patient ever had cellulitis? ☐ Yes ☐ No					
In the past year, has the patient had cellulitis in the affected areas due to the swelling?					
☐ Yes ☐ No If yes, How many times:					
In the past year, has the patient been admitted to hospital as a result of cellulitis?					
☐ Yes ☐ No If yes, How many times:					
9. Main Categories of Treatment within Complex Decongestive Therapy (check all that apply)					
☐ None	☐ Physiotherapy (not massage)	☐ Debulking / lipoedema / lymphatic surgery			
☐ Skin care advice	☐ Compression garment	☐ Exercise advice			
☐ Wound dressing	☐ Multilayer bandage	☐ Cellulitis advice			
☐ Antibiotic	☐ Compression wrap	☐ Psychological support			
☐ Massage (including lymphatic drainage)	☐ Pneumatic compression pumps	☐ Other (specify) _____			
10. Site of Swelling (check all that apply)					
☐ Head	☐ Vulva	☐ L fingers	☐ L toes	☐ R fingers	☐ R toes
☐ Face	☐ Scrotum	☐ L hand	☐ L foot	☐ R hand	☐ R foot
☐ Eyes	☐ Penis	☐ L lower arm	☐ L lower leg	☐ R lower arm	☐ R lower leg
☐ Lips		☐ L upper arm	☐ L upper leg	☐ R upper arm	☐ R upper leg
☐ Cheek		☐ L shoulder	☐ L buttocks	☐ R shoulder	☐ R buttocks
☐ Tongue		☐ L upper chest/breast	☐ L abdomen	☐ R upper chest/breast	☐ R Abdomen
11. Wound Area					
Does the patient have a wound? ☐ Yes ☐ No					
If Yes, (check all that apply)					
Site of wound:					
☐ Arm/hand	☐ Leg	☐ Foot/ankle	☐ Head/neck		
☐ Sacrum/buttocks					
☐ Abdomen	☐ Back	☐ Breast			
Type of wound:					
☐ Leg/foot ulcer	☐ Pressure ulcer	☐ Surgical wound (closed)			
☐ Dehisced wound	☐ Burn				

☐ Other (specify)

12. Access to Treatment

	Yes	No	NA
1. Is this patient's entire treatment for lymphoedema/chronic oedema available free within the healthcare system or covered by health insurance?	☐	☐	☐
2. If this patient's treatment for lymphoedema/chronic oedema is not free within the healthcare system or not covered by health insurance are they able to pay for care?	☐	☐	☐
3. Is specialist lymphoedema treatment available for this patient within a reasonable travelling distance for this patient?	☐	☐	☐
4. Does the distance/ lack of transport arrangements deter/prevent this patient from accessing specialist treatment?	☐	☐	☐
5. Is this patient's lymphoedema/wound preventing discharge from hospital into the community?	☐	☐	☐
6. Is this patient's lymphoedema/wound the main reason for them remaining in a long-term care facility?	☐	☐	☐
7. Is this patient's lymphoedema/wound the main reason for them remaining in long-term home care?	☐	☐	☐

13. Subjective Control of Swelling

In your opinion, is the swelling well controlled? ☐ Yes ☐ No ☐ Don't know

A2.8: LIMPRINT details of swelling tool

(Smaller font and size to original, adapted for dissertation margins)

Date:		Details of Swelling Tool		Site Number	
Day	Month	Year		Patient Number	

1. Current Swelling	
Press the site of swelling for 30 seconds; a pit remains upon removal of pressure.	
Does the area of swelling "pit"?	☐ Yes ☐ No
Tissues in swollen area are predominantly:	☐ Soft ☐ Hard
Is there significant shape distortion in the affected limb?	☐ Yes ☐ No

2. Has the patient been told the reason for the swelling? ☐ Yes ☐ No

3. Circumference or Volume Measurements		
Which limb(s) are swollen? ☐ Arm ☐ Leg ☐ Both		
* if you have the equipment to measure limb volume then limb circumference is not required		
** please measure both right and left side of limbs that have swelling.		
Arm(s)	Right	Left
Mid upper arm 10cm above elbow	cm	cm
Forearm 10cm below elbow	cm	cm
Arm volume measurements (where available)	ml	ml
Leg(s)	Right	Left
20cm above the centre of the patella	cm	cm
20cm below the centre of the patella	cm	cm
Leg volume measurements (where available)	ml	ml

4. Stemmers Sign

Stemmer's test results in either a positive or negative sign for lymphoedema. To perform it, try to pinch and lift a skin fold at the base of the second toe or middle finger. If you can pinch and lift the skin, Stemmer's sign is negative. If you can't, the sign is positive.

	Right		Left	
Hand	☐ Positive	☐ Negative	☐ Positive	☐ Negative
Foot	☐ Positive	☐ Negative	☐ Positive	☐ Negative

5. Severity of the Swelling - ISL Severity Staging (check one)	
☐ ISL stage I	This represents early onset of the condition where there is accumulation of tissue that subsides with limb elevation. The oedema may be pitting at this stage.
☐ ISL stage II	Limb elevation alone rarely reduces swelling and pitting is manifest.
☐ ISL stage III	The tissue is hard (fibrotic) and pitting is absent. Skin changes such as thickening, hyperpigmentation, increased skin folds, fat deposits and warty overgrowths develop.

A2.9: EQ-5D questionnaire

Date:

Day

Month

Year

Site Number

Patient Number

Quality of Life Tool EQ-5D

Complete both the EQ-5D and LYMQOL tools for both upper and lower limbs.

Whenever possible, the patient should complete each instrument for himself or herself. Please indicate what statements best describe your own health state today.

1. Mobility (check one)

- ☐ I have no problems in walking about
☐ I have some problems walking about
☐ I am confined to a bed

2. Self Care (check one)

- ☐ I have no problems with self care
☐ I have some problems washing or dressing myself
☐ I am unable to wash or dress myself

3. Usual Activities: e.g. work, study, housework, family or leisure activities (check one)

- ☐ I have no problems with performing my usual activities
☐ I have some problems with performing my usual activities
☐ I am unable to perform my usual activities

4. Pain / Discomfort (check one)

- ☐ I have no pain or discomfort
☐ I have some moderate pain or discomfort
☐ I have extreme pain or discomfort

5. Anxiety / Depression (check one)

- ☐ I am not anxious or depressed
☐ I am moderately anxious or depressed
☐ I am extremely anxious or depressed

6. To help people say how good or bad a health state is we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0.

We would like you to indicate on this scale how good or bad your own health is today, in your opinion. Please do this by drawing a line in the box to the right to whichever point on the scale indicates how good or bad your health state is today.

Best
imaginable
health state

100

90

80

70

60

50

40

30

20

10

0

Worst
imaginable
health state

A2.10: LYMQOL questionnaire**Page 1****Date:**

Day	Month	Year			

Site Number

----------------------	----------------------

Patient Number

----------------------	----------------------	----------------------	----------------------	----------------------

Quality of Life Tool
LYMQOL – Upper Limb

Do you have swelling in your upper limb?
☐ Yes ☐ No

If No, go to page 2

7. How much does your swollen arm affect the following daily activities (Check one that best applies)

	Not at all	A little	Quite a bit	A lot
Your occupation	☐	☐	☐	☐
Your housework	☐	☐	☐	☐
Combing your hair	☐	☐	☐	☐
Dressing yourself	☐	☐	☐	☐
Your writing	☐	☐	☐	☐
Your eating	☐	☐	☐	☐
Washing yourself	☐	☐	☐	☐
Cleaning your teeth	☐	☐	☐	☐

8.

	Not at all	A little	Quite a bit	A lot
How much does it affect your leisure activities/social life?	☐	☐	☐	☐
How much do you have to depend on other people?	☐	☐	☐	☐
How much do you feel the swelling affects your appearance?	☐	☐	☐	☐
How much difficulty do you have finding clothes to fit?	☐	☐	☐	☐
How much difficulty do you have finding clothes you would like to wear?	☐	☐	☐	☐
Does the swelling affect how you feel about yourself?	☐	☐	☐	☐
Does the swelling affect your relationships with other people?	☐	☐	☐	☐
Does your lymphedema cause you pain?	☐	☐	☐	☐
Do you have any numbness in your swollen arm?	☐	☐	☐	☐
Do you have any 'pins and needles' or tingling in your swollen arm?	☐	☐	☐	☐
Does your swollen arm feel weak?	☐	☐	☐	☐

9. In the past week (Check one that best applies)

	Not at all	A little	Quite a bit	A lot
Have you had trouble sleeping?	☐	☐	☐	☐
Have you had difficulty concentrating on things, e.g., reading?	☐	☐	☐	☐
Have you felt tense?	☐	☐	☐	☐
Have you felt worried?	☐	☐	☐	☐
Have you felt irritable?	☐	☐	☐	☐
Have you felt depressed?	☐	☐	☐	☐
Does your swollen arm feel heavy?	☐	☐	☐	☐
Do you feel tired?	☐	☐	☐	☐

10. Overall how you would rate your quality of life at present?

(Circle one number)

0 1 2 3 4 5 6 7 8 9 10
Poor Excellent

Patient Number				
-----------------------	--	--	--	--

Page 2

Quality of Life Tool

LYMOOL – Lower Limb

Do you have swelling in your lower limb? ☐ Yes ☐ No
If no, tool is complete

11. How much does your swollen leg affect the following daily activities

(Check one that best applies)

	Not at all	A little	Quite a bit	A lot
Your walking	☐	☐	☐	☐
Your ability to bend, e.g. to tie shoelaces or cut toenails	☐	☐	☐	☐
Your ability to stand	☐	☐	☐	☐
Your ability to get up from a chair	☐	☐	☐	☐
Your occupation	☐	☐	☐	☐
Your ability to do housework	☐	☐	☐	☐

12. How much does your swollen leg affect the following questions

(Check one that best applies)

	Not at all	A little	Quite a bit	A lot
How much does the swelling affect your leisure activities?	☐	☐	☐	☐

How much do you have to depend on other people?	☐	☐	☐	☐
How much do you feel it affects your appearance?	☐	☐	☐	☐
How much difficulty do you have finding clothes to fit?	☐	☐	☐	☐
How much difficulty do you have finding clothes you would like to wear?	☐	☐	☐	☐
How much difficulty in finding shoes to fit?	☐	☐	☐	☐
How much difficulty in finding socks/tights/stockings to fit?	☐	☐	☐	☐
Does the swelling affect how you feel about yourself?	☐	☐	☐	☐
Does the swelling affect your relationships with other people?	☐	☐	☐	☐
Does your lymphedema cause you pain?	☐	☐	☐	☐
Do you have any numbness in your swollen leg?	☐	☐	☐	☐
Do you have any 'pins and needles' or tingling in your swollen leg?	☐	☐	☐	☐
Does your swollen leg feel weak?	☐	☐	☐	☐
Does your swollen leg feel heavy?	☐	☐	☐	☐

13. In the past week (Check one that best applies)				
	Not at all	A little	Quite a bit	A lot
Have you had trouble sleeping?	☐	☐	☐	☐
Have you had difficulty concentrating on things, e.g., reading?	☐	☐	☐	☐
Have you felt tense?	☐	☐	☐	☐
Have you felt worried?	☐	☐	☐	☐
Have you felt irritable?	☐	☐	☐	☐
Have you felt depressed?	☐	☐	☐	☐

14. Overall how you would rate your quality of life at present?

(Circle one number)

0 **1** **2** **3** **4** **5** **6** **7** **8** **9** **10**
Poor **Excellent**

A2.11: SF-36 questionnaire

(Smaller font and size to original, adapted for dissertation margins)

SF-36 Questionnaire

(Rand 36-Item Short Form Health Survey 1.0, developed at RAND as part of the Medical Outcomes Study)

Date_____

Participant Study ID#_____

1. In general, would you say your health is:

Excellent..... 1
 Very good..... 2
 Good..... 3
 Fair..... 4
 Poor..... 5

2. **Compared to 1 year ago**, how would you rate your health in general **now**?

Much better now than 1 year ago..... 1
 Somewhat better now than 1 year ago..... 2
 About the same..... 3
 Somewhat worse now than 1 year ago..... 4
 Much worse now than 1 year ago..... 5

The following items are about activities you might do during a typical day.
Does your health now limit you in these activities? If so, how much?

CIRCLE ONE NUMBER ON EACH LINE

Yes Limited a lot	Yes limited a little	No not limited At all
-------------------------	----------------------------	-----------------------------

3. **Vigorous activities**, such as
 running, lifting heavy objects,
 participating in strenuous sports

1 2 3

4. **Moderate activities**, such as
 moving a table, pushing a vacuum
 cleaner, bowling or playing golf

1 2 3

5. Lifting or carrying groceries

1 2 3

6. Climbing **several** flights of stairs

1 2 3

7. Climbing **one** flight of stairs

1 2 3

8. Bending, kneeling or stooping

1 2 3

9. Walking **more than a mile**

1 2 3

10. Walking **several blocks**

1 2 3

11. Walking **one block**

1 2 3

12. Bathing or dressing yourself

1 2 3

During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities **as a result of your physical health?**

CIRCLE ONE NUMBER ON EACH LINE

- | | Yes | No |
|---|------------|-----------|
| 13. Cut down the amount of time you spent on work or other activities | 1 | 2 |
| 14. Accomplished less than you would like | 1 | 2 |
| 15. Were limited in the kind of work or other activities | 1 | 2 |
| 16. Had difficulty performing the work or other activities (for example, it took extra effort | 1 | 2 |

During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities **as a result of any emotional problems** (such as feeling depressed or anxious)

CIRCLE ONE NUMBER ON EACH LINE

- | | Yes | No |
|---|------------|-----------|
| 17. Cut down the amount of time you spent on work or other activities | 1 | 2 |
| 18. Accomplished less than you would like | 1 | 2 |
| 19. Didn't do work or other activities as carefully as usual | 1 | 2 |
| 20. During the past 4 weeks , to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors or groups? | | |

(circle 1 number)

- Not at all..... 1
 Slightly..... 2
 Moderately..... 3
 Quite a bit..... 4
 Extremely..... 5

21. How much **bodily** pain have you had in the **past 4 weeks?**
(circle 1 number)

- None..... 1
 Very mild..... 2
 Mild..... 3
 Moderate..... 4
 Severe..... 5
 Very severe..... 6

22. During the **past 4 weeks**, how much did **pain** interfere with your normal work (including both work outside the home **and** housework)

(circle 1 number)

Not at all..... 1
 A little bit..... 2
 Moderately..... 3
 Quite a bit..... 4
 Extremely..... 5

These questions are about how you feel and how things have been with you **during the past 4 weeks**. For each question, please give the 1 answer that comes closest to the way you have been feeling. **How much of the time during the past 4 weeks...**

CIRCLE ONE NUMBER ON EACH LINE

All of the Time	Most of the Time	A Good Bit of the Time	Some of the Time	A Little of the Time	None of the Time
-----------------------	------------------------	------------------------------	------------------------	----------------------------	------------------------

23. Did you feel full of pep?

1 2 3 4 5 6

24. Have you been a very nervous person?

1 2 3 4 5 6

25. Have you felt so down in the dumps that nothing could cheer you up?

1 2 3 4 5 6

26. Have you felt calm and peaceful?

1 2 3 4 5 6

27. Did you have a lot of energy?

1 2 3 4 5 6

28. Have you felt downhearted and blue?

1 2 3 4 5 6

29. Did you feel worn out?

1 2 3 4 5 6

30. Have you been a happy person?

1 2 3 4 5 6

31. Did you feel tired?

1 2 3 4 5 6

32. During the **past 4 weeks**, how much of the time has your **physical health or emotional problems** interfered with your social activities (like visiting with friends, relatives, etc.)?

- All of the time..... 1
 Most of the time..... 2
 Some of the time.... 3
 A little of the time.... 4
 None of the time..... 5

How TRUE or FALSE is each of the following statements for you?

CIRCLE ONE NUMBER ON EACH LINE

Definitely True	Mostly True	Don't Know	Mostly False	Definitely False
--------------------	----------------	---------------	-----------------	---------------------

33. I seem to get sick a little easier than other people
 1 2 3 4 5
34. I am as healthy as anybody I know
 1 2 3 4 5
35. I expect my health to get worse.
 1 2 3 4 5
36. My health is excellent
 1 2 3 4 5

A2.12: GAD-7 questionnaire

GAD-7 Questionnaire

Date_____

Participant Study ID#_____

Over the last 2 weeks, how often have you been bothered by the following problems? <i>(Use "✓" to indicate your answer)</i>	Not at all	Several days	More than half the days	Nearly every day
1. Feeling nervous, anxious or on edge	0	1	2	3
2. Not being able to stop or control worrying	0	1	2	3
3. Worrying too much about different things	0	1	2	3
4. Trouble relaxing	0	1	2	3
5. Being so restless that it is hard to sit still	0	1	2	3
6. Becoming easily annoyed Or irritable	0	1	2	3
7. Feeling afraid as if something awful might happen	0	1	2	3

(For office coding: Total Score T_____ = _____ + _____ + _____)

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A2.13: PHQ-9 questionnaire

Patient Health Questionnaire-9 (PHQ-9)

Date _____

Participant Study ID# _____

Over the last 2 weeks, how often have you been bothered by any of the following problems? (Use "✓" to indicate your answer)	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3

FOR OFFICE CODING _____ + _____ + _____ + _____
=Total Score: _____

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all Somewhat difficult Very difficult Extremely difficult

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A3: Study forms (Stage 2)

A3.1: Invitation letter (Stage 2)

The Stage 2 participant information sheet is identical to Stage 1 with the following alterations/additions:

If you agree to participate in this study, information would be collected when you come to hospital for your clinic appointments. The aim of the study is to determine if any leg swelling present before weight loss surgery improves afterwards.

When you attend hospital for your pre-op. assessment, a member of the study team will check if you would like to take part.

A3.2: Information sheet (Stage 2)

The Stage 2 participant information sheet was identical to Stage 1 with the following alterations/additions:

What is the purpose of the study?

Persistent leg swelling (chronic leg oedema) is quite a common condition.....Our experience suggests it is particularly common in people with weight problems and may improve following weight loss surgery. We therefore aim to examine in more detail changes in swelling after such surgery.

Why have I been invited?

You are being invited to take part because you have been referred for bariatric surgery at Royal Derby Hospital. We are hoping to invite 75 patients to take part in this study.

What will happen to me if I take part?

If you agree to take part, you will be required to be assessed: at your appointment before you undergo bariatric surgery and at your routine follow-up appointments 3, 6, and 12 months after surgery. (The assessments would all take place when you come to the clinic for your routine appointments.) Several assessments are necessary in order to determine, using the measurement methods, whether any leg measurement changes are a result of fat loss, fluid loss, or both. Each assessment is expected to take 50 minutes and will involve completing up to 5 questionnaires and a clinical assessment which will check if you have swelling or not.

- **Questionnaires**

If swelling is not found to be present, we will ask you to complete 4 questionnaires; if swelling is found to be present, we will ask you to complete 5 questionnaires.

- **Clinical assessment**

- **Perometer**

We will measure the size and shape of your legs. This can be undertaken by one of two methods depending on your mobility. If you need to stay in a chair or examination couch during the assessment, we will measure the size of your legs at different points using a tape measure. However, if we are able to, we will use a device called a Perometer. You will be asked to stand with one leg in the frame of the Perometer while it is moved up and down your leg. The frame contains lights which are used to measure the size and shape of the limb. This is a non-painful method for calculating limb shape and size.

What are the possible benefits of taking part?

One benefit to taking part is that we may find that you have swelling and there could be direct benefits in improvement of your swelling as a result of bariatric surgery.

A3.3: Letter sent to GP (Stage 2)

The Stage 2 GP letter was identical to Stage 1 with the following alterations/additions:

The purpose of this study is to assess the changes in chronic oedema following bariatric surgery at Royal Derby Hospital. After bariatric surgery, the participants will be followed up for a year.

A3.4: Case report form (Stage 2, before surgery) (Smaller font and size to original)

CASE REPORT FORM

STUDY TITLE: Prevalence and Impact of Chronic Oedema in a Population of Patients Prior to and Following Bariatric Surgery (STAGE 2)

PRE-OPERATIVE ASSESSMENT

R&D Reference Number:

Participant Study ID No

--	--	--

Date of Assessment (dd/mm/yyyy): / /.....

Type of Facility: Out-Patient

CRF Final Version 1 (23rdMar16)

The Stage 2 pre-operative CRF is quite similar to the Stage 1 CRF. Therefore, the questions unique to the Stage 2 pre-operative CRF are listed below.

- **Before the *Presence and Classification of Swelling/Oedema* section:**

Type of bariatric surgery: Insertion of Gastric Balloons
 Insertion of Gastric Band
 Laparoscopic Gastric Bypass
 Sleeve Gastrectomy

- **Before the *Bioimpedance* section:**

Limb Volume Measurements:

Is leg swelling: (select one) Unilateral / Bilateral / None present

Measurements obtained? (Circle one and complete the appropriate section)

Perometer / Manual Full / Manual Shortened / None taken

(If "None taken", skip to bioimpedance)

Leg Perometer Measurement: N/A ☐

Please record the volume of right and left leg:

Measurement length: 53mm - mm

	Measurement 1 (mls)	Measurement 2 (mls)
Right Leg		
Left Leg		

Manual Measurements Full Length – N/A ☐

Please record the circumference of right and left, lower and upper leg:

Lower Leg Measurements	Right Leg (cm)	Left Leg (cm)
2cm above medial malleolus		
6cm above medial malleolus		
10cm above medial malleolus		
14cm above medial malleolus		
18cm above medial malleolus		
22cm above medial malleolus		
26cm above medial malleolus		
30cm above medial malleolus		
34cm above medial malleolus		
38cm above medial malleolus		
42cm above medial malleolus		
46cm above medial malleolus		
50cm above medial malleolus		

Upper Leg Measurements	Right Leg (cm)	Left Leg (cm)
4cm above the knee		
8cm above the knee		
12cm above the knee		
16cm above the knee		
20cm above the knee		
24cm above the knee		
28cm above the knee		
32cm above the knee		
36cm above the knee		
40cm above the knee		
44cm above the knee		

48cm above the knee		
52cm above the knee		
Total volumes (ml)		

- **The last page:**

IN CASE OF PATIENT WITHDRAWAL

All dates in **DD/MMM/YYYY** format

Date of patient's Withdrawal from the study: __ / __ / __ __

☐ Tick if N/A

Primary reason for Withdrawal

☐

- 1 Adverse Event
- 2 Protocol Violation
- 3 Withdrawal of Consent
- 4 Death
- 5 Loss to follow up
- 6 Other, please specify
- 7 N/A

A3.5: Case report form (Stage 2, after surgery)

CASE REPORT FORM

**STUDY TITLE: Prevalence and Impact of Chronic Oedema in a
Population of Patients Prior to and Following Bariatric Surgery
(STAGE 2)**

POST-OPERATIVE ASSESSMENT: months

R&D Reference Number:

Participant Study ID No

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Date of Assessment (dd/mm/yyyy): / /.....

Type of Facility: Out-Patient

CRF Final Version 1 (23rdMar16)

The Stage 2 post-operative CRF is quite similar to the Stage 2 pre-operative CRF. Therefore, the questions unique to the Stage 2 post-operative CRF are listed below.

- The Medical History section:***

Relevant medical history - precipitating factors:

Arthritis: Yes ☐ No ☐

If yes, provide details:

Any change since the last assessment?

.....

Diabetes: Yes ☐ No ☐

If yes, provide details:

Any change since the last assessment?

.....

Heart disease: Yes ☐ No ☐

If yes, provide details:

Any change since the last assessment?

.....

Hypertension: Yes ☐ No ☐

If yes, provide details:

Any change since the last assessment?

.....

Liver disease: Yes ☐ No ☐

If yes, provide details:

Any change since the last assessment?

.....

Neurological disorder: Yes ☐ No ☐

If yes, provide details:

Any change since the last assessment?

.....

Obstructive sleep apnoea: Yes ☐ No ☐

If yes, provide details:

Any change since the last assessment?

.....

Peripheral arterial disease: Yes ☐ No ☐

If yes, provide details:

Any change since the last assessment?

.....

Renal disease: Yes ☐ No ☐

If yes, provide details:

Any change since the last assessment?

.....

Other co-morbidities/complications (of obesity/oedema) Yes ☐ No ☐

If yes, provide details:

Any change since the last assessment?

.....

Other co-morbidities/complications (of obesity/oedema) Yes ☐ No ☐

If yes, provide details:

Any change since the last assessment?

.....

Any complications (study/non-study related): Yes ☐ No ☐

If yes, provide details: hypertension

.....

wound infection

.....

other

.....

Blood test results **Date:** N/A ☐

HbA1c (glycated haemoglobin):

List of medications before surgery:

Any change in medications? YES/NO If yes, provide details:

.....

• **Adjusted Presence and Classification of Swelling/Oedema section**

Presence and Classification of Swelling/Oedema

1. Does the patient have any swelling? Yes / No (circle one)

(If no, skip to question 9)

2. Does the area of swelling pit? Yes / No

2a. **If the swelling does pit**, please detail site(s) where pitting oedema is present (circle all that apply):

L toes / L foot / L lower leg / L upper leg / L buttocks / L abdomen

R toes / R foot / R lower leg / R upper leg / R buttocks / R abdomen

Vulva / Scrotum / Penis

Other

3. Are the tissues in the swollen area predominantly: Soft / Hard / N/A

4. Is there significant shape distortion in the affected limb?

Yes / No / N/A

5. What is the severity of the swelling (ISL Severity Staging)?

ISL stage

ISL stage I – This represents early onset of the condition where there is accumulation of tissue that subsides with limb elevation. The oedema may be pitting at this stage.

ISL stage II - Limb elevation alone rarely reduces swelling and pitting is manifest.

ISL stage III - The tissue is hard (fibrotic) and pitting is absent. Skin changes such as thickening, hyperpigmentation, increased skin folds, fat deposits and warty overgrowths develop.

• **Adjusted Skin Condition section**

Skin Condition

6. Stemmers sign:

Left Foot (circle only one): Positive / Negative / Equivocal

Right Foot (circle only one): Positive / Negative / Equivocal

7. Skin Conditions: Yes / No If yes, where?

7a. If yes, what type of skin conditions: (circle all that apply)

Eczema / Varicose eczema / Chronic lipodermatosclerosis /

Other (Specify)

8. In the patient's opinion, has the swelling: improved / grown worse / stayed the same / Don't know

9. History of Deep Vein Thrombosis (DVT) since last assessment?

Yes / No

9a. If yes, please detail site(s) and date(s) of DVT diagnosis (date:):

.....

- **Adjusted Wound Assessment + Precipitating Factors sections**

Wound Assessment (if applicable)

10. Has there been any change since the last assessment (wounds/ulcers healed or developed, etc.)?

.....
.....

PRECIPITATING FACTORS

11. Has the patient had cellulitis since the last assessment? Yes / No

(If no, skip to question 12)

11a. If **yes**: how many times

11b. Since the last assessment, has the patient had cellulitis in the affected areas due to the swelling? Yes / No

If **yes**, how many times

11c. Since the last assessment, has the patient been admitted to hospital as a result of cellulitis? Yes / No

If **yes**, how many times

12. Is the participant currently receiving treatment for oedema?

Yes / No

12a. If yes, are they receiving compression? Yes / No?

13. In the patient's opinion, is the swelling controlled? Yes / No /

Don't know

- **Last page**

END OF STUDY

Did the patient complete the study according to the protocol?

☐

1= Yes **0**= No

All dates in **DD/MMM/YYYY** format

Date of patient's Completion of study: __ / __ / __

☐

Tick if N/A

Date of patient's Withdrawal from the study: __ / __ / __

☐

Tick if N/A

Primary reason for Withdrawal

☐

1 Adverse Event

2 Protocol Violation

3 Withdrawal of Consent

4 Death

5 Loss to follow up

6 Other, please specify

7 N/A

Page 7 of 7

A4: Participant data (Stage 1)

A4.1: Demographic details (Stage 1)

Participant ID Number	Date of Assessment	Age	Gender	Weight (kg)	Height (m)
001	25/08/2016	51	F	152.2	1.65
002	25/08/2016	55	M	144.6	1.65
005	08/09/2016	35	F	147.2	1.69
006	08/09/2016	64	F	124.2	1.56
007	15/09/2016	52	F	140.0	1.63
008	15/09/2016	56	F	141.6	1.65
010	22/09/2016	50	M	180.2	1.75
011	22/09/2016	36	M	160.4	1.81
014	29/09/2016	43	M	236.0	1.93
017	06/10/2016	55	F	101.2	1.58
018	06/10/2016	47	M	156.0	1.89
023	27/10/2016	54	F	134.4	1.70
024	03/11/2016	52	M	126.0	1.71
025	10/11/2016	44	M	136.2	1.79
026	10/11/2016	39	M	209.2	1.89
029	17/11/2016	24	F	149.8	1.65
030	17/11/2016	23	F	116.6	1.69
031	24/11/2016	52	M	185.0	1.78
032	24/11/2016	68	F	113.4	1.52
033	24/11/2016	25	F	122.4	1.61
034	01/12/2016	54	F	144.0	1.62
035	01/12/2016	49	F	141.2	1.57
038	08/12/2016	64	F	119.2	1.54
039	08/12/2016	31	M	184.0	1.87
040	15/12/2016	23	F	155.6	1.68
041	15/12/2016	50	F	139.8	1.65
042	22/12/2016	23	F	130.4	1.59
044	29/12/2016	30	F	136.0	1.65
049	12/01/2017	51	F	106.0	1.54
050	12/01/2017	54	F	142.6	1.55
051	12/01/2017	56	M	120.0	1.64

Participant ID Number	BMI (kg/m²)	Level of obesity	Lower body mobility	Upper body mobility
001	55.9	Morbidly obese (MO)	Walks unaided (WU)	Full range
002	53.0	MO	Walks with aid (WA)	Limited
005	51.5	MO	WU	Full
006	51.0	MO	WA	Limited
007	52.7	MO	WU	Full
008	52.0	MO	WA	Full
010	58.8	MO	WU	Full
011	48.9	MO	WU	Full
014	63.5	MO	WA	Limited
017	40.6	MO	WU	Full
018	43.7	MO	WU	Full
023	46.5	MO	WA	Limited
024	43.1	MO	WU	Full
025	42.5	MO	WU	Full
026	58.6	MO	WU	Full
029	55.0	MO	WA; for long walks.	Full
030	40.8	MO	WU	Full
031	58.4	MO	WU	Full
032	49.1	MO	WA	Limited
033	47.2	MO	WA; stick.	Full
034	54.8	MO	WA; sometimes due to arthritis.	Full
035	57.3	MO	WU	Full
038	50.2	MO	WA; frame, mobility scooter.	Limited
039	52.7	MO	WU	Full
040	55.1	MO	WU	Full
041	51.3	MO	WU; but mobility limited.	Limited
042	51.6	MO	WU	Full
044	50.0	MO	WU	Full
049	44.8	MO	WA	Full
050	59.3	MO	WU	Full
051	44.6	MO	WA	Full

A4.2: Skin conditions and wound assessment (Stage 1)

Participant ID Number	Stemmers sign (LF)	Stemmers sign (RF)
001	Negative (Neg)	Neg
002	Neg	Neg
005	Neg	Neg
006	Neg	Pos
007	Equivocal (Eq)	Eq. For both legs: able to lift but not fully.
008	Positive (Pos)	Pos
010	Neg	Pos
011	Neg	Neg
014	Neg	Neg
017	Eq	Eq
018	Neg	Neg
023	Pos	Pos
024	Neg	Neg
025	Neg	Neg
026	Neg	Neg
029	Neg	Neg
030	Neg	Neg
031	Neg	Neg
032	Neg	Neg
033	Neg	Neg
034	Neg	Neg
035	Neg	Neg
038	Neg	Neg
039	Pos	Pos
040	Neg	Neg
041	Neg	Neg
042	Neg	Neg
044	Neg	Neg
049	Neg	Neg
050	Pos	Pos
051	Neg	Pos

Participant ID Number	Skin conditions?
001	N
002	N. But, both lower legs: dry (also bumps on left lower leg), hard skin.
005	N
006	Y; left and right lower legs, chronic lipodermatosclerosis.
007	Y; left and right lower legs; varicose eczema, chronic lipodermatosclerosis.
008	Y; lower legs, chronic lipodermatosclerosis.
010	Y; lower legs, haemosiderin staining.
011	
014	Y; left and right lower legs, chronic lipodermatosclerosis.
017	N
018	N
023	Y; left lower leg, dry skin.
024	
025	
026	Y; right lower leg, eczema.
029	Y; upper and lower legs, healed bite and anxiety scratch marks.
030	
031	Y; left and right lower legs; chronic lipodermatosclerosis, darkened skin.
032	N
033	
034	
035	
038	N
039	Y; left and right lower legs; eczema, lymphangiectasia.
040	N
041	N
042	
044	
049	
050	Y; right and left lower legs; dry skin, itchy.
051	N

Participant ID Number	DVT (with details)	Wound present (with details)
001	N	N
002	N	N
005	N	N
006	N	N. However, 1 week ago, the left leg leaked water for 2-3 days.
007	N	N
008	N	N. Healed wounds from cuts. Sensitive skin: bruising easily.
010	N	N
011	N	N
014	N	N. Lower leg (right and left) blisters.
017	N	N
018	N	N
023	N	N
024	Y	N
025	N	
026	N	Y. Right lower leg ulcer. Healed surgical wounds from right knee operations.
029	N	N
030	N	N
031	Y. 16 years ago, heparin medication, hospital. Left upper leg.	N
032	N	N
033	N	N. Healed surgical scar on left ankle.
034	N	N
035	N	N
038	N	N
039	N	Y. Pressure Ulcer: unanswered question. Right and left lower leg ulcers.
040	N	N
041	N	N
042	N	N
044	N	N
049	N	N
050	N	N
051	Y. Blood clots in both legs: left leg, 2001; right leg, 2008-2009? Possibly 2013? PE: May 2013	N

A4.3: Cellulitis history (Stage 1)

This table lists the participants with a history of cellulitis (or being told that they have cellulitis). The other participants said that they had not had cellulitis.

Participant ID Number	Participants with History of Cellulitis?
006	No. GP said cellulitis. But, the participant was not unwell. She had red inflamed legs and antibiotics (which worked) to bring the redness down.
007	Y. Definite cellulitis, twice. First: right leg, second: left leg. In past year, cellulitis in affected areas due to swelling, twice. In past year, admitted to hospital as a result of cellulitis; once.
008	Yes, once. Left leg, May 2015. Preventive antibiotics taken after every cut, etc. on left leg. In past year, cellulitis in affected areas due to swelling; once. In past year, admitted to hospital as a result of cellulitis; once.
014	Yes, once. End of nose (end of 2015), right lower leg; antibiotics given which helped, felt unwell. In past year, cellulitis in affected areas due to swelling; once: right leg. In past year, admitted to hospital as a result of cellulitis; twice: right leg, nose.
023	Yes, once. Right leg, as a child. Antibiotics. Felt unwell. GP was called and prescribed medication.
026	Yes, once. 2010: hospital and antibiotics.
031	Yes, once. 2-3 years ago. Antibiotics. Left lower leg.
038	Yes, once. Painful. Antibiotics. Unwell. Left lower leg, 1 week ago. In past year, cellulitis in affected areas due to swelling; once.
039	Yes, once; December 2015. Left lower leg. Led to the lymphoedema. In past year, cellulitis in affected areas due to swelling; once. In past year, admitted to hospital as a result of cellulitis; once.

A4.4: Classification of oedema (Stage 1)

Participant ID Number	Swelling present?	Pitting swelling?	Tissues in swollen area
001	Y	Y; left and right feet.	Soft
002	Y	Y; left and right: feet and lower legs.	Soft
005	Y	Y. Left and right lower legs. Left and right lower arms, both with negative Stemmers signs on the hands.	Soft
006	Y	Y; left and right: feet and lower legs.	Soft
007	Y	Y; left and right: feet and lower legs.	Soft
008	Y	Y; left foot and lower leg, right foot, right wrist (negative Stemmer's sign).	Soft
010	Y	Y; left foot and lower leg, right foot and lower leg.	Soft
011	N		
014	Y	Y; left foot and lower leg, right lower leg.	Soft
017	Yes, but NOT chronic oedema. Left and right lower arms, left and right lower legs.	N	Soft
018	Y	Y; left and right lower legs.	Soft
023	Y	Y; left foot and lower leg, right foot and lower leg.	Soft
024	N	N	
025	N		
026	Y	Y; left and right lower legs.	Soft
029	Yes, but NOT chronic oedema. Right ankle.	N	Soft
030	N	N	
031	Y	Y. Slight pitting. Left and right lower legs.	Hard
032	Y	Y; left and right lower legs.	Soft
033	N	N	
034	N	N	
035	N		
038	Y	Y. Left foot and lower leg. Right lower leg (Left upper leg and abdomen, right upper leg and abdomen: Question Mark).	Soft
039	Y	Y. Left foot and lower leg, Right foot and lower leg. 2 lumps on pubic area: unchecked, possible swelling.	Soft
040	N	N	
041	Y	Y; left lower leg.	Soft
042	N		
044	N		
049	Y	Y; left and right lower legs.	Soft
050	Y	Y; left and right lower legs, left and right ankles.	Soft
051	Y	Y; left and right lower legs, left and right ankles.	Soft

Participant ID Number	ISL stage	Duration of swelling/oedema
001	1	Was not aware of the swelling.
002	1	5-10 years
005	1	1-2 years
006	2	2-5 years
007	1	2-5 years
008	1	Greater than 10 years (Furosemide for 4-5 days = legs thinner; fluid retention)
010	1	Greater than 10 years (no one in his family suffers/ed from swollen legs as far as he is aware)
014	Stage 1. Swelling decreases after legs have been up, but they always stay red.	2-5 years (about 4 years. Weight increases = swelling increases)
017	1	2-5 years
018	1	Less than 6 months (participant has known about the swelling for 1-2 months)
023	Stage 1. Swelling down by morning.	Less than 6 months
026	1	Greater than 10 years (his right leg has had swelling for greater than 10 years. In the last 6 months, both legs have had swelling)
029	1	2-5 years
031	2	Greater than 10 years
032	1	Greater than 10 years (15 years ago)
038	1	1-2 years
039	2	6 months - 1 year (December 2015)
041	1	5-10 years (before the spinal surgery)
049	1	2-5 years
050	1	2-5 years
051	1	Greater than 10 years (2000-2001 - swelling started at the time of the first blood clot)

A4.5: Medical history (Stage 1)

(Participants not listed in this table did not have the listed medical conditions.)

Participant ID Number	Arthritis	Diabetes	Heart disease
001	N	Y; Type 2 (T2).	N
002	Yes (Y); degenerative disc disease.	Y; T2, insulin controlled.	N
006	Y; osteoarthritis (OA): back, neck, arms, fingers and right ankle.	N	N
007	N	N	Y; right heart failure (6 months ago), still treated. Echo: preserved left ventricular systolic function.
008	Y; OA: knees and ankles. Right ankle collapsed, has been wearing a boot for the past 18 months.	N	N
010	Y; right knee.	N	N
011	Y; right knee.	N	N
014	No (N); not diagnosed, but he thinks he has rheumatoid arthritis.	Y; T2.	Possible angina (AG). Seen cardiologist in Birmingham City Hospital - no AG. Extra beat.
017	N; although testing for it at present.	N; although currently testing.	Y; atrial fibrillation.
018	N	N	N; had palpitations in the past.
023	N	Y; T2, from 3 years ago.	N
024	N	Y; T2, developed in June 2009.	Y; ischaemic heart disease, April 2009. Heart attack (HA), age 44 (April 2009).
025	N	Y; T2, diagnosed in 2007. "Diet" controlled.	Y; AG, very occasional chest tightness. Angiogram - 2008? Coronary heart disease (CHD).
029	Y; right ankle after operation; falling trauma, 3-4 years ago.	N	N
031	Possibly. If so, widespread.	Y; T2, diagnosed in 2011.	Y; HA: 9 years ago (2007).
032	Y; OA.	Borderline.	N
033	Y; knees and ankles. Upcoming scans.	N	N
034	Y; OA: both knees. Considered for surgery if her weight decreases.	N	N
035	Y; hip.	N	N
038	Y; OA: left shoulder and knees.	Y; T2 for 10yrs, on insulin.	Y; AG. CHD. 2014: myocardial perfusion scan - mild severity stress induced ischaemia.
042	N	Borderline.	N
049	Y; OA: right knee.	Y; T2, diagnosed last year.	N
050	Y; OA: left knee and fingers (lumps). Left knee needs operation.	N	N
051	Y; OA: both knees.	Y; T2.	N

Participant ID Number	Hypertension	Neurological disorder	Obstructive sleep apnoea	Renal disease
001	Y; medication control.	N	N	N
002	N; but has medication.	N	Y; using continuous positive airway pressure (CPAP) machine.	N
005	Y; no medication.	N	N	N
007	N	N	Y; using CPAP machine (UCM), from 6 weeks ago. Good response.	Y; chronic kidney disease (CKD). Estimated glomerular filtration rate (eGFR) = 50.
010	N	N	Y; UCM.	N
011	N	N	No, but possible. Tests have been recommended and the participant has been referred for sleep studies.	N
014	Y; medication.	N	Y; given CPAP machine, but not using it due to panic attacks.	N
017	N	N	No, although currently testing. Epworth Score: 19.	N
018	N	N	Debatable.	N
025	N	Y; previous epilepsy up to age 15.	Y; UCM.	N
029	N	N	N; but medical notes had a question mark for obstructive sleep apnoea (OSA).	N
030	N	N	N; but possible test. Epworth score: 13.	N
031	Y; medication. Obesity hypertension, 2003.	N	Y; using inspiratory positive airway pressure (IPAP) machine. Epworth Score: 7. Unlimited.	N
032	N	N	Y; UCM.	N
034	Y; medication.	N	Y; UCM. Diagnosed 2 months ago.	N
038	Y; medication.	N	N	Y; cysts on kidneys. October 2012: CKD, Stage 3A without proteinuria.
041	Y; medication.	N	Suspected OSA. Needs sleep studies. Snoring. Epworth score: 3.	N
044	Y; occasional.	N	N	N
049	Y	N	Y; UCM.	N
050	Y; medication.	N	Y; UCM. Really helps.	N
051	N	Y; mini stroke, 5 years ago.	Has CPAP machine, but does not normally use it due to the dryness it causes. Struggles with sleeping.	N

Participant ID Number	Other co-morbidities/complications
002	1. Degenerative disc disease. Going to have back surgery - implant. 2. Mild glaucoma.
005	Polycystic ovary syndrome (PCOS).
006	1. Right fused ankle. 2. Back: soft tissue damage, due to car accidents. 3. Hypothyroid. 4. Lymphoedema in right leg. 5. Recurrent cellulitis in leg.
011	Reactive hypoglycemia.
014	1. Lymphoedema. Last saw the lymphoedema nurse in November 2015. 2. Asthma. 3. Fractured spine. 4. Vitamin D deficiency. 5. Possible fibromyalgia. 6. Hayfever. 7. Depression. 8. Hidradenitis suppurativa. 9. Possible bipolar disorder.
017	1. Fibromyalgia. 2. Hypothyroid. Thyroidectomy at 18.
018	Persistent, mild depression (DEP).
023	1. Problems with feet circulation. 2. Nerve damage in back, due to 2008 operation, which led to damage in legs. 3. Asthma. 4. Pseudo meningocele + spinal damage from draining fluid 5. Cholecystectomy.
024	1. 1998 - prolapsed lumbar intervertebral disc. 2. Hyperlipidaemia in 2001. 3. Nasal polyp, 2001. Nasal polypectomy, 2002. 4. Increased cholesterol.
025	Post-traumatic stress, early 2005.
026	1. Previous broken right ankle. 2. Right knee: in 2005 - dislocated knee + torn ligaments + ligament reconstruction + wound infections after surgery, about 2010 - haematoma which burst, resulting in surgery.
029	1. Anxiety and DEP. 2. Cholecystectomy. Needing reoperations due to bile leak. 3. Possible anaemia. 4. Broken right ankle due to falling trauma, 3-4 years ago.
030	1. Sometimes: weight-related fungal rashes around breasts. 2. PCOS? 3. Anxiety.
031	1. Chronic obstructive pulmonary disease (COPD). 2. Paraumbilical/epigastric hernia repair in 2002. 3. Mild pedal oedema. 4. Heart: left ventricle mildly dilated. 5. Some posterior wall hypokinesis.
032	1. Fibromyalgia. 2. Laparotomy: about 15 years ago, due to endometriosis. 3. Bilateral knee replacement. 4. Total abdominal hysterectomy and bilateral salpingo-oophorectomy.
033	1. Borderline personality disorder. 2. Due to mental health breakdown in 2013: deliberate car crash, both feet and right knee were fractured.
034	1. Pre-diabetes: impaired glucose tolerance. 2. DEP. 3. Occasional heartburn, mild.
035	1. Asthma. Using inhalers. 2. Co Endometriosis. 3. Stress incontinence. 4. Hip pain.
038	1. Sigmoidoscopy (diarrhoea) = normal. 2. Blood sugar level between 6 and 11, few hypos if any. 3. Enlarged liver.
039	1. Lymphoedema in both legs, 2015. Cellulitis in 2015. 2. Asymptomatic gallstones. 3. Hypospadias in infancy.
040	1. DEP. 2. Womb surgery.
041	1. Back pains. Spinal decompression surgery, lumbar - L3-5, in 2013 and 2015. Spinal nerves now stuck together with scar tissue. 2. Difficult airway/intubation for anesthesia. 3. Pancreatitis, which led to cholecystectomy. 4. Appendectomy.
042	1. PCOS. 2. Asthma. Using inhalers. 3. Cholecystectomy in 2015. 4. Fatty liver? 5. Impaired glucose tolerance.
044	Right-sided abdominal pain - musculoskeletal?
049	1. Osteoporosis. 2. Broken left ankle. 3. Depression. 4. Laparoscopy at age 21. 5. CIN 1, early cancer of the uterus?
050	1. Knee pain. 2. DEP. 3. Pain: hips, bottom of back, and legs.
051	Previous pulmonary embolism and deep vein thromboses.

A4.6: Medications (Stage 1)

Participant ID Number	List of current medications
001	Metformin (1 gram), twice a day; Glucalazide (80mg), twice a day; Sinvastatin (40mg), once a day; Lisinopril (20mg), once a day.
002	Bisoprolol (2.5mg); Losartan (50mg), once a day; Bumetanide (2mg), once a day; Sinvastatin (40mg), once a day; Vitamin D; Insulin Humalog Mix 25.
006	Furosemide (40 mg); Pregabalin (150mg), twice a day; LT (levothyroxine treatment) (50 micrograms); Co-codamol.
007	Bisoprolol (7.5mg); Spironolactone (25mg); Furosemide (120mg/day); Warfarin.
008	Furosemide (40mg); Venlafaxine; Morphine; Omeprazole; Naproxen.
011	Co-codamol.
014	Bisoprolol; Metformin (2 grams); Citalopram (30mg); Atorvastatin; Aspirin; Lansoprazole; Loratidine; Gabapentin; Amitriptyline; Laxatives; Salbutamol inhaler
017	NOAC? Ribaroxaban; Levothyroxine (125 micrograms); Fluoxetine (20mg); Pregabalin (150mg); Bisoprolol
018	None listed
023	Metformin; Oxycodone; Amitriptyline; Fluticasone; Ipratroprium; Salmeterol; Quinine (300mg); Meloxicam; Mirtazapine
024	Metformin (1 gram), twice a day; Atorvastatin; Bisoprolol (2.5mg); Clopidogrel; Aspirin (75mg)
025	Aspirin (75mg); Bisoprolol (5mg); Monomax SR 60 (Isosorbide Mononitrate) (60mg); Adalat LA 20 (20mg); Lansoprazole (20mg); Atorvastatin (80mg); Fentofibrate (micro ionised) (160mg); Omacor (1 gram); Citalopram (40mg), 2 per day; Oxcarbazepine (300mg), 2 per day
029	Sertraline (100mg), once daily
030	Fluoxetine (40mg); Contraceptive implant
031	Aspirin; Furosemide (80mg); Metformin; Ramipril; Clenil modulate; Salbutamol; Amlodipine; Bisoprolol; Simvastatin (20mg)
032	Allopuranol; Paracetamol; Orlistat; Amitriptyline; Vitamin D; Atorvastatin
033	Quetiapine; Duloxetine; Oramorph
034	Paracetamol; Tramadol; Ramipril; Amlodipine; Citalopram
035	Naproxen; Orlistat; Mirena coil; Duloxetine
038	Humulin I; NovoRapid Penfil Insulin with meals, carbohydrate monitoring; Metformin (1 gram), twice a day; Aspirin; Atorvastatin; Blood pressure tablets
040	Fluoxetine - 6 months
041	Ramipril (2.5mg capsules), one a day; Sertraline (100mg) tablets, one a day; Paracetamol (500mg) tablets, 2 four times a day; Amitriptyline (50mg) tablets, one at night; Omeprazole (20mg) gastro-resistant capsules, one or two a day; Oxycodone (10mg capsules), 1 four times a day (2 tablets if necessary at times); Cetirizine (10mg tablets), one a day
042	Fostair inhaler; Ventolin; Metformin; Cerelle
044	Tramadol (in the afternoon); Codeine (in the afternoon)
049	Enalapril (20mg); Atorvastatin (20mg); Metformin MR (500mg), twice a day; Proven (10mg)
050	Ramipril (10mg), once a day; Amlodipine (10mg), once a day; Indapamide (2.5mg), once a day; Lansoprazole (30mg), once a day; Paroxetine (20mg), once a day
051	Metformin; Warfarin; Atorvastatin (10mg); Ramitidine (300mg at night)

A4.7: Blood test results (Stage 1)

Participant ID Number	Blood Test Results Date	FBC - Hb (g/L)	HbA1c (mmol/mol)	LFT - Albumin (g/L)	TFT - TSH (mU/L)	UE - eGFR (mL/min/1.73m ²)	BNP result (ng/L)
001	25/08/16	140	43 (T2 Diabetes)	36	Not Recorded (N/R)	>60	N
002	26/08/16	126	69 (T2 Diabetes)	38	0.94	>60	154
005	08/09/16	155	36	36	5.12	>60	N
006	08/09/16	147	38	42	1.88	>60	81
007	15/09/16	N/R	35	35	N/R	47 (Chronic Kidney Disease)	862 - Right heart failure (6 months ago), still treated.
008	15/09/16	134	38	35	2.50	>60	N
010	22/09/16	145	N/R	39	3.50	>60	N
011	22/09/16	151	31	43	1.76	>60	N
014	16/09/16	159	46 (T2 Diabetes)	40	0.88	>60	N
018	06/10/16	177	33	39	1.64	>60	N
023	27/10/16	155	50 (T2 Diabetes)	35	2.32	>60	259 - Use clinical judgement for heart failure.
024	03/11/16	165	64 (T2 Diabetes)	41	2.51	>60	N
025	10/11/16	155	41	36	1.22	>60	N
030	17/11/16	148	29	40	2.10	>60	N
031	24/11/16	N/R	04/11/16 - 49 (T2 Diabetes)	04/11/16 - 41	N/R	25/11/16 - >60	25/11/16 - 671 - Heart attack: 9 years ago (2007).
032	24/11/16	N/R	05/12/16 - 43 (Borderline Diabetes)	N/R	N/R	N/R	N
034	01/12/16	141	42	39	1.69	>60	N
035	01/12/16	150	28	42	3.77	>60	N
038	08/12/16	28/11/16 - 115	N/R	07/11/16 - 40	07/11/16 - 2.38	28/11/16 - 48 - Cysts on kidneys. CKD, Stage 3A without proteinuria.	N
041	15/12/16	130	38	40	N/R	>60	N
042	22/12/16	146	33	40	2.44	>60	N
049	12/01/17	145	44 (T2 Diabetes)	33	2.03	>60	N
050	12/01/17	136	50 (T2 Diabetes)	39	1.83	>60	N

A4.8: EQ-5D questionnaire data and analysis (Stage 1)

Participant ID Number	Health State	Mobility	Self	Active	Pain	Depress	const01	const02	Euroqol
001	97.0	0	0	0	0	0	0	0	1
002	6.5	0.069	0.104	0.036	0.386	0	0.081	0.269	0.055
005	75.0	0	0	0	0.123	0.071	0.081	0	0.725
006	86.5	0.069	0	0.036	0.123	0.071	0.081	0	0.620
007	60.0	0	0	0	0.123	0	0.081	0	0.796
008	40.0	0.069	0.104	0.094	0.386	0.071	0.081	0.269	-0.074
010	70.0	0.069	0	0.036	0.123	0	0.081	0	0.691
011	54.0	0.069	0	0.036	0.123	0.071	0.081	0	0.620
014	0	0.069	0.104	0.036	0.386	0.236	0.081	0.269	-0.181
017	80.0	0.069	0.104	0.036	0.386	0.071	0.081	0.269	-0.016
018	50.0	0	0	0.036	0.123	0.071	0.081	0	0.689
023	50.0	0.069	0.104	0.036	0.386	0	0.081	0.269	0.055
024	95.0	0	0	0	0	0	0	0	1
025	60.0	0	0	0	0	0.071	0.081	0	0.848
026	75.0	0	0	0	0	0	0	0	1
029	40.0	0.069	0	0.036	0.123	0.071	0.081	0	0.620
030	77.0	0	0	0	0	0.071	0.081	0	0.848
031	Patient left before study assessment was completed.								
032	68.0	0.069	0	0.036	0.123	0	0.081	0	0.691
033	50.0	0.069	0.104	0.036	0.386	0.071	0.081	0.269	-0.016
034	30.0	0.069	0	0	0.123	0.071	0.081	0	0.656
035	70.0	0.069	0	0.036	0.123	0	0.081	0	0.691
038	0	0.069	0	0.094	0.386	0	0.081	0.269	0.101
039	90.0	0	0	0	0.123	0	0.081	0	0.796
040	50.0	0	0	0	0	0.236	0.081	0.269	0.414
041	30.0	0.069	0.104	0.036	0.386	0.071	0.081	0.269	-0.016
042	70.0	0	0	0	0.123	0	0.081	0	0.796
044	70.0	0.069	0	0	0.386	0	0.081	0.269	0.195
049	70.0	0.069	0	0.036	0.123	0.071	0.081	0	0.620
050	40.0	0.069	0	0.036	0.386	0.071	0.081	0.269	0.088
051	75.0	0	0	0.036	0.386	0	0.081	0.269	0.228

A4.9: GAD-7 and PHQ-9 questionnaire data (Stage 1)

Participant ID Number	GAD-7 Score	PHQ-9 Score	PHQ-9: Q10
001	0	0	
002	0	3	Extremely difficult
005	6	7	Somewhat difficult
006	14	20	Extremely difficult
007	12	13	Not difficult at all
008	15	20	Very difficult
010	1	8	Very difficult
011	10	16	Very difficult
014	21	27	Extremely difficult
017	20	14	
018	12	21	Very difficult
023	1	8	Not difficult at all
024	0	3	Somewhat difficult
025	9	12	
026	3	2	Not difficult at all
029	8	19	Somewhat difficult
030	14	19	Somewhat difficult
031	4	3	
032	Unable to locate = missing data.		
033	14	20	Extremely difficult
034	4	15	Not difficult at all
035	10	9	Somewhat difficult, Very difficult
038	0	15	Not difficult at all
039	2	8	
040	18	13	Somewhat difficult
041	8	15	Somewhat difficult
042	2	2	
044	Not found = missing data		
049	Did not complete: missing data	10 (+ 1 unanswered question)	Somewhat difficult
050	10	13	Very difficult
051	5	13	

A4.10: LYMQOL questionnaire data (Stage 1)

(Participants with no swelling have been removed from this table.)

Participant ID Number	Function	Appearance	Symptoms	Mood	Overall Quality of Life
001	1	1	1	1	9
002	3.6	3.4	3.8	1	5
005	UL: 1, LL: 1.4	UL: 1.4, LL: 2.4	UL: 1.3, LL: 1.4	UL: 2, LL: 2	UL: 7, LL: 7
006	3	3.3	2.4	1.8	6
007	2.6	4	3	3	7
008	UL: 2.8, LL: 4	UL: 3.6, LL: 3.7	UL: 1.8, LL: 2.2	UL: 2.2, LL: 2.3	UL: 2, LL: 2
010	1.6	2.7	1.2	1.2	8
014	3.7	2.1	4	4	0
017	Swelling present, but NOT chronic oedema	Swelling present, but NOT chronic oedema	Swelling present, but NOT chronic oedema	Swelling present, but NOT chronic oedema	Swelling present, but NOT chronic oedema
018	1.9	1.1	1	3.3	6
023	1.9	1.3	1.8	1.2	5
026	1.9	2	1.4	1.3	8
029	Swelling present, but NOT chronic oedema	Swelling present, but NOT chronic oedema	Swelling present, but NOT chronic oedema	Swelling present, but NOT chronic oedema	Swelling present, but NOT chronic oedema
031	Patient left before study assessment was completed.				
032	1.3	2.3	1	1.2	7
038	3.9	4	4	1.7	0
039	1	1.6	1.3	1.7	8
041	1	1.9	2.2	2.2	3
049	2.1	1.9	1.8	1	10
050	1.3	2.3	1.4	3.3	3
051	2.1	1.9	1.6	2.3	5

A4.11: SF-36 questionnaire data (Stage 1)

Participant ID Number	Physical Functioning	Role Limitations due to Physical Health	Role Limitations due to Emotional Problems	Energy/Fatigue	Emotional Well Being	Social Functioning	Pain	General Health	General Health (Compared to 1 Year Ago)
001	100	100	100.0	75	96	100.0	90.0	90	50
002	0	0	100.0	25	100	25.0	0	40	25
005	80	100	0	50	68	50.0	57.5	35	50
006	5	0	0	15	76	75.0	32.5	75	25
007	55	75	66.7	25	60	37.5	22.5	30	50
008	5	0	0	35	64	12.5	0	20	25
010	30	0	100.0	40	80	62.5	57.5	35	50
011	75	50	66.7	25	48	37.5	22.5	50	25
014	0	0	0	0	0	0	0	0	0
017	25	25	33.3	45	28	12.5	0	15	0
018	70	100	33.3	10	32	37.5	45.0	35	50
023	30	0	33.3	25	84	100.0	0	45	50
024	85	50	33.3	25	80	100.0	100.0	70	50
025	75	50	33.3	40	56	62.5	100.0	65	100
026	55	50	100.0	45	92	100.0	67.5	65	50
029	55	50	0	15	32	12.5	57.5	40	50
030	45	0	33.3	20	52	37.5	55.0	40	0
031	Patient left before study assessment was completed.								
032	5	25	33.3	55	100	100.0	22.5	45	50
033	5	0	0	15	56	25.0	22.5	50	50
034	20	25	66.7	45	52	62.5	45.0	30	25
035	30	50	100.0	40	88	62.5	57.5	40	50
038	10	0	0	30	76	0	0	30	0
039	80	100	66.7	55	72	75.0	100.0	75	75
040	65	100	100.0	50	56	100.0	100.0	15	50
041	35	0	66.7	10	80	25.0	22.5	25	25
042	80	100	100.0	65	88	75.0	80.0	55	75
044	80	50	66.7	40	96	100.0	0	45	50
049	50	100	100.0	65	84	75.0	77.5	50	100
050	20	0	0	10	68	62.5	10.0	55	50
051	0	0	9.0	55	52	0	10.0	40	25

A4.12: Summary of statistical results from EQ-5D, GAD-7 and PHQ-9 questionnaire data (Stage 1)

(Missing Data - EQ-5D: participant left before study assessment completion, GAD-7: participant did not complete questionnaire, GAD-7 and PHQ-9: two participants' questionnaires not located)

Statistical Results	EQ-5D (Euroqol)	GAD-7	PHQ-9
Histogram	Normally Distributed	Normally Distributed	Normally Distributed
Number of participants	30	28	29
Missing Data	1	3	2
Mean (Standard Deviation)	0.49 (0.37)	7.96 (6.42)	12 (6.87)
With Oedema			
Number of participants	18	17	18
Missing Data	1	2	1
Mean (Standard Deviation)	0.44 (0.40)	6.71 (6.33)	11.44 (7.63)
Without Oedema			
Number of participants	12	11	11
Missing Data		1	1
Mean (Standard Deviation)	0.56 (0.34)	9.91 (6.33)	12.91 (6.11)
Difference between the means	-0.12	-3.20	-1.47
95% Confidence Intervals (around mean difference)	Lower: -0.40 & Higher: 0.17	Lower: -8.24 & Higher: 1.83	Lower: -6.93 & Higher: 4.00
T-Test			
Levene's Test	0.143	0.725	0.382
p value	0.410	0.203	0.587

A4.13: Summary of statistical results from LYMQOL (lower limb) data (Stage 1)

(Missing Data: participant had oedema but did not complete LYMQOL questionnaire)

Statistical Results	LYMQOL Function	LYMQOL Appearance	LYMQOL Symptoms
Histogram	Normally Distributed	Normally Distributed	Skewed
With Oedema			
Number of participants	18	18	18
Missing Data	1	1	1
Mean (Standard Deviation)	2.18 (1.04)	2.38 (0.95)	
95% Confidence Intervals (around the mean)	Lower: 1.66 & Higher: 2.70	Lower: 1.91 & Higher: 2.85	
Median (Interquartile Range)			1.7 (1.28 to 2.55)
95% Confidence Intervals (around the median)			Lower: 1.33 & Higher: 2.34
Statistical Results	LYMQOL Mood	LYMQOL Quality of Life	
Histogram	Skewed	Normally Distributed	
With Oedema			
Number of participants	18	18	
Missing Data	1	1	
Mean (Standard Deviation)		5.5 (2.92)	
95% Confidence Intervals (around the mean)		Lower: 4.05 & Higher: 6.95	
Median (Interquartile Range)	1.75 (1.20 to 2.48)		
95% Confidence Intervals (around the median)	Lower: 1.20 & Higher: 2.30		

A4.14: Summary of statistical results from SF-36 questionnaire data (Stage 1)

(Missing Data: participant left before study assessment completion)

Statistical Results	SF-36 - Physical Function	SF-36 - Role Limitations (Physical Health)	SF-36 - Role Limitations (Emotional Problems)
Histogram	Normally Distributed	Normally Distributed	Skewed
Number of participants	30	30	30
Missing Data	1	1	1
Mean (Standard Deviation)	42.33 (31.40)	40 (40.26)	
Median (Interquartile Range)			33.30 (0 to 100)
With Oedema			
Number of participants	18	18	18
Missing Data	1	1	1
Mean (Standard Deviation)	35 (32.36)	36.11 (45.55)	
Median (Interquartile Range)			33.30 (0 to 100)
Without Oedema			
Number of participants	12	12	12
Mean (Standard Deviation)	53.33 (27.58)	45.83 (31.68)	
Median (Interquartile Range)			50.00 (33.00 to 91.68)
Difference between means	-18.33	-9.72	
95% Confidence Intervals (around mean difference)	Lower: -41.67 & Higher: 5.00	Lower: -38.62 & Higher: 19.17	
Difference between medians			-16.70
95% Confidence Intervals (around median difference)			Lower: -72.01 & Higher: 38.61
T-Test			
Levene's Test	0.518	0.010	
p value	0.119	0.496	Mann-Whitney U Test: 0.570

Statistical Results	SF-36 - Energy/Fatigue	SF-36 - Emotional Well Being	SF-36 - Social Functioning
Histogram	Normally Distributed	Skewed	Normally Distributed
Number of participants	30	30	30
Missing Data	1	1	1
Mean (Standard Deviation)	35 (19.03)		54.17 (34.48)
Median (Interquartile Range)		70.00 (52 to 85)	
With Oedema			
Number of participants	18	18	18
Missing Data	1	1	1
Mean (Standard Deviation)	34.72 (21.52)		52.08 (36.44)
Median (Interquartile Range)		76.00 (63 to 86)	
Without Oedema			
Number of participants	12.00	12.00	12.00
Mean (Standard Deviation)	35.42 (15.44)		57.29 (32.62)
Median (Interquartile Range)		56.00 (49 to 86)	
Difference between the means	-0.69		-5.21
95% Confidence Intervals (around mean difference)	Lower: -15.48 & Higher: 14.09		Lower: -31.92 & Higher: 21.50
Difference between medians		20.00	
95% Confidence Intervals (around median difference)		Lower: -1.01 & Higher: 41.01	
T-Test			
Levene's Test	0.162	Using Squared Data - 0.685	0.497
p value	0.924	0.165	0.693

Statistical Results	SF-36 - Pain	SF-36 - General Health	SF-36 - General Health (compared to 1 year ago)
Histogram	Normally Distributed	Normally Distributed	Normally Distributed
Number of participants	30	30	30
Missing Data	1	1	1
Mean (Standard Deviation)	41.83 (35.55)	43.50 (19.83)	42.50 (25.55)
With Oedema			
Number of participants	18	18	18
Missing Data	1	1	1
Mean (Standard Deviation)	34.17 (33.49)	43.89 (21.93)	41.67 (24.25)
Without Oedema			
Number of participants	12	12	12
Mean (Standard Deviation)	53.33 (36.86)	42.92 (17.12)	43.75 (28.45)
Difference between means	-19.17	0.97	-2.08
95% Confidence Intervals (around mean difference)	Lower: -45.77 & Higher: 7.44	Lower: -14.43 & Higher: 16.38	Lower: -21.92 & Higher: 17.75
T-Test			
Levene's Test	0.880	0.448	0.708
p value	0.151	0.898	0.831

A4.15: Full comparison of SF-36 questionnaire scores with HSE normative data (Stage 1)

	Female 16-24		Male 25-34	
	Study Mean (n=4, NCO)	HSE Population Norm	Study Mean (n=1, CO)	HSE Population Norm
Physical Functioning	61.3	90	80.0	94
Role Limitations due to Physical Health	62.5	90	100.0	91
Role Limitations due to Emotional Problems	58.3	84	66.7	90
Energy/Fatigue	37.5	63	55.0	68
Emotional Well Being (Mental Health in HSE Population Norm file)	57.0	73	72.0	78
Social Functioning	56.3	85	75.0	90
Pain	73.1	80	100.0	84
General Health	37.5	70	75.0	74
	Female 25-34		Female 35-44	
	Study Mean (n=2, NCO)	HSE Population Norm	Study Mean (n=1, CO)	HSE Population Norm
Physical Functioning	42.5	90	80.0	87
Role Limitations due to Physical Health	25.0	88	100.0	84
Role Limitations due to Emotional Problems	33.4	85	0	85
Energy/Fatigue	27.5	62	50.0	61
Emotional Well Being (Mental Health in HSE Population Norm file)	76.0	73	68.0	73
Social Functioning	62.5	86	50.0	86
Pain	11.3	80	57.5	78
General Health	47.5	74	35.0	73
	Male 35-44			
	Study Mean (n=4)	Study Mean (n=2, CO)	Study Mean (n=2, NCO)	HSE Population Norm
Physical Functioning	51.3	27.5	75.0	91
Role Limitations due to Physical Health	37.5	25.0	50.0	89
Role Limitations due to Emotional Problems	50.0	50.0	50.0	89
Energy/Fatigue	27.5	22.5	32.5	66
Emotional Well Being (Mental Health in HSE Population Norm file)	49.0	46.0	52.0	77
Social Functioning	50.0	50.0	50.0	88
Pain	47.5	33.8	61.3	82
General Health	45.0	32.5	57.5	73

	Male 45-54			
	Study Mean (n=3)	Study Mean (n=2, CO)	Study Mean (n=1, NCO)	HSE Population Norm
Physical Functioning	61.7	50.0	85.0	87
Role Limitations due to Physical Health	50.0	50.0	50.0	84
Role Limitations due to Emotional Problems	55.5	66.7	33.3	86
Energy/Fatigue	25.0	25.0	25.0	66
Emotional Well Being (Mental Health in HSE Population Norm file)	64.0	56.0	80.0	77
Social Functioning	66.7	50.0	100.0	87
Pain	67.5	51.3	100.0	78
General Health	46.7	35.0	70.0	69
	Female 45-54			
	Study Mean (n=8)	Study Mean (n=6, CO)	Study Mean (n=2, NCO)	HSE Population Norm
Physical Functioning	42.5	48.3	25.0	82
Role Limitations due to Physical Health	43.8	45.8	37.5	80
Role Limitations due to Emotional Problems	66.7	61.1	83.4	84
Energy/Fatigue	36.9	35.0	42.5	60
Emotional Well Being (Mental Health in HSE Population Norm file)	76.5	78.7	70.0	74
Social Functioning	65.6	66.7	62.5	85
Pain	40.6	37.1	51.3	74
General Health	45.6	49.2	35.0	70
	Female 55-64			
	Study Mean (n=4)	Study Mean (n=3, CO)	Study Mean (n=1, NCO)	HSE Population Norm
Physical Functioning	11.3	6.7	25.0	72
Role Limitations due to Physical Health	6.3	0	25.0	72
Role Limitations due to Emotional Problems	8.3	0	33.3	81
Energy/Fatigue	31.3	26.7	45.0	60
Emotional Well Being (Mental Health in HSE Population Norm file)	61.0	72.0	28.0	73
Social Functioning	25.0	29.2	12.5	83
Pain	8.1	10.8	0	69
General Health	35.0	41.7	15.0	65

	Male 55-64		Female 65-74	
	Study Mean (n=2, CO)	HSE Population Norm	Study Mean (n=1, CO)	HSE Population Norm
Physical Functioning	0	76	5.0	62
Role Limitations due to Physical Health	0	75	25.0	64
Role Limitations due to Emotional Problems	54.5	84	33.3	78
Energy/Fatigue	40.0	64	55.0	59
Emotional Well Being (Mental Health in HSE Population Norm file)	76.0	78	100.0	74
Social Functioning	12.5	84	100.0	82
Pain	5.0	74	22.5	69
General Health	40.0	64	45.0	64

A4.16: Bioimpedance assessment - right (Stage 1)

Participant ID Number	WBA R1 (FN)	WBA R1 (RZ)	WBA R1 (RI)	WBA R1 (RI/RZ)
001	obe-jb-01	536.83	403.65	0.7519
002	obe-rs-02	408.38	261.68	0.6408
005	obe-sp-005-5710	495.69	347.16	0.7004
006	obe-nf-006-5725	497.42	370.56	0.7450
007	obe-jg-007-5740	420.82	302.02	0.7177
010	obe-jb-010-5768	367.07	262.68	0.7156
011	obe-gg-011-5781	486.23	343.26	0.7060
014	obe-pc-014-5828	375.48	272.05	0.7245
017	obe-kc-017-5860	552.24	396.72	0.7184
018	obe-jk-018-5873	508.99	364.44	0.7160
023	obe-gp-023-5942	410.69	303.76	0.7396
024	obe-wm-024-5956	533.83	351.15	0.6578
025	obe-ma-025-5971	444.45	308.70	0.6946
026	obe-dd-026-5985	424.78	308.92	0.7272
029	obe-cd-029-6041	542.98	395.49	0.7284
030	obe-lb-030-6029	553.15	394.71	0.7136
032	obe-lp-032-6058	494.86	351.19	0.7097
033	obe-gk-033-6071	480.32	354.54	0.7381
034	obe-dc-034-0090	426.83	299.15	0.7009
035	obe-kc-035-0103	563.23	410.98	0.7297
038	obe-pb-038-6354	437.79	326.06	0.7448
039	obe-jw-039-6372	369.08	241.60	0.6546
040	obe-dw-040-6388	541.67	379.85	0.7013
041	obe-ja-041-6401	421.68	294.49	0.6984
042	obe-kh-042-6416	468.35	340.56	0.7271
044	obe-ht-044-6443	573.95	398.56	0.6944
049	obe-jt-049-6523	443.68	335.24	0.7556
050	obe-sk-050-6536	411.92	290.33	0.7048
051	obe-cl-051-6548	418.35	272.61	0.6516

Participant ID Number	WBA R2 (FN)	WBA R2 (RZ)	WBA R2 (RI)	WBA R2 (RI/RZ)
001	obe-jb-01	536.49	403.64	0.7524
002	obe-rs-02	392.88	284.56	0.7243
005	obe-sp-005-5711	497.97	348.64	0.7001
006	obe-nf-006-5726	488.74	384.13	0.7860
007	obe-jg-007-5741	421.46	302.21	0.7171
010	obe-jb-010-5769	373.63	264.15	0.7070
011	obe-gg-011-5782	487.73	343.93	0.7052
014	obe-pc-014-5829	377.54	272.53	0.7219
017	obe-kc-017-5861	553.13	397.44	0.7185
018	obe-jk-018-5874	509.64	363.93	0.7141
023	obe-gp-023-5943	411.02	304.27	0.7403
024	obe-wm-024-5957	533.62	350.76	0.6573
025	obe-ma-025-5972	444.87	308.97	0.6945
026	obe-dd-026-5986	424.70	309.36	0.7284
029	obe-cd-029-6042	542.56	396.15	0.7301
030	obe-lb-030-6030	554.61	396.45	0.7148
032	obe-lp-032-6059	496.73	351.60	0.7078
033	obe-gk-033-6072	476.87	353.41	0.7411
034	obe-dc-034-0091	426.38	299.34	0.7020
035	obe-kc-035-0104	563.82	411.57	0.7300
038	obe-pb-038-6355	437.74	327.86	0.7490
039	obe-jw-039-6373	374.06	243.61	0.6513
040	obe-dw-040-6389	543.41	381.54	0.7021
041	obe-ja-041-6402	421.75	294.68	0.6987
042	obe-kh-042-6417	475.46	342.98	0.7214
044	obe-ht-044-6444	575.30	399.38	0.6942
049	obe-jt-049-6524	443.65	335.32	0.7558
050	obe-sk-050-6537	411.39	290.92	0.7072
051	obe-cl-051-6549	417.89	272.92	0.6531

Participant ID Number	RA1 (FN)	RA1 (RZ)	RA1 (RI)	RA1 (RI/RZ)
001	obe-jb-01	290.51	211.01	0.7263
002	obe-rs-02	0	0	0
005	obe-sp-005-5712	282.39	195.60	0.6927
006	obe-nf-006-5727	330.49	253.21	0.7662
007	obe-jg-007-5742	239.94	169.69	0.7072
010	obe-jb-010-5770	222.36	143.33	0.6446
011	obe-gg-011-5783	249.34	167.73	0.6727
014	obe-pc-014-5830	219.13	159.35	0.7272
017	obe-kc-017-5862	250.10	183.63	0.7342
018	obe-jk-018-5875	258.17	183.84	0.7121
023	obe-gp-023-5944	269.49	196.25	0.7282
024	obe-wm-024-5958	232.96	152.87	0.6562
025	obe-ma-025-5973	216.73	153.38	0.7077
026	obe-dd-026-5987	234.04	165.66	0.7078
029	obe-cd-029-6043	317.74	229.51	0.7223
030	obe-lb-030-6031	273.25	201.53	0.7375
032	obe-lp-032-6060	233.92	164.71	0.7041
033	obe-gk-033-6073	258.74	190.76	0.7373
034	obe-dc-034-0092	220.55	154.02	0.6983
035	obe-kc-035-0105	298.90	212.59	0.7112
038	obe-pb-038-6356	247.90	177.83	0.7173
039	obe-jw-039-6374	238.99	151.93	0.6357
040	obe-dw-040-6390	264.51	184.15	0.6962
041	obe-ja-041-6403	225.73	157.13	0.6961
042	obe-kh-042-6418	247.04	185.97	0.7528
044	obe-ht-044-6445	301.66	210.32	0.6972
049	obe-jt-049-6525	249.86	187.97	0.7523
050	obe-sk-050-6538	227.46	158.45	0.6966
051	obe-cl-051-6550	209.61	121.92	0.5817

Participant ID Number	RA2 (FN)	RA2 (RZ)	RA2 (RI)	RA2 (RI/RZ)
001	obe-jb-01	290.25	210.33	0.7247
002	obe-rs-02	0	0	0
005	obe-sp-005-5713	283.38	195.97	0.6915
006	obe-nf-006-5729	327.56	250.33	0.7642
007	obe-jg-007-5743	240.52	170.06	0.7071
010	obe-jb-010-5772	227.94	142.85	0.6267
011	obe-gg-011-5784	248.31	167.50	0.6746
014	obe-pc-014-5831	218.28	159.18	0.7292
017	obe-kc-017-5863	250.38	183.50	0.7329
018	obe-jk-018-5876	259.44	183.85	0.7086
023	obe-gp-023-5945	269.49	196.76	0.7301
024	obe-wm-024-5959	231.32	151.27	0.6539
025	obe-ma-025-5974	217.95	154.41	0.7085
026	obe-dd-026-5988	233.84	165.77	0.7089
029	obe-cd-029-6044	317.73	229.59	0.7226
030	obe-lb-030-6032	273.92	201.36	0.7351
032	obe-lp-032-6061	234.15	164.71	0.7034
033	obe-gk-033-6074	258.78	191.02	0.7382
034	obe-dc-034-0093	220.43	153.92	0.6983
035	obe-kc-035-0106	299.16	212.59	0.7106
038	obe-pb-038-6357	247.31	178.22	0.7206
039	obe-jw-039-6375	239.44	152.01	0.6349
040	obe-dw-040-6391	264.74	184.42	0.6966
041	obe-ja-041-6404	225.75	157.59	0.6981
042	obe-kh-042-6419	246.78	185.42	0.7514
044	obe-ht-044-6446	299.68	209.03	0.6975
049	obe-jt-049-6526	249.65	187.72	0.7519
050	obe-sk-050-6539	230.01	159.56	0.6937
051	obe-cl-051-6551	207.94	122.09	0.5871

Participant ID Number	RL1 (FN)	RL1 (RZ)	RL1 (RI)	RL1 (RI/RZ)
001	obe-jb-01	220.53	173.16	0.7852
002	obe-rs-02	143.69	108.87	0.7577
005	obe-sp-005-5714	194.14	138.63	0.7141
006	obe-nf-006-5730	133.36	115.06	0.8628
007	obe-jg-007-5744	153.87	115.21	0.7487
010	obe-jb-010-5773	132.93	106.69	0.8026
011	obe-gg-011-5785	209.87	157.33	0.7497
014	obe-pc-014-5832	138.66	100.32	0.7235
017	obe-kc-017-5864	272.68	194.79	0.7144
018	obe-jk-018-5878	200.80	154.16	0.7677
023	obe-gp-023-5946	142.64	111.73	0.7833
024	obe-wm-024-5960	268.05	176.97	0.6602
025	obe-ma-025-5975	204.40	141.51	0.6923
026	obe-dd-026-5989	167.63	128.40	0.7660
029	obe-cd-029-6045	201.55	152.10	0.7547
030	obe-lb-030-6033	254.65	177.45	0.6968
032	obe-lp-032-6063	243.70	175.80	0.7214
033	obe-gk-033-6075	188.65	142.24	0.7540
034	obe-dc-034-0094	185.31	132.90	0.7172
035	obe-kc-035-0107	235.57	182.64	0.7753
038	obe-pb-038-6358	169.34	138.78	0.8195
039	obe-jw-039-6377	110.04	78.27	0.7113
040	obe-dw-040-6393	255.91	185.76	0.7259
041	obe-ja-041-6405	174.14	124.95	0.7175
042	obe-kh-042-6420	197.74	143.41	0.7252
044	obe-ht-044-6447	248.93	172.65	0.6936
049	obe-jt-049-6527	174.94	134.89	0.7711
050	obe-sk-050-6540	161.02	118.39	0.7353
051	obe-cl-051-6552	180.44	134.09	0.7431

Participant ID Number	RL2 (FN)	RL2 (RZ)	RL2 (RI)	RL2 (RI/RZ)
001	obe-jb-01	220.78	173.35	0.7852
002	obe-rs-02	143.64	108.84	0.7577
005	obe-sp-005-5715	194.50	138.99	0.7146
006	obe-nf-006-5731	133.72	114.91	0.8593
007	obe-jg-007-5745	154.06	115.39	0.7490
010	obe-jb-010-5774	133.24	107.01	0.8031
011	obe-gg-011-5786	210.56	158.17	0.7512
014	obe-pc-014-5833	138.51	100.38	0.7247
017	obe-kc-017-5865	273.16	194.88	0.7134
018	obe-jk-018-5880	200.58	154.16	0.7686
023	obe-gp-023-5947	142.49	111.92	0.7855
024	obe-wm-024-5961	268.64	177.33	0.6601
025	obe-ma-025-5976	204.70	141.42	0.6909
026	obe-dd-026-5990	167.57	128.74	0.7683
029	obe-cd-029-6046	201.72	152.39	0.7555
030	obe-lb-030-6034	254.97	177.77	0.6972
032	obe-lp-032-6064	243.37	176.32	0.7245
033	obe-gk-033-6076	188.79	142.63	0.7555
034	obe-dc-034-0095	185.30	133.19	0.7188
035	obe-kc-035-0108	236.13	182.48	0.7728
038	obe-pb-038-6359	169.44	139.07	0.8208
039	obe-jw-039-6378	110.30	78.36	0.7104
040	obe-dw-040-6394	255.75	186.89	0.7308
041	obe-ja-041-6406	173.58	124.93	0.7197
042	obe-kh-042-6421	198.17	143.30	0.7231
044	obe-ht-044-6448	248.70	172.85	0.6950
049	obe-jt-049-6528	175.00	135.21	0.7726
050	obe-sk-050-6541	161.30	118.12	0.7323
051	obe-cl-051-6553	180.22	133.87	0.7428

A4.17: Bioimpedance assessment - left (Stage 1)

Participant ID Number	WBA L1 (FN)	WBA L1 (RZ)	WBA L1 (RI)	WBA L1 (RI/RZ)
001	obe-jb-01	535.60	404.68	0.7556
002	obe-rs-02	370.71	274.69	0.7410
005	obe-sp-005-5703	493.33	350.40	0.7103
006	obe-nf-006-5717	467.12	356.61	0.7634
007	obe-jg-007-5734	450.39	328.85	0.7301
010	obe-jb-010-5762	380.22	263.86	0.6940
011	obe-gg-011-5775	508.60	358.57	0.7050
014	obe-pc-014-5822	359.97	252.63	0.7018
017	obe-kc-017-5852	524.14	374.73	0.7149
018	obe-jk-018-5866	596.01	393.88	0.6609
023	obe-gp-023-5936	435.36	322.59	0.7410
024	obe-wm-024-5949	558.84	363.83	0.6510
025	obe-ma-025-5965	443.07	303.99	0.6861
026	obe-dd-026-5979	445.84	323.80	0.7263
029	obe-cd-029-6035	526.43	384.16	0.7297
030	obe-lb-030-6023	551.80	396.36	0.7183
032	obe-lp-032-6052	485.29	350.31	0.7219
033	obe-gk-033-6065	484.67	360.34	0.7435
034	obe-dc-034-0084	390.15	270.58	0.6935
035	obe-kc-035-0096	559.81	410.31	0.7329
038	obe-pb-038-6348	432.86	323.22	0.7467
039	obe-jw-039-6360	349.68	230.28	0.6585
040	obe-dw-040-6382	522.78	364.66	0.6975
041	obe-ja-041-6395	411.00	293.54	0.7142
042	obe-kh-042-6409	475.54	345.72	0.7270
044	obe-ht-044-6436	577.42	407.91	0.7064
049	obe-jt-049-6517	462.68	353.17	0.7633
050	obe-sk-050-6529	425.48	296.88	0.6978
051	obe-cl-051-6542	428.53	294.79	0.6879

Participant ID Number	WBA L2 (FN)	WBA L2 (RZ)	WBA L2 (RI)	WBA L2 (RI/RZ)
001	obe-jb-01	535.55	403.67	0.7537
002	obe-rs-02	371.90	275.75	0.7415
005	obe-sp-005-5704	493.62	350.20	0.7095
006	obe-nf-006-5718	468.35	358.01	0.7644
007	obe-jg-007-5735	458.98	332.19	0.7238
010	obe-jb-010-5763	398.62	266.37	0.6682
011	obe-gg-011-5776	510.32	359.48	0.7044
014	obe-pc-014-5823	360.37	253.30	0.7029
017	obe-kc-017-5853	524.79	374.86	0.7143
018	obe-jk-018-5867	604.33	396.07	0.6554
023	obe-gp-023-5937	433.90	324.09	0.7469
024	obe-wm-024-5950	562.52	366.70	0.6519
025	obe-ma-025-5966	440.57	303.69	0.6893
026	obe-dd-026-5980	444.99	323.65	0.7273
029	obe-cd-029-6036	526.44	384.98	0.7313
030	obe-lb-030-6024	552.21	396.42	0.7179
032	obe-lp-032-6053	487.84	350.33	0.7181
033	obe-gk-033-6066	484.77	360.97	0.7446
034	obe-dc-034-0085	391.08	270.83	0.6925
035	obe-kc-035-0097	559.31	411.29	0.7354
038	obe-pb-038-6349	432.27	324.33	0.7503
039	obe-jw-039-6361	348.34	230.14	0.6607
040	obe-dw-040-6383	523.80	365.28	0.6974
041	obe-ja-041-6396	410.34	294.12	0.7168
042	obe-kh-042-6410	477.00	345.70	0.7247
044	obe-ht-044-6437	576.07	408.56	0.7092
049	obe-jt-049-6518	462.81	353.81	0.7645
050	obe-sk-050-6530	426.66	297.67	0.6977
051	obe-cl-051-6543	419.11	289.12	0.6898

Participant ID Number	LA1 (FN)	LA1 (RZ)	LA1 (RI)	LA1 (RI/RZ)
001	obe-jb-01	250.95	135.94	0.5417
002	obe-rs-02	213.82	154.17	0.7210
005	obe-sp-005-5705	281.64	202.24	0.7181
006	obe-nf-006-5719	306.06	229.60	0.7502
007	obe-jg-007-5736	256.14	182.13	0.7111
010	obe-jb-010-5764	244.10	144.65	0.5926
011	obe-gg-011-5777	276.42	194.18	0.7025
014	obe-pc-014-5824	202.86	142.14	0.7007
017	obe-kc-017-5854	246.69	180.52	0.7318
018	obe-jk-018-5868	339.85	247.84	0.7293
023	obe-gp-023-5938	286.48	201.86	0.7046
024	obe-wm-024-5952	255.72	165.66	0.6478
025	obe-ma-025-5967	201.62	138.62	0.6875
026	obe-dd-026-5981	237.60	169.06	0.7115
029	obe-cd-029-6037	308.61	223.71	0.7249
030	obe-lb-030-6025	264.20	196.88	0.7452
032	obe-lp-032-6054	246.06	171.93	0.6987
033	obe-gk-033-6067	262.03	193.13	0.7371
034	obe-dc-034-0086	218.01	147.89	0.6784
035	obe-kc-035-0098	304.90	217.34	0.7128
038	obe-pb-038-6350	278.21	204.14	0.7338
039	obe-jw-039-6367	232.72	150.11	0.6450
040	obe-dw-040-6384	235.52	165.36	0.7021
041	obe-ja-041-6397	227.10	160.50	0.7067
042	obe-kh-042-6411	244.84	177.31	0.7242
044	obe-ht-044-6439	290.03	203.10	0.7003
049	obe-jt-049-6519	269.03	207.67	0.7719
050	obe-sk-050-6531	239.37	164.64	0.6878
051	obe-cl-051-6544	208.95	136.20	0.6518

Participant ID Number	LA2 (FN)	LA2 (RZ)	LA2 (RI)	LA2 (RI/RZ)
001	obe-jb-01	299.02	210.98	0.7056
002	obe-rs-02	214.16	154.41	0.7210
005	obe-sp-005-5706	281.96	202.74	0.7190
006	obe-nf-006-5720	304.63	229.11	0.7521
007	obe-jg-007-5737	257.17	182.31	0.7089
010	obe-jb-010-5765	248.59	147.58	0.5937
011	obe-gg-011-5778	277.22	195.13	0.7039
014	obe-pc-014-5825	203.23	142.68	0.7021
017	obe-kc-017-5855	247.29	181.12	0.7324
018	obe-jk-018-5870	333.80	252.52	0.7565
023	obe-gp-023-5939	283.57	205.00	0.7229
024	obe-wm-024-5953	256.69	166.21	0.6475
025	obe-ma-025-5968	201.43	138.73	0.6887
026	obe-dd-026-5982	237.98	169.37	0.7117
029	obe-cd-029-6038	307.93	223.54	0.7259
030	obe-lb-030-6026	263.64	197.33	0.7485
032	obe-lp-032-6055	246.39	171.90	0.6977
033	obe-gk-033-6068	261.78	193.27	0.7383
034	obe-dc-034-0087	218.11	147.90	0.6781
035	obe-kc-035-0099	304.97	217.34	0.7127
038	obe-pb-038-6351	278.37	204.22	0.7336
039	obe-jw-039-6368	236.01	152.40	0.6457
040	obe-dw-040-6385	231.45	162.80	0.7034
041	obe-ja-041-6398	226.66	160.04	0.7061
042	obe-kh-042-6412	246.62	184.28	0.7472
044	obe-ht-044-6440	289.95	203.19	0.7008
049	obe-jt-049-6520	269.42	208.44	0.7737
050	obe-sk-050-6532	238.55	164.54	0.6898
051	obe-cl-051-6545	208.43	136.13	0.6531

Participant ID Number	LL1 (FN)	LL1 (RZ)	LL1 (RI)	LL1 (RI/RZ)
001	obe-jb-01	212.38	166.48	0.7839
002	obe-rs-02	138.89	109.41	0.7877
005	obe-sp-005-5708	191.75	135.87	0.7086
006	obe-nf-006-5723	140.45	115.11	0.8196
007	obe-jg-007-5738	153.95	116.11	0.7542
010	obe-jb-010-5766	140.02	110.38	0.7883
011	obe-gg-011-5779	203.74	145.55	0.7144
014	obe-pc-014-5826	137.93	100.17	0.7262
017	obe-kc-017-5856	244.00	170.28	0.6979
018	obe-jk-018-5871	210.08	158.39	0.7540
023	obe-gp-023-5940	149.53	118.95	0.7955
024	obe-wm-024-5954	273.55	181.75	0.6644
025	obe-ma-025-5969	213.41	148.40	0.6954
026	obe-dd-026-5983	182.10	136.09	0.7473
029	obe-cd-029-6039	196.19	144.58	0.7369
030	obe-lb-030-6027	257.44	179.12	0.6958
032	obe-lp-032-6056	226.22	165.43	0.7313
033	obe-gk-033-6069	193.08	149.42	0.7739
034	obe-dc-034-0088	153.47	108.56	0.7074
035	obe-kc-035-0101	228.77	175.08	0.7653
038	obe-pb-038-6352	132.94	109.51	0.8238
039	obe-jw-039-6370	101.49	74.92	0.7382
040	obe-dw-040-6386	260.65	179.47	0.6885
041	obe-ja-041-6399	160.22	119.15	0.7437
042	obe-kh-042-6413	207.85	148.69	0.7154
044	obe-ht-044-6441	244.60	177.69	0.7265
049	obe-jt-049-6521	172.06	132.55	0.7704
050	obe-sk-050-6533	164.23	120.75	0.7352
051	obe-cl-051-6546	176.83	130.89	0.7402

Participant ID Number	LL2 (FN)	LL2 (RZ)	LL2 (RI)	LL2 (RI/RZ)
001	obe-jb-01	212.40	166.88	0.7857
002	obe-rs-02	139.19	109.73	0.7883
005	obe-sp-005-5709	191.95	136.17	0.7094
006	obe-nf-006-5724	140.68	114.80	0.8160
007	obe-jg-007-5739	154.15	116.02	0.7526
010	obe-jb-010-5767	140.35	110.35	0.7862
011	obe-gg-011-5780	204.09	145.90	0.7149
014	obe-pc-014-5827	138.17	100.38	0.7265
017	obe-kc-017-5859	244.02	170.44	0.6985
018	obe-jk-018-5872	209.98	158.63	0.7555
023	obe-gp-023-5941	149.53	119.10	0.7965
024	obe-wm-024-5955	273.67	181.93	0.6648
025	obe-ma-025-5970	213.64	148.14	0.6934
026	obe-dd-026-5984	181.76	136.21	0.7494
029	obe-cd-029-6040	196.10	144.90	0.7389
030	obe-lb-030-6028	257.87	180.11	0.6985
032	obe-lp-032-6057	226.79	164.80	0.7267
033	obe-gk-033-6070	193.06	149.67	0.7753
034	obe-dc-034-0089	153.54	108.66	0.7077
035	obe-kc-035-0102	229.08	175.47	0.7660
038	obe-pb-038-6353	133.08	114.34	0.8592
039	obe-jw-039-6371	101.39	75.11	0.7408
040	obe-dw-040-6387	261.30	180.04	0.6890
041	obe-ja-041-6400	160.36	119.44	0.7448
042	obe-kh-042-6414	208.92	149.80	0.7170
044	obe-ht-044-6442	244.89	177.75	0.7258
049	obe-jt-049-6522	172.29	132.57	0.7695
050	obe-sk-050-6534	164.48	120.61	0.7333
051	obe-cl-051-6547	176.53	130.86	0.7413

A4.18: Tissue dielectric constant data (Stage 1)

Participant ID Number	Additional Information	Foot (R1)	Foot (R2)	Foot (R3)	Foot (L1)	Foot (L2)	Foot (L3)
002		53.4	54.3	52.7	52.3	50.9	51.8
005		44.2	42.2	44.4	42.0	42.6	42.8
006		58.5	58.1	55.7	46.5	52.1	50.2
007		49.6	50.2	48.1	49.1	49.0	48.8
010		30.6	30.7	31.2	35.9	35.7	35.6
011		28.8	30.2	30.4	33.6	33.6	32.4
014		36.9	37.6	37.7	38.8	39.4	37.5
017		33.5	32.2	31.5	44.9	45.0	44.3
018		37.6	38.1	38.1	32.6	32.7	32.4
023		52.6	52.7	52.3	53.8	53.9	53.1
024	Below knee, left set: picture linked with measurements possibly indicates local swelling.	31.1	30.7		31.9	32.3	
025		46.1	47.2	47.6	37.0	38.0	39.2
026		42.0	40.3	42.5	43.3	43.2	43.8
029		36.5	36.7		43.9	45.2	43.7
030		35.5	35.2	35.5	35.4	34.8	
032		26.2	25.1	26.4	29.6	29.8	29.9
033		34.2	34.2		29.5	29.5	
034		41.3	41.2	41.9	41.6	41.6	
035		41.2	41.0		36.6	36.1	36.4
038		42.8	39.2		37.7	37.2	
039		47.7	46.5		38.7	37.5	38.0
040		28.2	29.0		29.9	29.7	
041		50.7	49.1		42.3	41.2	
042	Foot measurements, C.I. Comment: the high TDC measurements for both feet and the sock marks indicate the possibility of swelling present.	44.3	43.0	47.0	40.3	41.9	39.3
044		38.0	38.9		38.4	38.3	37.7
049		38.7	41.6	43.9	50.4	49.1	
050		43.8	42.5		41.1	43.8	
051		33.1	34.9		34.2	34.9	

Participant ID Number	Ankle (R1)	Ankle (R2)	Ankle (R3)	Ankle (L1)	Ankle (L2)	Ankle (L3)
002	46.1	45.5	46.7	46.4	47.3	48.8
005	30.7	30.1	26.6	34.7	33.1	34.2
006	42.8	41.5	41.6	39.5	37.4	38.9
007	34.6	36.0	35.0	36.1	37.8	38.2
010	28.2	28.0	28.2	21.4	22.8	21.7
011	25.4	25.8	25.9	26.0	26.0	26.7
014	30.0	30.5	30.3	30.3	30.6	31.3
017	32.1	31.4	32.4	29.3	28.7	29.3
018	31.2	31.4	31.8	31.1	31.5	31.3
023	39.3	39.2		44.1	44.1	43.9
024	23.9	24.7	24.7	25.8	25.9	25.3
025	34.8	35.5	35.1	37.4	37.2	37.2
026	35.0	33.7	35.3	34.6	33.7	33.9
029	32.3	31.9		40.3	38.5	39.8
030	28.9	28.5	30.2	26.8	28.2	
032	23.6	23.8		25.3	25.2	
033	28.4	30.1	29.8	32.1	31.3	
034	33.2	33.5	33.5	34.1	33.1	
035	22.9	22.4		23.4	23.4	22.7
038	34.1	35.1		37.7	36.5	
039	42.7	43.3	40.9	42.4	41.9	
040	29.9	30.1		31.2	29.9	
041	44.4	46.1		42.6	42.3	44.5
042	37.4	37.4	37.9	34.3	30.3	31.7
044	28.7	29.8		28.5	30.9	
049	32.0	32.0		34.9	34.9	35.7
050	38.3	35.7		36.3	35.7	
051	25.9	26.2		24.8	24.8	

Participant ID Number	Below Knee (R1)	Below Knee (R2)	Below Knee (R3)	Below Knee (L1)	Below Knee (L2)	Below Knee (L3)
002	41.4	43.6	43.2	47.4	46.6	46.5
005	40.6	40.8	40.8	34.8	34.9	34.5
006	43.8	43.7	42.6	41.5	42.3	41.7
007	48.6	47.0	47.6	51.5	51.5	51.5
010	35.8	34.4	35.4	42.4	42.1	41.9
011	26.0	26.0	26.2	26.0	26.0	26.6
014	30.4	30.4	30.2	34.7	32.9	33.6
017	28.9	28.2	28.5	28.8	26.6	27.8
018	32.3	33.7	32.5	36.2	34.8	35.1
023	36.2	36.2	35.9	39.1	39.3	38.7
024	29.4	28.9		34.9	35.0	34.5
025	37.3	36.9	38.1	41.0	40.2	40.1
026	33.9	32.1	31.7	32.3	32.4	32.6
029	30.3	30.5		35.6	36.1	
030	30.8	30.9		35.9	35.8	
032	31.0	32.1	32.2	36.1	34.7	34.7
033	33.2	32.3		33.2	32.3	
034	36.2	36.2		41.4	42.3	41.9
035	31.7	31.3		29.9	29.9	
038	44.0	42.5	41.9	48.7	48.9	
039	31.5	28.0	29.9	35.4	32.5	29.3
040	31.8	32.0		32.1	32.3	
041	39.1	38.7		41.2	41.4	
042	32.5	32.4	32.1	32.5	32.5	
044	28.5	27.8		28.4	27.6	
049	53.3	59.0	47.7	49.9	55.1	46.3
050	52.4	51.5		47.8	45.6	
051	28.6	27.4		25.0	25.3	

Participant ID Number	Above Knee (R1)	Above Knee (R2)	Above Knee (R3)	Above Knee (L1)	Above Knee (L2)	Above Knee (L3)
002	37.5	38.4	38.6	39.3	39.0	39.0
005	31.8	32.4	32.3	30.6	31.7	30.5
006	27.1	26.9	27.2	28.8	28.9	28.1
007	29.9	29.7	29.7	30.7	30.9	30.8
010	39.7	39.7	39.1	28.5	28.0	27.4
011	28.0	27.1	27.6	28.0	27.3	27.1
014	28.3	30.1	29.0	32.1	31.6	30.6
017	25.9	25.3	25.6	25.5	26.5	26.3
018	29.0	30.3	31.3	29.1	30.0	29.9
023	26.8	26.8	27.3	26.4	26.2	26.2
024	24.7	25.1		27.1	27.9	27.5
025	35.7	35.6	35.3	35.6	35.9	34.6
026	32.5	32.1	30.9	31.9	32.7	32.5
029	25.9	26.1		26.3	26.5	
030	28.8	28.2		28.5	28.4	
032	28.8	29.3		30.7	31.3	
033	29.5	29.5		28.9	29.3	
034	29.7	29.7	29.7	29.9	29.8	
035	27.4	26.8		26.9	27.1	
038	27.3	27.1		30.7	30.2	
039	32.0	31.9		34.1	32.6	
040	29.9	29.9		29.9	30.7	32.0
041	35.9	35.4		35.9	35.7	
042	32.6	32.7		33.1	33.1	
044	28.9	28.7		28.4	28.0	
049	32.8	32.8	32.6	27.4	27.9	28.1
050	30.0	31.0		31.0	31.9	
051	25.2	22.1		20.7	22.7	

Participant ID Number	Below Groin (R1)	Below Groin (R2)	Below Groin (R3)	Below Groin (L1)	Below Groin (L2)	Below Groin (L3)
002	37.9	36.4	36.8	39.3	38.9	39.6
005	28.5	29.0	29.0	30.4	30.7	30.8
006	25.4	25.5	24.2	25.2	24.6	24.5
007	25.2	25.5	25.3	27.2	27.3	27.7
010	31.6	29.5	30.3	26.4	26.4	26.7
011	23.4	22.8	22.8	24.0	24.9	25.2
014	36.2	34.2	36.2	36.5	36.2	36.2
017	23.8	23.9	24.2	25.5	25.4	25.7
018	27.7	27.3	28.9	27.0	26.9	26.3
023	24.2	24.2	24.5	22.5	22.5	
024	26.0	26.7	25.8	26.2	25.7	25.9
025	32.6	33.2	33.4	27.6	29.9	30.8
026	29.8	29.9		32.3	32.3	
029	30.0	30.3		29.1	30.1	
030	28.2	28.0		28.0	27.5	
032	34.5	34.8		36.7	36.9	
033	27.1	26.7		29.5	30.3	29.5
034	33.7	34.3		36.1	35.9	
035	24.5	25.1	24.6	23.5	23.5	
038	27.1	25.4		28.4	28.5	
039	34.1	34.1		33.8	32.4	
040	34.9	35.7		34.8	34.5	
041	30.1	29.3		26.7	27.6	
042	30.8	31.1		32.8	30.7	31.3
044	32.8	33.3		31.3	33.3	
049	33.9	34.9		31.8	33.3	
050	35.0	36.3		32.0	32.0	
051	18.3	19.8		22.1	24.1	

Participant ID Number	Abdominal Wall (R1)	Abdominal Wall (R2)	Abdominal Wall (R3)	Abdominal Wall (L1)	Abdominal Wall (L2)	Abdominal Wall (L3)
002	44.3	44.3	44.6	48.2	46.4	47.6
005	35.1	33.6	33.1	37.7	37.8	37.2
006	24.7	25.0	25.2	27.5	26.0	26.5
007	41.8	40.6	41.0	40.8	41.0	41.0
010	52.4	52.4	52.4	39.1	37.6	38.5
011	32.0	30.3	31.7	33.5	33.0	33.5
014	31.6	31.6	32.7	32.5	33.9	33.00
017	26.3	26.0	26.6	28.5	28.7	28.5
018	33.0	32.9	32.9	35.3	35.1	35.8
023	30.4	30.4		28.8	28.8	
024	30.9	31.2	29.2	28.5	28.5	28.6
025	32.6	32.3	34.2	36.7	38.7	36.8
026	37.1	37.7	35.7	34.9	34.9	
029	33.3	33.1		33.3	34.3	34.5
030	30.1	29.7		29.5	29.5	
032	31.6	31.5		36.8	37.2	
033	34.7	34.9		34.6	34.7	
034	28.8	28.1	29.3	26.6	26.2	
035	26.6	26.4	27.4	28.3	28.0	
038	32.0	31.0		30.7	31.0	
039	27.7	28.3		27.9	28.4	
040	36.9	36.9		36.6	35.7	
041	33.6	34.1		32.4	32.3	
042	35.7	35.5		36.2	35.8	
044	37.8	36.8		30.1	31.1	
049	28.4	27.9		27.4	26.3	
050	28.7	28.3		30.1	30.3	
051	26.7	25.9		25.2	22.4	

A4.19: Bioimpedance whole body analysis data (CO, Stage 1)

Participant ID Number	TBW (litres) - R	TBW (litres) Average - R	TBW (litres) - L	TBW (litres) Average - L
001 (CO)	42.56 42.55	42.56	42.40 42.52	42.46
002 (CO)	58.99 53.61	56.30	54.40 54.25	54.33
005 (CO)	49.35 49.22	49.29	48.81 48.85	48.83
006 (CO)	39.22 37.41	38.32	39.83 39.70	39.77
007 (CO)	50.31 50.31	50.31	47.24 47.07	47.16
010 (CO)	66.11 66.15	66.13	63.46 67.02	65.24
014 (CO)	80.14 80.16	80.15	85.17 84.97	85.07
017 (CO)	36.10 36.06	36.08	37.57 37.57	37.57
018 (CO)	38.25 38.32	38.29	37.30 37.25	37.28
023 (CO)	51.70 51.63	51.67	49.63 49.32	49.48
026 (CO)	68.69 68.58	68.64	66.60 66.58	66.59
032 (CO)	38.80 38.81	38.81	38.62 38.70	38.66
038 (CO)	41.42 41.17	41.30	41.62 39.47	40.55
039 (CO)	79.17 78.86	79.02	81.60 81.55	81.58
041 (CO)	52.49 52.46	52.48	52.19 52.05	52.12
049 (CO)	38.87 38.86	38.87	37.38 37.31	37.35
050 (CO)	48.92 48.79	48.86	48.36 48.28	48.32
051 (CO)	53.25 53.17	53.21	49.70 50.30	50.00

Participant ID Number	ECF (litres) - R	ECF (litres) Average - R	ECF (litres) - L	ECF (litres) Average - L
001 (CO)	25.66 25.67	25.67	25.70 25.70	25.70
002 (CO)	30.27 31.06	30.67	32.29 32.22	32.26
005 (CO)	27.63 27.55	27.59	27.72 27.71	27.72
006 (CO)	23.41 23.69	23.55	24.41 24.37	24.39
007 (CO)	28.88 28.85	28.87	27.60 27.26	27.43
010 (CO)	37.83 37.39	37.61	36.07 35.81	35.94
014 (CO)	46.46 46.29	46.38	47.78 47.75	47.77
017 (CO)	20.74 20.72	20.73	21.48 21.46	21.47
018 (CO)	21.90 21.89	21.90	19.72 19.53	19.63
023 (CO)	30.63 30.61	30.62	29.46 29.53	29.50
026 (CO)	39.97 39.98	39.98	38.70 38.75	38.73
032 (CO)	22.02 21.96	21.99	22.30 22.23	22.27
038 (CO)	24.72 24.72	24.72	24.90 24.33	24.62
039 (CO)	41.47 41.10	41.29	42.99 43.10	43.05
041 (CO)	29.30 29.30	29.30	29.81 29.84	29.83
049 (CO)	23.56 23.56	23.56	22.92 22.90	22.91
050 (CO)	27.56 27.59	27.58	26.97 26.92	26.95
051 (CO)	27.77 27.79	27.78	27.33 27.73	27.53

Participant ID Number	ICF (litres) - R	ICF (litres) Average - R	ICF (litres) - L	ICF (litres) Average - L
001 (CO)	16.90 16.88	16.89	16.70 16.82	16.76
002 (CO)	28.72 22.54	25.63	22.11 22.03	22.07
005 (CO)	21.72 21.67	21.70	21.09 21.14	21.12
006 (CO)	15.81 13.72	14.77	15.42 15.33	15.38
007 (CO)	21.43 21.46	21.45	19.63 19.82	19.73
010 (CO)	28.27 28.76	28.52	27.38 31.21	29.30
014 (CO)	33.68 33.87	33.78	37.39 37.23	37.31
017 (CO)	15.36 15.34	15.35	16.09 16.11	16.10
018 (CO)	16.35 16.44	16.40	17.58 17.72	17.65
023 (CO)	21.07 21.01	21.04	20.17 19.80	19.99
026 (CO)	28.71 28.60	28.66	27.90 27.83	27.87
032 (CO)	16.78 16.84	16.81	16.32 16.47	16.40
038 (CO)	16.70 16.45	16.58	16.71 15.14	15.93
039 (CO)	37.71 37.76	37.74	38.61 38.46	38.54
041 (CO)	23.19 23.16	23.18	22.38 22.21	22.30
049 (CO)	15.31 15.30	15.31	14.47 14.41	14.44
050 (CO)	21.35 21.21	21.28	21.39 21.35	21.37
051 (CO)	25.48 25.39	25.44	22.37 22.56	22.47

Participant ID Number	FFM (kg) - R	FFM (kg) Average - R	FFM (kg) - L	FFM (kg) Average - L
001 (CO)	58.15 58.13	58.14	57.93 58.08	58.01
002 (CO)	80.59 73.23	76.91	74.32 74.11	74.22
005 (CO)	67.42 67.24	67.33	66.68 66.73	66.71
006 (CO)	53.58 51.11	52.35	54.41 54.24	54.33
007 (CO)	68.74 68.73	68.74	64.53 64.31	64.42
010 (CO)	90.31 90.36	90.34	86.69 91.55	89.12
014 (CO)	109.48 109.50	109.49	116.35 116.08	116.22
017 (CO)	49.32 49.26	49.29	51.32 51.33	51.33
018 (CO)	52.26 52.36	52.31	50.96 50.89	50.93
023 (CO)	70.63 70.53	70.58	67.81 67.38	67.60
026 (CO)	93.83 93.69	93.76	90.98 90.96	90.97
032 (CO)	53.00 53.01	53.01	52.77 52.86	52.82
038 (CO)	56.58 56.25	56.42	56.85 53.93	55.39
039 (CO)	108.16 107.73	107.95	111.47 111.41	111.44
041 (CO)	71.70 71.66	71.68	71.29 71.11	71.20
049 (CO)	53.10 53.08	53.09	51.07 50.97	51.02
050 (CO)	66.83 66.66	66.75	66.07 65.95	66.01
051 (CO)	72.75 72.64	72.70	67.89 68.71	68.30

Participant ID Number	FM (kg) - R	FM (kg) Average - R	FM (kg) - L	FM (kg) Average - L	BMI (kg/m ²)
001 (CO)	94.05 94.07	94.06	94.27 94.12	94.20	55.90
002 (CO)	64.01 71.37	67.69	70.28 70.49	70.39	53.11
005 (CO)	79.78 79.96	79.87	80.52 80.47	80.50	51.54
006 (CO)	70.62 73.09	71.86	69.79 69.96	69.88	51.04
007 (CO)	71.26 71.27	71.27	75.47 75.69	75.58	52.69
010 (CO)	89.89 89.84	89.87	93.51 88.65	91.08	58.84
014 (CO)	126.52 126.50	126.51	119.65 119.92	119.79	63.36
017 (CO)	51.88 51.94	51.91	49.88 49.87	49.88	40.54
018 (CO)	48.94 48.84	48.89	50.24 50.31	50.28	40.54
023 (CO)	63.77 63.87	63.82	66.59 67.02	66.81	46.51
026 (CO)	115.37 115.51	115.44	118.22 118.24	118.23	58.56
032 (CO)	60.40 60.39	60.40	60.63 60.54	60.59	49.08
038 (CO)	62.62 62.95	62.79	62.35 65.27	63.81	50.26
039 (CO)	75.84 76.27	76.06	72.53 72.59	72.56	52.62
041 (CO)	68.10 68.14	68.12	68.51 68.69	68.60	51.35
049 (CO)	52.90 52.92	52.91	54.93 55.03	54.98	44.70
050 (CO)	75.77 75.94	75.86	76.53 76.65	76.59	59.35
051 (CO)	47.25 47.36	47.31	52.11 51.29	51.70	44.62

A4.20: Bioimpedance whole body analysis data (NCO, Stage 1)

Participant ID Number	TBW (litres) - R	TBW (litres) Average - R	TBW (litres) - L	TBW (litres) Average - L
011 (NCO)	55.92	55.90	54.34	54.30
	55.87		54.26	
024 (NCO)	48.20	48.23	47.22	47.09
	48.25		46.96	
025 (NCO)	56.31	56.30	57.13	57.10
	56.28		57.07	
029 (NCO)	43.46	43.42	44.28	44.23
	43.37		44.18	
030 (NCO)	41.65	41.58	41.43	41.43
	41.50		41.43	
033 (NCO)	42.08	42.09	41.51	41.47
	42.10		41.43	
034 (NCO)	58.94	58.92	63.19	63.19
	58.89		63.18	
035 (NCO)	44.92	44.90	44.91	44.85
	44.87		44.79	
040 (NCO)	46.95	46.88	48.34	48.32
	46.80		48.29	
042 (NCO)	43.67	43.63	43.23	43.26
	43.59		43.29	
044 (NCO)	9.26	9.26	9.07	9.06
	9.25		9.05	

Participant ID Number	ECF (litres) - R	ECF (litres) Average - R	ECF (litres) - L	ECF (litres) Average - L
011 (NCO)	31.56	31.53	30.63	30.60
	31.50		30.56	
024 (NCO)	25.37	25.37	24.60	24.55
	25.37		24.50	
025 (NCO)	31.26	31.25	31.33	31.39
	31.24		31.45	
029 (NCO)	25.33	25.34	25.86	25.86
	25.35		25.86	
030 (NCO)	23.76	23.74	23.80	23.80
	23.72		23.79	
033 (NCO)	24.87	24.93	24.72	24.72
	24.99		24.72	
034 (NCO)	24.33	24.34	25.83	25.81
	24.35		25.79	
035 (NCO)	19.27	19.27	19.35	19.36
	19.26		19.36	
040 (NCO)	26.32	26.30	26.95	26.94
	26.27		26.92	
042 (NCO)	25.41	25.28	25.15	25.13
	25.15		25.10	
044 (NCO)	5.14	5.14	5.12	5.13
	5.13		5.13	

Participant ID Number	ICF (litres) - R	ICF (litres) Average - R	ICF (litres) - L	ICF (litres) Average - L
011 (NCO)	24.36 24.37	24.37	23.71 23.70	23.71
024 (NCO)	22.84 22.88	22.86	22.62 22.46	22.54
025 (NCO)	25.05 25.04	25.05	25.80 25.63	25.72
029 (NCO)	18.13 18.03	18.08	18.42 18.32	18.37
030 (NCO)	17.88 17.77	17.83	17.63 17.64	17.64
033 (NCO)	17.21 17.11	17.16	16.78 16.71	16.75
034 (NCO)	34.61 34.54	34.58	37.36 37.39	37.38
035 (NCO)	25.65 25.62	25.64	25.56 25.43	25.50
040 (NCO)	20.63 20.53	20.58	21.38 21.37	21.38
042 (NCO)	18.26 18.44	18.35	18.08 18.19	18.14
044 (NCO)	4.12 4.12	4.12	3.95 3.92	3.94

Participant ID Number	FFM (kg) - R	FFM (kg) Average - R	FFM (kg) - L	FFM (kg) Average - L
011 (NCO)	76.39 76.32	76.36	74.23 74.13	74.18
024 (NCO)	65.85 65.91	65.88	64.51 64.15	64.33
025 (NCO)	76.93 76.88	76.91	78.04 77.97	78.01
029 (NCO)	59.37 59.25	59.31	60.49 60.36	60.43
030 (NCO)	56.89 56.69	56.79	56.60 56.60	56.60
033 (NCO)	57.48 57.52	57.50	56.70 56.60	56.65
034 (NCO)	80.51 80.44	80.48	86.33 86.31	86.32
035 (NCO)	61.37 61.30	61.34	61.35 61.19	61.27
040 (NCO)	64.15 63.93	64.04	66.03 65.96	66.00
042 (NCO)	59.65 59.55	59.60	59.06 59.13	59.10
044 (NCO)	12.66 12.64	12.65	12.39 12.36	12.38

Participant ID Number	FM (kg) - R	FM (kg) Average - R	FM (kg) - L	FM (kg) Average - L	BMI (kg/m ²)
011 (NCO)	84.01 84.08	84.05	86.17 86.27	86.22	48.96
024 (NCO)	60.15 60.09	60.12	61.49 61.85	61.67	43.09
025 (NCO)	59.27 59.32	59.30	58.16 58.23	58.20	42.51
029 (NCO)	90.43 90.55	90.49	89.31 89.44	89.38	55.02
030 (NCO)	59.71 59.91	59.81	60.00 60.00	60.00	40.82
033 (NCO)	64.92 64.88	64.90	65.70 65.80	65.75	47.22
034 (NCO)	63.49 63.56	63.53	57.67 57.69	57.68	54.87
035 (NCO)	79.83 79.90	79.87	79.85 80.01	79.93	57.28
040 (NCO)	91.45 91.67	91.56	89.57 89.64	89.61	55.13
042 (NCO)	70.75 70.85	70.80	71.34 71.27	71.31	51.58
044 (NCO)	-11.26 -11.24	-11.25	-10.99 -10.96	-10.98	0.51

A4.21: Summary of statistical results from fluid measurement (WBA) data (Stage 1)

[Missing Data: seven participants did not complete bioimpedance assessment or were excluded from total bioimpedance/WBA analysis due to invalidity (see A4.21 for further information)]

Statistical Results	TBW (Litres) - R	TBW (Litres) - L	ECF (Litres) - R	ECF (Litres) - L
Histogram	Skewed	Skewed	Skewed	Skewed
Number of participants	24	24	24	24
Missing Data	7	7	7	7
Mean (Standard Deviation)				
Median (Interquartile Range)	48.55 (42.21 to 56.30)	47.74 (41.72 to 56.41)	25.99 (24.44 to 31.11)	26.40 (24.57 to 31.19)
With Oedema				
Number of participants	14	14	14	14
Missing Data	5	5	5	5
Mean (Standard Deviation)				
Median (Interquartile Range)	50.99 (40.69 to 66.76)	48.90 (40.36 to 65.58)	28.33 (24.43 to 38.20)	27.48 (24.56 to 36.64)
Without Oedema				
Number of participants	10	10	10	10
Missing Data	2	2	2	2
Mean (Standard Deviation)				
Median (Interquartile Range)	45.89 (43.09 to 56.00)	45.97 (42.81 to 55.00)	25.31 (24.19 to 27.54)	25.47 (24.36 to 27.86)
Difference between the means				
95% Confidence Intervals (around mean difference)				
Difference between the medians	5.10	2.93	3.02	2.01
95% Confidence Intervals (around median difference)	Lower: -9.06 & Higher: 19.26	Lower: -11.43 & Higher: 17.30	Lower: -4.36 & Higher: 10.39	Lower: -4.51 & Higher: 8.53
T-Test				
Levene's Test	Using Natural Log Data:	Using Reciprocal	Using Natural Log	Using Reciprocal
p value	0.336	0.600	0.068	0.092

Statistical Results	ICF (Litres) - R	ICF (Litres) - L	FFM (kg) - R	FFM (kg) - L
Histogram	Normal	Skewed	Skewed	Skewed
Number of participants	24	24	24	24
Missing Data	7	7	7	7
Mean (Standard Deviation)	22.85 (6.33)			
Median (Interquartile Range)		21.38 (16.98 to 25.67)	66.32 (57.66 to 76.91)	65.21 (56.99 to 77.06)
With Oedema				
Number of participants	14	14	14	14
Missing Data	5	5	5	5
Mean (Standard Deviation)	23.14 (7.13)			
Median (Interquartile Range)		20.68 (16.28 to 28.23)	69.66 (55.59 to 91.20)	66.81 (55.13 to 89.58)
Without Oedema				
Number of participants	10	10	10	10
Missing Data	2	2	2	2
Mean (Standard Deviation)	22.45 (5.34)			
Median (Interquartile Range)		21.96 (18.02 to 25.56)	62.69 (58.86 to 76.50)	62.80 (58.49 to 75.14)
Difference between the means	0.69			
95% Confidence Intervals (around mean difference)	Lower: -4.86 & Higher: 6.23			
Difference between the medians		-1.28	6.97	4.01
95% Confidence Intervals (around median difference)		Lower: -8.12 & Higher: 5.56	Lower: -12.38 & Higher: 26.32	Lower: -15.63 & Higher: 23.64
T-Test				
Levene's Test	0.232	Using Natural Log Data:	Using Natural Log Data:	Using Reciprocal
p value	0.800	0.852	0.336	0.600

Statistical Results	FM (kg) - R	FM (kg) - L	BMI (kg/m ²) - R	BMI (kg/m ²) - L
Histogram	Skewed	Skewed	Normal	Normal
Number of participants	24	24	24	24
Missing Data	7	7	7	7
Mean (Standard Deviation)			51.55 (5.96)	51.55 (5.96)
Median (Interquartile Range)	71.04 (61.00 to 88.42)	70.85 (60.86 to 88.59)		
With Oedema				
Number of participants	14	14	14	14
Missing Data	5	5	5	5
Mean (Standard Deviation)			52.90 (5.75)	52.90 (5.75)
Median (Interquartile Range)	71.57 (62.19 to 90.92)	71.48 (63.01 to 91.86)		
Without Oedema				
Number of participants	10	10	10	10
Missing Data	2	2	2	2
Mean (Standard Deviation)			49.65 (6.02)	49.65 (6.02)
Median (Interquartile Range)	67.85 (60.04 to 85.66)	68.53 (59.55 to 87.01)		
Difference between the means			3.25	3.25
95% Confidence Intervals (around mean difference)			Lower: -1.78 & Higher: 8.29	Lower: -1.78 & Higher: 8.29
Difference between the medians	3.72	2.95		
95% Confidence Intervals (around median difference)	Lower: -15.42 & Higher: 22.85	Lower: -16.40 & Higher: 22.29		
T-Test				
Levene's Test	Using Natural Log Data:	Using Natural Log Data:	0.641	0.641
p value	0.720	0.542	0.193	0.193

A4.22: Excluded Stage 1 participants from bioimpedance data

Participant ID Number	Exclusion Reason	Exclusion Information
005	Invalid bioimpedance results	Participant had both upper and lower limb pitting oedema (having primary lymphoedema or genetically prone to having lymphoedema). Without a control arm, bioimpedance was invalid.
008	No bioimpedance	Participant could not lay on her back (at that time, bioimpedance was only completed lying down).
017	Invalid bioimpedance results	Participant had both upper and lower limb non-pitting swelling (potentially lipoedema).
018	Invalid WBA results	The wrong participant data (age, gender, height, weight) was used.
031	No bioimpedance	Participant left before study assessment was completed.
041	Invalid bioimpedance results	Participant only had oedema in her left lower limb, therefore bioimpedance was invalid.
044	Invalid WBA results	The results were inaccurate.

A4.23 Summary of statistical results from R_{zero} and $R_{infinity}$ data (Stage 1)

(See A4.21 for Missing Data information)

	Right	Left	Right	Left
Statistical Results	R_0 upper limb / R_0 lower limb	R_0 upper limb / R_0 lower limb	(R_i/R_0) lower limb / (R_i/R_0) upper limb	(R_i/R_0) lower limb / (R_i/R_0) upper limb
Histogram	Skewed	Normal	Skewed	Skewed
Number of participants	26	26	26	26
Missing Data	5	5	5	5
Mean (Standard Deviation)		1.45 (0.38)		
Median (Interquartile Range)	1.31 (1.14 to 1.57)		1.06 (1.01 to 1.10)	1.05 (1.02 to 1.10)
With Oedema				
Number of participants	15	15	15	15
Missing Data	4	4	4	4
Mean (Standard Deviation)		1.61 (0.36)		
Median (Interquartile Range)	1.43 (1.29 to 1.69)		1.08 (1.03 to 1.13)	1.08 (1.04 to 1.15)
Without Oedema				
Number of participants	11	11	11	11
Missing Data	1	1	1	1
Mean (Standard Deviation)		1.18 (0.233)		
Median (Interquartile Range)	1.19 (1.06 to 1.27)		1.02 (0.98 to 1.05)	1.03 (0.98 to 1.04)
Difference between the means		0.43		
95% Confidence Intervals (around mean difference)		Lower: 0.16 & Higher: 0.69		
Difference between the medians	0.24		0.06	0.05
95% Confidence Intervals (around median difference)	Lower: 0.023 & Higher: 0.46		Lower: 0.00 & Higher: 0.12	Lower: -0.00 & Higher: 0.11
T-Test				
Levene's Test		0.219		
p value	Mann-Whitney U: 0.019	0.003	Mann-Whitney U: 0.027	Mann-Whitney U: 0.005

A4.24: Summary of statistical results from fluid measurement (specific sites) data (Stage 1)

(Missing Data: two assessments where the TDC machine was not working or was not charged enough and one participant left before study assessment completion)

Statistical Results	Right Foot	Left Foot	Right Ankle	Left Ankle
Histogram	Normally Distributed	Normally Distributed	Normally Distributed	Normally Distributed
Number of participants	28	28	28	28
Missing Data	3	3	3	3
Mean (Standard Deviation)	40.26 (8.05)	39.78 (6.79)	32.78 (6.23)	33.19 (6.61)
With Oedema				
Number of participants	16	16	16	16
Missing Data	3	3	3	3
Mean (Standard Deviation)	42.91	41.90 (7.20)	34.82 (6.76)	35.20 (7.22)
Without Oedema				
Number of participants	12	12	12	12
Mean (Standard Deviation)	36.72 (5.95)	36.95 (5.21)	30.07 (4.35)	30.51 (4.75)
Difference between the means	6.19	4.95	4.75	4.69
95% Confidence Intervals (around mean difference)	Lower: 0.25 & Higher: 12.13	Lower: -0.10 & Higher: 10.00	Lower: 0.15 & Higher: 9.35	Lower: -0.25 & Higher: 9.63
T-Test				
Levene's Test	0.293	0.245	0.111	0.200
p value	0.042	0.054	0.044	0.062

Statistical Results	Right Below Knee	Left Below Knee	Right Above Knee	Left Above Knee
Histogram	Skewed	Normally Distributed	Normally Distributed	Normally Distributed
Number of participants	28	28	28	28
Missing Data	3	3	3	3
Mean (Standard Deviation)		36.99 (7.29)	30.05 (3.82)	29.93 (3.49)
Median (Interquartile Range)	32.66 (30.35 to 40.27)			
With Oedema				
Number of participants	16	16	16	16
Missing Data	3	3	3	3
Mean (Standard Deviation)		39.85 (7.61)	30.97 (4.17)	30.54 (3.91)
Median (Interquartile Range)	37.50 (31.97 to 43.23)			
Without Oedema				
Number of participants	12	12	12	12
Mean (Standard Deviation)		33.17 (4.89)	28.81 (3.02)	29.12 (2.80)
Median (Interquartile Range)	31.18 (28.69 to 32.65)			
Difference between the means		6.67	2.16	1.43
95% Confidence Intervals (around mean difference)		Lower: 1.50 & Higher: 11.85	Lower: -0.77 & Higher: 5.09	Lower: -1.31 & Higher: 4.16
Difference between the medians	6.32			
95% Confidence Intervals (around median difference)	Lower: 1.00 & Higher: 11.65			
T-Test				
Levene's Test	Using Reciprocal Data: 0.030	0.067	0.302	0.552
p value	0.003	0.014	0.142	0.294

Statistical Results	Right Below Groin	Left Below Groin	Right Abdominal Wall	Left Abdominal Wall
Histogram	Normally Distributed	Normally Distributed	Skewed	Normally Distributed
Number of participants	28	28	28	28
Missing Data	3	3	3	3
Mean (Standard Deviation)	29.55 (4.67)	29.65 (4.49)		32.70 (5.19)
Median (Interquartile Range)			31.76 (28.56 to 35.40)	
With Oedema				
Number of participants	16	16	16	16
Missing Data	3	3	3	3
Mean (Standard Deviation)	29.88 (5.09)	29.97 (4.96)		33.28 (6.12)
Median (Interquartile Range)			31.76 (28.24 to 36.11)	
Without Oedema				
Number of participants	12	12	12	12
Mean (Standard Deviation)	29.12 (4.21)	29.23 (3.94)		31.94 (3.74)
Median (Interquartile Range)			32.18 (29.02 to 35.40)	
Difference between the means	0.77	0.74		1.33
95% Confidence Intervals (around mean difference)	Lower: -2.95 & Higher: 4.49	Lower: -2.84 & Higher: 4.32		Lower: -2.78 & Higher: 5.45
Difference between the medians			-0.42	
95% Confidence Intervals (around median difference)			Lower: -5.34 & Higher: 4.50	
T-Test				
Levene's Test	0.642	0.271	Using Reciprocal Data: 0.326	0.173
p value	0.675	0.673	0.705	0.512

A4: Participant Data (Stage 2)

A4.25: End of study analysis (Stage 2)

Information about the participants who withdrew from the study is provided. All other participants will continue to be assessed.

Participant ID Number	Patient withdrawal date	Primary withdrawal reason	Other reason
003	14/NOV/2016		Participant was unable to have bariatric surgery due to the presence of dense adhesions throughout the abdomen.
021	12/DEC/2016	Withdrawal of consent	

A4.26: Demographic details (Stage 2)

Participant ID Number	Date of Assessment	Age	Gender	Weight (kg)	Height (m)
003	01/09/2016	59	F	144.3	1.59
004	01/09/2016	55	M	174.2	1.69
009	20/09/2016	52	F	143.4	1.72
012	27/09/2016	59	F	128.2	1.66
013	28/09/2016	50	M	145.2	1.71
015	30/09/2016	45	M	183.3	1.72
016	03/10/2016	55	F	126.3	1.59
019	06/10/2016	50	F	124.2	1.64
020	07/10/2016	60	F	130.0	1.57
021	17/10/2016	48	F	142.2	1.61
022	17/10/2016	61	F	96.3	1.59
027	11/11/2016	54	F	131.6	1.75
028	16/11/2016	48	M	134.0	1.85
036	02/12/2016	54	M	137.3	1.81
037	07/12/2016	44	F	118.3	1.66
043	28/12/2016	27	F	114.3	1.60
045	04/01/2017	74	M	125.6	1.75
046	04/01/2017	56	F	101.2	1.62
047	06/01/2017	56	F	157.8	1.64
048	11/01/2017	43	F	134.2	1.62
052	13/01/2017	51	F	137.4	1.65

Participant ID Number	BMI (kg/m²)	Level of obesity	Lower body mobility	Upper body mobility
003	57.1	MO	WA	Limited
004	61.0	MO	WU	Full
009	48.5	MO	WA	Full
012	45.9	MO	WA	Full
013	49.7	MO	WU	Full
015	61.4	MO	WU	Limited
016	50.0	MO	WA	Full
019	46.2	MO	WA	Full
020	52.8	MO	WU	Full
021	54.9	MO	WA	Full
022	38.1	O	WU	Full
027	43.0	MO	WU	Full
028	39.4	O	WA; sometimes	Full
036	41.5	MO	WU	Full
037	42.9	MO	WU	Full
043	44.7	MO	WU	Full
045	41.0	MO	WU	Full
046	38.6	O	WU	Full
047	58.8	MO	WA; if it is a long way.	Full
048	51.1	MO	WU	Full
052	50.4	MO	WU	Full

A4.27: Skin and wound assessment (Stage 2)

Participant ID Number	Stemmers sign (LF)	Stemmers sign (RF)
003	Pos	Pos
004	Neg	Neg
009	Pos	Pos
012	Pos	Pos
013	Neg	Neg
015	Neg	Neg
016	Neg	Neg
019	Neg	Neg
020	Neg	Pos
021	Pos	Neg
022	Neg	Neg
027	Neg	Neg
028	Neg	Neg
036	Neg	Neg
037	Neg	Neg
043	Neg	Neg
045	Eq	Eq. For both legs: could not lift but thought this was due to the lack/thinness of skin present.
046	Eq	Eq. For both legs: almost can pinch.
047	Pos	Pos
048	Neg	Neg
052	Neg	Neg

Participant ID Number	Skin conditions?	DVT (with details)	Wound present (with details)
003	Y; both legs: lower legs, chronic lipodermatosclerosis.	N	Y. Left leg: wound, ulcer, lower leg; Right leg: the wound has healed, ulcer, lower leg.
004	N	N	N
009	Y; left and right lower legs; chronic lipodermatosclerosis,	N	N
012	Y; left and right lower legs, chronic lipodermatosclerosis.	N	N. But slight cut on right ankle crease.
013		N	N
015		N	N
016	Y; left and right lower legs; dry skin, chronic inflammation.	N	N
019		N	N
020	Y; right lower leg, darkened skin pigmentation.	N	Y. From kitten scratch, but not healing quickly. Right lower leg.
021	N	N	N
022		N	N
027	N	Y. Right lower leg. 15 years ago, after an operation.	N
028		N	N
036	N	N	Healed ulcers/wounds, 1-2 years ago.
037		N	N
043		N	N
045	Y; left and right lower legs, chronic lipodermatosclerosis.	N	Healed: right lower leg, dog scratches.
046		N	N
047	Y; left lower leg, eczema.	N	N
048	N	N	N
052		N	N

A4.28: Cellulitis history (Stage 2)

This table lists the participants with a history of cellulitis (or being told that they have cellulitis). The other participants said that they had not had cellulitis.

Participant ID Number	Participants with History of Cellulitis?
009	N. Both legs, "recurring cellulitis", antibiotics take the edge off, not really feeling unwell. More than 6 times. In past year, cellulitis in affected areas due to swelling, more than 6 times.
012	Uncertain. She could not remember if she felt unwell or needed antibiotics for her leg. Left leg: calf, right abdomen; occurring several times (both sites). Uncertain if in past year, cellulitis was in affected areas due to swelling (uncertain: leg, no: abdomen). Uncertain if admitted to hospital as a result of cellulitis (if yes, once: leg).
016	Not that she can remember (symptoms-wise).
027	Y. Right upper and lower leg, once: 2 years ago.
036	Y. Right lower leg, end of 1998, once.

A4.29: Classification of oedema (Stage 2)

Participant ID Number	Swelling present?	Pitting swelling?	Tissues in swollen area
003	Y	Y; left foot and lower leg, right foot and lower leg	Soft
004	Y	Y; left foot and lower leg, right foot and lower leg	Soft
009	Y	Y; left foot and lower leg, right foot and lower leg, right hand (negative Stemmer's sign)	Soft
012	Y	Y; left toes and foot; right toes and foot; left and right hands: non-pitting swelling, negative Stemmers sign.	Soft
013	N		
015	N		
016	Y	Y; left and right lower legs	Hard
019	N		
020	Y	Y; right toes, left foot and lower leg, and right foot and lower leg	Soft
021	Y	Y; left foot and lower leg, right foot and lower leg	Soft
022	N		
027	N		
028	N	N	
036	Y	Y; left and right lower leg	Soft
037	N		
043	N	N	
045	Y	Y; left foot and lower leg, right foot and lower leg, left and right ankles	Soft
046	N		
047	Y; Left foot, both hands (between the knuckles)	Y; right foot, left hand (wedding ring)	Soft
048	Y	Y; left and right lower legs	Soft
052	N		

Participant ID Number	ISL stage	Duration of swelling/oedema
003	2	5-10 years. 2008 started.
004	1	
009	1	5-10 years.
012	2	Greater than 10 years.
016	Stage 2. After sleeping, swelling does improve.	5-10 years.
020	1	Greater than 10 years.
021	1	5-10 years.
036	1	Greater than 10 years. 1996/1997.
045	2	2-5 years.
047	1	Greater than 10 years. Nearly 30 years ago.
048	1	2-5 years.

A4.30: Medical history (Stage 2)

(Participants not listed in this table did not have the listed medical conditions.)

Participant ID Number	Arthritis	Diabetes	Heart disease
003	Y; right ankle	Y; 2 or 3 weeks diagnosed, T2.	Y; atrial fibrillation.
009	Y; OA in knees, ankles, hips, left shoulder, possibly fingers.	N	N
012	Y; 30 years: rheumatoid arthritis, widespread.	N	N
013	Y; inside of knees.	N	N
015	Y; OA	Y; T2	N
016	Y; OA; knees, left hip	N; although was T2, no tablets since February.	N
019	Y; OA in knees	N	N
021	Y; knees	Y; T2	N
022	Y; hips	Y; T2: insulin and metformin tablets.	Y; slight angina, on medication
027	Y; OA in right knee and left foot	Y; T2: tablet-controlled,	N
028	N.	Y; T2: controlled, Metformin, Lixisenatide; non-insulin dependant diabetes mellitus	N
036	Y; OA, widespread; hips, knees, and lower back	N	N
037	N.	Y; T2, tablet-controlled.	N
045	Y; OA; little bit, ankles and knees	Y; T2: diagnosed 2000, on oral medication, good control.	N
046	Y; knees and spine	Y; T2, diagnosed 2011, on insulin and medication, well controlled.	Y; controlled AG, ischemic heart disease, coronary angiogram: 2011.
047	N.	Y	2
048	N.	Y	2
052	N.	Y; T2, on medication, stable.	2

Participant ID Number	Hypertension	Liver disease	Neurological disorder	Obstructive sleep apnoea	Renal disease
003	Y; 2 or 3 weeks diagnosed	Y. 2001: non-alcoholic fatty liver (recorded in previous lymphoedema clinic notes). Current blood tests: clear.	Y; mini stroke 2 years ago, leading to her having warfarin.	N	Y; Chronic kidney disease, eGFR: 35
004	Y; Blood pressure tablets	N	N	N	N
009	Y; HRT for 20 years, leading to high blood pressure	N	N	Y; mask and machine, diagnosed 3 years ago.	N
012	Y; medication	N	N	N	N
013	N	N	N	N. No longer uses machine, Epworth score: 14. Used CPAP, had a trial and sleep studies (11/2015) but since he lost weight, he has not needed to use the machine.	N
015	N	N	N	Y; CPAP machine.	N
016	N; although had in the past.	N	N	N	N
019	Y; medication	N	Y; epilepsy: temporal lobe, diagnosed 2010, last fit 2-3 years ago.	N	N
020	Y	N	N	Y; very mild: given CPAP, but does not use it; Epworth Score: 21.	N
021	Y; medication	N	N	N	N
022	Y; very high (resistant hypertension)	N	N	N	N
027	Y; medication	N	N	Y; CPAP.	N
028	Y; medication	N	N	N	N
036	N	N	N	Y; CPAP machine, Epworth Score: 7.	N
037	Y; medication	N	N	N	N
045	Y; treatment	N	N	N	N
046	Y; stable on medications	N	N	Y; CPAP machine.	N
047	N	N	N	Y; sleep apnoea machine.	N
052	Y; stable, due to being on medication.	N	N	N	N

Participant ID Number	Other co-morbidities/complications
003	Lipolymphoedema.
004	1. Possible arthritis in spine. 2. Borderline diabetes. 3. Cramps in legs. 4. DEP and anxiety.
009	1. Mild DEP. 2. Fibromyalgia. 3. Hiatus hernia. 4. Lymphoedema. 5. Vaginal hysterectomy, leading to laparotomy in 1993. 6. Appendix removed in 1975. 7. Lapcolecystectomy, 2005. 8. Bladder repair.
012	1. Back: disc not fitting properly. 2. OA in right hip, hip replacement pending after bariatric surgery. 3. Fibromyalgia. 4. Varicose veins. Surgery, early 90s. 5. Hand surgery. 6. Oophrectomy. 7. Total hysterectomy. 8. Sterilised laparoscopies.
013	Vasectomy: 2000.
015	1. Gout. 2. Osteoporosis: spine, will get worse. 3. Bent left knee; has brace, but not using it at present. 4. Joint pain. 5. Depression. 6. Asthma. 7. Pins and needles in both hands. 8. Raised lipids. 9. Gastroscopy.
016	1. Crumbling discs 2. Swelling in legs. 3. TMJ: 03/16. 4. Hypothyroidism. 5. GORD. 6. Cholecystectomy: 96.
019	1. Anxiety and DEP. 2. Raised lipids. 3. Hayfever. 4. General anesthetic: 1997, ward, sutures to abdomen. 5. Laparoscopic cholecystectomy: 10+ years ago.
020	1. Primary lymphoedema - diagnosed by Professor Moffatt. 2. Underactive thyroid: GP monitors. 3. Polycystic ovary syndrome.
021	1. Chronic knee pain. 2. Lap Cholecystectomy: 2007. 3. C-Section x 2. 4. Vertigo. 5. LIS: 2015, fatty liver.
022	1. COPD. 2. Asthma. 3. DEP. 4. C Section: spinal anesthetic. 5. Bladder repair: 1990s. 6. TAH and BSO: 1991. 7. Left humerus: CRIF surgery. 8. ENT surgery

Participant ID Number	Other co-morbidities/complications
027	1. Venous insufficiency. 2. Hernia repair in her tummy. 3. TMJ problems. 4. DEP. 5. C-section. 6. Hypercholesterolaemia: statins.
028	1. Degenerative spine discs: lumbar disc degeneration. 2. Anxiety and DEP. 3. Asthma: continued inhalers. 4. Chronic right knee pain with limited mobility. 5. Excision of benign fibroepithelial polyp on neck (2016). 6. Excision of benign mole on back (2016). 7. Hypercholesterolaemia: medication.
036	1. Right knee - no cartilage. 2. Low bone density. 3. Anxiety/DEP. 4. Bilateral hip replacement: 2005/2006. 5. Varicose veins removed: 1999. 6. Shoulder operation: 2008.
037	1. Underactive thyroid, GP monitors. 2. Sciatica. 3. Diarrhoea, IBD ruled out. 4. DEP. 5. Diathermy cautery - 2000.
043	1. Polycystic ovaries syndrome - diagnosed at 17. 2. Controlled GORD. 3. Aged 10 - dental extractions. 4. 2010: gluing of pilonidal sinus. 5. 2006: Grommet insertion + left myringoplasty.
045	1. Torn ligaments in knee, physio has started/to start. 2. Very deaf, wears hearing aids. 3. Gallbladder removed: 2015. 4. Previous polyps on colon. 5. Poor eye sight. 6. TB gene carrier. 7. Hypercholesterolaemia.
046	1. GORD. 2. Hypothyroid. 3. Tonsillectomy. 4. Laparotomy for colo-vesical fistula: 2013. 5. Open cholecystectomy: 32 years ago. 6. Chronic back pain. 7. Hypercholesterolaemia.
047	1. Damaged back and left upper thigh - nerve pain/numb. 2. Sciatica in right leg. 3. Severe back pain. 4. Hiatus hernia. 5. GORD emergency. 6. Ovarian cystectomy [omental mass biopsy (removal of a massive ovarian cyst that encompassed bilateral salpingo-oophorectomy, the cyst contained over 10 litres of fluid but was benign), 2012 - led to being in the intensive treatment unit] and laparotomy. 7. Recurring salivary gland infections. 8. C-Section. 9. Chronic back pain.
048	1. Asthma: inhalers. 2. Possible PCOS. 3. GORD. 4. Frozen right shoulder. 5. DEP. 6. Grommets. 7. C-Section.
052	1. Psoriasis, very occasionally. 2. Carpal tunnel syndrome - decompression (left). 3. Tonsillectomy: age 3. 4. Hypercholesterolaemia? - statin. 5. Fractured arm: needed a general anesthetic to reset.

A4.31: Medications (Stage 2)

Participant ID Number	List of current medications
003	Warfarin (3-4mg); Atorvastatin (40mg), night; Bisoprolol (7.5mg), once a day; Codeine (PRN); Duloxetine (60mg); Pro D3, once a day; Quinine Sulphate (30mg), AN; Paracetamol; Glyptin.
004	Multivitamins with iron; Citalopram (20mg) (at 08:00); Indapamide (2.5mg) (at 08:00); Ramipine (10mg) (at 08:00)
009	Airomir (inhaler); Amitriptyline (25mg) at night; Furosemide (20mg), once a day; Lansoprazole (15mg) daily; Ramopril (5mg) at night; Citalopram (20mg) daily; Qvar; Matrifen patches (12 micrograms an hour); Multivitamins
012	Omeprazole; Amlodipine; Atenolol; MST (30mg), twice a day; Amitriptyline; Paracetamol; Senna (as necessary); Hydroxychloroquine, twice a day; Irbesartan; Naproxen; Gabapentin, three times a day; Folic Acid
013	None listed
015	Adcal D3 (750mg x 2) twice daily; Alendronic Acid (70mg), 1 weekly; Allopurinol (100mg), 1 daily; Atorvastatin (10mg), 1 daily; Gliclazide (80mg x 2) daily; Cetirizine (10mg), 1 daily; Dapagliflozin (10mg), 1 daily; Fluoxetine (20mg x 2) daily; Fostair inhaler; Furosemide (40mg), 1 daily; Gabapentin, (300mg), 1 tablet; Naproxen (500mg x 1) twice daily; Montelukast (10mg), 1 at night; Nefopam (30mg x 2 tablets); Ramipril (2.5mg), 1 daily; Ventolin Evohaler; Liraglutide; Lansoprazole (15mg), 1 once daily; Metformin (500mg x 2) twice daily
016	Simvastatin (20mg); Citalopram (20mg); Levothyroxine (200 micrograms); Paracetamol (as and when)
019	Lansoprazole (30mg), once daily (c/o Naproxen: being taken with Lansoprazole); Lamotrigine (250mg), once daily at night; Codeine phosphate (30mg), as needed, 4 times a day; Paracetamol (1g), 4 times a day, as needed; Cetirizine (10mg), once daily; Candesartan (4mg), once daily; Naproxen (500mg), twice daily, as needed
020	Bendroflumethiazide (2.5mg); Cetirizine (10mg); Citalopram (20mg); Co-codamol; Levothyroxine (250 micrograms); Losartan (100mg)
021	Lansoprazole (30mg), twice a day; Indapamide (1.5mg); Ramipril (10mg); Metformin (500mg); Naproxen (500mg), twice per day; Amlodipine (10mg)
022	Omeprazole (20mg); Salbutamol Inhaler; Verapamil (240mg); Metformin (1 gram), twice a day; Aspirin (75mg); Candesartan (32mg); Fostair (200mg), 2 puffs twice a day; GTN spray; Indapamide (1.5mg); Spironolactone (25mg); Humalog (6-10 units), 3 times a day with meals; Ipratropium inhaler (1-2 puffs), 3 times a day; Loratadine (10mg); Moxonidine (300 micrograms)
027	Amlodipine (5mg), once a day at night; Furosemide (40mg), once a day in the morning; Lansoprazole (15mg), once a day in the morning; Metformin: once a day in the morning; Paracetamol; Naproxen (500mg), twice daily; Norethisterone (5mg, as per cycle); Telmisartan (40mg), once a day at night; Simvastatin (20mg), once a day at night; Multivitamins

Participant ID Number	List of current medications
028	Amlodopine (10mgs), once daily; Atorvastatin (20mgs), once daily; Doxazosin (2mgs), once daily; Gaviscon; Lixisenatide injection (stopped whilst on liver diet); Metformin (500mgs), 1 with breakfast and tea, 2 at lunch; Qvar inhaler; Ramipril (10mgs), once daily; Sertraline (100mgs), once daily
036	Tramadol (50mg), 3 times a day; Iron and vitamins
037	Amlodipine (5mg), once daily; Atorvastatin (20mg), once daily; Levothyroxine (125 micrograms), once daily; Metformin (500mg), twice daily
043	Omeprazole, prn (as necessary)
045	Amitriptyline; Calcichew; Furosemide (40mg); Gliclazide (80mg); Losartan (50mg); Metformin (500mg); Simvastatin (40mg); Paracetamol (500mg); Gabapentin (300mg); Indapamide (2.5mg)
046	Tyrocaine; Aspirin (75mg); Bendroflumethiazide (2.5mg); Bisoprolol; Clonidine (25mg); Dapagliflozin; Repronex XL; Gabapentin (100mg); Glyceryl trinitrate (GTN), 3 times a year; Insuman comb; Sinvastatin; Lansoprazole (30mg); Levothyroxine (100mg); Losartan (100mg); Metformin (500mg); Orlistat (120mg)
047	Codliver oil; Pregabalin (225mg), BD; Vitamin B Complex; Ranitidine (150mg), BD; Codeine Phosphate (15mgs), 1-2 four times a day; Multivitamins
048	Naproxen (500mg), twice a day; Citalopram (10mg), once a day; Lansoprazole, once a day; Mini Pill
052	Multivitamins; Gliclazide (80mgs), 8am; Lisinapril (20mgs), 8am; Simvastatin (40mgs), 10pm; Metformin (1 gram), twice a day; Iron tablets, 6-7 years ago

A4.32: Blood test results (Stage 2)

Participant ID Number	Blood Test Results Date	FBC - Hb (g/L)	HbA1c (mmol/mol)	LFT - Albumin (g/L)	TFT - TSH (mIU/L)	UE - eGFR (mL/min/1.73m ²)
003	01/09/2016	137	N/R	35	N/R	35
004	01/09/2016	160	44	41	1.05	>60
009	20/09/2016	136	42	42	N/R	>60
012	27/09/2016	138	32	39	2.24	>60
013	28/09/2016	157	Database: "Unable to obtain results"	44	2.43	>60
015	30/09/2016	154	51	38	2.05	>60
016	03/10/2016	135	30	38	0.39	>60
019	06/10/2016	142	34	41	1.67	>60
020	07/10/2016	150	39	18/10/16: 31	0.71	18/10/16: >60
021	17/10/2016	143	45	41	N/R	>60
022	17/10/2016	124	N/R	45	N/R	41
027	11/11/2016	150	40	45	N/R	>60
028	16/11/2016	170	08/09/16: 47	46	N/R	>60
036	02/12/2016	156	32	38	N/R	>60
037	07/12/2016	137	46	42	1.98	>60
043	28/12/2016	126	N/R	38	18/11/16 - 1.98	>60
045	04/01/2017	153	42 (T2)	43	N/R	51 - CKD, Stage 3
046	04/01/2017	136	51 (T2)	40	0.47	>60
047	06/01/2017	155	N/R	38	N/R	>60
048	11/01/2017	148	37 (T2)	41	N/R	>60
052	13/01/2017	146	41 (T2)	40	N/R	>60

A4.33: Classification of oedema (Stage 2, after surgery)

Participant ID Number	Swelling present?	Pitting swelling?	Additional Information
012	Y	Y. Left toes, foot and lower leg; right toes, foot and lower leg; left and right hands: knuckles.	Wearing lymphoedema bandage stockings. Left and right toes: researcher assessed. Left and right feet and lower legs: wearing stockings for these areas (according to participant: right leg red due to soreness, left leg: looks normal). Left and right knuckles: non-pitting swelling, negative Stemmers sign.
016	Y	Y. Left and right lower legs	
020	Y	Y. Left foot and lower leg, Right foot and lower leg	
027	N		
028	N		

Participant ID Number	Tissues in swollen area	ISL stage
012	Soft	2
016	Soft	Stage 2. Hard to pit, but still the same in the morning.
020	Soft	1

A4.34: Demographic details (Stage 2, after surgery)

Participant ID Number	Additional Information	Number of months	Date of Assessment	Age	Gender
012	"6 week" post-op appointment. 14 weeks, 6 days after surgery (NOT including the surgery or post-op appointment dates).	>3	24/01/2017	59	F
016	"6 week" post-op appointment. 14 weeks, 6 days after surgery (NOT including the surgery or post-op appointment dates).	>3	23/01/2017	55	F
020	"6 week" post-op appointment. 11 weeks, 3 days after surgery (NOT including the surgery or post-op appointment dates).	>2	06/01/2017	61	F
027	"6 week" post-op appointment. 7 weeks, 6 days after surgery (NOT including the surgery or post-op appointment dates).	<2	13/01/2017	54	F
028	"6 week post-op appointment. 7 weeks, 3 days after surgery (NOT including the surgery or post-op appointment dates).	<2	17/01/2017	48	M

Participant ID Number	Weight (kg)	Height (m)	BMI (kg/m²)	Level of obesity	Lower body mobility	Upper body mobility
012	116.2	1.66	42.2	MO	WA; mobility scooter	Limited
016	117.2	1.59	46.3	MO	WA	Full
020	118.4	1.57	48	MO	WU	Full
027	116.6	1.75	38	O	WU	Full
028	120.8	1.84	35.6	O	WA; sometimes	Full

A4.35: EQ-5D questionnaire data and analysis (Stage 2)

Participant ID Number	Health State	Mobility	Self	Active	Pain	Depress	const01	const02	Euroqol
003	41.0	0.069	0.104	0.094	0.386	0.236	0.081	0.269	-0.239
004	60.0	0.069	0.104	0	0.123	0.071	0.081	0	0.552
009	50.0	0.069	0	0	0.123	0.071	0.081	0	0.656
012	60.0	0.069	0.104	0.036	0.123	0	0.081	0	0.587
013	70.0	0	0	0	0.123	0	0.081	0	0.796
015	70.0	0.069	0.104	0.036	0.386	0.071	0.081	0.269	-0.016
016	40.0	0.069	0.104	0.036	0.386	0.071	0.081	0.269	-0.016
019	60.0	0.069	0	0	0.123	0	0.081	0	0.727
020	80.0	0.069	0	0.036	0.123	0	0.081	0	0.691
021	60.0	0.069	0.104	0.036	0.123	0	0.081	0	0.587
022	30.0	0.069	0	0.036	0.123	0.071	0.081	0	0.620
027	81.5	0	0	0	0.123	0	0.081	0	0.796
028	65.0	0.069	0	0.036	0.123	0.071	0.081	0	0.620
036	60.0	0.069	0	0.036	0.123	0	0.081	0	0.691
037	100.0	0	0	0	0	0	0	0	1.000
043	65.0	0	0	0	0	0	0	0	1.000
045	90.0	0.069	0	0	0.123	0	0.081	0	0.727
046	47.0	0.069	0	0.036	0.123	0.071	0.081	0	0.620
047	65.0	0.069	0.104	0.036	0.386	0.071	0.081	0.269	-0.016
048	80.0	0	0	0	0.123	0	0.081	0	0.796
052	98.0	0	0	0	0	0	0	0	1.000

A4.36: GAD-7 and PHQ-9 questionnaire data (Stage 2)

Participant ID Number	GAD-7 Score	PHQ-9 Score	PHQ-9 - Q10
003	21	24	Extremely difficult
004	14	12	Not difficult at all
009	7	16	Somewhat difficult
012	0	5	Not difficult at all
013	0	1	Not difficult at all
015	10	18	Somewhat difficult
016	7	16	Very difficult
019	0	0	
020	0	4	
021	4	0	
022	18	20	Somewhat difficult
027	2	6	Not difficult at all
028	12	16	Somewhat difficult
036	0	2	Not difficult at all
037	0	0	
043	6	6	Somewhat difficult
045	0	2	Somewhat difficult
046	16	18	Very difficult
047	6	9	Very difficult
048	3	2	Somewhat difficult
052	0	0	Not difficult at all

A4.37: Summary of statistical results of EQ-5D, GAD-7 and PHQ-9 data (Stage 2)

Statistical Results	EQ-5D (Euroqol)	GAD-7	PHQ-9
Histogram	Skewed - Transformed	Skewed - Transformed	Skewed - Transformed
Number of participants	21	21	21
Median (Interquartile Range)	0.66 (0.57 to 0.80)	4.00 (0 to 11.00)	6.00 (1.50 to 16.00)
With Oedema			
Number of participants	11	11	11
Median (Interquartile Range)	0.59 (-0.02 to 0.69)	4.00 (0 to 7.00)	5.00 (2.00 to 16.00)
Without Oedema			
Number of participants	10	10	10
Median (Interquartile Range)	0.76 (0.62 to 1.00)	4.00 (0 to 13.00)	6.00 (0 to 18.00)
Difference between the medians	-0.17	0	-1.00
95% Confidence Intervals (around the median difference)	Lower: -0.58 & Higher: 0.24	Lower: -7.77 & Higher: 7.77	Lower: -11.69 & Higher: 9.69
T-Test			
Levene's Test	Using EQ-5D Squared Data: 0.224	Using GAD-7 Square Root Data: 0.424	Using PHQ-9 Square Root Data: 0.242
p value	0.040	0.922	0.743

A4.38: LYMQOL questionnaire data (Stage 2)

(Participants with no swelling have been removed from this table.)

Participant ID Number	Function	Appearance	Symptoms	Mood	Overall Quality of Life
003	4	4	3.4	4	0
004	1.6	1.7	1.4	1.5	Missing Data
009	UL: 1.5, LL: 3.75	UL: 3.2, LL: 3.6	UL: 1.8, LL: 3	UA: 2, LL: 1.8	UL: 5, LL: 5
012	UL: 2.7, LL: 3.9	UL: 2.4, LL: 3.6	UL: 1.8, LL: 1.8	UL: 1.5, LL: 1.5	UL: 7, LL: 7
016	3.6	3.7	3.4	2.3	4
020	3.5	4	2.4	1	7
021	1	2.4	1.6	1	8
036	1.1	1.6	1	1.3	6
045	1.9	1.6	2	1	9
047	UL: 1.2, LL: 2.7	UL: 3.4, LL: 3.6	UL: 2.5, LL: 2.4	UL: 1.7, LL: 1.8	UL: 3, LL: 3
048	1.4	1.7	1.4	1	6

A4.39: Summary of statistical results from LYMQOL (lower limb) data (Stage 2)

(Missing Data: participant did not answer this question)

Statistical Results	LYMQOL Function	LYMQOL Appearance	LYMQOL Symptoms
Histogram	Skewed	Skewed	Normally Distributed
With Oedema			
Number of participants	11	11	11
Mean (Standard Deviation)			2.16 (0.83)
95% Confidence Intervals (around the mean)			Lower: 1.61 & Higher: 2.72
Median (Interquartile Range)	2.70 (1.40 to 3.75)	3.6 (1.70 to 3.70)	
95% Confidence Intervals (around the median)	Lower: 1.31 & Higher: 3.79	Lower: 1.67 & Higher: 3.79	
Statistical Results	LYMQOL Mood	LYMQOL Quality of Life	
Histogram	Skewed	Normally Distributed	
With Oedema			
Number of participants	11	10	
Missing Data	0	1	
Mean (Standard Deviation)		5.50 (2.64)	
95% Confidence Intervals (around the mean)		Lower: 3.62 & Higher: 7.39	
Median (Interquartile Range)	1.5 (1.00 to 1.80)		
95% Confidence Intervals (around the median)	Lower: 1.00 & Higher: 1.94		

A4.40: SF-36 questionnaire data (Stage 2)

Participant ID Number	SF-36 - Physical Functioning	SF-36 - Role Limitations due to Physical Health	SF-36 - Role Limitations due to Emotional Problems	SF-36 - Energy/Fatigue	SF-36 - Emotional Well Being	SF-36 - Social Functioning	SF-36 - Pain	SF-36 - General Health	SF-36 - General Health (Compared to 1 Year Ago)
003	5.0	0	0.0	0	24	0.0	22.5	10	25
004	56.3	100	100.0	45	56	62.5	45.0	55	75
009	15.0	0	0.0	0	56	50.0	10.0	50	25
012	0.0	0	100.0	45	92	25.0	22.5	30	25
013	30.0	100	100.0	45	88	100.0	90.0	75	100
015	15.0	0	33.3	35	44	62.5	45.0	25	50
016	10.0	0	33.3	15	44	25.0	0.0	45	50
019	70.0	100	100.0	80	76	100.0	90.0	70	100
020	65.0	100	100.0	30	84	100.0	100.0	70	50
021	20.0	50	100.0	70	84	62.5	22.5	65	50
022	10.0	75	100.0	40	68	50.0	45.0	10	50
027	70.0	75	100.0	75	88	100.0	57.5	75	75
028	60.0	75	0.0	50	40	25.0	55.0	40	75
036	25.0	0	100.0	55	76	62.5	45.0	80	100
037	95.0	100	100.0	75	100	100.0	100.0	65	100
043	85.0	100	100.0	60	84	100.0	90.0	65	50
045	60.0	50	33.3	45	68	87.5	77.5	65	75
046	10.0	0	0.0	15	20	25.0	22.5	20	25
047	20.0	25	66.7	25	68	50.0	12.5	85	50
048	85.0	25	100.0	30	92	75.0	32.5	70	100
052	100.0	100	100.0	85	100	100.0	100.0	85	75

A4.41: Summary of statistical results from SF-36 questionnaire data (Stage 2)

Statistical Results	SF-36 - Physical Function	SF-36 - Physical Health	SF-36 - Emotional Problems
Histogram	Skewed - Transformed	Skewed	Skewed
Number of participants	21	21	21
Median (Interquartile Range)	30 (12.50 to 70.00)	50 (0 to 100.00)	100 (33.30 to 100.00)
With Oedema			
Number of participants who completed the questionnaire	11	11	11
Median (Interquartile Range)	20 (10.00 to 60.00)	25 (0 to 50.00)	100 (33.30 to 100.00)
Without Oedema			
Number of participants	10	10	10
Median (Interquartile Range)	65 (13.75 to 87.50)	87.5 (56.25 to 100)	100 (24.98 to 100.00)
Difference between the medians	-45	-62.50	0
95% Confidence Intervals (around the median difference)	Lower: -89.94 & Higher: -0.06	Lower: -112.74 & Higher: -12.26	Lower: -55.46 & Higher: 55.46
T-Test			
Levene's Test	Using SF-36 Square Root		
p value	0.144	Mann-Whitney U Test: 0.048	Mann-Whitney U Test: 0.627

Statistical Results	SF-36 - Energy/Fatigue	SF-36 - Emotional Well Being	SF-36 - Social Functioning
Histogram	Normally Distributed	Normally Distributed	Normally Distributed
Number of participants	21	21	21
Mean (Standard Deviation)	43.81 (24.90)	69.14 (23.80)	64.88 (32.02)
With Oedema			
Number of participants	11	11	11
Mean (Standard Deviation)	32.73 (22.06)	67.64 (21.28)	54.55 (29.19)
Without Oedema			
Number of participants who completed the questionnaire	10	10	10
Mean (Standard Deviation)	56.00 (22.83)	70.8 (27.39)	76.25 (32.52)
Difference between the means	-23.27	-3.16	-21.70
95% Confidence Intervals (around the mean difference)	Lower: -43.78 & Higher: -2.76	Lower: -25.45 & Higher: 19.12	Lower: -49.88 & Higher: 6.47
T-Test			
Levene's Test	0.774	0.332	0.366
p value	0.028	0.770	0.123

Statistical Results	SF-36 - Pain	SF-36 - General Health	SF-36 - General Health (compared to 1 year ago)
Histogram	Normally Distributed	Normally Distributed	Normally Distributed
Number of participants who completed the questionnaire	21	21	21
Mean (Standard Deviation)	51.67 (33.18)	55.00 (23.93)	63.10 (26.95)
With Oedema			
Number of participants who completed the questionnaire	11	11	11
Mean (Standard Deviation)	35.46 (30.10)	56.82 (22.17)	56.82 (27.59)
Without Oedema			
Number of participants who completed the questionnaire	10	10	10
Mean (Standard Deviation)	69.50 (27.66)	53.00 (26.79)	70.00 (25.82)
Difference between the means	-34.05	3.82	-13.18
95% Confidence Intervals (around the mean difference)	Lower: -60.54 & Higher: -7.55	Lower: -18.56 & Higher: 26.19	Lower: -37.66 & Higher: 11.30
T-Test			
Levene's Test	0.802	0.240	0.832
p value	0.015	0.725	0.274

A4.42: Full comparison of SF-36 scores with HSE normative data (Stage 2)

	Female 25-34	
	Study Mean (n=1, NCO)	HSE Population Norm
Physical Functioning	85.0	90
Role Limitations due to Physical Health	100.0	88
Role Limitations due to Emotional Problems	100.0	85
Energy/Fatigue	60.0	62
Emotional Well Being (Mental Health in HSE Population Norm file)	84.0	73
Social Functioning	100.0	86
Pain	90.0	80
General Health	65.0	74

	Female 35-44			
	Study Mean (n=2)	Study Mean (n=1, CO)	Study Mean (n=1, NCO)	HSE Population Norm
Physical Functioning	90.0	85.0	95.0	87
Role Limitations due to Physical Health	62.5	25.0	100.0	84
Role Limitations due to Emotional Problems	100.0	100.0	100.0	85
Energy/Fatigue	52.5	30.0	75.0	61
Emotional Well Being (Mental Health in HSE Population Norm file)	96.0	92.0	100.0	73
Social Functioning	87.5	75.0	100.0	86
Pain	66.3	32.5	100.0	78
General Health	67.5	70.0	65.0	73

	Male 45-54			
	Study Mean (n=4)	Study Mean (n=1, CO)	Study Mean (n=3, NCO)	HSE Population Norm
Physical Functioning	32.5	25.0	35.0	87
Role Limitations due to Physical Health	43.75	0.0	58.3	84
Role Limitations due to Emotional Problems	58.325	100.0	44.4	86
Energy/Fatigue	46.25	55.0	43.3	66
Emotional Well Being (Mental Health in HSE Population Norm file)	62	76.0	57.3	77
Social Functioning	62.5	62.5	62.5	87
Pain	58.75	45.0	63.3	78
General Health	55	80.0	46.7	69

	Female 45-54			
	Study Mean (n=5)	Study Mean (n=2, CO)	Study Mean (n=2, NCO)	HSE Population Norm
Physical Functioning	55.0	17.5	70.0	82
Role Limitations due to Physical Health	65.0	25.0	87.5	80
Role Limitations due to Emotional Problems	80.0	50.0	100.0	84
Energy/Fatigue	62.0	35.0	77.5	60
Emotional Well Being (Mental Health in HSE Population Norm file)	80.8	70.0	82.0	74
Social Functioning	82.5	56.3	100.0	85
Pain	56.0	16.3	73.8	74
General Health	69.0	57.5	72.5	70
	Female 55-64			
	Study Mean (n=7)	Study Mean (n=5, CO)	Study Mean (n=2, NCO)	HSE Population Norm
Physical Functioning	17.1	20.0	10.0	72
Role Limitations due to Physical Health	28.6	25.0	37.5	72
Role Limitations due to Emotional Problems	57.1	60.0	50.0	81
Energy/Fatigue	24.3	23.0	27.5	64
Emotional Well Being (Mental Health in HSE Population Norm file)	57.1	62.4	44.0	73
Social Functioning	39.3	40.0	37.5	83
Pain	32.1	31.5	33.8	69
General Health	38.6	48.0	15.0	65
	Male 55-64		Male 65-74	
	Study Mean (n=1, CO)	HSE Population Norm	Study Mean (n=1, CO)	HSE Population Norm
Physical Functioning	56.3	76	60.0	70
Role Limitations due to Physical Health	100.0	75	50.0	68
Role Limitations due to Emotional Problems	100	84	33.3	81
Energy/Fatigue	45.0	64	45.0	64
Emotional Well Being (Mental Health in HSE Population Norm file)	56.0	78	68.0	78
Social Functioning	62.5	84	87.5	83
Pain	45.0	74	77.5	75
General Health	55.0	64	65.0	62

A4.43: Limb volume data (Stage 2)

Participant ID Number	Leg swelling	Perometer measurement length (mm)	Volume measurement: RL1 (mls)	Volume measurement: RL2 (mls)	RL average (mls)
003	Bilateral	424	7583	7510	7546.5
004	Bilateral	452	4908	4956	4932.0
009	Bilateral	617	11071	11227	11149.0
012	Bilateral	462	5650	5641	5645.5
013	None present	509	6220	6319	6269.5
015	None present	518	8886	8853	8869.5
016	Bilateral	485	7241	7344	7292.5
019	None present	447	6955	6843	6899.0
020	Bilateral	527	9695	9581	9638.0
021	Bilateral	541	7704	7782	7743.0
022	None present	640	7507	6501	7004.0
027	None present	673	8436	8466	8451.0
028	None present	682	8517	8226	8371.5
036	Bilateral	560	6441	6373	6407.0
037	None present	617	9877	9847	9862.0
043	None present	541	6921	6882	6901.5
045	Bilateral	621	7954	7825	7889.5
046	None present	588	6228	6109	6168.5
047	Bilateral	462	8298	8439	8368.5
048	Bilateral	584	11565	11549	11557.0
052	None present	570	7488	7350	7419.0

Participant ID Number	Perometer measurement length (mm)	Volume measurement: LL1 (mls)	Volume measurement: LL2 (mls)	LL average (mls)
003	424	8900	8511	8705.5
004	452	4752	4751	4751.5
009	617	10143	10215	10179.0
012	462	6124	6452	6288.0
013	509	6098	6118	6108.0
015	518	8861	8805	8833.0
016	485	7820	7836	7828.0
019	447	6931	6855	6893.0
020	527	8917	8915	8916.0
021	541	7702	7569	7635.5
022	640	7001	6375	6688.0
027	673	8405	8378	8391.5
028	682	8253	8260	8256.5
036	560	6248	6358	6303.0
037	617	9535	8989	9262.0
043	541	7040	7050	7045.0
045	621	7775	7834	7804.5
046	588	6287	6322	6304.5
047	462	8139	8709	8424.0
048	584	11627	11568	11597.5
052	570	8400	7403	7901.5

A4.44: Limb volume data (Stage 2, after surgery)

Participant ID Number	Q14. Leg swelling	Perometer measurement length (mm)	Volume measurement: RL1 (mls)	Volume measurement: RL2 (mls)	RL average (mls)
012	Bilateral	462	7543	7406	7474.5
016	Bilateral	485	7126	7097	7111.5
020	Bilateral	527	9060	9235	9147.5
027	None present	673	7908	7876	7892.0
028	None present	682	7675	7557	7616.0

Participant ID Number	Perometer measurement length (mm)	Volume measurement: LL1 (mls)	Volume measurement: LL1 (mls)	LL average (mls)
012	462	7528	7369	7448.5
016	485	7731	7797	7764.0
020	527	8524	9060	8792.0
027	673	7833	7815	7824.0
028	682	7533	7543	7538.0

A4.45: Bioimpedance assessment - right (Stage 2)

Participant ID Number	WBA R1 (FN)	WBA R1 (RZ)	WBA R1 (RI)	WBA R1 (RI/RZ)
003	obe-ts-003-5687	483.52	320.66	0.6632
009	obe-rc-009-5754	530.31	405.89	0.7654
012	obe-ml-012-5795	524.08	405.33	0.7734
013	obe-dr-013-5811	438.60	290.85	0.6631
015	obe-jb-015-5843	436.61	294.32	0.6741
019	obe-gn-019-5888	498.13	377.50	0.7578
020	obe-lc-020-5901	471.77	348.68	0.7391
021	obe-jv-021-5915	549.92	383.16	0.6968
022	obe-pe-022-5927	554.80	381.35	0.6874
027	obe-kr-027-5998	497.21	336.89	0.6776
028	obe-dc-028-6016	506.49	344.65	0.6805
036	obe-lk-036-0116	455.62	305.88	0.6713
037	obe-tj-037-6341	536.99	368.34	0.6859
043	obe-cc-043-6429	643.23	440.94	0.6855
045	obe-dg-045-6456	505.70	377.31	0.7461
046	obe-mbr-046-6468	554.76	401.27	0.7233
047	obe-sb-047-6497	551.00	409.80	0.7437
048	obe-cg-048-6510	453.83	311.56	0.6865
052	obe-jb-052-6573	552.61	401.67	0.7269

Participant ID Number	WBA R2 (FN)	WBA R2 (RZ)	WBA R2 (RI)	WBA R2 (RI/RZ)
003	obe-ts-003-5688	477.82	333.39	0.6977
009	obe-rc-009-5755	530.65	406.37	0.7658
012	obe-ml-012-5796	525.91	406.30	0.7726
013	obe-dr-013-5813	439.00	292.12	0.6654
015	obe-jb-015-5844	436.37	294.56	0.6750
019	obe-gn-019-5889	499.67	377.97	0.7564
020	obe-lc-020-5902	472.82	349.51	0.7392
021	obe-jv-021-5916	551.51	385.49	0.6990
022	obe-pe-022-5928	554.75	381.79	0.6882
027	obe-kr-027-5999	497.71	337.79	0.6787
028	obe-dc-028-6017	506.85	344.92	0.6805
036	obe-lk-036-0117	457.33	306.70	0.6706
037	obe-tj-037-6342	535.68	368.87	0.6886
043	obe-cc-043-6430	643.03	441.19	0.6861
045	obe-dg-045-6457	505.98	378.22	0.7475
046	obe-mbr-046-6469	555.49	401.66	0.7231
047	obe-sb-047-6498	552.47	415.45	0.7520
048	obe-cg-048-6511	454.17	311.79	0.6865
052	obe-jb-052-6574	553.27	402.06	0.7267

Participant ID Number	RA1 (FN)	RA1 (RZ)	RA1 (RI)	RA1 (RI/RZ)
003	obe-ts-003-5689	315.55	225.30	0.7140
009	obe-rc-009-5756	320.15	239.09	0.7468
012	obe-ml-012-5797	284.73	212.46	0.7462
013	obe-dr-013-5816	227.75	144.01	0.6323
015	obe-jb-015-5845	241.09	149.28	0.6192
019	obe-gn-019-5890	293.78	222.17	0.7562
020	obe-lc-020-5903	298.26	217.05	0.7277
021	obe-jv-021-5917	294.30	204.49	0.6948
022	obe-pe-022-5929	267.60	181.08	0.6767
027	obe-kr-027-6000	234.18	163.79	0.6994
028	obe-dc-028-6018	221.74	148.24	0.6685
036	obe-lk-036-0118	258.93	166.49	0.6430
037	obe-tj-037-6343	266.77	186.45	0.6989
043	obe-cc-043-6431	284.31	197.27	0.6939
045	obe-dg-045-6458	275.47	202.34	0.7345
046	obe-mbr-046-6470	276.37	202.76	0.7337
047	obe-sb-047-6499	303.30	231.40	0.7629
048	obe-cg-048-6512	240.01	167.45	0.6977
052	obe-jb-052-6575	279.26	250.74	0.8979

Participant ID Number	RA2 (FN)	RA2 (RZ)	RA2 (RI)	RA2 (RI/RZ)
003	obe-ts-003-5690	315.97	226.13	0.7157
009	obe-rc-009-5757	319.60	239.09	0.7481
012	obe-ml-012-5798	284.57	212.38	0.7463
013	obe-dr-013-5817	229.00	144.07	0.6291
015	obe-jb-015-5846	241.27	149.41	0.6193
019	obe-gn-019-5891	256.59	244.93	0.9546
020	obe-lc-020-5904	299.63	217.64	0.7264
021	obe-jv-021-5918	294.65	204.52	0.6941
022	obe-pe-022-5930	267.48	181.45	0.6784
027	obe-kr-027-6001	234.60	164.00	0.6991
028	obe-dc-028-6019	221.10	148.16	0.6701
036	obe-lk-036-0119	258.76	166.71	0.6443
037	obe-tj-037-6344	266.80	186.77	0.7000
043	obe-cc-043-6432	284.13	197.46	0.6950
045	obe-dg-045-6459	276.40	203.12	0.7349
046	obe-mbr-046-6471	275.81	202.95	0.7358
047	obe-sb-047-6500	303.27	231.54	0.7635
048	obe-cg-048-6513	240.31	167.25	0.6960
052	obe-jb-052-6576	314.89	223.34	0.7093

Participant ID Number	RL1 (FN)	RL1 (RZ)	RL1 (RI)	RL1 (RI/RZ)
003	obe-ts-003-5691	163.51	127.42	0.7793
009	obe-rc-009-5758	187.03	150.64	0.8054
012	obe-ml-012-5799	226.09	177.93	0.7870
013	obe-dr-013-5818	189.25	135.49	0.7159
015	obe-jb-015-5847	169.01	127.89	0.7567
019	obe-gn-019-5892	179.18	136.29	0.7606
020	obe-lc-020-5905	147.45	115.31	0.7820
021	obe-jv-021-5919	236.20	168.48	0.7133
022	obe-pe-022-5931	258.21	182.87	0.7082
027	obe-kr-027-6002	243.29	161.58	0.6641
028	obe-dc-028-6020	259.00	180.65	0.6975
036	obe-lk-036-0120	177.06	128.08	0.7234
037	obe-tj-037-6345	246.30	169.82	0.6895
043	obe-cc-043-6433	328.72	224.29	0.6823
045	obe-dg-045-6460	206.71	158.27	0.7657
046	obe-mbr-046-6472	259.36	187.53	0.7230
047	obe-sb-047-6501	225.63	167.77	0.7436
048	obe-cg-048-6514	191.88	130.71	0.6812
052	obe-jb-052-6577	214.10	164.17	0.7668

Participant ID Number	RL2 (FN)	RL2 (RZ)	RL2 (RI)	RL2 (RI/RZ)
003	obe-ts-003-5701	239.45	164.99	0.6890
009	obe-rc-009-5759	186.98	150.59	0.8054
012	obe-ml-012-5801	227.88	178.21	0.7820
013	obe-dr-013-5820	189.82	135.49	0.7138
015	obe-jb-015-5848	169.21	128.21	0.7577
019	obe-gn-019-5893	179.28	136.48	0.7613
020	obe-lc-020-5906	147.74	115.80	0.7838
021	obe-jv-021-5920	237.06	167.35	0.7059
022	obe-pe-022-5932	258.20	182.88	0.7083
027	obe-kr-027-6003	243.10	161.71	0.6652
028	obe-dc-028-6021	258.64	180.87	0.6993
036	obe-lk-036-0121	176.97	128.46	0.7259
037	obe-tj-037-6346	245.74	170.28	0.6929
043	obe-cc-043-6434	329.04	224.67	0.6828
045	obe-dg-045-6461	207.22	158.74	0.7660
046	obe-mbr-046-6473	259.02	187.80	0.7250
047	obe-sb-047-6502	225.49	167.96	0.7449
048	obe-cg-048-6515	192.03	130.66	0.6804
052	obe-jb-052-6578	214.27	164.29	0.7667

A4.46: Bioimpedance assessment – left (Stage 2)

Participant ID Number	WBA L1 (FN)	WBA L1 (RZ)	WBA L1 (RI)	WBA L1 (RI/RZ)
003	obe-ts-003-5694	455.69	303.99	0.6671
009	obe-rc-009-5747	542.17	420.36	0.7753
012	obe-ml-012-5789	531.76	403.13	0.7581
013	obe-dr-013-5803	430.00	285.42	0.6638
015	obe-jb-015-5835	443.51	309.75	0.6984
019	obe-gn-019-5881	479.50	361.52	0.7540
020	obe-lc-020-5895	479.99	350.60	0.7304
021	obe-jv-021-5908	541.39	381.03	0.7038
022	obe-pe-022-5921	559.21	393.01	0.7028
027	obe-kr-027-5992	501.37	339.47	0.6771
028	obe-dc-028-6006	514.37	350.66	0.6817
036	obe-lk-036-0110	476.18	320.48	0.6730
037	obe-tj-037-6335	551.92	395.87	0.7173
043	obe-cc-043-6423	651.67	457.88	0.7026
045	obe-dg-045-6450	499.22	372.92	0.7470
046	obe-mbr-046-6462	500.80	359.61	0.7181
047	obe-sb-047-6491	555.73	414.40	0.7457
048	obe-cg-048-6504	481.31	347.63	0.7223
052	obe-jb-052-6567	546.63	402.75	0.7368

Participant ID Number	WBA L2 (FN)	WBA L2 (RZ)	WBA L2 (RI)	WBA L2 (RI/RZ)
003	obe-ts-003-5695	455.65	301.76	0.6623
009	obe-rc-009-5748	543.40	421.17	0.7751
012	obe-ml-012-5790	532.06	404.60	0.7604
013	obe-dr-013-5805	431.22	286.82	0.6651
015	obe-jb-015-5836	448.44	312.13	0.6960
019	obe-gn-019-5882	480.94	362.73	0.7542
020	obe-lc-020-5896	479.48	351.03	0.7321
021	obe-jv-021-5910	546.14	380.51	0.6967
022	obe-pe-022-5922	559.31	392.36	0.7015
027	obe-kr-027-5993	501.43	340.35	0.6788
028	obe-dc-028-6007	512.68	349.92	0.6825
036	obe-lk-036-0111	476.05	320.03	0.6723
037	obe-tj-037-6336	552.40	395.82	0.7165
043	obe-cc-043-6424	653.87	460.00	0.7035
045	obe-dg-045-6451	498.85	373.60	0.7489
046	obe-mbr-046-6463	502.02	360.47	0.7180
047	obe-sb-047-6492	556.00	414.43	0.7454
048	obe-cg-048-6505	481.25	347.57	0.7222
052	obe-jb-052-6568	547.89	402.36	0.7344

Participant ID Number	LA1 (FN)	LA1 (RZ)	LA1 (RI)	LA1 (RI/RZ)
003	obe-ts-003-5696	335.60	239.56	0.7138
009	obe-rc-009-5750	318.39	237.03	0.7445
012	obe-ml-012-5791	277.34	202.41	0.7298
013	obe-dr-013-5807	220.70	144.33	0.6540
015	obe-jb-015-5838	262.72	171.58	0.6531
019	obe-gn-019-5883	282.24	204.93	0.7261
020	obe-lc-020-5897	295.03	212.28	0.7195
021	obe-jv-021-5911	285.37	192.53	0.6747
022	obe-pe-022-5923	278.52	190.88	0.6853
027	obe-kr-027-5994	242.45	170.21	0.7020
028	obe-dc-028-6008	229.26	150.47	0.6563
036	obe-lk-036-0112	266.52	171.49	0.6434
037	obe-tj-037-6337	271.57	194.85	0.7175
043	obe-cc-043-6425	313.03	226.73	0.7243
045	obe-dg-045-6452	265.78	190.90	0.7183
046	obe-mbr-046-6464	263.06	192.33	0.7311
047	obe-sb-047-6493	298.26	223.46	0.7492
048	obe-cg-048-6506	237.49	169.07	0.7119
052	obe-jb-052-6569	282.18	245.90	0.8714

Participant ID Number	LA2 (FN)	LA2 (RZ)	LA2 (RI)	LA2 (RI/RZ)
003	obe-ts-003-5697	336.08	240.42	0.7154
009	obe-rc-009-5751	286.65	259.43	0.9050
012	obe-ml-012-5792	277.70	202.90	0.7306
013	obe-dr-013-5808	220.58	144.15	0.6535
015	obe-jb-015-5839	270.24	177.04	0.6551
019	obe-gn-019-5884	296.93	206.63	0.6959
020	obe-lc-020-5898	295.36	213.18	0.7218
021	obe-jv-021-5912	285.61	192.33	0.6734
022	obe-pe-022-5924	278.00	190.94	0.6868
027	obe-kr-027-5995	242.42	170.49	0.7033
028	obe-dc-028-6009	228.57	150.34	0.6577
036	obe-lk-036-0113	265.61	171.58	0.6460
037	obe-tj-037-6338	271.47	195.28	0.7193
043	obe-cc-043-6426	313.15	227.00	0.7249
045	obe-dg-045-6453	267.84	192.26	0.7178
046	obe-mbr-046-6465	262.06	192.24	0.7336
047	obe-sb-047-6494	298.36	223.68	0.7497
048	obe-cg-048-6507	236.59	168.86	0.7137
052	obe-jb-052-6570	283.13	244.19	0.8625

Participant ID Number	LL1 (FN)	LL1 (RZ)	LL1 (RI)	LL1 (RI/RZ)
003	obe-ts-003-5698	113.26	-37.19	-0.3284
009	obe-rc-009-5752	203.34	161.63	0.7949
012	obe-ml-012-5793	237.04	186.07	0.7850
013	obe-dr-013-5809	185.07	126.46	0.6833
015	obe-jb-015-5840	173.66	129.54	0.7459
019	obe-gn-019-5886	179.50	139.73	0.7784
020	obe-lc-020-5899	160.69	122.51	0.7624
021	obe-jv-021-5913	238.26	173.26	0.7272
022	obe-pe-022-5925	253.86	185.31	0.7300
027	obe-kr-027-5996	238.66	157.78	0.6611
028	obe-dc-028-6013	258.97	183.34	0.7080
036	obe-lk-036-0114	187.82	135.71	0.7226
037	obe-tj-037-6339	260.58	187.57	0.7198
043	obe-cc-043-6427	312.89	214.08	0.6842
045	obe-dg-045-6454	206.19	163.58	0.7933
046	obe-mbr-046-6466	221.60	156.12	0.7045
047	obe-sb-047-6495	239.08	179.98	0.7528
048	obe-cg-048-6508	223.40	159.49	0.7139
052	obe-jb-052-6571	209.66	161.12	0.7685

Participant ID Number	LL2 (FN)	LL2 (RZ)	LL2 (RI)	LL2 (RI/RZ)
003	obe-ts-003-5699	118.54	-31.61	-0.2667
009	obe-rc-009-5753	203.81	161.48	0.7923
012	obe-ml-012-5794	237.25	186.41	0.7857
013	obe-dr-013-5810	184.96	126.58	0.6844
015	obe-jb-015-5841	174.02	129.78	0.7458
019	obe-gn-019-5887	179.59	139.67	0.7777
020	obe-lc-020-5900	160.62	122.75	0.7642
021	obe-jv-021-5914	238.92	173.62	0.7267
022	obe-pe-022-5926	254.05	185.62	0.7306
027	obe-kr-027-5997	238.02	157.89	0.6633
028	obe-dc-028-6014	259.29	183.65	0.7083
036	obe-lk-036-0115	187.91	135.83	0.7228
037	obe-tj-037-6340	259.32	187.64	0.7236
043	obe-cc-043-6428	313.00	214.41	0.6850
045	obe-dg-045-6455	205.38	162.99	0.7936
046	obe-mbr-046-646	221.86	156.52	0.7055
047	obe-sb-047-6496	239.27	179.80	0.7515
048	obe-cg-048-6509	223.32	159.12	0.7125
052	obe-jb-052-6572	209.88	161.04	0.7673

A4.47: Tissue dielectric constant data (Stage 2)

Participant ID Number	Foot (R1)	Foot (R2)	Foot (R3)	Foot (L1)	Foot (L2)	Foot (L3)
003	38.7	38.6	37.4	36.8	35.9	36.5
004	46.8	46.4	44.9	48.5	46.0	44.4
012	39.1	39.5	39.2	44.5	44.4	43.5
013	40.7	38.2	40.3	40.2	41.8	41.4
015	36.7	36.6	35.0	35.3	35.3	34.6
016	45.7	43.7	44.2	48.4	48.2	47.2
019	37.6	37.9	37.4	37.9	39.3	39.7
020	45.8	46.7	46.4	49.4	49.2	
021	31.7	31.7		34.2	35.1	36.1
022	41.1	41.4	41.6	30.0	30.5	32.1
027	38.5	38.2		39.5	38.5	37.2
028	40.1	37.6	38.6	42.7	39.8	41.9
036	47.8	48.4		43.9	44.3	
037	37.0	37.6		51.0	48.3	48.0
043	23.9	24.4		26.9	26.4	
045	47.2	49.3		49.1	48.3	
046	40.5	43.2		42.9	42.4	
047	40.5	40.3		35.4	33.9	
048	38.5	39.3		38.7	37.0	
052	27.7	30.9		31.7	30.3	

Participant ID Number	Ankle (R1)	Ankle (R2)	Ankle (R3)	Ankle (L1)	Ankle (L2)	Ankle (L3)
003	21.1	20.9	21.6	17.4	17.2	19.5
004	28.5	28.9	28.2	31.6	31.3	31.6
012	30.3	32.6	30.6	40.7	39.1	41.2
013	30.9	31.1	31.1	34.1	33.9	33.8
015	27.8	28.5	26.8	25.8	26.2	24.7
016	34.8	33.3	33.3	31.4	31.6	29.7
019	25.5	25.7	24.0	26.9	25.1	26.8
020	33.4	32.9		30.0	30.2	
021	27.9	27.6	27.1	28.7	29.3	
022	28.0	26.9	26.0	25.8	24.9	24.3
027	24.8	24.5		28.6	26.6	26.7
028	35.3	35.3	35.6	38.6	37.5	
036	24.8	26.0	25.9	42.1	39.7	39.4
037	28.5	28.5		38.0	41.3	37.4
043	25.2	26.7	27.0	24.5	23.1	22.3
045	57.9	58.4		59.5	60.3	
046	33.3	32.7		32.9	32.9	
047	23.5	25.0		15.0	13.6	
048	29.2	28.2		30.7	30.7	
052	21.9	24.2		25.5	25.3	

Participant ID Number	Below Knee (R1)	Below Knee (R2)	Below Knee (R3)	Below Knee (L1)	Below Knee (L2)	Below Knee (L3)
003	33.3	32.5	33.3	26.9	26.0	26.2
004	28.9	29.5	29.9	30.1	29.2	28.5
012	34.0	35.5	35.1	30.0	30.0	30.3
013	36.1	36.6	36.5	39.5	40.6	38.8
015	29.7	30.4	29.1	34.0	32.1	32.7
016	39.7	39.5	40.2	32.9	32.9	32.7
019	33.0	33.1	32.8	32.9	32.9	32.9
020	43.1	44.1		47.7	47.3	
021	29.9	30.4		31.8	31.7	
022	43.8	43.8	46.1	38.4	39.0	38.8
027	33.5	33.1		35.4	35.1	
028	33.0	33.1		35.9	35.9	36.3
036	40.7	42.2		41.6	39.8	39.1
037	35.2	34.9		33.7	33.6	
043	24.7	23.5	23.3	26.4	26.4	
045	42.6	41.9		41.1	41.0	
046	37.5	34.9		38.4	40.3	
047	33.9	33.6		37.5	37.7	
048	33.3	32.7		32.9	32.9	
052	23.7	23.3		30.4	31.6	

Participant ID Number	Above Knee (R1)	Above Knee (R2)	Above Knee (R3)	Above Knee (L1)	Above Knee (L2)	Above Knee (L3)
003	22.2	21.5	21.9	19.9	20.3	20.5
004	36.4	36.3	36.2	33.2	33.5	34.4
012	29.8	30.5	30.5	24.2	24.2	23.6
013	31.7	30.4	31.1	32.7	30.6	32.4
015	29.3	27.9	29.9	24.3	24.9	24.0
016	26.6	27.9	28.3	33.5	33.7	35.6
019	30.5	31.6	31.4	33.1	33.1	33.5
020	28.2	29.0		28.8	28.8	
021	26.9	27.1		25.1	25.8	
022	26.9	26.9		27.2	27.2	
027	29.0	28.5		35.9	33.5	33.7
028	30.4	29.4		30.0	28.9	
036	34.1	34.8		35.8	34.9	
037	35.9	35.7		36.1	36.4	
043	23.2	23.2	23.4	22.4	22.4	22.3
045	36.1	37.5		35.7	35.3	
046	32.1	32.5		35.9	35.3	
047	31.3	30.7		31.3	31.4	
048	30.6	29.4		28.7	29.7	
052	25.1	25.4		27.4	27.1	

Participant ID Number	Below Groin (R1)	Below Groin (R2)	Below Groin (R3)	Below Groin (L1)	Below Groin (L2)	Below Groin (L3)
003	23.5	23.8	22.1	22.9	21.5	21.5
004	35.8	36.1	36.5	33.8	34.1	33.8
012	26.0	25.5	25.5	24.6	23.3	23.1
013	34.7	34.4	33.4	25.3	27.2	27.4
015	35.4	36.4	36.5	32.7	32.2	31.4
016	26.1	25.8	26.2	32.7	33.1	33.1
019	27.5	29.9	27.7	27.7	28.5	28.4
020	29.6	29.2		28.3	28.1	
021	29.3	30.6		27.3	28.2	28.2
022	27.4	27.4		28.4	29.0	
027	29.0	29.4		35.8	35.3	
028	29.8	30.6	31.1	32.7	32.7	
036	26.1	26.2		29.1	27.5	
037	33.1	32.8		33.8	35.3	
043	23.4	23.8		20.5	21.9	21.0
045	22.3	24.2		23.9	24.0	
046	30.8	30.4		35.7	35.4	
047	32.8	31.8		33.6	29.9	35.1
048	30.7	32.2		30.5	31.3	
052	25.9	26.5		26.3	26.8	

Participant ID Number	Abdominal Wall (R1)	Abdominal Wall (R2)	Abdominal Wall (R3)	Abdominal Wall (L1)	Abdominal Wall (L2)	Abdominal Wall (L3)
003	29.4	28.2	29.5	35.5	33.1	33.1
004	28.6	29.0	28.5	33.5	34.1	34.1
012	50.3	48.5	50.7	29.5	29.4	29.5
013	30.5	31.2	31.3	33.5	34.1	34.2
015	38.8	36.8	36.8	34.5	35.1	33.2
016	24.9	24.9	25.5	31.8	30.5	30.8
019	32.7	32.5	32.1	33.1	33.2	32.9
020	33.6	33.4		32.9	32.4	32.6
021	29.1	29.4		31.0	31.5	32.3
022	29.7	29.7		30.3	30.8	
027	32.3	31.5		33.1	33.5	
028	29.6	29.1	29.0	25.1	25.3	25.9
036	32.4	31.7		30.3	29.8	
037	38.7	37.6		37.1	37.0	37.1
043	22.9	23.5		24.8	24.8	
045	24.0	21.9		27.6	28.4	
046	32.2	32.1		31.5	31.4	
047	39.0	38.5		34.1	35.9	
048	37.6	37.7		40.8	38.7	
052	23.4	21.7		24.3	25.1	

A4.48: Summary of statistical results from limb volume data (Stage 2)

Statistical Results	Right Lower Limb Mean	Left Lower Limb Mean
Histogram	Normally Distributed	Normally Distributed
Number of participants	21	21
Mean (Standard Deviation)	7827.81 (1698.60)	7815.02 (1547.27)
With Oedema		
Number of participants	11	11
Mean (Standard Deviation)	8015.32 (2089.57)	8039.318 (1890.87)
Without Oedema		
Number of participants	10	10
Mean (Standard Deviation)	7621.55 (1212.42)	7568.30 (1103.77)
Difference between the means	393.77	471.02
95% Confidence Intervals (around the mean difference)	Lower: -1188.72 & Higher: 1976.25	Lower: -963.00 & Higher: 1905.04
T-Test		
Levene's Test	0.221	0.307
p value	0.609	0.500

A4.49: Bioimpedance whole body analysis data (CO, Stage 2)

Participant ID Number	TBW (litres) - R	TBW (litres) Average - R	TBW (litres) - L	TBW (litres) Average - L
003 (CO)	48.51	47.51	50.17	50.35
	46.50		50.53	
009 (CO)	43.61	43.59	42.36	42.34
	43.57		42.32	
012 (CO)	39.92	39.90	40.42	40.35
	39.88		40.27	
020 (CO)	41.96	41.93	42.00	41.97
	41.89		41.93	
021 (CO)	42.90	42.79	42.91	43.01
	42.68		43.10	
036 (CO)	67.02	66.97	64.93	64.97
	66.91		65.00	
045 (CO)	45.31	45.26	45.64	45.59
	45.20		45.54	
047 (CO)	42.49	42.21	42.13	42.14
	41.92		42.14	
048 (CO)	48.94	48.93	44.70	44.70
	48.92		44.70	

Participant ID Number	ECF (litres) - R	ECF (litres) Average - R	ECF (litres) - L	ECF (litres) Average - L
003 (CO)	25.73	25.83	26.76	26.77
	25.93		26.77	
009 (CO)	26.81	26.81	26.42	26.40
	26.80		26.38	
012 (CO)	24.83	24.80	24.59	24.59
	24.77		24.58	
020 (CO)	24.84	24.82	24.55	24.56
	24.80		24.57	
021 (CO)	23.89	23.87	24.14	24.07
	23.85		24.00	
036 (CO)	26.58	26.55	25.81	25.81
	26.51		25.81	
045 (CO)	27.09	27.09	27.33	27.34
	27.08		27.34	
047 (CO)	25.32	25.30	25.18	25.18
	25.27		25.17	
048 (CO)	26.86	26.85	25.83	25.83
	26.84		25.83	

Participant ID Number	ICF (litres) - R	ICF (litres) Average - R	ICF (litres) - L	ICF (litres) Average - L
003 (CO)	22.78	21.67	23.41	23.59
	20.56		23.77	
009 (CO)	16.80	16.79	15.95	15.95
	16.77		15.94	
012 (CO)	15.10	15.11	15.83	15.76
	15.11		15.69	
020 (CO)	17.12	17.11	17.44	17.40
	17.09		17.36	
021 (CO)	19.01	18.92	18.77	18.94
	18.83		19.10	
036 (CO)	40.44	40.42	39.11	39.15
	40.40		39.19	
045 (CO)	18.22	18.17	18.32	18.26
	18.12		18.20	
047 (CO)	17.17	16.91	16.96	16.97
	16.64		16.97	
048 (CO)	22.09	22.08	18.87	18.87
	22.07		18.87	

Participant ID Number	FFM (kg) - R	FFM (kg) Average - R	FFM (kg) - L	FFM (kg) Average - L
003 (CO)	66.27	64.90	68.54	68.79
	63.52		69.03	
009 (CO)	59.58	59.55	57.87	57.84
	59.52		57.81	
012 (CO)	54.54	54.51	55.22	55.12
	54.48		55.01	
020 (CO)	57.32	57.28	57.37	57.33
	57.23		57.28	
021 (CO)	58.60	58.45	58.62	58.75
	58.30		58.88	
036 (CO)	91.55	91.48	88.70	88.75
	91.41		88.80	
045 (CO)	61.90	61.83	62.36	62.29
	61.75		62.21	
047 (CO)	58.05	57.66	57.56	57.56
	57.26		57.56	
048 (CO)	66.86	66.85	61.06	61.07
	66.83		61.07	

Participant ID Number	FM (kg) - R	FM (kg) Average - R	FM (kg) - L	FM (kg) Average - L	BMI (kg/m ²)
003 (CO)	78.03	79.41	75.76	75.52	57.08
	80.78		75.27		
009 (CO)	83.82	83.85	85.53	85.56	48.47
	83.88		85.59		
012 (CO)	73.66	73.69	72.98	73.09	46.52
	73.72		73.19		
020 (CO)	72.68	72.73	72.63	72.68	52.74
	72.77		72.72		
021 (CO)	83.60	83.75	83.58	83.45	54.86
	83.90		83.32		
036 (CO)	45.75	45.82	48.60	48.55	41.91
	45.89		48.50		
045 (CO)	63.70	63.78	63.24	63.32	41.01
	63.85		63.39		
047 (CO)	99.75	100.15	100.24	100.24	58.67
	100.54		100.24		
048 (CO)	67.34	67.36	73.14	73.14	51.14
	67.37		73.13		

A4.50: Bioimpedance whole body analysis data (NCO, Stage 2)

Participant ID Number	TBW (litres) - R	TBW (litres) Average - R	TBW (litres) - L	TBW (litres) Average - L
013 - NCO	57.16	57.05	57.87	57.76
	56.93		57.64	
015 - NCO	61.45	61.42	58.71	58.60
	61.39		58.48	
019 - NCO	41.12	41.12	42.41	42.36
	41.12		42.31	
022 - NCO	37.34	37.32	36.32	36.35
	37.29		36.38	
027 - NCO	51.38	51.32	51.13	51.07
	51.26		51.00	
028 - NCO	54.55	54.54	53.89	53.92
	54.52		53.95	
037 - NCO	43.37	43.32	40.70	40.71
	43.27		40.72	
043 - NCO	36.22	36.21	35.03	34.97
	36.19		34.90	
046 - NCO	36.95	36.94	39.86	39.83
	36.93		39.80	
052 - NCO	41.83	41.82	41.53	41.57
	41.80		41.61	

Participant ID Number	ECF (litres) - R	ECF (litres) Average - R	ECF (litres) - L	ECF (litres) Average - L
013 - NCO	30.32	30.31	30.72	30.69
	30.30		30.66	
015 - NCO	33.12	33.13	32.78	32.66
	33.13		32.53	
019 - NCO	25.00	24.98	25.65	25.63
	24.95		25.60	
022 - NCO	20.51	20.51	20.41	20.41
	20.51		20.40	
027 - NCO	27.83	27.82	27.68	27.68
	27.81		27.67	
028 - NCO	29.67	29.67	29.37	29.40
	29.66		29.43	
037 - NCO	23.78	23.80	23.35	23.35
	23.82		23.34	
043 - NCO	19.85	19.85	19.67	19.65
	19.85		19.63	
046 - NCO	21.38	21.37	22.89	22.88
	21.36		22.86	
052 - NCO	24.33	24.32	24.50	24.49
	24.31		24.47	

Participant ID Number	ICF (litres) - R	ICF (litres) Average - R	ICF (litres) - L	ICF (litres) Average - L
013 - NCO	26.84	26.74	27.15	27.07
	26.64		26.98	
015 - NCO	28.33	28.30	25.93	25.94
	28.26		25.94	
019 - NCO	16.12	16.15	16.77	16.75
	16.17		16.72	
022 - NCO	16.82	16.80	15.91	15.95
	16.78		15.98	
027 - NCO	23.55	23.50	23.45	23.39
	23.45		23.33	
028 - NCO	24.88	24.87	24.52	24.52
	24.86		24.52	
037 - NCO	19.59	19.53	17.35	17.37
	19.46		17.38	
043 - NCO	16.37	16.36	15.35	15.31
	16.34		15.27	
046 - NCO	15.57	15.57	16.97	16.96
	15.57		16.94	
052 - NCO	17.50	17.50	17.03	17.09
	17.49		17.15	

Participant ID Number	FFM (kg) - R	FFM (kg) Average - R	FFM (kg) - L	FFM (kg) Average - L
013 - NCO	78.09	77.94	79.05	78.90
	77.78		78.74	
015 - NCO	83.95	83.91	80.20	80.05
	83.87		79.89	
019 - NCO	56.17	56.17	57.94	57.87
	56.17		57.80	
022 - NCO	51.01	50.98	49.62	49.66
	50.95		49.70	
027 - NCO	70.19	70.11	69.85	69.76
	70.03		69.67	
028 - NCO	74.52	74.50	73.63	73.67
	74.48		73.70	
037 - NCO	59.25	59.19	55.60	55.62
	59.12		55.63	
043 - NCO	49.48	49.46	47.85	47.77
	49.44		47.68	
046 - NCO	50.48	50.47	54.45	54.41
	50.45		54.37	
052 - NCO	57.14	57.13	56.74	56.80
	57.11		56.85	

Participant ID Number	FM (kg) - R	FM (kg) Average - R	FM (kg) - L	FM (kg) Average - L	BMI (kg/m ²)
013 - NCO	67.11	67.27	66.15	66.31	49.66
	67.42		66.46		
015 - NCO	99.35	99.39	103.10	103.26	61.96
	99.43		103.41		
019 - NCO	68.03	68.03	66.26	66.33	46.18
	68.03		66.40		
022 - NCO	45.29	45.32	46.68	46.64	38.09
	45.35		46.60		
027 - NCO	61.41	61.49	61.75	61.84	42.97
	61.57		61.93		
028 - NCO	59.48	59.50	60.37	60.34	39.37
	59.52		60.30		
037 - NCO	59.05	59.12	62.70	62.69	42.93
	59.18		62.67		
043 - NCO	64.82	64.84	66.45	66.54	44.65
	64.86		66.62		
046 - NCO	50.72	50.74	46.75	46.79	38.56
	50.75		46.83		
052 - NCO	80.26	80.28	80.66	80.61	50.47
	80.29		80.55		

A4.51: Summary of statistical results from fluid measurement (WBA) data (Stage 2)

(Missing data: two participants could not complete the bioimpedance assessment)

Statistical Results	TBW (Litres) - R	TBW (Litres) - L	ECF (Litres) - R	ECF (Litres) - L
Histogram	Skewed	Normally Distributed	Normally Distributed	Normally Distributed
Number of participants	19	19	19	19
Missing Data	2	2	2	2
Mean (Standard Deviation)		45.92 (8.05)	25.67 (3.27)	25.65 (3.16)
Median (Interquartile Range)	43.32 (41.12 to 51.32)			
With Oedema				
Number of participants	9	9	9	9
Missing Data	2	2	2	2
Mean (Standard Deviation)		46.16 (7.63)	25.77 (1.13)	25.62 (1.10)
Median (Interquartile Range)	43.59 (42.07 to 48.22)			
Without Oedema				
Number of participants	10	10	10	10
Mean (Standard Deviation)		45.71 (8.81)	25.58 (4.50)	25.68 (4.35)
Median (Interquartile Range)	42.57 (37.23 to 55.17)			
Difference between the means		0.44	0.19	-0.07
95% Confidence Intervals (around mean difference)		Lower: -7.58 & Higher: 8.45	Lower: -3.08 & Higher: 3.46	Lower: -3.23 & Higher: 3.10
Difference between the medians	1.02			
95% Confidence Intervals (around median difference)	Lower: -8.17 & Higher: 10.21			
T-Test				
Levene's Test	Using Natural Log Data: 0.152	0.223	0.002	0.003
p value	0.848	0.908	0.898	0.963

Statistical Results	ICF (Litres) - R	ICF (Litres) - L	FFM (kg) - R	FFM (kg) - L
Histogram	Skewed	Skewed	Skewed	Normally Distributed
Number of participants	19	19	19	19
Missing Data	2	2	2	2
Mean (Standard Deviation)				62.74 (10.99)
Median (Interquartile Range)	18.17 (16.79 to 23.50)	17.40 (16.75 to 23.59)	59.19 (56.17 to 70.11)	
With Oedema				
Number of participants	9	9	9	9
Missing Data	2	2	2	2
Mean (Standard Deviation)				63.06 (10.42)
Median (Interquartile Range)	18.17 (16.85 to 21.88)	18.26 (16.46 to 21.27)	59.55 (57.47 to 65.88)	
Without Oedema				
Number of participants	10	10	10	10
Mean (Standard Deviation)				62.45 (12.03)
Median (Interquartile Range)	18.52 (16.31 to 25.34)	17.23 (16.55 to 24.88)	58.16 (50.85 to 75.36)	
Difference between the means				0.60
95% Confidence Intervals (around mean difference)				Lower: -10.35 & Higher: 11.56
Difference between the medians	-0.35	1.03	1.39	
95% Confidence Intervals (around median difference)	Lower: -5.51 & Higher: 4.82	Lower: -4.56 & Higher: 6.62	Lower: -11.17 & Higher: 13.95	
T-Test				
Levene's Test	Using Reciprocal Data: 0.764	Using Reciprocal Data: 0.71	Using Natural Log Data: 0.152	0.223
p value	0.929	0.857	0.848	0.909

Statistical Results	FM (kg) - R	FM (kg) - L	BMI (kg/m ²) - R	BMI (kg/m ²) - L
Histogram	Normally Distributed	Normally Distributed	Normally Distributed	Normally Distributed
Number of participants	19	19	19	19
Missing Data	2	2	2	2
Mean (Standard Deviation)	69.82 (15.49)	70.36 (15.73)	47.75 (7.05)	47.75 (7.05)
With Oedema				
Number of participants	9	9	9	9
Missing Data	2	2	2	2
Mean (Standard Deviation)	74.50 (15.20)	75.06 (14.44)	50.27 (6.30)	50.27 (6.30)
Without Oedema				
Number of participants	10	10	10	10
Mean (Standard Deviation)	65.60 (15.26)	66.14 (16.35)	45.48 (7.21)	45.48 (7.21)
Difference between the means	8.91	8.93	4.78	4.78
95% Confidence Intervals (around mean difference)	Lower: -5.86 & Higher: 23.67	Lower: -6.08 & Higher: 23.93	Lower: -1.81 & Higher: 11.37	Lower: -1.81 & Higher: 11.37
T-Test				
Levene's Test	0.932	0.911	0.948	0.948
p value	0.220	0.227	0.144	0.144

A4.52: Bioimpedance assessment - right (Stage 2, after surgery)

Participant ID Number	WBA R1 (FN)	WBA R1 (RZ)	WBA R1 (RI)	WBA R1 (RI/RZ)
012	Due to the patient wearing lymphoedema stockings, the machine gave either: abnormal readings or zero readings. Therefore, the patient could NOT be assessed.			
016	obe-fb-016-6639	442.69	352.54	0.7964
020	obe-lc-020-6483	430.79	331.15	0.7687
027	obe-kr-027-6561	517.12	365.21	0.7062
028	obe-dc-028-6586	492.67	352.09	0.7147
Participant ID Number	WBA R2 (FN)	WBA R2 (RZ)	WBA R2 (RI)	WBA R2 (RI/RZ)
016	obe-fb-016-6640	440.73	351.92	0.7985
020	obe-lc-020-6484	431.74	331.11	0.7669
027	obe-kr-027-6562	516.70	366.00	0.7083
028	obe-dc-028-6587	491.14	352.18	0.7171
Participant ID Number	RA1 (FN)	RA1 (RZ)	RA1 (RI)	RA1 (RI/RZ)
016	obe-fb-016-6642	265.40	211.07	0.7953
020	obe-lc-020-6485	271.04	206.76	0.7628
027	obe-kr-027-6563	248.23	181.09	0.7295
028	obe-dc-028-6588	231.66	163.03	0.7037
Participant ID Number	RA2 (FN)	RA2 (RZ)	RA2 (RI)	RA2 (RI/RZ)
016	obe-fb-016-6643	239.97	232.77	0.9700
020	obe-lc-020-6486	271.30	206.90	0.7626
027	obe-kr-027-6564	247.90	181.75	0.7332
028	obe-dc-028-6589	231.80	162.99	0.7031
Participant ID Number	RL2 (FN)	RL2 (RZ)	RL2 (RI)	RL2 (RI/RZ)
016	obe-fb-016-6645	145.52	122.26	0.8402
020	obe-lc-020-6488	140.83	109.03	0.7742
027	obe-kr-027-6566	251.18	172.84	0.6881
028	obe-dc-028-6592	236.82	175.76	0.7422
Participant ID Number	RL1 (FN)	RL1 (RZ)	RL1 (RI)	RL1 (RI/RZ)
016	obe-fb-016-6644	145.60	122.39	0.8406
020	obe-lc-020-6487	140.80	109.17	0.7754
027	obe-kr-027-6565	250.75	172.27	0.6870
028	obe-dc-028-6590	236.99	175.63	0.7411

A4.53: Bioimpedance assessment - left (Stage 2, after surgery)

Participant ID Number	WBA L1 (FN)	WBA L1 (RZ)	WBA L1 (RI)	WBA L1 (RI/RZ)
016	obe-fb-016-6633	465.19	368.69	0.7926
020	obe-lc-020-6476	442.27	341.96	0.7732
027	obe-kr-027-6555	501.44	355.15	0.7083
028	obe-dc-028-6580	497.86	359.77	0.7226
Participant ID Number	WBA L2 (FN)	WBA L2 (RZ)	WBA L2 (RI)	WBA L2 (RI/RZ)
016	obe-fb-016-6634	464.18	369.38	0.7958
020	obe-lc-020-6477	442.83	342.50	0.7734
027	obe-kr-027-6556	500.62	354.88	0.7089
028	obe-dc-028-6581	498.25	360.74	0.7240
Participant ID Number	LA1 (FN)	LA1 (RZ)	LA1 (RI)	LA1 (RI/RZ)
016	obe-fb-016-6635	282.42	222.66	0.7884
020	obe-lc-020-6478	273.04	210.91	0.7725
027	obe-kr-027-6557	236.21	171.87	0.7276
028	obe-dc-028-6582	232.52	166.48	0.7160
Participant ID Number	LA2 (FN)	LA2 (RZ)	LA2 (RI)	LA2 (RI/RZ)
016	obe-fb-016-6636	282.26	223.28	0.7910
020	obe-lc-020-6479	272.35	209.09	0.7677
027	obe-kr-027-6558	237.15	172.06	0.7255
028	obe-dc-028-6583	232.08	166.32	0.7166
Participant ID Number	LL1 (FN)	LL1 (RZ)	LL1 (RI)	LL1 (RI/RZ)
016	obe-fb-016-6637	146.04	121.54	0.8322
020	obe-lc-020-6480	149.84	116.62	0.7783
027	obe-kr-027-6559	244.97	172.13	0.7027
028	obe-dc-028-6584	244.32	180.04	0.7369
Participant ID Number	LL2 (FN)	LL2 (RZ)	LL2 (RI)	LL2 (RI/RZ)
016	obe-fb-016-6638	145.94	121.82	0.8347
020	obe-lc-020-6481	150.05	116.30	0.7751
027	obe-kr-027-6560	245.79	172.29	0.7010
028	obe-dc-028-6585	245.09	180.37	0.7359

A4.54: Bioimpedance whole body analysis data (Stage 2, after surgery)

Participant ID Number	TBW (litres) - R	TBW (litres) Average - R	TBW (litres) - L	TBW (litres) Average - L	
016 (CO)	37.73	37.73	36.70	36.65	
	37.72		36.59		
020 (CO)	41.41	41.44	40.43	39.45	
	41.46		38.47		
027 (NCO)	46.12	46.06	46.94	46.94	
	46.00		46.94		
028 (NCO)	50.91	50.88	49.98	49.92	
	50.84		49.85		
Participant ID Number	ECF (litres) - R	ECF (litres) Average - R	ECF (litres) - L	ECF (litres) Average - L	
016 (CO)	24.85	24.89	24.04	24.06	
	24.92		24.08		
020 (CO)	25.58	25.56	25.13	24.82	
	25.54		24.51		
027 (NCO)	26.04	26.05	26.58	26.60	
	26.05		26.61		
028 (NCO)	29.09	29.12	28.89	28.89	
	29.15		28.88		
Participant ID Number	ICF (litres) - R	ICF (litres) Average - R	ICF (litres) - L	ICF (litres) Average - L	
016 (CO)	12.88	12.84	12.66	12.59	
	12.80		12.51		
020 (CO)	15.83	15.88	15.30	14.63	
	15.92		13.96		
027 (NCO)	20.08	20.02	20.36	20.35	
	19.95		20.34		
028 (NCO)	21.81	21.75	21.08	21.03	
	21.68		20.97		
Participant ID Number	FFM (kg) - R	FFM (kg) Average - R	FFM (kg) - L	FFM (kg) Average - L	
016 (CO)	51.54	51.54	50.14	50.06	
	51.53		49.98		
020 (CO)	56.57	56.61	55.23	53.89	
	56.64		52.55		
027 (NCO)	63.00	62.92	64.12	64.13	
	62.84		64.13		
028 (NCO)	69.54	69.50	68.27	68.19	
	69.45		68.10		
Participant ID Number	FM (kg) - R	FM (kg) Average - R	FM (kg) - L	FM (kg) Average - L	BMI (kg/m ²)
016 (CO)	65.66	65.67	67.06	67.14	46.36
	65.67		67.22		46.36
020 (CO)	61.83	61.80	63.17	64.51	48.03
	61.76		65.85		48.03
027 (NCO)	53.60	53.68	52.48	52.48	38.07
	53.76		52.47		38.07
028 (NCO)	51.26	51.31	52.53	52.62	35.68
	51.35		52.70		35.68

A4.55: Summary of statistical results from R_{zero} and $R_{infinity}$ data (Stage 2)

	Right	Left	Right	Left
Statistical Results	R_0 upper limb / R_0 lower limb	R_0 upper limb / R_0 lower limb	R_i/R_0 lower limb / R_i/R_0 upper limb	R_i/R_0 lower limb / R_i/R_0 upper limb
Histogram	Normally Distributed	Skewed	Normally Distributed	Skewed
Number of participants	19	19	19	19
Missing Data	2	2	2	2
Mean (Standard Deviation)	1.30 (0.30)	1.34 (0.45)	1.03 (0.08)	0.95 (0.34)
Median (Interquartile Range)		1.20 (1.06 to 1.49)		1.05 (0.96 to 1.08)
With Oedema				
Number of participants	9	9	9	9
Missing Data	2	2	2	2
Mean (Standard Deviation)	1.46 (0.27)		1.04 (0.05)	
Median (Interquartile Range)		1.30 (1.19 to 1.67)		1.06 (0.98 to 1.10)
Without Oedema				
Number of participants	10	10	10	10
Mean (Standard Deviation)	1.14 (0.24)		1.02 (0.10)	
Median (Interquartile Range)		1.14 (1.02 to 1.40)		1.03 (0.94 to 1.08)
Difference between the	0.32		0.02	
95% Confidence Intervals (around mean difference)	Lower: 0.08 & Higher: 0.57		Lower: -0.05 & Higher: 0.10	
Difference between the		0.16		0.03
95% Confidence Intervals (around median difference)		Lower: -0.23 & Higher: 0.55		Lower: -0.06 & Higher: 0.13
T-Test				
Levene's Test	0.924	Using Reciprocal Data: 0.881	0.114	
p value	0.013	0.073	0.504	Mann-Whitney U: 0.566

A4.56: Summary of statistical results from fluid measurement (specific sites) data (Stage 2)

(Missing Data: assessment where TDC machine was not charged enough)

Statistical Results	Right Foot	Left Foot	Right Ankle	Left Ankle
Histogram	Normally Distributed	Normally Distributed	Skewed	Skewed
Number of participants	20	20	20	20
Missing Data	1	1	1	1
Mean (Standard Deviation)	39.31 (6.06)	39.99 (6.62)		
Median (Interquartile Range)			28.10 (25.20 to 32.54)	30.40 (25.44 to 37.02)
With Oedema				
Number of participants	10	10	10	10
Missing Data	1	1	1	1
Mean (Standard Deviation)	42.17 (5.34)	42.45 (5.86)		
Median (Interquartile Range)			28.62 (25.24 to 33.31)	30.8 (26.26 to 40.35)
Without Oedema				
Number of participants	10	10	10	10
Mean (Standard Deviation)	36.46 (5.56)	37.53 (6.69)		
Median (Interquartile Range)			27.34 (24.97 to 31.52)	26.79 (25.30 to 34.96)
Difference between means	5.72	4.92		
95% Confidence Intervals (around mean difference)	Lower: 0.59 & Higher: 10.84	Lower: -0.99 & Higher: 10.82		
Difference between medians			1.28	4.01
95% Confidence Intervals (around median difference)			Lower: -4.13 & Higher: 6.69	Lower: -7.02 & Higher: 15.05
T-Test				
Levene's Test	0.722	0.911		Using Natural Log Data: 0.307
p value	0.031	0.097	Mann-Whitney U: 0.496	0.790

Statistical Results	Right Below Knee	Left Below Knee	Right Above Knee	Left Above Knee
Histogram	Normally Distributed	Normally Distributed	Normally Distributed	Normally Distributed
Number of participants	20	20	20	20
Missing Data	1	1	1	1
Mean (Standard Deviation)	34.50 (5.81)	34.77 (5.29)	29.87 (4.04)	29.99 (4.90)
With Oedema				
Number of participants	10	10	10	10
Missing Data	1	1	1	1
Mean (Standard Deviation)	36.13 (5.19)	34.95 (6.47)	30.39 (4.57)	29.79 (5.23)
Without Oedema				
Number of participants	10	10	10	10
Mean (Standard Deviation)	32.86 (6.19)	34.59 (4.14)	29.34 (3.61)	30.20 (4.81)
Difference between means	3.27	0.37	1.05	-0.42
95% Confidence Intervals (around mean difference)	Lower: -2.09 & Higher: 8.64	Lower: -4.74 & Higher: 5.47	Lower: -2.82 & Higher: 4.91	Lower: -5.14 & Higher: 4.31
T-Test				
Levene's Test	0.889	0.12	0.549	0.871
p value	0.216	0.882	0.577	0.855

Statistical Results	Right Below Groin	Left Below Groin	Right Abdominal Wall	Left Abdominal Wall
Histogram	Normally Distributed	Normally Distributed	Skewed	Normally Distributed
Number of participants	20	20	20	20
Missing Data	1	1	1	1
Mean (Standard Deviation)	29.13 (3.98)	29.31 (4.45)		31.70 (3.91)
Median (Interquartile Range)			31.45 (28.78 to 36.48)	
With Oedema				
Number of participants	10	10	10	10
Missing Data	1	1	1	1
Mean (Standard Deviation)	28.35 (4.22)	28.46 (4.23)		32.53 (3.35)
Median (Interquartile Range)			30.65 (27.80 to 37.93)	
Without Oedema				
Number of participants	10	10	10	10
Mean (Standard Deviation)	29.91 (3.79)	30.17 (4.72)		30.86 (4.41)
Median (Interquartile Range)			31.45 (27.72 to 33.69)	
Difference between means	-1.56	-1.7		1.67
95% Confidence Intervals (around mean difference)	Lower: -5.33 & Higher: 2.20	Lower: -5.92 & Higher: 2.51		Lower: -2.00 & Higher: 5.36
Difference between medians			-0.80	
95% Confidence Intervals (around median difference)			Lower: -9.22 & Higher: 7.62	
T-Test				
Levene's Test	0.569	0.588	Using Natural Log Data: 0.420	0.277
p value	0.395	0.407	0.591	0.351

A4.57: Tissue dielectric constant data (Stage 2, after surgery)

Participant ID Number	Foot (R1)	Foot (R2)	Foot (L1)	Foot (L2)
012	Foot, ankle and below knee site measurements: not possible due to stockings.			
016	41.4	43.6	52.6	53.2
020	60.8	59.1	58.5	60.8
027	42.4	44.9	39.4	41.7
028	50.9	48.4	47.6	45.4

Participant ID Number	Ankle (R1)	Ankle (R2)	Ankle (L1)	Ankle (L2)
016	30.2	31.9	31.9	31.6
020	36.9	35.5	31.1	33.5
027	29.0	27.0	34.0	33.6
028	43.3	40.6	36.8	38.3

Participant ID Number	Below Knee (R1)	Below Knee (R2)	Below Knee (L1)	Below Knee (L2)
016	43.2	43.2	40.0	41.7
020	46.9	48.3	44.0	43.2
027	48.3	47.6	42.5	40.1
028	32.6	35.3	42.0	41.1

Participant ID Number	Above Knee (R1)	Above Knee (R2)	Above Knee (L1)	Above Knee (L2)
012	33.7	34.0	29.3	30.7
016	37.3	36.4	37.2	37.7
020	29.0	29.2	29.4	29.6
027	29.7	32.8	38.5	35.6
028	36.6	35.1	33.7	33.7

Participant ID Number	Below Groin (R1)	Below Groin (R2)	Below Groin (R3)	Below Groin (L1)	Below Groin (L2)	Below Groin (L3)
012	29.5	28.5		29.6	29.7	
016	35.0	33.1		34.2	34.5	36.4
020	29.1	30.6		28.7	27.5	
027	30.3	35.1	34.5	32.7	35.2	
028	32.3	32.8		32.8	34.7	

Participant ID Number	Abdominal Wall (R1)	Abdominal Wall (R2)	Abdominal Wall (L1)	Abdominal Wall (L2)	Abdominal Wall (L3)
012	66.4	67.6	34.2	34.4	34.6
016	33.5	33.8	38.7	38.3	
020	38.2	36.8	38.2	38.0	
027	27.1	25.8	29.1	29.3	
028	34.8	35.5	38.0	38.0	