Quality of life and other outcomes of breast reduction surgery

by

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LIST OF ABBREVIATIONS

ASA	American Society of Anesthesiologists
AUD	Australian dollars
BMI	Body mass index
BP	Bodily Pain (SF-36 scale)
BSA	Body surface area
CEAC	Cost-effectiveness acceptability curve
CEP	Cost-effectiveness plane
CI	Confidence interval
CUA	Cost-utility analysis
ES	Effect size
GH	General Health (SF-36 scale)
HRQoL	Health-related quality of life
ICER	Incremental cost-effectiveness ratio
MBSRQ	Multidimensional Body-Self Relations Questionnaire
MCS	SF-36: Mental Component Summary
MH	Mental Health (SF-36 scale)
MID	Minimal important difference
MSAC	Medical Services Advisory Committee
N	Number
NICE	National Institute of Clinical Excellence
OR	Odds ratio
PBAC	Pharmaceutical Benefits Advisory Committee

PCS	SF-36: Physical Component Summary
PF	Physical Function (SF-36 scale)
PRO	Patient-reported outcome
PROM	Patient-reported outcome measure
QALY	Quality-adjusted life year
RE	Role Emotional (SF-36 scale)
RP	Role Physical (SF-36 scale)
SD	Standard deviation
SEM	Standard error of measurement
SF	Social Functioning (SF-36 scale)
SF-6D	Short Form six-dimensional
SF-36	Short Form-36 questionnaire
SF-36v2	Short Form-36 version 2 questionnaire
SRM	Standardised response mean
UK	United Kingdom
US	United States of America
VT	Vitality (SF-36 scale)
WHO	World Health Organisation

THESIS SUMMARY

The effectiveness of breast reduction surgery for women with symptomatic mammary hypertrophy has been established by previous studies but questions have remained about whether restrictions to accessing breast reduction surgery, based on particular criteria, are appropriate. This thesis is a comprehensive body of work on the health benefits of breast reduction surgery, evidence for restrictions and cost-effectiveness.

The introductory chapter of this thesis presents a review of the literature relating to the health burden associated with breast hypertrophy; and the reported health gains following breast reduction surgery. A review of the assessment of outcomes following surgery through post-operative complications and patient-reported outcomes is included. This chapter highlights the inconsistencies and limitations described in existing research studies. The final section of Chapter 1 details the increasing importance of economic evaluations in weighing up the costs and benefits of medical interventions.

This thesis reports on research which aimed to provide insight into the health burden of breast hypertrophy and the clinical- and cost-effectiveness of breast reduction surgery in improving health-related quality of life (HRQoL) within the Australian healthcare system. Chapter 2 describes a prospective outcome study in Australian women before and up to 12-months after breast reduction surgery. This study details the recruitment of a control group of women with breast hypertrophy who did not undergo surgery for comparison. HRQoL was assessed using validated patient-reported outcome measures (PROMs) including the Short Form-36 (SF-36) and Multi-Dimensional Body-Self Relations Questionnaire (MBSRQ). This chapter describes the comparison of outcomes to normative data and demonstrates the effectiveness of surgery in improving HRQoL to levels of the general population. The analysis extended to assess whether women benefit from surgery regardless of participant and clinical factors, including commonly scrutinised factors such as body mass index and resection weight.

Normative data provides a valuable clinical reference point for clinicians to compare scores from women undergoing breast reduction surgery, enabling a better understanding of the health burden of breast hypertrophy and the health benefits of breast reduction surgery. Chapter 3 was designed to derive normative BREAST-Q data from women within the Australian general population; prior to this study, normative BREAST-Q data was limited to a United States population. A comparison of normative population data demonstrated that differences exist when comparing HRQoL between populations, emphasizing the importance of using country-specific normative data wherever possible.

Chapter 4 examines the satisfaction and wellbeing in women before and 12-months after breast

reduction surgery using the BREAST-Q Reduction module. The use of a condition-specific questionnaire in combination with the generic instruments described in Chapter 2 provides a comprehensive assessment of patient-reported outcomes following surgery. Minimal important difference estimates remain undetermined for this PROM and were established in this study to further enhance interpretability and provide clinical relevance of BREAST-Q scores.

Limited evidence exists as to the long-term health benefits of breast reduction surgery. A prospective study establishing the long-term outcomes following breast reduction surgery is detailed in Chapter 5. This study provides a follow-up of women who underwent surgery and were included in the studies described in Chapter 2 and Chapter 4.

Chapter 6 describes the estimation of breast and body volume in women with breast hypertrophy before and after surgery using a series of techniques including anthropometric measurements, water displacement and three-dimensional laser scanning.

In an era of limited healthcare resources, evidence assessing the cost-effectiveness of breast reduction surgery is important to support the maintenance of funding by healthcare decision-makers. Chapter 7 details an economic evaluation of breast reduction surgery within the Australian public healthcare setting. HRQoL gains were assessed using the SF-6D and effectiveness of surgery was measured in terms of cost per quality-adjusted life years (QALYs) gained.

The final chapter summarises the evidence presented in this thesis that breast hypertrophy is a chronic and painful health condition and establishes the effectiveness of surgery in improving HRQoL to levels of the general population. This thesis established that women benefit from surgery regardless of patient and clinical characteristics, including those commonly used as restrictive criteria for access to surgery and insurance coverage in many countries and jurisdictions worldwide. This thesis provides strong evidence to demonstrate the clinical- and cost-effectiveness of surgery, supporting the inclusion of this procedure in publicly funded health systems.

DECLARATION

I certify that this thesis:

1. does not incorporate without acknowledgment any material previously submitted for a degree or diploma in any university; and
2. to the best of my knowledge and belief, does not contain any material previously published or written by another person except where due reference is made in the text.

Signed:

Tamara Crittenden

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PUBLICATIONS

The following is a list of publications which were generated from the work contained within this thesis:

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Crittenden T, Watson DI, Ratcliffe, J, Griffin, P, Dean, NR on behalf of the AFESA Research Group
BMJ Open 2020; 10(2): e031804.

2019 **Outcomes of Breast Reduction Surgery using the BREAST-Q: A Prospective Study and Comparison with Normative Data.**
Crittenden T, Griffin P, Watson DI, Ratcliffe JR, Dean NR
Plastic and Reconstructive Surgery 2019; Nov; 144: 1034-1044.

2019 **Breast reduction surgery improves health-related quality of life in women with breast hypertrophy: a comparison to other surgical interventions.**
Crittenden T, Watson DI, Ratcliffe, J, Dean, NR
Quality of Life Research 2019; 28: S115-S115.

2018 **Measuring breast volume in hypertrophy: laser scanning or water displacement?**
Crittenden T, Veitch D, Henneberg M, Burford K, van Essen P, Deut K, Lomax E, Griffin P, Dean NR
Australasian Journal of Plastic Surgery 2018; 1(2): 33-40.

2018 **Normative data for the BREAST-Q Reduction module in an Australian population.**
Crittenden T, Watson D, Ratcliffe J, Dean NR
Quality of Life Research 2018; 27(S1): S56-S57.

PRESENTATIONS

The following is a list of presentations which were generated from the work contained within this thesis:

2019 **Breast reduction surgery provides symptomatic relief and improves health-related quality of life in women with breast hypertrophy.**
Crittenden, T., Watson, D., Ratcliffe, J., Griffin, P., & Dean, N.R.
Presenter: Tamara Crittenden
Oral presentation at the Plastic Surgery Congress (PSC) 2019, Melbourne, Australia.

2019 **Quality of life in women who undergo breast reduction surgery: a prospective outcome study and comparison with normative data.**
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Presenter: Tamara Crittenden
Oral presentation at the Plastic Surgery Congress (PSC) 2019, Melbourne, Australia.

2019 **Breast reduction surgery improves health-related quality of life in women with breast hypertrophy: a comparison to other surgical interventions.**
Crittenden, T., Watson, D., Ratcliffe, J. & Dean, N.R.
Presenter: Tamara Crittenden
Poster presentation at the International Society for Quality of Life Research (ISOQOL) 26th Annual Conference 2019, San Diego, USA (International meeting).

2018 **Normative data for the BREAST-Q Reduction Module in an Australian Population.**
Crittenden, T., Watson, D., Ratcliffe, J. & Dean, N.R.
Presenter: Tamara Crittenden
Poster presentation at the International Society for Quality of Life Research (ISOQOL) 25th Annual Conference 2018, Dublin, Ireland (International meeting).
Awarded Student Poster Presentation Finalist.

2017 **Does Bilateral Breast Reduction Surgery Improve the Health Burden of Macromastia?**
Crittenden, T., Watson, D., Ratcliffe, J., Griffin, P., & Dean, N.R.
Presenter: Tamara Crittenden
Oral presentation at Flinders Health Research Week 2017, Flinders Centre for Innovation in Cancer, Adelaide, Australia.

1. LITERATURE REVIEW

1.1 Introduction

A body of literature has established that breast hypertrophy can have a significant impact on daily activities and the quality of life of affected women. It is a cause of considerable physical and psychosocial impairment. Effects of breast hypertrophy include persistent back, neck, shoulder and breast pain; painful bra strap grooving into shoulders; chronic skin rashes; poor body posture; hand tingling; difficulty performing physical activities including exercise; and psychological symptoms such as poor body image and low self-esteem (Blomqvist et al., 2000, Gonzalez et al., 1993, Guthrie et al., 1998, Kerrigan et al., 2001, Sigurdson et al., 2007b). Breast reduction surgery provides symptomatic relief in most cases and considerably improves the health-related quality of life (HRQoL) and wellbeing in women suffering from the functional symptoms of breast hypertrophy (Chao et al., 2002, Klassen et al., 1996, Mello et al., 2010, Singh and Losken, 2012, Thoma et al., 2007). Despite the evidence, breast reduction surgery is often regarded more as a cosmetic rather than a functional procedure by the general public and many medical professionals (Blomqvist et al., 2000, Frey et al., 2014, Taylor et al., 2004).

Traditionally surgical outcomes are measured by morbidity, mortality and hospital complications data (Devlin, 2010). However, when the primary goal of a surgical intervention is to improve patient quality of life and function, it would seem logical to measure function and quality of life to assess how well the surgery is achieving those goals. Patient-reported outcome measures (PROMs) enable the measurement of outcome according to the patient's own experience and opinion. Healthcare providers and clinicians worldwide are increasingly recognising the valuable information that PROMs provide for clinical practice improvement, patient advocacy, in support of research studies, and for the comparison of outcomes using alternative techniques or medical interventions (Cano et al., 2009, Pusic et al., 2011). There is considerable literature investigating surgical outcomes, risk factors for complications and HRQoL after breast reduction. However, there are contradictory findings and comparison difficulties that remain, particularly in the measurement of post-operative complications. In addition, there have been no outcome studies in Australian women and no comprehensive comparison between objective physical body measurements and patient-reported outcomes in the current literature.

The increasing demand for breast reduction surgery and increasing pressure to constrain healthcare spending has led to lengthy waiting times and restrictions placed on surgery in numerous countries and jurisdictions worldwide (Breuning et al., 2010, Klassen et al., 1996, Koltz et al., 2013, Nguyen et al., 2008, O'Blenes et al., 2006, Seitchik, 1995). Often these restrictions or denials are centred on body mass index or a minimum amount of resected breast tissue in order to qualify for surgery and are poorly supported by evidence. Clinical comparative effectiveness

research (CER) is an inclusive model of research that utilises best evidence to assess “what works best”, “for whom” and “under what circumstances?” (Chalkidou et al., 2009, Selby et al., 2012, Sox, 2010). Understanding the clinical effectiveness of breast reduction surgery would be useful at both a patient and clinician level but also for healthcare funders and the wider community. Furthermore, establishing the cost-effectiveness of breast reduction surgery would be valuable; that is, to assess whether this surgery significantly improves HRQoL and at what cost to the Australian healthcare system. There remains the need for reliable, high quality studies to assist clinicians and health care decision-makers in determining appropriate levels of access to breast reduction surgery.

This chapter provides a comprehensive literature review on the health burden of breast hypertrophy, the effectiveness of breast reduction surgery, and the measure of outcomes including complications and health-related quality of life. Also included in this chapter is an overview of breast volume assessment and the economic evaluation of breast reduction surgery.

1.2 Breast hypertrophy

Breast hypertrophy, otherwise known as macromastia, is poorly defined in the literature and has no universally accepted definition. Intrinsic to the concept of this condition is the overdevelopment of breasts such that the weight of the breasts causes significant symptoms. Usually it is implied that both breasts are affected, but the term can also be used in the more unusual situation of one breast overdeveloping (developmental breast asymmetry). Juvenile macromastia is a subcategory of breast hypertrophy where an alarmingly rapid and continued breast growth occurs during puberty, usually as an abnormal response to hormonal stimuli. Gigantomastia is used to refer to cases of extreme breast enlargement (Dancey et al., 2008, Wolfswinkel et al., 2013).

Symptomatic breast hypertrophy causes a physical functional deficit and is associated with psychological distress and a reduced quality of life in women. Eighty percent of women with breast hypertrophy have tolerated symptoms that originated during puberty (Corriveau and Jacobs, 1990). The aetiology of breast hypertrophy is not well understood but its development is thought to be a multifactorial process involving factors such as hormonal change including adolescence and pregnancy, genetics, medication and obesity. Although studies exploring the relationship between body mass and breast size have presented inconsistent findings (Benditte-Klepetko et al., 2007, Brown et al., 2012, Findikcioglu et al., 2013, Vandeput and Nelissen, 2002), obesity is very common in adult women with breast hypertrophy with prevalence ranging from 24% to 43.5% (Cruz-Korchin et al., 2002, Roehl et al., 2008, Wagner and Alfonso, 2005). Although there is therefore evidence of a relationship between obesity and breast hypertrophy, pre-operative weight loss does not provide effective relief from symptoms of breast hypertrophy (Collins et al., 2002).

1.2.1 Symptoms of breast hypertrophy

Breast hypertrophy is a cause of considerable physical and psychosocial impairment in women.

Women often endure physical symptoms such as chronic back, neck, shoulder and breast pain; difficultly in carrying out daily activities and exercise; painful bra strap grooving into shoulders (Figure 1.1); chronic skin rashes; headaches; poor body posture; and numbness or tingling in their hands. Ducic and colleagues noted that 69% of patients with macromastia reported chronic headaches or migraines at their surgical consultation (Ducic et al., 2010). Starley et al. found women with breast hypertrophy experience reduced lung function and suggested that heavy breasts decreases chest wall compliance (Starley et al., 1998). It is also been shown that breast hypertrophy alters a woman's centre of gravity (Letterman and Schurter, 1980), increasing spinal curvature which can lead to degenerative changes in the spine (Benditte-Klepetko et al., 2007) and musculoskeletal pain (Coltman et al., 2019b). Coltman and colleagues found that women with large hypertrophic breasts participated in significantly less total physical activity than their counterparts, and suggested that breast size should be acknowledged as a potential barrier to women participating in physical activity (Coltman et al., 2019a).

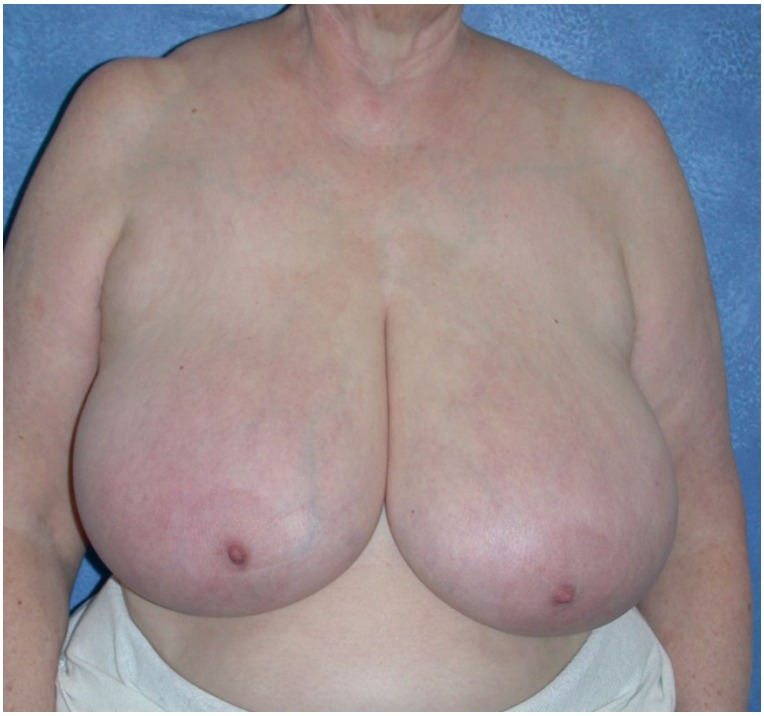


Figure 1.1. Shoulder grooving due to breast hypertrophy

Psychological symptoms in women with breast hypertrophy may include poor body image, embarrassment, low self-esteem, poor psychosexual function, depression and anxiety (Beraldo et al., 2016, Singh and Losken, 2012). Up to one third of women who present for breast reduction surgery have clinical evidence of anxiety or depression, or both (Faria et al., 1999, Guthrie et al., 1998, Iwuagwu et al., 2006a, Saariniemi et al., 2011a, Saariniemi et al., 2009). Breast mass has been correlated with depression, with the finding that the higher the breast mass was in the study population, the greater the incidence of depressive symptoms according to studies using the Beck

Depression Inventory (BDI) (Benditte-Klepetko et al., 2007). Social problems related to the large size of the breast include poor fitting clothing, unwanted attention, low self-esteem and feeling uncomfortable in body image and sexual relationships.

Breast hypertrophy is a chronic health problem that has been proven to significantly affect health and quality of life (Blomqvist et al., 2000). The combination of physical pain and psychological symptoms in breast hypertrophy produce a substantial negative impact on quality of life.

1.3 Breast reduction surgery

Breast reduction surgery, also known as reduction mammoplasty, has been shown to be the most effective treatment for breast hypertrophy in women; weight loss, hormonal therapy and physical therapy have had very little success (Benditte-Klepetko et al., 2007, Collins et al., 2002). Relief of disabling symptoms is the primary motivator for most women who are pursuing breast reduction surgery. As an example, Davis et al. reported that 91% of patients in their study stated that relief of their symptoms was the primary reason for deciding to have the operation (Davis et al., 1995). Surgery provides almost immediate symptomatic relief in most cases including decreased shoulder, back, and neck pain, reduced headaches and considerably improves the health-related quality of life and wellbeing in women suffering from the functional symptoms of breast hypertrophy (Berberoglu et al., 2015, Blomqvist et al., 2000, Foreman et al., 2009, Mello et al., 2010). Freire et al. reported that surgery improved functional capacity and reduced pain in the lower back, shoulders, and neck of patients with breast hypertrophy (Freire et al., 2007). Studies have also reported that surgery results in a significant improvement in the body posture of patients (Chao et al., 2002, Sahin et al., 2013) and a reduced or discontinued use of analgesia (Miller et al., 1995, Schnur et al., 1997). Breast reduction surgery has also been shown to improve oncologic surveillance by facilitating breast self-examinations (Brown et al., 2008), as an option in women with breast cancer and macromastia (Losken et al., 2017), and as a risk-reduction surgery option (Tarone et al., 2004).

Having large breasts often makes exercise difficult and leads to a more sedentary lifestyle; reduction surgery facilitates an increase in physical activity and exercise (Boschert et al., 1996). In fact, Brown and colleagues reported that 100 percent of women found exercising easier and were able to participate in more rigorous forms of exercise post-operatively (Brown et al., 2008). Breast reduction surgery has also been shown to increase work capacity and productivity in patients with breast hypertrophy (Atterhem et al., 1998, Cabral et al., 2017b).

Psychologically, breast reduction surgery has a positive impact on the symptoms of anxiety and depression (Beraldo et al., 2016, Berberoglu et al., 2015, Cerovac et al., 2005, Chadbourne et al., 2001, Chahraoui et al., 2006, Faria et al., 1999, Iwuagwu et al., 2006a, Perez-Panzano et al., 2017, Romeo et al., 2010, Saariniemi et al., 2009, Saariniemi et al., 2011b). Saariniemi et al.

conducted a prospective randomised trial to assess levels of anxiety and depression in an operative group and compared this to women who underwent conservative treatment. They found a significant reduction in anxiety and depression in the surgical group (Saariniemi et al., 2009). In a subsequent study, women were followed for up to 5 years after surgery and it was found that the improvement in anxiety and depression was long lasting (Saariniemi et al., 2011b). Improvement in self-esteem (Mello et al., 2010, Saariniemi et al., 2009, Sabino Neto et al., 2008, Shakespeare and Postle, 1999) and psychosexual function (Cerovac et al., 2005, Romeo et al., 2010) have also been reported following breast reduction surgery.

Despite the reported health benefits of breast reduction surgery, some members of the general public, medical professionals and health insurance providers often mistakenly think of the surgery as a “cosmetic” procedure rather than a functional operation (Frey et al., 2014). This is in spite of the finding that breast reduction surgery not only reduces pain and functional problems, but also increases and normalises the quality of life in these patients (Blomqvist et al., 2000, Miller et al., 2005, Mundy et al., 2017c, O'Blenes et al., 2006). This highlights the effectiveness of surgery; quality of life and wellbeing are significantly improved to a level that is equal to that of the general population. Further research into the “normalisation” effect after surgery is warranted, as there are a limited number of studies on this comparison in the literature.

1.4 Indications for surgery and variations between jurisdictions

Whilst the precise prevalence of breast hypertrophy is unknown, it is believed to be increasing. Reduction mammoplasty is a common procedure in plastic surgery and is one of the most frequently performed breast surgeries worldwide. In the United States of America, the American Society of Plastic Surgeons (ASPS) reported that 100,969 breast reductions were performed in 2016 (American Society of Plastic Surgeons, 2016). This number represents a 19% increase since 2000. In Australia, breast reduction surgery statistics are difficult to collate, as surgery may take place in the public hospital, private hospital or cosmetic setting and there are currently no reporting requirements from surgeons. Data from the Australian Institute of Health and Welfare (AIHW) indicates that 7102 bilateral breast reduction surgeries were performed in 2017/18, an 104% increase since 2000/01 in which 3481 surgeries were recorded (Australian Institute of Health and Welfare, 2019b). However, the release of surgical data by Australian state and territory or by clinical setting is currently restricted outside of the Department of Health and related agencies, and therefore it is difficult to ascertain where these increases have occurred.

The demand for elective surgery procedures including breast reduction surgery is increasing in many countries worldwide and health systems do not have the resources to meet this need (Curtis et al., 2010). Consequently, access to surgery is often limited and waiting lists are long. A study of insurance company medical policies revealed they are “uniformly inconsistent with peer-reviewed,

published indications for breast reduction surgery", resulting in women with a medical need for surgery denied coverage (Nguyen et al., 2008). Health care funders and third-party providers have placed restrictions on access to surgery that commonly focus on the obese population or a minimum weight of reduction. For example, in Sweden only women at a normal weight (body mass index (BMI) 19 to 24.9 kg/m^2 in the age group <50 years and BMI ≤26.9 kg/m^2 in the age group ≥50 years) and large breasts (volume ≥800 mL per breast) have access to breast reduction surgery through the public health system (Eggert et al., 2009, Hansson et al., 2014). This is also the situation in Spain and many other countries. In the United Kingdom, reduction mammoplasty is a "postcode lottery" and is available in some areas of the National Health Service (NHS), whilst in many areas it is a restricted procedure (Klassen et al., 1996, Royal College of Surgeons of England, 2016, Wraight et al., 2007). In the province of Nova Scotia, a patient with symptoms of mammary hyperplasia must have a BMI of less than 27 kg/m^2 to qualify for insurance coverage. In other regions, there are different insurance criteria (O'Blenes et al., 2006). In the United States and Canada, health care insurance providers often stipulate a minimum amount of breast tissue be resected in order to qualify for surgery with many using a body surface area (BSA)-adjusted value scale described by Schnur and colleagues (Schnur et al., 1991). However, evidence from the literature relating to a BMI cut-off point or a minimum resection weight does not support these restrictions, as it has been shown that symptom relief and improvement in health-related quality of life are independent of these factors (Blomqvist et al., 2000, Cole and Shakespeare, 1998, Collins et al., 2002, Dabbah et al., 1995, Gonzalez et al., 2012, Nguyen et al., 2008, Spector and Karp, 2007, Spector et al., 2008, Strong and Hall-Findlay, 2015, Wagner and Alfonso, 2005). As an example, a minimum 500 grams per breast of resected tissue is commonly required for reimbursement despite the fact that clinical studies have shown that amounts as little as 205 grams per breast result in significant clinical improvement (Nguyen et al., 2008).

In Australia, an 'Elective surgery access policy' was released by the Victorian Government for indications for surgery in Victorian public health services. In the case of breast reduction surgery, surgery is indicated for patients with a BMI less than 30 kg/m^2 where clinical symptoms are present (Victorian Government Department of Human Services, 2015). Whilst in Tasmania this procedure is restricted to patients with a BMI less than 35 kg/m^2 and requires exceptional clinical indications for surgery; chronic head, neck and back ache (where pain is due to breast size) and/or chronic intertrigo (Tasmanian Government Department of Health and Human Services, 2015). In New South Wales, bilateral breast reduction surgery is listed as a cosmetic surgical procedure that should not routinely be performed in public hospitals, except in the instance of severe disability due to breast size (NSW Government Department of Health, 2012). Similarly, in Western Australia breast reduction (not performed as part of cancer treatment) is on the excluded procedures list; the surgical procedure should not be routinely performed unless approval is given by the appropriate executive (Government of Western Australia, 2017). Whereas in the Australian Capital Territory

reduction mammoplasty is an excluded procedure and should not be performed in public hospitals with the exception of gross breast asymmetry in patients under 21 and virginal (juvenile) hypertrophy (ACT Government, 2016). In South Australia, reduction mammoplasty is also on the restricted procedures list. However, it may be performed if justified on true clinical grounds; to rectify poor posture, to relieve back or shoulder pain or to relieve discomfort caused by grooves from the brassiere strap (Government of South Australia SA Health, 2018). In short, there is inequitable access to breast reduction surgery within Australian public hospitals and access for patients is ultimately reliant upon state and local policies. Furthermore, the Australian Medicare Benefits Schedule (MBS) does allow breast reduction surgery for a rebate in private hospitals, therefore recognising that it is a functional procedure that justifies tax-payer funding.

As rising economic pressure continues to enforce changes and restrictions on the health care system, it has become increasingly important to demonstrate the clinical effectiveness and long-term health benefits of breast reduction surgery. No such studies currently exist in the Australian health care setting.

1.5 Varying elective surgery restrictions between jurisdictions – methods and evidence

Worldwide, a wide variety of systems exists to allocate resources in health care, none of which provide the perfect model. It is impossible for public health care systems to fund every procedure for every patient. This has led to 'rationing' of health care in public health systems. Whilst this is an essential process in health care and is driven by an excess in demand for scarce or limited resources, it has the potential to create inequity and raises a number of complex moral, legal and ethical concerns. The term when used in health care often has negative connotations as many people believe that it is not reasonable or ethical to place arbitrary limits on access to care.

Procedures performed for non-life threatening conditions are the first to be scrutinised when services have to be rationed (Breuning et al., 2010). Rationing means that some patients who, despite having a surgically treatable condition, will not receive surgical treatment and may be forced to endure symptoms and a reduced quality of life. In the United Kingdom, there have been reports on the rationing of surgery by the NHS on the basis of geographical location, resulting in a "postcode lottery" (Royal College of Surgeons of England, 2014). The report found that 73% of Clinical Commissioning Groups (CCGs) reviewed were not following NICE and clinical guidelines for referral for hip replacements and 44% required patients to meet various thresholds before they were referred for hip replacements. A subsequent report in 2016 by the Royal College of Surgeons of England (RCS) was prompted by concerns of further evidence of rationing of surgery by the NHS and that some patients, smokers and the overweight, were soft targets for NHS savings (Royal College of Surgeons of England, 2016). Whilst surgeons and medical professionals recognise that ceasing smoking and weight loss is potentially beneficial to surgical

outcomes, they have never proposed a ban to such patients. As an example, clinical guidance by NICE and the RCS states that 'patient-specific factors such as age, gender, smoking, obesity and co-morbidity should not be barriers to referral' for joint surgery (National Institute for Health and Clinical Excellence, 2014b). Despite this, 39% of clinical commissioning groups have a policy on BMI for hip and knee replacement surgery, with the cut-off threshold varying by CCG location. Given that 65% of men and 58% of women were reported as either overweight or obese in England in 2014, a significant proportion of the population could be affected by these BMI restrictions. Withholding treatment based on the basis of age has been reported by Evans, and is "best documented in substandard treatment of acute myocardial infarction and other forms of heart disease, where it leads to premature deaths and unnecessary disability" (Evans, 1997). A report by RCS and Age UK found that despite a population that is older and fitter than ever before, elective surgical treatment rates across a range of common conditions declined steadily for the over-65's (Royal College of Surgeons of England, 2012). In the United States (US), most health care is privately funded and therefore is rationed based on the ability to pay; you get what you or your employer can afford. Whereas, in the public system in the US, rationing is by long waiting lists, high patient co-payments and limited payments to doctors and hospitals. Rationing by price means that there is no triaging system according to need; privately insured patients have access to expensive surgeries and treatment, whilst the uninsured are denied access to even the most basic care (Singer, 2009).

In the Australian public health system, access to elective surgery is prioritised through the use of waiting lists using broad urgency categories; surgeons are principally responsible for making decisions for placing patients on waiting lists, urgency of care and selecting patients from the waiting list for surgery. The lack of uniform and specific guidelines about patients' need for surgery is a shortcoming of the Australian health system and does not assure equity of access (Curtis et al., 2010). In Victoria, substantial variability has been observed in the use of urgency categories across surgeons and hospitals (Russell et al., 2003). Furthermore, variation in waiting times for surgery according to socioeconomic status and remoteness have been observed in Australia and reveal an inconsistency in access to elective surgery (Australian Institute of Health and Welfare, 2008).

Clinicians are increasingly faced with moral and professional challenges in making appropriate decisions for a patient's individual treatment needs. Limited resources in the public health setting has forced rationing of health care resources and restrictions that are often not evidence-based; both have the potential to threaten equity of access to surgical treatment.

1.6 Surgical techniques

Surgery to reduce overly large breasts was first reported upon in the sixteenth century by German

Hans Schaller who is believed to have carried out the first successful breast amputation. However, it was Johann Friedrich Dieffenbach in 1848 who was the first to describe a breast reduction resection using an incision in the inframammary fold. Over the years, surgical techniques have been modified and refined in order to achieve both aesthetic and functional outcomes.

There is no single breast reduction technique that can be applied to all breasts and each technique has its advantages and limitations. Each individual patient is unique, and a surgeon must adapt their technique appropriately in order to achieve the functional improvement and most aesthetically pleasing result (Antony et al., 2013, Dex et al., 2008, Greco and Noone, 2017, Hall-Findlay, 2004, McCulley and Hudson, 2001).

Various techniques have been described in the literature with different skin incision and pedicle patterns. The Wise “keyhole” pattern incision was developed in 1956 (Wise, 1956) and further described in 1977 (Robbins, 1977). The inferior pedicle Wise breast reduction (inverted T-scar) is still one of the most frequently used procedures (Okoro et al., 2008, Rohrich et al., 2004). However, the disadvantages of the technique are the potential for “bottoming-out” of the lower pole over time and long scars that may detract from the overall aesthetic result. Claude Lassus reported the first limited incision technique in 1964 using a vertical reduction technique (Lassus, 1970). In the last decade, some surgeons have adopted modifications on the vertical or limited incision techniques that have become popular (Hall-Findlay, 2004, Lejour et al., 1990). However, limited incision techniques are preferred less by surgeons as the degree of hypertrophy and ptosis increases (Okoro et al., 2008). Additional limited incision techniques have been described using periareolar approaches (Goes, 1996, Hammond, 1999) and L-shaped scars (Bozola, 1990).

1.7 Surgical complications

Reduction mammoplasty is a very effective surgical procedure to improve function, quality of life and relieve painful symptoms associated with large breasts. However, the surgery does not come without its risk of complications. Risk factors for complications are a major determinant in surgical planning and this has become an important area of research. Post-operative complications after breast reduction can include wound healing problems, wound infection, skin necrosis, fat necrosis, seroma, haematoma, altered nipple sensation, nipple loss, asymmetry and abnormal scarring.

The reported rate of complications in the literature is highly variable, from 4% to as high as around 50% (Atterhem et al., 1998, Bauermeister et al., 2019, Bikhchandani et al., 2007, Blomqvist, 1996, Cogliandro et al., 2017a, Cunningham et al., 2005, Dabbah et al., 1995, Fischer et al., 2014, Guemes et al., 2016, Gust et al., 2013, Hanwright et al., 2013, Hernanz et al., 2016, Lewin et al., 2014, Manahan et al., 2015, Mello et al., 2010, Miller et al., 2005, Nelson et al., 2014a, O'Blenes et al., 2006, Platt et al., 2003, Roehl et al., 2008, Scott et al., 2005, Setala et al., 2009, Shah et al., 2011, Shakespeare and Cole, 1997, Simpson et al., 2019, Srinivasaiah et al., 2014, Young et al.,

2019, Zubowski et al., 2000). However, this sizeable variation may be explained by the lack of comparability between studies: many researchers evaluate limited numbers of patients; studies may not include a range of surgical techniques; results may be based on a single surgeon's experience; there is a lack of clarity on what constitutes a 'complication'; and the majority of the larger studies are retrospective surgical database searches and do not necessarily capture all complication data specific to reduction mammoplasty surgery. Parikh and colleagues conducted a literature review to analyse the quality of complication reporting in plastic surgery, including reduction mammoplasty (Parikh et al., 2018). The authors demonstrated inconsistencies in the reporting of complication outcomes in the plastic surgery literature and highlighted the need for the development and implementation of standardised reporting guidelines to accurately, efficiently, and reproducibly report complication data for core plastic surgery procedures.

In a large single-centre retrospective review of 2142 consecutive breast reduction procedures, Manahan et al. reported that common complications were related to wounds (14.9%) and scars (14.5%), along with fat necrosis (8.2%), infections (7.3%) and seroma (1.2%) (Manahan et al., 2015). In another retrospective study, it was found that complications occurred in 32% of the patients within 30 days of surgery, the most common being infection at the surgical site (16%) followed by delayed wound healing (10%) (Lewin et al., 2014). Whilst Bikhchandani and colleagues reported a lower complication rate of 19%, with T-junction necrosis (11.2%), infection (5.5%) and wound dehiscence (2.2%) being the most common complications (Bikhchandani et al., 2007). However, the authors highlighted that delayed healing, one of the commonly reported complications in other studies, was not recorded in their study due to the difficulties in accurately defining delayed healing in a retrospective study (Bikhchandani et al., 2007).

In a prospective study by a Spanish team of researchers, a complication rate of 27.3% was reported with partial cutaneous dehiscence (11.6%) the most common complication followed by haematoma (3.3%) (Perez-Panzano et al., 2016). In the prospective Breast Reduction Assessment: Value and Outcomes (BRAVO) study of 179 patients, the complication rate was 43%, with healing complications representing the most common complication (21.6%) (Cunningham et al., 2005). The BRAVO study originated to address deficiencies in previous research describing outcomes of breast reduction surgery by using a prospective, controlled, multi-centre study design with a comprehensive set of standardised outcome measures. Outcome studies, both retrospective and prospective, predominantly agree that wound healing complications are the primary problem following breast reduction surgery.

In large population-based analyses of reduction mammoplasty surgeries using the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) surgical database, studies have reported the overall incidence of complications between 4% and 8.7% (Fischer et al., 2014, Gust et al., 2013, Nelson et al., 2014a, Simpson et al., 2019, Young et al., 2019). However,

whilst use of the NSQIP database may facilitate large study numbers, it has limitations in that it only captures early post-operative complications within 30 days and does not include many complications specific to breast surgery such as delayed wound healing, haematoma, seroma, hypertrophic scarring, and nipple necrosis. Given that delayed wound healing is widely reported to be the most common complication following reduction mammoplasty, the lower complication rates reported by studies using the NSQIP database are perhaps not surprising.

The Clavien-Dindo Classification (CDC) is a validated grading tool that allows the classification of surgical complications. The CDC grades complications based on the medical intervention required to treat the complications following operative procedures (Dindo et al., 2004). This tool provides a simple, standardised and reproducible approach of objectively ranking surgical outcomes and is valid and applicable across a wide range of surgical specialties (Clavien et al., 2009). The CDC is widely accepted ranking system for classifying surgical complications and overcomes the inconsistency in reporting of complications using terms such as “minor”, “major”, or “severe” complications. A single retrospective study has used the Clavien-Dindo Classification to report complications following breast reduction surgery. Winter et al. reported an overall complication rate of 63%; 48% had a Grade I, 9% a Grade II, 1% a Grade IIIA, and 5% a Grade IIIB operative complication (Winter et al., 2017). The use of an objective classification of complications following breast reduction surgery would allow a more accurate and objective comparison of the incidence and severity of complications following this procedure.

1.7.1 Risk factors for complications

The study of factors affecting surgical outcome is an area of research that is widely reported in the literature. A number of factors such as body mass index, age, resection weight, smoking, diabetes, operative technique and chronic steroid use have been implicated as risk factors for complications following breast reduction surgery (Table 1.1). When present, these factors can delay the healing process, increase morbidity, and affect the overall aesthetic result. However, the number of prospective, adequately powered studies examining these factors is limited and there are comparison difficulties between many of the existing studies. Furthermore, almost all of the risk factors associated with complications have contradictory outcomes in the literature (Table 1.1).

Table 1.1. Summary of literature of major risk factors for complications

Risk factor	Supporting evidence			Refuting evidence		
	Study	*n*	*Type*	*Study*	*n*	*Type*
Smoking	(Young et al., 2019)	9110	R	(Bauermeister et al., 2019)	938	R
	(Simpson et al., 2019)	16,812	R	(Guemes et al., 2016)	121	P
	(Winter et al., 2019)	804	R	(Roehl et al., 2008)	179	P
	(Theocharidis et al., 2018)	4912	R	(Karamanos et al., 2015)	2779	R
	(Hillam et al., 2017)	13,503	R	(Henry et al., 2009)	485	R
	(Baltodano et al., 2017)	7068	R	(Hanwright et al., 2013)	2507	R
	(Fischer et al., 2014)	3538	R			
	(Zhang et al., 2016)	10,593	M			
	(Manahan et al., 2015)	2142	R			
	(Cunningham et al., 2005)	179	P			
	(Bikhchandani et al., 2007)	402	R			
	(Bartsch et al., 2007)	50	P			
	(Schumacher, 2005)	71	R			
	(Srinivasaiah et al., 2014)	67	P			
	(Lewin et al., 2014)	512	R			
	(Gravante et al., 2008)	87	P			
	(Shah et al., 2011)	306	R			
	(Chan et al., 2006)	173	R			
Body Mass Index	(Bauermeister et al., 2019)	938	R	(Eggert et al., 2009)	65	P
	(Simpson et al., 2019)	16,812	R	(Roehl et al., 2008)	179	P
	(Winter et al., 2019)	804	R	(Cunningham et al., 2005)	179	P
	(Baltodano et al., 2017)	7068	R	(Schumacher, 2005)	71	R
	(Manahan et al., 2015)	2142	R	(Wagner and Alfonso, 2005)	186	R
	(Nelson et al., 2014a)	4545	R			
	(Henry et al., 2009)	485	R	(Setala et al., 2009)	273	R
	(Zubowski et al., 2000)	395	R	(Guemes et al., 2016)	121	P
	(Platt et al., 2003)	30	P	(Webb et al., 2012)	67	R
	(Zhang et al., 2016)	10,593	R	(Tadiparthi and Liew, 2008)	206	R
	(Srinivasaiah et al., 2014)	67	P	(Gamboa-Bobadilla and Killingsworth, 2007)	86	R
	(Fischer et al., 2014)	3538	R			
	(Karamanos et al., 2015)	2779	R	(Hanwright et al., 2013)	2507	R
	(Shah et al., 2011)	306	R			
	(Myung and Heo, 2017)	6904	M			
	(Gust et al., 2013)(BMI ≥39)	2492	R			
	(Chen et al., 2011)	8000	R			
	(Chun et al., 2012)	675	R			
	(Lahiri et al., 2006)	43	P			
	(Platt et al., 2003)	30	P			
	(Atterhem et al., 1998)	242	R			
	(Gulcelik et al., 2011)	286	R			
	(Stevens et al., 2008)	444	R			
	(Baldwin et al., 2010)	40	P			
	(O'Grady et al., 2005)	133	R			
	(Blomqvist, 1996)	291	R			
Age	(Young et al., 2019)	9110	R	(Baltodano et al., 2017)	7068	R
	(Simpson et al., 2019)	16,812	R	(Nelson et al., 2014b)	3537	R
	(Srinivasaiah et al., 2014)	67	P	(Zhang et al., 2016)	10,593	R
	(Shermak et al., 2011)	1192	R	(Henry et al., 2009)	485	R
				(Roehl et al., 2008)	179	P
				(Schumacher, 2005)	71	R
				(Braig et al., 2016)	50	R
				(Setala et al., 2009)	273	R
				(Guemes et al., 2016)	121	P
				(Shah et al., 2011)	306	R
				(Cunningham et al., 2005)	179	P
				(Hanwright et al., 2013)	2507	R
				(Hunter-Smith et al., 2012)	283	R

Risk factor	Supporting evidence			Refuting evidence		
	Study	*n*	*Type*	*Study*	*n*	*Type*
Resected specimen weight	(Bauermeister et al., 2019)	938	R	(Wagner and Alfonso, 2005)	186	R
	(Winter et al., 2019)	804	R			
	(Zubowski et al., 2000)	395	R	(Zhang et al., 2016)(>1000g)	10,593	R
	(Srinivasaiah et al., 2014)	67	P			
	(Lewin et al., 2014)	512	R	(Roehl et al., 2008)	179	P
	(Gravante et al., 2008)	87	P	(Hunter-Smith et al., 2012)	283	R
	(Shah et al., 2011)	306	R			
	(Setala et al., 2009)	273	R			
	(Henry et al., 2009)	485	R			
	(Cunningham et al., 2005)	179	P			
	(Schnur et al., 1997)	328	R			
Diabetes	(Young et al., 2019)	9110	R	(Bauermeister et al., 2019)	938	R
	(Simpson et al., 2019)	16,812	R	(Manahan et al., 2015)	2142	R
	(Lewin et al., 2014)	512	R	(Fischer et al., 2014)	3538	R
	(Eggert et al., 2009)	65	P	(Hanwright et al., 2013)	2507	R
				(Henry et al., 2009)	485	R
				(Roehl et al., 2008)	179	P
Cardiac disease	(Manahan et al., 2015)	2142	R	(Fischer et al., 2014)	3538	R
Nipple-to-sternal notch distance	(Bauermeister et al., 2019)	938	R			
	(Manahan et al., 2015)	2142	R			
	(Lewin et al., 2014)	512	R			
Operating time	(Simpson et al., 2019)	16,812	R			
	(Hanwright et al., 2013)	2507	R			
Operative technique	(Derby et al., 2016) (pedicle technique)	317	R	(Bauermeister et al., 2019)	938	R
				(Kemaloglu and Ozocak, 2018)	50	P
				(Ogunleye et al., 2017)	124	P
				(Roehl et al., 2008)	179	P
				(Antony et al., 2013)	150	R
				(Hunter-Smith et al., 2012)	283	R
Chronic steroid use	(Simpson et al., 2019)	16,812	R	(Hanwright et al., 2013)	2507	R
	(Barcha and Ranzer, 2018)	17,058	R			
	(Hillam et al., 2017)	13,503	R			
	(Baltodano et al., 2017)	7068	R			

P, prospective study; R, retrospective study; M, meta-analysis; n, number of participants

Zhang and colleagues performed a meta-analysis of 16 unique studies, including 10,593 patients, examining risk factors for complications in order to address the inconsistencies surrounding the predictors of complications after reduction mammoplasty (Zhang et al., 2016). They found that smoking and a BMI greater than or equal to 30 kg/m^2 increased the risk of complications. Patients who were obese or irradiated were found to be more likely to develop infections, and smokers experienced a higher incidence of wound dehiscence than non-smokers. The authors found no association between age ≥50 years or a combined tissue resection weight ≥1000 grams and post-operative complications (Zhang et al., 2016).

Smoking

In previous outcome studies in plastic surgery, smoking has been shown to significantly increase post-operative morbidity. Chang et al. found a 4.4% incidence of flap necrosis after free TRAM flap reconstruction in smokers compared with 0.8% in non-smokers (Chang et al., 2000); and Manassa et al. reported that smokers had 3.2-fold increased chance of developing wound healing complications than non-smokers following abdominoplasty surgery (Manassa et al., 2003). Perhaps surprisingly, disagreement exists in the literature regarding the effect of smoking on patient outcomes following reduction mammoplasty.

Simpson and colleagues conducted the largest retrospective analysis of 16,812 reduction mammoplasties from 2006 to 2015 using the NSQIP database and found that smoking was associated with an increased risk of total complications (OR, 1.39; $p = 0.001$) but not with major complications (Simpson et al., 2019). In another study of 9110 patients, Young and colleagues aimed to identify pre-operative risk factors and to identify any increased complication risk in patients older than 60 years and found that smoking was found to be a statistically significant risk factor for superficial surgical site infection and deep space infection regardless of age (Young et al., 2019). Hillam and colleagues conducted a multicentre retrospective analysis of 13,503 reduction mammoplasties from 2009–2014 using the NSQIP database to specifically evaluate smoking as a risk factor. They found that smokers had a higher likelihood of any wound complication following surgery compared to non-smokers (OR 1.72; $p < 0.001$) (Hillam et al., 2017). This finding was supported by the study by Winter and colleagues using the Clavien-Dindo Classification system (Winter et al., 2019). In another study using the NSQIP database, Fischer et al. retrospectively reviewed 3538 reduction mammoplasty patients from 2005–2010. They concurred with Hillam et al. that smoking increased the risk of overall surgical complications (OR, 1.7; $p < 0.001$), and that active smoking was a strong predictor of major surgical complications (Fischer et al., 2014). Interestingly, findings from another study of 2779 patients using the NSQIP database are contradictory to this. The authors found no significant association between smoking and wound complication (Karamanos et al., 2015). However, as mentioned previously, a limitation of these studies and others using the NSQIP database is that follow-up data is only for 30 days post-operatively; surgical technique information is not collected including laterality and tissue

resection weight; and the database captures general complications and therefore does not capture surgery-specific complications such as delayed wound healing, haematomas, nipple necrosis or scarring. In a retrospective review of 938 patients at a single institution, Bauermeister and colleagues found smoking history was not associated with an increased risk of complications (Bauermeister et al., 2019).

Further studies have indicated that smokers are at increased risk of developing complications compared to non-smokers (Bartsch et al., 2007, Cunningham et al., 2005, Gravante et al., 2008, Srinivasaiah et al., 2014). Bikhchandani et al. found that smokers were 2.3 times more likely to develop a complication (Bikhchandani et al., 2007). Similarly, Schumacher and colleagues reported the incidence of wound complications to be 3.4 times higher in smokers (Schumacher, 2005). In a recent meta-analysis and systematic review on the role of smoking in plastic surgery elective procedures, Theocharidis and colleagues found that tobacco use is found to significantly increase the overall number of post-operative complications following breast reduction surgery (OR, 2.35; $p < 0.001$) (Theocharidis et al., 2018). Furthermore, the authors found that smoking was linked to an increased incidence of skin necrosis, infection, wound separation, delayed wound healing and re-operation. In a retrospective review of 173 consecutive patients who underwent bilateral reduction mammoplasty, Chan et al. found that smokers were 1.6 times more likely to have a wound healing problem, but interestingly patients who ceased smoking at least 4 weeks before surgery had the same complication rate as non-smokers. As a result, the authors suggested the introduction of urine nicotine testing at the preadmission clinic and prior to the operation to provide objective verification of patients' smoking history, minimize morbidity, and enable healthcare cost savings (Chan et al., 2006).

Body mass index

Numerous studies have evaluated the incidence of post-operative complications following reduction mammoplasty in the obese patient. However, reported findings have been somewhat inconsistent and contradictory, creating confusion as to whether surgery be postponed in the obese patient or whether pre-operative counselling regarding risk factors is more appropriate. Whilst many studies indicate that there is a higher rate of overall complications with increasing BMI, the majority of these complications are often minor and do not affect satisfaction and overall outcome of the patient (Bauermeister et al., 2019, Fischer et al., 2014, Nelson et al., 2014a, Shah et al., 2011).

Myung and Heo recently conducted a systematic review and meta-analysis in order to clarify the relationship between obesity and surgical complications after reduction mammoplasty (Myung and Heo, 2017). The review found 26 studies, 22 of which were retrospective, that reported surgical complication risk and patient body weight, 11 concluded that obesity is not a risk factor and 15

reporting that high BMI increases risk of surgical complications. A meta-analysis was conducted on 12 studies which met the quality criteria, including 6904 patients (3752 obese and 3152 non-obese), undergoing reduction mammoplasty. The authors found that obese patients had a higher relative risk of surgical complications (RR 1.38) and tissue necrosis (RR 2.01) and that the risk gradually increases with an increase in the severity of obesity. However, the authors concluded that the risk is not extremely high when compared to the risk for other types and surgeries and that there is no reason to exclude or to postpone surgery in obese patients (Myung and Heo, 2017).

Population based studies of reduction mammoplasty using the NSQIP database have all concurred on the finding that BMI is an independent risk factor for complications (Fischer et al., 2014, Hillam et al., 2017, Karamanos et al., 2015, Nelson et al., 2014a, Simpson et al., 2019). Furthermore, when stratified by WHO obesity classification, morbidly obese patients (BMI >40 kg/m^2) were twice as likely as normal weight patents to experience surgical complications. Interestingly, obesity did not appear to be an independent risk factor for major surgical complications (deep infection and/or unplanned return to the operating room) (Fischer et al., 2014). In a study investigating obesity and early complications in 4545 reduction mammoplasty patients, Nelson et al. found a significant increase with increasing obesity class, with morbidly obese patients at highest risk of complications, particularly wound infection and dehiscence. The authors encouraged appropriate pre-operative counselling as opposed to declining surgery in the obese patient (Nelson et al., 2014a).

Age

As women age, the ability to heal and respond to injury lessens. Several studies have reported on the detrimental effect of age on outcomes following breast reduction surgery. In a retrospective study of 1192 consecutive patients undergoing reduction mammoplasty over a 10-year period, Shermak et al. proposed that women older than 50 years were more likely to experience infection (OR, 2.7; p = 0.003) and there was a trend towards wound healing problems and re-operative wound debridement. The authors hypothesised that hormonal deficiency may partially account for this finding (Shermak et al., 2011). Young and colleagues conducted a retrospective study of 9110 patients using the NSQIP database to identify any increased complication risk in patients aged 60 years and above and found that age does have an impact on outcomes and complication risk, with a higher rate of total complications and an increased risk of cerebral vascular accidents, myocardial infarction, and readmission (Young et al., 2019). In a prospective study 67 patients, the authors found that the probability of a patient developing a complication increases for older age patients (Srinivasaiah et al., 2014). In contrast, the BRAVO study found that delayed healing correlated inversely with age, with every year of increasing age decreasing the likelihood of having wound-healing complications by 7% (Cunningham et al., 2005). Interestingly, Roehl et al. found that complication rate was most frequent in those aged 30 to 39 years, although the authors could

not explain the reason for this finding (Roehl et al., 2008).

A meta-analysis of 16 studies demonstrated that an age of 50 years and older bears no relationship to complications in reduction mammoplasty compared to younger patients less than 50 years (Zhang et al., 2016). Additionally, Braig et al. conducted a study specifically evaluating the impact of increasing age on breast reduction surgery and found that age is not a contraindication for surgery, although noted that patient counselling is essential around age-related expectations and specific complications (Braig et al., 2016). The finding that age is not an independent risk factor for complications is supported by several other studies (Table 1.1) (Baltodano et al., 2017, Hanwright et al., 2013, Henry et al., 2009, Hillam et al., 2017, Hunter-Smith et al., 2012, Nelson et al., 2014b, Schumacher, 2005, Setala et al., 2009, Shah et al., 2011).

Co-morbidities and other risk factors

Whilst the majority of the research into risk factors for complications following reduction mammoplasty explores the effect of smoking and obesity, there are limited studies into the effect of co-morbidities such as diabetes mellitus. In a large retrospective review of records from 9110 women undergoing reduction mammoplasty between 2013 and 2015, Young and colleagues found that diabetes was found to be a significant risk factor for readmission, regardless of age (Young et al., 2019). In a prospective study of 65 women undergoing reduction mammoplasty, Eggert et al. found that diabetes was a risk factor for wound infection. However, small numbers limit this study to some degree (Eggert et al., 2009). In a larger retrospective study of 512 consecutive women who underwent bilateral breast reduction, diabetes was found to be an independent risk factor for necrosis of the areola (OR, 8.22; $p = 0.003$). The authors also found that a longer suprasternal notch-to-nipple distance (SND) and tissue resection weight were significant and independent predictors of postsurgical complications (Lewin et al., 2014). This is supported by the findings of Setala and colleagues (Setala et al., 2009) and Bauermeister and colleagues (Bauermeister et al., 2019) in a retrospective review of 273 and 938 consecutive cases, respectively. In contrast, in a retrospective analysis of 2142 reduction mammoplasties, Manahan et al. did not find associations with comorbidities including diabetes and hypertension. However, they found that a greater degree of pre-operative ptosis was associated with increased rates of fat necrosis (OR, 2.14; $p = 0.03$) and wound healing problems (OR, 2.6; $p = 0.002$). Nipple-to-sternal notch distances greater than 41cm were associated with infections (OR, 4.3; $p = 0.02$) and major wounds (OR 13.3; $p = 0.04$), while SND more than 43cm led to increased seroma rates (OR, 24.4; $p = 0.006$) (Manahan et al., 2015). Using the NSQIP database, Fischer et al. reported that diabetes, alcohol use, COPD and cardiovascular risk factors were not significantly associated with complications (Fischer et al., 2014). Unfortunately, Zhang and colleagues stated that it was not possible to evaluate diabetes in their meta-analysis of risk factors in reduction mammoplasty as there were too few related studies (Zhang et al., 2016). This reinforces the importance of further study into the impact of diabetes on

surgical outcomes following breast reduction. In a retrospective analysis of 94,140 plastic surgery cases comprising 17,058 reduction mammoplasties, Barcher and Ranza found that chronic steroid use was a significant risk factor for post-operative wound complications (OR, 2.2; $p = 0.001$) (Barcha and Ranzer, 2018). This finding is further supported by several other published studies (Baltodano et al., 2017, Hillam et al., 2017, Simpson et al., 2019).

Despite the risks of postsurgical complication, breast reduction surgery remains a beneficial intervention for symptomatic relief and improved quality of life in women suffering from symptomatic macromastia. Although there is contradictory evidence regarding the factors which are associated with an increased risk of complications, the overwhelming majority of studies ultimately support that reduction mammoplasty should be accessible, with the appropriate pre-operative counselling, to all women with symptomatic breast hypertrophy.

The clinical effectiveness of breast reduction surgery has been established by previous research studies. Likewise, the risks of post-operative morbidity following surgery have been highlighted. What is a far more complex concept and one that is not well reported in the literature is how these two fields relate to one another. That is, how much importance does the patient place on short-term complications when considering long-term outcomes? A 'trade-off' in decision-making exists which is largely dependent upon an individual's perspective and what their priorities are in what are they willing to accept or give up in order to have something else (Gawande, 2015, McNutt, 2004). Trade-offs happen every day in health care. Clinicians have to make choices every day on the trade-off between positive outcomes and potential risks for their patients. They also may need to make trade-offs in following regulations of their organisation versus doing what they think is right for their patients. Patients themselves make trade-offs and have to choose between their own health care options that they often know very little about. Breast reduction surgery entails risks and sacrifices, but the expected benefits include improved long-term 'quality of life' and wellbeing. However, ultimately it is the patient alone who truly knows how they will feel about adverse outcomes and how much they are willing to compromise for long-term gain. It is anticipated that this thesis will provide quantitative evidence as to both the risks and benefits of surgery to assist women in making informed decisions prior to undergoing surgery.

High levels of satisfaction are reported by the vast majority of women following breast reduction surgery. Between 78% and 100% of patients who have undergone surgery report they would have the surgery again or would recommend it to others (Atterhem et al., 1998, Collins et al., 2002, Dabbah et al., 1995, Davis et al., 1995, Faria et al., 1999, Godwin et al., 2014, Godwin et al., 1998, Makki and Ghanem, 1998, Schnur et al., 1997). This is despite a reported complication rate of up to 53%; the majority of patients seem to accept the 'trade-off' between sometimes less than ideal outcomes and aesthetic results because the overall positive health benefits outweigh the short-term negative issues that may arise. For example, Godwin and colleagues conducted a study to

evaluate the difference between patient and surgeon opinion on the aesthetic outcome of reduction mammoplasty. Thirty-four women who were at least one-year post-surgery were asked to evaluate the appearance of their breasts. Patients' satisfaction with their outcome of surgery significantly exceeded that of the surgical panel. Scars were found to be the biggest issue for patients; 35% of women said the appearance of post-operative scars was 'unacceptable' and 53% of these patients underwent additional corrective procedures. Yet remarkably, 94% of women stated that they would have the surgery again or recommend it to a friend (Godwin et al., 1998). The functional benefits and long-term satisfaction gained by women following breast reduction surgery appear to compensate for less than perfect outcomes in the majority of women.

1.8 Health-related quality of life and patient-reported outcome measures

1.8.1 Health-related quality of life (HRQoL)

Surgical outcomes are traditionally measured by morbidity, mortality and rate of complications. Whilst these measures continue to be important, the aims of the majority of procedures performed in reconstructive surgery are to improve a patient's health-related quality of life (HRQoL) and improve or restore function. In 1948, the Constitution of the World Health Organization (WHO) defined health in its broader sense as "a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity" (WHO, 1947). Quality of life and, more specifically, 'health-related quality of life' (HRQoL) is a broad and complex concept for which there is no universally accepted definition. HRQoL relates to factors directly affecting an individual's health and wellbeing; it is multi-dimensional and describes the physical, role functional and emotional aspects of functioning and wellbeing. HRQoL is subjective and is therefore best reported from the patient's own perspective.

An important outcome measure of the impact of a health condition and the success of surgical intervention is the patient's own perception of the outcome. In reconstructive and aesthetic surgery, there is often a profound difference in the patient's assessment of their outcome when compared to that of the surgeon (Cano et al., 2009). Breast hypertrophy is not a life-threatening condition and quality of life outcome studies have become an important way to assess the beneficial effects of such medical interventions.

1.8.2 Measurement of HRQoL with patient-reported outcome measures

Patient-reported outcome measures (PROMs) are questionnaire-based and enable the patient to have a "voice" in the clinical setting. They measure HRQoL and examine the physical, psychological, emotional, social and functional outcomes of reconstructive surgery. This is in contrast to the traditional aesthetic assessment of outcome according to the surgeon. PROMs are increasingly becoming an important part of clinical practice in plastic surgery internationally for

several reasons. Firstly, to provide strong evidence to support that surgery improves function and quality of life. This information is valuable in an era of increasing restrictions on access to certain medical procedures. Secondly, the utilisation of outcome instruments enables the comparison to new or alternative surgical techniques, some of which are more costly, as to whether they are actually superior from a patient perspective. Thirdly, PROMs are being adopted by regulatory bodies which recognise the validity in capturing patient-centred data which can only be provided by PROMs (Cano et al., 2009, Voineskos et al., 2018).

There are several different types of PROMs: generic questionnaires that examine the quality of life and general wellbeing across patient and population groups, e.g. the Short Form-36 (SF-36); surgery-specific instruments are more sensitive to capture symptoms and outcomes specific to a condition, e.g. BREAST-Q; and preference-based measures such as the Short Form Six-Dimension (SF-6D) (derived from the SF-36), the EuroQol (EQ-5D) and the Health Utilities Index (HUI) which generate utility scores for the calculation of quality-adjusted life years (QALYs) for application in economic evaluation (Figure 1.2).

Generic instruments

- Short Form-36 (SF-36)
- Multidimensional Body-Self Relations Questionnaire (MBSRQ)
- Rosenberg Self-Esteem Scale

Surgery-specific instruments

- BREAST-Q
- Breast-Related Symptoms Questionnaire (BRSQ)
- Breast Reduction Assessed Severity Scale (BRASS)
- Modified Breast Evaluation Questionnaire (mBEQ)

Preference-based measures

- Short Form Six-Dimension (SF-6D)
- Health Utilities Index (HUI)
- 15-dimensional (15D)
- EuroQol EQ-5D (EQ-5D)

Figure 1.2. Common instruments to measure HRQoL outcomes of breast surgery

1.8.3 Challenges of interpreting HRQoL data

The multi-dimensional and subjective nature of HRQoL data can make interpretation of change in scores difficult. Many factors can predict an individual's HRQoL and it is unlikely that all of these will be captured in any one or several HRQoL instruments, no matter how comprehensive they may be. Other contributing factors, both known and unknown, and life events will undoubtedly affect responses. This becomes increasingly relevant in longitudinal HRQoL research studies

conducted over multiple time points.

An important factor in interpretation of HRQoL data is what is the “minimal important difference” (MID)? The MID, from the patient-perspective, can be defined as ‘the smallest difference in score in the domain of interest which patients perceive as beneficial and which would mandate, in the absence of troublesome side effects and excessive cost, a change in the patient’s management’ (Jaeschke et al., 1989, p. 408). Whilst is useful to obtain quantitative scores to measure and compare quality of life before and after a health intervention, the value is somewhat limited if we do not know what is considered a meaningful change in the context of the clinical setting. For example, there is no known universal magnitude to establish a clinically important difference on the SF-36 subscales. However, a rule of thumb of a 10-point change on 100-point quality of life scales has been recommended (King, 1996). Estimates of minimal important clinical difference are particularly important when HRQoL instruments are used as the primary measure of outcome in randomised clinical trials and for power calculations in clinical research. However, this threshold may vary depending on the context of disease, disease severity, by population characteristics and by type of outcome instruments; highlighting the importance of estimating MID based on the specific clinical setting (Jayadevappa et al., 2017). Two broad strategies for estimation of MID are commonly used to interpret changes in HRQoL scores following a medical intervention or treatment: (1) anchor-based; and (2) distribution-based approaches (Crosby et al., 2003, King, 2011, Lydick and Epstein, 1993). Anchor-based methods express changes in HRQoL scores by linking specific scales to known variables of clinical relevance or to patient- or clinician-derived ratings of change (Guyatt et al., 2002, Jaeschke et al., 1989, Musoro et al., 2018). Distribution-based methods are based on the statistical distribution of HRQoL scores (Wyrwich et al., 2005), and are often suggested to support anchor-based estimates (Revicki et al., 2008). To date, there are no established estimates of what represents a clinically meaningful change for any of the validated generic or condition-specific patient-reported outcome measures utilised in studies of women with breast hypertrophy undergoing breast reduction surgery.

Another challenge relating to the interpretation of quality of life scores in longitudinal outcome studies is the “response shift” phenomenon. Schwartz and Sprangers define this as when individuals undergo a change in health state they may change their “internal standards, values, or the conceptualization of quality of life” (Schwartz and Sprangers, 1999). That is, due to the self-report and subjective nature of HRQoL measurements, the mechanism by which people assess or quantify their HRQoL could change over time. These changes may be reflected in perceived quality of life scores to be greater or smaller than what they actually are. Response shift is a natural process that has the potential to distort the interpretation of change in HRQoL scores over time and affect what represents a ‘true’ change. For example, patients undergoing cancer treatment may adapt to their increased symptom level or impaired HRQoL that the disease or treatment cause, and patients’ internal standard of measurement may be changed. Response

shifts in this situation may therefore occur during the course of the disease, or during the course of a treatment (Brazier et al., 2017, Sprangers, 1996).

An issue in longitudinal HRQoL studies is the likelihood of missing data and loss to follow-up of participants. In observational studies over time, participants may miss appointments or fail to complete questionnaires at different study time points. The interpretation of the change in HRQoL scores can be significantly affected in this scenario. For example, missing HRQoL data in cancer trials can be problematic as it is likely that the data are not missing randomly; if patients whose condition has deteriorated are not completing their HRQoL questionnaires, HRQoL may be overestimated and may not capture the full side-effects of treatment. Statistical approaches are employed to handle missing data, from simple approaches such as complete case analysis, to more sophisticated imputation-based approaches (Brazier et al., 2017, pp. 271-275).

In summary, the interpretation is HRQoL scores in research studies should be carefully made with respect to these challenges and biases.

1.9 Review of HRQoL research in breast reduction surgery

Research studies have highlighted that breast reduction surgery is of significant benefit to women with macromastia, in terms of improving health-related quality of life (HRQoL). In 1996, Klassen and colleagues introduced the use of validated and self-reported instruments for the assessment of outcomes following breast reduction surgery (Klassen et al., 1996). Validated HRQoL tools such as the SF-36 and the BREAST-Q questionnaire have been valuable for measuring the improvement in quality of life following breast reduction surgery. However, there have been no outcome studies performed in Australian women, and no comprehensive comparison between physical assessment and patient-reported outcomes.

A systematic review of the literature of studies conducted between 1966 and 2006 by Pusic et al., exploring the use of patient-reported health outcomes instruments in breast surgery studies, identified 227 health outcomes questionnaires. Of these, only one patient-reported outcomes instrument, the Breast-Related Symptoms Questionnaire (BRSQ), was developed and validated for use in the cosmetic and reconstructive breast surgery population. The authors concluded that there was a lack of availability of validated, condition or surgery specific instruments for breast surgery and that whilst generic instruments play an important complementary role, they are not sensitive enough to detect the full spectrum of changes after breast surgery (Pusic et al., 2007a). To fill this gap, Pusic and colleagues developed the four modules of the BREAST-Q (augmentation, reconstruction, mastectomy and reduction) in order to study the unique outcomes of breast surgery from the patients' perspective (Pusic et al., 2009). Subsequently, a systematic review of patient-reported outcome measures used in 95 studies of reduction mammoplasty patients was conducted; the authors emphasizing that using a combination of validated generic

measures and breast-specific surveys is preferred and provide a more accurate assessment of patient outcomes (Lonie et al., 2019).

1.9.1 Generic PROMs

1.9.1.1 Short Form-36

The Short Form-36 Health Survey (SF-36) is a generic instrument which has broad applicability and is the most commonly used instrument globally to measure the general health across population and patient groups. The SF-36 was developed as part of the Medical Outcomes Study (MOS), with the main objective of developing a measure to monitor the outcomes of medical care (Ware and Sherbourne, 1992). An advantage of the SF-36 is that it can be used to compare the burden of various disease states and interventions, for comparison to normative populations, and individual responses can be transformed with a SF-6D scoring algorithm to facilitate economic evaluations (Brazier et al., 2017, Brazier et al., 2002, Norman et al., 2014). In a systematic review of PROMs in breast surgery, the SF-36 was found to be the most widely used instrument in cosmetic and reconstructive breast surgery studies. However, the authors stated that whilst generic instruments play an important complementary role in patient-reported outcome studies, they may not be sensitive or responsive enough to detect changes as a result of surgery or capture all aspects of outcome after breast surgery (Pusic et al., 2007a).

Perez-Panzano et al. conducted a prospective study of quality of life and patient satisfaction after breast reduction surgery in a short- and long-term evaluation of 121 patients with symptomatic macromastia (Perez-Panzano et al., 2016). Symptom-specific questionnaires were used to assess patient satisfaction and the SF-36 was used to assess quality of life. They found an improvement in quality of life in all SF-36 domains in the long-term at one year after surgery. At the one-month assessment, all of the domain scores were significantly higher except physical functioning and social functioning, which did improve but not significantly. Role Physical was the only domain which deteriorated one month after surgery, although this was regarded as foreseeable due to the convalescence period after surgery (Perez-Panzano et al., 2016). Blomqvist and colleagues conducted a prospective study to assess the HRQoL in 49 women with breast hypertrophy who underwent reduction mammoplasty (Blomqvist et al., 2000). They found that reduction mammoplasty resulted in significantly improved quality of life in all eight domains of the SF-36 post-operatively. They also found that results were similar at 6- and 12-months post-surgery, indicating long-term improvement. Furthermore, they found that these patients were normalised in health-related quality of life, with no statistically significant differences between the patients and age-matched control population (Blomqvist et al., 2000). Other studies had similar findings of improvement in HRQoL across all domains of the SF-36 when assessing outcomes beyond the initial convalescence period following surgery (Behmand et al., 2000, Collins et al., 2002, Klassen et al., 1996, Mello et al., 2010). Thoma et al. conducted a prospective study of 52 patients using the SF-36 pre-operatively and again at 1-, 6- and 12-months after breast reduction surgery. The

authors found that the improvement from 1 month after surgery was maintained to 1 year after surgery (Thoma et al., 2007). However, the authors only reported physical and mental summary scores as opposed to all SF-36 domains. Iwuagwu et al. conducted a randomised-controlled trial of a surgical group compared to a non-surgical group who received physiotherapy. Using the SF-36, they found that surgery resulted in considerable improvement in physical and mental summary scores whilst conservative treatment was not effective in providing relief from symptoms of breast hypertrophy and improving HRQoL (Iwuagwu et al., 2006b).

Despite the apparent breadth of literature on HRQoL in women undergoing breast reduction surgery using the SF-36 at various follow-up time points, there remain comparison problems and gaps in the literature. This study will address some of these limitations by being a prospective, longitudinal study with adequate participant numbers with control groups for comparison and the collection of HRQoL data as the primary measure of outcome using several validated patient-reported outcome measures.

1.9.1.2 MBSRQ

The Multi-Dimensional Body-Self Relations Questionnaire (MBSRQ) is a validated patient-reported outcome measure for the assessment of body image. The full, 69-item version consists of seven factor subscales: (1) appearance evaluation; (2) appearance orientation; (3) fitness evaluation; (4) fitness orientation; (5) health evaluation; (6) health orientation; and (7) illness orientation. There are also three additional MBSRQ subscales: body areas satisfaction scale; (2) overweight preoccupation; and (3) self-classified weight (Cash and Pruzinsky, 1990). Two forms of the MBSRQ are available, the full version and the MBSRQ-Appearance Scales (MBSRQ-AS).

The MBSRQ has been used in combination with additional PROMs in a number of studies investigating breast hypertrophy and the outcome of breast reduction surgery (Collins et al., 2002, Cunningham et al., 2005, Kerrigan et al., 2001, Thoma et al., 2013, Thoma et al., 2005). Comparison studies of women with breast hypertrophy who are seeking breast reduction surgery, hypertrophy control subjects, and normal control subjects have revealed that, pre-operatively, surgical candidates scored worse on the appearance evaluation of the MBSRQ questionnaire than the two control groups. In addition, the hypertrophy control subjects scored worse than the normal control subjects did. The authors concluded that breast hypertrophy has a significant impact on women's quality of life as measured by the MBSRQ and other validated self-report instruments (Collins et al., 2002, Kerrigan et al., 2001). In a prospective study, Thoma et al. found that the mean MBSRQ score before surgery was 2.3 and at 12 months after surgery had improved to 3.2, nearing the adult female normative score of 3.36 (Thoma et al., 2007).

A systematic review of patient-reported outcome instruments in cosmetic, functional and reconstructive breast surgery, conducted by Pusic and colleagues, criticised the use of the MBSRQ as a standalone measure of outcome in this patient population as the questions do not

address relevant body image concerns such as scarring and breast size. However, the authors argued that generic instruments such as the MBSRQ play an important complementary role in outcome studies (Pusic et al., 2007a).

1.9.1.3 Rosenberg Self-Esteem Scale

The Rosenberg Self-Esteem scale (RSE) is a widely-used self-report measure of self-esteem (Rosenberg, 1965). It is comprised of 10-items answered on a four-point Likert scale. The scale ranges from a score of 0 to 30, in which higher scores indicate higher self-esteem. Klassen and colleagues (Klassen et al., 1996) first described using the RSE to demonstrate a significant improvement in self-esteem after breast reduction surgery. Similar findings have since been reported in other outcome studies (Hermans et al., 2005, Kececi et al., 2015, Mello et al., 2010, Miller et al., 2005, O'Blenes et al., 2006, Shakespeare and Cole, 1997).

1.9.2 Condition or surgery-specific PROMs

1.9.2.1 BREAST-Q

The BREAST-Q is a condition specific patient-reported outcome questionnaire that was developed and validated to measure patient satisfaction and quality of life following cosmetic, functional and reconstructive breast surgery (Pusic et al., 2009). Individual modules were generated to assess unique outcomes related to specific types of breast surgery; breast reconstruction, breast augmentation, mastectomy, and breast reduction. The BREAST-Q underwent full development and validation using the three-stage approach described previously by Cano et al., including item generation (individual questions are developed from patient interviews, experts and literature), item reduction (field test to finalise questions), and psychometric evaluation (final questionnaire administered to a large population to assess data quality, validity, reliability and responsiveness) (Cano et al., 2009). The conceptual framework of the BREAST-Q was developed following literature review and qualitative interviews with breast surgery patients in order to identify six key themes and form the framework of patient satisfaction and quality of life among breast surgery patients (Figure 1.3) (Klassen et al., 2009, Pusic et al., 2009).

Image removed due to copyright restriction. Original can be accessed at:

https://journals.lww.com/plasreconsurg/Abstract/2009/08000/Development_of_a_New_Patient_Reported_Outcome.1.aspx

Figure 1.3. BREAST-Q conceptual framework
Source: (Pusic et al., 2009)

Satisfaction with breasts — Relates to women's satisfaction with their breasts with reference to size, shape, symmetry, cleavage, positioning, how natural their breasts look and feel both clothed and unclothed, and how their breasts sit in proportion to the rest of their body. There are also post-operative only items such as the location and appearance of scars.

Satisfaction with outcome — Relates to an overall level of satisfaction with the outcome of breast surgery.

Psychosocial wellbeing — Relates to the effect of breast surgery on their psychosocial wellbeing with items that ask about body image and confidence in social settings, emotional health and self-esteem.

Sexual wellbeing — Relates to the way a woman's breast condition and surgery impact on her sexual life and body-image issues when clothed and unclothed.

Physical wellbeing — Relates mainly to chest and upper body symptoms and how these impact on physical function and participation in activities before and after breast surgery.

Satisfaction with care — Relates to patient satisfaction with the overall process of care. This domain represents a key area in the patient's overall assessment of the surgery. There are three main subthemes: satisfaction with information pre-operatively; satisfaction with the care provided by the plastic surgeon; and satisfaction with office staff and other members of the medical team.

Satisfaction with information — Items cover possible risks and complications, healing and recovery time, and breast appearance and scarring. The patient's relationship with the plastic surgeon was a key area and items cover whether or not they felt comfortable, had their questions answered,

understood what they wanted, and whether they felt the surgeon had provided adequate follow-up after surgery.

A review of the literature on the use of the BREAST-Q in surgical research from 2009 to 2015, conducted by Cohen and colleagues, yielded 49 peer-reviewed articles that met the inclusion criteria (Cohen et al., 2016b). Of these, four references used the BREAST-Q Reduction module questionnaire (Carty et al., 2012, Coriddi et al., 2013, Gonzalez et al., 2012, Gurunluoglu et al., 2013). In the largest of these studies, Carty and colleagues conducted a retrospective study of 279 women who had undergone breast reduction surgery between 1995 and 2007. They found that older patients were more satisfied with their breasts than younger patients after reduction mammoplasty, and they also found no difference in satisfaction with outcome and/or breasts based on surgeon's age or experience (Carty et al., 2012). Gonzalez and colleagues conducted a 10-year retrospective analysis of patient satisfaction and surgeon experience in 178 women who had previously undergone breast reduction surgery. The authors found that breast reduction surgery had a positive impact on quality of life and that no difference was found in satisfaction with outcome by quantity of breast tissue removed. However, the limitations of this study were a low response rate, the lack of pre-operative BREAST-Q data, and that only the item responses (i.e. the raw data) rather than scored BREAST-Q data was used in the analysis, which was not in line with the design or the intended use of the instrument (Gonzalez et al., 2012). Retrospective studies are, by their very nature, unable to provide pre-operative HRQoL levels and therefore assume that all respondents had an approximately equal baseline level of satisfaction and wellbeing before surgery. In addition, these studies lack the longitudinal tracking of patients following surgery and often include a broad range of follow-up time following surgery that may alter patient satisfaction responses.

Coriddi and colleagues completed the only prospective study that was included in the systematic review by Cohen et al (Cohen et al., 2016b, Coriddi et al., 2013). Using the BREAST-Q before and 6 weeks after surgery they found that breast reduction significantly improves satisfaction with breast, psychosocial, sexual, and physical wellbeing, and that overall satisfaction with outcome is highly correlated with satisfaction with breasts after surgery. However, this study was limited by a small sample size and, furthermore, only a small subset of participants completed both pre- and post-operative questionnaires.

Cogliandro and colleagues in Italy conducted the largest outcome study using the BREAST-Q in 414 breast reduction patients (Cogliandro et al., 2017a). However, this study was also retrospective in design and therefore even though the authors reported a high level of patient satisfaction following surgery, there was no pre-operative data to serve as a baseline for comparison. In addition to this, there was a very broad range of time since surgery and this could have affected patient responses. Following on from this study, the authors presented data in a

short letter from a prospective study of 156 women who completed the BREAST-Q pre- and 6 months post-surgery. Whilst the authors reported a statistically significant improvement across three of the four common BREAST-Q domains, an unusual finding in this study was the significant decrease in physical wellbeing scores following surgery (Cogliandro et al., 2017b). In contrast, prospective studies by Cohen and colleagues (Cohen et al., 2016a) and Cabral and colleagues (Cabral et al., 2017a) found a significant improvement in all four of the BREAST-Q scales. Whilst the study by Cohen et al. has the advantage of being prospective in nature, the results are limited by a small sample size and furthermore, not all of these patients completed the BREAST-Q at each study time point. During the course of this thesis, a prospective study of outcomes following reduction mammoplasty using the BREAST-Q was published. The authors reported a significant improvement in all four BREAST-Q domains when comparing pre- to one year post-surgery in 156 women in Sweden (Lewin et al., 2019). However, a limitation of this study was the restrictive inclusion criteria as per the Swedish national guidelines for breast reduction (BMI <25 kg/m^2 if younger than 50 years and BMI <27 kg/m^2 if older than 50 years; plus breast volume ≥800 cm^3 with physical problems) and a low response rate among women who answered both the pre-operative and post-operative questionnaires (45%).

Despite there being several studies published using the BREAST-Q to assess patient outcomes following breast reduction surgery, there still remains the need for high quality, longitudinal, and most importantly, prospective studies. Further to this, there have been no outcome studies using the BREAST-Q Reduction questionnaire in Australian women.

1.9.2.2 BRSQ

Breast-Related Symptoms Questionnaire (BRSQ) is a validated 13-item scale uniquely developed to measure symptoms associated with breast hypertrophy. The focus of the instrument is on breast symptoms and physical symptoms and/or limitations due to breast hypertrophy and does not include general QoL issues or satisfaction with breast appearance. The BRSQ was developed for use in the BRAVO study and subsequently underwent further validation studies (Kerrigan et al., 2001). The instrument is scored from 0 (corresponds to having all 13 symptoms all the time) to 100 (corresponds to no symptoms). In a prospective multi-centre study using the BRSQ, Valtonen et al. found that breast reduction surgery significantly improved breast-related symptoms and HRQoL (Valtonen et al., 2014). Thoma and colleagues utilised the BRAVO instruments (BRSQ, MBSRQ, SF-36) to assess HRQoL before and at 1, 6, and 12 months after surgery. The authors also found that breast-related symptom scores significantly improved after surgery (Thoma et al., 2007). This is supported by the findings of other studies (Collins et al., 2002, Kerrigan et al., 2002, Lewin et al., 2019).

In a randomised-controlled trial, the Finnish version of the BRSQ was used to compare outcomes of a surgical group versus a control group. The authors found that the surgical patients had

significantly less reported breast-associated symptoms or pain when compared with the non-surgical group at the six month follow-up (Saariniemi et al., 2008a).

Whilst well-validated, the BRSQ does not capture the full spectrum of HRQoL related to breast reduction surgery as it fails to address issues around psychosocial and sexual functioning, body image, aesthetics, satisfaction with care and overall quality of life.

1.9.2.3 BRASS

The Breast Reduction Assessed Severity Scale (BRASS) is a 39-item questionnaire using the five point Likert scale for measuring the burden of breast hypertrophy (Sigurdson et al., 2007a). The instrument comprises five subscales: (1) physical implications; (2) poor self-concept; (3) body pain; (4) negative social interactions; and (5) physical appearance. In a test of criterion validity, the BRASS subscale analysis showed moderate though significant correlations with conceptually similar domains from the Short Form-36 and the Rosenberg Self-Esteem scale and correlated strongly with the Breast-Related Symptoms (BRSQ) score. Despite its reliability, the instrument has been criticised for focusing solely on capturing physical symptoms and psychological issues and the absence of items or scales that measure post-operative outcomes including scarring and pain (Reavey et al., 2011).

Kececi and colleagues conducted a prospective cohort study of 94 patients with breast hypertrophy who underwent breast reduction and found a significant post-operative improvement in all domains of the BRASS (Kececi et al., 2015). However, this study utilised a Turkish translation of the BRASS, which had been validated in a group of women presenting with breast hypertrophy (Kececi et al., 2013). However, it has been argued that this version of the BRASS has limited validity due to by the absence of a post-operative cohort to ensure that the questionnaire is responsive to change and lacks the additional dimensions to address surgery-specific post-operative issues which are included in instruments such as the BREAST-Q (Kerrigan, 2013).

1.9.2.4 mBEQ

The Breast Evaluation Questionnaire (BEQ) was initially developed and validated on 1244 women seeking breast augmentation surgery and is comprised of 55-item scale (Anderson et al., 2006). The instrument addresses three subscales of breast comfort and satisfaction: (1) Comfort not fully dressed; (2) comfort fully dressed; and (3) satisfaction. The scores range from 0 (very dissatisfied/uncomfortable) to 100 (very satisfied/comfortable). However, the applicability in using the BEQ to assess outcomes following other types of breast surgery as recommended by the developers, such as breast reduction and reconstruction, has been questioned (Pusic et al., 2007b). Subsequently, a modified Breast Evaluation Questionnaire (mBEQ) version was developed and validated to specifically measure the outcomes of breast reduction surgery (Lewin et al., 2018). The authors state that the mBEQ assesses important aspects of breast hypertrophy and may provide additional information about psychosocial morbidity in comparison with the

BREAST-Q Reduction module. Lewin and colleagues presented findings of a prospective study using the modified mBEQ to demonstrate that reduction mammoplasty improves psychosocial issues associated with breast hypertrophy (Lewin et al., 2019).

1.9.3 Preference-based measures

Preference-based measures provide a single index score that quantifies a patient or population's state of health-related quality of life. These are typically represented on the quality adjusted life years (QALY) scale whereby a utility score of 0 corresponds to being dead and a utility score of 1 corresponds to full health (Brazier et al., 2017). Utilities facilitate the classification of the HRQoL associated with different diseases or conditions on a common scale and are especially useful in economic evaluations of health interventions. The Short Form Six-Dimensional (SF-6D), 15-dimensional (15D), EuroQol-5D (EQ-5D), Quality of Well-Being Scale Self-Administered (QWB-SA), and Health Utilities Index Mark 2 (HUI2) and Mark 3 (HUI3) are commonly used generic preference-based instruments.

Preference-based measures of quality of life, were first described in the area of plastic surgery almost two decades ago. Kerrigan and colleagues reported a utility score for living with breast hypertrophy of 0.86, which was lower (i.e. worse) than expected and was comparable with the reported burden of living with other health conditions, such as moderate angina (0.90) and a kidney transplant (0.84) (Kerrigan et al., 2000). Similarly, Thoma et al, using the HUI3, reported a HRQoL utility score of 0.76 before surgery and 0.89 at one year after surgery, with a difference of 0.13 (Thoma et al., 2007). The burden of breast hypertrophy is comparable to reports for other chronic conditions: 0.77 for heart disease; 0.78 for arthritis; 0.78 for epilepsy; 0.79 for diabetes; and 0.81 for back problems (Mittmann et al., 1999).

In a prospective study of 80 patients using the 15D instrument before and 6 months after surgery, Tykka et al. found that mean HRQoL score increased from 0.916 to 0.939 (Tykka et al., 2010). In another study, Saariniemi et al. also conducted a cost-utility analysis using the 15D pre-operatively and at a mean follow-up time point of 4 years on 73 patients who underwent reduction mammoplasty. They describe a utility score of 0.847 at baseline and 0.930 at follow-up, with a mean improvement of 0.083 (Saariniemi et al., 2012). The minimal clinically important difference in the 15D and the HUI is ≥0.03, highlighting that these studies all agree that reduction mammoplasty significantly improves HRQoL (Drummond, 2001, Sintonen, 2001). Araujo described a considerably lower pre-operative utility index of 0.63, increasing to 0.73 six months post-operatively, using the SF-6D (Araujo et al., 2014).

There have been no utility studies performed on women with breast hypertrophy in Australia in order to compare with the burden with other health conditions and to perform a health economic evaluation of breast reduction surgery.

1.9.4 Factors influencing the HRQoL of women following breast reduction surgery

Studies have shown that patients express a high level of satisfaction and improved quality of life following breast reduction (Carty et al., 2012, Cohen et al., 2016a, Coriddi et al., 2013, Davis et al., 1995, Gonzalez et al., 2012, Makki and Ghanem, 1998, Perez-Panzano et al., 2016, Scott et al., 2005). However, there are several factors which have the potential to influence the level of change in HRQoL in women with breast hypertrophy following surgery: body mass index; tissue resection weight; age; surgical technique; surgical complications; time since surgery; pre-operative breast symmetry; and degree of hypertrophy.

In the prospective study of patents undergoing breast reduction surgery using the BRAVO instruments, a positive relationship was found between breast resection weight and body mass index (Thoma et al., 2007). However, the authors established that the patients' body mass index did not affect the change in HUI scores. This demonstrates that women with breast hypertrophy of all body weights, obese or non-obese, can benefit from reduction surgery. The authors also found that tissue resection weight was not significantly associated with the change in HUI scores. That is, all women benefit from surgery regardless of the amount of tissue removed at surgery (Thoma et al., 2007). This is supported by Collins et al. in the finding that all patients benefited regardless of body weight or tissue resection weight (Collins et al., 2002). In a retrospective chart review, Wagner et al. also found that there was no correlation between BMI or the volume of tissue resected and the relief of symptoms (Wagner and Alfonso, 2005). Guemes and colleagues evaluated the effect of reduction mammoplasty on quality of life using the SF-36 in obese patients compared with non-obese. They found that quality of life significantly improved following surgery in both obese and non-obese groups (Guemes et al., 2016). This is supported by the findings of Eggert and colleagues (Eggert et al., 2009).

In 2017, a retrospective study was conducted to determine if the quantity of tissue removed at surgery had any influence on patient satisfaction as measured by the BREAST-Q; the researchers found that quality of life and satisfaction were similar irrespective of resection weight, BMI, and surgical technique (Menéndez-Cardo et al., 2017). Cabral and colleague's study also supported these findings and found no association between BMI, age or resection weight on BREAST-Q satisfaction and wellbeing scores (Cabral et al., 2017a). In addition, overall satisfaction with outcome has been shown to be associated with satisfaction with breast appearance, further supporting the importance of thorough pre-operative counselling in relation to patients ideals on post-operative breast size and shape (Cabral et al., 2017a, Coriddi et al., 2013).

Cogliandro and colleagues conducted the largest study of 414 participants using the BREAST-Q Reduction module. They found that participants who presented with severe asymmetry and breast hypertrophy were more satisfied than others were. Limitations of this study include a retrospective

design and lack of pre-operative baseline BREAST-Q data (Cogliandro et al., 2017a).

In a retrospective study, Carty and colleagues found that BREAST-Q 'satisfaction with breasts' and 'satisfaction with outcome' scores were unaffected by gains in operative efficiency with increasing surgeon experience (Carty et al., 2012). They also found that patients older than 40 years demonstrated significantly higher satisfaction with breasts scores than younger patients. This is believed to be due to a variety of factors including more realistic expectations following surgery and that older patients have lived with symptoms of macromastia for a longer duration and therefore may find a greater degree of relief. Furthermore, this study demonstrated that patients who had post-operative skin necrosis demonstrated significantly reduced satisfaction scores. In contrast, studies have found no relationship between post-operative complications and satisfaction scores using the SF-36 and MBSRQ instruments (Cunningham et al., 2005). A recent article by Cohen et al. conducted the only study using the BREAST-Q to determine the temporal relationship on satisfaction and wellbeing scores (Cohen et al., 2016a). In a study of 20 patients, they found that HRQoL scores significantly improved following reduction mammoplasty and that this was maintained during the post-operative period.

Whilst a large number of studies have investigated factors that influence the satisfaction and HRQoL outcomes following reduction surgery, there exists a research gap. There have been no outcome studies performed in Australian women, and no studies to date have provided a comprehensive comparison between physical assessment of body shape and patient-reported outcomes. In addition, the quantity of prospective studies in the current literature with sufficient participant numbers for subgroup analyses is lacking.

1.9.5 Comparison of women with breast hypertrophy with the general population

Research that describes the health-related quality of life of women with symptomatic breast hypertrophy who undergo breast reduction surgery is useful in its own right. However, the comparison with scores from a reference population, such as normative data from the general population, provides a clinical reference point and enables a better understanding of the health burden of breast hypertrophy and the success of breast reduction surgery. The availability of normative values provides a valuable benchmark and allows findings from research studies to be placed into context for what is considered 'normal' for a given population. Population-based reference data that can be further categorised according to variables such as gender and age demographics is particularly useful for describing populations. However, normative data is not readily available for many PROMs.

Normative values for the general population are available for the original Short-Form 36 (SF-36) in Australia (Australian Bureau of Statistics, 1997, Watson et al., 1996) and in numerous countries worldwide as part of the International Quality Of Life Assessment (IQOLA) project including

Denmark, France, Germany, Italy, Japan, the Netherlands, Norway, Sweden, Spain, the United Kingdom, the United States (Gandek et al., 1998), and in Canada (Hopman et al., 2000). Population-based normative data for the revised “international version” of the SF-36, the SF-36 Version 2 (SF-36V2), are available for Australia (Hawthorne et al., 2007, Marin et al., 2009), the United States (Maglinte et al., 2012, Ware et al., 2000), New Zealand (Frieling et al., 2013), Sweden (Taft et al., 2004), and the United Kingdom (Jenkinson et al., 1999). Normative values for condition-specific HRQoL instruments may be advantageous over those from a more generic instrument as they focus on relevant disease and treatment-specific issues. The recent publication of normative data for the most commonly used breast surgery-specific instrument, the BREAST-Q, for the United States population provides a valuable comparison for assessing the outcome of reconstructive breast surgery (Mundy et al., 2017a, Mundy et al., 2017b, Mundy et al., 2017c). Despite some recognised limitations of the study in regard to population diversity, this HRQoL normative data provides a benchmark or reference point and provides a greater context to the burden of disease and the effectiveness of surgical intervention when interpreting HRQoL scores. Additional normative data from a more diverse and different population, such as that of the Australian population, would further enhance the knowledge for ongoing and future outcome studies in reconstructive breast surgery. Furthermore, evidence has shown that there are potentially important differences when comparing the HRQoL within the Australian population to other populations (Frieling et al., 2013, Hawthorne et al., 2007). This highlights the importance of utilising country-specific HRQoL population norm data for accurate comparison in outcome studies wherever possible. The availability of normative breast-related quality of life data in Australian women is lacking and is an important area for further research and investigation.

Evidence from several international research studies demonstrates that women with symptomatic breast hypertrophy have a considerable health deficit and impaired quality of life compared to women in the general population (Blomqvist and Brandberg, 2004, Kececi et al., 2015, Klassen et al., 1996, Miller et al., 2005, Mundy et al., 2017c, O'Blenes et al., 2006, Saariniemi et al., 2008b, Shakespeare and Cole, 1997). These studies also report that surgical intervention provides symptomatic relief and improves health-related quality of life to such an extent that they ‘normalise’ post-operatively to that of the general population. For example, O’Blenes and colleagues conducted a prospective study to assess HRQoL in 57 women pre-operatively and at 6- and 21.5-months following reduction mammoplasty. When comparing to age-matched, female Canadian normative SF-36 scores, the authors found that health deficits were eliminated at 6 months following surgery and showed a normalisation effect within the 21.5 months after surgery (O'Blenes et al., 2006). This finding is supported by other published studies comparing HRQoL in women undergoing breast reduction surgery to population norms using generic HRQoL instruments (Behmand et al., 2000, Blomqvist and Brandberg, 2004, Blomqvist et al., 2000, Collins et al., 2002, Eggert et al., 2009, Faria et al., 1999, Hernanz et al., 2016, Kececi et al., 2015, Kerrigan et al.,

2001, Klassen et al., 1996, Lewin et al., 2019, Shakespeare and Cole, 1997). In the publication by Mundy and colleagues in 2017, a comparison was made between the generated United States normative BREAST-Q Reduction module data and previously published pre- and post-operative data by Coriddi and colleagues (Coriddi et al., 2013, Mundy et al., 2017c). The authors highlighted the health burden and reduced quality of life associated with breast hypertrophy, and in turn demonstrated the success of breast reduction surgery to increase breast-related HRQoL to normative levels. Notably, all of these studies comparing HRQoL in women with breast hypertrophy and following breast reduction surgery have been conducted overseas, predominantly in the United States (Behmand et al., 2000, Collins et al., 2002, Coriddi et al., 2013, Kerrigan et al., 2001, Mundy et al., 2017c), Canada (Miller et al., 2005, O'Blenes et al., 2006) or Sweden (Blomqvist and Brandberg, 2004, Blomqvist et al., 2000, Eggert et al., 2009, Lewin et al., 2019).

1.10 Assessment of breast volume and body shape

1.10.1 Breast volume measurement

A variety of techniques have been described in the literature to fulfil the need for an accurate and objective measurement of breast volume in the clinical setting: magnetic resonance imaging, mammography, plaster casting, Grossman-Roudner plastic cups, water-displacement, anthropometric measurement and 3D surface imaging (Bulstrode et al., 2001, Howes et al., 2017, Kovacs et al., 2007, Kwong et al., 2020, Lee et al., 2016, Longo et al., 2013, Losken et al., 2005, Muslu et al., 2019, Qiao et al., 1997, 1986, Sigurdson and Kirkland, 2006, Smith et al., 1986, Wang et al., 2019, Wesselius et al., 2018). The accurate and objective assessment of breast volume plays an important role in breast reduction, reconstruction, developmental asymmetry and augmentation. In women with breast hypertrophy this is important for pre-operative planning and may aid intraoperative decision-making regarding the amount of tissue to be taken from each breast to achieve breast symmetry, or in cases where removal of a minimum amount of breast tissue is required to justify proceeding to surgery (Boukovalas et al., 2019, Descamps et al., 2008, Dvoracek et al., 2019, Eder et al., 2013, Kocak et al., 2011, Sommer et al., 2002, Wamalwa et al., 2018, Wampler et al., 2019). Accurate estimation of breast volume and predicted tissue resection weight also promotes improved counsel to the patient and provides a valuable guide to training surgeons.

Traditionally, the pre-operative measurement of breast volume and the amount of tissue to be resected in breast reduction surgery is estimated by jugular notch to nipple distance or other measurements, which are not necessarily well validated. In a situation where a woman is undergoing post-mastectomy breast reconstruction the most accurate method for measuring breast tissue volume for reconstruction is the Archimedes method of water displacement of the mastectomy specimen (Yip et al., 2012). In terms of measuring breast tissue volume in the intact state such as candidates for breast reduction surgery, MRI is reported as being the most accurate.

However, MRI is expensive and not accessible to all. Three-dimensional laser scanning has been demonstrated to be a valid method of breast volume measurement, but some centres may lack access to either a 3D laser scanner or other forms of 3D imaging. Water displacement of the intact breast as a method has been used in some centres since 1970, but has not previously been validated against other more modern methods (Bouman, 1970).

1.10.2 Body shape assessment

Body mass index (BMI) is commonly used as a criterion for surgery in patients presenting for breast reduction surgery. However, there is not always a clear relationship between BMI and breast size and the appropriateness of BMI as a selection criterion in this patient group is debatable (Benditte-Klepetko et al., 2007, Findikcioglu et al., 2013, Katch et al., 1980, Vandeput and Nelissen, 2002). Distinct clinical anthropometric measurements of fixed skeletal and soft tissue landmarks provide a useful tool in the evaluation of body and breast size pre-operatively and following surgical procedures. As an example, the linear measurement of the suprasternal notch to nipple distance is widely used by surgeons to evaluate breasts pre-operatively and to assess the outcome of breast surgery. In women with breast hypertrophy, increasing breast mass is associated with the inferior migration of the nipple, resulting in a larger measurement (Khan and Bayat, 2008). Whilst previous studies have investigated the relationship of suprasternal notch to nipple distance and surgical outcomes, there are limited studies evaluating other anthropometric variables related to breast and body size. In addition, studies exploring the relationship between BMI and the physical symptoms associated with large breasts have presented conflicting findings (Dabbah et al., 1995, Gonzalez et al., 1993, Miller et al., 1995, Netscher et al., 2000). In women with breast hypertrophy, the influence of body shape on physical symptoms and health-related quality of life is scarcely reported in the literature. Furthermore, the effect of disproportionality (breast size as a proportion of overall body size) is an important area for further research.

1.11 Economic evaluation of breast reduction surgery

In addition to clinical effectiveness, evidence to assess the cost effectiveness of interventions is becoming increasingly important for health care decision-makers due to limited resources and the comparatively larger number of treatment options available. Making rational decisions requires decision-makers to weigh up the costs and benefits of a treatment option and compare to other interventions in order to decide which are the most beneficial for informing optimal treatment pathways for patients and for driving health system efficiencies. Measurement and valuation of health-related quality of life using validated outcome measures is increasingly being employed to measure treatment success and provide comparative data between different medical interventions. As an example, the generic SF-36 questionnaire is commonly utilised worldwide across a wide variety of specialties as a measure of health outcome. However, it may be unclear how improvement or change in one area of health compares to an improvement or change in another.

For this reason, a single measure of quality of life may be employed to enable simpler comparisons between treatments. In the case of the SF-36, this led to the development of the SF-6D, providing a single preference-based utility score (on the 0 to 1 being dead to full health quality-adjusted life years (QALY) scale) from the 36-items specifically for application in economic evaluations (Brazier et al., 2002). Whilst the National Institute of Clinical Excellence (NICE) in the United Kingdom, which provides guidance on which treatments and care types are available from the National Health Service (NHS) in England and Wales, has mandated the EQ-5D as the preferred measure of HRQoL (National Institute for Health and Clinical Excellence, 2014a), guidelines from the Pharmaceutical Benefits Advisory Committee (PBAC) and Medical Services Advisory Committee (MSAC) in Australia are not so prescriptive and advocate the use of any generic preference-based health outcome measure as long as it is justified (Medical Services Advisory Committee, 2016, Pharmaceutical Benefits Advisory Committee, 2016). In this context, outcomes using generic measures, as opposed to condition-specific measures, are in principle valued consistently across all healthcare treatments and programmes.

Health utility scores are commonly used to value the benefits of health care which are measured in terms of quality-adjusted life years (QALYs). QALYs attempt to provide a measure which combines both length of life and health-related quality of life into a single measure and are used in cost-utility analyses (Brazier et al., 2017). In the United Kingdom, NICE has adopted the cost per QALY as its main measure of outcome. This ratio incorporates the incremental cost associated with an intervention with its incremental benefits (defined in terms of QALYS) (Dakin et al., 2015, Rawlins and Dillon, 2005, Rawlins and Culyer, 2004). It is then possible to directly compare a new intervention with existing treatments to determine which is the most cost-effective option. However, this approach may be limited by the lack of information for many medical interventions. Despite the published evidence on the health gains of breast reduction surgery, it is possible that without comprehensive evidence relating to its cost-effectiveness it may be mistaken as a cosmetic or lifestyle intervention rather than a functional operation.

Research assessing the cost-effectiveness of breast reduction surgery is scarce and has only been described in a few countries worldwide including the United Kingdom (Taylor et al., 2004), Finland (Saariniemi et al., 2012, Tykka et al., 2010), Canada (Thoma et al., 2014) and Brazil (Araujo et al., 2014). In the study by Taylor and colleagues in the United Kingdom, the cost per QALY for reduction mammoplasty was found to be between £4733 and £5729. However, the HRQoL data was obtained from a Swedish study, whilst the cost data was from the United Kingdom (Taylor et al., 2004). In addition, this study only reported the cost per QALY and did not separately report the number of QALYs gained. In Finland, the average direct hospital costs for reduction mammoplasty was approximately €3601 and the mean cost per QALY gained was €1180 (Saariniemi et al., 2012). In another Finnish study, the mean direct costs were found to be comparable at €3383, yet the cost per QALY of €3638 was considerably higher using the same 15D utility instrument but

over a shorter 6 month follow-up period (Tykka et al., 2010). Thoma and colleagues performed a prospective study on 52 women using the Health Utilities Index Mark 3 scores and found that patients who undergo breast reduction surgery have an average lifetime gain of 5.32 quality-adjusted life years, which is equivalent to each patient living an extra 5.32 years in perfect health (Thoma et al., 2007). Whilst this study advanced the understanding of the health burden of breast hypertrophy on health-related quality of life health burden in comparison to other chronic health conditions, and the expected lifetime benefits of breast reduction surgery, the authors did not present the utility value or cost per QALY data to enable further comparison. Subsequently, the authors conducted a randomised-controlled trial to compare the cost-effectiveness of vertical scar reduction in comparison to inverted T-shaped reduction mammoplasty (Thoma et al., 2014). The authors found that inverted T-shaped reduction dominated vertical scar reduction from the Ministry of Health perspective by being slightly less costly ($3090.06 versus $3106.58 in 2012 Canadian dollars) and slightly more effective (0.87 quality-adjusted life-years versus 0.86 quality-adjusted life-years).

Despite some limitations in current published studies in this area, preliminary evidence argues that the cost-effectiveness and cost per QALY for breast reduction surgery compares favourably to other medical interventions. Whilst NICE in the United Kingdom rejects the use of an absolute cost per QALY threshold (Rawlins and Culyer, 2004), it's stated 'range of acceptable cost effectiveness' is between £20,000-£30,000 (Devlin and Parkin, 2004). The cost per QALY ratio for reduction mammoplasty of between £4733 and £5729 was found to be very favourable when compared with interventions approved by NICE; for example Etanercept and infliximab for rheumatoid arthritis at a cost per QALY of £27,000 - £35,000, Infliximab for Crohn's disease at £27,500 (Taylor et al., 2004) and £5623 for a total knee replacement (Dakin et al., 2012).

Given the reported gains in health-related quality of life in many international studies, a thorough economic evaluation of breast reduction surgery in Australia is warranted to provide the necessary information that decision-makers need to objectively maintain Australian government funding of this surgery within the healthcare system.

2. A PROSPECTIVE STUDY OF WOMEN UNDERGOING BREAST REDUCTION SURGERY: CLINICAL OUTCOMES AND HEALTH-RELATED QUALITY OF LIFE

A version of this chapter has been accepted as an original article for publication in *BMJ Open* journal (Crittenden et al., 2020); attached as Appendix A. A comparison of the magnitude of change in SF-36 scores between surgical interventions was presented at the 2019 International Society for Quality of Life Research (ISOQOL) 26th annual conference in San Diego, USA (Crittenden et al., 2019a).

2.1 Introduction

Breast reduction surgery is a common plastic surgery procedure and it has previously been shown to be effective for relieving pain and functional problems associated with breast hypertrophy (Blomqvist et al., 2000, Freire et al., 2007, Klassen et al., 1996, Mello et al., 2010, Thoma et al., 2007), whereas conservative approaches to treatment such as physiotherapy, hormonal therapy and weight loss have much less impact (Collins et al., 2002, Iwuagwu et al., 2006b). However, despite existing evidence to support the efficacy of breast reduction surgery, this has not translated to policy in many countries and jurisdictions worldwide. As described in Chapter one, within the Australian public hospital system, access to breast reduction surgery for patients is variable and is ultimately reliant upon state and local policies. Similarly, in the United Kingdom, reports on the rationing of surgery by the National Health Service (NHS) on the basis of geographical location has resulted in a "postcode lottery" (Royal College of Surgeons of England, 2014, Wraight et al., 2007). In 2018, reports from the NHS England 'Evidence-Based Interventions Programme' proposed to restrict funding for procedures it considers 'unnecessary', to save money and eliminate unwarranted clinical variation (Iacobucci, 2018). The inclusion of breast reduction surgery as a 'procedure of limited effectiveness' implies that it is a marginal and low priority procedure in comparison to other medical interventions (NHS England, 2018). However, labelling breast reduction surgery an 'ineffective' and 'unnecessary' procedure might be misleading and inaccurate, with little evidence to support this claim. Furthermore, restrictive access policies are in place in both public and private sectors in many countries and jurisdictions worldwide; often these restrictions are based on body mass index or a minimum weight of breast resection at surgery (Breuning et al., 2010, Frey et al., 2014, Klassen et al., 1996, Koltz et al., 2013, Nguyen et al., 2008, NHS England, 2018, O'Blenes et al., 2006, Royal College of Surgeons of England, 2014, Seitchik, 1995, Taylor et al., 2004, Wraight et al., 2007). The validity of such criteria might not be evidence-based, resulting in women with a medical need for surgery being denied access to it.

The Short Form-36 (SF-36) is a well-established and widely-utilised indicator of patient-reported outcome for evaluating the burden of disease states and the outcomes of medical interventions

and was therefore chosen as the primary outcome measure for this study (Ware and Sherbourne, 1992); with the Multidimensional Body-Self Relations Questionnaire (MBSRQ) used to further assess body image and health status (Brown et al., 1990, Cash and Pruzinsky, 1990). An ongoing challenge of interpreting changes in health-related quality of life (HRQoL) measures following medical treatments is defining a threshold as to what constitutes a clinically meaningful change. The interpretation of HRQoL scores based solely on statistical significance may be misleading because small differences in scores can be statistically significant even in the absence of the change being clinically meaningful (Lydick and Epstein, 1993, Osoba et al., 1998). The minimal important difference (MID) has become a standard approach for interpreting the clinical relevance of changes in scores of patient-reported outcomes such as HRQoL and can be defined as the smallest difference in HRQoL score that is perceived as beneficial or important by a patient or clinician (Jaeschke et al., 1989, p. 408). However, there is no universal measure of MID as this threshold may vary due to many factors including; population groups, type of disease, disease severity, between different health measures or clinical context (Jaeschke et al., 1989, King, 2011, Musoro et al., 2018). MID estimates for interpreting SF-36 scores in women undergoing breast reduction surgery are currently undetermined and are limited to rule-of-thumb approaches such as a 10-point change on 100-point subscales (King, 1996), and universal estimates for the SF-36 summary measures recommended by the developers (Frendl and Ware, 2014, Ware et al., 1995). Given that the SF-36 is the most frequently used patient-reported outcome measure in studies of women undergoing breast reduction surgery worldwide (Lonie et al., 2019), condition-specific estimates of MIDs provide valuable information for use in both the clinical setting, and for interpretation of findings from research studies.

The primary aim of this study was to longitudinally assess health-related quality of life (HRQoL) in women with breast hypertrophy before and after breast reduction surgery, and to compare these outcomes to control groups of women with breast hypertrophy not undergoing surgery, and also to a normative female reference population. Secondly, this study aimed to assess the impact of patient demographics and surgical characteristics including, but not limited to, those commonly used as selection criteria for access to surgery and insurance coverage on pre-operative HRQoL scores and the long-term improvement in HRQoL following surgery. Finally, this study aimed to estimate thresholds of minimal important difference for the SF-36 in patients for the interpretation of the change in scores in women with breast hypertrophy who underwent breast reduction surgery

2.2 Participants and methods

2.2.1 Design and participants

2.2.1.1 Surgical cohort

A prospective cohort study was performed at Flinders Medical Centre in Adelaide, Australia. Ethics approval was obtained for this project from the local Southern Adelaide Clinical Human

Research Ethics Committee (SAC HREC approval number 118.056) (Appendix B). All women aged 18 years and over with symptomatic breast hypertrophy who were assessed for bilateral breast reduction surgery between April 2007 and February 2016 were informed of the study. Women who were unable to complete written questionnaires or refused to participate, were excluded from the study. Participants were provided with the information sheet and written informed consent was obtained.

Participants who consented to the study were assessed prospectively pre-operatively and at 3, 6 and 12 months following bilateral breast reduction surgery. Participants were asked to complete the Short-Form-36 version 2 (SF-36v2), Multi-Dimensional Body-Self Relations Questionnaire (MBSRQ) and adjunct study-specific questionnaire at each of the four study time points. Participant characteristics including age, height, weight and smoking status were recorded at the time of enrolment. Intraoperatively, the surgical technique and weight of tissue resected from each breast was documented. Hospital records were used to determine the American Society of Anesthesiologists (ASA) Physical Status Classification System status (American Society of Anesthesiologists, 2014), length of hospital stay, number of outpatient clinic appointments relating to the surgery, and complications leading to re-hospitalisation or a further operative procedure within the 12 months follow-up period. Standardised clinical photography was performed at all four study timepoints.

Breast and body measurements were performed pre-operatively and 12 months post-operatively using a Cyberware WBX three-dimensional laser body scanner (Cyberware, Monterey, USA), anthropometric measurements and water displacement. These measurements are described in detail in Chapter 6.

2.2.1.2 Breast hypertrophy control cohort

A control group of women with breast hypertrophy who were actively seeking breast reduction surgery through Flinders Medical Centre but had not yet had surgery were recruited for comparison. Women aged 18 years and above who were referred to Flinders Medical Centre by their general practitioner for consultation for bilateral breast reduction surgery were invited to participate in the study. The breast hypertrophy control group of women were identified from two sources: either new referrals on the waiting list for an outpatient consultation with a consultant plastic surgeon, or those who were on the surgical admissions waiting list. This non-surgical cohort represents an appropriate reference to compare HRQoL to those in the surgical cohort as they too were presenting with symptoms of breast hypertrophy and were followed up for the same 12-month timeframe without undergoing surgical intervention. Women who were unable to complete written questionnaires, had breast reduction surgery during the study, or did not return study questionnaires, were excluded from the study. Ethics approval was obtained for this study from the Southern Adelaide Clinical Human Research Ethics Committee (SAC HREC approval

number 73.17) (Appendix C).

Eligible participants were mailed study information and questionnaires. Consenting participants were required to self-complete and return the SF-36v2 and MBSRQ questionnaire and provide information for relevant variables such as age, height, weight, bra cup size and health status at baseline and again at 12 months after enrolment.

2.2.2 Outcome measures

2.2.2.1 Short-Form 36 (SF-36)

The Short Form-36 Health Survey (SF-36) is a generic instrument which has broad applicability and is widely used in the medical literature to measure the general health-related quality of life across population and patient groups (Ware and Sherbourne, 1992). The SF-36 version 2 (SF-36v2) used in this study is an updated version of the original SF-36 questionnaire and contains 36 items which form and assess health across eight subscales: (1) physical functioning; (2) role physical; (3) bodily pain; (4) general health; (5) vitality; (6) social functioning; (7) role emotional; and (8) mental health (Appendix D) (Table 2.1). Questionnaire responses were transformed using QualityMetric Health Outcomes™ Scoring Software for Microsoft Windows and as per the SF-36v2 scoring manual to provide the eight subscales a score between 0 and 100, with higher scores indicating better health (Ware et al., 2000). The subscales were converted into two summary scores: Physical Component Score (PCS) and Mental Component Score (MCS) using norm-based methods and scoring coefficients from the Australian general population (Hawthorne et al., 2007).

For comparison purposes, general female population normative scores were obtained from the 2008 South Australian Health Omnibus Survey dataset (Marin et al., 2009, Population Research and Outcome Studies Unit, 2008), with scores weighted to correspond to the age distribution of the study participants.

Table 2.1 Dimensions of the SF-36v2

Dimension	Description	No. items
Physical Functioning (PF)	Limitations in carrying out a range of physical activities because of health problems.	10
Role Physical (RP)	Limitations in performing regular daily activities because of physical health problems.	4
Bodily Pain (BP)	Intensity of bodily pain or discomfort and the extent to which pain interferes with their normal activities.	2
General Health (GH)	General health perceptions.	5
Vitality (VT)	Energy and fatigue.	4
Social Functioning (SF)	Limitations in social activities due to physical or emotional problems.	2
Role Emotional (RE)	Limitations in usual role activities because of emotional problems.	3
Mental Health (MH)	Psychological distress and well-being.	5
Physical Component (PCS)	Physical health summary.	35
Mental Component (MCS)	Mental health summary.	35

2.2.2.2 Multidimensional Body-Self Relations Questionnaire (MBSRQ)

The Multidimensional Body-Self Relations Questionnaire (MBSRQ) is a validated patient-reported outcome measure for the assessment of self-attitude aspects of body image, physical activity and health (Brown et al., 1990, Cash and Pruzinsky, 1990). Two forms of the MBSRQ are available, the full version and the MBSRQ-Appearance Scales (MBSRQ-AS). The full, 69-item version consists of seven factor subscales: (1) appearance evaluation; (2) appearance orientation; (3) fitness evaluation; (4) fitness orientation; (5) health evaluation; (6) health orientation; and (7) illness orientation. There are also three additional MBSRQ subscales: body areas satisfaction scale (BASS); (2) overweight preoccupation; and (3) self-classified weight (Cash and Pruzinsky, 1990) (Table 2.2). In this study, the full version of the MBSRQ questionnaire was utilised and scores were generated from one to five according to the revised algorithms provided by Cash (Cash, 2000) (Appendix E). Higher scores on evaluation scales indicate the person feels more satisfied in relation to either the construct (i.e. appearance, fitness or health), whereas higher scores for orientation scales indicates a greater importance that a respondent places on the construct. Previously published normative data from the United States population was used for comparison (Cash, 2000).

Table 2.2 Dimensions of the MBSRQ

Dimension	Description	No. items
Appearance evaluation	Feelings of physical attractiveness or unattractiveness; satisfaction or dissatisfaction with one's looks.	7
Appearance orientation	Extent of investment in one's appearance.	12
Fitness evaluation	Feelings of being physically fit or unfit.	3
Fitness orientation	Extent of investment in being physically fit or athletically competent.	13
Health evaluation	Feelings of physical health and/or the freedom from physical illness.	6
Health orientation	Extent of investment in a physically healthy lifestyle.	8
Illness orientation	Extent of reactivity to being or becoming ill.	5
Body areas satisfaction scale	Similar to the Appearance Evaluation subscale, except that the BASS taps satisfaction with discrete aspects of one's appearance.	9
Overweight preoccupation	This scale assesses a construct reflecting fat anxiety, weight vigilance, dieting, and eating restraint.	4
Self-classified weight	This scale reflects how one perceives and labels one's weight, from very underweight to very overweight.	2

2.2.2.3 Adjunct questionnaire

Supplementary study-specific questionnaires were completed at each study timepoint. Pre-operatively, participants were asked to state: (1) number of days off work in the last six months from symptoms relating to their breast condition; and (2) spending on medications and treatments (creams, pain relief etc.) due to symptoms from their breast condition. Post-operatively, in addition to the aforementioned questions participants were also asked: (3) whether they would choose to have the surgery again if they had their time over; (4) whether they experienced any new health issues or a worsening of an existing health issue that was not related to the surgery; and (5) whether or not they experienced any complications from the surgery.

2.2.2.4 Assessment of surgical complications

A comprehensive complications checklist was completed prospectively by the treating doctor at the following approximate timepoints; 4 weeks, 3 months, 6 months, and 12 months following surgery (Appendix F). Complications were subsequently graded according to the Clavien-Dindo Classification (CDC) (Clavien et al., 2009, Dindo et al., 2004), a standardised grading system for surgical complications based on the medical intervention required to treat the complication (Table 2.3). The CDC provides a validated approach to classifying surgical complications and enables an objective, standardised and reproducible comparison of surgical complications; avoiding subjective

interpretation and overcoming limitations with the comparison of surgical complications between surgeons, across institutions and treatment modalities.

Table 2.3 Clavien-Dindo classification of surgical complications

Grade	Definition
Grade I	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions. Allowed therapeutic regimens are: drugs as antiemetics, antipyretics, analgetics, diuretics, electrolytes, and physiotherapy. This grade also includes wound infections opened at the bedside
Grade II	Requiring pharmacological treatment with drugs other than such allowed for grade I complications. Blood transfusions and total parenteral nutrition are also included.
Grade III	Requiring surgical, endoscopic or radiological intervention.
Grade IIIa	Intervention not under general anaesthesia
Grade IIIb	Intervention under general anaesthesia
Grade IV	Life-threatening complication (including CNS complications)* requiring IC/ICU management
Grade IVa	Single organ dysfunction (including dialysis)
Grade IVb	Multiorgan dysfunction
Grade V	Death due to the intervention

*Brain haemorrhage, ischemic stroke, subarachnoidal bleeding, but excluding transient ischemic attacks.
CNS, central nervous system; IC, intermediate care; ICU, intensive care unit.

For analysis purposes, surgical complications graded using the CDC system in this study were further categorised into two groups: (1) CDC grades I and II were classified as minor complications; and (2) CDC grades III and above were classified as major complications.

2.2.3 Distribution-based estimates of MID

The minimal important difference (MID) was estimated for the SF-36 scores by applying distribution-based techniques. The most common distribution-based approaches use sample variability, either at baseline, after follow-up or using the change between timepoints. Half a standard deviation of the baseline scores has been suggested to serve as a default value for important patient-perceived change on HRQoL measures (Norman et al., 2003). This approach is the most frequently reported distribution-based criterion for determination of the MID (Ousmen et al., 2018). The 0.2 SD and 0.3 SD have also been suggested as a useful starting point to estimate MID, with a corresponding effect size (ES) calculated as the mean difference (or change) in score divided by the standard deviation of the baseline score, with a treatment effect size of 0.2 to 0.5

suggested as minimally important (Cohen, 1988, Crosby et al., 2003, Kazis et al., 1989, King, 2011, Samsa et al., 1999). This MID can be used to evaluate change both within-persons and between-persons.

The standardised response mean (SRM) is similar to the effect size but is defined as the mean score change divided by the standard deviation of that change score (Liang et al., 1990). This method therefore factors in the variability of the change between measurements whereas the effect size does not, and therefore the SRM is not as dependent on the heterogeneity of the sample at baseline. As per interpretation of the effect size, values of 0.2, 0.5 and 0.8 SRM have been proposed to represent small, moderate and large change, respectively (Crosby et al., 2003).

Another commonly used method that can be used to benchmark the change in HRQoL scores by approximating the MID is the standard error of measurement (SEM). The SEM is calculated using the sample standard deviation and the reliability coefficient (*r*) of the instrument ($\mathrm{SEM} = \mathrm{SD}\sqrt{1-r}$); in this study the Cronbach's alpha was used as an estimate of reliability for each individual SF-36 scale and summary measure in the calculation of SEM. A value of 1 SEM change threshold has been recommended for defining the MID (Norman et al., 2003, Wyrwich et al., 1999a, Wyrwich et al., 1999b).

2.2.4 Statistical analysis

Statistical analyses were performed using SPSS v25.0 statistical software (IBM Corp., Armonk, N.Y.). Descriptive statistics including mean, standard deviation and 95% confidence interval were computed for continuous variables. Comparisons between groups were made using *t* tests for continuous data and chi-square tests for categorical data, with Fisher's exact test as appropriate.

Linear mixed-models were used to assess the significance of changes in SF-36 scores for the surgical cohort pre-operatively and 3, 6, and 12 months post-operatively, where the dependent variable was each SF-36 scale and time was the fixed effect. For each SF-36 scale, a change score was calculated using the score obtained at the last available assessment, with a higher score representing a greater improvement from baseline.

Pearson correlation coefficients were calculated to assess the linear association between SF-36 scores and baseline participant and clinical characteristics; variables that showed a significant association were entered into the regression model. For any two independent variables with high correlation ($r > 0.8$), one was chosen to be included in the regressions model rather than both. Candidate variables included age, body mass index (BMI), pre-operative breast volume, bra cup size, tissue resection weight (grams), breast asymmetry, and ratio of breast to body volume. Variables were continuous except for bra cup size which was categorised into six groups as follows: D, DD, E, F, G and ≥H cup. Multiple linear regression was used to assess whether any of

the collected socio-demographic or clinical variables were predictive of firstly, SF-36 PCS score at baseline, and secondly, with the change in SF-36 PCS scores from baseline to 12-months after surgery.

The analysis of surgical complications was conducted using several approaches, including the grade of complications and the presence or absence of any complication. Any complication was defined by whether or not a patient experienced at least one of the complications listed on the comprehensive assessment checklist, with the incidence reported as the number of cases (percentages). Bivariate analysis was performed between any complication and potential baseline participant and clinical variables using an independent samples *t*-test for continuous variables or a chi-square or Fisher's exact test for categorical variables. Logistic regression was then conducted to explore potential relationships between any complication (dependent dichotomous variable) and candidate predictor variables (independent variables). Variables of interest included patient age, BMI, smoking status, presence of diabetes, total tissue resection weight at surgery, operative time, bra cup size, pre-operative breast volume and sternal-notch-to-nipple distance. From this model, adjusted odds ratios with associated 95% confidence interval were estimated for each explanatory variable as measures of association with any complication.

The World Health Organisation (WHO) definition of obesity was used to classify patients with a BMI <30 kg/m^2 as non-obese and those with BMI ≥30 kg/m^2 as obese (World Health Organization, 2018). BMI was further divided into six categories for statistical analysis based on the WHO classification: underweight (<18.5 kg/m^2); normal weight (18.5–24.9 kg/m^2); overweight (25–29.9 kg/m^2); obese class I (30–34.9 kg/m^2); obese class II (35–39.9 kg/m^2); and obese class III (≥40 kg/m^2). A one-way analysis of variance (ANOVA) was used to compare mean SF-36 scores between BMI groups, with a Dunnett's two-tailed post-hoc test used to compare participants of a normal weight to higher BMI categories.

For all analyses, statistical significance was established at a *p*-value of less than 0.05.

Sample size was determined *a priori* and a minimum sample size of 98 patients per group was calculated to give 80% power at a two-sided significance level of 5% to detect a mean difference of 10-points with an estimated standard deviation of 25-points in the SF-36 questionnaire score.

2.3 Results

2.3.1 Study participants

2.3.1.1 Surgical cohort

Of 251 participants who completed a baseline assessment and underwent bilateral breast reduction surgery, 209 (83.3%) completed at least one post-operative follow-up assessment and were included in the study group for analysis. Missing data were due to participants repeatedly not

attending appointments or choosing to not complete and return the study questionnaires at some time points. Twenty-three participants formally withdrew from the study following surgical intervention.

Participant demographics for the surgical cohort are summarised in Table 2.4. The mean age at surgery was 42.6 ± 13.4 years. The mean sternal notch-to-nipple distances were 32.7 ± 4.5 cm and 32.4 ± 4.5 cm for the right and left breasts, respectively. The majority of participants (64%) were classified as obese with a body mass index greater than or equal to 30 kg/m^2. The mean total weight of breast tissue resected at surgery was 1338 g ± 817 g. An inferior pedicle breast reduction technique was the most commonly used approach (161/209, 77%), followed by a superior pedicle technique (35/209, 17%). The average hospital stay was 2.3 days.

Baseline characteristics were compared between participants who were lost to follow-up or declined to attend subsequent study assessments and those who completed at least one post-operative assessment. No difference was observed for age, body mass index, tissue weight resected or pre-operative SF-36 scales and summary scores except for the mental health scale, where non-respondents had a lower mean score of 6.8-points less than responders (p = 0.034).

2.3.1.2 Breast hypertrophy control cohort

Study questionnaires were initially posted to 350 women with breast hypertrophy who were not scheduled for surgery; 160 (46%) completed and returned the questionnaires at baseline, and of these 124 responded again 12 months later. Twenty-four of those contacted to participate in the study underwent breast reduction surgery during the study timeframe and were therefore excluded. Participant demographics for the hypertrophy control cohort are summarised in Table 2.4.

There were no statistically significant differences in characteristics including age, body mass index, obesity status, or smoking history between the surgical group and hypertrophy control group.

Table 2.4 Baseline characteristics of participants.

	Surgical cohort	Hypertrophy control cohort	*p*-value of difference[†]
No. of participants	209	124	
Mean (SD; range) age (years)	42.6 (13.4; 18 to 72)	45.3 (13.1; 20 to 79)	0.079
Age group (years):			
18–24	24 (12)	12 (10)	
25–34	38 (18)	15 (12)	
35–44	64 (31)	26 (21)	
45–54	41 (20)	43 (34)	
55–64	31 (15)	21 (18)	
≥ 65	11 (5)	7 (6)	
Mean (SD) BMI (kg/m^2)	32.7 (6.0)	32.2 (6.1)	0.468
Obesity status:			
Non-obese (<30 kg/m^2)	71 (34)	48 (39)	0.326
Obese (≥30 kg/m^2)	138 (66)	74 (61)	
Missing	0 (0)	2 (0)	
Smoking status:			
Non-smoker	108 (52)	78 (63)	0.243
Current smoker	35 (17)	14 (11)	
Ex-smoker <12 months	15 (7)	5 (5)	
Ex-smoker >12 months	47 (23)	25 (20)	
Missing	4 (0)	2 (0)	
Bra cup size:			
≤D	13 (6)	4 (3)	
DD	43 (21)	13 (11)	
E	50 (24)	19 (15)	
F	46 (22)	27 (22)	
G	35 (17)	37 (30)	
≥H	19 (10)	19 (15)	
Missing	3 (0)	5 (0)	
ASA status:			
1 (normal healthy)	82 (39)	-	
2 (mild systemic disease)	101 (48)	-	
3 (severe systemic disease)	19 (9)	-	
Mean (SD) operating time (min)	168 (38)	-	

Values are numbers (percentages) unless stated otherwise.

[†] Using independent samples *t*-test or chi-square test as appropriate.

2.3.2 Clinical outcomes in the surgical cohort

Overall, 92 participants (44%) experienced at least one complication within the 12 months following breast reduction surgery; with 117 patients (56%) experiencing no surgical complications. Classification of surgical complications for each of the 209 patients according to the Clavien-Dindo Classification (CDC) system were as follows: Grade I (*n* = 39, 19%); Grade II (*n* = 38, 18%); Grade IIIa (*n* = 5, 2%); and Grade IIIb (*n* = 10, 5%). There were no Grade IV or Grade V complications. Minor complications, classified as CDC Grade I and Grade II, accounted for the majority (77/92, 83.7%) of all post-operative complications.

Wound healing problems were the most frequent cause of post-operative complications (*n* = 39, 19%). These were predominantly wound healing problems requiring dressings (*n* = 34, 16.3%). Importantly, this study was very inclusive of surgical complications and given that incomplete wound healing at 4 weeks may not be reported as a complication in other studies, if these cases were excluded from the reported complications then the incidence reduced to 28% (58 participants). The most common cause of Grade II complications was wound infections requiring oral antibiotics (*n* = 36, 17%), prescribed by either one of the hospital doctors in the treating team or by a community general practitioner. It should be noted that the reporting of a wound infection did not require a positive bacterial growth on laboratory testing or a raised white cell count; therefore, it may be that some women who were prescribed antibiotics by their general practitioner may have had wound inflammation rather than true infection. Small wound debridement and minor scar excision under local anaesthesia were the treatments for Grade IIIa complications (*n* = 5, 2%). Revisional surgery under general anaesthesia (Grade IIIb) was required for five patients (2.4%) for evacuation of a haematoma, and nine patients (4.3%) had subsequent procedures for revision of surgical scars or to correct standing cone deformities or 'dog-ears'. As for post-operative sequelae, a total of 20 patients (9.6%) reported noticeable breast asymmetry; and 19 patients (9.1%) noted altered nipple sensation at their final post-operative review, with 5 patients reporting hyper-sensation and 14 stating reduced nipple sensation following surgery.

Using bivariate analysis, smoking status, sternal notch-to-nipple distance and total tissue resection weight were significantly associated with an increased incidence of any complication (Table 2.5). In contrast, there was no significant association between obesity status and the incidence of surgical complications, with the incidence of complications in non-obese participants (25/71, 35.2%) and obese participants (67/138, 48.6%). There were also no differences in the incidence of major complications (CDC grade III and above) based on obesity status, with incidences of 5/71 (7.0%) in non-obese and 10/138 (7.2%) in obese cases ($X^2 = 3.7$, $p = 0.158$). The increased prevalence of any complication in obese participants was due to minor complications (CDC grade I and II), with 57 (41%) of obese participants experiencing a minor complication in comparison to 20 (28%) of non-obese participants. Age, ASA status, diabetes and operating time were not associated with an increased incidence of complications.

Table 2.5 Association between participant and clinical characteristics and any complication

	No Complication (*n* = 117)	Complication (*n* = 92)	*p*-value of difference[†]
Age, years	42.5 (13.4)	42.8 (13.4)	0.839
Pre-operative breast volume,[‡] ml	1710.6 (590)	1751 (650)	0.661
SND distance,[¥] cm	32.0 (4.2)	33.4 (4.8)	0.046
Total resection weight, g	1192.3 (637.4)	1506.8 (974.4)	0.006
Operative time, min	167 (39)	169 (38)	0.770
Obesity (BMI ≥30 kg/m^2)	71 (61%)	67 (73%)	0.078
Smoking	11 (9%)	24 (26%)	0.002
Diabetes	4 (2%)	6 (3%)	0.349
ASA status			
1	43 (37%)	39 (14%)	0.638
2	58 (50%)	43 (47%)	
3	12 (13%)	7 (8%)	

[†] Using an independent two-sample *t*-test for continuous variables and a chi-square test for categorical variables.

[‡] Average of left and right breast volumes.

[¥] Average of left and right breast sternal notch-to-nipple (SND) distances.

A logistic regression analysis was performed to assess the impact of baseline participant and clinical characteristics on the likelihood that participants will experience any complication. The model contained nine independent variables at baseline: age, smoking status, diabetes, BMI, sternal notch-to-nipple distance, pre-operative breast volume, bra cup size, total weight of tissue resection, and operating time. The full logistic regression model containing all predictors was statistically significant (X^2 = 40.6, p = 0.001), indicating that the model was able to distinguish between patients who did and did not experience any post-operative complication. The model explained between 26.5% (Cox and Snell R^2) and 35.4% (Nagelkerke R^2) of the variance in any complication, and correctly classified 72.7% of cases. As shown in Table 2.6, smoking status was the only independent variable that made a unique statistically significant contribution to the model. Current smokers and those who were reformed less than 12-months were both 9.7-times more likely to have any complication.

Table 2.6 Logistic regression of risk factors for complications

Variable	*B*	SE	*p*	Odds ratio	95% CI for odds ratio
Age, years	0.025	0.02	0.175	1.02	0.99 to 1.06
BMI, kg/m^2	0.123	0.13	0.310	1.13	0.89 to 1.43
Total resection weight, g	0.001	0.001	0.400	1.00	0.99 to 1.02
Operative time, min	0.0001	0.0001	0.582	1.00	1.0 to 1.0
Pre-operative breast volume, ml	-0.001	0.001	0.234	1.00	0.99 to 1.0
Sternal notch-to-nipple distance, cm	0.146	0.091	0.103	1.16	0.97 to 1.38
Smoking†					
Current smoker	2.27	0.68	0.001	9.72	2.6 to 36.7
Ex-smoker <12 months	2.27	0.75	0.003	9.73	2.2 to 42.5
Ex-smoker >12 months	0.32	0.54	0.556	1.38	0.48 to 3.98
Diabetes‡					
Yes	0.98	1.52	0.284	2.67	0.44 to 16.1

† Compared with non-smoker.

‡ Compared with non-diabetic.

2.3.3 Health-related quality of life outcomes using the SF-36

The SF-36 was completed pre-operatively and at least once post-operatively by 209 surgical participants; 191 (91%) completed the post-operative questionnaires at 3 months, 183 (88%) at 6 months and 193 (92%) at 12 months. When compared with previously published age-adjusted normative data for the female Australian population (Marin et al., 2009), mean baseline SF-36 scores for the surgical cohort were significantly lower across all scales ($p < 0.001$) (Table 2.7). A comparison of mean pre-operative and 3 month post-operative SF-36 scores showed that scores were significantly higher across all eight SF-36 subscales ($p < 0.001$) (Table 2.7), such that they reached the level of the normative population (Figure 2.1). Mean SF-36 PCS and MCS scores significantly improved following surgery, increasing by 10.2 (95% CI; 8.2 to 12.1) and 9.2 points (95% CI; 6.9 to 11.6), respectively ($p < 0.001$) (Table 2.7 and Table 2.8). SF-36 scores were stable at 6- and 12-months post-surgery and linear mixed-model analysis showed no significant difference from those at 3 months post-surgery.

Mean baseline SF-36 scores for women in the breast hypertrophy control group were significantly lower than the normative population across all dimensions (Table 2.7). At 12 months post-baseline, SF-36 scores showed no significant improvement and remained significantly lower than population norms (Figure 2.2) and post-operative scores for women in the surgical cohort (Table 2.7). Mean SF-36 PCS and MCS summary scores for women in the breast hypertrophy control group were significantly lower than those who underwent breast reduction surgery, with a mean difference of 10.6 (95% CI; 8.3 to 12.8) and 11.1 points (95% CI; 8.2 to 13.9), respectively ($p < 0.001$) (Table 2.7).

Table 2.7 Mean (SD) SF-36 scores for participants in the surgical cohort, hypertrophy control cohort and normative female population

SF-36 scale	Normative† (*n* = 1551)	Hypertrophy Control Cohort		Surgical Cohort			
		Baseline (*n* = 160)	12 months (*n* = 124)	Pre-operative (*n* = 209)	3 months post-operative (*n* = 190)	6 months post-operative (*n* = 181)	12 months post-operative (*n* = 191)
Physical function	84.2 (19.1)	64.7 (24.2)	61.1 (25.5)	61.0 (25.4)	80.1 (22.3)	80.8 (24.2)	83.4 (22.1)
Role physical	82.0 (24.8)	58.3 (28.7)	58.1 (29.2)	56.0 (28.3)	79.5 (23.7)	81.1 (25.4)	81.3 (25.1)
Bodily pain	73.0 (21.4)	39.8 (22.5)	37.9 (21.2)	38.5 (21.5)	67.4 (24.1)	67.6 (27.6)	71.6 (25.9)
General health	70.2 (22.2)	49.7 (21.8)	49.8 (22.4)	57.9 (21.7)	69.1 (19.8)	69.5 (19.8)	70.4 (19.1)
Vitality	57.3 (20.9)	36.7 (19.7)	35.1 (21.0)	39.7 (20.2)	57.7 (20.4)	58.6 (19.1)	58.9 (19.7)
Social function	82.6 (24.3)	55.2 (29.0)	55.1 (27.4)	57.1 (27.9)	78.8 (25.9)	79.4 (25.9)	81.4 (23.4)
Role emotional	88.3 (20.3)	62.8 (30.3)	60.2 (28.6)	61.7 (28.9)	80.1 (25.1)	82.3 (23.1)	84.6 (22.2)
Mental health	77.0 (18.2)	58.8 (22.8)	56.1 (21.0)	59.8 (20.2)	73.7 (18.7)	73.8 (18.4)	74.3 (18.6)
Physical Component Score	49.7 (9.7)	39.6 (9.3)	39.3 (9.9)	39.7 (9.7)	48.9 (9.2)	49.0 (10.3)	49.9 (9.9)
Mental Component Score	47.6 (11.4)	36.2 (14.6)	35.1 (13.2)	37.0 (13.2)	45.4 (11.9)	45.7 (11.5)	46.2 (11.6)

† Source: Age-standardised normative data from the South Australian female population (Marin et al., 2009).

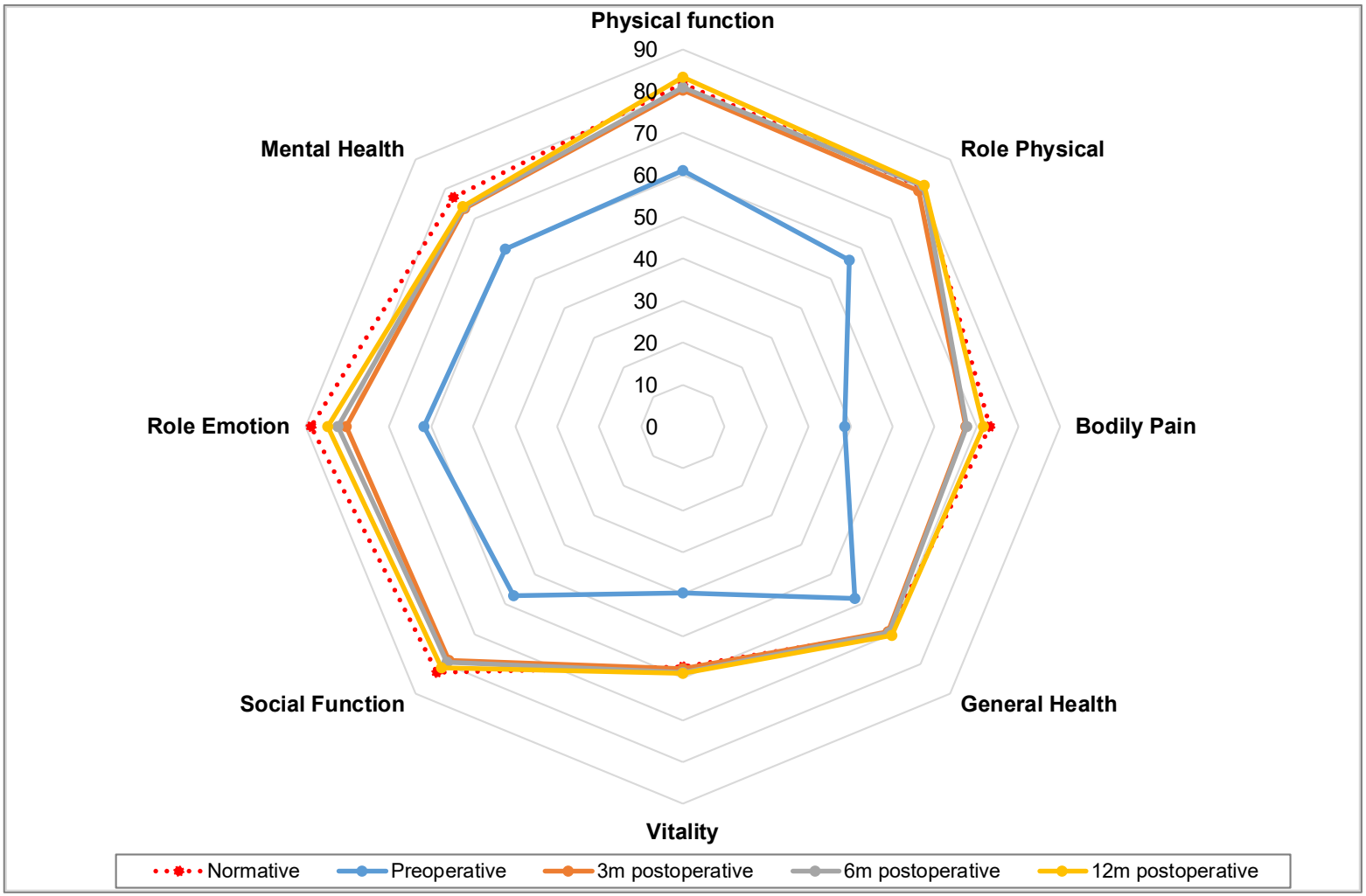


Figure 2.1 Comparison of mean pre-operative and post-operative SF-36 scores in surgical participants with age-standardised female population norms

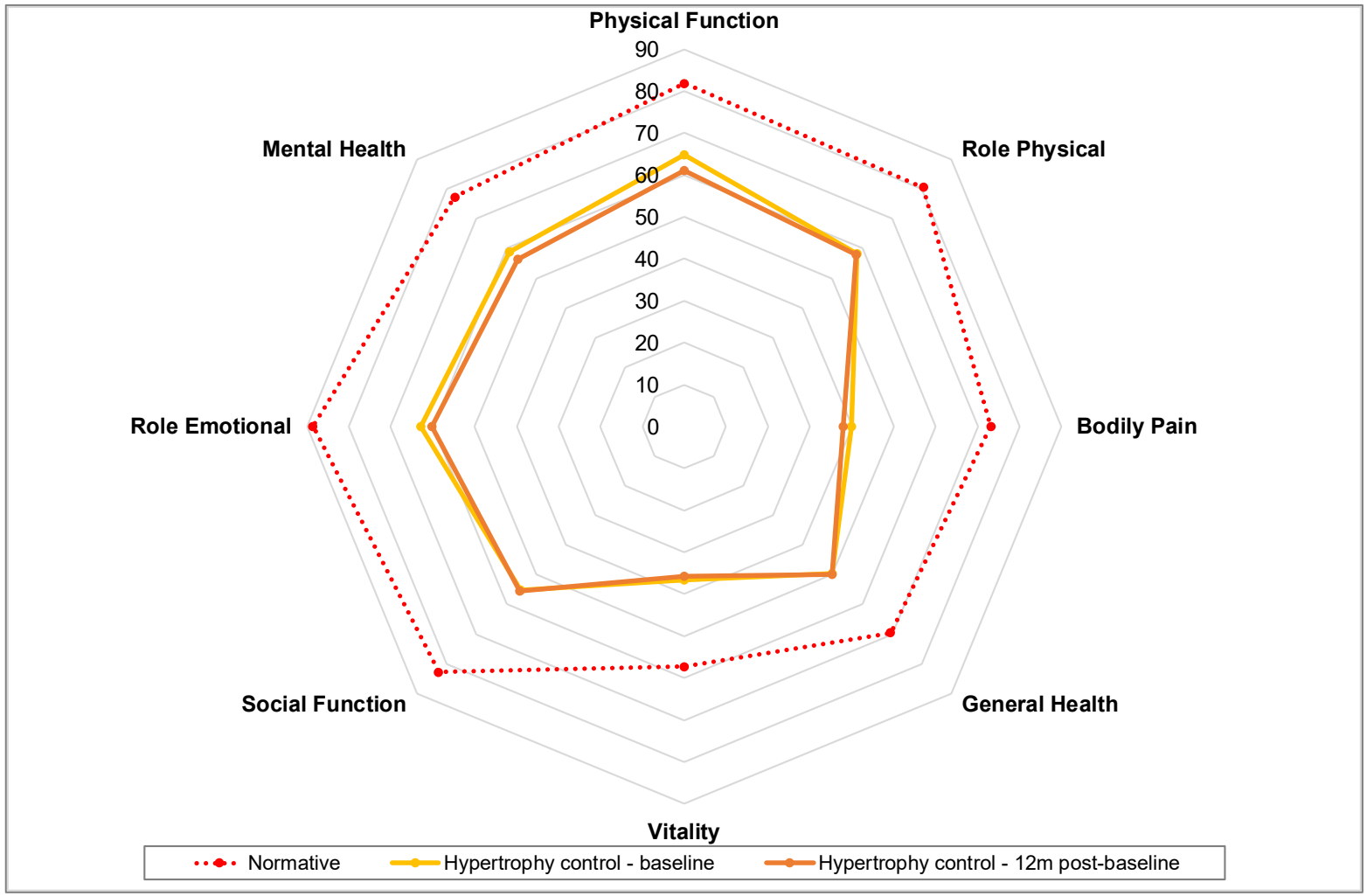


Figure 2.2 Comparison of mean baseline and 12-months post-baseline SF-36 scores in the breast hypertrophy control group with age-standardised female population norms

Table 2.8 summarises the mean changes in SF-36 subscales and summary scores from baseline to each follow-up timepoint in the surgical cohort and the breast hypertrophy control cohort. Within the surgical cohort, there were statistically significant improvements in SF-36 scores across all scales and summary scales. Corresponding effect sizes at 12-months post-operative ranged from a moderate effect of 0.58 for General Health, with the remaining seven subscales and both summary measures exhibiting a large effect size according to Cohen's criteria, ranging up to 1.53 for Bodily Pain. In contrast, scores did not improve within the breast hypertrophy control cohort, with scores for the Physical Functioning scale significantly lower by 4.4-points (95% CI, 0.67 to 7.9) when comparing baseline to 12-months (p = 0.02).

Table 2.8 Mean (95% CI) change in SF-36 scores in the breast hypertrophy control cohort and surgical cohort

SF-36 scale	Hypertrophy control cohort	Surgical cohort			
	Baseline to 12m post-baseline	Baseline to 3m post-operative	Baseline to 6m post-operative	Baseline to 12m post-operative	Effect size (95% CI)‡
Physical function	-4.3 (-7.9 to -0.7)**	19.1 (14.5 to 23.7)*	19.8 (15.1 to 24.5)*	22.3 (17.7 to 27.0)*	0.94 (0.64–1.24)
Role physical	-0.82 (-5.3 to 3.6)	23.5 (18.4 to 28.6)*	25.0 (19.9 to 30.2)*	25.3 (20.2 to 30.4)*	0.95 (0.65–1.25)
Bodily pain	-1.97 (-5.7 to 1.7)	28.9 (24.0 to 33.7)*	29.1 (24.2 to 34.0)*	33.0 (28.2 to 37.9)*	1.39 (1.08–1.71)
General health	0.55 (-2.5 to 3.6)	11.2 (7.2 to 15.2)*	11.6 (7.6 to 15.6)*	12.5 (8.5 to 16.4)*	0.61 (0.32–0.90)
Vitality	-1.6 (-4.5 to 1.2)	18.0 (14.1 to 21.9)*	18.8 (14.9 to 22.8)*	19.2 (15.3 to 23.1)*	0.96 (0.66–1.26)
Social function	0.32 (-4.3 to 4.9)	21.6 (16.5 to 26.7)*	22.3 (17.1 to 27.5)*	24.3 (19.2 to 29.4)*	0.94 (0.65–1.24)
Role emotional	-1.71 (-6.6 to 3.2)	18.4 (13.5 to 23.4)*	20.6 (15.5 to 25.6)*	22.8 (17.9 to 27.8)*	0.89 (0.59–1.19)
Mental health	-2.9 (-6.2 to 0.5)	13.9 (10.2 to 17.7)*	14.1 (10.3 to 17.9)*	14.5 (10.8 to 18.3)*	0.75 (0.45–1.04)
Physical Component Score	-0.7 (-2.1 to 0.7)	9.2 (7.3 to 11.2)*	9.3 (7.3 to 11.3)*	10.2 (8.2 to 12.1)*	1.04 (0.74–1.34)
Mental Component Score	-1.08 (-3.2 to 1.0)	8.4 (6.0 to 10.8)*	8.7 (6.3 to 11.2)*	9.2 (6.9 to 11.6)*	0.74 (0.45–1.03)

* Differences between pre-operative versus post-operative scores in the surgical cohort were significant at the p <0.001 level.

** Differences between baseline versus 12 months post-baseline scores in the breast hypertrophy control cohort were significant at the p <0.05 level.

‡ Effect size was calculated as the mean difference between groups (12m post-operative – baseline), divided by the pooled standard deviation for the two groups.

2.3.3.1 Distribution-based estimates of MID for the SF-36

Minimal important difference (MID) estimates from the distribution-based analyses for each scale of the SF-36 are presented in Table 2.9. The SEM, 0.2 SD, 0.3 SD and 0.5 SD are presented based on baseline SF-36 scores, and the 0.2 SRM and 0.3 SRM were computed as a measure of effect size based on the change in SF-36 scores from baseline to 12 months following surgery. MID estimates for the SF-36 instrument varied for each individual subscale, ranging from 6 to 9-points using the 0.3 SRM, and 10 to 14-points using the one-half a standard deviation approach. MID estimates were lower using the standard error of measurement analyses based on the reliability of each subscale and ranged from 6 to 10-points. The distribution-based estimates for change scores were similar to those based on baseline scores, mostly within 1-point range (i.e. when comparing 0.2 SD to 0.2 SRM, and 0.3 SD to 0.3 SRM). For the norm-based SF-36 physical and mental summary scales, MID estimates were 5-points and 7-points using half a standard deviation, respectively; SRM estimates were slightly smaller at 3 and 4 points, respectively.

Table 2.9 Summary of distribution-based estimates of clinical significance (MID)

	Pre-surgery				Change from pre- to 12m post-surgery	
SF-36 scale	**0.2SD**	**0.3 SD**	**0.5 SD**	**1 SEM**	**0.2 SRM**	**0.3 SRM**
Physical function	5.1	7.6	12.7	6.2	4.8	7.2
Role physical	5.7	8.5	14.2	6.6	5.7	8.5
Bodily pain	4.3	6.5	10.8	8.3	5.2	7.9
General health	4.3	6.5	10.9	8.9	4.3	6.4
Vitality	4.0	6.1	10.1	7.8	4.4	6.7
Social function	5.6	8.4	14.0	9.7	5.6	8.4
Role emotional	5.8	8.7	14.5	7.6	5.7	8.5
Mental health	4.0	6.1	10.1	7.8	4.2	6.3
Physical component score	1.9	2.9	4.9	2.2	2.0	3.1
Mental component score	2.6	4.0	6.6	3.5	2.8	4.1

The mean change in SF-36 scores from baseline to 12 months in participants who underwent breast reduction surgery was in excess of MID threshold estimates based on a rule-of-thumb 10-point change on 100-point quality of life scales (King, 1996) or a 0.5 SD default value for patient-perceived important change (Norman et al., 2003), as well as additional distribution-based MID estimates derived in this study, in all eight SF-36 subscales. In addition, the mean change in SF-36 PCS and MCS scores was in excess of both the developer-recommended 3-point MID threshold, as well as condition-specific distribution-based estimates derived in this study. This is in contrast to scores for women in the breast hypertrophy control cohort which remained significantly lower and did not improve over the course of the study across all SF-36 subscales and summary measures. This finding is shown in Figure 2.3 by plotting the mean change from baseline to 12-

months in both surgical and hypertrophy control groups in comparison to the one-half standard deviation estimate of MID.

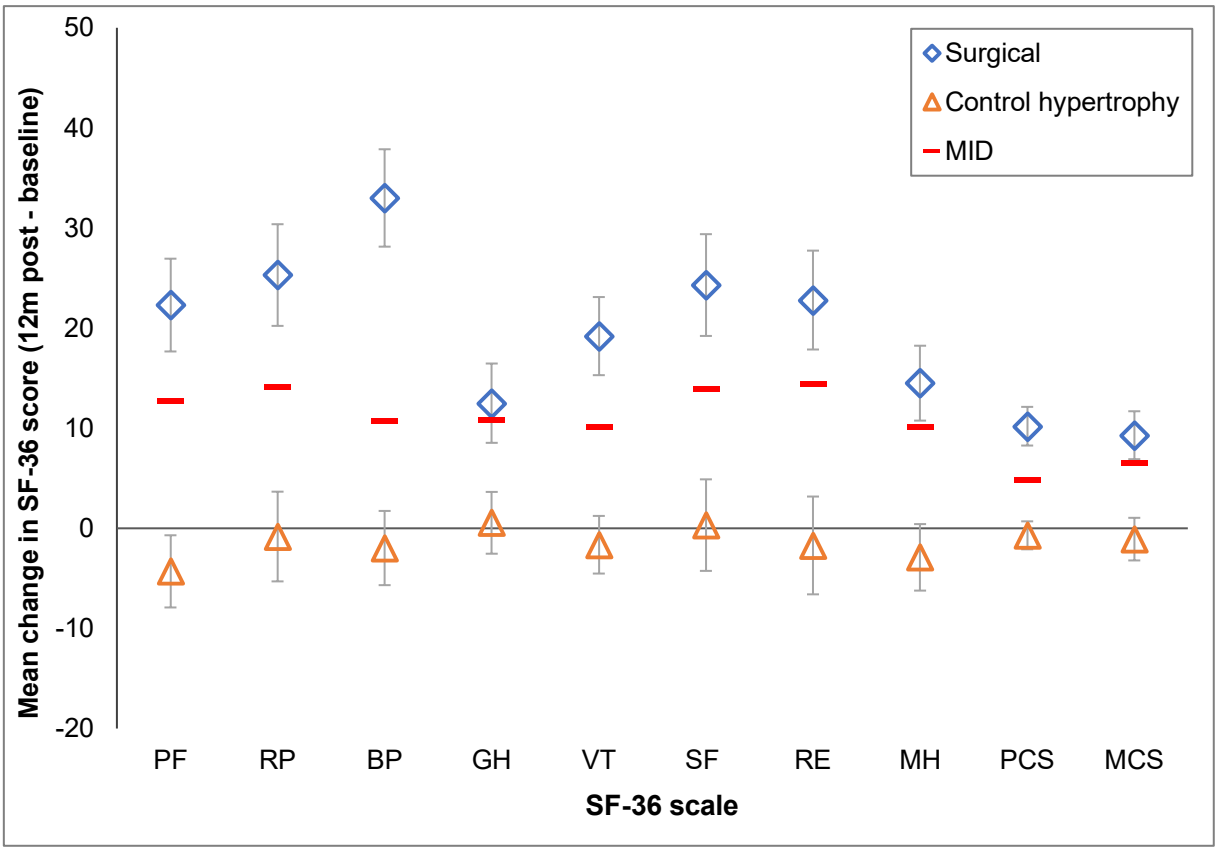


Figure 2.3 Mean change in SF-36 scores from baseline to 12-months for surgical and breast hypertrophy control cohorts in comparison to MID estimates (0.5 SD).

Error bars represent 95% confidence intervals.

2.3.3.2 Comparing the improvement in health-related quality of life with other surgical interventions

The improvement in SF-36 physical and mental summary scores in women who underwent surgery in this study were compared to existing studies which describe 12-month post-operative outcomes from other surgical interventions (Table 2.10). Breast reduction surgery provided a greater gain in SF-36 PCS scores than a coronary artery bypass graft and hernia repair and the improvement was similar to that experienced by patients undergoing total knee replacement surgery (Figure 2.4). The improvement in SF-36 MCS scores following breast reduction surgery exceeded that of all other surgical procedures (Figure 2.5).

Table 2.10 Mean improvement in SF-36 PCS and MCS scores between surgical interventions

Reference	Surgical Intervention	Pre-op PCS	Post-op PCS	Mean change in SF-36 PCS	Pre-op MCS	Post-op MCS	Mean change in SF-36 MCS	*n*
This study	*Bilateral breast reduction*	*39.7*	*49.9*	*10.2*	*37.0*	*46.2*	*9.2*	*191*
(Pivec et al., 2015)	Total knee replacement	33.0	47.8	14.8	52.9	55.9	3.0	281
(Stickles et al., 2001)	Total hip replacement	28.0	41.2	13.2	51.2	53.9	2.7	551
(Muller-Nordhorn et al., 2004)	Coronary artery bypass graft	36.0	43.0	7.3	45.0	50.0	4.3	412
(Polly et al., 2007)	Lumbar fusion (spine)	26.6	40.0	13.4	n/a	n/a	n/a	1826
(Rogmark et al., 2016)	Incisional hernia repair	41.6	49.5	8.1	50.2	52.3	1.7	124
(Faulconbridge et al., 2013)	Bariatric surgery	37.7	46.4	8.7	43.1	45.5	2.4	36

PCS, SF-36 Physical Component Score; MCS, SF-36 Mental Component Score; mean change in SF-36 score from pre-operative to 12 months post-operative; n/a, not applicable; *n*, number of participants.

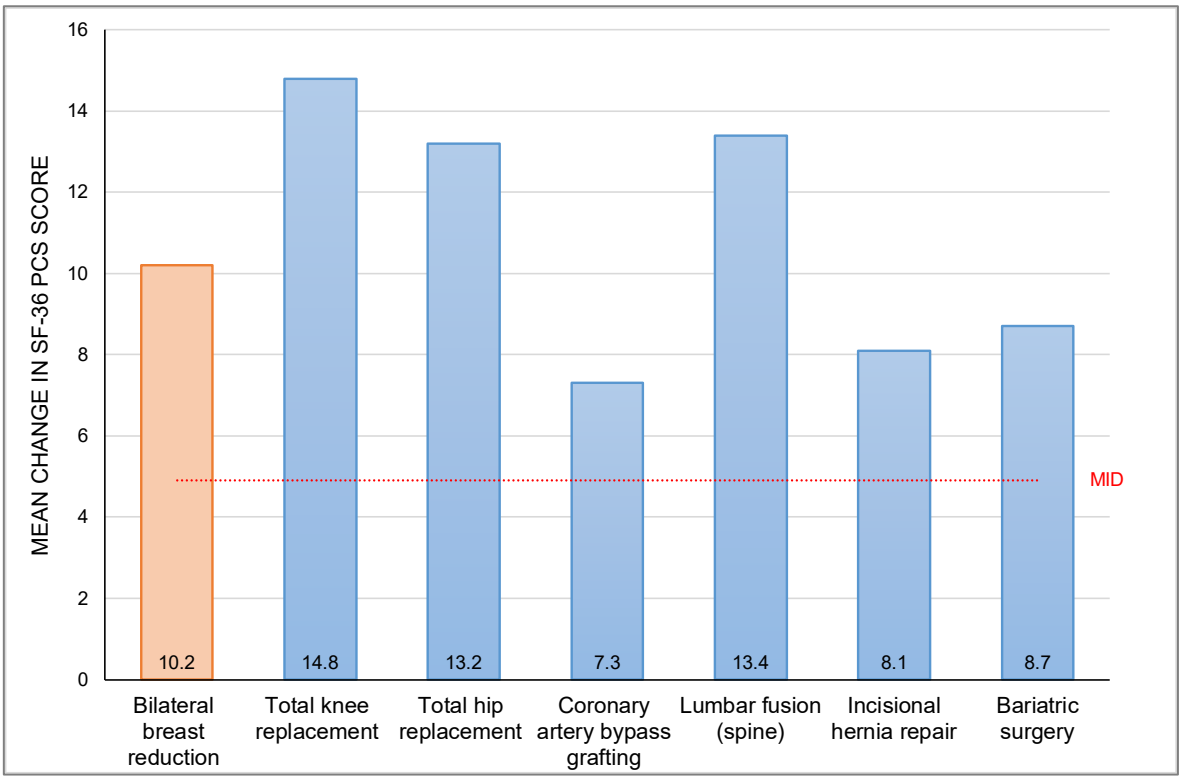


Figure 2.4 Mean improvement in SF-36 Physical Component Summary (PCS) scores at 12m post-operative.

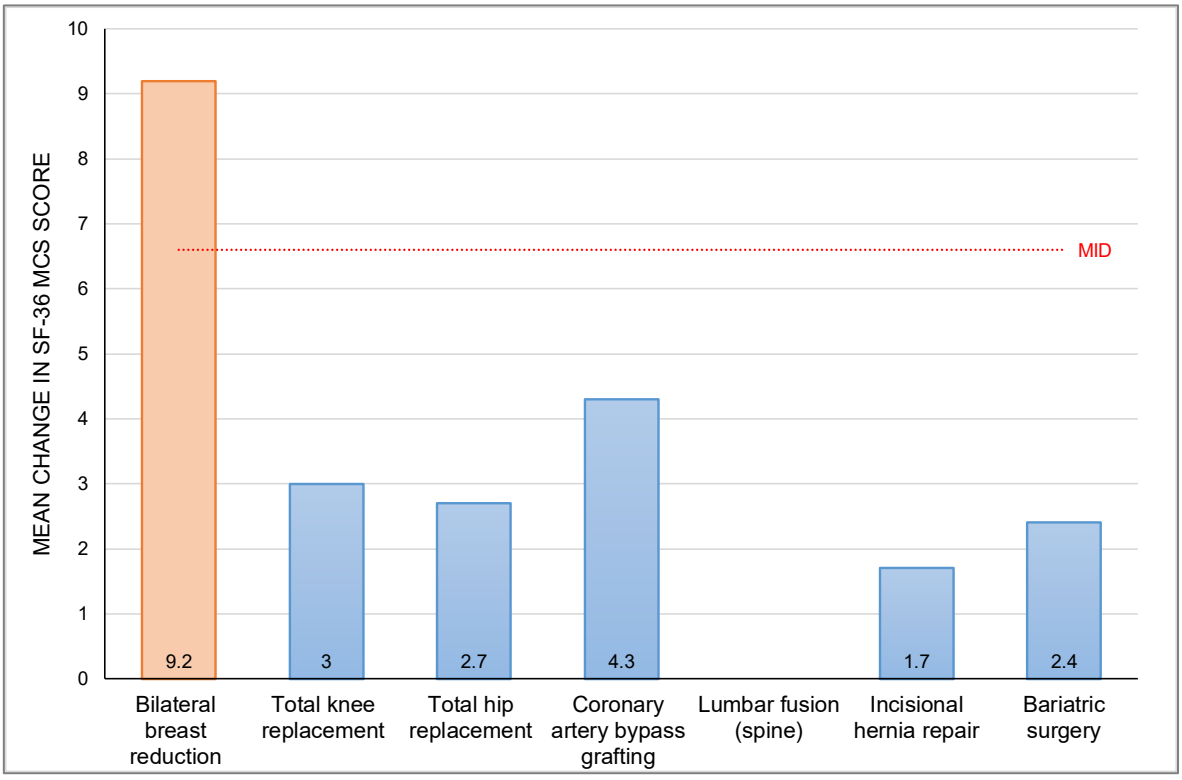


Figure 2.5 Mean improvement in SF-36 Mental Component Summary (MCS) scores at 12m post-operative.

2.3.3.3 The impact of participant characteristics on health-related quality of life and benefit of surgical intervention

There was a significant positive correlation between baseline body mass index (BMI) and the total amount of breast tissue resected at surgery. That is, as BMI increased there was an associated increase in the amount of breast tissue removed (Pearson $r = 0.645$, $p < 0.001$) (Figure 2.6).

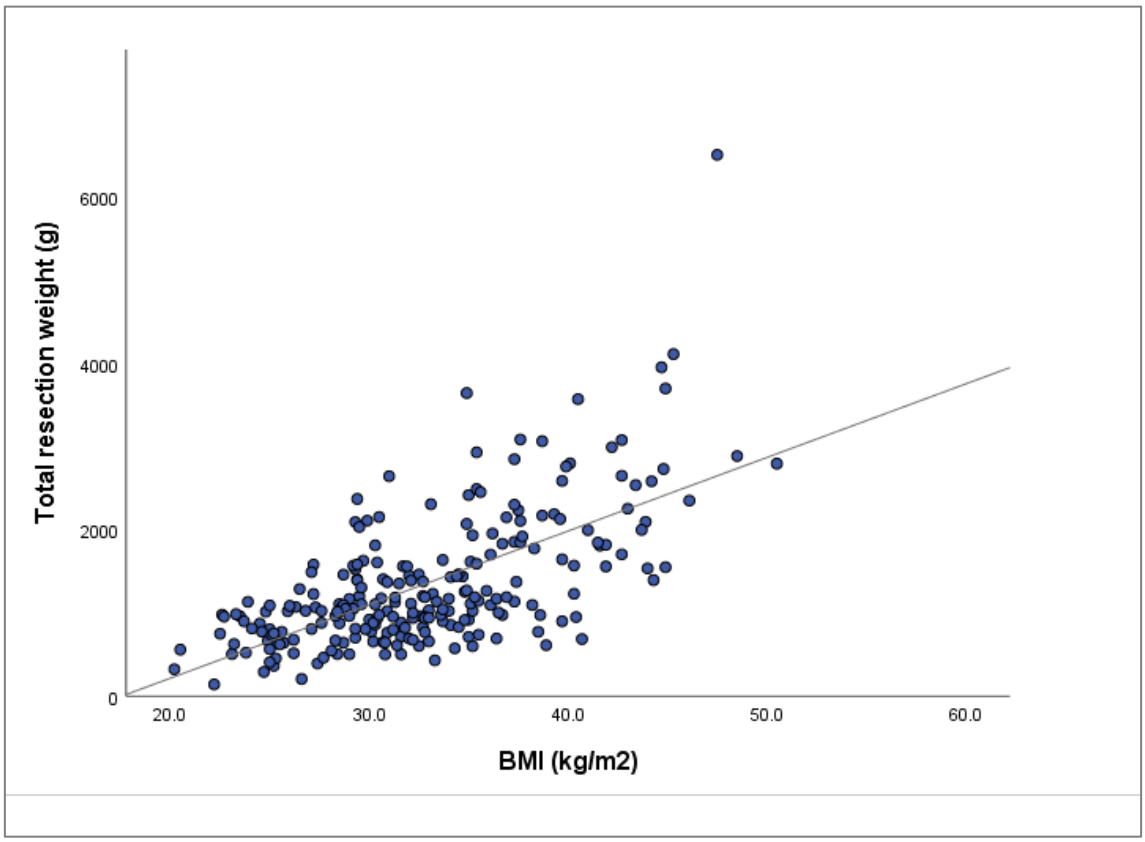


Figure 2.6 Relationship between body mass index and tissue resection weight at surgery

When exploring the change in individual SF-36 subscale scores following surgery, scores for obese women (BMI ≥30 kg/m^2) improved equally, if not greater than, their non-obese counterparts (BMI <30 kg/m^2) following surgery, reaching statistical significance for the physical functioning subscale (Table 2.11).

Table 2.11 Comparison of mean change in SF-36 scores following surgery in non-obese and obese participants

SF-36 scale	Mean change (95% CI)		Difference in means (95% CI)	*p*-value of difference‡
	Non-obese (*n* = 71)	Obese (*n* = 138)		
Physical function	16.1 (11.2 to 22.1)	23.4 (19.5 to 27.3)	6.8 (0.03 to 13.5)	0.050
Role physical	19.4 (12.4 to 26.3)	25.9 (21.2 to 30.5)	6.5 (-1.7 to 14.7)	0.121
Bodily pain	28.6 (22.8 to 34.5)	32.3 (27.8 to 36.9)	3.7 (-3.9 to 11.4)	0.337
General health	10.2 (6.0 to 14.3)	12.2 (8.4 to 16.0)	2.0 (-4.1 to 8.2)	0.516
Vitality	18.9 (14.8 to 23.1)	18.3 (14.2 to 22.4)	-0.7 (-7.2 to 5.9)	0.842
Social function	23.6 (17.8 to 29.4)	21.9 (16.6 to 27.2)	-1.7 (-10.2 to 6.8)	0.701
Role emotional	18.9 (12.8 to 25.0)	22.5 (17.2 to 27.8)	3.6 (-5.0 to 12.2)	0.409
Mental health	14.9 (11.4 to 18.5)	13.0 (9.2 to 16.9)	-1.9 (-7.9 to 4.1)	0.532

‡ Using an independent *t*-test.
Obesity status: non-obese (<30 kg/m^2), obese (≥30 kg/m^2)

When exploring baseline SF-36 PCS scores, a significant negative correlation was found between SF-36 PCS scores and age (r = -0.13), BMI (r = -0.30), tissue resection weight (r = -0.26), degree of breast hypertrophy (r = -0.28) and ratio of breast to body volume (r = -0.19). Multivariate regression of candidate variables against baseline SF-36 PCS scores found BMI to be the only variable significantly related to pre-operative SF-36 PCS scores (R^2 = 0.16, p < 0.001). Following on from the regression analysis, this finding was supported with the results of the one-way ANOVA which was conducted to explore the impact of pre-operative BMI class on baseline SF-36 PCS scores. Participants were divided into five groups according to the WHO classification: normal weight, overweight, obese class I, obese class II, and obese class III. No participants were in the underweight category and therefore this was not included in the analysis. There was a statistically significant difference in baseline SF-36 PCS scores between the BMI categories (p < 0.001), with Dunnett's post-hoc test (two-tailed) revealing baseline SF-36 PCS scores were lower for patients within each of the 3 classes of obesity when compared to participants of a 'normal weight': (i) normal weight vs obese class I (mean difference = 6.3-points; 95% CI: 1.6 to 11.1, p = 0.006); (ii) normal weight vs obese class II (mean difference = 10.0-points; 95% CI: 4.8 to 15.1; p < 0.001); and (iii) non-obese vs obese class III (mean difference = 7.8-points; 95% CI: 2.2 to 13.5, p = 0.003). Scores were lower for 'overweight' participants in comparison to those of a normal weight, but the mean difference of 4.3-points but this did not reach statistical significance. The results comparing baseline SF-36 PCS score based on BMI classification are shown graphically in Figure 2.7.

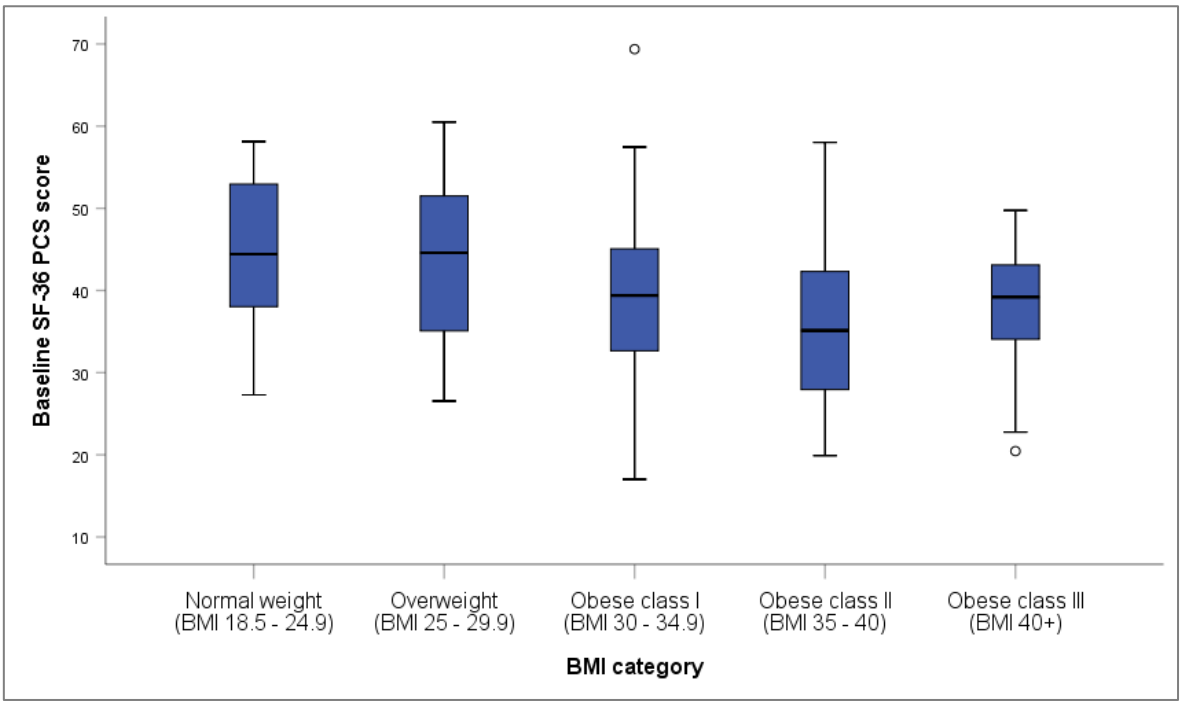


Figure 2.7 Baseline SF-36 PCS scores for BMI categories

Multivariate linear regression analysis was also used to analyse predictors of the change in SF-36 PCS score following surgery and showed that improvement in SF-36 PCS scores was not significantly associated with any of these factors.

When stratifying the surgical participants by post-operative complication status, patients with and without a complication had significant improvements in SF-36 scores between baseline and 12 months in all eight SF-36 subscales as well as physical and mental summary scores (Table 2.12). When comparing the improvements in SF-36 scores following surgery between the groups based on the presence or absence of any complication, there were no significant differences in change in SF-36 scores across all eight subscales and summary measures ($p > 0.05$).

Table 2.12 Comparison of mean change in SF-36 scores by complication status

SF-36 scale	Mean change (95% CI)		Difference in means (95% CI)	*p*-value of difference‡
	No complication (*n* = 117)	Any complication (*n* = 92)		
Physical function	20.1 (15.9 to 24.2)	22.4 (17.3 to 27.6)	-2.4 (-8.9 to 4.1)	0.475
Role physical	25.0 (19.8 to 30.4)	21.9 (15.9 to 27.8)	3.2 (-4.7 to 11.1)	0.429
Bodily pain	33.3 (28.4 to 38.2)	28.3 (22.8 to 33.7)	5.0 (-2.3 to 12.3)	0.176
General health	11.2 (7.4 to 15.0)	11.9 (7.4 to 16.5)	-0.75 (-6.6 to 5.2)	0.801
Vitality	18.7 (14.4 to 23.1)	18.3 (13.9 to 22.6)	0.48 (-5.7 to 6.7)	0.879
Social functioning	24.1 (19.0 to 29.3)	20.4 (13.8 to 26.9)	3.8 (-4.4 to 11.9)	0.364
Role emotional	20.2 (14.9 to 25.5)	22.6 (16.2 to 29.1)	-2.5 (-10.7 to 5.8)	0.556
Mental health	13.1 (9.2 to 17.0)	14.4 (10.2 to 18.6)	-1.3 (-7.0 to 4.5)	0.662
Physical summary	10.3 (8.3 to 12.3)	9.1 (6.9 to 11.3)	1.2 (-1.7 to 4.2)	0.418
Mental summary	9.2 (6.5 to 12.0)	9.5 (6.5 to 12.4)	-0.2 (-4.2 to 3.8)	0.915

* Mean change between 12 month post-operative and pre-operative scores.
‡ Independent samples *t*-test.

2.3.4 Quality of life outcomes using the MBSRQ

Mean MBSRQ scores for surgical and breast hypertrophy control participants are summarised in Table 2.13. When compared with previously published normative data from women within the United States general population, women with breast hypertrophy have significantly lower baseline scores for all scales. Within the surgical cohort, a comparison of mean pre-operative and 3 month post-operative MBSRQ scores showed that scores significantly improved in Appearance Evaluation, Fitness Evaluation, Health Evaluation, Health Orientation, Body Areas Satisfaction and Self-classified Weight ($p < 0.05$) (Table 2.13 and Figure 2.8). MBSRQ scores were stable at 6- and 12-months post-surgery and linear mixed-model analysis showed no significant difference from those at 3 months post-surgery.

Women with breast hypertrophy who were awaiting breast reduction surgery displayed lower mean scores across all subscales of the MBSRQ instrument in comparison to population norms (Table 2.13). Whereas women who underwent surgery displayed a significant improvement in scores across six scales of the MBSRQ, a comparison of mean baseline and 12-month scores for women in the breast hypertrophy control group showed that scores did not improve over time. In fact, mean scores for women in the breast hypertrophy control group remained low and unchanged over the course of the study, with the exception of Appearance Evaluation and Appearance Orientation which significantly declined over the 12-month period ($p < 0.05$) (Table 2.13). When comparing the surgical cohort and the breast hypertrophy control cohort at their final assessment, women who underwent surgery were more satisfied with their appearance, fitness levels, reported being in better health and were more satisfied with their body than those who did not undergo surgery (Table 2.13).

Table 2.13 Mean (SD) MBSRQ scores for participants in the surgical and breast hypertrophy control cohorts in comparison with populations norms

	Surgical group				Hypertrophy control		Normative¥
	Preop (n = 209)	3m postop (n=190)	6m postop (n = 183)	12m postop (n = 191)	Baseline (n = 161)	12m post (n = 124)	(n = 1070)
Appearance Evaluation	1.96 (0.64)	2.81 (0.70)*	2.83 (0.79)	2.87 (0.77) †	2.02 (0.66)	1.93 (0.58) ‡	3.36 (0.87)
Appearance Orientation	3.57 (0.75)	3.53 (0.60)	3.53 (0.61)	3.50 (0.60)	3.63 (0.64)	3.53 (0.64) ‡	3.91 (0.60)
Fitness Evaluation	3.10 (0.78)	3.31 (0.79)*	3.30 (0.86)	3.35 (0.80) †	3.05 (0.85)	2.95 (0.84)	3.48 (0.97)
Fitness Orientation	2.94 (0.64)	3.03 (0.61)	3.03 (0.65)	3.06 (0.68) †	2.86 (0.68)	2.86 (0.58)	3.20 (0.85)
Health Evaluation	2.99 (0.72)	3.29 (0.78)*	3.34 (0.73)	3.32 (0.75) †	2.86 (0.75)	2.84 (0.74)	3.86 (0.80)
Health Orientation	3.62 (0.62)	3.44 (0.59)*	3.54 (0.56)	3.50 (0.60) †	3.38 (0.64)	3.31 (0.64)	3.75 (0.70)
Illness Orientation	3.04 (0.78)	3.14 (0.75)	3.14 (0.80)	3.13 (0.77)	3.19 (0.82)	3.22 (0.74)	3.21 (0.84)
Body Areas Satisfaction	2.47 (0.56)	2.93 (0.61)*	2.99 (0.63)	3.00 (0.62) †	2.48 (0.58)	2.46 (0.58)	3.23 (0.74)
Overweight Preoccupation	3.31 (0.83)	3.17 (0.85)	3.16 (0.91)	3.23 (0.80)	3.34 (0.94)	3.34 (0.90)	3.03 (0.96)
Self-classified Weight	4.14 (0.71)	4.00 (0.64)*	3.98 (0.64)	4.00 (0.62)	4.00 (0.82)	4.09 (0.62)	3.57 (0.73)

* denotes significant difference ($p < 0.05$) between pre-operative and 3m post-operative scores using linear mixed-model analysis.
† denotes significant difference ($p < 0.05$) between 12m post-operative scores for the surgical group and 12m post-baseline scores for the hypertrophy control group using an independent samples *t*-test.
‡ denotes significant difference ($p < 0.05$) between baseline and 12m post-baseline scores in the hypertrophy control group using a paired *t*-test.
¥ Normative scores from females within the United States population (Cash, 2000).

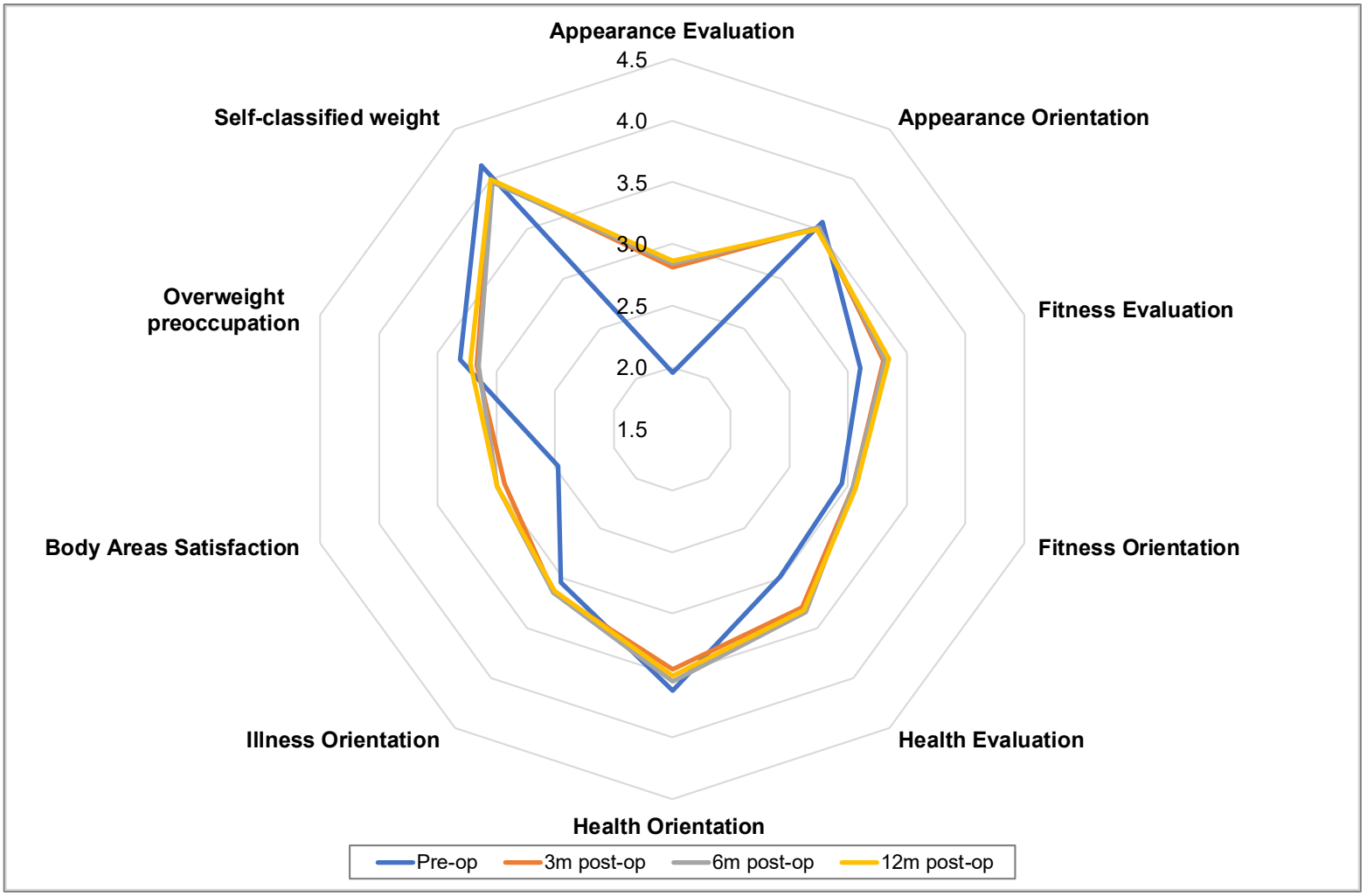


Figure 2.8 Mean MBSRQ scores for surgical participants

2.3.5 Adjunct questions

The majority of participants (204/209, 97.6%) responded in the post-operative questionnaire that they would have the surgery again, whilst others were either unsure (4/209, 1.9%) or would not have surgery again (1/209, 0.5%). Following surgery, participants on average spent less money on medications and treatments (AU$26.41 vs AU$5.73 per month, $p < 0.001$) and took fewer days off work (4.5 days vs 0.1 days in the previous 6-month period, $p = 0.009$) when compared to before surgery. In contrast, no significant differences were observed in the breast hypertrophy control cohort when comparing spending on medications and number of days off work between baseline and 12 months following enrolment, with both remaining significantly higher than post-operative surgical participants ($p < 0.001$).

Surgical participants were asked to self-report whether or not they experienced any complications from the surgery; 115 (55%) stated they did not, 61 (29%) reported they did have a complication, and 11 (5%) were unsure. Surgical participants were also asked whether they experienced any new health issues or a worsening of an existing health issue that was not related to the surgery; 138 (66%) did not, 41 (20%) stated yes, and 8 (4%) were unsure. There were 22 cases (10%) of missing data for this supplementary study questionnaire.

2.4 Discussion

Findings from this prospective cohort study demonstrate that women with symptomatic breast hypertrophy have impaired quality of life compared to those in the general population. At baseline, participants in both the surgical and control breast hypertrophy groups scored significantly lower than the female general population in all SF-36 subscales, with pain being the most prominent. Surgical participants' quality of life improved following breast reduction to such an extent that the health deficits were eliminated at 3 months following surgery and quality of life was 'normalised' to levels equivalent to that of the general population across all dimensions. This normalisation effect was stable across 12 months follow-up. The SF-36 health gain ranged from 14.5 to 33.1 points for individual scale scores, and this exceeded the minimally important difference threshold estimates based on a rule-of-thumb of a 10-point change on 100-point sub-scales (King, 1996). Furthermore, estimates of the minimal important difference were derived from this study using a series of distribution-based analyses for each SF-36 subscale, with MIDs using the 0.5 SD and SEM approaches close to 10-points for many scales. Accordingly, the improvement in HRQoL exceeded all MID estimates in women who underwent surgery across all eight SF-36 subscales, supporting the proposition that breast reduction surgery provides a clinically relevant health benefit to women.

The finding that breast reduction surgery improves health-related quality of life to levels of the general population is supported by existing studies using the SF-36 within the literature (Blomqvist and Brandberg, 2004, Blomqvist et al., 2000, Kececi et al., 2015, Klassen et al., 1996, Miller et al., 2005, O'Blenes et al., 2006, Shakespeare and Cole, 1997). Interestingly, findings from a Swedish study in 2019 are contradictory to this and report that scores for General Health, Physical Functioning and Mental Health decreased at 1 year following surgery; with scores remaining significantly lower than population norms for these scales as well as the Vitality scale (Lewin et al., 2019). The authors did not comment on possible reasons for the post-operative decrease in scores across these scales. In addition, these findings are unexpected given that large gains were reported in physical and psychosocial wellbeing using another patient-reported outcome instrument in this study.

Secondary aims of this study were to investigate factors which have the potential to influence the level of improvement in quality of life following surgery: body mass index; degree of hypertrophy; bra cup size; age; pre-operative breast symmetry, disproportionality and weight of tissue resection at surgery. Several of these factors are frequently used to restrict access to breast reduction surgery, none of which are based on high quality evidence. In this study the improvement in health-related quality of life was independent of these factors, suggesting that all women with symptomatic breast hypertrophy can benefit from this surgery regardless of commonly scrutinised factors. This is of clinical relevance as it highlights the fact that women with a higher body mass

index or those with a lower weight of resection benefit as much as others requesting this surgery and should not be discriminated against based on criteria-based restrictions. The finding that symptom relief and improvement in health-related quality of life are not impacted by BMI and weight of resection is consistent with existing studies using the SF-36 (Collins et al., 2002, Eggert et al., 2009, Guemes et al., 2016, Lewin et al., 2019). In spite of these findings access restrictions for breast reduction surgery are in place in many countries including Australia, despite a lack of supporting evidence. The current study aims to contribute to the gap in the literature in the comprehensive assessment of the impact of patient and clinical characteristics on health-related quality of life outcomes following surgery.

When assessing the summary measures of health for the SF-36, the intervention effect of breast reduction surgery in our study was well in excess of the minimal clinically important difference for SF-36 physical and mental component score, which has been recommended by the developers as a 3-point change (Frendl and Ware, 2014, Ware et al., 1995, Ware et al., 1994). Furthermore, the mean change in SF-36 PCS and MCS scores following breast reduction surgery in this study were greater than the study-specific MID estimates of 4.9-points and 6.6-points using the half a standard deviation approach which has been recognised as a more universally accepted important difference (Norman et al., 2003). These MIDs for the SF-36 PCS and MCS were similar to published findings in patients undergoing surgery for degenerative cervical myelopathy, with scores reported as 4.63 and 6.76-points, respectively (Badhiwala et al., 2018). The improvements in the SF-36 physical component score at one year following surgery were comparable to those of other widely-accepted surgical interventions such as total hip and total knee replacement (Pivec et al., 2015), spinal fusion (Polly et al., 2007), bariatric surgery (Faulconbridge et al., 2013), and coronary artery bypass graft surgery (Muller-Nordhorn et al., 2004). The improvements in the mental component score following breast reduction surgery actually exceeded those of all other interventions cited. Breast reduction surgery is a relatively inexpensive procedure, and the improvement in health-related quality of life provides evidence as to the comparative effectiveness of this intervention in relieving the health burden and the functional symptoms of breast hypertrophy.

When assessing patient-reported outcomes using the MBSRQ, surgical patients rated their appearance significantly higher after breast reduction and rated themselves as being more physically fit post-operatively, despite their fitness orientation remaining unchanged. Importantly women who underwent surgery rated their bodies to be in better health following surgery and were more invested in leading a healthier lifestyle post-operatively. They rated themselves to be more content with areas of their body and viewed themselves as less overweight following surgery. These findings are consistent with an existing study using the MBSRQ in patients undergoing breast reduction surgery (Collins et al., 2002), and with prior outcome studies that used only the appearance evaluation subscale (Kerrigan et al., 2001, Thoma et al., 2013, Thoma et al., 2005).

To the author's knowledge, this study is the first to report the prospective assessment of surgical complications following breast reduction surgery using the standardised Clavien-Dindo Classification (CDC) system. An overall surgical complication rate of 44% was reported in this study, this is slightly lower than the rate of 63% reported in the retrospective study by Winter and colleagues using the CDC grading (Winter et al., 2017), and comparable with existing prospective studies such as the multi-institutional BRAVO study (Cunningham et al., 2005). However, this rate is slightly higher than those reported by previous studies (Guemes et al., 2016, Perez-Panzano et al., 2016, Srinivasaiah et al., 2014). This finding reiterates the need for standardised reporting of surgical complications, with the discrepancies likely to be attributable to inconsistencies in the collection and reporting of complications data. Whilst this study reported a relatively high infection rate of 17%, this figure included the prescription of oral antibiotics by General Practitioners outside of the hospital system, which may have been provided for presumed infection and without confirmation of bacterial infection by microbiological tests. It is acknowledged this may have overestimated the occurrence of surgical site infection in this study. This study also supports previous findings of no significant difference in the complication rate based on obesity status (Cunningham et al., 2005, Guemes et al., 2016, Wagner and Alfonso, 2005); further advocating that surgery should not be restricted to only those patients with a low BMI as the health benefits were found to outweigh the risks of post-operative complication. Lastly, whilst 44% of patients in this study experienced a surgical complication, no differences were found in the improvement in health-related quality of life across all dimensions between those who experienced a complication and those who did not.

A potential limitation of this study was the participant response rate for the breast hypertrophy control cohort was relatively low at 46 percent, which may be due to the recruitment process via postal questionnaire. Furthermore, whilst the total follow-up period for this cohort was 12 months, the intermediate timepoints of 3 and 6 months that were collected in the surgical cohort were not included in this cohort, although the consistency of outcomes at baseline and 12 months suggest that 3 and 6 month outcomes are likely to have been similar. Finally, estimation of the minimal important difference for the SF-36 patient-reported outcome in this study was limited to distribution-based approaches. Whilst there is a lack of consensus as to the best approach to approximate the minimal important difference, a more optimal approach may have been a combination of both anchor- and distribution-based methods if suitable clinical anchors were available (Revicki et al., 2008).

The strengths of this study were the prospective design, the relatively large sample size, and the inclusion of a non-surgical control sample of women with breast hypertrophy who were recruited from the same waiting list as those in the surgical cohort. Given the non-surgical hypertrophy control group were found to have a similar health deficit to the surgical cohort at baseline and showed no improvement in HRQoL over time, this cohort provided a meaningful reference to

accurately assess the impact of surgery on HRQoL. In addition, the post-operative outcomes described in this study included multiple time points over a 12-month period. Additionally, our surgical cohort were not biased by restrictions that have been reported in previous studies based on a minimum weight of resection or body mass index and therefore includes a broad spectrum across these variables. This is particularly important as it enables the accurate assessment of these factors as potential predictors of the change in health-related quality of life and outcomes of surgery and overcomes these limitations.

2.5 Conclusion

Breast hypertrophy is a painful condition which is effectively treated by breast reduction surgery. The marked improvement in quality of life following breast reduction surgery is comparable to other widely accepted and publicly funded surgical interventions. This study highlights that the improvement in quality of life following surgery is independent of traditionally used criteria based on body mass index or a minimum weight of resection and demonstrates the health benefits of surgery occur regardless of these factors. This confirms the clinical effectiveness of breast reduction surgery and supports the proposition that there is no justification for excluding women based on criteria such as body mass index or the extent of breast hypertrophy.

3. GENERATION OF AUSTRALIAN GENERAL POPULATION REFERENCE DATA FOR INTERPRETING THE BREAST-Q

A summary of the normative BREAST-Q data generated in this study was presented at the International Society for Quality of Life Research (ISOQOL) 25th annual conference in Dublin, Ireland (Crittenden et al., 2018b) and a version of this chapter has been published as an original article in the *Plastic and Reconstructive Surgery* journal (Crittenden et al., 2019b); attached as Appendix M.

3.1 Introduction

Health-related quality of life (HRQoL) data from a reference population such as the general population provides a valuable clinical reference point or as a benchmark for the interpretation of HRQoL data in outcome studies. General population reference values are available for generic instruments such as the Short Form-36 and have provided a valuable comparator for the assessment and interpretation of outcomes following breast reduction surgery. However, research studies have shown that potentially important differences exist when comparing HRQoL values between countries (Frieling et al., 2013, Hawthorne et al., 2007, Hopman et al., 2000, Mercieca-Bebber et al., 2019, Nolte et al., 2019, Norman et al., 2013). This highlights the importance of utilising country-specific population norms wherever possible for the accurate interpretation of HRQoL data in the clinical setting and for research studies. Furthermore, age and gender have been shown to influence patient-reported outcome scores and therefore is important to incorporate these key characteristics and distributions for general population reference values (Hjermstad et al., 1998).

Normative data for the BREAST-Q Reduction questionnaire provides valuable information as to the levels of breast-related satisfaction and quality of life within the general female population, enabling a better understanding of the health burden associated with breast hypertrophy and the health benefits of breast reduction surgery. However, normative BREAST-Q data are currently limited to a single population, the United States of America (Mundy et al., 2017c). Given that the BREAST-Q is one of the most widely used patent-reported outcome measures in breast surgery worldwide, the generation and reporting of Australian population-based reference data for comparison to women undergoing surgery provides an important contribution to the literature and a valuable reference for clinical care and future research studies.

The primary aim of this study was therefore to derive Australian general population reference values for the BREAST-Q Reduction module. This data will provide a population-specific comparison for the interpretation of HRQoL outcome data in women with breast hypertrophy who underwent breast reduction surgery (described in Chapter 4). Secondary aims were to explore the

association between socio-demographic characteristics and BREAST-Q scale scores, and to compare Australian values with United States BREAST-Q general population reference values.

3.2 Methods

3.2.1 Participant recruitment

Australian women aged 18 years and above who were registered members of a national online survey panel (Pureprofile Pty Ltd, Sydney, New South Wales, Australia; www.pureprofile.com) were invited to participate in the study in April 2018. Consenting respondents who self-reported as being without a history of breast cancer or breast surgery and not actively seeking breast surgery were eligible to participate in this study. Participants who were accepted into the study after answering the eligibility screening question and completed the questionnaire received a small monetary compensation (AUD$3). Ethics approval was obtained from the Social and Behavioural Research Ethics Committee at Flinders University (SB REC approval number 7848) (Appendix G).

3.2.2 Data collection

Participants were required to self-complete the pre-operative version of the BREAST-Q Reduction module and provide information for the following relevant variables: age, height, weight, bra cup size, post code, employment status and health status. Participants within the normative study cohort were distributed across age and geographical variables in a manner consistent with the national representation population breakdown from the 2016 Census conducted by the Australian Bureau of Statistics (Australian Bureau of Statistics, 2016a). The corresponding target percentages for the age groups, taken from the Census, were as follows: 18–24 years (11.8%), 25–34 years (18.5%), 35–44 years (17.3%), 45–54 years (17.1%), 55–64 years (15.1%) and 65 years and above (20.2%). Target distribution across geographical variables according to the census breakdown were as follows: New South Wales (32.0%); Victoria (25.6%); Queensland (20.0%); South Australia (7.0%); Western Australia (10.5%); Australian Capital Territory (1.7%); Tasmania (2.1%); and Northern Territory (1.0%).

A Socio-Economic Indexes for Areas (SEIFA) measure of relative socio-economic status, the Index of Relative Socio-economic Disadvantage (IRSD), was obtained from postcodes; where a low index score indicates relatively greater disadvantage and a high index score indicates relative lack of disadvantage within an area (Australian Bureau of Statistics, 2016c). The SEIFA measure refers to the level of socio-economic status of the area in which the respondent lives, so is a broad measure of socio-economic status. IRSD scores were stratified into quintiles for further statistical analysis.

3.2.3 The BREAST-Q

The BREAST-Q Reduction module is a validated condition-specific patient-reported outcome

measure that was developed to specifically evaluate the outcomes of breast reduction surgery (Pusic et al., 2009). The BREAST-Q Reduction pre-operative module was used in this study to evaluate breast-related satisfaction and HRQoL in women within the general population (Appendix H). The instrument comprises Likert-type item responses across independently functioning patient satisfaction and wellbeing scales. The pre-operative version of the BREAST-Q comprises the following scales: Satisfaction with Breasts (*n* = 11 items), Psychosocial Wellbeing (*n* = 9 items), Sexual Wellbeing (*n* = 5 items) and Physical Wellbeing (*n* = 14 items). Questionnaire responses were transformed using Q-Score software (New York, N.Y.) to generate a score between 0 and 100, where a score of 0 is the minimum score and 100 is the maximum score and indicates the highest level of satisfaction or wellbeing. Administration of the electronic version of the BREAST-Q has previously been found to be psychometrically valid (Fuzesi et al., 2017).

3.2.4 Normative data from the United States

Normative data for the BREAST-Q Reduction module was first described in women within the United States population (Mundy et al., 2017c). Participants were recruited via the Army of Women (AOW), an online community of women, with and without breast cancer, started in 2008 by the Dr. Susan Love Research Foundation, with a mission to promote breast cancer research. An electronic survey link was sent to registered members and participants who self-reported they met the inclusion criteria were able to complete the pre-operative version of the BREAST-Q questionnaire and study-specific questions including demographic information, bra cup size, height and weight. Inclusion criteria included women aged 18 years and above, with no prior history of breast cancer or breast surgery, and the ability to complete an online questionnaire in English. A limited raw dataset from the Army of Women United States study was kindly made available by the authors under formal agreement with Dartmouth-Hitchcock Clinic, New Hampshire, United States of America (Appendix J). The dataset was therefore able to be used in a comprehensive comparison to generated Australian norms and analysis of the association between socio-demographic variables and BREAST-Q scores described in this chapter.

A comparison of age composition was made between the United States normative population sample and published age and sex composition data from the 2016 United States Census (United States Census Bureau, 2016).

3.2.5 Statistical analysis

Descriptive statistics for the four BREAST-Q scales were calculated, including the mean, standard deviation, 95% confidence intervals and the percent scoring at the lowest value (floor) and the highest value (ceiling). Cronbach's alpha coefficient was used to assess internal consistency (reliability) of the four multi-item BREAST-Q scales. A coefficient of 0.70 and above was considered acceptable. Comparisons of BREAST-Q scores were made between groups using an independent samples *t*-test, or a one-way analysis of variance (ANOVA) for three or more groups.

Socio-demographic variables were presented using descriptive summary statistics, or categorised and expressed as frequencies and percentages. Body mass index (BMI) was calculated from reported height and weight values (kg/m^2) and categorised into non-obese (less than 30 kg/m^2) and obese (greater than or equal to 30 kg/m^2) status according to the World Health Organisation (WHO) classification (World Health Organization, 2018). Participant age was stratified into the following six subgroups: 18–24 years, 25–34 years, 35–44 years, 45–54 years, 55–64 years and 65 years and above. Bra cup size data were categorised into the following groups: less than A cup, A, B, C, D, DD, and greater than DD cup size. Bra cup size and age were further stratified into 2 groups for analysis: less than D cup and greater than or equal to D cup size, and less than 40 years versus greater than or equal to 40 years. Categorical variables were compared using Chi-square (X^2) statistics or Fisher's exact test as appropriate. Socio-demographic data from the population sample were compared with corresponding Australian general population reference values from the Australian Bureau of Statistics 2016 (Australian Bureau of Statistics, 2016a) using X^2 test to examine the representativeness of the study sample.

Multiple linear regression analysis was conducted to determine which socio-demographic variables were predictors for individual BREAST-Q scale scores derived from women in the Australian general population. Candidate variables included age, BMI, bra cup size, presence of a chronic health condition/s, employment status and Index of Relative Socio-economic Disadvantage (IRSD). Age and BMI were entered into the regression model as continuous variables; all other socio-demographic variables were categorical.

Socio-demographic characteristics and unadjusted mean BREAST-Q scores were compared between Australia and the United States population samples using a X^2 test or independent samples *t*-test, as appropriate. Cohen's *d* was used to provide a measure of effect size and was computed as the mean difference between groups divided by the pooled standard deviation for the two groups. Effect sizes were interpreted according to the thresholds established by Cohen as follows: <0.20, trivial; 0.20 to 0.50, small; >0.50 to 0.80, moderate; and >0.80, large (Cohen, 1988). To account for the differences in participant age distributions between the Australian and United States population samples when investigating differences in BREAST-Q scale scores, a one-way analysis of covariance (ANCOVA) model was used with age included as a potential confounder.

Statistical significance was established at a *p*-value of less than 0.05. Statistical analyses were performed using SPSS v25.0 statistical software (IBM Corp., Armonk, N.Y.).

3.3 Results

3.3.1 Participant characteristics

Normative BREAST-Q Reduction Module data were obtained from 513 female panellists within the Pureprofile Australia organisation. A total of 18 (3.4%) women were either ineligible or chose not

to proceed with participation in the study after viewing the study information page and eligibility screening question. Participant demographics from the Australian normative cohort are summarised in Table 3.1. The median patient age was 45 years (range, 18 to 88 years) with a mean body mass index of 27.8 ± 7.0 kg/m^2. The majority of women were non-obese with a body mass index of less than 30 kg/m^2 (*n* = 356, 69%) and 43% of women had a bra size of at least a D cup. A chronic health condition was reported by 29% of respondents (*n* = 148). Most women were employed in either a part-time (*n* = 143, 28%) or full-time basis (*n* = 119, 23%).

The age distribution for the normative study is summarised in Table 3.1. Distribution of participants across the geographical variable were as follows: New South Wales (*n* = 164, 32%); Victoria (*n* = 133, 25.9%); Queensland (*n* = 101, 19.7%); South Australia (*n* = 36, 7.0%); Western Australia (*n* = 55, 10.7%); Australian Capital Territory (*n* = 8, 1.6%); Tasmania (*n* = 13, 2.5%); and Northern Territory (*n* = 3, 0.6%). Concerning age and geographical distribution, the sample was statistically representative of the Australian general female population, [$X^2(5) = 0.123$, $p = 1.0$] and [$X^2(5) = 0.195$, $p = 1.0$], respectively. Furthermore, the proportion of participants who were obese in the population sample was 31%; this was not significantly different from the Australian population data in which 30.2% of females were classed as obese (BMI ≥30 kg/m^2) (Australian Bureau of Statistics, 2018).

Table 3.1 Participant socio-demographic characteristics

Characteristic	No. (%)
Sample size	513
Age, years	
Mean age ± SD	46.1 ± 17.0
Median (range)	45 (18–88)
Age group (years):	
18–24	62 (12)
25–34	99 (19)
35–44	88 (17)
45–54	87 (17)
55–64	75 (15)
≥65	102 (20)
Mean BMI ± SD, kg/m^2	27.8 ± 7.0
Obesity status:	
Non-obese (BMI < 30 kg/m^2)	356 (69)
Obese (BMI ≥ 30 kg/m^2)	157 (31)
Bra cup size:	
<A	1 (0.2)
A	33 (6)
B	96 (19)
C	153 (30)
D	111 (22)
DD	69 (13)
>DD	50 (10)
Chronic health condition?	
Yes	148 (29)
No	365 (71)
Employment status	
Full-time	119 (23)
Part-time	143 (28)
Voluntary work	3 (1)
Homemaker	84 (16)
Student	26 (5)
Retired	85 (17)
Unable to work/disabled	21 (4)
Unemployed	24 (5)
Other	8 (2)
Index of Relative Socio-economic Disadvantage	
Lowest quintile	78 (15)
Low quintile	94 (18)
Middle quintile	122 (24)
High quintile	106 (21)
Highest quintile	113 (22)

Values are numbers (percentage) unless stated otherwise. *BMI*, body mass index

3.3.2 Australian normative BREAST-Q Reduction module scores

Mean normative BREAST-Q scores from the general Australian population derived in this study are summarised in Table 3.2 and ranged from 49 to 71 on a transformed scale from 0 to 100.

Table 3.2 Australian normative BREAST-Q Reduction module scores

Scale	*n*	Mean	SD
Satisfaction with Breasts	513	52	17
Psychosocial Wellbeing	513	55	22
Sexual Wellbeing	473	49	24
Physical Wellbeing	513	71	13

Satisfaction with breasts, Psychosocial Wellbeing and Physical Wellbeing were scored for all 513 (100%) study participants. The Sexual Wellbeing scale was completed by 473 participants (92.2%). It is important to note that the Sexual Wellbeing scale was the only scale in which participants could respond 'not applicable' to some or all individual items.

Summary statistics for individual items and Cronbach's alpha coefficients for the multi-item scales are presented for reference in Appendix K. Internal consistency reliability coefficients, estimated by Cronbach's alpha, ranged from 0.89 to 0.97 on the four scales. These high coefficients supported scale reliability and validity. There did not appear to be a strong floor effect (proportion of subjects receiving the minimum possible score) or ceiling effect (proportion of subjects receiving the maximum possible score) in any of the four BREAST-Q scales. Item response frequencies from the Australian normative study are shown for each BREAST-Q scale: Satisfaction with Breasts (Figure 3.1), Psychosocial Wellbeing (Figure 3.2), Sexual Wellbeing (Figure 3.3) and Physical Wellbeing (Figure 3.4).

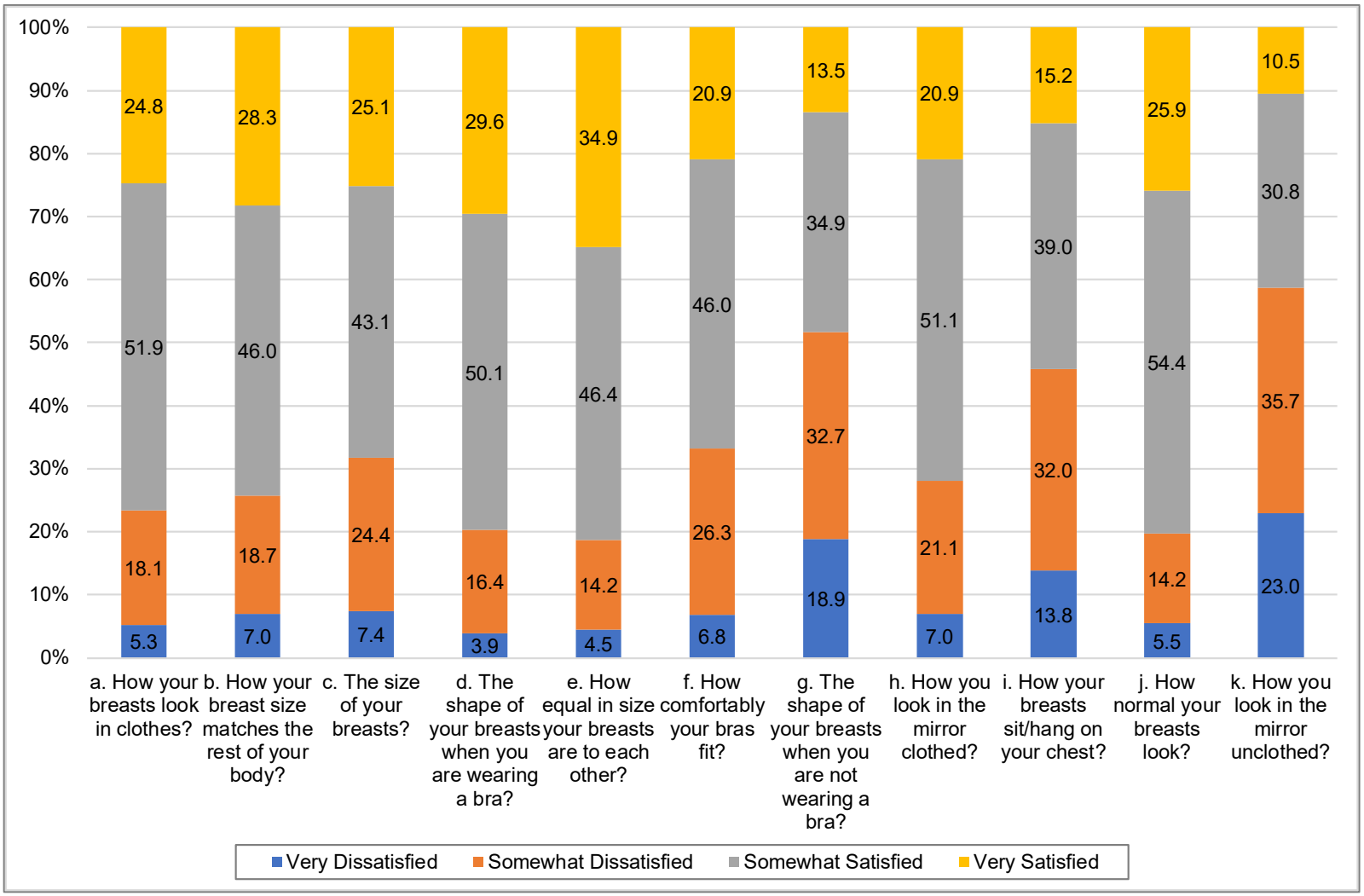


Figure 3.1 Item response frequencies 'Satisfaction with Breasts'

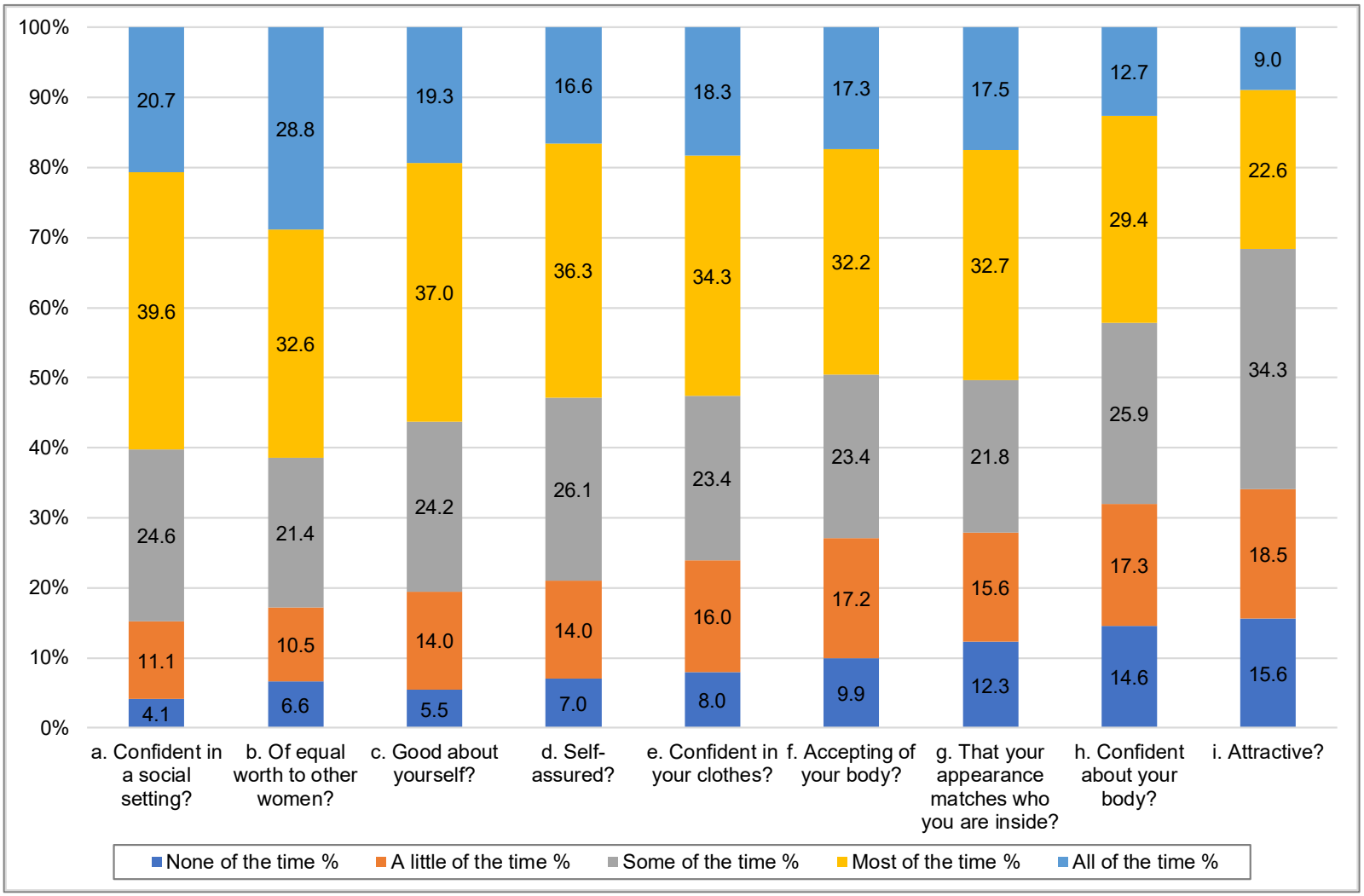


Figure 3.2 Item response frequencies 'Psychosocial Wellbeing'

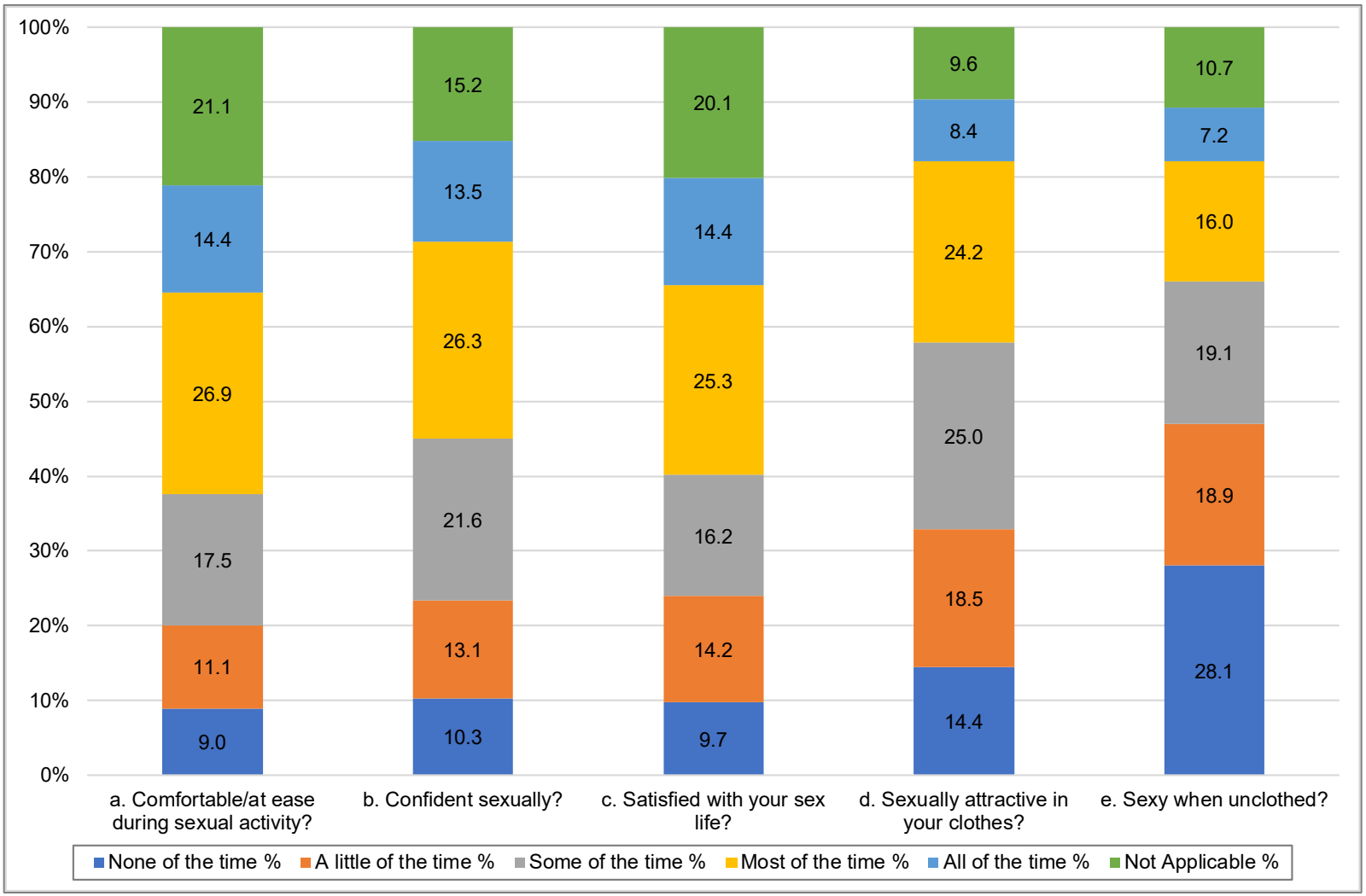


Figure 3.3 Item response frequencies 'Sexual Wellbeing'

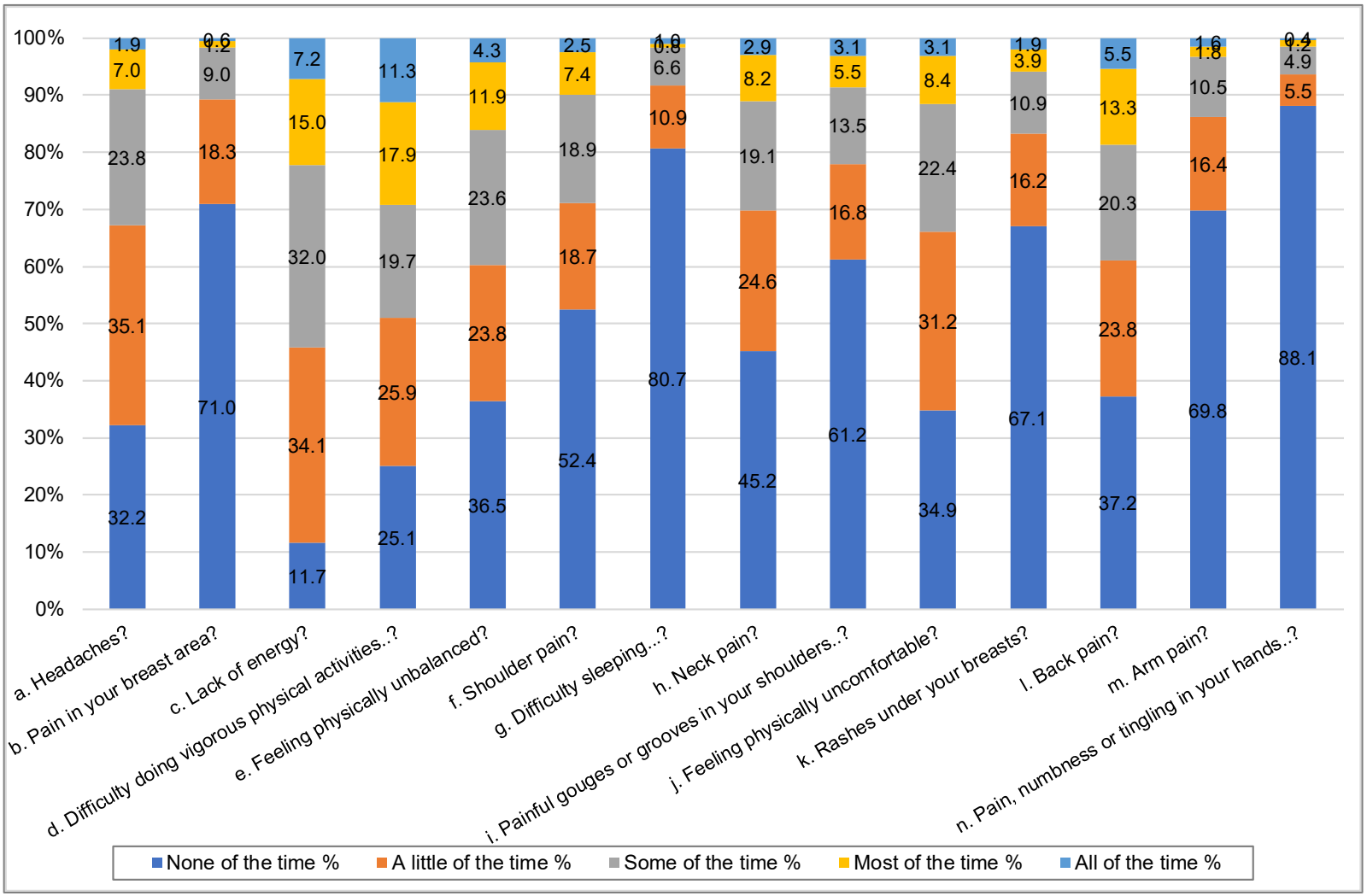


Figure 3.4 Item response frequencies 'Physical Wellbeing'

Normative BREAST-Q scores with relevant co-variables across the four scales which constitute the pre-operative version are shown in Figure 3.5 and are summarised in Table 3.3. An independent samples *t*-test was conducted to compare BREAST-Q scale scores between socio-demographic categorical variables. Participants with a higher BMI of 30 kg/m^2 or greater were found to have lower BREAST-Q scores across all scales when compared to those with a lower BMI of less than 30 kg/m^2 ($p < 0.001$). Participants who self-reported having a chronic health condition were also found to have significantly lower BREAST-Q scores across all scales ($p < 0.001$). Participants aged 40 years and above were found to have higher BREAST-Q scores in Satisfaction with Breasts ($p = 0.014$), Psychosocial Wellbeing *(*$p < 0.001$) and Physical Wellbeing scales ($p = 0.038$). In contrast, no significant differences were observed for age in the Sexual Wellbeing scale ($p = 0.404$). When comparing bra cup size, those with a bra cup size at least D cup had significantly lower scores for Physical Wellbeing when compared to those with a smaller cup size ($p = 0.002$), whilst scores for the other three scales were not significantly different. An Index of Relative Socio-economic Disadvantage (IRSD) quintile was recorded for each participant and no significant differences were found when comparing BREAST-Q scores across all four scales using a one-way ANOVA.

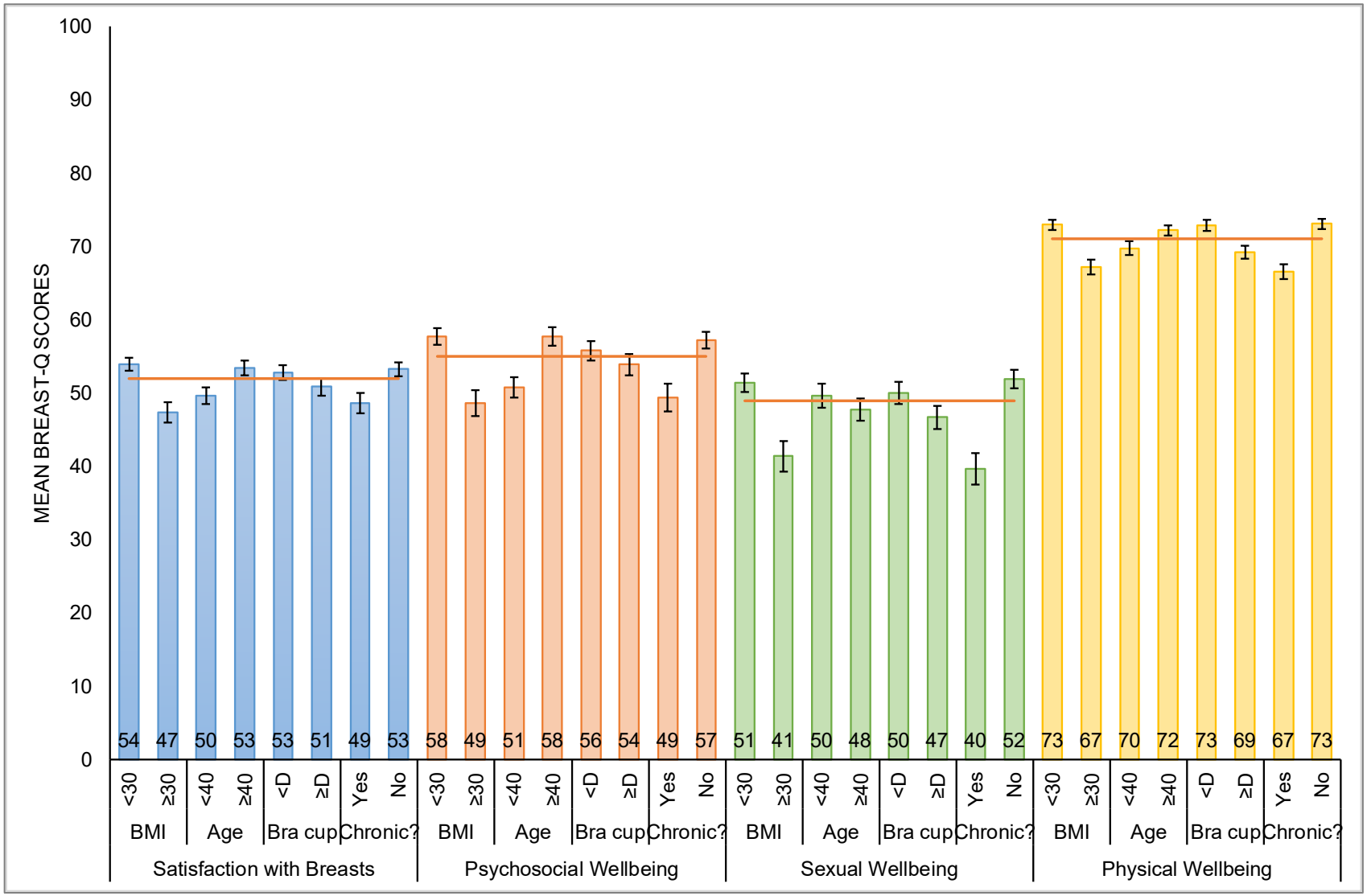


Figure 3.5 Normative BREAST-Q Reduction module pre-operative scores

Error bars represent 95% confidence intervals. *Orange line* indicates mean score for individual BREAST-Q scales; *BMI*, body mass index; *Bra cup*, bra cup size; *Chronic?*, chronic health condition?

Table 3.3 Australian normative BREAST-Q scores by socio-demographic characteristics

	Satisfaction with breasts		Psychosocial Wellbeing		Sexual Wellbeing		Physical Wellbeing	
Variable	***n***	**mean (SD)**	***N***	**mean (SD)**	***n***	**mean (SD)**	***n***	**mean (SD)**
Age								
18–24	62	49.8 (13.7)	62	50.0 (19.8)	56	50.0 (24.1)	62	70.0 (12.6)
25–34	99	50.2 (16.1)	99	51.9 (19.9)	98	50.9 (23.1)	99	68.9 (13.7)
35–44	88	48.8 (18.4)	88	49.1 (21.6)	84	43.7 (23.6)	88	70.3 (12.8)
45–54	87	49.7 (16.1)	87	52.0 (22.3)	83	47.5 (23.4)	87	70.5 (12.8)
55–64	75	56.6 (18.1)	75	59.9 (21.3)	68	50.5 (24.8)	75	74.4 (12.7)
65+	102	56.1 (18.6)	102	64.8 (21.6)	84	49.0 (25.0)	102	73.2 (13.0)
BMI								
<30 kg/m^2	356	54.0 (16.7)	356	57.7 (21.3)	336	51.4 (23.4)	356	73.0 (12.9)
≥30 kg/m^2	157	47.4 (17.8)	157	48.6 (21.7)	137	41.4 (23.9)	157	67.2 (12.5)
Bra cup size								
< D cup	283	52.8 (17.0)	283	55.8 (21.8)	258	50.1 (24.2)	283	72.9 (13.0)
≥ D cup	230	50.9 (17.6)	230	53.9 (21.9)	215	46.7 (23.6)	230	69.2 (12.9)
Chronic health condition?								
Yes	148	48.6 (17.0)	148	49.4 (23.0)	131	39.6 (25.0)	148	66.6 (11.7)
No	365	53.3 (17.3)	365	57.2 (21.0)	342	51.9 (22.7)	365	73.1 (13.1)
Employment status								
Full-time	119	52.9 (17.1)	119	55.0 (23.2)	118	48.9 (23.1)	119	71.2 (14.1)
Part-time	143	50.8 (17.8)	143	54.8 (20.0)	135	50.8 (23.2)	143	71.2 (13.2)
Voluntary work	3	58.7 (11.0)	3	61.3 (27.7)	3	49.7 (18.3)	3	67.7 (4.2)
Homemaker	84	51.0 (19.2)	84	50.8 (22.7)	83	48.3 (24.5)	84	71.9 (13.4)
Student	26	49.7 (10.6)	26	51.8 (17.4)	19	44.2 (24.1)	26	71.2 (11.0)
Retired	85	56.1 (17.3)	85	64.6 (19.6)	69	50.5 (25.1)	85	73.6 (11.1)
Unable to work	21	48.0 (18.0)	21	45.4 (24.1)	20	33.0 (25.0)	21	63.9 (12.1)
Unemployed	24	45.8 (13.0)	24	45.5 (23.5)	20	44.7 (25.4)	24	67.6 (14.1)
Other	8	55.5 (12.6)	8	60.8 (13.5)	6	50 .0 (22.6)	8	70.4 (14.4)
IRSD								
Lowest quintile	78	51.9 (17.6)	78	54.1 (22.3)	70	46.6 (22.4)	78	71.2 (13.2)
Low quintile	94	49.2 (16.4)	94	52.8 (23.1)	83	47.8 (25.0)	94	72.0 (14.1)
Middle quintile	122	52.7 (18.2)	122	55.1 (21.9)	114	45.0 (25.2)	122	70.6 (12.8)
High quintile	106	53.1 (18.0)	106	56.4 (21.9)	99	51.2 (22.3)	106	71.2 (13.0)
Highest quintile	113	52.3 (16.1)	113	55.8 (20.5)	107	51.7 (24.0)	113	71.4 (12.7)
All participants	513	51.9 (17.3)	513	55.0 (21.8)	473	48.5 (24.0)	513	71.2 (13.1)

3.3.3 Predictors of BREAST-Q scale scores

Multiple linear regression analysis was employed to determine which independent socio-demographic variables, if any, predicted each of the four individual BREAST-Q scale scores from the Australian general population sample. Regression models for each of the four BREAST-Q scales are shown in Table 3.4. Multiple regression models were run to predict BREAST-Q scale scores from candidate variables including age, BMI, bra cup size and presence of a chronic health condition. Results of the multiple linear regression indicated that age, BMI and the presence of a chronic health condition were statistically significantly independent predictors of 'Satisfaction with Breasts', $F(4, 508) = 14.6$, $p < 0.001$, R^2 of 0.103, explaining 10.3% of the variance in the data. Age, BMI and chronic health condition were significant independent predictors of 'Psychosocial Wellbeing', $F(4, 508) = 29.3$, $p < 0.001$, R^2 of 0.187, explaining 18.7% of variance in the BREAST-Q scale. Of the four candidate variables, BMI and chronic health condition were significant independent predictors of 'Sexual Wellbeing', $F(4, 468) = 13.2$, $p < 0.001$, R^2 of 0.101, explaining 10.1% of the variation in the wellbeing scale. Age, BMI, bra cup size and chronic health condition were significant independent predictors of 'Physical Wellbeing', $F(4, 508) = 22.7$, $p < 0.011$, R^2 of 0.152, explaining 15.2% of variance in the data.

Table 3.4 Multiple linear regression models for BREAST-Q scales

Variable	Coefficient (β)	Standard error	95% CI	*P*-value
Satisfaction with breasts				
Intercept	49.6	5.16	39.5 to 59.7	< 0.001
Age	-0.24	0.05	0.15 to 0.33	< 0.001
BMI	-0.65	0.12	-0.88 to 0.41	< 0.001
Bra cup size	0.49	0.58	-0.65 to 1.63	0.400
Chronic health condition	4.19	1.67	0.90 to 7.47	0.013
Psychosocial Wellbeing				
Intercept	45.5	6.21	33.3 to 57.7	< 0.001
Age	0.45	0.05	0.34 to 0.55	< 0.001
BMI	-1.01	0.14	-1.29 to -0.73	< 0.001
Bra cup size	0.83	0.70	-0.54 to 2.20	0.233
Chronic health condition	7.74	2.01	3.79 to 11.7	< 0.001
Sexual Wellbeing				
Intercept	47.1	7.46	32.5 to 61.8	< 0.001
Age	0.11	0.07	-0.02 to 0.24	0.109
BMI	-0.81	0.17	-1.15 to -0.47	< 0.001
Bra cup size	0.34	0.83	-1.29 to 1.96	0.685
Chronic health condition	10.1	2.44	5.33 to 14.92	< 0.001
Physical Wellbeing				
Intercept	67.9	3.79	60.5 to 75.4	< 0.001
Age	0.17	0.03	0.11 to 0.24	< 0.001
BMI	-0.36	0.09	-0.53 to -0.18	< 0.001
Bra cup size	-1.26	0.43	-2.10 to -0.43	0.003
Chronic health condition	6.41	1.23	4.00 to 8.83	< 0.001

3.3.4 Comparison of socio-demographic characteristics between normative population samples

Socio-demographic characteristics were compared between the previously published United States study (Mundy et al., 2017c) and the Australian population sample described in this study. Table 3.5 summarises the comparison of socio-demographic characteristics between population samples. The demographic characteristics of respondents were significantly different between the two population samples across all described variables including age, body mass index, employment status, and presence of a chronic health condition. Notably, the mean age for the US and Australian population sample was 54.7 years (SD 12.5) and 46.1 years (SD 17.0), respectively, with a mean difference of 8.6 years (95% CI, 7.2 to 10.1 years) ($p < 0.001$). Furthermore, the age distribution across categories was significantly different across the two groups as summarised in Table 3.5 ($p < 0.001$).

Whilst the normative BREAST-Q data derived for the Australian population in this study is considered representative of the general population by age and geographical breakdown (refer Section 3.3.1), a comparison of the published age and sex composition data from the 2016 United States Census (United States Census Bureau, 2016) indicates that this may not be the case for the United States data. According to the United States Census, the age distribution of females per age group were as follows: 9.2% (18–24 years); 13.5% (25–34 years); 12.5% (35–44 years); 13.4% (45–54 years); 13.1% (55–64 years); and 16.2% (65 years and above). In contrast, the age breakdown for the US normative study was: 0.5% (18–24 years); 7.7% (25–34 years); 14.2% (35–44 years); 20.0% (45–54 years); 33.3% (55–64 years); and 24.0% (65 years and above). A X^2 test demonstrated the age distribution of the population sample in the US study was therefore significantly different from the United States Census population breakdown and is potentially biased and represented by a higher proportion of participants of older age (X^2 (5) = 17.4; p = 0.004).

Table 3.5 Comparison of participant socio-demographics between normative population samples

Variable	Australia	United States	*p*-value
No.	513	1206	
Mean age (SD), years	46.1 (17.0)	54.7 (12.5)	< 0.001
Median age (range), years	45 (18 – 88)	57 (20 – 86)	
Age group (years):			< 0.001
18–24	62 (12)	6 (0.5)	
25–34	99 (19)	93 (8)	
35–44	88 (17)	171 (14)	
45–54	87 (17)	241 (20)	
55–64	75 (15)	402 (33)	
65+	102 (20)	289 (24)	
Mean BMI (SD), kg/m^2	27.8 (6.96)	26.8 (6.03)	0.004
Obesity status			
Non-obese (BMI <30kg/m^2)	356 (69)	912 (76)	0.004
Obese (BMI ≥30 kg/m^2)	157 (31)	286 (24)	
Employment status			< 0.001
Full-time	119 (23)	511 (43)	
Part-time	143 (28)	168 (14)	
Voluntary	3 (1)	33 (3)	
Homemaker	84 (16)	85 (7)	
Student	26 (5)	16 (1)	
Retired	85 (17)	326 (27)	
Unable to work or disabled	21 (4)	12 (1)	
Unemployed or seeking employment	24 (5)	19 (2)	
Other	8 (2)	32 (3)	
Bra cup size			0.022
<A	1 (0.2)	22 (2)	
A	33 (6)	90 (8)	
B	96 (19)	287 (24)	
C	153 (30)	320 (27)	
D	111 (22)	232 (19)	
DD	69 (13)	149 (12)	
>DD	50 (10)	100 (8)	
Chronic health condition?			< 0.001
Yes	148 (29)	596 (50)	
No	365 (71)	606 (50)	

Values are number (%) unless stated otherwise.

3.3.5 Comparison of normative BREAST-Q scores between normative population samples

Normative BREAST-Q Reduction module data were compared between the United States (Mundy et al., 2017c) and Australian general population reference values derived in this study. Table 3.6 compares the unadjusted mean scores for the four BREAST-Q scales. An independent *t*-test confirmed that the Australian mean scores were significantly lower than United States norms across all four pre-operative BREAST-Q scales, in particular for the Psychosocial Wellbeing scale with a mean difference of 13-points (95% CI, 10.5 to 14.6 points). Effect size calculations show a small effect in Satisfaction with Breasts, Sexual Wellbeing and Physical Wellbeing when comparing normative reference values between the two population samples. A moderate effect size was found when comparing population norms in the Psychosocial Wellbeing scale.

Table 3.6 Comparison of unadjusted normative BREAST-Q Reduction module scores for the United States of America and Australia

	United States of America†				Australia				Difference in means (95% CI)	*p*-value	Effect size‡ (95% CI)
	N	Mean	SD	95% CI	*N*	Mean	SD	95% CI			
Satisfaction with Breasts	1205	56.7	16.3	56.1 – 57.9	513	51.9	17.3	50.4 – 53.4	4.7 (3.0 – 6.4)	<0.001	0.29 (0.19 – 0.39)
Psychosocial Wellbeing	1205	67.5	19.0	66.9 – 69.1	513	55.0	21.8	53.1 – 56.8	12.5 (10.5 – 14.6)	<0.001	0.63 (0.52 – 0.73)
Sexual Wellbeing	1024	55.2	19.4	53.8 – 56.2	473	48.5	24.0	46.4 – 50.7	6.7 (4.4 – 9.0)	<0.001	0.32 (0.21 – 0.43)
Physical Wellbeing	1205	75.7	10.9	75.4 – 76.6	513	71.2	13.1	70.1 – 72.4	4.5 (3.3 – 5.7)	<0.001	0.39 (0.28 – 0.49)

† Source: (Mundy et al., 2017c).
‡ Effect size was calculated as the mean difference between groups, divided by the pooled standard deviation for the two groups.

The difficulty when comparing mean scores across multiple normative studies is that there are differences in the age distribution of the samples. Presentation of overall mean scores for health-related quality of life in a population sample may mask important differences in the distribution of scores across different socio-demographic variables. Given the significant differences in the age distribution between the two normative population samples (Table 3.5), a one-way ANCOVA was conducted to compare each of the four BREAST-Q scale scores between Australian and United States population samples whilst controlling for age. Results of the ANCOVA found a statistically significant difference remained when comparing the two normative studies across all four BREAST-Q scales after adjustment for age (Table 3.7).

A comprehensive comparison of BREAST-Q scores for the four scales stratified by socio-demographic characteristics for the Australian and United States population samples is shown in supplementary tables (Appendix L).

Table 3.7 Comparison of age-adjusted normative BREAST-Q Reduction module scores

	United States of America			Australia			Difference in means (95% CI)	*p*-value of difference
	N	**Mean**	**95% CI**	***N***	**Mean**	**95% CI**		
Satisfaction with Breasts	1205	56.5	55.5 – 57.4	513	52.3	50.9 – 53.8	4.1 (2.4 – 5.9)	<0.001
Psychosocial Wellbeing	1205	66.7	65.6 – 67.8	513	56.6	54.8 – 58.3	10.1 (8.0 – 12.2)	<0.001
Sexual Wellbeing	1024	55.3	54.0 – 56.6	473	48.3	46.4 – 50.3	7.0 (4.6 – 9.4)	<0.001
Physical Wellbeing	1205	75.6	74.9 – 76.2	513	71.7	70.6 – 72.7	3.9 (2.7 – 5.1)	<0.001

3.4 Discussion

This study is the first to report Australian general population reference values for the BREAST-Q Reduction module. These values establish the levels of breast-related satisfaction and quality of life within the female general population and provide a valuable population-specific comparison for the interpretation of BREAST-Q scores for women with breast hypertrophy undergoing surgery. Such comparisons facilitate the ability to quantify the impact of a condition or disease on health-related quality of life, and also the success of a surgical intervention in comparison to levels within the general population.

Within the normative study, participants of an older age were found to report higher scores in three out of the four scales: Satisfaction with Breasts, Psychosocial Wellbeing and Physical Wellbeing. Furthermore, a larger body mass index and presence of a chronic health condition was found to be associated with lower scores in all BREAST-Q scales of participant satisfaction and quality of life than their respective comparison groups. Increased bra cup size was associated with lower Physical Wellbeing scores. These findings are in agreement with the study by Mundy and colleagues (Mundy et al., 2017c) and highlight the importance of capturing socio-demographic information and comorbidities when conducting health-related quality of life studies.

Prior to this study, published general population reference values for the BREAST-Q Reduction module were limited to a single study and were based on data from the United States population. An interesting finding from this study was that sizeable differences were found in mean BREAST-Q scores when comparing Australian values to reported United States norms, in particular for Psychosocial Wellbeing. A number of reasons for this difference between general population reference values might be postulated, whether it is something related to the Australian population or whether it is due to variations in the populations sampled within each study. It is possible that participants in the United States study recruited through the Army of Women, with a primary focus of connecting breast cancer researchers with women with and without breast cancer, had a different awareness and motivation for participating in the study which may have impacted their responses. When comparing socio-demographic characteristics between the two normative studies pronounced differences were observed, particularly in the age distribution of the population samples. Whilst it was plausible that this may have accounted for the observed differences in BREAST-Q scores as age is often an important predictor of self-reported health status (Hjermstad et al., 1998), on comparison of age-adjusted BREAST-Q scores the significant differences remained between the two general population samples across all four BREAST-Q scales. This finding highlights the importance of utilising country-specific norms for quality of life studies wherever possible, as potentially important differences do exist between populations. Furthermore, this finding is consistent with previous studies which have identified differences between reference values in Australia and those from other countries for various health-related

quality of life measures including the Short Form-36, Short Form-6D, EQ-5D and EORTC QLQ-C30 (Frieling et al., 2013, Hawthorne et al., 2007, McCaffrey et al., 2016, Mercieca-Bebber et al., 2019, Norman et al., 2013, Roser et al., 2019, Watson et al., 1996). As an example of the importance of using country-specific reference values, the threshold for a small but clinically important difference has been estimated by a rule-of-thumb approach as 10-points on a 100-point scale (King, 1996). When comparing 'Psychosocial Wellbeing', the United States reference value for this scale is 10.1-points higher than the Australian reference value generated in this study; which therefore represents a clinically meaningful difference; the interpretation of a mean score for a patient presenting for and undergoing breast reduction surgery in Australia would therefore be inaccurate if compared with the United States reference values.

Strengths of this study include the generation of population-specific reference values for the BREAST-Q in order to provide an accurate comparison for the interpretation of health-related quality of life between surgical patients and population norms (see Chapter 4). Furthermore, the population sample described in this study was representative of the general Australian population breakdown by age and geographical location. This enforces the likelihood that this study captured an accurate representation of women in the general population, and overcomes limitations described in the normative study from the US population sample which was potentially biased by not being representative of the age distribution of the United States general population. This is particularly important given that this study demonstrated that age was a significant predictor of BREAST-Q scores in three out of the four pre-operative scales. Finally, given that the BREAST-Q is the most widely used patient-reported outcome measure in breast surgery, this study is valuable because it provides general population reference data for the BREAST-Q Reduction module from a second, diverse population set, and highlights that within this context potentially important differences exist in health-related quality of life between populations.

This study has several potential limitations that should be noted. Firstly, the Pureprofile panel used for participant recruitment in this study consists exclusively of members of the public who voluntarily enrol to complete surveys, and this might introduce an element of selection bias. Bias could be attributable to various factors including: the self-selection of a biased population sample by Pureprofile; or participants who elect to complete online surveys may not represent the population at large. Secondly, data was not collected on socio-demographic characteristics including income, country of birth, marital status and highest level of education, so we could not assess the representativeness of our population sample across these variables. Despite these limitations, online survey organisations represent an efficient method of obtaining a large, representative sample of the general population and consistent with country-specific population breakdown distribution across factors including age and geographic variables. Finally, whilst we have reported normative data from a second diverse population sample, the normative values were derived from another relatively wealthy country. The absence of data from low- and middle-income

counties means it is unlikely that this can be representative of worldwide normative data.

3.5 Conclusion

This study reports the first BREAST-Q Reduction module general population reference values specific to Australia, and only the second set of population reference values reported globally. These values will assist in the interpretation of BREAST-Q scale scores for Australian women with breast hypertrophy who undergo reduction mammaplasty, both in existing data and in future studies. This study confirmed that general population reference values for HRQoL measures may differ between populations and highlights the importance of utilising country-specific normative data wherever possible for the accurate interpretation of HRQoL scores in the clinical setting. Lastly, findings from this study highlight the importance of presenting socio-demographic data together with patient-reported outcome data and note which characteristics have a significant influence on HRQoL outcome data.

4. OUTCOMES OF BREAST REDUCTION SURGERY USING THE BREAST-Q: A PROSPECTIVE STUDY AND COMPARISON WITH NORMATIVE DATA

A version of this chapter has been published as an original article in the Plastic and Reconstructive Surgery journal (Crittenden et al., 2019b); attached as Appendix M.

4.1 Introduction

The BREAST-Q is a condition-specific patient-reported outcome measure that was developed and validated by Pusic and colleagues to assess patient satisfaction and HRQoL following cosmetic, functional and reconstructive breast surgery (Pusic et al., 2009). Most reported studies using the BREAST-Q Reduction module to assess outcomes following breast reduction surgery have been limited by their retrospective design, and lack of comparison of scores with a pre-operative baseline (Cabral et al., 2017a, Cogliandro et al., 2017a, Cohen et al., 2016a, Coriddi et al., 2013, Correa et al., 2018, Gonzalez et al., 2012). The generation of Australian population reference values for the BREAST-Q described in Chapter 3 provides a population-specific benchmark for the interpretation of scores derived from the surgical and breast hypertrophy control cohorts detailed in this chapter. Finally, in order to further provide a meaningful interpretation of HRQoL scores, an estimate for the minimal important difference (MID) for the BREAST-Q Reduction module was established. To date, no published MID estimates exist for the reduction version of the BREAST-Q patient-reported outcome measure.

This chapter describes a prospective study using the BREAST-Q to assess outcomes following breast reduction surgery. The primary objective was to assess breast-related satisfaction and health-related quality of life in Australian women with breast hypertrophy before and after breast reduction surgery. Secondary objectives were to compare levels of breast-related satisfaction and wellbeing in a control group of women with breast hypertrophy who did not undergo surgery; and compare to normative data derived from an Australian population (Chapter 3) and to previously published United States norms. Finally, many providers commonly determine the medical necessity for reduction mammaplasty using the Schnur sliding scale based on body surface area-adjusted minimum resection weight calculations; a scale which was never intended for this purpose and has since been misused (Dvoracek et al., 2019, Koltz et al., 2013, Schnur, 1999, Schnur et al., 1991). This study therefore aimed to evaluate the influence of factors including a minimum weight of resection on HRQoL outcomes following breast reduction surgery.

4.2 Participants and methods

4.2.1 Surgical cohort

The participants in the surgical cohort are introduced and described in detail in Chapter 2. However, a point of difference in this study was that participants self-completed the condition-specific BREAST-Q Reduction module patient-reported outcome measure at two timepoints, pre-operatively and 12 months post-operatively. In addition, the number of participants within the surgical cohort described in this chapter was lower as the BREAST-Q patient-reported outcome measure was not developed until after the commencement of this study and was introduced into the study in March of 2010.

This study therefore includes women aged 18 years and above with symptomatic breast hypertrophy who were eligible for bilateral breast reduction surgery between March 2010 and February 2016. A detailed description of participant recruitment and data collected for surgical participants is detailed in Chapter 2 section 2.2.1. In brief, age, height, weight, bra cup size and smoking status were recorded at the time of enrolment. Intraoperatively, the surgical technique and weight of tissue resected from each breast was documented. Post-operatively, a "comprehensive complications assessment" checklist was completed by one of the doctors in the treating team (Appendix F).

Pre-operative height and weight measurements were used to calculate body surface area (BSA) for individual surgical participants using the DuBois and DuBois formula: BSA (m^2) = 0.007184 x height (cm)$^{0.725}$ x weight (kg)$^{0.425}$ and the patients were subsequently divided into two groups depending on whether or not they met Schnur's 22nd percentile criteria based on BSA and required volume of tissue resected at surgery (Schnur et al., 1991).

4.2.2 Breast hypertrophy control cohort

The participants in the breast hypertrophy control cohort are introduced and described in detail in Chapter 2 section 2.2.1. In brief, eligible participants were mailed study information and questionnaires and consenting participants were required to self-complete and return the BREAST-Q questionnaire and provide information for relevant variables such as age, height, weight, bra cup size and health status at a baseline time-point and 12 months following.

4.2.3 The BREAST-Q

The BREAST-Q condition-specific patient-reported outcome measure is described in detail in Chapter 3. In this study, the BREAST-Q Reduction module was used to evaluate breast-related satisfaction and HRQoL in women with breast hypertrophy who underwent breast reduction surgery, in a control group of women with breast hypertrophy, and a comparison made to normative population BREAST-Q data generated in Chapter 3. The pre-operative version of the

BREAST-Q comprises the following scales: Satisfaction with Breasts, Psychosocial Wellbeing, Sexual Wellbeing and Physical Wellbeing (Appendix H). Additionally, the post-operative version includes: Satisfaction with Outcome (*n* = 8 items), Satisfaction with Nipple (*n* = 5 items), Satisfaction with Information (*n* = 12 items), Satisfaction with Surgeon (*n* = 12 items), Satisfaction with Medical Staff (*n* = 7 items) and Satisfaction with Office Staff (*n* = 7 items) (Pusic et al., 2009) (Appendix I). Questionnaire responses were transformed using the Q-Score software (New York, NY; http://qportfolio.org/score-breast-q-reduction-mastopexy) to generate a score between 0 and 100, where a score of 0 is the minimum score and 100 is the maximum score and indicates the highest level of satisfaction or wellbeing.

4.2.4 Minimal important difference estimates

Distribution-based methods were used to estimate a clinically meaningful change, or MID, in BREAST-Q scores. Distribution-based approaches rely on statistical methods to express an effect in terms of providing a measure of sample variability to estimate the MID. Four alternate distribution-based approaches were used to estimate a clinically meaningful change in BREAST-Q scores including: one-half a standard deviation; effect size; standardised response mean; and standard error of measurement. These approaches were described in detail in Chapter 2 section 2.2.3.

4.2.5 Statistical analysis

Statistical analyses were performed using SPSS v25.0 statistical software (IBM Corp., Armonk, N.Y.). Descriptive statistics including mean, standard deviation and 95% confidence intervals (CI) were computed for continuous variables. To assess the significance of changes in HRQoL, mean pre-operative and 12 months post-operative BREAST-Q scores were compared using a paired *t*-test for dependent samples. Change effect size statistics were computed as the mean difference between pre-operative and post-operative BREAST-Q scores divided by the standard deviation (SD) of the baseline score. Change effect sizes were interpreted according to the thresholds established by Cohen as follows: <0.20, trivial; 0.20 to 0.50, small; >0.50 to 0.80, moderate; and >0.80, large (Cohen, 1988). Comparisons were made between groups using a two-sample *t*-test for continuous data and a difference in means with 95% confidence intervals. A chi-square or Fisher's exact test were used to compare categorical variables between groups. BREAST-Q scores from the surgical cohort were compared to Australian population normative data using an independent samples *t*-test. The Pearson correlation coefficient (*r*) was used to investigate the strength of association between two continuous variables. Multiple linear regression analysis was used to explore the relationship between BREAST-Q scores and independent demographic variables. Statistical significance was established at a *p*-value of less than 0.05.

4.3 Results

4.3.1 Study participants

4.3.1.1 Surgical cohort

One hundred and sixty-eight eligible participants who underwent reduction mammaplasty between March 2010 and February 2016 completed the BREAST-Q questionnaire pre-operatively and 156 completed the questionnaire post-operatively. Of these, 132 participants (76%) completed the BREAST-Q Reduction module at both time points. Participant demographics from the surgical cohort are summarised in Table 4.1. The median age was 42 years (range, 18 to 72 years) with a mean ± SD body mass index (BMI) of 32.1 ± 5.7 kg/m^2. The mean total weight of breast tissue resected at surgery was 1298.7 ± 824.7 grams. The inferior pedicle was used in the majority (78%) of surgeries, with the superomedial in 19%.

4.3.1.2 Breast hypertrophy control cohort

Study questionnaires were initially posted to 350 women; 160 respondents (46%) completed and returned the questionnaires at baseline and of these, 124 responded 12 months later. Twenty-two of those contacted to participate in the study underwent breast reduction surgery during the study timeframe and were therefore ineligible to participate. Participant demographics for the hypertrophy control cohort are summarised in Table 4.1. The mean participant age was 45.6 years (range, 20 to 79 years) and the mean BMI was 31.6 ± 6.4 kg/m^2. The most common bra cup sizes were F (23%) and G (28%).

There were no statistically significant differences in baseline characteristics of participants who completed BREAST-Q questionnaires at both study timepoints including age, BMI, obesity status, or smoking history between the surgical group and hypertrophy control group (Table 4.1).

Table 4.1 Baseline characteristics of participants.

Variable	Surgical cohort (*n* = 132)	Hypertrophy control cohort (*n* = 124)	P value of difference[†]
Median (range) age (years)	42 (18 – 72)	47 (20 – 79)	
Mean (± SD) age (years)	42.1 ± 13.6	45.3 ± 13.1	0.058
Age group (years):			
18–24	17 (13)	12 (9.7)	
25–34	24 (18)	15 (12.1)	
35–44	42 (32)	26 (21.0)	
45–54	25 (19)	43 (34.7)	
55–64	17 (13)	21 (16.9)	
65+	6 (5)	7 (5.6)	
Mean (± SD) BMI (kg/m^2)	32.1 ± 5.7	32.1 ± 6.0	0.960
Obesity status:			0.519
non-obese (BMI <30 kg/m^2)	47 (36)	49 (39.5)	
obese (BMI ≥30 kg/m^2)	85 (64)	74 (59.7)	
Missing	0 (0)	1 (0)	
Smoking Status:			0.686
Non-smoker	77 (58)	79 (63.7)	
Current	21 (16)	14 (11.3)	
Ex-smoker <12 months	8 (6)	6 (4.8)	
Ex-smoker >12 months	26 (20)	25 (20.2)	
Bra cup size:			
C	1 (0.76)	0 (0)	
D	5 (3.8)	4 (3.2)	
DD	31 (23.5)	13 (10.5)	
E	29 (22.0)	19 (15.3)	
F	27 (20.0)	27 (21.8)	
G	23 (17)	37 (29.8)	
H	7 (5)	15 (12.1)	
>H	8 (6)	4 (3.2)	
Missing	0 (0)	5 (4)	

Values are numbers (percentages) unless stated otherwise.

† Using independent samples *t*-test or chi-square test as appropriate.

4.3.2 BREAST-Q scores before and after breast reduction surgery

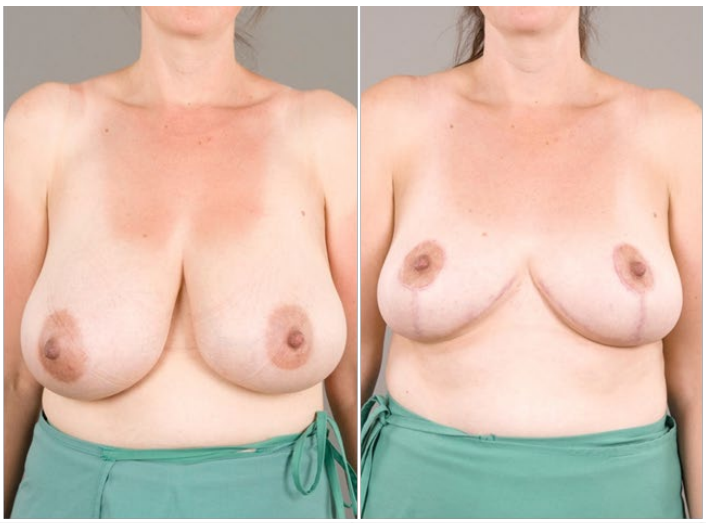
Summary statistics for the BREAST-Q scores measured in the surgical participants are presented in Table 4.3. Statistically significant improvements were found across all BREAST-Q scales measured pre- and post-operatively; Satisfaction with Breasts, Psychosocial Wellbeing, Sexual Wellbeing, and Physical Wellbeing, when compared to pre-operative scores ($p < 0.001$) (Table 4.2). Satisfaction with Breasts improved with a mean ± SD change of 51.4 ± 20.3; Psychosocial Wellbeing improved with a mean change of 36.9 ± 21.7; Sexual Wellbeing improved with a mean change of 31.4 ± 25.0; and Physical Wellbeing improved with a mean change of 32.7 ± 17.9. Change effect size calculations show a very large effect in all BREAST-Q scales when comparing pre-operative and post-operative scores: Satisfaction with breasts (effect size 3.6; 95% CI, 3.2 to 3.9); Psychosocial Wellbeing (effect size 2.2; 95% CI, 1.9 to 2.5); Sexual Wellbeing (effect size 1.6; 95% CI, 1.3 to 1.9); and Physical Wellbeing (effect size 2.3; 95% CI, 2.0 to 2.7).

Table 4.2 BREAST-Q scores before and after breast reduction surgery

Scale	*n*	Mean (SD)		Mean change (95% CI)	*p*-value[‡]
		Pre-operative score	Post-operative score		
Satisfaction with Breasts	132	21.9 (10.9)	73.3 (17.3)	51.4 (47.9 – 54.9)	<0.001
Psychosocial Wellbeing	132	32.4 (12.8)	69.3 (19.8)	36.9 (33.1 – 40.6)	<0.001
Sexual Wellbeing	111	30.4 (17.6)	61.9 (22.1)	31.4 (26.7 – 36.1)	<0.001
Physical Wellbeing	132	44.0 (15.5)	76.6 (12.1)	32.7 (29.6 – 35.7)	<0.001

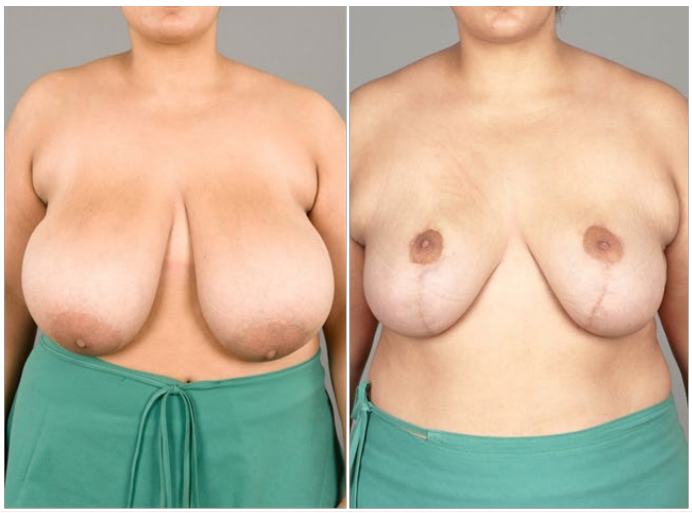
[‡] Paired-samples *t*-test.

Patient photos before and 12-months after breast reduction surgery demonstrate BREAST-Q scores at both time points, with the magnitude of change represented with by the percentage increase in scores following surgery (Figure 4.1 and Figure 4.2).



BREAST-Q scale	Pre-operative	12m post-operative	% change
Satisfaction with breasts	23	90	291%
Psychosocial Wellbeing	43	77	79%
Sexual Wellbeing	46	100	204%
Physical Wellbeing	56	79	41%

Figure 4.1 Pre- and post-operative photos of a patient who underwent an inferior pedicle Wise pattern breast reduction with corresponding BREAST-Q scores



BREAST-Q scale	Pre-operative	12m post-operative	% change
Satisfaction with breasts	29	57	97%
Psychosocial Wellbeing	30	70	133%
Sexual Wellbeing	40	56	40%
Physical Wellbeing	30	61	103%

Figure 4.2 Pre- and post-operative photos of a patient who underwent a Hall-Findlay pattern breast reduction with corresponding BREAST-Q scores

An independent *t*-test was conducted to compare BREAST-Q scores between socio-demographic categorical variables. Figure 4.3 demonstrates that participants with a higher BMI of 30 kg/m^2 or greater (n = 85, 64%) had a significantly greater mean change in Satisfaction with Breasts (p = 0.027), Psychosocial Wellbeing (p = 0.031), and Physical Wellbeing (p = 0.003) than those with a body mass index less than 30 kg/m^2 (n = 47, 36%) when comparing pre-operative to 12 month post-operative scores. Whilst participants with a higher BMI were also found to have a greater improvement following surgery in 'Sexual Wellbeing', this difference did not reach statistical significance (p = 0.101). Participants aged 40 years and above had a greater mean change in Satisfaction with Breasts (p = 0.050) and Psychosocial Wellbeing (p = 0.022) than those less than 40 years of age (Figure 4.3).

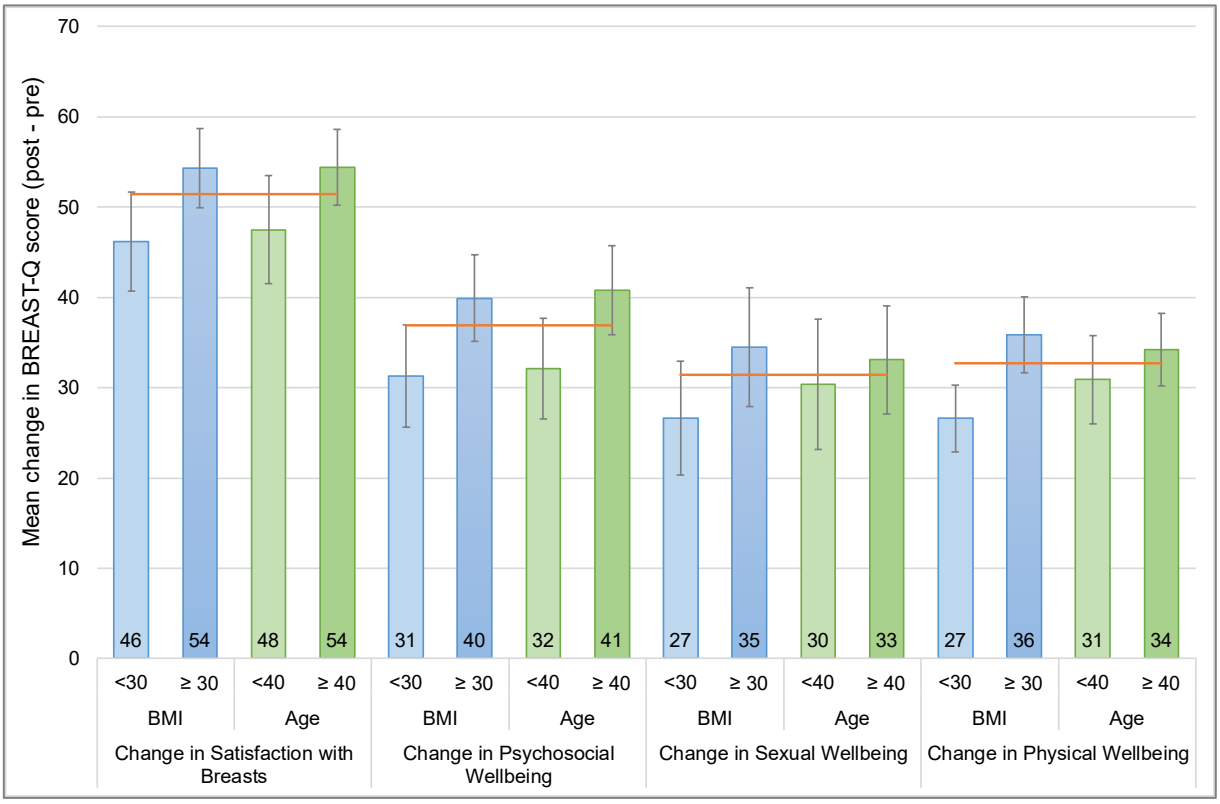


Figure 4.3 Mean change in BREAST-Q scores following surgery.

Error bars represent 95% confidence intervals. Orange line indicates mean score for individual BREAST-Q scales.

Mean change in BREAST-Q scores was not significantly different between patients who had a post-operative surgical complication and those who did not (Table 4.3).

Table 4.3 Significance of surgical complications on mean change (SD) in BREAST-Q scores

Scale	Surgical complication		Difference in means (95% CI)	*p*-value
	Yes (*n* = 45)	No (*n* = 87)		
Satisfaction with Breasts	52.1 (21.3)	51.0 (19.8)	-1.1 (-8.5 to 6.3)	0.77
Psychosocial Wellbeing	34.1 (19.7)	38.3 (22.7)	4.2 (-3.6 to 12.1)	0.29
Sexual Wellbeing	30.0 (24.8)	32.3 (25.2)	2.3 (-7.5 to 12.1)	0.64
Physical Wellbeing	31.3 (17.7)	33.3 (18.1)	2.0 (-4.5 to 8.5)	0.55

4.3.3 BREAST-Q scores in women with breast hypertrophy awaiting surgery

Mean BREAST-Q scores for women in the breast hypertrophy control group who did not undergo breast reduction surgery during the 12-month study follow-up are described in Table 4.4. BREAST-Q scores were lower when comparing 12 months to baseline scores across all scales, with scores for Sexual Wellbeing reaching statistical significance using a paired samples *t*-test (p = 0.01).

Table 4.4 BREAST-Q scores in the breast hypertrophy control group

Scale	*n*	Mean (SD)		Mean change (95% CI)	*p*-value
		Baseline score	12m post-baseline score		
Satisfaction with Breasts	124	22.1 (12.1)	20.3 (12.0)	-1.8 (-3.9 – 0.2)	0.08
Psychosocial Wellbeing	124	29.0 (13.8)	27.8 (14.8)	-1.2 (-3.2 – 0.8)	0.23
Sexual Wellbeing	110	25.1 (17.2)	21.4 (16.1)	-3.7 (-6.5 – 0.9)	0.01
Physical Wellbeing	124	42.1 (14.9)	41.2 (16.1)	-0.9 (-3.2 – 1.4)	0.44

Mean BREAST-Q scores for women in the breast hypertrophy control group remained significantly lower than post-operative scores for women who underwent surgery across all scales: Satisfaction with breasts (mean difference 53.0-points; 95% CI, 49.4 to 56.7, $p < 0.001$); Psychosocial Wellbeing (mean difference 41.5-points; 95% CI, 37.1 to 45.8, $p < 0.001$); Sexual Wellbeing (mean difference 39.3-points; 95% CI, 34.0 to 44.5, $p < 0.001$); and Physical Wellbeing (mean difference 35.4-points; 95% CI, 31.9 to 38.9, $p < 0.001$).

4.3.4 Distribution-based estimates of MID

Table 4.5 presents the range of estimated minimal important difference (MID) values for each scale of the Reduction module of the BREAST-Q. MID estimates varied by scale, ranging from 6-points to 9-points based on the one-half standard deviation approach, and 5-points to 8-points using the one-third standardised response mean. MID estimates were lower using the standard error of

measurement analyses based on the reliability of each subscale and ranged from 2.9-points to 6.4-points.

Table 4.5 BREAST-Q Reduction module minimal important difference estimates

Scale	Distribution-based approach				MID estimate	
	0.5 SD	0.2 SRM	0.3 SRM	SEM	Based on 0.5 SD	Based on 0.3 SRM
Satisfaction with Breasts	5.5	4.1	6.1	3.3	6	6
Psychosocial Wellbeing	6.4	4.3	6.5	2.9	6	7
Sexual Wellbeing	8.8	5.0	7.5	4.7	9	8
Physical Wellbeing	7.8	3.6	5.4	6.4	8	5

The improvement in BREAST-Q scores in participants who underwent breast reduction surgery was well in excess of all estimates of minimal important difference across all four scales. This finding is shown in Figure 4.4 by plotting the mean change from baseline to 12-months in both surgical and hypertrophy control groups in comparison to the one-half standard deviation estimate of minimal important difference.

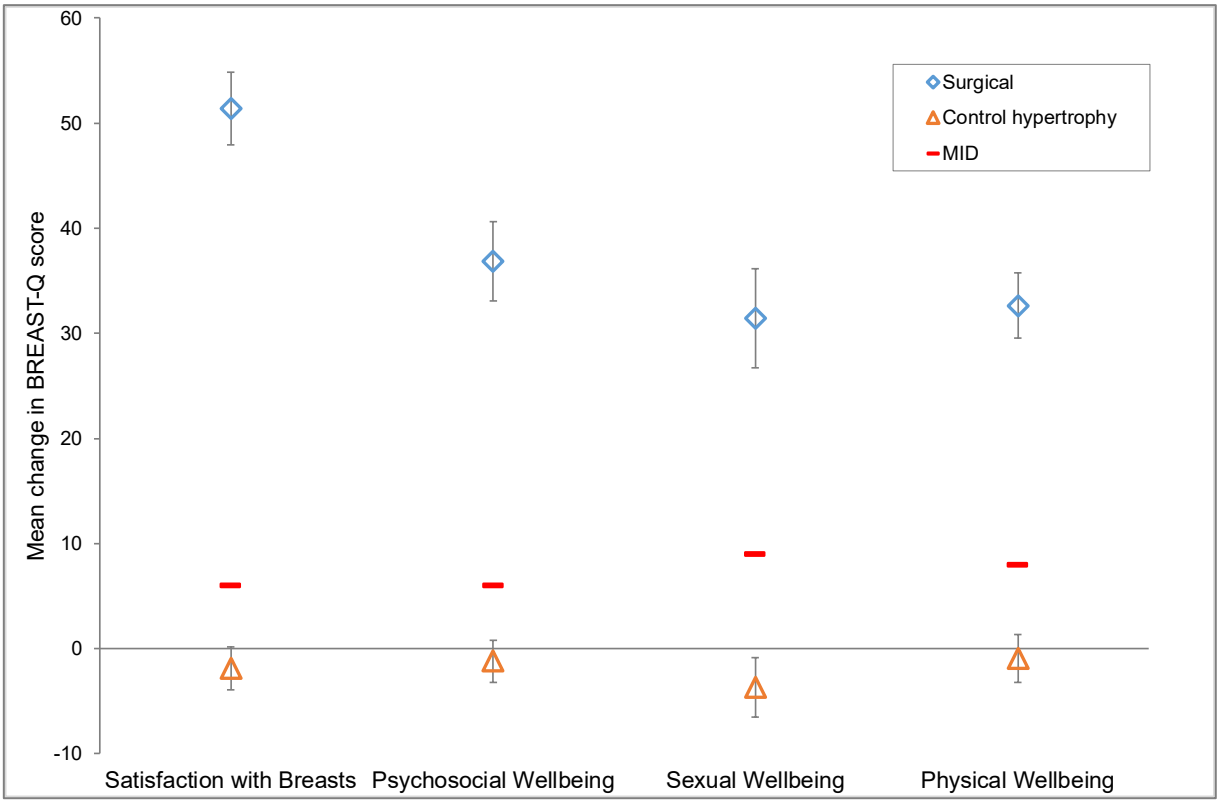


Figure 4.4 Mean change in BREAST-Q scores from baseline to 12-months for surgical and breast hypertrophy control groups in comparison to MID estimate.

Error bars represent 95% confidence intervals.

4.3.5 Comparison of BREAST-Q scores between women with breast hypertrophy and women in the general Australian population

Normative BREAST-Q scores generated from Australian women (Chapter 3) were compared to scores from patients in the surgical cohort with symptomatic breast hypertrophy who proceeded to reduction mammaplasty. Figure 4.5 demonstrates mean BREAST-Q scores for surgical patients before and 12 months after surgery in comparison to norms for Australia and the United States. In comparison to normative values, women with breast hypertrophy who were awaiting surgery had significantly lower BREAST-Q scores pre-operatively across all scales ($p < 0.001$). Post-operatively, mean scores significantly improved to levels at least that of the normative Australian population.

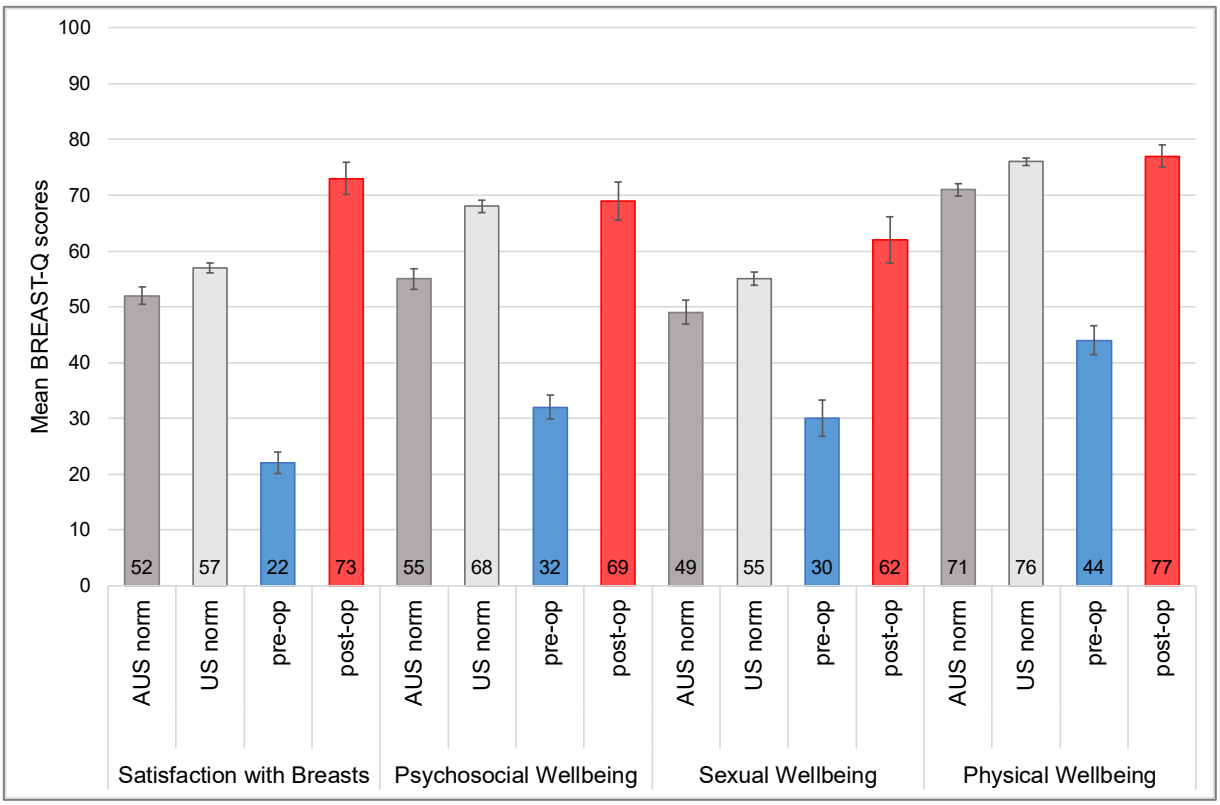


Figure 4.5 Comparison of surgical patient group mean BREAST-Q scores before and after reduction surgery to normative scores for Australia and the United States.

Error bars represent 95% confidence intervals.

Mean BREAST-Q scores from "satisfaction" scales that are captured in the post-operative version are presented in Figure 4.6. High levels of satisfaction were observed across all scales included in the post-operative version. As an example, the mean score for overall 'Satisfaction with Outcome' was 87-points at 12-months following surgery.

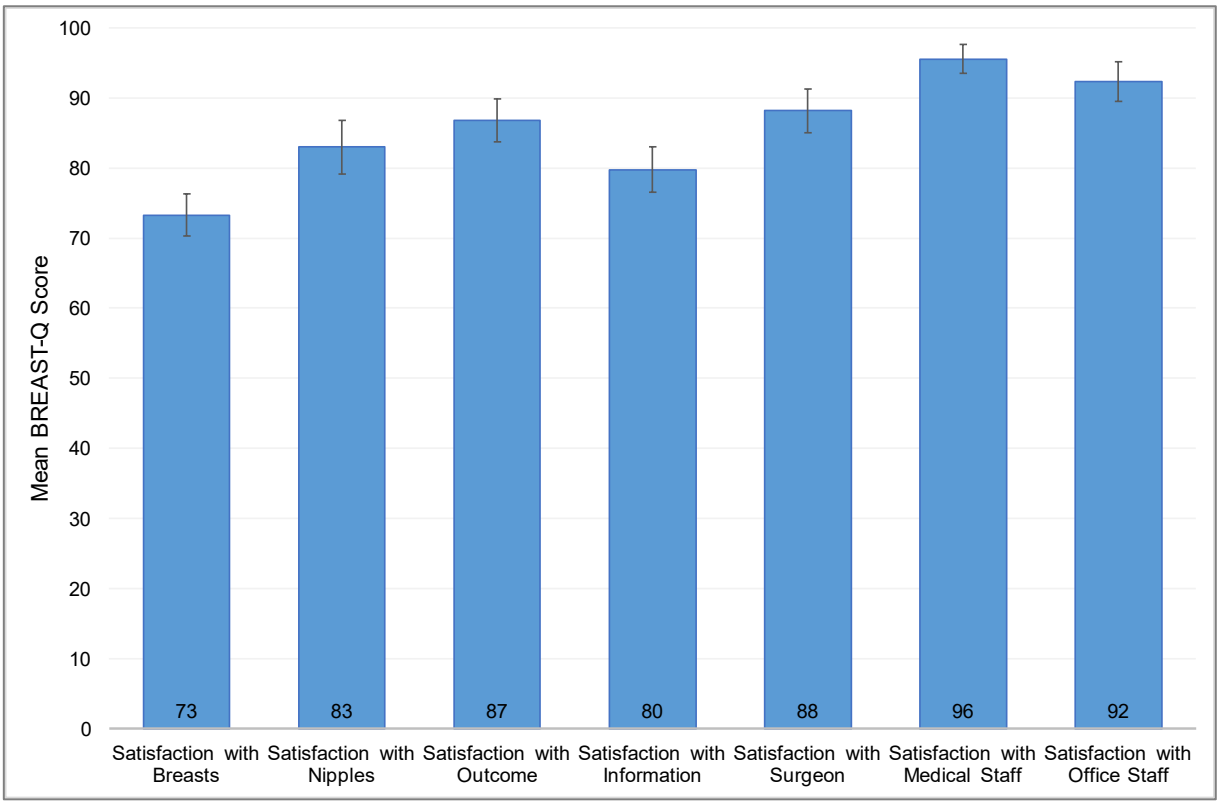


Figure 4.6 Post-operative only BREAST-Q Reduction Module satisfaction scale scores. Error bars represent 95% confidence intervals.

Results of the Pearson correlation indicated that there was a strong, positive association between Satisfaction with Outcome and Satisfaction with Breasts ($r = 0.7$; $p < 0.001$), Satisfaction with Surgeon ($r = 0.7$; $p < 0.001$) and Satisfaction with Information ($r = 0.6$; $p < 0.001$) (Table 4.6). Weak positive correlations were observed between Satisfaction with Outcome and the remaining BREAST-Q scales.

Table 4.6 Correlation between Satisfaction with Outcome and post-operative BREAST-Q scales

Scale	Pearson's r	*p* value
Satisfaction with Breast	0.7	< 0.001
Psychosocial Wellbeing	0.3	0.001
Sexual Wellbeing	0.3	0.001
Physical Wellbeing	0.4	< 0.001
Satisfaction with Information	0.6	< 0.001
Satisfaction with Nipples	0.4	< 0.001
Satisfaction with Surgeon	0.7	< 0.001
Satisfaction with Medical Staff	0.3	< 0.001
Satisfaction with Office Staff	0.2	0.013

When considering 12-month outcomes, no differences in 'Satisfaction with Outcome' BREAST-Q scores were found between patients who experienced a complication (mean 85.1, SD 16.6) and those who did not (mean 87.6, SD 18.0). Participants aged 40 years and older (mean 90.0, SD 13.6) had significantly higher mean Satisfaction with Outcome scores than younger participants (mean 82.5, SD 21.3; $p = 0.015$). Patients with a higher body mass index of 30 kg/m^2 or greater were found to have significantly higher outcome scores (Table 4.7). Scores were not significantly different between participants who met traditional insurance criteria requirements (Schnur sliding scale and the 500g minimum rule) and those who did not (Table 4.7).

Table 4.7 Validity of traditional insurance selection criteria for coverage of breast reduction surgery and 'Satisfaction with Outcome' BREAST-Q Scores

		Satisfaction with Outcome			
		n	**Mean**	**SD**	***p* value**
BMI (kg/m^2)	<30	47	82.8	15.6	0.046
	≥30	85	88.9	18.2	
Eligible by Schnur Sliding Scale 22 percentile criterion?†	Yes	81	88.1	14.7	0.394
	No	49	85.8	21.2	
Eligible by 500 g per breast Minimum Rule?‡	Yes	73	88.2	14.8	0.324
	No	57	85.3	20.4	

† Source: Schnur et al., 1991.

‡ Source: Seitchik, 1995.

4.4 Discussion

Health-related quality of life (HRQoL) outcome studies reported from the patient's perspective provide an important measure of the impact of a health condition and the success of surgical interventions (Brazier et al., 2017). Research studies using generic HRQoL instruments such as the Short Form-36 (SF-36) have highlighted that breast reduction surgery is of significant benefit to women with breast hypertrophy, providing relief of symptoms and improved quality of life, often to a level greater than that of the general population (Behmand et al., 2000, Blomqvist and Brandberg, 2004, Collins et al., 2002, Kececi et al., 2015, Klassen et al., 1996, Miller et al., 2005, O'Blenes et al., 2006, Saariniemi et al., 2008a, Shakespeare and Cole, 1997). However, it has been found that whilst generic instruments play an important complementary role in patient-reported outcome studies, they may not be sensitive or responsive enough to detect changes as a result of surgery or to capture all aspects of outcome after breast surgery (Pusic et al., 2007a). The development of validated condition-specific patient-reported outcome instruments such as the BREAST-Q have facilitated outcome studies exploring the unique outcomes of breast surgery from the patients' perspective (Pusic et al., 2009).

Previous outcome studies have utilised the BREAST-Q Reduction module to explore patient satisfaction and health-related quality of life in women with breast hypertrophy. In the largest retrospective study to date, Cogliandro et al. utilised the BREAST-Q to report high levels of patient satisfaction and wellbeing following breast reduction surgery (Cogliandro et al., 2017a). However, retrospective studies such as this are limited by their inability to provide pre-operative health-related quality of life levels and therefore assume that all respondents had an approximately equal baseline level of satisfaction and wellbeing before surgery (Andrade et al., 2018, Carty et al., 2012, Derby et al., 2016, Gonzalez et al., 2012, Krucoff et al., 2019, Menéndez-Cardo et al., 2017). Furthermore, the broad range of time since surgery could have affected patient responses in these studies. Whilst several prospective studies demonstrate a statistically significant improvement in BREAST-Q scores following reduction mammaplasty, most are limited by a relatively small sample size and in some studies there was minimal overlap in patients who completed the BREAST-Q at each study time point (Cohen et al., 2016a, Coriddi et al., 2013).

Although no known magnitude has previously been determined to establish a minimal clinically important difference for the change in BREAST-Q Reduction module scores following surgical intervention, a rule of thumb of a 10-point change on 100-point quality of life scales (King, 1996) or one-half a standard deviation has been suggested as a default value for patient-perceived important change on health-related quality of life measures (Cano et al., 2014, Norman et al., 2003). Whereas minimal important difference estimates have been described for the augmentation module (Cano et al., 2014) and the reconstruction module (Voineskos et al., 2020) of the BREAST-Q, estimates for the reduction module remain undetermined. This study is the first to describe a minimal important difference estimate for the reduction module of the BREAST-Q, enhancing the interpretability of scores for both patients and clinicians as to what represents a meaningful change. Accordingly, results from this study demonstrate that reduction mammaplasty is of significant health benefit to women with symptomatic breast hypertrophy and provides a clinically important improvement in all areas of patient satisfaction and health-related quality of life. Furthermore, this study provides evidence that the considerable health benefits of reduction mammaplasty are comprehensive and the marked improvement in satisfaction and quality of life is experienced by patients regardless of characteristics including body mass index, age or a minimum resection. Additionally, patients with a higher body mass index and older women who may be ineligible for surgery according to restrictions in some jurisdictions were found to have an even greater level of improvement in satisfaction with breasts, physical wellbeing and psychosocial wellbeing than their respective comparison groups. The surgical cohort were not biased by restrictions that previous studies have reported based on body mass index or resection weight and therefore includes a broad spectrum across these variables (Andrade et al., 2018, Cabral et al., 2017a, Eggert et al., 2009, Freire et al., 2004, Lewin et al., 2019, Mello et al., 2010, Miller et al., 2005, Thoma et al., 2013, Thoma et al., 2007). No differences were found in improvement in

quality of life between those patients meeting traditional insurance cut-offs including Schnur sliding scale and the 500-gram per breast minimum rule and those who did not. This study therefore supports previous findings that there is no evidence or rationale to justify any policy that restricts funding for reduction mammaplasty based on arbitrary cut-offs for body mass index or a minimum weight of reduction (Chao et al., 2002, Collins et al., 2002, Kerrigan et al., 2002, Nguyen et al., 2008, Spector et al., 2008, Strong and Hall-Findlay, 2015, Thoma et al., 2007, Wagner and Alfonso, 2005).

Despite over one-third of women experiencing a surgical complication, there were no differences in either the change in scores in all four BREAST-Q scales or with the overall satisfaction with outcome of surgery between those patients who experienced a post-operative complication and those who did not. This finding supports the results described in chapter 2 using the SF-36 instrument and highlights that the overall health benefits and improvement in quality of life gained by women following breast reduction surgery appear to compensate for the negative impact of post-operative complications following surgery in the majority of cases.

This study found that women reported high scores for satisfaction with outcome following surgery. This BREAST-Q scale is important as it represents the overall level of patient satisfaction with the results of surgery. Post-operative Satisfaction with Outcome was found to be greater in participants with a higher BMI and in older women than their respective comparison groups. In contrast, eligibility by traditional insurance requirements including the Schnur sliding scale or 500-gram minimum rule was not found to be predictive of satisfaction with outcome. These findings strongly refute the validity of traditional selection criteria for coverage by insurance providers or restrictions on access to surgery based on body mass index and a minimum resection weight.

Overall patient Satisfaction with Outcome following surgery was found to be strongly correlated with Satisfaction with Surgeon, Satisfaction with Breasts and Satisfaction with Information scales. Conversely, only weak associations were observed with remaining BREAST-Q scales. These findings highlight the central importance of the doctor-patient relationship and managing patient expectations (Yip et al., 2015). Our findings confirm those of Coriddi and colleagues who reported that satisfaction with outcome was strongly correlated with satisfaction with breast appearance (Coriddi et al., 2013).

The comparison of generated norms to BREAST-Q data from participants in the surgical cohort confirmed that breast hypertrophy represents a significant health impairment to women, with pre-operative scores significantly lower in all areas of satisfaction and health-related quality of life. At one year following reduction mammaplasty, mean scores significantly increased across all BREAST-Q scales to levels at least that of the norm. This finding demonstrates the long-term health benefits and success of breast reduction surgery in bringing satisfaction and quality of life to

levels of the general female population. This study facilitated the comparison of normative BREAST-Q data to a prospective study of women undergoing reduction surgery and therefore addresses previous gaps in the literature (Mundy et al., 2017c).

A potential limitation of this study is the administration of the BREAST-Q questionnaire to the surgical cohort at a post-operative time point of 12 months. Whilst this has affirmed the long-term benefits of breast reduction surgery on patient satisfaction and HRQoL, for comparative purposes the addition of a shorter post-operative time point may also have been informative. Secondly, estimation of the minimal important difference was limited to the use of distribution-based approaches in the absence of a clinical anchor; existing studies have shown that using a combination of distribution-based and anchor-based approaches in a process of triangulation provides the most accurate estimates (Revicki et al., 2008).

Strengths of this study include the prospective design and relatively large sample size for the surgical cohort. The post-operative outcomes described were at 12 months, beyond the convalescence period following surgery, and therefore represent an appropriate measure of long-term outcomes for comparison to population norms. This study is the first to describe a minimal important difference estimate for the reduction module of the BREAST-Q, providing a valuable threshold as to what represents a clinically meaningful change. Furthermore, the generation of corresponding population-specific normative BREAST-Q data enabled an accurate comparison for the interpretation of health-related quality of life between surgical patients and population norms.

4.5 Conclusion

This study demonstrates that breast reduction surgery significantly improves the breast-related satisfaction and health-related quality of life in women. Women with breast hypertrophy presenting for reduction mammaplasty have a significant health burden and reduced quality of life, which is significantly improved following surgery to levels of the general population. This study provides strong evidence to support the health benefits and clinical effectiveness of breast reduction surgery and establishes that indications for surgery should not be restricted to women who meet traditional insurance coverage based on body mass index or a minimum resection.

5. LONG-TERM OUTCOMES OF BREAST REDUCTION SURGERY

5.1 Introduction

Previous studies have described outcomes following breast reduction surgery using validated patient-reported outcome measures (PROMs) to assess health-related quality of life (HRQoL); however, the majority of these have been limited to a relatively short-term follow-up of up to 12-months after surgery. Whilst findings from these studies are important, there remains a need to evaluate patient-reported outcomes beyond the short-term to understand the full health benefits and effectiveness of surgery.

Of the existing studies evaluating patient satisfaction and health-related quality of life outcomes in the longer-term following surgery, few have been of prospective design (Blomqvist and Brandberg, 2004, O'Blenes et al., 2006, Saariniemi et al., 2011b); and retrospective studies remain the primary source of research output in the literature (Bai et al., 2019, Carty et al., 2012, Cogliandro et al., 2017a, Gonzalez et al., 2012, Hermans et al., 2005, Janik et al., 2019, Krucoff et al., 2019, Menéndez-Cardo et al., 2017). However, these studies are limited by their design and by the absence of baseline assessments of patient satisfaction and quality of life for which to compare long-term outcomes following surgery. Consequently, these studies are unable to assess whether or not levels of health-related quality of life in patients who underwent surgery several years prior remain stable or return to baseline levels in the longer-term. Additionally, these studies assume that all women presenting for breast reduction surgery have equal levels of wellbeing and health-related quality of life.

Finally, the prospective long-term assessment of patient-reported outcomes following breast reduction surgery using validated condition-specific outcome measures has yet to be explored in the literature. The use of the BREAST-Q patient-reported outcome instrument (Pusic et al., 2009) in this study provides valuable information for evaluating and gaining a better understanding the long-term outcomes specifically related to breast hypertrophy and breast reduction surgery.

This study aims to build on the 12-month patient-reported outcomes from the original prospective cohort study (described in Chapter 2 and Chapter 4) by evaluating the long-term health benefits and patient satisfaction up to 12 years following breast reduction surgery. To ensure a consistent and comprehensive comparison of long-term outcomes after surgery, a combination of both generic and condition-specific validated patient-reported outcome measures were administered as per the original study. The goals of this study were therefore to evaluate the long-term outcomes of breast reduction surgery, and to compare these levels of health-related quality of life several years after surgery to country-specific population reference data. It is anticipated that information

from the present study will inform clinicians, patients, and health care funders and providers about the expected long-term quality of life benefits of surgery and further support the clinical effectiveness of surgery for women with symptomatic breast hypertrophy.

5.2 Participants and methods

5.2.1 Participant recruitment

A long-term follow-up study was conducted within the Department of Plastic and Reconstructive Surgery at Flinders Medical Centre between March and August of 2019. Eligible participants were identified from the study database of women who underwent bilateral breast reduction surgery and consented to participate in the original prospective cohort study with 12-month follow-up detailed in Chapter 2 and Chapter 4. Inclusion criteria included women aged 18 years and above who consented to participate in the original study and underwent breast reduction surgery. Exclusion criteria were: participants who did not proceed to bilateral breast reduction surgery; participants who had withdrawn from the original study; participants who were identified from the electronic hospital system as deceased; and participants who were identified from the electronic hospital system as having had a breast cancer diagnosis. Ethics and governance approval were obtained for this study from the local Southern Adelaide Clinical Human Research Ethics Committee (SAC HREC approval number 299.18) (Appendix N).

For this long-term follow-up study, demographic information for potential participants was accessed from the original study database and checked for updated information and eligibility through the electronic hospital system. A letter of invitation (Appendix O), participant information sheet (Appendix P) and study questionnaires were mailed to eligible participants. Participants who were willing to complete and return study questionnaires by mail consented to participate in this study. A follow-up phone call was made to non-responders in an attempt to ascertain their reasons for non-response or to obtain permission to mail out a subsequent study questionnaire pack if required.

5.2.2 Patient-reported outcome measures

The validated patient-reported outcome measures selected for this study were the same questionnaires introduced and discussed in detail in Chapter 2 and Chapter 4. In brief, the Short Form-36 version 2 (SF-36v2) (Appendix D) and BREAST-Q Reduction module post-operative version (Appendix I) were used to capture patient-reported satisfaction and health-related quality of life. The BREAST-Q and SF-36 instruments provide a transformed score on a scale between 0 and 100, with higher scores representing greater satisfaction or quality of life. The Multidimensional Body-Self Relations Questionnaire (MBSRQ) (Appendix E) was used for the assessment of self-attitudinal aspects of the body-image and weight-related constructs. MBSRQ scales were calculated on a scale between one and five, with a higher score on orientation scales

indicating a greater emphasis on one's looks or appearance and higher scores on evaluation scales indicating a person feels more satisfied in relation to the construct (i.e. appearance, fitness or health) (Cash, 2000).

Comparisons were made between long-term follow-up outcome scores and normative values for each of the validated patient-reported outcome instruments used in this study. For the BREAST-Q, general Australian female population reference values were generated and were described previously in Chapter 3. Normative data from the general female Australian population for the SF-36v2 were obtained from the 2008 South Australian Health Omnibus Survey dataset (Marin et al., 2009, Population Research and Outcome Studies Unit, 2008), with scores for each subscale weighted to correspond to the age distribution of the study participants. MBSRQ normative scores for females have been previously published by the developers of the instrument (Cash, 2000).

5.2.3 Adjunct questionnaires

A supplementary customised questionnaire was included to assess long-term patient satisfaction and outcomes following breast reduction surgery and to obtain relevant participant socio-demographic information. Participants were asked a series of questions including: (1) whether they would choose to have breast reduction surgery again if they had their time over; (2) whether or not surgery has alleviated the symptoms due to having large breasts; (3) whether they would recommend surgery to a relative or friend; (4) whether any further surgery was performed on their breasts since the original breast reduction surgery; (5) whether they experienced any new chronic/long-term health issues or a worsening of an existing health issue since surgery; and (6) current height, weight and bra cup size.

A standard issue hospital patient health questionnaire was administered to capture comprehensive information of self-reported health issues and medical co-morbidities (Appendix Q).

5.2.4 Statistical analysis

Descriptive statistics including mean, standard deviation and 95% confidence interval were computed for continuous socio-demographic variables and health-related quality of life outcome scores. Categorical variables were presented as counts and percentages. Participant characteristics were analysed using an independent *t*-test for continuous variables or a χ^2 test for categorical variables. Linear mixed-model analysis was used to assess the significance of changes in HRQoL scores for the surgical cohort over time (pre-operatively, 3-, 6-, 12-months post-operatively, and long-term post-operative follow-up), where the dependent variable was each individual health-related quality of life scale and time was the fixed effect. An independent *t*-test was used to compare long-term outcome scores between groups, or when comparing long-term outcomes with normative population reference scores. An analysis of covariance (ANCOVA) was used to assess long-term patient-reported outcome scores with participant characteristics

(categorical) as a fixed-factor and baseline scores as a covariate.

Not all participants in the original study who were assessed following surgery agreed to participate in this long-term follow-up study. To evaluate selection bias, a χ^2 test and independent *t*-test were used in a comparison of participant characteristics of responders and non-responders.

Statistical analyses were performed using SPSS v25.0 statistical software (IBM Corp., Armonk, N.Y.) and a *p*-value of less than 0.05 was considered statistically significant.

5.3 Results

5.3.1 Study participants

Participant recruitment and study completion rates are summarised in Figure 5.1. In summary, a total of 231 participants who remained enrolled at the completion of the original prospective study (Chapter 2) were screened for eligibility. Of these, 14 potential participants were excluded: 4 had a breast cancer diagnosis; 3 were deceased; 2 had undergone other types of breast surgery; and 5 were omitted due to ongoing psychological issues (1 hospitalised in a drug dependency facility and 4 with recent hospitalisations for psychiatric admissions). Therefore, a total of 217 eligible participants were invited to participate in this long-term follow-up postal questionnaire survey. Of these, 103 participants completed and returned study questionnaires and were included in the long-term follow-up cohort, yielding a total response rate of 47.5%.

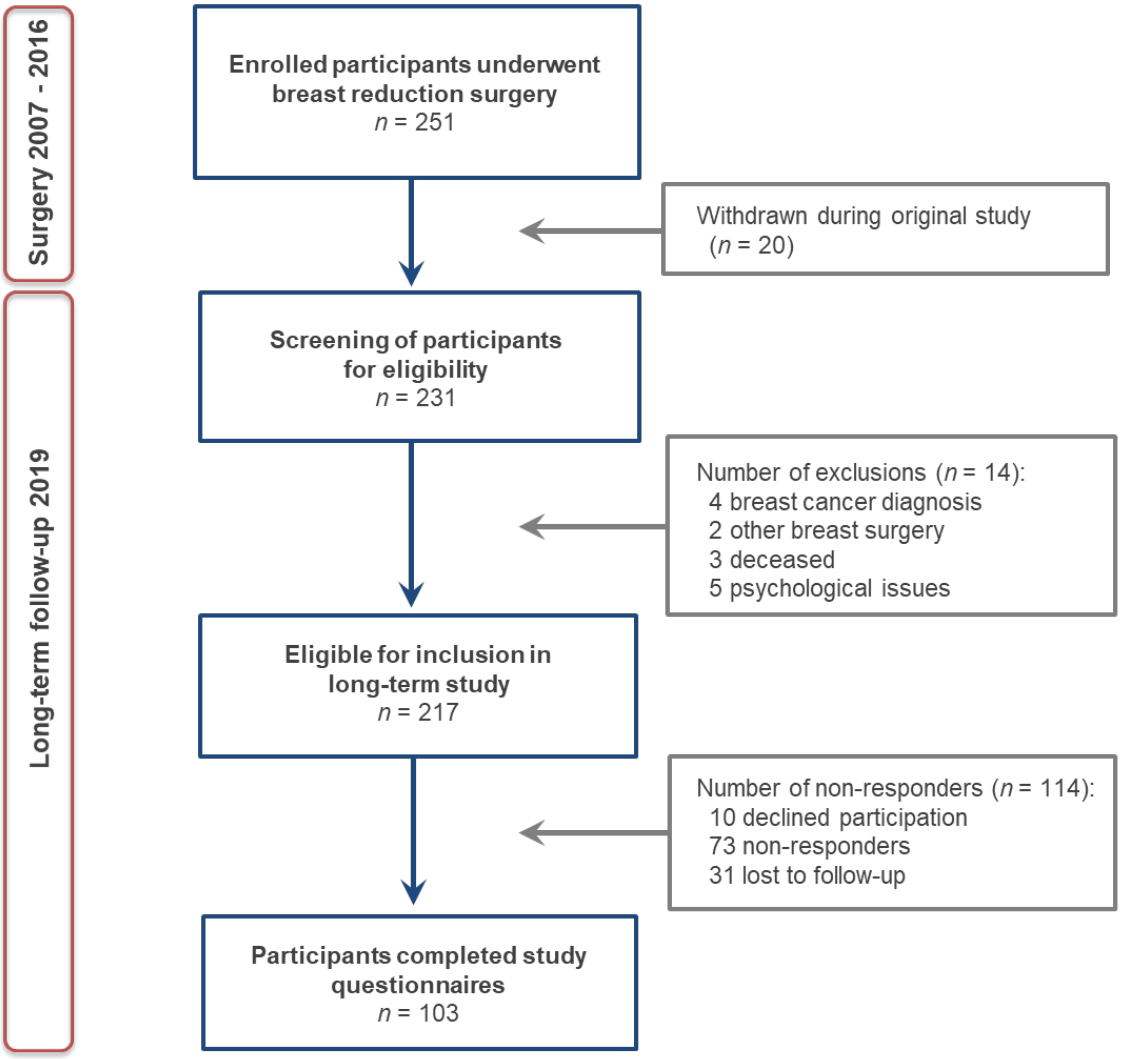


Figure 5.1 Study flow-chart

5.3.2 Participant characteristics

Participant demographics for those in the surgical cohort who consented to the long-term follow-up study are summarised in Table 5.1. Median age at follow-up was 48 years (range, 22 to 81 years) with a median follow-up time since surgery of 6.0 years (range, 3 to 12 years). The mean body mass index at follow-up was 32.0 ± 6.2 kg/m^2, with the majority of participants (52%) classified as obese (≥30 kg/m^2). The proportion of participants reporting the presence of medical co-morbidities at the long-term follow-up are presented in Table 5.1 and were as follows: diabetes (8%), hypertension (12%), asthma (22%), chronic pain (20%) and mental health problems including anxiety (19%) and depression (20%).

Table 5.1 Participant characteristics

Characteristic	Value (%)
Study number, *n*	103
Age at surgery, years	43.3 ± 13.6
Median (range)	42 (18 to 73)
Current age, years	
Mean ± SD	49.7 ± 13.6
Median (range)	48 (22 to 81)
Time since surgery, years	
Mean ± SD	6.8 ± 2.5
Median (range)	6.0 (3 to 12)
BMI, kg/m^2	
Mean ± SD	32.0 ± 6.2
Obesity status	
Non-obese (<30 kg/m^2)	40 (39)
Obese (≥30 kg/m^2)	53 (52)
Missing	10 (10)
Bra cup size	
A	0 (0)
B	3 (3)
C	28 (28)
D	31 (30)
DD	18 (18)
>DD	16 (16)
Missing	7 (7)
Co-morbidities (*n* = 93)	
Diabetes	
No	85 (83)
Yes	8 (8)
Hypertension	
No	81 (79)
Yes	12 (12)
Asthma	
No	70 (68)
Yes	23 (22)
Chronic pain	
No	72 (70)
Yes	21 (20)
Anxiety	
No	73 (71)
Yes	20 (19)
Depression	
No	72 (70)
Yes	21 (20)

Values are numbers (percentages) unless stated otherwise.

5.3.3 Non-responders

Participant characteristics were compared between those who elected to participate by returning study questionnaires and those who either did not respond or declined to participate in the long-term follow-up study. Demographic and clinical characteristics were similar between responders and non-responders, with no significant differences observed in relevant variables including age at surgery, body mass index, and amount of breast tissue resected at surgery, or current age at long-term follow-up. Table 5.2 provides a summary of these findings.

Table 5.2 Comparison of participant characteristics between responders and non-responders

	Mean (SD)		Difference in means (95% CI)	*p*- value[†]
	Responders (*n* = 103)	Non-responders (*n* = 114)		
Age at surgery, y	43.3 (13.6)	41.2 (12.5)	2.1 (-1.4 – 5.6)	0.25
BMI, kg/m^2	32.2 (5.9)	33.6 (5.6)	1.33 (-0.2 – 2.9)	0.09
Resection weight, g	1259 (693)	1430 (821)	169 (-43.8 – 383.4)	0.12
Age (long-term), y	49.7 (13.6)	48.3 (13.3)	1.43 (-2.2 – 5.0)	0.44

[†] Using an independent samples *t*-test.

5.3.4 Long-term patient-reported outcome scores

5.3.4.1 Short Form-36

Summary statistics for SF-36 subscale and summary scores measured in a long-term outcome assessment for women who underwent bilateral breast reduction surgery are presented in Table 5.3. A comparison between SF-36 scores up to 12 months post-operative from the original study and long-term post-operative scores showed that scores remained stable and significantly higher than baseline over time, with no significant differences found in all eight SF-36 subscales or physical and mental summary scales (Figure 5.2). When compared with previously published age-adjusted normative data for the female Australian population (Marin et al., 2009), long-term SF-36 scores for women who underwent surgery several years prior remained comparable and no significant difference was found across seven of the eight SF-36 scales or physical and mental summary scales ($p > 0.05$). In contrast, mean scores for 'bodily pain' at the long-term review were slightly lower than normative values, with a mean difference of 5.7 points (95% CI, 1.24 to 10.2; $p = 0.02$).

Table 5.3 Mean (SD) SF-36 scores for surgical participants over time in comparison to normative data

	Normative‡	Pre-operative	Post-operative			
SF-36 scale	**(*n* = 1551)**	**(*n* = 209)**	**3 months (*n* = 190)**	**6 months (*n* = 181)**	**12 months (*n* = 191)**	**Long-term (*n* = 103)**
Physical function	84.2 (19.1)	61.0 (25.4)	80.1 (22.3)	80.8 (24.2)	83.4 (22.1)	82.6 (21.5)
Role physical	82.0 (24.8)	56.0 (28.3)	79.5 (23.7)	81.1 (25.4)	81.3 (25.1)	81.6 (24.7)
Bodily pain	73.0 (21.4)	38.5 (21.5)	67.4 (24.1)	67.6 (27.6)	71.6 (25.9)	67.4 (24.7)*
General health	70.2 (22.2)	57.9 (21.7)	69.1 (19.8)	69.5 (19.8)	70.4 (19.1)	68.1 (21.8)
Vitality	57.3 (20.9)	39.7 (20.2)	57.7 (20.4)	58.6 (19.1)	58.9 (19.7)	57.4 (19.4)
Social function	82.6 (24.3)	57.1 (27.9)	78.8 (25.9)	79.4 (25.9)	81.4 (23.4)	82.4 (23.4)
Role emotional	88.3 (20.3)	61.7 (28.9)	80.1 (25.1)	82.3 (23.1)	84.6 (22.2)	85.2 (22.9)
Mental health	77.0 (18.2)	59.8 (20.2)	73.7 (18.7)	73.8 (18.4)	74.3 (18.6)	73.6 (18.8)
Physical Component Score	49.7 (9.7)	39.7 (9.7)	48.9 (9.2)	49.0 (10.3)	49.9 (9.9)	48.9 (9.6)
Mental Component Score	47.6 (11.4)	37.0 (13.2)	45.4 (11.9)	45.7 (11.5)	46.2 (11.6)	46.7 (11.5)

‡ Age-standardised normative data for females from the South Australian Health Omnibus Survey (SAHOS) 2008 (Marin et al., 2009).

* denotes significant difference between normative and long-term SF-36 scores ($p < 0.05$).

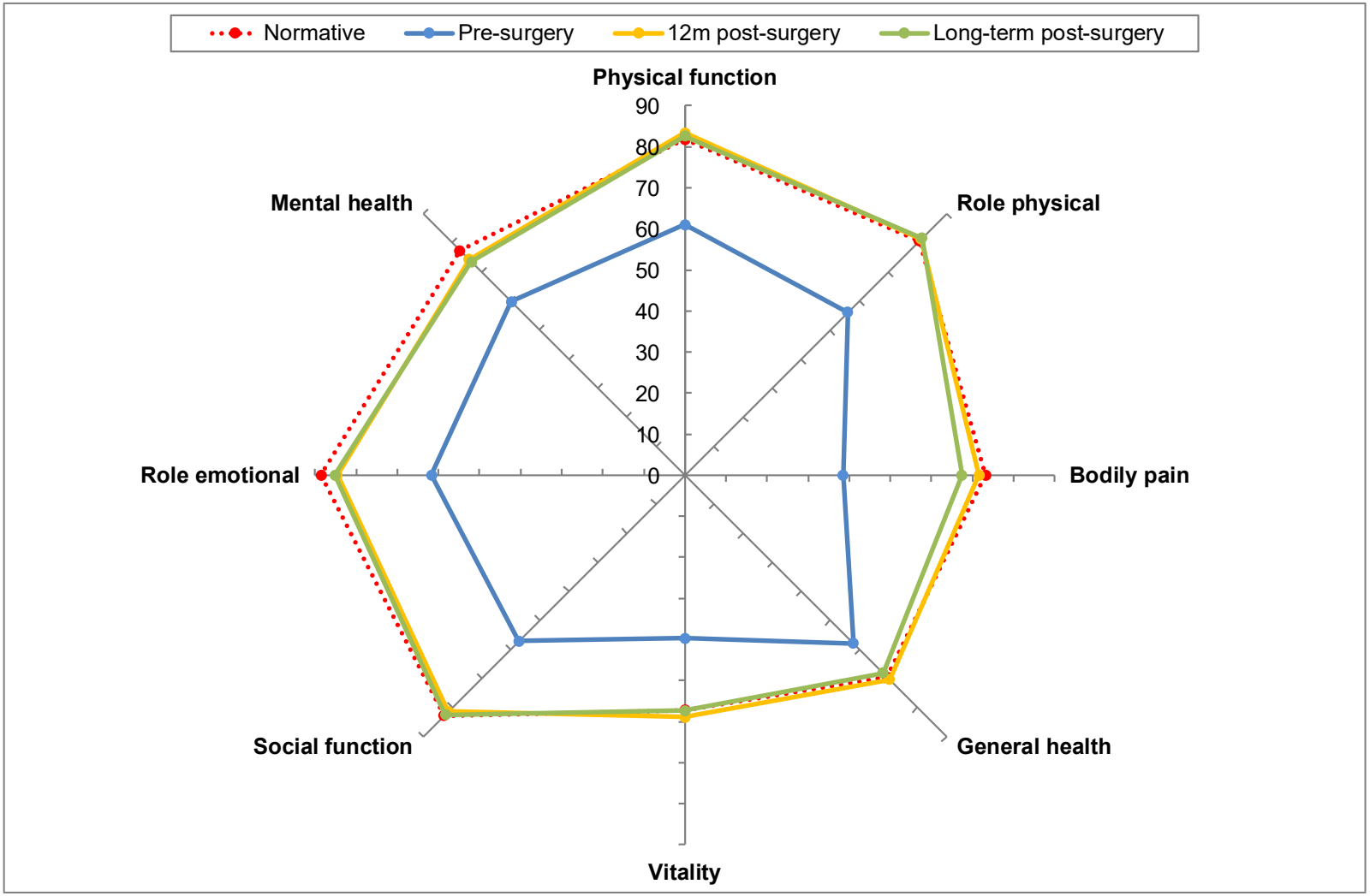


Figure 5.2 Mean SF-36 subscale scores over time compared to female general population reference values

5.3.4.2 BREAST-Q

Mean BREAST-Q scores obtained pre-operatively and 12 months post-operatively (Chapter 4) were compared to long-term outcome scores and are presented in Table 5.4. As described in the previous study, statistically significant improvements were observed when comparing baseline to 12 months following surgery across all four BREAST-Q scales measured pre- and post-operatively ($p < 0.001$). In this long-term follow-up study, mean BREAST-Q scores were found to remain stable between 12 months post-operative and the long-term assessment, with no significant differences observed across all scales: satisfaction with breasts (mean difference, -3.1; 95% CI, -7.5 to 1.3; $p = 0.27$); psychosocial wellbeing (mean difference, 1.2; 95% CI, -3.8 to 6.2; $p = 0.61$); sexual wellbeing (mean difference, 3.8; 95% CI, -2.0 to 9.6; $p = 0.19$); and physical wellbeing (mean difference, -0.3; 95% CI, -3.6 to 3.0; $p = 0.72$) (Table 5.4 and Figure 5.3). Mean BREAST-Q scores at long-term follow-up remained significantly higher than baseline levels in all four scales ($p < 0.001$). In comparison to the normative data generated from women within the Australian general population (Chapter 3), long-term outcome scores remained stable and at levels above population norms (Figure 5.3).

Table 5.4 Summary of mean (SD) BREAST-Q scores in surgical participants over time

	Normative†	**Pre-operative**	**Post-operative**	
Scale	**(*n* = 513)**	**(*n* = 132)**	**12 months (*n* = 132)**	**Long-term (*n* = 103)**
Satisfaction with Breasts	51.9 (17.3)	21.9 (10.9)	73.3 (17.3)	70.2 (16.4)
Psychosocial Wellbeing	55.0 (21.8)	32.4 (12.8)	69.3 (19.8)	70.5 (18.3)
Sexual Wellbeing	48.5 (24.0)	29.3 (18.2)	60.6 (23.3)	64.4 (20.9)
Physical Wellbeing	71.2 (13.1)	44.0 (15.5)	76.6 (12.1)	76.3 (13.6)

† Normative BREAST-Q scores derived from the Australian general population (Chapter 3).

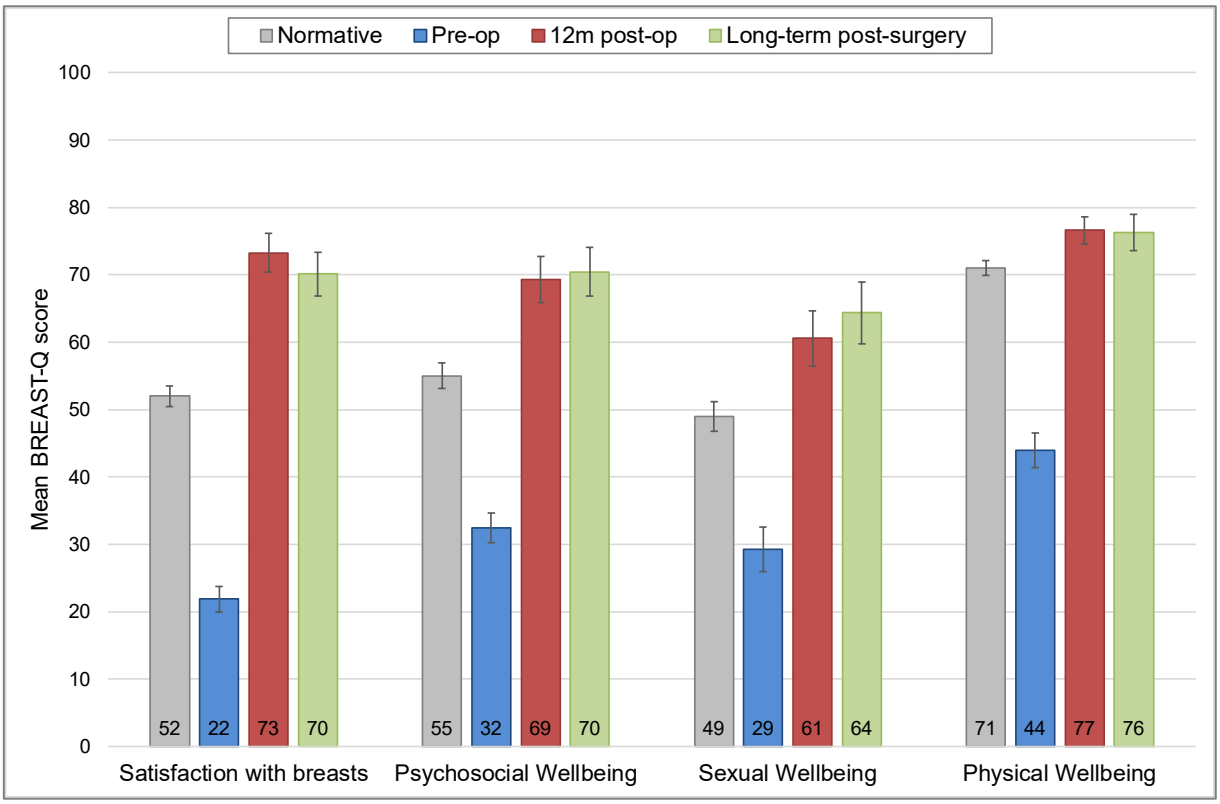


Figure 5.3 Mean BREAST-Q scores for surgical participants over time in comparison to population norms

Error bars represent 95% confidence intervals.

Table 5.5 presents a comparison of scores reported exclusively in the post-operative version of the BREAST-Q Reduction module between surgical participants at 12 months following surgery and long-term follow-up. Mean scores remained stable in the long-term across all six BREAST-Q scales measured post-operatively only, with no significant differences found in satisfaction with outcome, satisfaction with information, satisfaction with nipple, or satisfaction with surgeon, satisfaction with medical staff and satisfaction with office staff scales.

Table 5.5 Summary of post-operative BREAST-Q scale scores in surgical participants

Scale	Mean (SD)		Difference in means (95% CI)	*p*-value
	12 months post-operative	Long-term post-operative		
Satisfaction with outcome	86.7 (17.5)	87.1 (15.8)	0.4 (-3.9 – 4.7)	0.27
Satisfaction with information	79.8 (18.6)	81.8 (17.4)	2.0 (-2.7 – 6.7)	0.17
Satisfaction with nipple	82.3 (22.3)	82.5 (23.2)	0.2 (-5.6 – 6.1)	0.96
Satisfaction with surgeon	88.1 (18.4)	87.6 (19.3)	-0.5 (-5.4 – 4.4)	0.64
Satisfaction with medical staff	95.6 (12.0)	94.7 (12.5)	-0.9 (-4.1 – 2.3)	0.86
Satisfaction with office staff	92.3 (16.4)	94.0 (12.8)	1.7 (-2.2 – 5.6)	0.60

5.3.4.3 MBSRQ

Mean MBSRQ scores for women who underwent bilateral breast reduction surgery are summarised in Table 5.6. When compared with scores obtained at the final 12-months post-operatively assessment in the original study (Chapter 2), scores remained stable and were not significantly different in the longer-term follow-up across all MBSRQ scales with the exception of 'appearance orientation' and 'fitness orientation'. Mean scores for these two scales were significantly lower at long-term follow-up, with a mean difference of 0.18 points (95% CI, 0.04 to 0.32; $p = 0.03$) and 0.17 points (95% CI, 0.01 to 0.34; $p = 0.048$), respectively. This finding demonstrates women placed less importance on their appearance and fitness at the long-term follow-up when compared to 12 months post-operatively.

When compared to scores reported pre-operatively, scores remained significantly higher at the long-term follow-up for 'appearance evaluation' (mean difference 0.85; 95%CI, 0.68 to 1.02, $p < 0.001$), 'health evaluation' (mean difference 0.20; 95%CI, 0.06 to 0.34, $p = 0.005$) and 'body areas satisfaction score' (mean difference 0.51; 95%CI, 0.37 to 0.64, $p < 0.001$). In contrast, scores were significantly lower for 'appearance orientation' (mean difference -0.33; 95%CI, -0.48 to -0.18, $p < 0.001$), 'health orientation' (mean difference -0.25; 95%CI, -0.35 to -0.14, $p < 0.001$), and 'self-classified weight' (mean difference -0.19; 95%CI, -0.33 to 0.05, $p = 0.08$). This finding demonstrates that even several years after breast reduction surgery women continued to be more satisfied with their appearance, reported being in better health and were more satisfied with their body than those who did not undergo surgery despite placing less importance on their appearance and health than they did before surgery. The results for the MBSRQ scores at each timepoint are presented in Figure 5.4.

Table 5.6 Comparison of mean (SD) MBSRQ scores over time for surgical participants

	Pre-operative	Post-operative			
Scale	**(*n* = 209)**	**3 months (*n* = 190)**	**6 months (*n* = 181)**	**12 months (*n* = 191)**	**Long-term (*n* = 103)**
Appearance evaluation	1.96 (0.64)	2.81 (0.70)*	2.83 (0.79)	2.87 (0.77)	2.84 (0.81)‡
Appearance orientation	3.57 (0.75)	3.53 (0.60)	3.53 (0.61)	3.50 (0.60)	3.32 (0.59)†,‡
Fitness evaluation	3.10 (0.78)	3.31 (0.79)*	3.30 (0.86)	3.35 (0.80)	3.23 (0.91)
Fitness orientation	2.94 (0.64)	3.03 (0.61)	3.03 (0.65)	3.06 (0.68)	2.89 (0.70)†
Health evaluation	2.99 (0.72)	3.29 (0.78)*	3.34 (0.73)	3.32 (0.75)	3.36 (0.82)‡
Health orientation	3.62 (0.62)	3.44 (0.59)*	3.54 (0.56)	3.50 (0.60)	3.44 (0.65)‡
Illness orientation	3.04 (0.78)	3.14 (0.75)	3.14 (0.80)	3.13 (0.77)	3.14 (0.81)
Body Areas Satisfaction Score	2.47 (0.56)	2.93 (0.61)*	2.99 (0.63)	3.00 (0.62)	2.97 (0.74)‡
Overweight preoccupation	3.31 (0.83)	3.17 (0.85)	3.16 (0.91)	3.23 (0.80)	3.13 (0.85)
Self-Classified Weight	4.14 (0.71)	4.00 (0.64)*	3.98 (0.64)	4.00 (0.62)	3.94 (0.81)‡

* denotes significant difference ($p < 0.05$) between pre-operative & 3-month post-operative scores using linear mixed-model analysis.

† denotes significant difference ($p < 0.05$) between 12-month post-operative and long-term post-operative scores

‡ denotes significant difference ($p < 0.05$) between pre-operative & long-term post-operative scores.

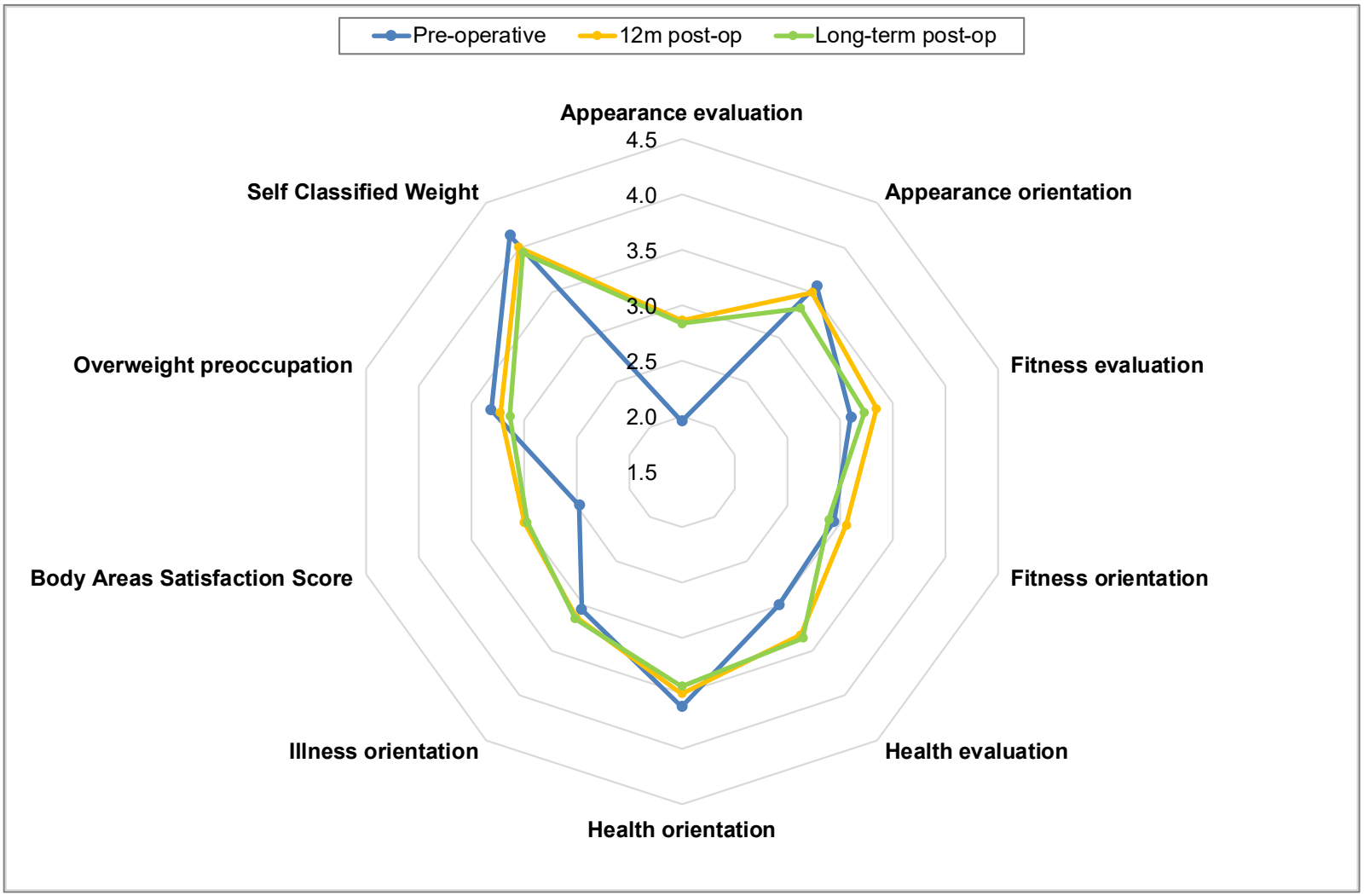


Figure 5.4 Mean MBSRQ scores pre-operatively versus scores at 12 months post-operative and long-term follow-up

5.3.4.4 Adjunct questionnaire

The majority of women (97/103, 94.3%) who underwent breast reduction surgery stated they would have their surgery again, if they had their time over; one participant replied that they would not have surgery again, and two (2/103, 1.9%) responded they were unsure. Three participants in the long-term follow-up study failed to answer the adjunct questionnaire. When asked whether or not breast reduction surgery alleviated the symptoms due to having large breasts, a total of 92 (89.3%) agreed; two participants (1.9%) disagreed; four (3.9%) were unsure; and five (4.9%) did not respond to this question. Most women (96/103, 93.2%) who underwent surgery would recommend it to a relative or friend; two (1.9%) were unsure; five (4.9%) did not respond; with no (0%) participants responding they would not recommend surgery. A total of ten participants (9.7%) stated they had further surgery on their breasts since the original surgery and of these 9 underwent revisional procedures related to the original breast reduction surgery and 1 participant had surgery for the removal of a benign breast lump; 80 (78%) had no further breast surgery; and 13 participants (12.6%) failed to respond to this question. Twenty participants (19%) stated they had experienced a new chronic or long-term health issue, or a worsening of an existing health issue in the time since their breast reduction surgery; 68 (66%) did not; and eight (7.8%) were unsure.

5.3.4.5 Other clinical outcomes

When comparing participant characteristics at baseline prior to surgery (Chapter 2) versus at long-term follow-up, there were no significant differences found in average weight of participants (mean 84.2 versus 84.6 kg, $p = 0.66$) or corresponding body mass index (32.0 versus 32.02 kg/m^2, $p = 0.949$). In contrast, a chi-square test showed that bra cup size remained significantly smaller at the long-term assessment (χ^2 (5) = 29.9, $p < 0.001$) when compared to preoperatively. Frequency distributions for bra cup sizes at baseline in comparison to those reported at the long-term follow-up assessment are presented in Figure 5.5.

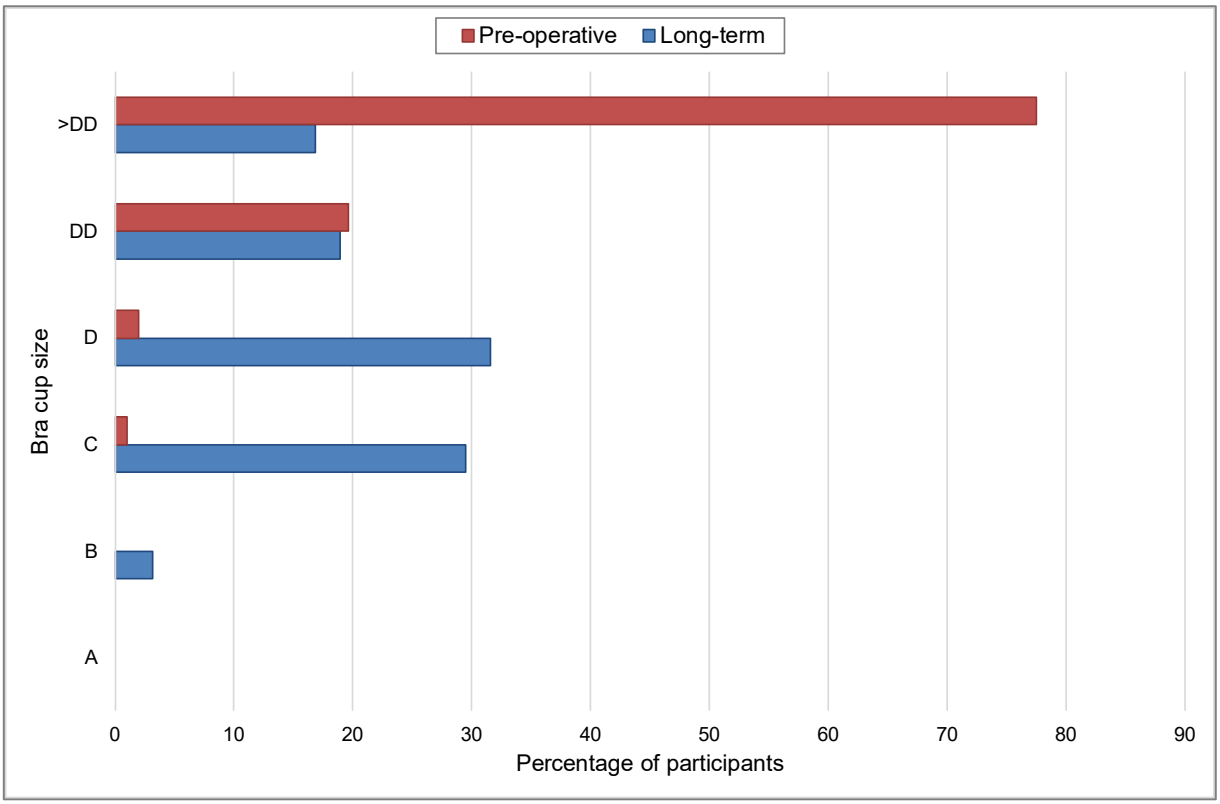


Figure 5.5 Bra cup size frequency distribution at pre-operative compared to long-term follow-up

5.3.5 Factors influencing long-term quality of life

Participants were categorised into the two groups based on BMI at the pre-operative assessment. A one-way ANCOVA was conducted to compare long-term BREAST-Q scores between non-obese (BMI <30 kg/m^2) and obese participants (BMI ≥30 kg/m^2) whilst controlling for baseline BREAST-Q scores. There were no significant differences found in long-term BREAST-Q scores between BMI groups in all scales measured both pre- and post-operatively: satisfaction with breasts, psychosocial wellbeing, sexual wellbeing and physical wellbeing. Summary statistics and mean differences between BMI groups are summarised in Table 5.7.

Table 5.7 Summary of adjusted long-term BREAST-Q scores by BMI category

Scale	Mean (SD)		Difference in means (95% CI)	*p*-value†
	Non-obese (*n* = 38)	Obese (*n* = 63)		
Satisfaction with Breasts	71.1 (15.5)	69.1 (15.2)	-1.9 (-9.5 to 5.6)	0.61
Psychosocial Wellbeing	70.1 (18.3)	71.7 (18.0)	1.5 (-7.6 to 10.6)	0.74
Sexual Wellbeing	68.6 (19.1)	67.1 (18.9)	-1.5 (-12.0 to 8.9)	0.77
Physical Wellbeing	76.2 (12.2)	76.4 (12.0)	0.2 (-5.8 to 6.2)	0.95

Non-obese <30 kg/m^2, obese ≥30 kg/m^2.

† Using an ANCOVA to compare BREAST-Q scale scores between groups after adjustment for preoperative BREAST-Q scores.

Post-operative BREAST-Q scales including satisfaction with outcome, satisfaction with nipple, satisfaction with information, satisfaction with surgeon, satisfaction with medical staff and satisfaction with office staff are not included in the pre-operative module and therefore do not have baseline values to be used as a covariate in the ANCOVA analysis. Therefore, an independent samples *t*-test was conducted to compare long-term BREAST-Q scores between obese and non-obese participants at baseline. There were no statistically significant differences between the two groups in all BREAST-Q scales. These findings are summarised in Table 5.8.

Table 5.8 Summary of unadjusted long-term BREAST-Q scores by BMI category

Scale	Mean (SD)		Difference in means (95% CI)	*p*-value†
	Non-obese (*n* = 38)	Obese (*n* = 63)		
Satisfaction with outcome	85.3 (14.6)	88.2 (16.5)	2.9 (-3.6 to 9.3)	0.38
Satisfaction with information	80.2 (16.1)	82.8 (18.2)	2.6 (-4.5 to 9.7)	0.47
Satisfaction with nipple	85.0 (21.6)	81.0 (24.2)	-4.0 (-13.5 to 5.4)	0.40
Satisfaction with surgeon	86.7 (20.5)	88.2 (18.7)	1.4 (-6.5 to 9.4)	0.72
Satisfaction with medical staff	94.8 (12.6)	94.7 (12.5)	-0.1 (-5.3 to 5.0)	0.95
Satisfaction with office staff	95.2 (12.1)	93.2 (13.2)	-2.0 (-7.2 to 3.3)	0.45

Non-obese <30 kg/m^2, obese ≥30 kg/m^2.

† Using an independent *t*-test to compare BREAST-Q scale scores between groups.

Patient-reported long-term SF-36 subscale and summary component scores were also compared between the two BMI groups using a one-way ANCOVA. While participants with a higher BMI reported lower scores for several subscales, in particular ‘role physical’, ‘bodily pain’ and ‘general health’ compared to participants with a lower BMI, this difference of 5.3-, 7.9- and 6.9-points, respectively, did not reach statistical significance. There were no statistically significant differences were found in all eight SF-36 subscales or physical and mental health summary measures between these groups whilst controlling for baseline SF-36 scores ($p > 0.05$). Table 5.9 provides a summary of the results.

Table 5.9 Summary of adjusted long-term SF-36 scores by BMI category

SF-36 scale	Mean (SD)		Difference in means (95% CI)	*p*-value†
	Non-obese (*n* = 38)	Obese (*n* = 63)		
Physical function	83.5 (19.8)	81.8 (19.5)	-1.7 (-10.0 to 6.6)	0.68
Role physical	85.1 (24.3)	79.8 (24.4)	-5.3 (-15.6 to 5.0)	0.31
Bodily pain	72.1 (24.3)	64.2 (23.2)	-7.9 (-18.2 to 2.3)	0.13
General health	72.2 (21.2)	65.3 (21.0)	-6.9 (-15.8 to 1.9)	0.12
Vitality	57.7 (18.9)	56.9 (18.9)	-0.8 (-8.7 to 7.0)	0.83
Social function	82.6 (22.2)	82.1 (22.0)	-0.5 (-9.8 to 8.7)	0.90
Role emotional	86.3 (22.5)	84.3 (22.6)	-2.0 (-11.4 to 7.4)	0.68
Mental health	73.3 (18.8)	73.5 (18.8)	0.2 (-7.6 to 8.0)	0.96
Physical Component Score	50.6 (8.9)	48.1 (9.0)	-2.5 (-6.4 to 1.3)	0.19
Mental Component Score	46.0 (11.3)	46.9 (11.4)	0.9 (-3.9 to 5.7)	0.71

Non-obese <30 kg/m^2, obese ≥30 kg/m^2.

† Using an ANCOVA to compare SF-36 scale scores between groups after adjustment for pre-operative scores.

The relationship between age and long-term quality of life outcome scores were explored using a one-way ANCOVA, controlling for pre-operative baseline scores. Participants were categorised into two groups according to their age at surgery of less than 40 years and 40 years and above. While older women reported higher scores for 'satisfaction with breasts' and 'psychosocial wellbeing', this difference of 5.3- and 6.0-points did not reach statistical significance (Table 5.10). In summary, there were no statistically significant differences found in long-term outcome scores between these age groups in all dimensions of the BREAST-Q (Table 5.10).

Table 5.10 Summary of adjusted long-term BREAST-Q scores by age category

Scale	Mean (SD)		Difference in means (95% CI)	*p*-value†
	< 40 years (*n* = 31)	≥ 40 years (*n* = 43)		
Satisfaction with Breasts	66.7 (15.0)	72.0 (13.5)	5.3 (-1.9 to 12.5)	0.15
Psychosocial Wellbeing	67.7 (17.2)	73.6 (17.4)	6.0 (-2.2 to 14.2)	0.15
Sexual Wellbeing	67.4 (18.9)	67.9 (18.5)	0.5 (-9.3 to 10.3)	0.91
Physical Wellbeing	74.8 (11.8)	77.4 (11.5)	2.6 (-2.9 to 8.2)	0.35

† Using an ANCOVA to compare BREAST-Q scale scores between groups after adjustment for pre-operative scores.

An independent samples *t*-test was conducted to compare long-term post-operative only BREAST-Q scores between older and younger participants. Older women age 40 years and above were found to have significantly higher scores for 'satisfaction with outcome' when compared to younger women with an average difference of 6.7-points ($p = 0.034$). There were no statistically significant differences in long-term BREAST-Q scores between the two groups in the remaining post-

operative scales. These findings are summarised in Table 5.11.

Table 5.11 Summary of unadjusted long-term BREAST-Q scores by age category

Scale	Mean (SD)		Difference in means (95% CI)	*p*-value
	Age <40 years (*n* = 42)	Age ≥40 years (*n* = 59)		
Satisfaction with outcome	83.2 (17.3)	89.9 (14.2)	6.7 (0.5 to 13.0)	0.034*
Satisfaction with information	79.3 (17.1)	83.6 (17.6)	4.3 (-2.6 to 11.3)	0.220
Satisfaction with nipple	77.9 (25.3)	85.8 (21.2)	7.9 (-1.4 to 17.1)	0.094
Satisfaction with surgeon	84.5 (20.4)	89.9 (18.3)	5.5 (-2.3 to 13.2)	0.164
Satisfaction with medical staff	93.3 (13.9)	95.7 (11.3)	2.4 (-2.6 to 7.4)	0.351
Satisfaction with office staff	92.4 (15.3)	95.2 (10.6)	2.8 (-2.3 to 8.0)	0.277

A one-way ANCOVA was conducted to compare long-term outcome scores using the SF-36 questionnaire between younger and older women, adjusting for baseline values before surgery. Statistically significant differences were observed in 'physical functioning' and 'role physical' scales. Mean scores were 11.2- and 10.3-points lower, respectively, in older women aged 40 years and above at surgery compared to younger women aged less than 40 years. When compared to previously published normative data stratified by age group it was found that this finding was consistent to that of the general population, with older women reporting significantly lower scores for 'physical functioning' and 'role physical' than younger women, with a 14.3 and 9.0-point difference, respectively. There were no statistically significant differences found between age groups in all other dimensions of the SF-36 (Table 5.12).

Table 5.12 Summary of adjusted long-term SF-36 scores by age category

SF-36 scale	Mean (SD)		Difference in means (95% CI)	*p*-value†
	<40 years (*n* = 40)	≥40 years (*n* = 60)		
Physical function	89.1 (18.6)	77.9 (18.4)	-11.2 (-18.9 to -3.5)	0.005*
Role physical	87.9 (23.8)	77.6 (24.0)	-10.3 (-20.1 to -0.6)	0.038*
Bodily pain	70.4 (24.6)	65.0 (24.0)	-5.4 (-15.4 to 4.5)	0.281
General health	66.6 (21.0)	68.7 (21.2)	2.1 (-6.5 to 10.7)	0.626
Vitality	59.7 (19.0)	55.6 (18.7)	-4.2 (-11.8 to 3.5)	0.283
Social function	85.0 (22.8)	80.5 (22.2)	-4.5 (-13.7 to 4.7)	0.332
Role emotional	87.4 (22.5)	83.4 (22.7)	-3.9 (-13.1 to 5.2)	0.395
Mental health	75.6 (19.0)	72.1 (18.7)	-3.5 (-11.2 to 4.2)	0.365
Physical Component Score	51.0 (8.6)	47.7 (8.6)	-3.3 (-6.9 to 0.3)	0.069
Mental Component Score	47.1 (11.4)	46.2 (11.4)	-0.9 (-5.7 to 3.8)	0.703

† Using an ANCOVA to compare SF-36 scale scores between groups after adjustment for pre-operative scores.

* Denotes statistical significance at $p < 0.05$ level.

5.4 Discussion

Patient-reported outcome measures utilised in long-term clinical outcome studies can provide valuable insight into the effectiveness and stability of medical or surgical interventions over time. Findings from this study using a combination of validated generic and condition-specific patient-reported outcome measures demonstrate that the positive health benefits and improved health-related quality of life are sustained for up to 12 years following breast reduction surgery. Furthermore, the comparison of long-term patient-reported outcomes with pre-operative scores demonstrated that health-related quality of life did not deteriorate to levels observed at baseline over time. This is a novel finding as existing outcome studies reporting a long-term follow-up have primarily been retrospective and were therefore unable to address this fundamental question (Bai et al., 2019, Carty et al., 2012, Cogliandro et al., 2017a, Gonzalez et al., 2012, Krucoff et al., 2019, Makki and Ghanem, 1998). In addition, this is the first study to use the BREAST-Q Reduction module to prospectively evaluate patient-reported outcomes beyond 1 year and compare patients' results to normative values; providing valuable insight as to whether patient-reported outcomes specific to breast reduction surgery change over time and in the longer-term.

This study found that years after undergoing breast reduction surgery patients continue to report a greater level of satisfaction and quality of life than levels observed prior to surgery, and in comparison to women within the general population across all BREAST-Q scales. Furthermore, the finding of a high level of long-term satisfaction with outcome is significant as this BREAST-Q scale represents a patient's overall appraisal of the results after surgery. In support of this finding, the majority of women reported a high level of long-term satisfaction and responded in an adjunct questionnaire that they would have surgery again or recommend surgery to a relative or friend; and almost 90 percent of respondents reported that breast reduction surgery had successfully alleviated the symptoms of having large breasts. Finally, this study demonstrates that the significant and long-term improvement in health-related quality of life following surgery is experienced by patients' regardless of patient factors including body mass index and age. In addition, consistent with the finding at the 12-month follow-up in the original study, older women continued to report a higher level of satisfaction with the overall outcome of surgery in the longer-term when compared to younger women.

While existing long-term outcome studies described in the literature using the BREAST-Q Reduction module have provided promising preliminary results, they have all been retrospective and interpretation is therefore limited as there are no baseline values for comparison. Accordingly, it is difficult to make meaningful comparisons to the findings of this prospective longitudinal study. Menéndez-Cardo et al. conducted a retrospective study using the post-operative version of the BREAST-Q to compare outcomes between vertical and inverted-T techniques; they reported a high level of long-term satisfaction with outcome, although scores were lower than those found in this

present study and the absence of any prior timepoint makes further interpretation of these findings difficult (Menéndez-Cardo et al., 2017). In 2019, a retrospective review describing the long-term follow-up of 37 young reduction mammaplasty patients less than 25 years of age using the BREAST-Q was conducted (Krucoff et al., 2019). The authors found that decades after surgery these patients reported high levels of breast-related quality of life when compared to normative population. Unfortunately, the analysis from this study focused on only four of the post-operative scales and therefore did not present information for long-term satisfaction with outcome for comparison; this was also the case in the retrospective study by Cogliandro and colleagues (Cogliandro et al., 2017a). In their 10 year retrospective analysis using the BREAST-Q, Gonzalez and colleagues did assess satisfaction with outcome and found that over 95% of patients were satisfied in the long-term following surgery; however, participants' responses for satisfaction with outcome were incorrectly reported as Likert item responses instead of being transformed to a 0 to 100 scale (Gonzalez et al., 2012). Nevertheless, the results of these aforementioned studies in conjunction with results of the current study provide evidence to demonstrate that breast reduction surgery provides a long-term improvement in quality of life outcomes for women with breast hypertrophy.

In this study, health-related quality of life outcomes as measured by the generic SF-36 instrument were consistent with findings from the BREAST-Q and were found to be stable in the longer-term up to 12 years after surgery and remained significantly higher than baseline levels in all eight subscales and summary measures. Furthermore, scores were equivalent to those from women within the general population in all quality of life scales with the exception of the 'bodily pain'. However, it is likely that this finding is due to ageing and is impacted by life events other than the surgery; with one-fifth of women reporting they had experienced either a new chronic health condition or worsening of an existing health issue since their surgery. These findings are consistent with a previously published study that demonstrated quality of life scores improve following surgery and are stable over time in a shorter-term follow-up. Blomqvist and Brandberg published a prospective study of 39 patients at 1 and 3 years post-operative using the SF-36 and demonstrated improved quality of life was stable at 3 years after surgery with only minor nonsignificant reductions found between 1 and 3 year assessments (Blomqvist and Brandberg, 2004). Notably, the authors also used a supplementary questionnaire assessing pain in six different body locations and found that whilst the reduction of bodily pain was still significantly lower when compared to baseline levels, there was a minor increase in levels of bodily pain between 1 and 3 years assessment, but this did not reach statistical significance. The finding of improved quality of life across all SF-36 scales in the longer-term is also consistent with a study exploring quality of life outcomes with a median follow-up time of 19.1 months following reduction mammoplasty in adolescents and young women aged 12 to 21 years (Nuzzi et al., 2019).

A number of existing studies have demonstrated that women with breast hypertrophy often display

a high level of dissatisfaction with their overall body image (Collins et al., 2002, Cunningham et al., 2005, Kerrigan et al., 2001, Sarwer et al., 1998, Thoma et al., 2013, Thoma et al., 2005). The results of the present study are consistent with this finding. In Chapter 2, patients who underwent breast reduction surgery were found to self-report improved levels of body image and overall evaluation of their appearance and health over a 12-month period. However, to the authors knowledge, no existing studies have assessed body image in women undergoing breast reduction surgery beyond this timeframe. Accordingly, this study demonstrates that the improved levels of body image satisfaction and evaluation of overall health and appearance continue well beyond this timeframe and are sustained for many years after breast reduction surgery. In addition, the finding that women continue to be less focused on their appearance and are more content with most areas of their body when compared to levels observed pre-operatively further demonstrates the ongoing health benefits of surgery.

Findings of this study have demonstrated the long-term health benefits in terms of improved health-related quality of life following breast reduction surgery. However, other factors including the potential for weight loss in the years following surgery and whether or not reduced breast size is sustained in the longer-term are also important outcomes. This study found that women reported wearing significantly smaller bra cup sizes in the long-term than at the pre-operative assessment. In contrast, no significant differences were found in body weight and corresponding BMI in the long-term follow-up after surgery when compared to baseline values. Therefore, although surgery did not result in any long-term weight loss, there was also no increase in average body weight or BMI in the longer-term. Weight gain is influenced by many external factors including lifestyle, diet, physical activity and hormonal changes in aging such as pregnancy and menopausal status; and in Australian women has been shown to steadily increase in younger (average 649g per year) and middle-aged women over time (average 492g per year) (Adamson L, 2007, Australian Longitudinal Study on Women's Health, 2005, Australian Longitudinal Study on Women's Health, 2018, Australian Longitudinal Study on Women's Health, 2019). Accordingly, weight gain in women who underwent breast reduction surgery several years prior was less than the rate observed in the general population over time. These findings are supported by existing studies that demonstrated the majority of patients tend to return to their original body weight up to 5 years following surgery (Bayramicli et al., 2017) or show a tendency towards a slight weight gain but at a slower rate than the general population (Pauzenberger et al., 2014). Whilst other studies have provided evidence contradictory to this, their follow-up was considerably shorter-term at less than two years following surgery (O'Blenes et al., 2006, Singh et al., 2010). Finally, given that this present study found patient satisfaction and quality of life were stable and did not deteriorate in the longer-term following surgery, it further demonstrates that these two factors are often independent of one another.

5.4.1 Strengths and limitations

A strength of this study was the prospective design and long-term follow-up of surgical participants previously enrolled in the original study with a 12-month follow-up (described in Chapter 2 and Chapter 4). Therefore, eligible participants in the present study had baseline preoperative and 12-month follow-up data for comparison to the longer-term outcomes. In addition, this study employed a series of validated generic and condition-specific patient-reported outcome questionnaires and the first study to prospectively assess the long-term outcomes of breast reduction surgery using the BREAST-Q instrument. These factors overcome limitations previously described in the literature describing long-term outcomes based on retrospectively designed studies or prospective studies with a small sample size. Finally, the comparison of long-term patient-reported outcomes to population-specific normative data, including generated population reference data for the BREAST-Q Reduction module described previously (Chapter 3), provides further insight into the expected patient satisfaction and sustained improvement in health-related quality of life following breast reduction surgery when compared to women in the general population.

This long-term outcome study has several potential weaknesses that should be noted. Achieving satisfactory response rates when administering questionnaires by post can present a challenge, with non-response reducing sample size and may introduce bias (Edwards et al., 2002). The follow-up of participants in the present study is incomplete; of the 217 participants from the original study who were eligible for participation in this study, 114 (52.5%) did not participate in the study, reducing study power and raising the possibility of bias. However, socio-demographic and clinical characteristics were found to be similar between responders and non-responders which suggests this long-term cohort provides an accurate representation of the original surgical cohort. Furthermore, this study remained adequately powered with 103 respondents to detect clinically meaningful changes in patient-reported outcomes and is in keeping with response rates reported by other long-term mail-out survey studies in the absence of ongoing contact with participants from their 12-month post-operative follow-up. Finally, the present study reports patient experiences and outcome data from one state, potentially limiting the generalisability of the findings.

5.5 Conclusion

This study assessed the long-term outcomes and patient-reported quality of life in women who underwent bilateral breast reduction surgery for symptomatic breast hypertrophy. This study demonstrated that patients report a high level of satisfaction with the outcome of surgery and experience the ongoing health benefits and improvement in quality of life for many years after surgery. In the long term, the significant improvement in patient satisfaction and health-related quality of life observed in the shorter-term following surgery is sustained and does not deteriorate to levels reported preoperatively over time. In a climate of increasingly constrained healthcare budgets, this study provides evidence as to the value of surgery in this population which continues

well beyond the short-term gains previously reported.

6. RELATIONSHIP BETWEEN BREAST AND BODY SIZE AND THE IMPROVEMENT IN HEALTH-RELATED QUALITY OF LIFE FOLLOWING BREAST REDUCTION SURGERY

A version of this chapter including the comparison of three-dimensional laser scanning to water displacement for the measurement of breast volume has been published as an original article in the Australasian Journal of Plastic Surgery; attached as Appendix R (Crittenden et al., 2018a).

6.1 Introduction

Measurement of breast volume plays an important role in breast reduction, reconstruction, developmental asymmetry and augmentation. In women with breast hypertrophy it is important for pre-operative planning, in intraoperative decision-making regarding the amount of tissue to be taken from each breast to achieve symmetry, and where removal of a minimum amount of breast tissue is required to justify surgery (Boukovalas et al., 2019, Descamps et al., 2008, Dvoracek et al., 2019, Hernanz et al., 2014, Kececi and Sir, 2014, Klassen et al., 1996, Kocak et al., 2011, Koltz et al., 2013, Nguyen et al., 2008, O'Blenes et al., 2006, Seitchik, 1995, Sommer et al., 2002, Wamalwa et al., 2018, Wampler et al., 2019). Accurate estimation of breast volume and predicted tissue resection weight also promotes improved counsel to the patient and provides a valuable guide to training surgeons.

A variety of techniques are described in the literature to fulfil the need for an accurate and objective measurement of breast volume in the clinical setting. These techniques include magnetic resonance imaging (MRI), mammography, plaster casting, Grossman-Roudner plastic cups, water displacement, anthropometric measurement and three-dimensional surface imaging (Bulstrode et al., 2001, Howes et al., 2017, Kovacs et al., 2007, Kwong et al., 2020, Lee et al., 2016, Longo et al., 2013, Losken et al., 2005, Muslu et al., 2019, Qiao et al., 1997, 1986, Sigurdson and Kirkland, 2006, Smith et al., 1986, Wesselius et al., 2018). In a situation where a woman is undergoing post-mastectomy breast reconstruction, the gold standard for measuring the breast tissue volume for reconstruction is the Archimedes method of water displacement of the mastectomy specimen (Yip et al., 2012). When measuring breast tissue volume in the intact state, such as in candidates for breast reduction surgery, MRI is reported as being the most accurate (Choppin et al., 2016). However, MRI is expensive and not always accessible. Three-dimensional (3D) laser scanning has also been demonstrated as a valid method of breast volume measurement (Howes et al., 2017, Kwong et al., 2020, Lee et al., 2016, O'Connell et al., 2015, Yip et al., 2012), but some centres lack access to this technology. Anthropometric measurements based on defined anatomic points from skeletal and soft tissue landmarks provide a fast and useful tool to assess breast aesthetics and predict breast volume (Brown et al., 2012, Longo et al., 2013, Muslu et al., 2019, Qiao et al., 1997, Sigurdson and Kirkland, 2006). Water displacement of the intact breast has

been used in some centres since 1970, but has not previously been validated against more recent methods (Bouman, 1970).

Research studies reporting on the relationship between breast size and body size and shape in women undergoing breast reduction surgery are limited. Whilst some studies have attempted to explore this relationship, many have relied on indirect proxy measures for body size including the use of BMI (Benditte-Klepetko et al., 2007), or have used substitute measures to estimate breast size including tissue resection weight (Findikcioglu et al., 2013) and bra cup size (Brown et al., 2012). Gaining a better understanding of whether factors such as the degree of breast hypertrophy or breast size as a proportion of body size have an impact on the improvement in health-related quality of life (HRQoL) following surgery is relevant both at a patient and clinician level but also for healthcare funders and the wider community worldwide.

The original aims of the surgical study described in Chapter 2 was not only to investigate the health benefits of breast reduction surgery but to also assess the effect of body shape or 'disproportionality' on HRQoL outcomes following surgery. In planning this study, it was hypothesised by the team of investigators that women with disproportionately large breasts in relation to their total body size would have a greater improvement in HRQoL following surgery than women with large breasts and a larger body size. In order to address this hypothesis, the original study was designed to include a comprehensive body shape assessment pre-operatively and at 12 months following breast reduction surgery with breast and body size measured using a series of approaches including water displacement, 3D laser scanning and anthropometric measurements. In this way, if it was determined there was a relationship between disproportionality and the level of improvement in HRQoL then this information could be used to generate a prioritisation system that was evidence-based in order to allow for fairer waiting lists within the public hospital system. Additionally, if this hypothesis was proven correct a further aim was to determine if anthropometric measurements or water displacement would be a simple and practical method for general practitioners to triage patients and determine eligibility for publicly funded surgery. Therefore, the primary objectives of this chapter were to evaluate the relationship of disproportionality on health-related quality of life outcomes following surgery; to investigate breast and body shape in women undergoing breast reduction surgery; and to compare and assess the validity of a series of techniques for measuring breast and body size in women with breast hypertrophy.

6.2 Participants and methods

6.2.1 Surgical participants

The participants in the surgical cohort are introduced and described in detail in Chapter 2 (Section 2.2.1). However, a point of difference in this study was that surgical participants underwent a comprehensive body shape assessment at two of the four timepoints; pre-operatively and at 12

months following surgery. Breast size was measured with 3 different methods: anthropometric measurements, three-dimensional (3D) laser scanning, and water displacement. Body size was measured with anthropometry, 3D laser scanning and through the conventional calculation of body mass index. A professor of anthropology (Professor Maciej Henneberg, University of Adelaide), certified anthropometrist (Daisy Veitch, SHARP Dummies Pty Ltd, Adelaide) and a public health physician (Professor David Ben-Tovim, Flinders University) were all involved in the original research design of this study with the plastic surgery team at Flinders Medical Centre.

6.2.2 Anthropometric body shape assessment

6.2.2.1 Surgical participants

A series of direct anthropometric body measurements were taken from surgical participants using a measuring tape and anthropometer with sliding calliper (GPM, Switzerland) as per International Standards Organisation (ISO) document 8559 (ISO 8559 (part 1), 2017). A standard set of direct measurements were performed by a criterion anthropometrist to assess the composition of the body and included: height, weight and body mass index; body circumferences (chest, bust, under-bust, intermammary fold, waist and hips); and point-to-point/width measurements including bust width, nipple-to-nipple distance, shoulder and hip width (Appendix S). Suprasternal notch-to-nipple distance was recorded in the preoperative consultation with the plastic surgeon.

A formula based on anthropometric measurements for the estimation of total breast volume was proposed by a Professor of Anthropological and Comparative Anatomy at the University of Adelaide, Professor Maciej Henneberg. This proposed formula was based on three anthropometric measurements (bust girth, under bust girth and bust width) and a geometric volume formula: Total breast volume = $(0.6667*\pi((\text{bust girth} - \text{under bust girth})/\pi)*(\text{bust width}/2)^2)/500000$

6.2.2.2 Normative anthropometry data

Normative anthropometric body data from 521 Australian female volunteers within the general population obtained from the 2009 Sharp Dummies Australian Body Sizing Survey was kindly provided by Daisy Veitch (SHARP Dummies Pty Ltd, Adelaide, Australia). Participants were represented across a broad range of variables including age, body weight and geographical location. Participant characteristics including age and weight were recorded. Anthropometric body measurements were performed by the same criterion anthropometrist employed in the assessment of surgical participants in the present study. One-dimensional anthropometric measurements included height, acromial height (shoulder to ground), waist height, bust width (nipple to nipple), bust girth, waist girth, hip girth, bi-acromial (shoulder) width, and hip width.

6.2.3 Measuring breast and body volume using a 3D laser scanner

Three-dimensional (3D) laser body scanning was performed using a Cyberware WBX scanner (Cyberware, Monterey, USA) and CySlice software (Headus Pty Ltd, Perth, Australia). The

Cyberware WBX scanner has four sets of laser heads and cameras that move vertically to scan the surface anatomy of subjects in the upright position. Breast and body volume was measured according to the published protocol described previously at our institution (Veitch et al., 2012). The accuracy of the Cyberware WBX 3D scanner for the measurement of breast volume has previously been established at our institution by comparison to water displacement of mastectomy specimens (Yip et al., 2012) and by comparison to magnetic resonance imaging (MRI) (Howes et al., 2017). Prior to scanning, the assessor placed 'landmarks' on subjects using palpation to demarcate selected anatomical areas and the breast perimeter. Figure 6.1 illustrates the application of landmarks on a large-breasted woman to section the breast from the torso for volume analysis.

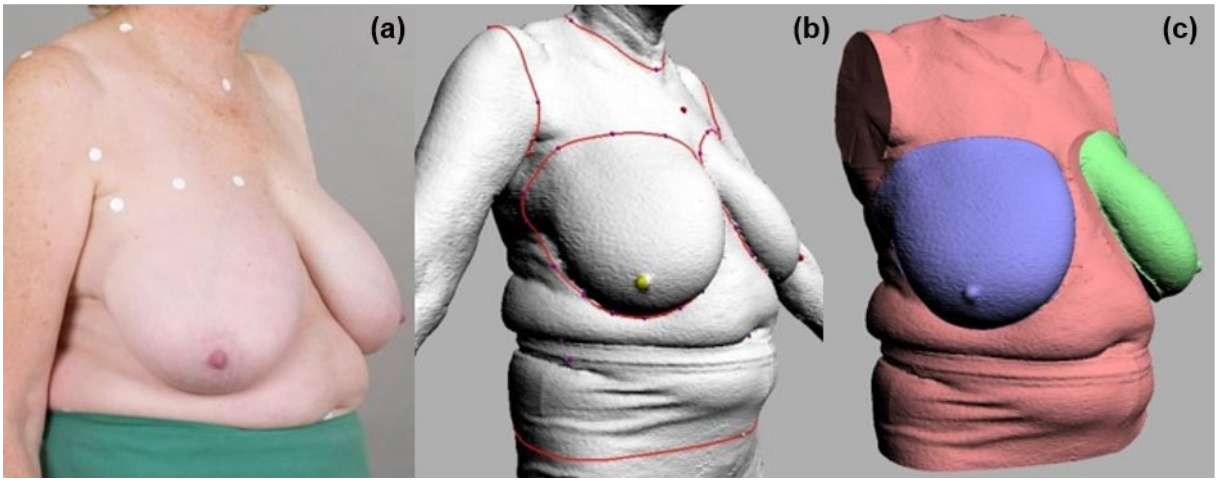


Figure 6.1 Volumetric analysis of the breast with Cyberware WBX 3D scanner.

(a) photography showing landmark placement following determination of breast borders by palpation, (b) scan image with outline of breast and torso boundary (c) CySlice image to section the breast portion of the scan from the torso. Source: (Crittenden et al., 2018a).

6.2.4 Water displacement for measuring breast volume

Water displacement measurements based on Archimedes' principle was performed on each breast to determine the volume, as described by Schultz et al. (Schultz et al., 1986). A large calibrated container was filled with warm water and the patient asked to individually immerse each breast into the container, using a specially modified surgical bed and ensuring that the superior and lateral edges of the breast were at water level (Figure 6.2). Individual breast volumes were then determined by the amount of water displaced.

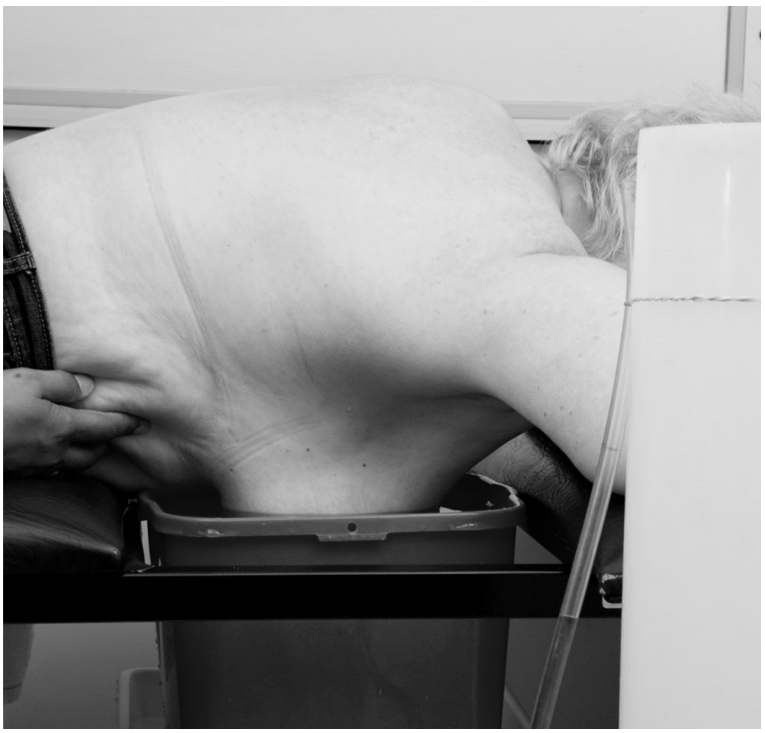


Figure 6.2 Water displacement technique

6.2.5 Statistical analysis

Descriptive statistics including mean, standard deviation and 95% confidence interval were computed for continuous variables. Measurements undertaken before and after surgery were compared using a paired samples *t*-test. An independent samples *t*-test was undertaken when comparing continuous variables between two different groups. A one-way analysis of variance (ANOVA) was used when comparing the mean measurements of more than two groups, with a post-hoc Tukey test to determine which of the groups differ. Pearson correlation coefficients (*r*) were calculated to assess the strength of linear association between two variables, including when comparing the two measurement techniques. Correlation coefficients less than 0.29 were described as weak, between 0.30 to 0.49 as moderate, and greater than or equal to 0.5 as strong (Cohen, 1988). The strength of any correlation between two measurement techniques was determined with a Bland-Altman analysis (Bland and Altman, 1995). This analysis plots the mean breast volume measurements for both techniques against their differences. If the two methods are comparable and in agreement then the differences should be small, and the mean of the differences should be close to zero. The 95% limits of agreement were formed using the mean difference in volumes ±1.96 standard deviation (SD) of the differences in volumes. Linear regression analysis was performed to assess proportional bias between the two measurement techniques. All analyses were performed using SPSS v25.0 statistical software (IBM Corp., Armonk, New York). All tests were two-sided and a *p*-value of less than 0.05 was regarded as statistically significant.

6.3 Results

6.3.1 Participants

A total of 251 participants were assessed pre-operatively and 190 participants at 12-months post-operatively. Clinical and demographic information for surgical participants was summarised previously in Chapter 2 (Section 2.3.1).

6.3.2 Missing data

The total numbers of surgical participants assessed by each measurement approach varied due to several factors. Firstly, water displacement for the measurement of breast volume was discontinued prior to study completion and therefore there were a lower number of participants with data for this technique. Secondly, on occasion participants had limited time and therefore not all assessments at each study timepoint may have been completed.

6.3.3 Anthropometric body shape assessment before and after breast reduction surgery

A total of 251 participants had anthropometric measurements at the pre-operative assessment and 190 participants at 12-months post-operatively. Table 6.1 summarises the comparison of these measurements before and after surgery. Bust girth, breast point-to-point (distance between breast apices) and nipple-to-nipple distance were found to significantly decrease following surgery. In contrast, no significant differences were found when comparing pre- and post-operative measurements for body weight, height, BMI, waist girth, under-bust girth, shoulder width and hip girth. Pre-operatively, mean sternal notch-to-nipple distance for the left breast was 32.4 cm (SD 4.4 cm, range 24 to 54 cm) and 32.7 cm (SD 4.5 cm, range 24 to 54 cm) for the right breast. When estimating breast volume using the proposed formula based on anthropometric measurements, preoperative mean total breast volume was 4267 mL (SD 1594 mL). At 12 months post-operatively mean total breast volume was significantly lower and estimated at 2906 mL (SD 846 mL).

When comparing the mean age of surgical participants (mean 41.9 years, SD 13.3) to women in the normal population sample (mean 41.7 years, SD 10.9; range 18 to 57 years), there were no significant differences found between the two groups (mean difference 0.16 years, 95% CI: -1.6 to 1.9; $p = 0.858$). Table 6.1 presents a comparison of anthropometric measurements between surgical participants and women within the general Australian population sample. In comparison to both baseline and post-operative measurements from surgical participants, women within the normal population sample had significantly lower measurements for body weight, BMI, bust girth, waist girth, hip girth, and nipple-to-nipple distance. In contrast, data were similar between these groups for shoulder width and height (stature).

Table 6.1 Anthropometric measurements for surgical participants in comparison to normative general population sample

	Surgical group		Mean difference (95% CI) pre-op vs 12m post-op; *p*-value[†]	Normative	Mean difference (95% CI) pre-op vs normal; *p*-value[‡]	Mean difference (95% CI) 12m post-op vs normal; *p*-value[‡]
	Pre-op (*n* = 251) Mean (SD)	12m post-op (*n* = 190) Mean (SD)		(*n* = 521) Mean (SD)		
Weight, kg	86.4 (17.5)	86.4 (17.0)	-0.50 (-1.3 to 0.27); 0.200	66.0 (9.3)	20.4 (18.5 to 22.3); <0.001	20.4 (18.4 to 22.4); <0.001
Height, mm	1619.3 (66.5)	1620.8 (65.5)	-2.1 (-3.2 to -0.91); 0.201	1627.3 (65.0)	-8.1 (-18.0 to 1.9); 0.111	-6.6 (-17.4 to 4.3); 0.234
BMI, kg/m^2	32.7 (5.9)	32.8 (5.8)	-0.14 (-0.5 to 0.18); 0.375	25.0 (3.6)	7.9 (7.2 to 8.6); <0.001	7.8 (7.1 to 8.5); <0.001
Bust girth, mm	1161.5 (125.2)	1113.9 (111.2)	47.6 (40.0 to 55.2); <0.001	947.8 (82.3)	216.3 (201.4 to 231.1); <0.001	166.2 (151.1 to 181.3); <0.001
Waist girth, mm	979.3 (129.3)	982.1 (130.2)	-2.8 (-10.2 to 4.2); 0.460	806.9 (89.1)	174.5 (158.3 to 190.7); <0.001	175.2 (158.3 to 192.1); <0.001
Hip girth, mm	1171.8 (128.9)	1178.5 (128.5)	-6.6 (-13.4 to 0.15); 0.055	1040.4 (76.2)	131.9 (117.3 to 146.5); <0.001	138.1 (122.6 to 153.5); <0.001
Shoulder width	366.0 (23.0)	366.4 (22.9)	-0.35 (-3.4 to 2.8); 0.825	368.5 (19.3)	-1.3 (-4.4 to 1.8); 0.410	-2.1 (-5.4 to 1.3); 0.230
Nipple-to-nipple, mm	240.8 (37.2)	214.6 (22.2)	26.9 (21.7 to 32.1); <0.001	189.5 (22.2)	51.5 (47.2 to 55.8); <0.001	25.2 (21.5 to 28.9); <0.001
Breast point-to-point	235.5 (29.1)	218.3 (20.8)	17.2 (13.6 to 20.8); <0.001	-	-	-
Under-bust girth	938.1 (113.4)	933.2 (105.4)	4.9 (-1.8 to 11.5); 0.148	-	-	-

[†] Paired samples *t*-test

[‡] Independent samples *t*-test

6.3.4 3D laser scanner

A total of 217 participants had 3D laser scans at baseline and 189 participants at 12 months post-operative. Descriptive statistics and mean comparisons before and after surgery for breast and body volumes measured by the 3D laser scanner are presented in Table 6.2. Breast and body volume measurements were compared for surgical participants with both a pre-operative and 12-month post-operative assessment using a paired samples *t*-test. A statistically significant difference was found when comparing individual breast volumes at baseline to 12-months post-operative measurements. Pre-operatively, mean total breast volume measured by 3D laser scanner was 3339 mL (range 1472 to 9622 mL). At 12 months post-operatively, mean total breast volume was significantly lower at 2193 mL (range 963 to 4392 mL). In contrast, no significant difference was found in total body volumes. This finding was consistent with the body mass index calculated from height and weight measurements at pre- and 12 months post-operative timepoints.

Table 6.2 Breast and body volumes measured by 3D scanner pre- and 12 months post-operative

3D scan volume (mL)	Mean (SD)		Difference in means (95% CI)	*p*-value
	Pre-operative (*n* = 162)	Post-operative (*n* = 162)		
Left breast	1697.9 (569.2)	1137.8 (318.6)	560.2 (494.0 to 626.3)	<0.001
Right breast	1641.3 (559.5)	1055.9 (290.7)	585.5 (514.1 to 656.8)	<0.001
Total breast	3339.2 (1115.1)	2193.6 (589.5)	1145.6 (1010.7 to 1280.5)	<0.001
Total body	89394.0 (17936.6)	89864.2 (17885.0)	-470.2 (-1149.3 to 508.8)	0.344

When comparing the change in breast volumes measured by the 3D laser scan to the weight of tissue resected from each breast at surgery, there was a strong positive correlation found (r = 0.851, $p < 0.001$). This finding is presented in Figure 6.3 below.

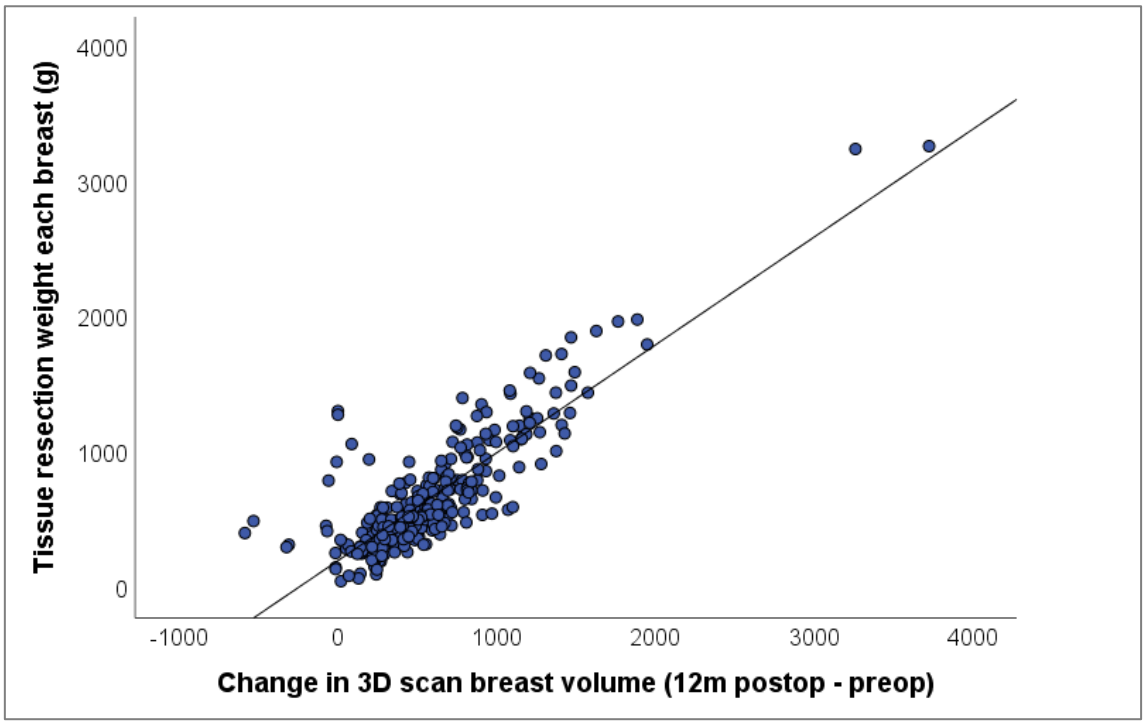


Figure 6.3 Relationship between the change in breast volume and weight of tissue resection at surgery

6.3.4.1 Relationship between breast volume and bra cup size

The relationship between pre-operative breast volume measured using the 3D laser scanner and patient-reported bra cup size was also assessed. While there was a trend of increasing breast volume with increasing bra cup size, there was considerable variability within cup size categories (Figure 6.4). Furthermore, correlation analysis revealed only a weak positive association between the two variables ($r = 0.338$, $n = 217$, $p < 0.001$). As an example, participants who self-reported a bra cup size of DD cup were found to have a mean breast volume of 3116 mL (SD 1303 mL) and ranged between 1601 mL and 9622 mL. A one-way ANOVA was conducted to compare mean breast volumes between bra cup size groups. A significant difference was found in mean breast volumes between the seven bra cup categories. However, post-hoc comparisons using the Tukey test indicated that only the mean breast volumes for I/J bra cup size were significantly different from; C/D cup size ($p < 0.001$), DD cup ($p < 0.001$), E/EE cup ($p = 0.001$), F/FF cup ($p = 0.002$), and G/GG cup ($p = 0.004$). Breast volumes for all other bra cup categories did not differ significantly from one another.

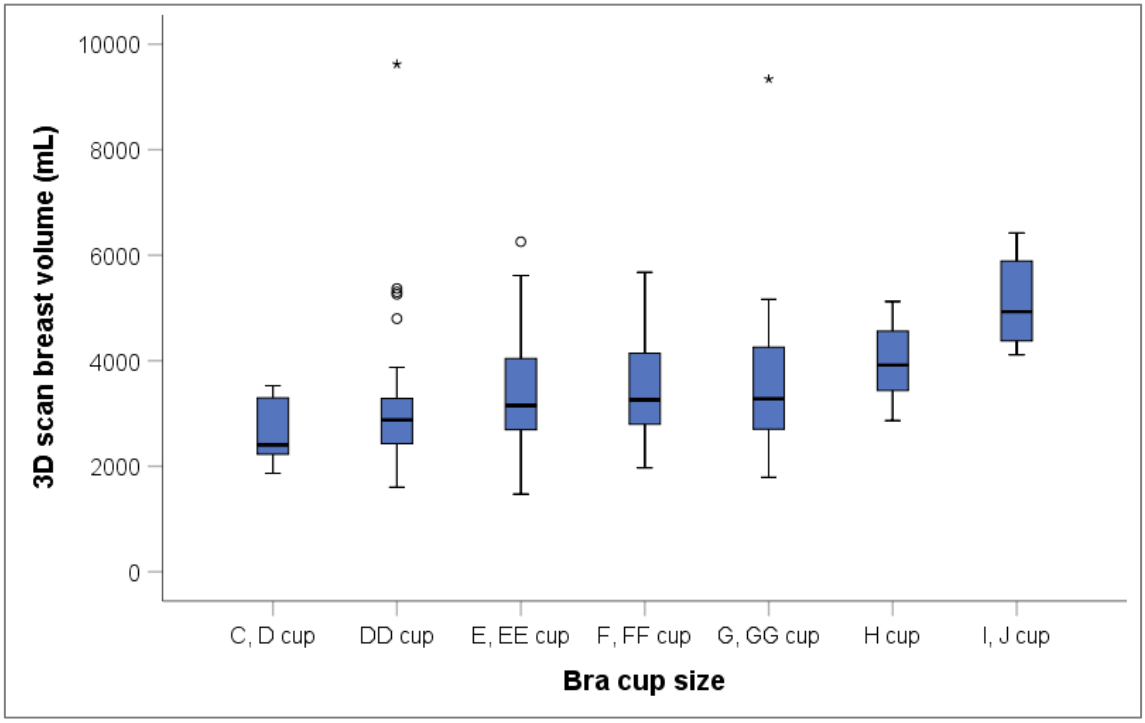


Figure 6.4 Distribution of measured breast volume by bra cup size

6.3.4.2 Relationship between breast volume and anthropometric variables

Correlation analysis was conducted to evaluate the relationship between pre-operative breast volume estimated using 3D laser scanner with anthropometric measurements (n = 217). Table 6.3 provides a summary of these findings and demonstrates that pre-operative breast volume was most strongly correlated with the amount of tissue resected at surgery, indicating that women with larger breasts had more breast tissue excised. Pre-operative breast volume also demonstrated a large positive correlation with sternal notch-to-nipple distance, bust girth, breast point-to-point distance, total body volume, weight and BMI. The association with these latter three variables indicates that heavier women or those with a larger body size tend to have larger breasts. All other variables showed a medium correlation with breast volume with the exception of height, which was found to have a weak association.

Table 6.3 Relationship between pre-operative breast volume and anthropometric and 3D scan volume variables

	Pearson's *r* correlation to preoperative breast volume	***p*-value**
3D scan total body volume	0.614	<0.001
Tissue resection weight	0.843	<0.001
Unisex chest girth	0.542	<0.001
Bust girth	0.687	<0.001
Under-bust girth	0.575	<0.001
Intermammary fold girth	0.505	<0.001
Nipple-to-nipple distance	0.580	<0.001
Breast point-to-point distance	0.612	<0.001
Suprasternal notch-to-nipple distance	0.723	<0.001
Bra cup size	0.320	<0.001
BMI	0.612	<0.001
Weight	0.613	<0.001
Height	0.153	0.025
Hip girth	0.563	<0.001
Waist girth	0.542	<0.001
Shoulder width	0.345	<0.001
Hip width	0.620	<0.001

6.3.4.3 Breast asymmetry

Individual breast volumes estimated by 3D laser scanning were used to evaluate the degree of breast asymmetry pre-operatively within the surgical cohort. Figure 6.5 presents the distribution and degree of breast asymmetry when comparing left breast to right breast volume at the baseline assessment. The median difference in volume between breasts was found to be 166 mL (mean 149.7 mL, SD 115.2 mL) and ranged from 1 mL to 532 mL, with a difference of greater than 200 mL found in 62 participants (28.6%). When assessing the degree of asymmetry between breasts as a proportion of total breast volume, the median degree of breast asymmetry was found to be 3.97% and ranged from 0% to 17.7%. The majority of participants were found to have mild asymmetry of less than 5% (138/217, 63.6%); 65 participants (30.1%) had between 5% and 10%; and 13 participants (6.3%) were found to have greater than 10% difference in volume between breasts.

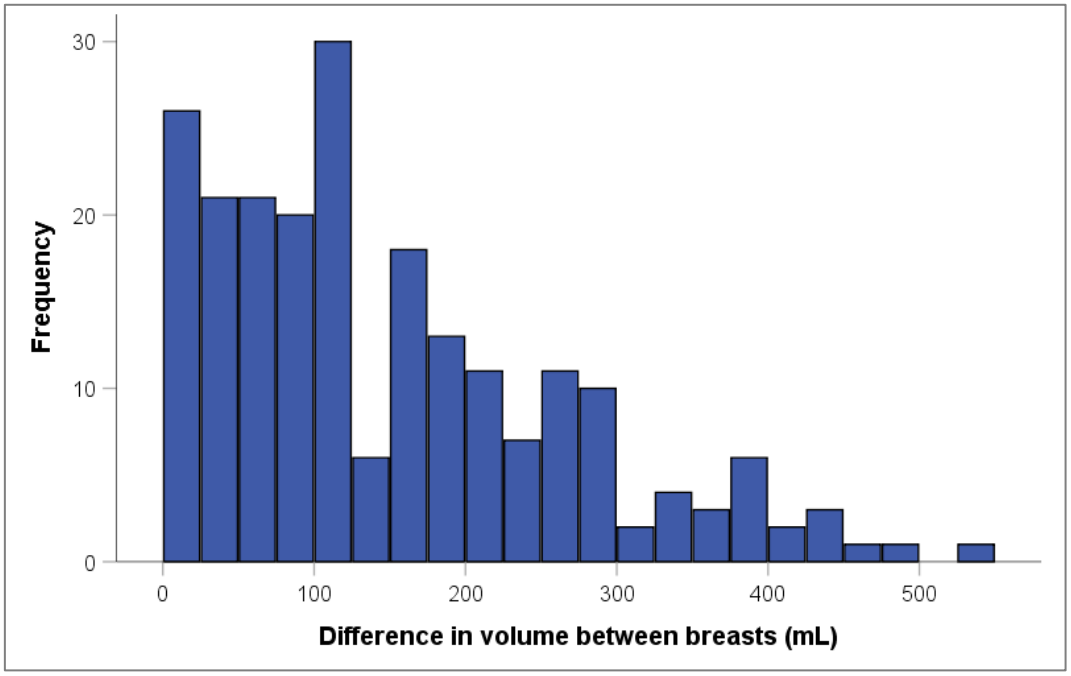


Figure 6.5 Frequency distribution of the degree of breast asymmetry at baseline assessment

6.3.4.4 Breast size as a proportion of body size

Using 3D scan breast volume measurements, the extent of 'disproportionality' was assessed using the total breast volume as a proportion of the total body volume at the pre-operative assessment. The frequency distribution is presented in Figure 6.6. The median ratio of breast to body volume was 3.74% and ranged from 1.49% to 7.88%. Breast volume as a proportion of total body volume was less than 5% for the majority of participants (197/217, 90.8%).

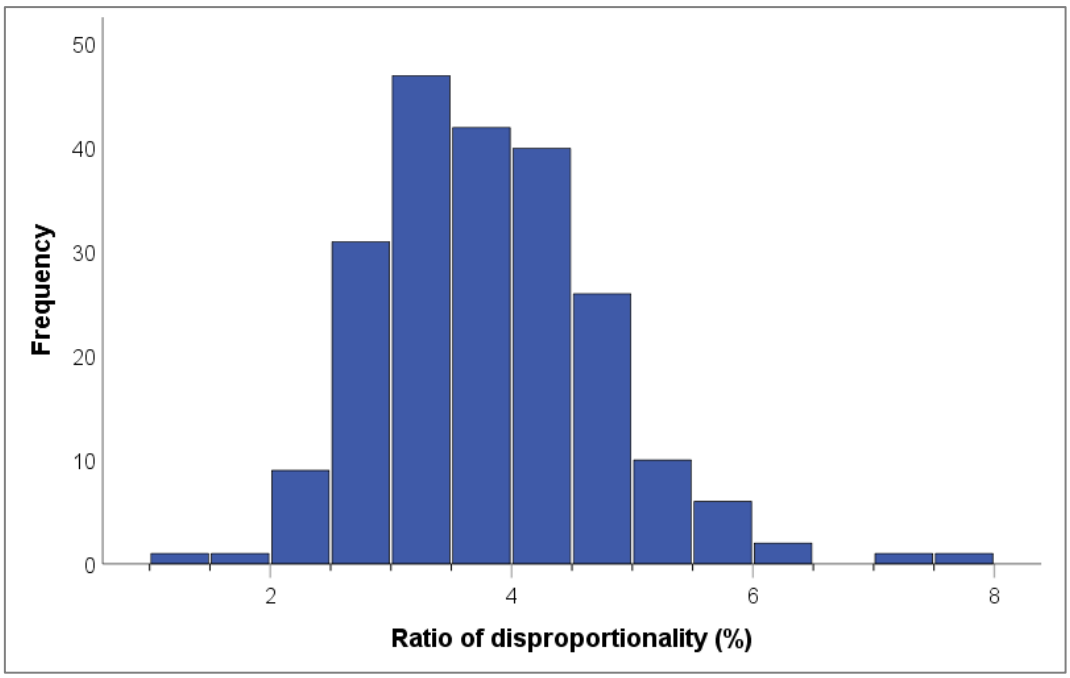


Figure 6.6 Frequency distribution of proportion of breast to body size

The relationship between the degree of disproportionality and the level of improvement in health-related quality of life following surgery as measured by the SF-36 physical summary scores (SF-36 PCS) was investigated using Pearson correlation analysis. It was found that there was no significant association between the two variables ($r = 0.137$, $p = 0.09$) (Figure 6.7).

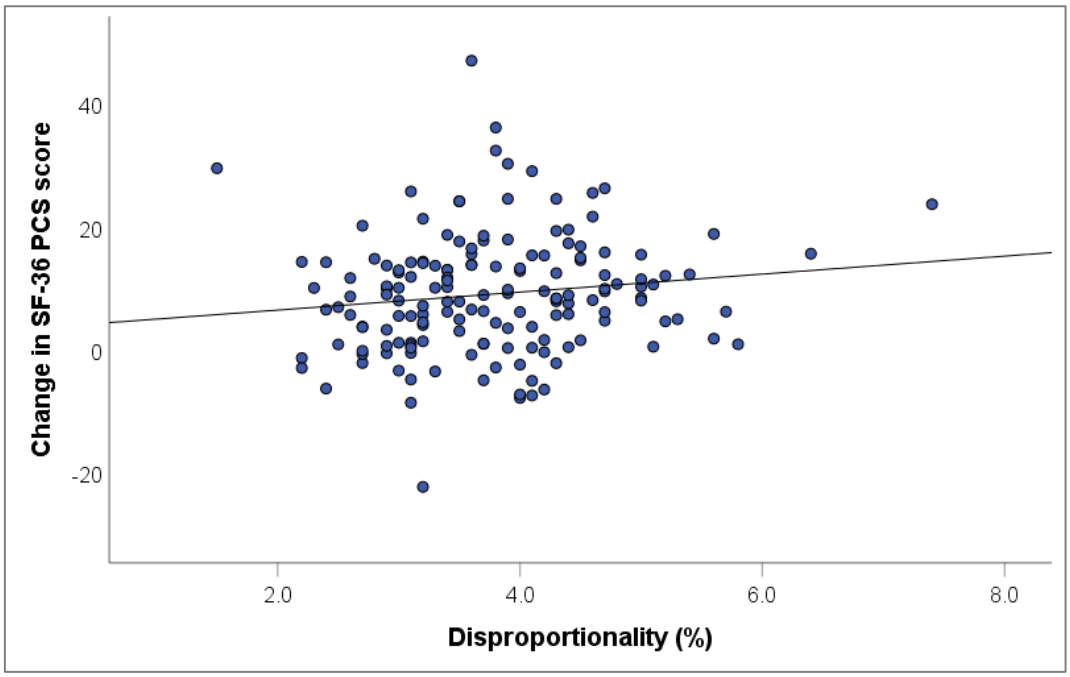


Figure 6.7 Relationship between disproportionality and change in SF-36 PCS score

The relationship between degree of disproportionality and the change in SF-36 mental summary scores (SF-36 MCS) was also evaluated using Pearson correlation analysis. There was no significant association found between the two variables (r = 0.10, p = 0.212) (Figure 6.8).

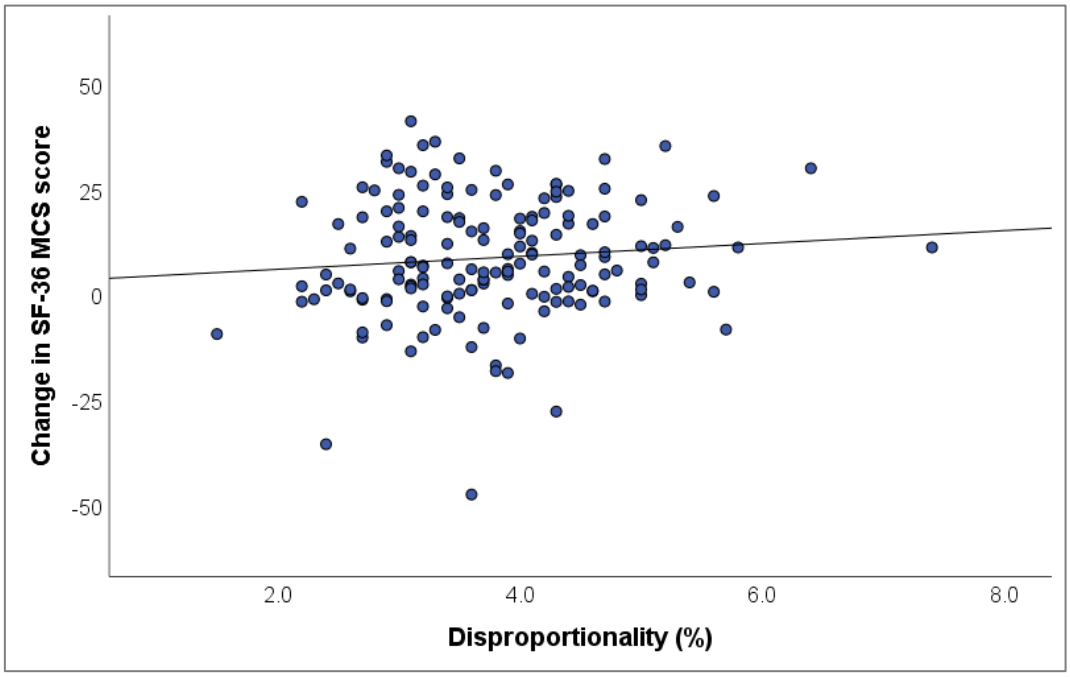


Figure 6.8 Relationship between disproportionality and change in SF-36 MCS score

6.3.4.5 Relationship between body volume and BMI

When comparing the total body volume measurement by 3D laser scanner to the calculated BMI from height and weight measurements at the baseline assessment, there was found to be a large positive correlation ($r = 0.915$, $p < 0.001$). This suggests a strong relationship between these two variables describing body size (Figure 6.9).

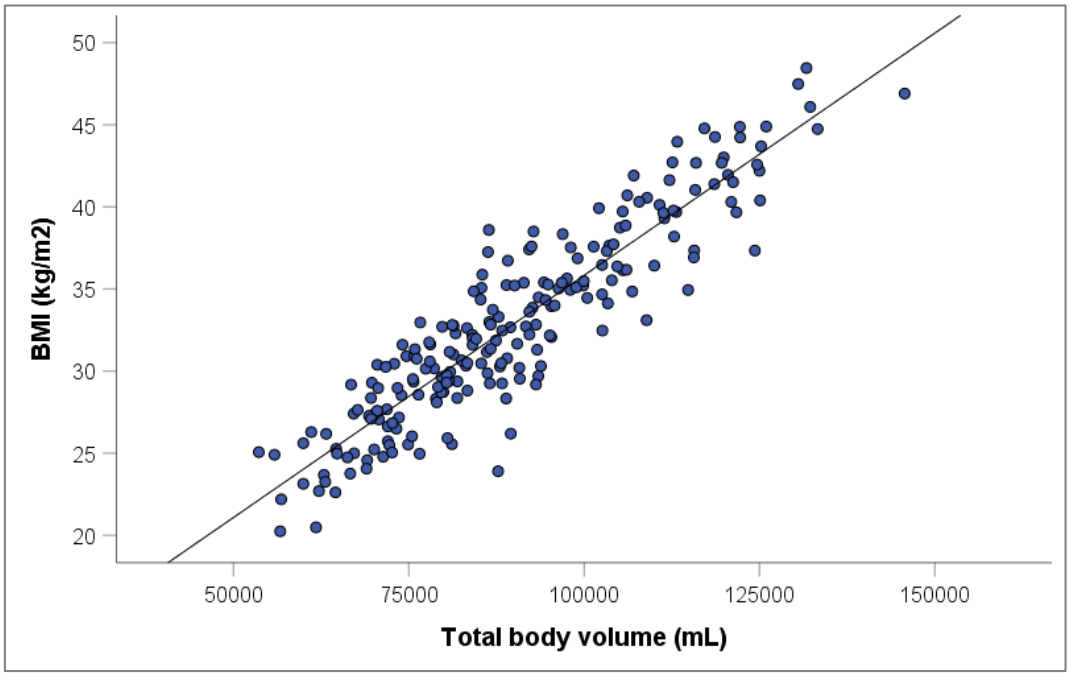


Figure 6.9 Relationship between total body volume and BMI

6.3.5 Water displacement

A total of 120 participants had water displacement measurements at the pre-operative assessment and 64 at the 12 months post-operative assessment. Mean (SD) breast volumes at baseline were found to be 1795.8 mL (839.2 mL) and 1791.5 mL (845.8 mL) for left and right breasts, respectively, with a mean total breast volume of 3587.3 mL (1667.2 mL). Post-operatively mean volumes were 929.5 mL (413.7 mL) and 916.9 mL (411.2 mL) for left and right breast volumes, respectively, with a mean total volume of 1846.4 mL (813.6 mL). Using a paired samples *t*-test, breast volumes were compared for those participants who completed both a pre- and post-operative assessment and these findings are presented in Table 6.4. Individual and total breast volumes were found to be significantly reduced at 12 months following surgery when compared to baseline.

Table 6.4 Breast volumes for surgical participants pre- and post-operatively

	Mean (SD) breast volume (mL)		Difference in means (95% CI)	*p*-value[†]
	Pre-operative (*n* = 62)	Post-operative (*n* = 62)		
Left breast	1716.2 (776.4)	915.7 (401.8)	800.5 (647.5 to 953.5)	<0.001
Right breast	1712.9 (772.0)	907.6 (407.7)	805.2 (646.2 to 964.3)	<0.001
Total breast	3429.1 (1519.5)	1823.3 (798.7)	1605.7 (1304.9 to 1906.5)	<0.001

[†] Paired samples *t*-test.

6.3.6 Comparison of breast volume measurement using 3D scan and water displacement

In comparing the individual breast volumes obtained from 3D laser scanning and water displacement, a Pearson correlation demonstrated a strong, positive linear association between the two different methods ($r = 0.89$, $n = 322$, $p < 0.001$), with higher volume estimates by 3D scanner measurement associated with higher volume estimates by water displacement (Figure 6.10).

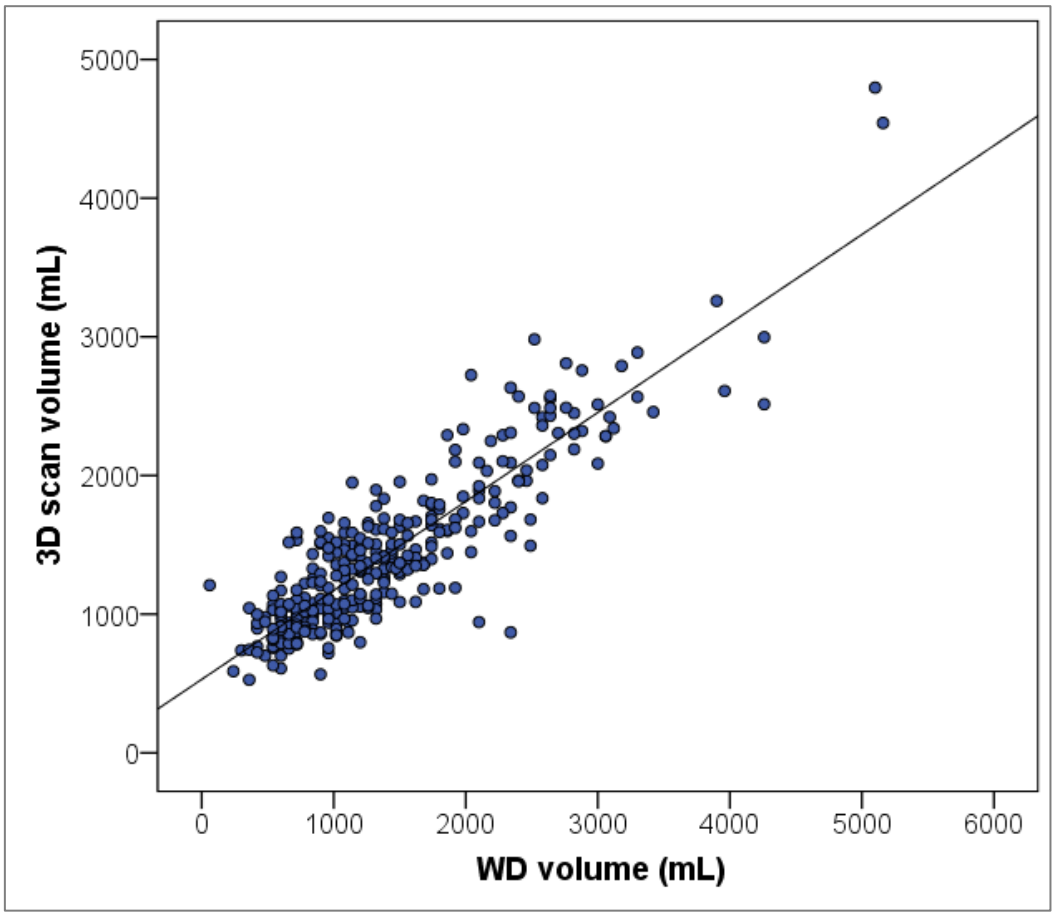


Figure 6.10 Pearson correlation of breast volume measurement – water displacement versus 3D laser scan

A Bland-Altman analysis was subsequently conducted to evaluate the level of agreement between the two methods. Figure 6.11 presents the results of the Bland-Altman plot showing the differences between the two techniques plotted against the averages of the two techniques. A mean difference of -21.7 mL with a standard deviation of 399 mL was found between the two techniques. While most values were within the 95% limits of agreement (±1.96 x SD) on the plot (a lower limit of -804 mL and an upper limit of 760 mL), the majority of the data points are widely spread across this range and do not lie close to zero, which would have been the case if there was good agreement between the measured values. This analysis demonstrated there was a large difference in measurement of breast volume using the two methods.

Linear regression analysis confirmed a degree of proportional bias, meaning that one method gave values that were consistently higher or lower than those of the other method. In this instance, the breast volumes obtained from water displacement tended to be larger than those from the 3D scanner, and the difference between the two methods increased as the mean volume increased. This is evident from the plot where there was a discernible trend for more points to be above the line of mean difference in volume as the mean volume increased (Figure 6.11).

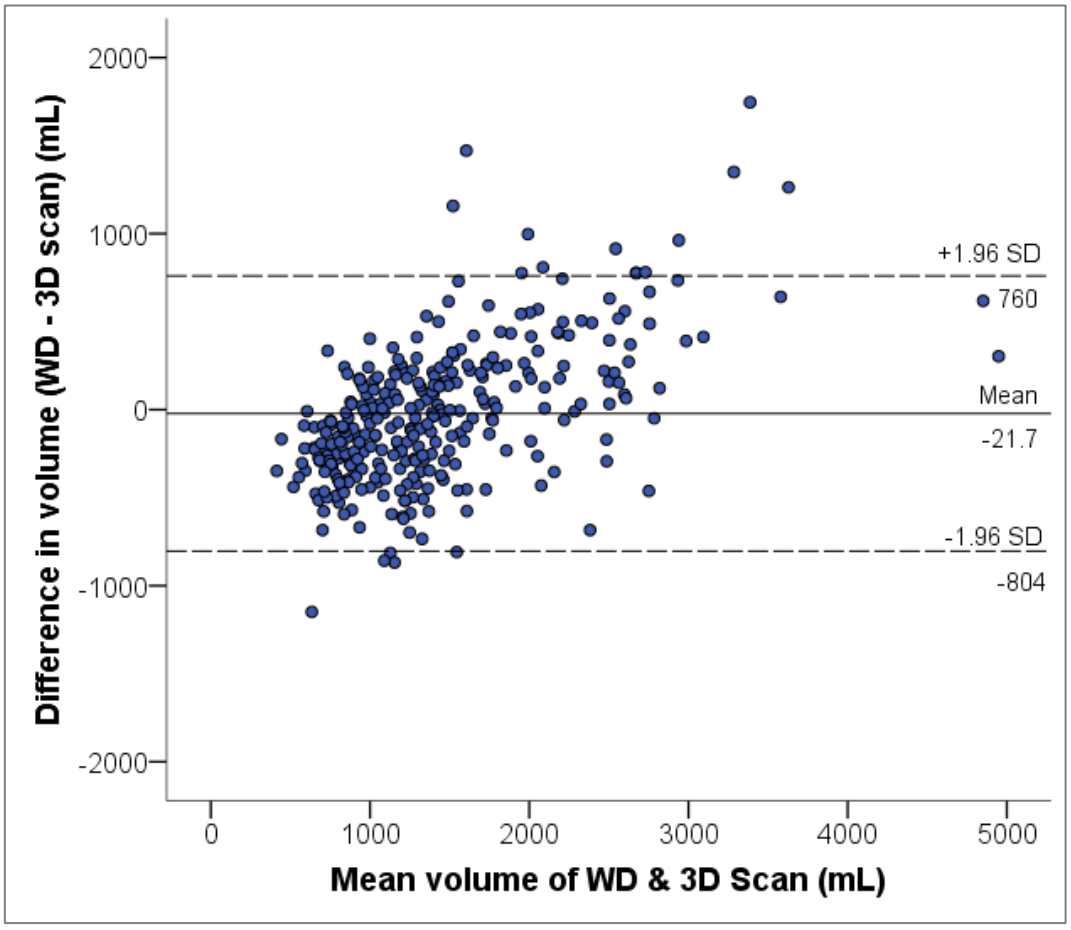


Figure 6.11 Bland-Altman plot of breast volume measured by water displacement and 3D scanning techniques.

The analyses therefore suggest that despite a strong linear correlation between the two methods of breast volume measurement, the measures have low agreement on actual values. The water displacement values were consistently larger than the 3D scan values. The greatest agreement in breast volume measurement between the two methods (within 10%) was seen for volumes between 1000 and 2000 mL (Figure 6.12).

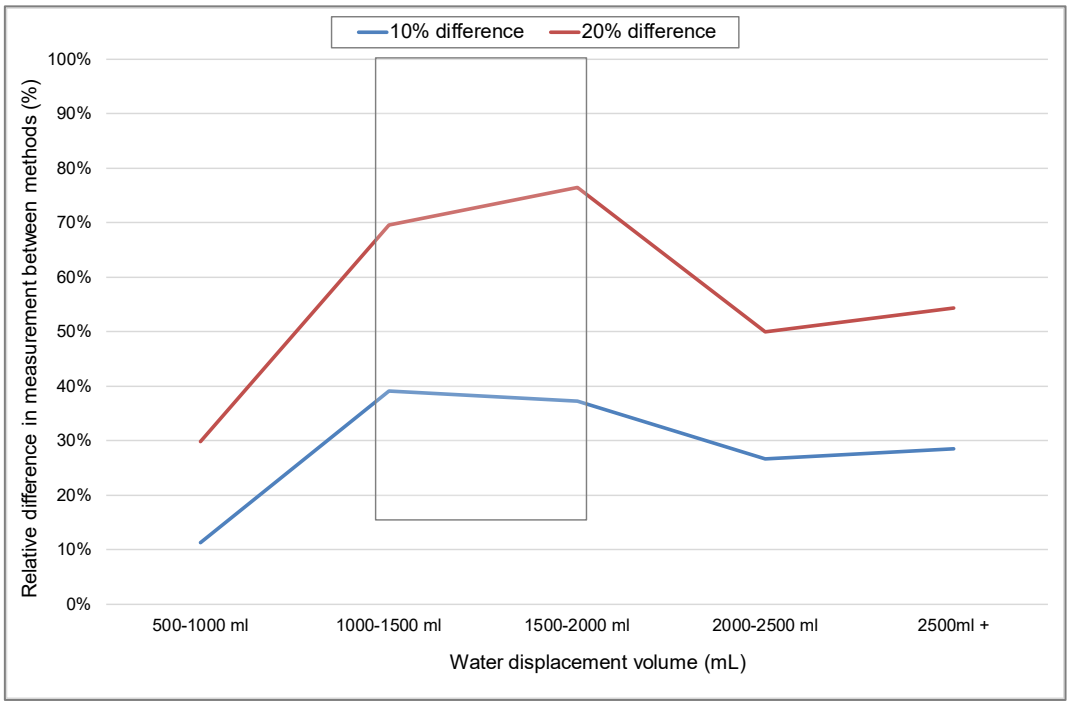


Figure 6.12 The level of agreement between the two methods.
Shaded area highlights the range of breast volumes with the highest level of agreement

6.3.7 Comparison of breast volume measurement using 3D scan and anthropometric formula

In comparing the total breast volumes obtained from 3D laser scanning and anthropometric formula, a Pearson correlation demonstrated a strong, positive linear association between the two different methods ($r = 0.72$, $n = 414$, $p < 0.001$), with higher volume estimates by 3D scanner measurement associated with higher volume estimates by the predictive formula (Figure 6.13).

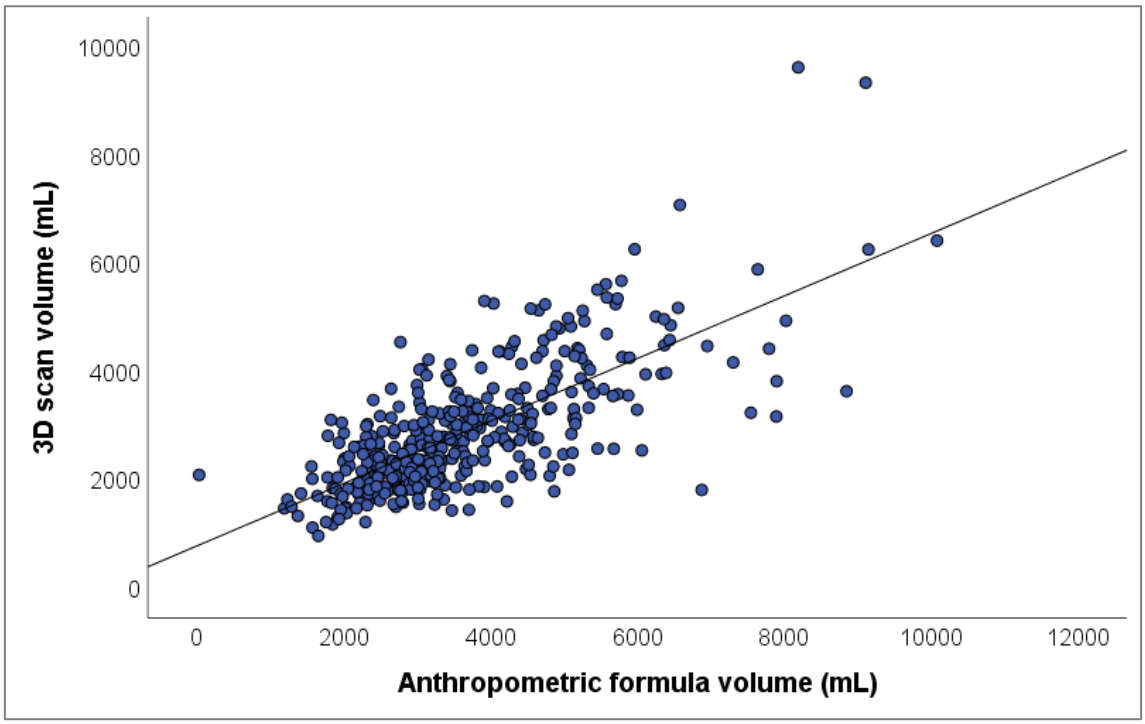


Figure 6.13 Pearson correlation of breast volume measurement – anthropometric formula versus 3D laser scan

A Bland-Altman analysis was subsequently conducted to evaluate the level of agreement between the two methods. Figure 6.14 presents the results of the Bland-Altman plot showing the differences between the two techniques plotted against the averages of the two techniques. A mean difference of 757 mL with a standard deviation of 993 mL was found between the two techniques. While most values were within the 95% limits of agreement (±1.96 x SD) on the plot (a lower limit of -1189 mL and an upper limit of 2703 mL), the majority of the data points are widely spread across this broad range and do not lie close to zero, which would have been the case if there was good agreement between the measured values. Furthermore, the limits of agreement were very large, and this analysis demonstrated there was a large difference in measurement of breast volume, with total breast volumes estimated by the anthropometric formula consistently larger than the 3D scan values. Therefore, despite a relatively strong linear correlation between the two methods of breast volume measurement, the measures have low agreement on actual values and the proposed anthropometric formula is therefore an unsuitable substitute for 3D laser scanning.

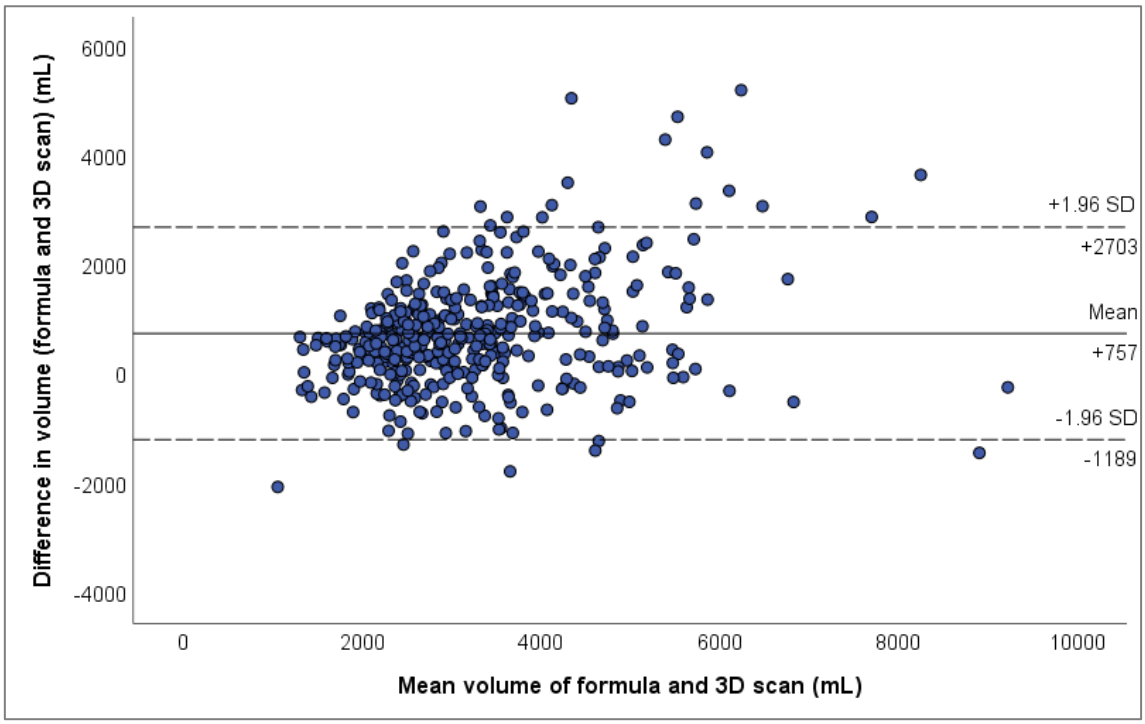


Figure 6.14 Bland-Altman plot of breast volume measured by anthropometric formula and 3D scanning techniques

6.4 Discussion

A large number of techniques for the objective measurement of breast volume have been described in the literature. However, these techniques often vary in accuracy and reliability and some are limited in their application to large-breasted patients. Many studies specifically on women with breast hypertrophy aim to develop a formula for estimating breast reduction weight in reduction mammoplasty rather than the assessment of breast volumes both before and after surgery (Appel et al., 2010, Boukovalas et al., 2019, Chan et al., 2019, Descamps et al., 2008, Dvoracek et al., 2019, Eder et al., 2007, Hernanz et al., 2014, Kececi and Sir, 2014, Kocak et al., 2011, Sommer et al., 2002, Wampler et al., 2019). This is most likely driven by restrictions placed on breast reduction surgery by healthcare providers or insurance companies which often require surgeons to predict a minimum weight of resected breast tissue. Although a formula to predict tissue resection weight is clinically useful, there remains a need for the accurate determination of absolute breast volumes both in planning breast surgery and in assessing outcomes following surgery.

In this study a series of approaches including anthropometry, 3D laser scanning and water displacement were used to measure breast and body size in women with breast hypertrophy who underwent breast reduction surgery. These measurements were invaluable in order to investigate the relationship between factors including degree of breast hypertrophy, breast asymmetry and

disproportionality on quality of life outcomes following surgery; and overcomes limitations associated with existing studies that have used indirect measures such as bra cup size or resection weight as a proxy to describe breast size. While it was hypothesised that factors including disproportionality may influence the health benefits of surgery and be used to establish an evidence-based system to prioritise patients presenting for surgery, results from this study demonstrate that there was no significant relationship between the ratio of disproportionality and the improvement in the physical or mental summary measures of the SF-36. This finding supports the conclusions described in previous chapters that the improvement in quality of life is independent of these factors and that restrictions on access to surgery based on variables including BMI, a minimum weight of resection or by the degree of disproportionality are not supported by evidence.

Findings from this study indicate that the majority of women with breast hypertrophy who presented for breast reduction surgery had a degree of breast asymmetry. Almost one-third of participants in this study were found to have a difference of greater than 200 mL between their breasts. This finding was consistent with a previous study by Tenna and colleagues who reported a difference of greater than 200g between breasts in 20% of their patients with breast hypertrophy (Tenna et al., 2012). Another important finding from the present study was that breast volume measured using 3D laser scanning was only weakly correlated with bra cup size in women with large breasts. This finding is consistent with another study which used anthropometric measurements to predict breast volume formula in women with breast hypertrophy (Sigurdson and Kirkland, 2006) and highlights that bra cup size is a poor indicator of breast volume for use in outcome studies exploring the relationship of breast volume to other clinical and outcome variables. Additionally, the results of this study demonstrate that breast size was found to be strongly correlated with body size and body mass index. In other words, women with a larger BMI and body volume tend to have larger breasts. This finding further demonstrates that BMI is an inappropriate exclusion criteria as women with a higher BMI are likely to have a larger breast volume and supports previous literature (Benditte-Klepetko et al., 2007, Brown et al., 2012). Finally, measurements using anthropometry and 3D scanning demonstrated that whilst breast size was found to significantly decrease following surgery, body size and composition measurements did not differ. This result was confirmed by the finding that BMI and body weight remained similar at pre- and post-operative timepoints.

The most accurate metric of true breast tissue volume is water displacement of mastectomy specimens, however, this is not applicable other than in post-mastectomy reconstruction scenarios (Kayar et al., 2011, Losken et al., 2005, Yip et al., 2012). Additionally, volume measurement of the intact breast has proven to be more variable due to the challenge of correctly differentiating breast tissue from the chest wall. Within the Plastic Surgery Unit at Flinders Medical Centre, 3D laser scanning has previously been validated as an accurate and reliable method of breast volume measurement and demonstrated equivalence in comparison to mastectomy volume (Yip et al.,

2012) and in comparison to breast volume measured by MRI (Howes et al., 2017). The present study further enhances the understanding of measuring breast volume using 3D laser scanning with a comparison to direct measurement of the intact breast by water displacement, and with a comparison to breast volumes measured by anthropometry in women with breast hypertrophy. The measurement of breast volumes by both 3D laser scan and water displacement showed a close association between the two techniques. However, it was found the water displacement method had a clear tendency to estimate a larger volume than the 3D scan. A possible explanation for the difference between techniques is that measurement of the intact breast volume using water displacement requires the patient to be in a prone position, which may change the form of the breast and add axillary or abdominal fat to the breast measurement. In contrast, patients are in the upright position for measurement with the 3D scanner. Another source of difference is that 3D scanning technology allows for a curved cut plane at the back of the breast where it can digitally follow the curved chest wall, while water displacement has by definition a flat cut plane at the water level. The water displacement technique is also highly dependent on the positioning of the patient. Alternative devices for the water displacement technique have been described to address the disadvantages of the immersion technique used in this study (Tezel and Numanoglu, 2000). This study therefore supports previous findings that, although water displacement is easily accessible and a low-cost option, the technique has relatively low accuracy for measurement of the intact breast due to poor reproducibility (Bulstrode et al., 2001, Henseler et al., 2011).

When comparing breast volume measurement by 3D laser scanning to anthropometric measurements for use in a predictive formula, it was found that the two methods had low agreement on values with the proposed formula resulting in significantly larger estimates of breast volume. This is likely explained by the limitations of the proposed formula which is based on geometric shape calculations when applied to large, ptotic breasts. This is consistent with the finding that whilst linear anthropometric measurements for use in predictive formula are fast and the costs are negligible, they are often less accurate and have been shown to be limited to estimates of breast volumes within a specific range (Longo et al., 2013, Qiao et al., 1997, Sigurdson and Kirkland, 2006). Therefore, the selection of the most appropriate formula and anthropometric measurements is crucial to their application in the clinical setting.

Strengths of this study include the relatively large sample size and that the data was collected prospectively. Furthermore, the manual positioning of landmarks prior to 3D scanning using palpation to accurately identify the margins of the breast base and control for potential location error, rather than relying on marking these points later in the scan image. Finally, while existing studies have relied on proxy measurements for breast and body volume such as tissue resection weight and BMI, the direct and accurate measurement of breast and body size in the present study provides a more comprehensive assessment to further enhance the assessment of outcomes

following surgery.

This study has several limitations that should be noted. Firstly, not all participants had breast volume measurements using all techniques at both the pre-operative and 12 months post-operative timepoints. It was decided that additional measurement by water displacement was too onerous for some patients given the commitments associated with voluntarily participating in the study. As a result, both of these techniques were performed on discrete subsets of patients at each timepoint. However, the majority of participants had an anthropometric body shape assessment and 3D scanning both pre- and post-operatively. Lastly, while a series of anthropometric measurements were taken to assess breast and body size, anatomic measurements specific to alternate published predictive anthropometric formulae to estimate breast volume were not performed. This limited the ability to explore the agreement between breast volume estimations using these predictive formulae and 3D scanning in the present study population.

6.5 Conclusion

This study measured breast and body size using water displacement, anthropometry and 3D laser scanning in women with large breasts undergoing breast reduction surgery. The degree of disproportionality in women with breast hypertrophy was not found to influence the improvement in health-related quality of life following surgery. Furthermore, breast size was strongly associated with body size and BMI, indicating that larger women tend to have a greater breast volume. Therefore, restrictive criteria or prioritised waiting lists based on BMI or disproportionality are not appropriate based on this evidence. Significant correlations were found between breast size and anthropometric variables, in particular sternal notch-to-nipple distance. In contrast, breast volume was found to be weakly associated with bra cup size, highlighting that cup size is not an accurate indicator of breast volume in clinical outcome studies. While this study found a strong association between the measurement of breast volumes using water displacement and 3D laser scanning techniques and anthropometric measurements and 3D scanning in women with breast hypertrophy, the methods had low agreement on actual values. While water displacement and anthropometry may be more convenient and accessible in clinical practice, 3D scanning remains preferable as it has been proven to be a more accurate and reliable technique for the determination of intact breast volume.

7. ECONOMIC EVALUATION OF BREAST REDUCTION SURGERY IN AUSTRALIA

7.1 Introduction

Measurement of health-related quality of life using validated outcome measures is increasingly being employed to measure the burden of disease and the impact of treatment and provide comparative data between different surgical and medical interventions. Traditionally, health economists attempt to guide priority-setting and resource allocation decisions by healthcare funders by measuring and valuing both the quality and quantity of health, typically measured in quality-adjusted life years (QALYs). The estimated QALY gain is often calculated from health utility scores, which provide a single measure of quality of life for a given health state, using the area under the curve approach (Matthews et al., 1990).

A cost-utility analysis is considered a subset of cost-effectiveness analysis and compares net costs against net health outcomes as measured by the QALY. As a cost-utility analysis provides a consistent unit of measure (incremental cost per QALY gained), direct comparisons can be made between funding options, and therefore this analysis is preferred by the Australian Government's Pharmaceutical Benefits Advisory Committee (PBAC) (Pharmaceutical Benefits Advisory Committee, 2016, Taylor and Jan, 2017) and Medical Services Advisory Committee (MSAC) (Medical Services Advisory Committee, 2016). The incremental cost-effectiveness ratio (ICER) threshold incorporates a society's willingness-to-pay in terms of the incremental cost for an incremental QALY gain. In Australia, while there is no explicit value, research studies have suggested that an acceptable threshold is AUD$50,000 per QALY gained (George et al., 2001, Henry et al., 2005). This implicit threshold was further supported when comparing ICERs in paired submissions to the PBAC in Australia versus NICE in the United Kingdom, the decision-making outcomes were found to be largely consistent in being above or below their corresponding threshold (Wang et al., 2018). More recently, Edney and colleagues proposed a lower estimate of AUD$28,033 per QALY gained for the ICER as a reference to inform value-based decision making in Australian health care system (Edney et al., 2018).

In an era of tight healthcare budgets, it has become increasingly important to quantify the value of surgical interventions for the treatment of non-life-threatening conditions such as breast hypertrophy. Despite published evidence on the health gains of breast reduction surgery, there is a lack of high-quality research internationally regarding the cost-effectiveness of surgery. In addition, there are no published studies from the Australian healthcare (Medicare) perspective.

The primary objective of this study was to conduct an economic evaluation of bilateral breast reduction surgery in the Australian public health system. This study describes findings of a

prospective outcome study with a 12-month follow-up and includes the comparison of surgical participants to a reference population of women with breast hypertrophy who did not undergo surgery. The results of this study, in terms of incremental costs per QALY gained, will help determine whether breast reduction surgery is justifiable for government funding within the Australian healthcare sector.

7.2 Participants and methods

7.2.1 Participants

The data for this health economic evaluation were obtained from the prospective cohort study described previously in Chapter 2, comprising a surgical cohort and a breast hypertrophy control cohort. All participants were referred to the Department of Plastic and Reconstructive Surgery, Flinders Medical Centre, Adelaide, South Australia. In summary, women who underwent bilateral breast reduction surgery completed assessments pre-operatively and at 3, 6 and 12 months following surgery. A control group of women with breast hypertrophy who were actively seeking breast reduction surgery but were not expected to undergo surgery within 12 months were recruited for comparison and completed study questionnaires via postal survey. Ethics approval was obtained for this study from the Southern Adelaide Clinical Human Research Ethics Committee (SAC HREC reference numbers 118.056 and 73.17) (Appendix B and Appendix C).

7.2.2 Healthcare costs

Direct hospital costs for the surgical intervention were determined from the Australian (Medicare) healthcare perspective. Flinders Medical Centre is a tertiary care teaching hospital with 593 beds capacity and is predominantly funded through the Australian Medicare Scheme. Individual patient costs were obtained from the Power Performance Management (PPM) system (PowerHealth Pty Ltd, Adelaide, Australia) using surgical procedure codes (International Statistical Classification of Diseases and Related Health Problems, Australian Modification, ICD-10-AM codes)(IHPA, 2018) including the hospital costs of the original surgical admission and hospital costs for all readmissions and outpatient appointments within 12 months of surgery. Cost data for hospital admission was captured at the individual patient level and included theatre costs, specialist costs, critical care, imaging, pathology, pharmacy, allied health, ward nursing, ward medical, ward supply and non-clinical salaries. All hospital costs within 12 months of surgery for outpatient clinical appointments, return to theatre admissions and revisional procedures were included in the analyses to capture all direct hospital costs associated with surgical intervention. Costs were inflation-adjusted to 2016 Australian dollars using the relevant consumer price index (CPI), as this was the final year of recruitment in the study (Australian Bureau of Statistics, 2016b). Indirect costs such as those incurred by the participant including productivity costs due to possible absence from work were not included.

7.2.3 Health-related quality of life

Health-related quality of life (HRQoL) was assessed using the Short Form-36 (SF-36) version 2 instrument (Ware and Sherbourne, 1992). Surgical participants competed the SF-36 questionnaire pre-operatively and again at 3, 6, and 12 months post-operatively. Participants in the breast hypertrophy control group who were awaiting consultation for surgery completed the questionnaire at baseline and at 12 months following. This was described in further detail in Chapter 2.

Responses to individual items from the SF-36 questionnaire can be used in economic evaluations by transformation of responses into a single SF-6D utility score. In this study, the preference-based scoring algorithm developed by Brazier and colleagues was used to calculate individual SF-6D health utility scores for participants at each study timepoint (Brazier et al., 2002). This original algorithm was derived from a general population sample from the United Kingdom (UK). An algorithm for Australian preference weights for the SF-6D utility has since been developed by Norman et al. and was also used to convert SF-36 responses to individual utility scores in this study (Norman et al., 2014). The algorithm calculates a SF-6D index score based on responses to 11 of the 36 items from 6 dimensions of the SF-36 questionnaire including Physical Functioning (items 3a, 3b, and 3j); Role Limitation due to physical problems (item 4c) and Role Limitation due to emotional problems (item 5b); Social Functioning (item 10); both bodily pain items (items 7 and 8); Mental Health (items 9b and 9f); and Vitality (item 9e) (Appendix D). The SF-6D defines utility values for 18,000 possible health states of the SF-36 on a scale, with a score of one representing full health and a health state equivalent to being dead valued at zero. Negative values indicate a poor health state considered worse than death.

For comparison purposes, population normative SF-36v2 scores were obtained from the 2008 South Australian Health Omnibus Survey (SAHOS), with de-identified raw data kindly provided by David Banham and Professor Robert Goldney, Department of Psychiatry, University of Adelaide. Normative SF-6D scores were then derived from the SF-36 responses from female respondents using the United Kingdom and Australian preference weights described previously. Normative SF-6D population data was age-standardised to correspond to the age distribution of the surgical participants.

7.2.4 Cost-utility analysis

Effectiveness of the surgical intervention was measured in terms of quality-adjusted life years (QALYs) gained. The QALY gain over the 12 month period was calculated at an individual patient level using SF-6D utility values and the area under the curve method (Drummond, 2005). A cost per QALY was calculated by dividing the mean costs by the mean number of QALYs gained to provide an estimate of cost-utility. Both unadjusted and adjusted QALYs (adjusted for any differences in SF-6D utility scores at baseline) were calculated. As there is no SF-6D data for the control group at the 3- and 6-months follow-up periods, only baseline and 12 months SF-6D data

were used in calculating the QALYs for the base case analysis. QALYs based on all four time-points in the intervention groups were also calculated and examined within a sensitivity analysis (see Section 7.2.5). For the base case, 12-month QALYs were extrapolated to a 10-year time horizon as HRQoL gains were shown to be maintained in this longer time period as described in Chapter 5. As per PBAC and MSAC guidelines, a discount rate of 5% per year was applied to QALY gains over any period beyond 1 year (Medical Services Advisory Committee, 2016, Pharmaceutical Benefits Advisory Committee, 2016). Calculations for discounting involve multiplying the value of costs and benefits for each year in the future using the formula: $(1/(1 + D)^y)$, where the discount rate is denoted by D and y is the number of years (Drummond, 2005). However, whilst the health gains from treatment were expected to last several years, the direct costs of surgery in this study were expected to be confined to the 12-month study period and were therefore not discounted.

The economic evaluation used in this study was a cost-utility analysis (CUA), with primary outcomes expressed in terms of QALYs. Secondary outcomes of the CUA were expressed as incremental costs per QALYs gained in order to determine the incremental cost effectiveness ratio (ICER). The ICERs were calculated as the differences in costs between the intervention and the control group divided by the difference in QALY gain: $ICER=C_a – C_b/E_a – E_b$, where C_a is the cost of the intervention, C_b is the cost of the control, E_a is the effectiveness of the intervention, and E_b is the effectiveness of the control. In this study, cost-effectiveness at willingness to pay thresholds of AUD$28,033 per QALY gained (Edney et al., 2018) and AUD$50,000 per QALY gained (Harris et al., 2008) were used for decision-making. Bootstrapping was used to account for uncertainty due to sampling variation in the ICER; and 5,000 paired estimates of mean differences in costs and outcomes (QALYs) were derived. The bootstrapped pairs were summarized in cost-effectiveness planes (CEPs) (Black, 1990). Figure 7.1 illustrates the decision rules for the four-quadrants of the incremental cost-effectiveness plane. In interpreting the results of the cost-effectiveness planes, observations that fall within the ‘north-west’ quadrant indicate the intervention is less effective and more costly than the comparator and therefore rejected; and in the ‘south-east’ quadrant the intervention is more effective and less costly than the comparator and therefore has an acceptable cost-effectiveness profile. Observations that fall within the ‘north-east’ quadrant are more effective and more costly than the comparator; and in the ‘south-west’ quadrant the intervention is considered to be less effective and less costly than the comparator, with both quadrants indicating the intervention is potentially acceptable. The probability of the intervention being more cost-effective compared to the control at varying willingness-to-pay thresholds was presented using cost-effectiveness acceptability curves (CEACs) (Fenwick et al., 2001).

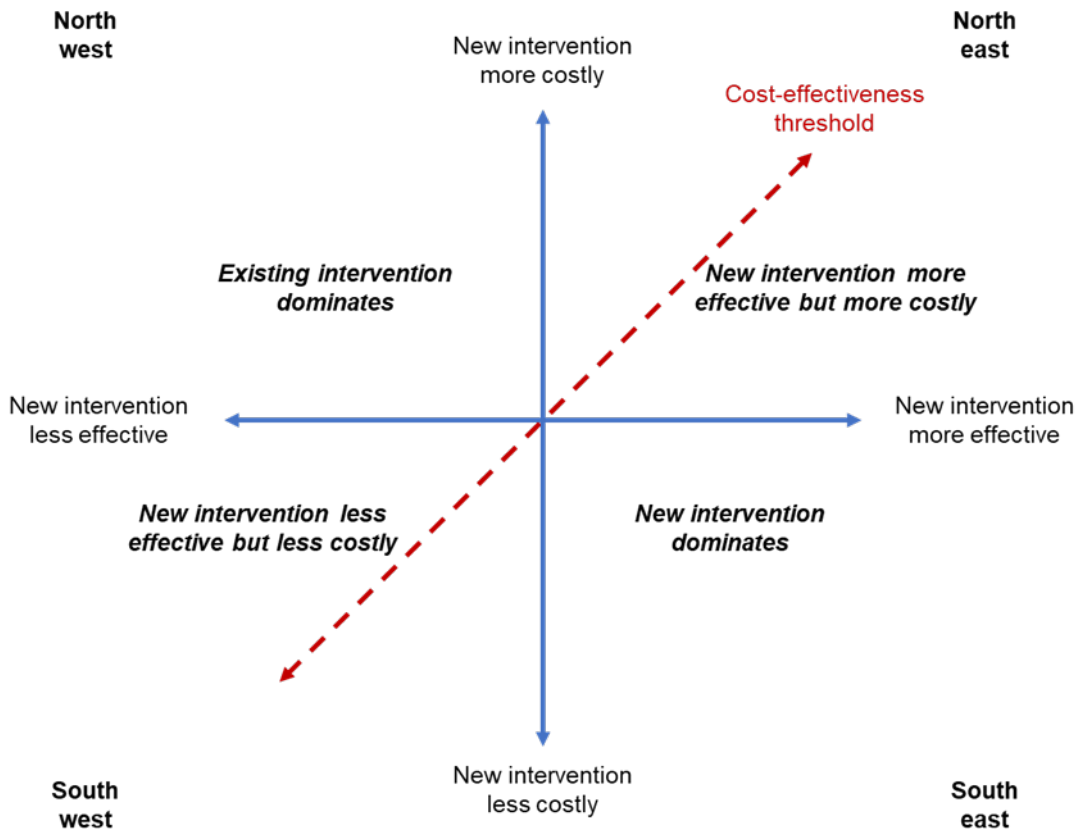


Figure 7.1 The cost-effectiveness plane.

The x-axis shows the difference in effectiveness between the new intervention and the existing and the y-axis shows the difference in cost.

Due to the presence of missing data on costs and outcomes, multiple imputation was used to account for missing values. Data was deemed to be missing at random (MAR) and imputed values were generated for cost and outcome variables using the multiple imputation with Predictive Mean Matching (PMM) algorithm, a method that matches the missing value to the observed value with the closest predicted estimate (Little, 1988, Rubin, 1986). The PMM method was used as the normality assumption for the SF-6D was violated, that is, the SF-6D scores were not normally distributed. A total of 50 multiple-imputed complete datasets were generated and the following variables were used to predict the missing values for the surgical cohort: age, height, weight, body mass index, smoking, bra cup size, and length of hospital stay. For the control cohort the variables used to predict missing values included age, height, weight, body mass index, smoking and bra cup size. The multiple imputed data is presented as the base case, with the complete case analysis explored in a sensitivity analysis.

7.2.5 Sensitivity analysis

Sensitivity analyses were performed to test the robustness of the base case results. The first sensitivity analysis focused on assessing the impact of missing cost and outcome data by

comparing results of the economic evaluation based on complete cases with those estimated using multiple imputation. The second sensitivity analysis explored using QALY estimates based on the four study timepoints in surgical intervention group in comparison to results based on baseline and 12-month follow-up only. The third sensitivity analysis considered 12-month QALYs extrapolated 40 years (average life years remaining) under the assumption that the HRQoL gain was maintained until the end of the statistical life expectancy for the study cohort with a mean age of 43 years; for females in Australia this was 84.6 years (Australian Institute of Health and Welfare, 2019a). Although this is not strictly accurate as HRQoL is known to deteriorate over time, this approach is widely used for the calculation of QALYs gained following medical interventions. Finally, all sensitivity analyses explored results using UK versus Australian preference-based weights for transforming the SF-36 responses to health utilities, and cost-effectiveness was determined at two different willingness-to-pay thresholds of $28,033 and $50,000 per QALY gained.

7.2.6 Statistical analysis

Statistical analyses were performed using SPSS v25.0 statistical software for Windows (IBM Corp., Armonk, N.Y.) and Stata statistical software version 16 (StataCorp, College Station, TX). Continuous variables were presented as mean values with standard deviations, and differences between groups as mean differences with 95% confidence intervals. Comparisons of participant socio-demographic variables were made between groups using an independent samples *t*-test. Categorical variables were expressed as frequencies (percentage) and were compared using chi-square (χ^2) statistics or Fisher's exact test as appropriate.

7.3 Results

A total of 251 participants were enrolled in the study and underwent bilateral breast reduction surgery. Of these, 209 (83.3%) completed at least one post-operative assessment; 191 (91%) at 3 months, 183 (88%) at 6 months and 193 (92%) at 12 months. Missing data were due to participants repeatedly not attending appointments or choosing to not complete and return the study questionnaires. Twenty-three participants formally withdrew from the study following surgical intervention and were therefore excluded from the analysis. A total of 159 (63.3%) participants completed all four study timepoints. Of these, 141 had no missing responses to items from the SF-36 questionnaire and therefore SF-6D utility scores were generated. This was the study group used for the complete case cost-utility analysis.

In the breast hypertrophy control group, study questionnaires were initially posted to 350 women on the waiting list; 160 (46%) completed and returned the questionnaires at baseline, and of these 124 responded again 12 months later. Of these, SF-6D utility scores were able to be generated from 119 participants in the control hypertrophy group and this was the study group used for the

complete case analysis. Baseline demographic characteristics from the surgical and hypertrophy control groups were similar between the two groups and are summarised in Table 7.1.

Table 7.1 Baseline characteristics of participants

Characteristic	Surgical intervention (*n* = 209)	Control hypertrophy (*n* = 124)	*p*-value†
Age mean (SD), years	42.6 (13.4)	45.3 (13.1)	0.079
BMI, mean (SD), kg/m^2	32.7 (6.0)	32.1 (6.0)	0.468
Obesity status:			
Non-obese <30 kg/m^2	71 (34)	48 (39)	0.326
Obese ≥30 kg/m^2	138 (66)	74 (61)	
Smoking status:			0.243
Non-smoker	108 (52)	78 (63)	
Current smoker	35 (17)	14 (11)	
Reformed < 1 year	15 (7)	5 (5)	
Reformed ≥ 1 year	47 (23)	25 (20)	

Values are numbers (percentages) unless stated otherwise.
† Using an independent samples *t*-test, X^2 or Fisher's exact test as appropriate.

7.3.1 Healthcare costs

Direct healthcare costs were calculated at the individual patient level for the original surgical admission and included relevant hospital costs for all readmissions and outpatient appointments within 12 months of surgery. A summary of the mean costs (in 2016 Australian dollars) for the surgical intervention across the 12-month period are shown in Table 7.2. The greatest cost was for the hospitalisation episode (AUD$9464), with outpatient clinic appointments providing an average additional cost of AUD$740 to the cost of the surgery. Any required return to theatre episodes and/or revisional procedures were included in the total direct hospital costs. A comparison of costing data from the National Hospital Cost Data Collection (NHCDC) Australian Public Hospitals Cost Report 2015 to 2016, Round 20, for AR-DRG version 8.0 reported the mean cost of surgery in an Australian public hospital to be AUD$9199.96, which is consistent with our findings (IHPA, 2018). The breast hypertrophy control group did not incur any direct hospital costs as they did not undergo any intervention during the study timeframe.

Table 7.2 Costs per participant for intervention and control groups over 12 months ($AUD)

Costs	Intervention Mean (SD)	Control Mean (SD)	Between-group difference (95% bootstrapped CI)
Base-case analysis (imputed)	*n* = 209	*n* = 124	
Direct cost – hospital stay	9464 (3621)	0.00 (0.00)	9464 (9244 to 9685)
Outpatient clinic consultation	250 (105)	0.00 (0.00)	250 (234 to 266)
Plastic surgery outpatient treatment	490 (320)	0.00 (0.00)	490 (458 to 522)
Total cost	10,204 (3719)	0.00 (0.00)	10,204 (9981 to 10,427)
Sensitivity analysis (complete cases)	*n* = 196	*n* = 124	
Direct cost – hospital stay	9370 (3624)	0.00 (0.00)	9370 (8859 to 9880)
Outpatient clinic consultation	250 (102)	0.00 (0.00)	250 (236 to 265)
Plastic surgery outpatient treatment	492 (311)	0.00 (0.00)	492 (448 to 536)
Total cost	10,112 (3728)	0.00 (0.00)	10,112 (9863 to 10,360)

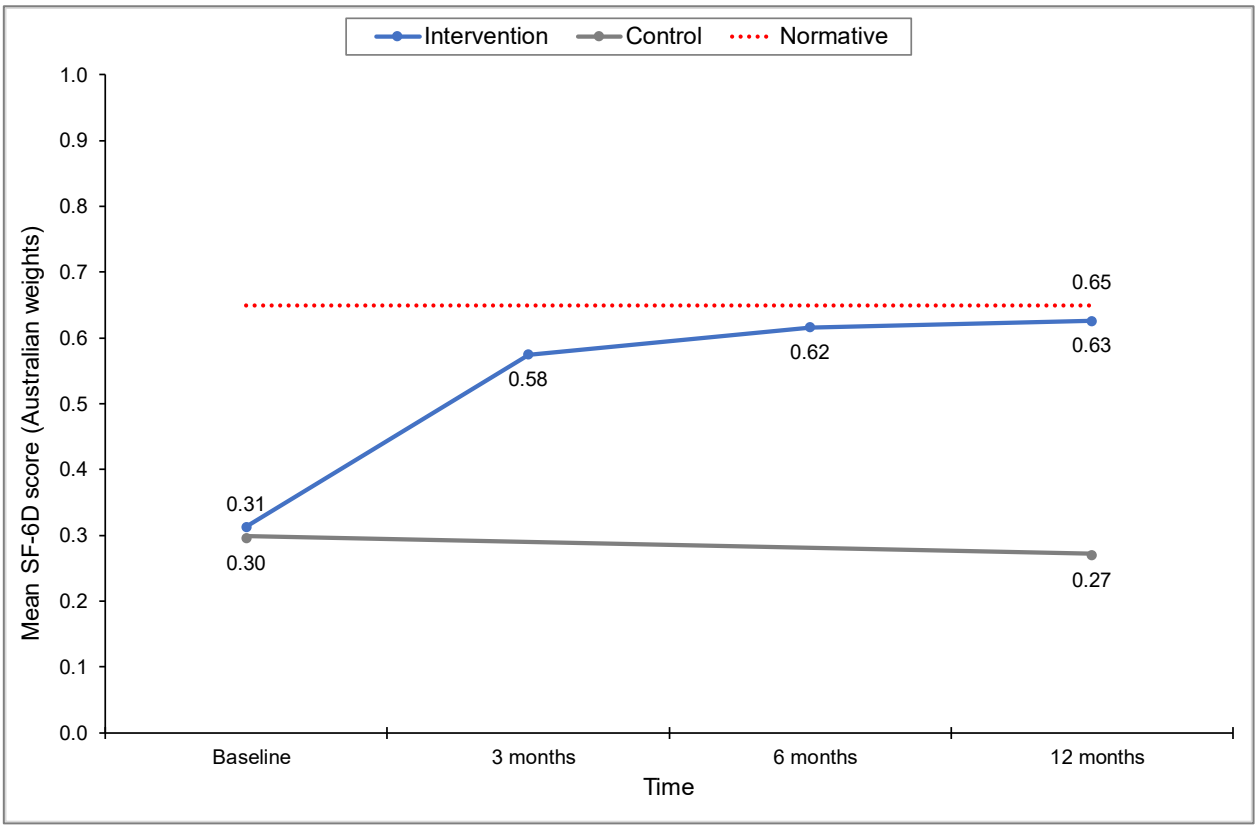
7.3.2 Outcomes

Health-related quality of life outcomes as assessed by the SF-6D and scored using both the Australian and UK scoring algorithms are presented in Figure 7.2. Utility scores in the surgical intervention group significantly increased from baseline to 3 months and remained stable at 6 and 12 months ($p < 0.001$). In contrast, health-related quality of life decreased in the control group from baseline to 12 months.

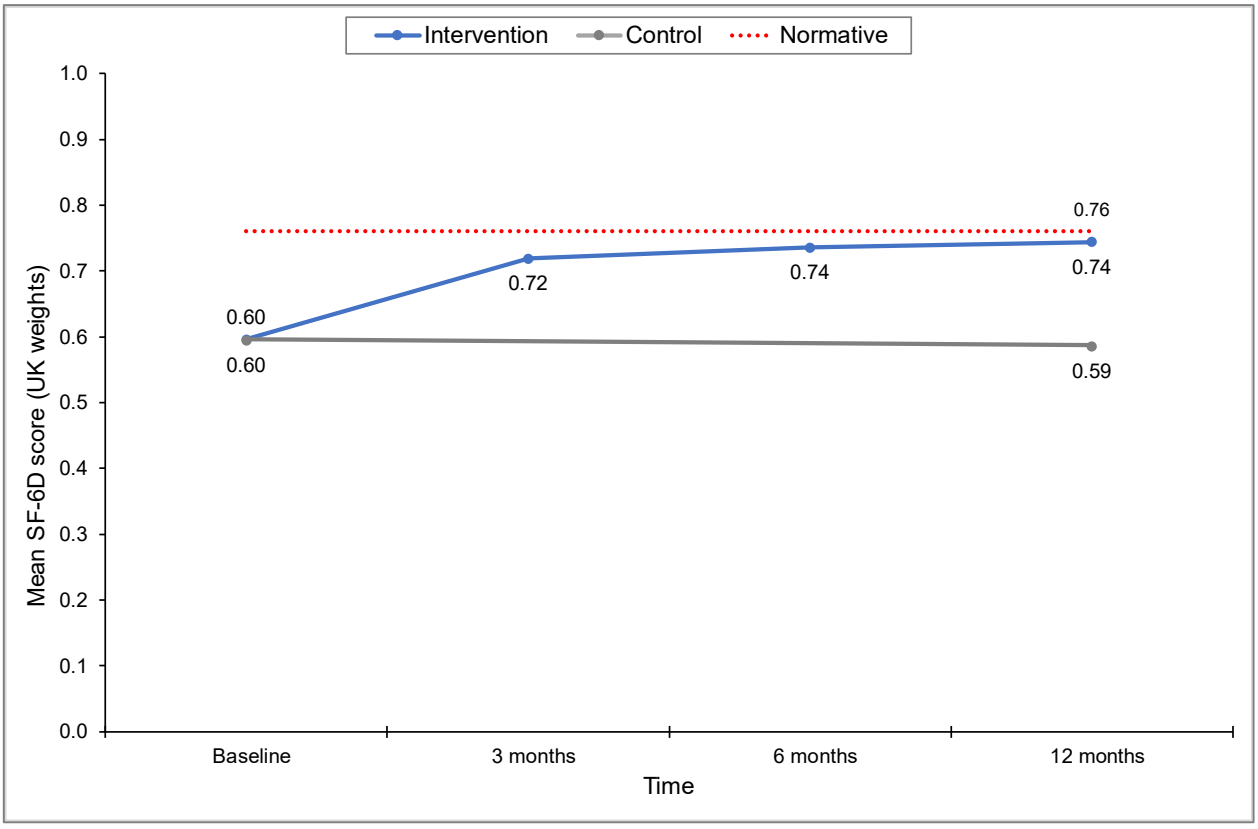
Australian female normative SF-6D values were derived from SF-36 data using the two different algorithms for comparison to study participants, resulting in an age-adjusted mean score of 0.65 (SD 0.04) (Australian weights) and 0.76 (SD 0.01) (Brazier's UK weights) from 1708 respondents. In comparison to population norms, participants with breast hypertrophy had significantly lower utility scores ($p < 0.001$). In the group who underwent surgical intervention, utility scores significantly increased (mean change 0.32 points using Australian weights and 0.15 points using UK weights) to levels equivalent to those of the normal population (Figure 7.2).

Within the 12-month time frame of the study, the QALY gains were higher for the surgical intervention group (mean 0.469, SD 0.223) than for the control (mean 0.283, SD 0.235), with a mean difference of 0.186 (95% CI, 0.163 to 0.210) when using Australian SF-6D scoring weights. Similarly, QALY gains in the intervention group (mean 0.670, SD 0.106) were higher than in the control group (mean 0.590, SD 0.100) with a mean difference of 0.080 (95% CI, 0.074 to 0.085) using Brazier's UK scoring algorithm.

Table 7.3 summarises SF-6D utility scores and QALYs gained for the surgical intervention and control groups. For the base case analysis, the adjusted QALY gains over a 10-year time horizon were higher for the surgical intervention group (mean difference of 1.519; 95% CI, 1.362 to 1.675) for the SF-6D Australian valuation and for the SF-6D UK valuation (mean difference of 0.690; 95% CI, 0.618 to 0.761). A similar pattern was observed with the unadjusted analyses and complete case analyses.



a. SF-6D scores based on Australian preference-based scoring weights



b. SF-6D scores based on UK preference-based scoring weights

Figure 7.2 Mean SF-6D utility scores for surgical intervention and control cohorts in comparison to age-adjusted normative data

Table 7.3 Utility scores and QALYs gained for the intervention and control groups

Variable	Australian Scoring Algorithm			UK Scoring Algorithm		
	Intervention Mean (SD)	Control Mean (SD)	Difference (Bootstrapped 95% CI)	Intervention Mean (SD)	Control Mean (SD)	Difference (Bootstrapped 95% CI)
Base case analysis (imputed cases)	*n* = 209	*n* = 124		*n* = 209	*n* = 124	
SF-6D scores						
Baseline	0.313 (0.263)	0.296 (0.267)	0.017 (-0.011, 0.045)	0.596 (0.116)	0.595 (0.116)	0.001 (-0.012, 0.015)
3 months	0.575 (0.287)	-		0.719 (0.141)	-	
6 months	0.616 (0.294)	-		0.736 (0.154)	-	
12 months	0.626 (0.277)	0.270 (0.257)	0.356 (0.322, 0.390)	0.744 (0.139)	0.585 (0.110)	0.159 (0.147, 0.170)
Unadjusted QALYs	4.094 (1.941)	2.467 (2.050)	1.627 (1.425, 1.828)	5.841 (0.922)	5.145 (0.868)	0.697 (0.648, 0.745)
Adjusted[a] QALYs			1.519 (1.362, 1.675)			0.690 (0.618, 0.761)
Length of inpatient stay, days	2.39 (0.88)	-	-	-	-	-
Sensitivity analysis (complete cases)[b]	*n* = 141	*n* = 119		*n* = 141	*n* = 119	
SF-6D scores						
Baseline	0.314 (0.259)	0.295 (0.262)	0.017 (-0.011, 0.045)	0.596 (0.114)	0.595 (0.114)	0.001 (-0.012, 0.015)
3 months	0.570 (0.270)	-		0.718 (0.133)	-	
6 months	0.612 (0.280)	-		0.734 (0.143)	-	
12 months	0.628 (0.265)	0.270 (0.256)	0.356 (0.322, 0.390)	0.744 (0.135)	0.585 (0.109)	0.159 (0.147, 0.170)
Unadjusted QALYs	4.152 (1.927)	2.447 (2.060)	1.705 (1.307, 2.102)	5.859 (0.922)	5.132 (0.081)	0.727 (0.533, 0.920)
Adjusted[a] QALYs			1.491 (1.020, 1.961)			0.683 (0.477, 0.889)
Length of inpatient stay, days	2.43 (0.87)	-	-	-	-	-
Sensitivity analysis (imputed cases – SF-6D values at all 4 timepoints used for QALY calculation in the intervention)						
Unadjusted QALYs	4.973 (1.883)	2.467 (2.050)	2.505 (2.216, 2.794)	6.245 (0.948)	5.145 (0.868)	1.101 (0.996, 1.204)
Adjusted[a] QALYs			2.419 (2.201, 2.637)			1.095 (0.991, 1.199)
Sensitivity analysis (imputed cases - QALYs gained over mean lifetime remaining years)						
Unadjusted QALYs	8.523 (4.041)	5.137 (4.269)	3.387 (2.967, 3.807)	12.16 (1.920)	10.71 (1.807)	1.451 (1.350, 1.551)
Adjusted[a] QALYs			3.162 (2.836, 3.488)			1.436 (1.288, 1.584)

[a] Predicted scores were adjusted for SF-6D utility score at baseline

[b] Study participants with complete information at baseline and 12-month outcomes

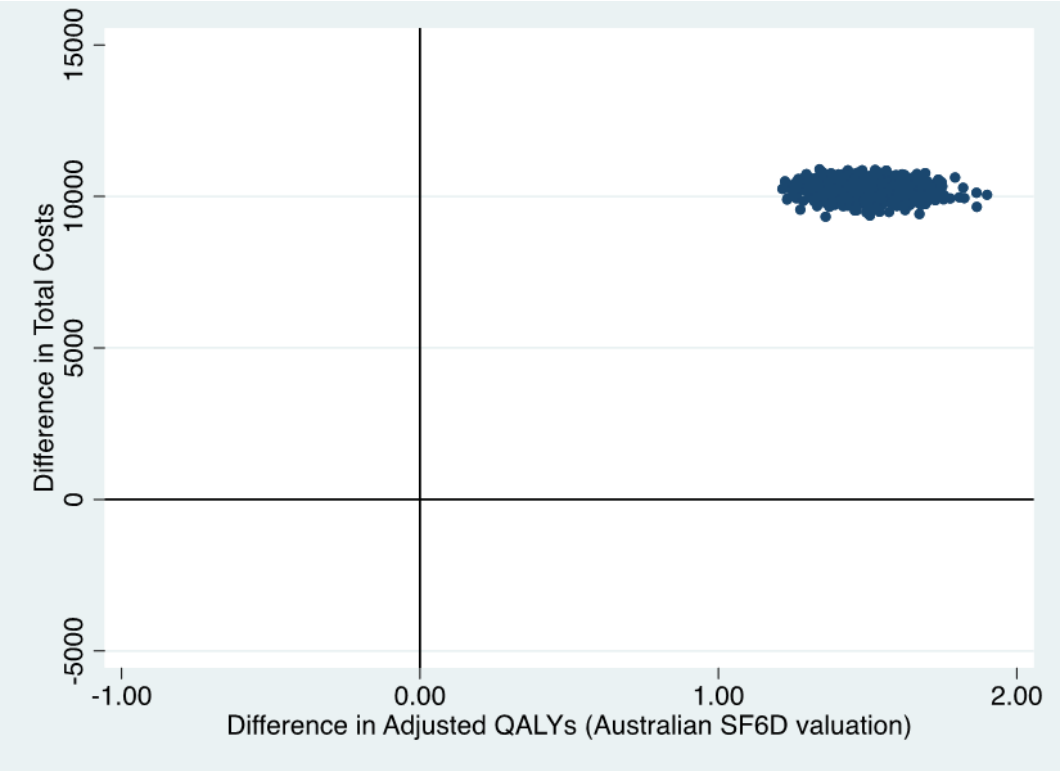
7.3.3 Cost-utility analysis

7.3.3.1 Base case analysis

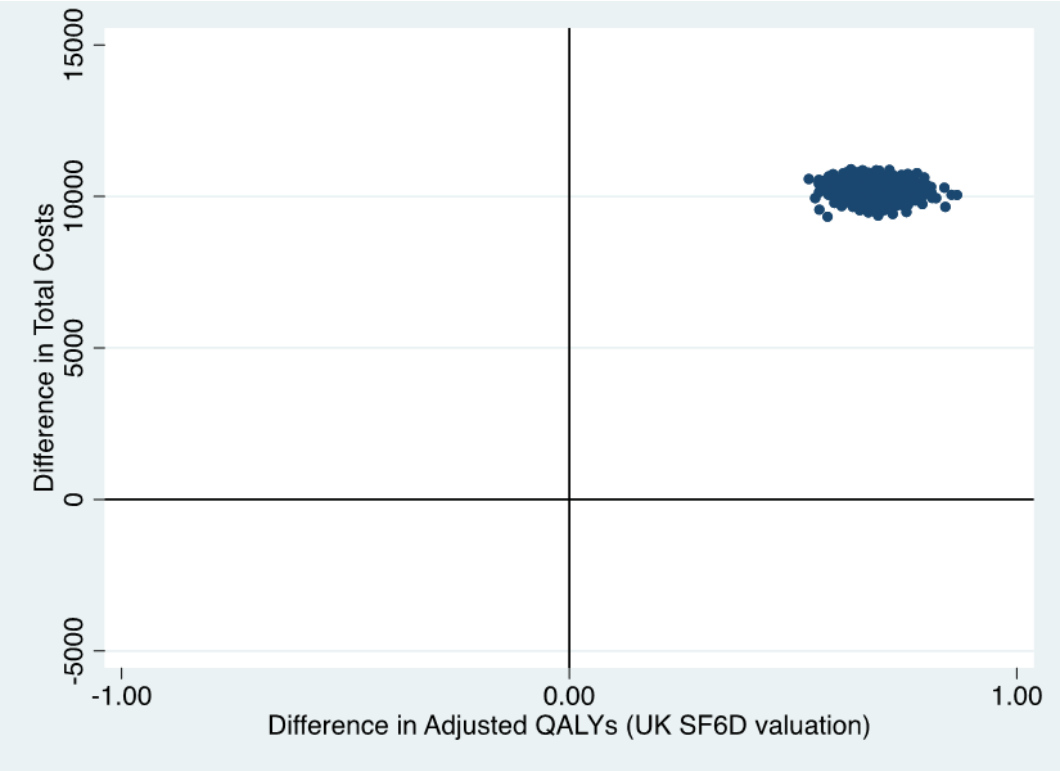
As the surgical intervention group was more expensive than the control group by $10,204 per patient (95% CI: $9,981 to $10,427), the intervention was associated with an incremental cost-effectiveness ratio (ICER) of $6,719 (95% CI: $6,142 to $6,919) per QALY gained (based on the Australian SF-6D valuation) and of $14,795 (95% CI: $13,811 to $15,215) per QALY gained (based on the UK SF-6D valuation).

Figure 7.3 presents the cost-effectiveness planes for the base case analysis in the present study based on UK and Australian preference weights. All (100%) of the bootstrapped paired estimates of mean differences in costs and outcomes appear within the north-east quadrant, indicating that the intervention provides better health outcomes but at a higher cost than the control comparator. The tight grouping of data points indicates a low level of variability in the data and therefore a relatively high degree of certainty in the cost-effectiveness results.

The cost-effectiveness acceptability curves (Figure 7.4) show the probability of the intervention being cost-effective at different willingness to pay thresholds. When the Australian SF-6D valuation is used, the intervention had a 94% probability of being cost-effective at the revised willingness to pay threshold of $28,033 per QALY gained, and 100% probability of being the cost-effective option at a willingness to pay threshold of $50,000 per QALY gained which is the implicit criterion used for assessing the cost-effectiveness of new pharmaceuticals and medical services in Australia (Harris et al., 2008). When the UK SF-6D valuation is used, the intervention again had a 74% probability of being cost-effective at a willingness to pay threshold of $28,033 per QALY gained, and 98% probability of being the cost-effective option at a willingness to pay threshold of $50,000 per QALY gained.

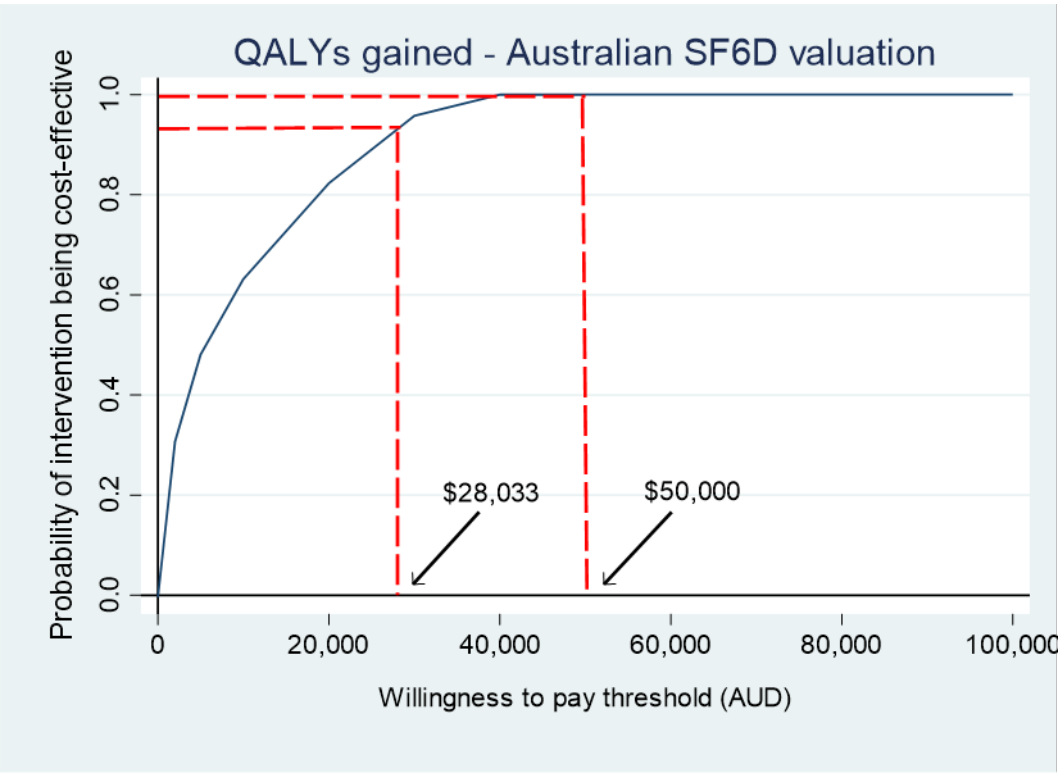


a. Cost-effectiveness plane for the difference in QALYs calculated using Australian weights over 10 years

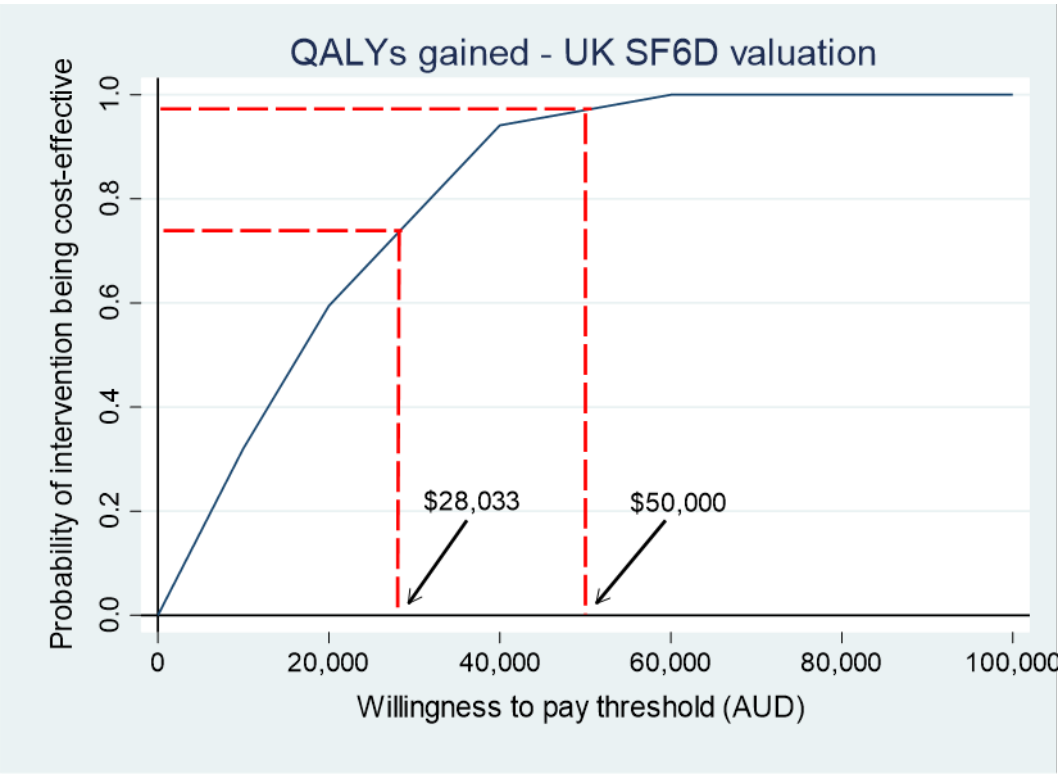


b. Cost-effectiveness plane for the difference in QALYs calculated using UK weights over 10 years

Figure 7.3 Cost-Effectiveness Planes



a. Differences in QALYs gained based on SF-6D utility scores calculated using Australian weights over 10 years



b. Differences in QALYs gained based on SF-6D utility scores calculated using UK weights over 10 years

Figure 7.4 Cost-Effectiveness Acceptability Curves

7.3.3.2 Sensitivity analysis

Sensitivity analyses were performed and found the results of the base case to be robust. Results of the sensitivity analyses are summarised in Table 7.3. In the base case analysis, multiple imputation was utilised to estimate missing data on costs (13 observations or 6.2%) and SF-6D utility scores at 12-months (16 observations or 7.7%). In the first sensitivity analysis, using the complete case dataset for analysis did not have an effect on the QALY gains or the incremental effectiveness over the 10-year time horizon (Table 7.3). The adjusted QALY gains over the 10-year time period were still higher for the surgical intervention group in comparison to the control group with a mean difference of 1.491 (95% CI: 1.020 to 1.961) for the SF-6D Australian valuation and a difference of 0.683 (95% CI: 0.477 to 0.889) for the SF-6D UK valuation. A similar pattern was observed with the unadjusted analyses. The surgical intervention group was more expensive than the control group by $10,112 per patient (95% CI: $9,863 to $10,360). The resultant ICERs were $6,784 per QALY gained (95% CI: $6,416 to $6,997) based on the Australian SF-6D valuation and $14,808 per QALY gained (95% CI: $13,681 to $15,964) based on the UK SF-6D valuation.

The second sensitivity analysis considered using imputed dataset of SF-6D values collected at 4 time points to calculate QALY gains over 10 years. The adjusted QALYs gains over the 10-year period were much higher for the surgical intervention group than the control group with a mean difference of 2.419 (95% CI: 2.201 to 2.637) for the SF-6D Australian valuation and a mean difference of 1.095 (95% CI: 0.991 to 1.199) for the SF-6D UK valuation. A similar pattern was observed with the unadjusted or complete-cases analyses. The resultant ICERs were $4218 (95% CI: $3980 to $4455) per QALY gained (based on the Australian SF-6D valuation) and $9319 (95% CI: $8615 to $9756) per QALY gained (based on the UK SF-6D valuation).

The final sensitivity analysis extrapolated QALY gains to estimated lifetime years remaining. The adjusted QALY gains were higher for the surgical intervention group than the control group with a mean difference of 3.162 (95% CI: 2.836 to 3.488) for the SF-6D Australian valuation and a difference of 1.436 (95% CI: 1.288 to 1.584) for the SF-6D UK valuation. The intervention was associated with an incremental cost-effectiveness ratio (ICER) of $3,227 per QALY gained (95% CI: $2,950 to $3,323) based on the Australian SF-6D valuation and $7,106 per QALY gained (95% CI: $6,633 to $7,308) based on the UK SF-6D valuation.

Results of each of the sensitivity analyses did not change the final interpretation of the study as the impact of the intervention still exceeded the control and all ICERs for the intervention were considerably lower than the recommended willingness-to-pay thresholds of $28,033 per QALY gained or $50,000 per QALY gained.

All cost-utility analyses were conducted using the two different scoring algorithms for the calculation of SF-6D utility scores based on UK and Australian population weights. A scatterplot

comparing SF-6D utility values calculated using the two algorithms is presented in Figure 7.5, with a line indicating perfect equivalence. It was apparent that substantial differences existed in the health utility values derived using each scoring approach, particularly in the lower scoring range. As an example, the Australian algorithm estimated health states for some participants to be valued below zero, meaning they were considered to represent a health state worse than death. In contrast, Brazier's UK algorithm did not estimate any health states to be below zero, and the minimum value was found to be with 0.3. This finding is consistent with that reported by the developers of the Australian algorithm based on normative data (Norman et al., 2014).

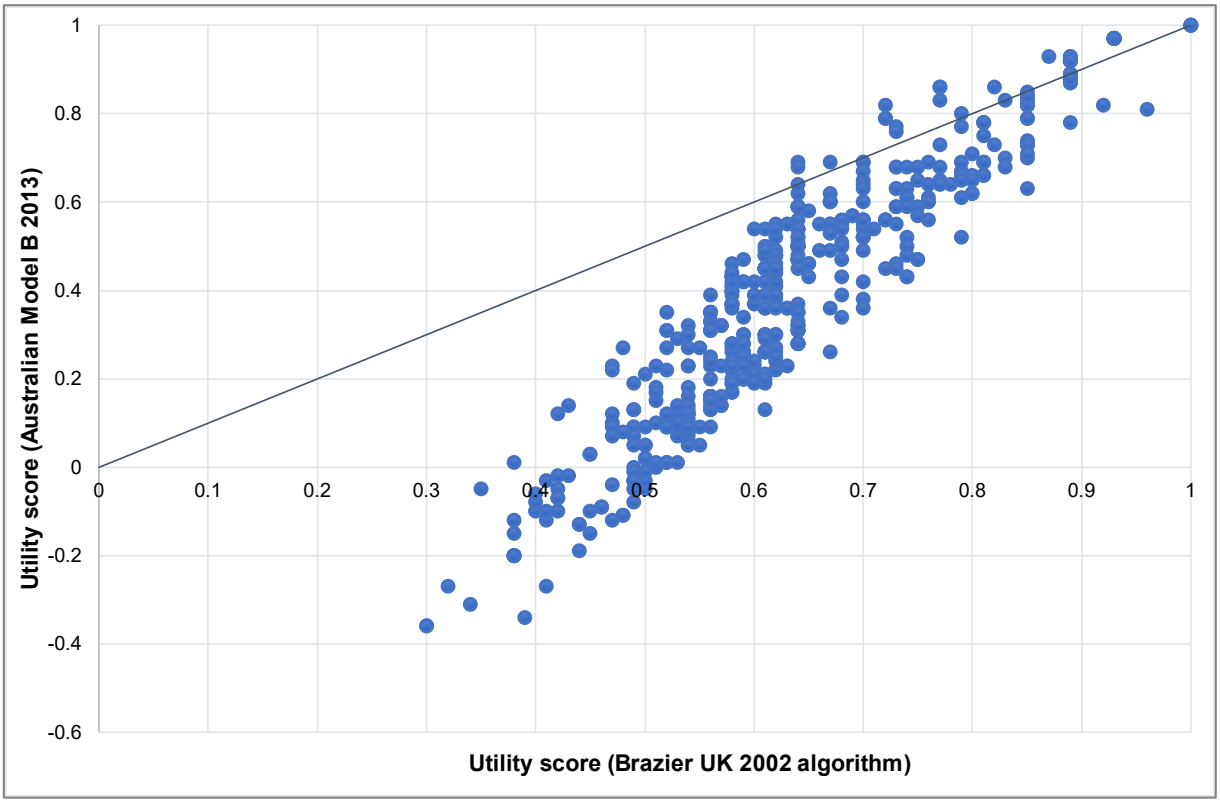


Figure 7.5 Comparison of health state using different algorithms

7.4 Discussion

The findings of this study indicate that women with breast hypertrophy who were awaiting surgery in both surgical and control hypertrophy groups reported a significantly lower health status in comparison to the female general population. Following surgery health utility scores significantly improved to levels equivalent to the general female population, demonstrating the effectiveness of surgery. The mean improvement in SF-6D health utility of 0.32-points using the Australian valuation or 0.15-points using the UK valuation following surgery is well in excess of the minimal important difference reported by Walters and Brazier who found that the SF-6D MID for 11 disease groups ranged from 0.011 to 0.097 with a mean of 0.041 (Walters and Brazier, 2005).

The analysis for this study focused on conducting an economic evaluation of breast reduction surgery to determine the likelihood of the intervention being regarded as cost-effective within the Australian public healthcare setting. Results from this study indicate that the cost-effectiveness of surgery is favourable within an Australian context. The finding that that the QALY gain following breast reduction surgery is considerable and at a reasonable cost to the health system, with a mean cost per QALY gained estimated at $6719 Australian dollars per QALY gained based on the Australian SF-6D valuation. Accordingly, results from the base-case analysis for this study show that the probability of breast reduction surgery being cost-effective was 100% at a willingness-to-pay $50,000 per QALY gained and 94% at the lower threshold of $28,033 per QALY gained. Therefore, under these reference criteria, the findings of our study demonstrate that surgery is justified for inclusion within the Australian healthcare system.

The time horizon of 10 years used in this analysis may be considered conservative as it is likely that the positive effects of breast reduction surgery continue over a longer period of time. Results from the long-term outcome study described in Chapter 5 support that the benefits of surgery were maintained and did not deteriorate over this follow-up. This finding provides reliable data to support that the cost-utility of surgery would be even more favourable given that the health benefits of surgery are likely to continue well beyond 10 years. This was confirmed with the results of the sensitivity analysis which extrapolated QALY gains over the average number of lifetime years remaining. Furthermore, the validity of the results was further strengthened by additional sensitivity analyses which demonstrated that changes in QALY calculations or choice of scoring algorithm did not change the main conclusions of the study.

Research assessing the cost-utility or cost-effectiveness of breast reduction surgery is limited and has only been described in a few countries worldwide including the United Kingdom (Taylor et al., 2004), Finland (Saariniemi et al., 2012, Tykka et al., 2010), Canada (Thoma et al., 2014) and Brazil (Araujo et al., 2014). Araujo and colleagues evaluated the cost-utility of reduction mammaplasty in the Brazilian public health system and reported a gain of 0.74 QALYs using the SF-6D from SF-36 data (Araujo et al., 2014). However, the average direct cost of surgery was low at R$391.47 (approximately £104 or AUD$130), corresponding to a cost per QALY of R$536.26 (approximately £142 or AUD$178). This cost-utility ratio reflects the extremely low compensation paid by funders to public hospitals and medical staff in Brazil. Unfortunately, further comparisons are limited as this study did not extrapolate QALY gains beyond the 6-month follow-up nor report any sensitivity analyses. In the United Kingdom, the cost per QALY for reduction mammaplasty was found to be between £4733 and £5729 (approximately AUD$9427 and AUD$11,411) with a three-year time horizon and was deemed to be cost-effective when compared to other interventions approved by NICE. However, HRQoL data using the SF-36 instrument was obtained from a Swedish study of 49 women, whilst the cost data was the average cost taken from the United Kingdom Department of Health Schedule of Reference Costs (Taylor et al., 2004). In addition, this study did not report

the number of QALYs gained or perform any sensitivity analyses. In Finland, the average direct hospital costs for reduction mammoplasty was approximately €3601 (approximately AUD$6408) and the mean cost per QALY gained was €1180 (approximately AUD$2100) (Saariniemi et al., 2012). In another Finnish study, the mean direct costs were found to be comparable at €3383 (approximately AUD$6020), however, the cost per QALY of €3638 (approximately AUD$6474) was considerably higher using the same 15D utility instrument (Tykka et al., 2010). Despite these differences, both of these studies found surgery to be cost-effective and to compare favourably with a number of other surgical procedures. Finally, Thoma and colleagues conducted a randomised-controlled trial to compare the cost-effectiveness of vertical scar reduction in comparison to inverted T-shaped reduction mammoplasty using the Health Utilities Index Mark 3 (Thoma et al., 2014). The authors found that inverted T-shaped reduction dominated vertical scar reduction from the Ministry of Health perspective by being slightly less costly ($3090.06 versus $3106.58 in 2012 Canadian dollars) and slightly more effective (0.87 quality-adjusted life years versus 0.86 quality-adjusted life years). In summary, whilst the comparison of findings from other economic evaluations may be problematic due to the variation between analyses with regard to factors including HRQoL instrument, health care system, currency values, perspective, time horizon and discount rate used, results from this study are consistent with previously published findings in supporting the cost-effectiveness of surgery.

In comparison to medical interventions for other chronic health conditions, findings from the present study provide evidence to demonstrate that the incremental cost per QALY gain following breast reduction surgery compares favourably. Assessing the effectiveness of surgery based on cost per QALY estimates enables other interventions with different outcome measures to be compared from within the Australian healthcare perspective to be compared to a societal willingness-to-pay threshold. Segal and colleagues investigated the cost-effectiveness of total hip replacement and total knee replacement for osteoarthritis in Australia and found surgery to be cost-effective at an estimated cost per QALY of AUD$7500 and AUD$10,000, respectively (Segal et al., 2004). James and colleagues evaluated the cost-utility of three types of bariatric surgery in comparison with usual care for the treatment of obesity in Australia and reported an ICER of between AUD$22,645 and AUD$27,253 (James et al., 2017). Foteff and colleagues evaluated the cost–utility of cochlear implantation in comparison to bilateral hearing aids in Australian adults and found an ICER of AUD$11,160 per QALY (Foteff et al., 2016). In 2014, Abell and Vote performed a comparative cost-effectiveness analysis of laser-assisted cataract surgery and conventional cataract surgery and found that whereas laser surgery was not cost-effective at AUD$92,862 per QALY, conventional cataract surgery was at AUD$4,378 per QALY gained (Abell and Vote, 2014). In summary, the cost per QALY gains following breast reduction compare favourably to other commonly implemented and widely accepted medical interventions within the Australian public healthcare setting.

7.4.1 Strengths and limitations

This study reports findings from the most comprehensive economic evaluation to date of the cost-effectiveness of breast reduction surgery. A major strength of this study was the prospective collection of patient-reported HRQoL outcome data at multiple time points for estimation of the cost-utility. This enabled the calculation of the QALY gain from baseline to the 12-month post-operative time-point based on responses from the patients themselves rather than being reliant on estimates by clinicians and health economists. In addition, this study captured costing data at an individual patient level, accounting for factors that may influence total costs including variations in length of stay, in-hospital complications and return to theatre episodes. Furthermore, costing data included additional costs accrued beyond the initial hospital admission including all hospital outpatient clinic appointments and any revisional procedures over the 12-month follow-up period. Whilst the compliance rate for this study was relatively high, a sensitivity analysis was performed to compare the complete case dataset to an imputed dataset. Results were similar, indicating that the impact of multiple imputation did not lead to biased results.

In estimating the SF-6D health utility score, a population-specific algorithm was used that was developed based on data from the Australian population (Norman et al., 2014) alongside the original algorithm by Brazier was based on data from the UK population (Brazier et al., 2002). While it may be hypothesized that the use of the updated scoring weights best represents the preferences of the Australian population, it is likely results of an economic evaluation would be sensitive to the choice of algorithm. Therefore, a strength of this study was that all analyses were conducted to explore the sensitivity of results using the two algorithms, with both revealing a beneficial cost per QALY below the incremental cost-effectiveness ratio.

This study had several potential limitations when assessing the economic value of surgery. While we included direct hospital costs for each surgical participant, our analysis did not account for indirect costs to the participant and their families such as loss of work due to periods of absence. In addition, the economic evaluation was not a randomised clinical trial and did not include indirect costing data for the control breast hypertrophy group such as time off work, GP visits, specialist consultations, physiotherapy and other associated expenses outside of the hospital setting, and/or hospitalisations attributable to the condition. However, it is assumed to be likely that the indirect costs at baseline would have been similar in both groups with symptoms of breast hypertrophy and would not significantly alter the conclusions from this study. Whilst HRQoL was prospectively captured at baseline and at 12 months follow-up, data was not collected at 3- and 6-months in the hypertrophy control cohort; therefore, the differences between surgical intervention and control groups used baseline and 12-month follow-up data points only. However, a sensitivity analysis explored the use of the four study timepoints for estimation of QALYs and found that this did not alter the conclusions of the study. In fact, using the four study timepoints resulted in an even more favourable cost-utility ratio given the marked improvement observed between baseline and 3

months post-operative utility scores which results in a greater area under the curve estimate for QALY calculations.

7.5 Conclusion

The findings of this cost-utility analysis demonstrate that bilateral breast reduction surgery for symptomatic breast hypertrophy is likely to be cost-effective in the Australian healthcare setting with incremental cost per QALY gained considerably lower than the implicit cost-effectiveness threshold. This conclusion was further supported by the finding that the cost-effectiveness acceptability curves showed that the intervention had a high probability of being cost-effectiveness over a range of willingness-to-pay values. This study provides clinical and economic evidence that surgery is justifiable for government funding within the Australian healthcare setting.

8. THESIS CONCLUSIONS

8.1 Summary of thesis

The main objective of this thesis was to comprehensively evaluate the health burden of breast hypertrophy and the clinical- and cost-effectiveness of breast reduction surgery in improving health-related quality of life in Australian women. To investigate this objective a comprehensive literature review was conducted (Chapter 1) and subsequently five studies were conducted: a longitudinal prospective cohort study using validated generic patient-reported outcome measures comprised of a surgical group and a non-surgical control group (Chapter 2); a normative study to derive population reference data for the BREAST-Q Reduction module (Chapter 3); a prospective cohort study using the condition-specific BREAST-Q outcome measure (Chapter 4); a long-term follow-up study to determine whether or not surgery delivers long-term health benefits (Chapter 5); and an economic evaluation study to evaluate the cost-effectiveness of surgery from the Australian healthcare perspective (Chapter 7). In addition, the objective measurement of breast and body volume was undertaken (Chapter 6) to enable the comprehensive comparison between physical assessment and patient-reported outcomes. A summary as to how these studies formed a cohesive body of work to address the research objectives is addressed in this chapter. Implications for practice and healthcare policy are also discussed along with future directions for further research studies in the field of in plastic and reconstructive surgery.

A prospective cohort study was conducted to evaluate the health burden of breast hypertrophy and the comparative effectiveness of breast reduction surgery in improving health-related quality of life. Participants in this study were women who underwent breast reduction surgery and were followed up for 12 months; and a comparison control cohort comprised women with breast hypertrophy who did not undergo surgery. The primary outcome measure was health-related quality of life measured pre-operatively and up to 12 months following using the Short Form-36 (SF-36) and the Multidimensional Body-Self Relations Questionnaire (MBSRQ). Secondary outcome measures included post-surgical complications. This study demonstrated that women with breast hypertrophy had significantly lower scores compared with population norms across all SF-36 scales. In the surgical cohort, SF-36 scores improved to such an extent within 3 months of surgery that the health deficits were eliminated and quality of life scores were ‘normalised’ to levels equivalent to that of the general population across all eight dimensions and summary measures of the SF-36. This improvement was found to be sustained at 6- and 12-months following surgery. In contrast, SF-36 scores for the breast hypertrophy controls remained at baseline across 12 months. When assessing the relationship between participant or clinical characteristics and patient-reported outcomes, the improvement in health-related quality of life was independent of traditionally used criteria based on breast resection weight and body mass index and demonstrates the health benefits of surgery regardless of these factors. Women who underwent surgery were also found to

report significantly improved MBSRQ scores for how they evaluated their overall health, fitness, appearance and body satisfaction. Finally, the marked improvement in the SF-36 physical summary score was proven to be comparable to other widely accepted and approved surgical procedures including total joint replacement, spinal fusion, bariatric surgery, hernia repair, and coronary artery bypass grafting which are not the subject of restrictive access policies that are commonly enforced for breast reduction surgery. In addition, the improvement in the mental summary score following surgery was found to exceed that of all other interventions cited. In summary, this study provided evidence as to the comparative effectiveness of breast reduction surgery in relieving the functional symptoms and impaired quality of life associated with breast hypertrophy.

In Chapter 3, normative data were derived for the BREAST-Q Reduction module from women within the Australian general population, describing only the second set of normative values for this instrument reported worldwide. This study was undertaken to provide population-specific reference data for comparison to BREAST-Q scores from the surgical and breast hypertrophy control cohort (described in Chapter 4). Within the normative study, participants with a higher BMI and those with a chronic health condition were found to have significantly lower scores across all four BREAST-Q scales when compared to their respective comparison groups. Participants aged 40 years and above were found to have significantly higher scores for satisfaction with breasts, psychosocial wellbeing and physical wellbeing than their younger counterparts. Women with a larger bra cup size were found to have significantly lower scores for physical wellbeing than those with a smaller cup size. In a comparison between derived Australian normative data and published United States norms, this study demonstrated significant differences existed in all four BREAST-Q domains of satisfaction and wellbeing and highlighted the importance of using population-specific normative data wherever possible for the accurate interpretation of health-related quality of life data in research studies and in the clinical setting.

Findings of the prospective outcome study using validated generic measures such as the SF-36 were complemented with the administration of the condition-specific BREAST-Q to participants within the surgical and breast hypertrophy control groups pre-operatively and at 12 months follow-up. This study found that women with breast hypertrophy had significantly lower health-related quality of life scores across all BREAST-Q scales when compared to normative data. Following surgery, scores were found to significantly increase to levels equivalent to that of the general population. This is in contrast to BREAST-Q scores for women in the breast hypertrophy control group, with scores remaining at baseline levels. When assessing the relationship between participant characteristics and improvement in BREAST-Q scores, participants with a higher BMI were found to have a significantly greater improvement following surgery than those with a lower BMI in satisfaction with breasts, psychosocial wellbeing and physical wellbeing. In contrast, the level of improvement in all four BREAST-Q scales was found to be similar between patients who

had a post-operative surgical complication and those who did not. Overall, a high level of patient satisfaction was found following surgery, and satisfaction with outcome was not found to be affected by the presence of surgical complications. Furthermore, this study demonstrated that surgery was of health benefit to all women, including those who do not meet traditional insurance criteria requirements such as the 500-gram minimum weight of resection or using Schnur's sliding scale.

A long-term prospective outcome study was undertaken to evaluate the health benefits and patient satisfaction several years following breast reduction surgery. Participants who underwent breast reduction surgery and were followed up in the original 12-month outcome study self-completed the same series of validated patient-reported outcome measures up to 12 years following surgery. This study demonstrated that the majority of women continue to report a high level of satisfaction with the outcome of surgery and experience the ongoing health benefits and improvement in quality of life for many years after surgery; with no significant differences found when comparing long-term outcome scores with those reported at 12-months post-operatively. Furthermore, the comparison of long-term outcome data with population-specific norms for the SF-36 and BREAST-Q in this study confirmed that health-related quality of life remains at levels of women in the general population and did not decline towards levels reported pre-operatively over time; highlighting the health benefits of surgery continue for many years. The significant long-term improvement in health-related quality of life and relief of painful symptoms promotes the provision of insurance coverage for surgery as a functional rather than cosmetic procedure.

The objective measurement of breast and body size was conducted before and after breast reduction surgery using a series of techniques including water displacement, 3D laser scanning and anthropometry. This enabled the investigation of the relationship between breast and body size, and the comparison between physical assessment and health-related quality of life outcomes following surgery. This was an area of research that warranted further investigation, with a limited number of existing studies relying on proxy measurements for breast and body size such as tissue resection weight, bra cup size and BMI. An important finding was that the level of disproportionality in women with breast hypertrophy did not influence the improvement in health-related quality of life following surgery. In addition, breast size was found to be strongly correlated with body size and BMI, indicating that larger women tend to have a greater breast volume and provides evidence to further support that restrictive criteria should not be based on these factors. In contrast, breast volume was found to be weakly associated with bra cup size, highlighting that cup size is not an accurate indicator of breast volume in clinical outcome studies. This study also assessed the validity of measuring breast tissue volume using water displacement of the intact breast and anthropometry in comparison to 3D laser scanning in women with breast hypertrophy. While a strong association was found between the measurement of breast volumes using water displacement and 3D laser scanning techniques and also between anthropometric measurements

and 3D laser scanning in women with breast hypertrophy, the methods had low agreement on actual values and 3D scanning was proven to be a more accurate and reliable method for the determination of breast volume.

An economic evaluation of bilateral breast reduction surgery within the Australian public healthcare system was undertaken. SF-36 responses from the original prospective outcome study comprising a surgical cohort and a breast hypertrophy control cohort were transformed to a single SF-6D health utility score using preference-based scoring weights from Australia and the United Kingdom. Effectiveness of the surgical intervention was measured in terms of quality-adjusted life years (QALYs) gained. The findings of this cost-utility analysis demonstrate that bilateral breast reduction surgery for symptomatic breast hypertrophy is likely to be considered cost-effective in the Australian healthcare setting with incremental cost per QALY gained of AUD$6719, which is considerably lower than the recommended cost-effectiveness threshold of AUD$28,033 per QALY gained.

8.2 Limitations

Further to the limitations highlighted in individual study chapters, this body of research has several overall potential limitations that should be noted. Firstly, the prospective cohort studies described in this thesis were conducted at a single institution, potentially limiting the generalisability of these findings. Secondly, it is important to acknowledge the possibility of reporting bias when using patient-reported outcome measures in this type of research. This is a valid concern for patients seeking surgical treatment who may feel their responses could determine their access to surgery. Whilst participants in this study were informed that their responses to the health-related quality of life questionnaires would not be used to determine their access to surgery, it is possible that participants still overestimated their symptoms. However, the potential for bias in the surgical cohort was considered to be low as the pre-operative questionnaires were completed after participants had already been assessed by a plastic surgeon and were scheduled for surgical admission. It was also conceivable that when completing the study questionnaires post-operatively participants may have responded more favourably and felt an expectation to please the surgical team. In order to minimise the potential influence of the clinician or treating team on patient responses, study questionnaires were mailed to participants and these were self-completed independent of the hospital setting. Whilst it is acknowledged that the potential for bias is an inevitable accompaniment of this type of research design and may affect the strength of the conclusions, there is also no solution to this problem and efforts were made to limit this influence wherever possible when undertaking this research.

8.3 Original contribution to knowledge

The studies that comprise this thesis have provided a significant original contribution to knowledge

in the practice of evidence-based medicine and in the field of patient-reported outcomes following breast reduction surgery in a number of ways. Firstly, this body of research details the first studies to evaluate the clinical effectiveness of breast reduction surgery for the treatment of symptomatic breast hypertrophy in Australian women. In addition, the use of a combination of validated generic and condition-specific patient-reported outcome measures enabled a comprehensive assessment of health-related quality of life outcomes. Normative population data and the recruitment of a non-surgical control group of women with breast hypertrophy who were referred for, but did not undergo, breast reduction surgery provided appropriate comparison groups and further strengthened the interpretation of outcomes.

This study reported the first general population reference values for the BREAST-Q Reduction module specific to Australia. The generation of normative data for the BREAST-Q from women within the Australian general population provided valuable insight into breast-related satisfaction and wellbeing in Australian women who were not pursuing breast surgery. This study established a valuable clinical reference point or benchmark for the interpretation of health-related quality of life scores; in turn providing new clinical context to better understand the health burden of breast hypertrophy or macromastia and the health benefits of breast reduction surgery. Prior to this normative data was limited to the United States population and findings from this study demonstrated that potentially significant differences existed when comparing health-related quality of life between populations. When assessing the relationship between participant socio-demographic characteristics and normative BREAST-Q scores it was found that some of these variables, in particular age, had a significant influence on scores. This finding highlighted the importance that the population sample in this study were representative of the Australian population across gender, age and geographical variables and therefore overcame limitations associated with the United States sample, which was found to be potentially biased by not being representative of the age distribution of the United States general population. Finally, given that the BREAST-Q is the most widely used patient-reported outcome measure in breast surgery, this study provides a valuable contribution to the literature as it presents normative data from a second, diverse population sample for use in both existing and future clinical or research studies.

The prospective design of the research studies in this thesis overcome the limitations associated with many existing outcome studies which are based on retrospective review. This is particularly important in patient-reported outcome studies evaluating quality of life, as retrospective studies lack baseline data and therefore make the considerable assumption that health-related quality of life is identical in all individuals when they present for surgery. In addition, retrospective studies are inflexible in the collection of clinical outcome data such as surgical complications as these studies are entirely dependent on the standard of medical record keeping or predetermined database fields collected at the time of surgery and are often limited to the early post-operative period. The complication data included in this thesis was recorded prospectively over multiple

post-operative timepoints and is the first study to report the prospective assessment of surgical complications following breast reduction surgery using a standardised grading system. This standardised reporting of surgical complications overcomes comparison difficulties that currently exist in the literature, with the sizeable discrepancies in the reporting of incidences and risk factors for complications likely to be attributable to inconsistencies in the collection and in the classification of complications data. In addition, this body of work included studies with a relatively large sample size to generate adequate power for further subgroup analyses; overcoming limitations associated with many existing prospective outcome studies have been limited by small sample sizes. Finally, another strength of this study was that post-operative outcomes were not limited to a single follow-up timepoint and were not restricted to the early outcomes during the convalescence period following surgery; outcomes in this study were assessed at multiple timepoints over a 12-month period and again in a long-term follow-up study.

The study evaluating the long-term outcomes of breast reduction surgery provides a significant contribution to knowledge with the finding that health-related quality of life remains stable up to 12 years after surgery and does not trend or decline to baseline levels. In addition, this study detailed a comparison of long-term outcome scores to population reference data and demonstrated that the health-related quality of life remained comparable over time. Whilst a small number of existing studies have explored long-term outcomes of surgery, the majority of these have been based on retrospective review and are limited by the lack of baseline data; and are therefore unable to address the important issue as to whether health-related quality of life returns to baseline values over time. In a climate of increasingly tight healthcare budgets, this study provides evidence as to the value in surgery which continues well beyond the short- to medium-term gains previously reported.

Research gaps have remained in this field due to inconsistencies reported in the literature regarding the relationship between participant characteristics and clinical factors and the outcomes of surgery. The surgical study cohort described in this thesis were not biased by restrictive access policies that have been reported in previous studies based on a minimum weight of resection or BMI and therefore includes a broad range across these variables. This was particularly important as it enabled the accurate assessment of these factors as potential predictors of the change in health-related quality of life and outcomes of surgery and therefore overcomes limitations associated with existing studies. Importantly, this study established that the improvement in health-related quality of life following surgery is independent of commonly used criteria including those based on breast size, BMI or a minimum weight of resection; highlighting that the validity of such criteria is poorly supported by evidence, potentially ruling out access to surgery for many women who would greatly benefit. This finding is not only relevant within the Australian public healthcare system where access to surgery is inconsistent and ultimately reliant on state and local policies, some of which include eligibility criteria based on BMI, but is also relevant on a global

scale. This body of work provides strong evidence-base to refute the validity of restrictions enforced by policymakers and healthcare funders in many countries and jurisdictions worldwide.

Finally, existing studies in the literature describing the cost-utility and cost-effectiveness of breast reduction surgery are scarce; and there are currently no studies from the Australian perspective. This thesis details a thorough economic evaluation and provides strong economic evidence that breast reduction surgery is a cost-effective intervention and is therefore justifiable for inclusion within the Australian public healthcare sector.

8.4 Future directions

Within the field of plastic and reconstructive surgery there are further areas where research is warranted to provide high-quality evidence to better inform and support clinical practice and healthcare policy. An example of this is abdominoplasty with surgical repair of the rectus diastasis following pregnancy. Similar to breast reduction, this surgery has commonly been subjected to ongoing restrictions and is often considered a cosmetic procedure rather than a functional operation by many policymakers and healthcare funders. In 2016, the item number for abdominoplasty (for repair of the rectus diastasis) was removed from the Australian Medicare Benefits Schedule (MBS) and is therefore this procedure is currently excluded within the Australian public hospital system. Therefore, there are no MBS-funded treatment options for patients with pregnancy-acquired rectus diastasis and who are nonresponsive to conservative treatments such as physiotherapy, exercise, lifestyle changes and painkillers. Preliminary studies suggest that abdominoplasty in women with pregnancy-acquired rectus diastasis reduces urinary incontinence symptoms, back pain and improves health-related quality of life. However, these existing studies have limitations including the lack of a control group and a risk of bias and unfortunately do not currently provide the high-quality evidence required to provide justification for inclusion within the healthcare system. Following on from the present study of outcomes following breast reduction surgery, conducting a well-designed prospective study using validated patient-reported outcome measures to compare outcomes in a surgical cohort in comparison to an appropriate control group to evaluate both the clinical-effectiveness and cost-effectiveness of abdominoplasty surgery for rectus diastasis following pregnancy within the Australian healthcare setting is therefore warranted. Furthermore, an investigation of the participant and clinical variables such as those included in this thesis and their relationship on the outcomes following surgery would offer a significant contribution. This study would be useful both at a clinical and patient level, but also to inform healthcare funders and policymakers to support the provision of funding and reinstate access to surgery in the future. Finally, the examination and investigation into biases in surgical and health care rationing more generally, and the relationship between degree of need to access healthcare and restrictions preventing that access, would be an important direction for future research studies.

8.5 Conclusion

Breast hypertrophy is a chronic health problem and the combination of pain and functional deficits has a significant impact on health-related quality of life in affected women. Breast reduction surgery is an effective intervention for providing symptomatic relief and improving health-related quality of life in Australian women to levels equivalent to that of the general population. The health benefits were found to be sustained over time and remain for many years following surgery. The improvement in health-related quality of life following surgery was comparable to other widely accepted and approved surgical interventions and was found to be independent of traditionally used restrictive criteria based on body mass index or a minimum weight of resection and demonstrates that the health benefits of surgery regardless of these factors. A comprehensive economic evaluation found that surgery is cost-effective and justifiable for inclusion within the Australian healthcare setting.

The collective findings from this body of research provide strong evidence as to the clinical- and cost-effectiveness of bilateral breast reduction surgery for the treatment of symptomatic breast hypertrophy in Australian women. The results from this research provide a contribution to knowledge and it is anticipated that this thesis will be a definitive piece of work to inform clinicians and the wider community, and to guide the Australian healthcare system in offering breast reduction services in the future.

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APPENDICES

Open access Original research

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Does breast reduction surgery improve health-related quality of life? A prospective cohort study in Australian women

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ABSTRACT

Objectives To assess the health burden of breast hypertrophy and the comparative effectiveness of breast reduction surgery in improving health-related quality of life.

Design Prospective cohort study.

Setting A major public tertiary care hospital in Australia.

Participants Women with symptomatic breast hypertrophy who underwent breast reduction surgery were followed for 12 months. A comparison control cohort comprised women with breast hypertrophy who did not undergo surgery.

Interventions Bilateral breast reduction surgery for women in the surgical cohort.

Main outcome measures The primary outcome measure was health-related quality of life measured preoperatively and at 3, 6 and 12 months postoperatively using the Short Form-36 (SF-36) questionnaire. Secondary outcome measures included post-surgical complications.

Results 209 patients in the surgical cohort completed questionnaires before and after surgery. 124 patients in the control hypertrophy cohort completed baseline and 12-month follow-up questionnaires. At baseline, both groups had significantly lower scores compared with population norms across all scales ($p<0.001$). In the surgical cohort significant improvements were seen across all eight SF-36 scales ($p<0.001$) following surgery. Within 3 months of surgery scores were equivalent to those of the normal population and this improvement was sustained at 12 months. SF-36 physical and mental component scores both significantly improved following surgery, with a mean change of 10.2 and 9.2 points, respectively ($p<0.001$). In contrast, SF-36 scores for breast hypertrophy controls remained at baseline across 12 months. The improvement in quality of life was independent of breast resection weight and body mass index.

Conclusion Breast reduction significantly improved quality of life in women with breast hypertrophy. This increase was most pronounced within 3 months of surgery and sustained at 12-month follow-up. This improvement in quality of life is comparable to other widely accepted surgical procedures. Furthermore, women benefit from surgery regardless of factors including body mass index and resection weight.

Strengths and limitations of this study

- This large prospective longitudinal study reports 12-month follow-up using a validated patient-reported outcome measure for health-related quality of life assessment.
- The completion rate of the study was 83% for participants who underwent surgery.
- Comparisons were made with a control cohort of women with breast hypertrophy not undergoing surgery, and also to a normative female reference population.
- This was a non-randomised study design.

INTRODUCTION

Breast reduction surgery is a common plastic surgery procedure and it has previously been shown to be effective for relieving pain and functional problems associated with breast hypertrophy,[1–5] whereas conservative approaches to treatment such as physiotherapy, hormonal therapy and weight loss have much less impact.[6 7] However, despite clear published evidence to the contrary, breast reduction surgery is often regarded more as a cosmetic rather than a functional procedure by the general public and many medical professionals.[1 8 9] This is in spite of the finding that breast hypertrophy is a chronic health problem and relief of physical symptoms is the primary motivator for most women who are pursuing breast reduction surgery.[10]

The increasing demand for breast reduction surgery and increasing pressure to constrain healthcare spending have led to lengthy waiting times and restrictions placed on surgery in numerous countries and jurisdictions worldwide.[4 11–15] While 'rationing' of healthcare is an essential process in public healthcare systems globally, it has the potential to threaten equity of access to surgical

treatment. Within the Australian public hospital system, access to breast reduction surgery for patients is ultimately reliant on state and local policies.[16–21] Similarly, in the UK, reports on the rationing of surgery by the National Health Service (NHS) on the basis of geographical location have resulted in a 'postcode lottery'.[22 23] In 2018, reports from the NHS England 'Evidence-Based Interventions Programme' proposed to restrict funding for procedures it considers 'unnecessary', to save money and eliminate unwarranted clinical variation.[24] The inclusion of breast reduction surgery as a 'procedure of limited effectiveness' implies that it is a marginal and low priority procedure in comparison to other medical interventions.[25] However, labelling breast reduction surgery an 'ineffective' and 'unnecessary' procedure might be misleading and inaccurate, with little evidence to support this claim. Furthermore, restrictive access policies are in place in both public and private sectors in many countries and jurisdictions worldwide; often these restrictions are based on body mass index (BMI) or a minimum weight of breast resection at surgery.[4 8 9 11–15 22 23 25] The validity of such criteria might not be evidence-based, resulting in women with a medical need for surgery being denied access to it.

The primary aim of this study was to longitudinally assess health-related quality of life (HRQoL) in women with breast hypertrophy before and after breast reduction surgery, and to compare these outcomes to control groups of women with breast hypertrophy not undergoing surgery, and also to a normative female reference population. The Short Form-36 (SF-36) is a well-established indicator of patient-reported outcome for evaluating the burden of disease states and the outcomes of medical interventions and was therefore chosen as the primary outcome measure for this study. Second, this study aimed to assess the impact of patient demographics and surgical characteristics including, but not limited to, those commonly used as selection criteria for access to surgery and insurance coverage on preoperative HRQoL scores and the long-term improvement in HRQoL following surgery.

METHODS

Design and participants

A prospective cohort study was performed at Flinders Medical Centre in Adelaide, Australia. All women aged 18 years and over with symptomatic breast hypertrophy who were assessed for bilateral breast reduction surgery between April 2007 and February 2018 were informed of the study. Patients who underwent breast reduction surgery comprised the surgery cohort. Patients who were referred for surgery and were placed on the waiting list but were not expected to undergo surgery within 12 months comprised the controls.

All participants who consented to the study were asked to complete the SF-36 questionnaire at set time points. For the surgical patients this was preoperatively and 3, 6 and 12 months postoperatively. For the control patients, the questionnaire was completed at baseline and again 12 months after enrolment. Data including age, height, weight, bra cup size, health status and smoking status were determined for all patients at baseline and again at follow-up. Women who were unable to complete written questionnaires or were enrolled in the control group and had breast reduction surgery within 12 months of enrolment, or who did not return study questionnaires, were excluded from the study.

Outcome measures

The SF-36 V.2 was used to measure the general HRQoL.[26] This contains 36 items which assess health across eight subscales. Questionnaire responses were transformed as per the SF-36 V.2 scoring manual to provide the eight subscales, each with a score between 0 and 100, with higher scores indicating better health.[27] The subscales were converted into two summary scores: Physical Component Summary (PCS) score and Mental Component Summary (MCS) score using norm-based methods and scoring coefficients from the Australian population.[28] For comparison purposes, general female population normative scores were obtained from the 2008 South Australian Health Omnibus Survey and scores weighted to correspond to the age distribution of the study participants.[29]

Sample size was determined a priori and a minimum sample size of 98 patients per group was calculated to give 80% power at a two-sided significance level of 5% to detect a mean difference of 10-points with an estimated SD of 25-points in the SF-36 questionnaire score.

Study-specific questionnaires, which asked about time off work and consumption and expenditure on medications, were administered at the baseline and 12-month postoperative time points. Participants in the surgical cohort were asked postoperatively whether they would have the surgery again if they had their time over. Additional data were collected pertaining to the surgical technique used, and the weight of breast tissue removed. Hospital records were used to determine the length of hospital stay, number of outpatient clinic appointments relating to the surgery and complications leading to re-hospitalisation, or a further operative procedure within the 12 months follow-up period. A comprehensive complications checklist was completed prospectively during the study by the treating doctor. Three-dimensional laser body scanning was performed preoperatively and at 12 months postoperatively using a Cyberware WBX scanner (Cyberware) and Cyslice software (Headus Pty Ltd). Breast and body volume were measured from the scan according to a protocol described previously.[30 31]

Statistical analysis

Statistical analyses were performed using SPSS V.25.0 statistical software (IBM Corp). Descriptive statistics including mean, SD and 95% CI were computed for continuous variables. Comparisons between groups were

made using t-tests for continuous data and χ^2 tests for categorical data, with Fisher's exact test as appropriate. Linear mixed models were used to assess the significance of changes in SF-36 subscale scores over multiple time points. For each SF-36 scale an improvement score was calculated using the score obtained at the last available assessment, with a higher score representing a greater improvement from baseline. Pearson correlation coefficients were calculated to assess the linear association between SF-36 scores and baseline participant and clinical characteristics; variables that showed a significant association were entered into the regression model. Candidate variables included age, BMI, preoperative breast volume, bra cup size, tissue resection weight (grams), breast asymmetry and ratio of breast to body volume. Variables were continuous except for bra cup size which was categorised into six groups as follows: D, DD, E, F, G and ≥H cup. Multiple linear regression was used to assess whether any of the collected sociodemographic or clinical variables were associated with first, SF-36 PCS score at baseline, and second, with the change in SF-36 PCS scores from baseline to 12 months after surgery. Statistical significance was accepted at a p value of less than 0.05.

Patient and public involvement

At the design stage of the study two group meetings were held with women with breast hypertrophy to discuss their perspective on the condition, deliver education material and discuss this study. In addition, one consumer was more extensively involved with the design of the study and trialling different methods of breast volume measurement. Study results will be disseminated to the public through presentations and local health newsletter.

Table 1 Baseline characteristics of participants

Characteristic	Surgical cohort (n=209)	Hypertrophy control cohort (n=124)	P value of difference*
Mean (SD; range) age (years)	42.6 (13.4; 18 to 72)	45.3 (13.1; 20 to 79)	0.079
Age group (years):			
18–24	24 (12)	12 (10)	
25–34	38 (18)	15 (12)	
35–44	64 (31)	26 (21)	
45–54	41 (20)	43 (34)	
55–64	31 (15)	21 (18)	
≥65	11 (5)	7 (6)	
Mean (SD) BMI (kg/m^2)	32.7 (6.0)	32.2 (6.1)	0.468
Obesity status:			
Non-obese (<30)	71 (34)	48 (39)	0.326
Obese (≥30)	138 (66)	74 (61)	
Missing	0 (0)	2 (0)	
Smoking status:			
Non-smoker	108 (52)	78 (63)	0.243
Current smoker	35 (17)	14 (11)	
Ex-smoker <12 months	15 (7)	5 (5)	
Ex-smoker >12 months	47 (23)	25 (20)	
Missing	4 (0)	2 (0)	
Bra cup size:			
≤D	13 (6)	4 (3)	
DD	43 (21)	13 (11)	
E	50 (24)	19 (15)	
F	46 (22)	27 (22)	
G	35 (17)	37 (30)	
≥H	19 (10)	19 (15)	
Missing	3 (0)	5 (0)	

Values are numbers (percentages) unless stated otherwise.
*Using independent samples t-test or χ^2 test as appropriate.
BMI, body mass index.

RESULTS

Surgical cohort

Of 251 participants who completed a baseline assessment and underwent bilateral breast reduction surgery, 209 (83.3%) completed at least one postoperative follow-up assessment and were included in the study group for analysis. Missing data were due to participants repeatedly not attending appointments or choosing to not complete and return the study questionnaires at some time points. Twenty-three participants formally withdrew from the study following surgical intervention. Baseline characteristics were compared between participants who were lost to follow-up and those who completed at least one postoperative assessment. No difference was observed for age, BMI, tissue weight resected or preoperative SF-36 scales and summary scores except for the mental health scale, where non-respondents had a lower mean score of 6.8 points less than responders (p=0.034).

Participant demographics for the surgical cohort are summarised in table 1. Preoperatively, mean total breast volume measured by 3D laser scanner was 3391 mL (range 1472–9622 mL). At 12 months postoperatively, mean total breast volume was 2184 mL (range 963 to 4392 mL). The mean total weight of breast tissue resected at surgery was 1338 g±817 g. An inferior pedicle breast reduction technique was the most commonly used approach (161/209, 77%), followed by a superior pedicle technique (35/209, 17%). The average hospital stay was 2.3 days. Fifty-nine patients (28%) experienced at least one surgical complication. Eight patients (3.8%) had subsequent procedures for revision of surgical scars or to correct 'dog-ears'.

The majority of participants (204/209, 97.6%) responded in the postoperative questionnaire that they would have the surgery again, while others were either unsure (4/209, 1.9%) or would not have surgery again (1/209, 0.5%). Following surgery, participants on average spent less money on medications and treatments (AU$26.41 vs AU$5.73 per month, p<0.001) and took fewer days off work (4.5 days vs 0.1 days in the previous 6-month period, p=0.009) when compared with before surgery. Using bivariate analysis, obesity was not associated with an increased incidence of surgical complications (p=0.323), with the incidence of complications in non-obese participants (17/71, 24%) and obese participants (42/138, 30%). Furthermore, there were no differences in the incidence of major complications based on obesity status.

The SF-36 was completed preoperatively and at least once postoperatively by 209 surgical participants; 191 (91%) completed the postoperative questionnaires at 3 months, 183 (88%) at 6 months and 193 (92%) at 12 months. When compared with previously published age-adjusted normative data for the female Australian population,[29] mean baseline SF-36 scores for the surgical cohort were significantly lower across all scales (p<0.001) (table 2). A comparison of mean preoperative and 3-month postoperative SF-36 scores showed that scores were significantly higher across all eight SF-36 subscales (p<0.001) (table 2) such that they reached the level of the normative population (figure 1). Mean SF-36 PCS and MCS scores significantly improved following surgery, increasing by 10.2 (95% CI; 8.2 to 12.1) and 9.2 (95% CI; 6.9 to 11.6) points, respectively (p<0.001) (figure 2 and online supplementary table S1). The mean change in SF-36 PCS and MCS scores was in excess of the developer-recommended 3-point minimal important difference (MID) threshold.[32 33] SF-36 scores were stable at 6 and 12 months post-surgery and linear mixed-model analysis showed no significant difference from those at 3 months post-surgery. The mean change in SF-36 scores from baseline to 12 months following surgery was in excess of MID threshold estimates based on a rule of thumb 10-point change on 100-point quality of life scales[34] or 0.5 SD default value for patient-perceived important change[35] in all eight SF-36 subscales (figure 2). SF-36 scores for obese women improved equally, if not greater than their non-obese counterparts following surgery, reaching statistical significance for the physical functioning subscale (table 3).

Breast hypertrophy control cohort

Study questionnaires were initially posted to 350 women with breast hypertrophy who were not scheduled for surgery; 160 (46%) completed and returned the questionnaires at baseline, and of these 124 responded again 12 months later. Twenty-four of those contacted to participate in the study underwent breast reduction surgery during the study time frame and were therefore excluded. Participant demographics for the hypertrophy control cohort are summarised in table 1. No significant differences were observed when comparing spending on medications and number of days off work between baseline and 12 months following enrolment, with both remaining significantly higher than postoperative surgical participants (p<0.001).

Mean baseline SF-36 scores for women in the breast hypertrophy control group were significantly lower than the normative population across all dimensions (table 2). At 12 months post-baseline, SF-36 scores showed no significant improvement and remained significantly lower than population norms (table 2) and postoperative scores for women in the surgical cohort (figure 2). Mean SF-36 PCS and MCS summary scores for women in the breast hypertrophy control group were significantly lower than those who underwent breast reduction surgery, with a mean difference of 10.6 (95% CI; 8.3 to 12.8) and 11.1 points (95% CI; 8.2 to 13.9), respectively (p<0.001) (table 2).

Comparing the improvement in HRQoL with other surgical interventions

The improvement in SF-36 physical and mental summary scores in women who underwent surgery in our study was compared with existing studies which describe 12-month postoperative outcomes from other surgical interventions

Table 2 Mean (95% CI) SF-36 scores for participants in the surgical cohort, hypertrophy control cohort and normative female population

SF-36 scale	Normative* (n=1551)	Hypertrophy control cohort		Surgical cohort			
		Baseline (n=160)	12 months (n=124)	Preoperative (n=209)	3 months postoperative (n=190)	6 months postoperative (n=181)	12 months postoperative (n=191)
PF	84.2 (83.2 to 85.2)	64.7 (60.9 to 68.6)	61.1 (56.7 to 65.7)	61.0 (57.6 to 64.5)	80.1 (76.9 to 83.3)	80.8 (77.3 to 84.4)	83.4 (80.2 to 86.5)
RP	82.0 (80.7 to 83.3)	58.3 (53.8 to 62.8)	58.1 (53.0 to 63.0)	56.0 (52.2 to 59.9)	79.5 (76.1 to 82.9)	81.1 (77.4 to 84.8)	81.3 (77.7 to 84.9)
BP	73.0 (71.9 to 74.1)	39.8 (36.3 to 40.4)	37.9 (34.2 to 41.7)	38.5 (35.6 to 41.5)	67.4 (63.9 to 70.8)	67.6 (63.6 to 71.7)	71.6 (67.9 to 75.2)
GH	70.2 (69.1 to 71.4)	49.7 (46.3 to 53.1)	49.8 (46.0 to 54.0)	57.9 (55.0 to 60.9)	69.1 (66.3 to 72.0)	69.5 (66.6 to 72.4)	70.4 (67.7 to 73.1)
VT	57.3 (56.2 to 58.3)	36.7 (33.6 to 39.8)	35.1 (31.3 to 38.8)	39.7 (37.0 to 42.5)	57.7 (54.8 to 60.6)	58.6 (55.8 to 61.3)	58.9 (56.1 to 61.7)
SF	82.6 (81.3 to 83.8)	55.2 (50.6 to 59.8)	55.1 (50.1 to 59.9)	57.1 (53.3 to 60.9)	78.8 (75.0 to 82.5)	79.4 (75.6 to 83.2)	81.4 (78.1 to 84.7)
RE	88.3 (87.2 to 89.3)	62.8 (58.0 to 67.5)	60.2 (55.4 to 65.7)	61.7 (57.8 to 65.7)	80.1 (76.5 to 83.7)	82.3 (78.9 to 85.7)	84.6 (81.4 to 87.7)
MH	77.0 (76.1 to 78.0)	58.8 (55.2 to 62.5)	56.1 (52.4 to 59.9)	59.8 (57.0 to 62.5)	73.7 (71.0 to 76.4)	73.8 (71.1 to 76.5)	74.3 (71.6 to 76.9)
PCS	49.7 (49.2 to 50.2)	39.6 (38.1 to 41.1)	39.3 (37.5 to 41.1)	39.7 (38.4 to 41.0)	48.9 (47.6 to 50.3)	49.0 (47.5 to 50.5)	49.9 (48.4 to 51.3)
MCS	47.6 (47.0 to 48.2)	36.2 (33.8 to 38.6)	35.1 (32.7 to 37.6)	37.0 (35.2 to 38.8)	45.4 (43.6 to 47.1)	45.7 (44.0 to 47.4)	46.2 (44.5 to 47.9)

*Source: age-standardised normative data from the South Australian female population.[29]
BP, Bodily pain; GH, General health; MCS, Mental Component Summary; MH, Mental health; PCS, Physical Component Summary; PF, Physical function; RE, Role emotional; RP, Role physical; SF-36, Short Form-36; SF, Social function; VT, Vitality.

(table 4). Breast reduction surgery provided a greater gain in SF-36 PCS scores than a coronary artery bypass graft and hernia repair and the improvement was similar to that experienced by patients undergoing total knee replacement surgery. The improvement in SF-36 MCS scores following breast reduction surgery exceeded that of all other surgical procedures.

The impact of participant characteristics on HRQoL and benefit of surgical intervention

There was a significant positive correlation between baseline BMI and the total amount of breast tissue resected at surgery. That is, as the BMI increased there was an associated increase in the amount of breast tissue removed (Pearson's r=0.641, p<0.001). When exploring baseline SF-36 PCS scores, a significant negative correlation was found between SF-36 PCS scores and age (r=−0.13), BMI (r=−0.30), tissue resection weight (r=−0.26), degree of breast hypertrophy (r=−0.28) and ratio of breast to body volume (r=−0.19). Multivariate linear regression of candidate variables against baseline SF-36 PCS scores found BMI to be the only variable significantly related to preoperative SF-36 PCS scores (R^2=0.16, p<0.001). Multivariate regression analysis was also used to analyse predictors of the change in SF-36 PCS score following surgery and showed that improvement in SF-36 PCS scores was not significantly associated with any of these factors.

DISCUSSION

Principal findings

Findings from this study demonstrate that women with symptomatic breast hypertrophy have impaired quality of life compared with those in the general population. At baseline, participants in both the surgical and control breast hypertrophy groups scored significantly lower than the female general population in all SF-36 subscales, with pain being the most prominent. Surgical participants quality of life improved following breast reduction to such an extent that the health deficits were eliminated at 3 months following surgery and quality of life was 'normalised' to levels equivalent to that of the general population across all dimensions. This normalisation effect was stable across 12 months follow-up. The SF-36 health gain ranged from 14.5 to 33.1 points, and this exceeded the minimally important difference threshold estimates of one-half a SD approach[35] or a rule-of-thumb of a 10-point change on 100-point subscales,[34] supporting the contention that breast reduction surgery provides a clinically relevant health benefit.

Secondary aims of this study were to investigate factors that have the potential to influence the level of improvement in quality of life following surgery: BMI, degree of hypertrophy, bra cup size, age, preoperative breast symmetry and weight of tissue resection at surgery. Several of these factors are frequently used to restrict access to breast reduction surgery, none of which are based on high-quality evidence. In our study the improvement in

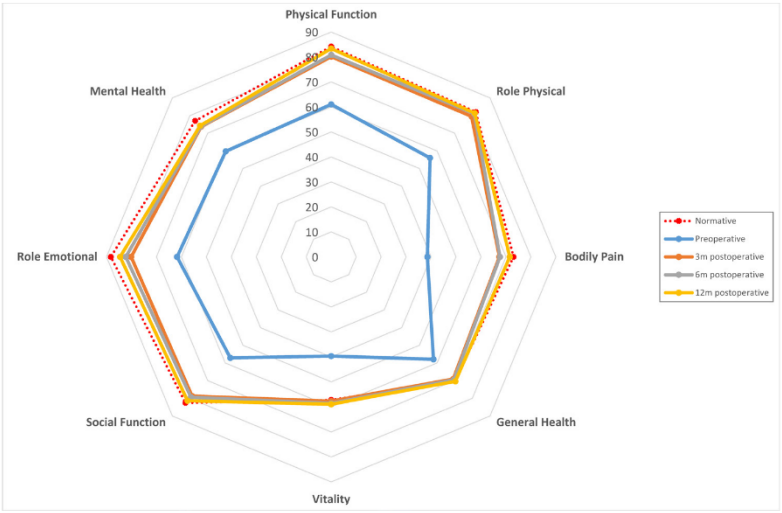

Figure 1 Comparison of mean preoperative and postoperative Short Form-36 scores with age-standardised female population norms (South Australian Health Omnibus Survey).[29]

HRQoL was independent of these factors, suggesting that all women with symptomatic breast hypertrophy can benefit from this surgery regardless of commonly scrutinised factors. This is of clinical relevance as it highlights that women with a higher BMI or those with a lower weight of resection benefit equally and should not be discriminated against based on criteria-based restrictions. Furthermore, there was no increase in the complication rate in the obese participants.

Comparison with other studies

The finding that women with symptomatic breast hypertrophy have a considerable health deficit and impaired quality of life compared with women in the general population is supported by existing studies within the literature.[4 14 36–39] These studies also report that surgical intervention provides symptomatic relief and improves HRQoL to levels of the general population. Our findings support those of Blomqvist *et al* and demonstrate that the improvement in quality of life is stable for up to 1 year after surgery, enabling women to return to levels of HRQoL that are similar to the normal population.[1]

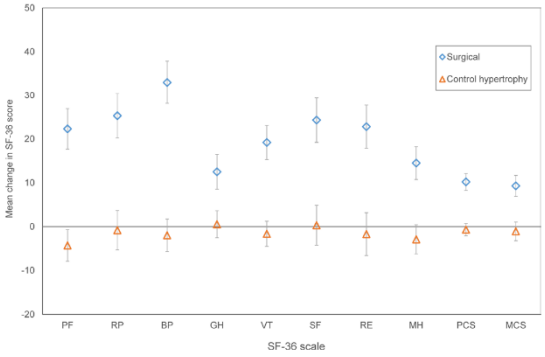

Figure 2 Mean change in Short Form-36 (SF-36) scores from baseline to 12 months for surgical and breast hypertrophy control groups. Error bars represent 95% CI. BP, bodily pain; GH, general health; MCS, mental component summary; MH, mental health; PCS, physical component summary; PF, physical function; RE, role emotional; RP, role physical; SF, social function, VT, vitality.

Our study demonstrated that symptom relief and improvement in HRQoL are not impacted by BMI or the removal of a minimum weight of resection. This finding is consistent with existing studies using the SF-36; however, two of these studies were potentially biased due to the BMI restrictions on their study populations.[6 40 41] Our study also supports previous findings of no significant difference in the complication rate based on obesity status.[41–43] In spite of these findings access restrictions for breast reduction surgery are in place in many countries, despite a lack of supporting evidence.

The intervention effect of breast reduction surgery in our study was well in excess of the minimal clinically important difference for SF-36 PCS and MCS scores, which has been recommended by the developers as a 3-point change.[32 33] The improvements in the SF-36 PCS score at 1 year following surgery were comparable to those of other widely accepted surgical interventions such as total hip and total knee replacement,[44] spinal fusion,[45] bariatric surgery[46] and coronary artery bypass graft surgery.[47] The improvements in the mental component score following breast reduction surgery actually exceeded those of all other interventions cited. Breast reduction surgery is a relatively inexpensive procedure, and the improvement in HRQoL provides evidence as to the comparative effectiveness of this intervention in

Table 3 Comparison of mean change (95% CI) in SF-36 scores following surgery in non-obese and obese participants

SF-36 subscale	Non-obese (n=71)	Obese (n=138)	Difference in means (95% CI)	P value of difference*
Physical function	16.1 (11.2 to 22.1)	23.4 (19.5 to 27.3)	6.8 (0.03 to 13.5)	0.050
Role physical	19.4 (12.4 to 26.3)	25.9 (21.2 to 30.5)	6.5 (–1.7 to 14.7)	0.121
Bodily pain	28.6 (22.8 to 34.5)	32.3 (27.8 to 36.9)	3.7 (–3.9 to 11.4)	0.337
General health	10.2 (6.0 to 14.3)	12.2 (8.4 to 16.0)	2.0 (–4.1 to 8.2)	0.516
Vitality	18.9 (14.8 to 23.1)	18.3 (14.2 to 22.4)	–0.7 (–7.2 to 5.9)	0.842
Social function	23.6 (17.8 to 29.4)	21.9 (16.6 to 27.2)	–1.7 (–10.2 to 6.8)	0.701
Role emotional	18.9 (12.8 to 25.0)	22.5 (17.2 to 27.8)	3.6 (–5.0 to 12.2)	0.409
Mental health	14.9 (11.4 to 18.5)	13.0 (9.2 to 16.9)	–1.9 (–7.9 to 4.1)	0.532

Obesity status: non-obese (<30 kg/m^2), obese (≥30 kg/m^2).
*Using an independent t-test.
SF-36, Short Form-36.

relieving the health burden and the functional symptoms of breast hypertrophy.

Strengths and limitations of this study

A potential limitation of our study was that the participant response rate for the breast hypertrophy control cohort was relatively low at 46%, which may be due to the recruitment process via postal questionnaire. Furthermore, while the total follow-up period for this cohort was 12 months, the intermediate time points of 3 and 6 months that were collected in the surgical cohort were not included in this cohort, although the consistency of outcomes at baseline and 12 months suggest that 3 and 6 month outcomes are likely to have been similar.

The strengths of our study were the prospective design, the relatively large sample size and the inclusion of a non-surgical control sample of women with breast hypertrophy who were recruited from the same waiting list as those in the surgical cohort. In addition, the postoperative outcomes described in this study included multiple time points over a 12-month period. In addition, our surgical cohort was not biased by restrictions that have been reported in previous studies based on a minimum weight of resection or BMI and therefore includes a broad spectrum across these variables. This is particularly important as it enables the accurate assessment of these factors as potential predictors of the change in HRQoL and outcomes of surgery and overcomes these limitations.

CONCLUSIONS AND POLICY IMPLICATIONS

Breast hypertrophy is a painful condition which is effectively treated by breast reduction surgery. The marked improvement in quality of life following breast reduction surgery is comparable to other widely accepted and approved surgical interventions. This study highlights that the improvement in quality of life following surgery is independent of traditionally used criteria based on BMI or a minimum weight of resection and demonstrates the health benefits of surgery regardless of these factors. This confirms the clinical effectiveness of breast reduction surgery and supports the contention that there is no justification for excluding women based on criteria such as BMI or the extent of breast hypertrophy.

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Table 4 Mean improvement in SF-36 PCS and MCS scores between surgical interventions

Reference	Surgical intervention	Preop PCS	Postop PCS	ΔPCS	Preop MCS	Postop MCS	ΔMCS	N
This study	Bilateral breast reduction	39.7	49.9	10.2	37.0	46.2	9.2	191
Pivec *et al*[44]	Total knee replacement	33.0	47.8	14.8	52.9	55.9	3.0	281
Stickles *et al*[48]	Total hip replacement	28.0	41.2	13.2	51.2	53.9	2.7	551
Muller-Nordhorn *et al*[47]	Coronary artery bypass grafting	36.0	43.0	7.3	45.0	50.0	4.3	412
Polly *et al*[45]	Lumbar fusion (spine)	26.6	40.0	13.4	n/a	n/a	n/a	1826
Rogmark *et al*[49]	Incisional hernia repair	41.6	49.5	8.1	50.2	52.3	1.7	124
Faulconbridge *et al*[46]	Bariatric surgery	37.7	46.4	8.7	43.1	45.5	2.4	36

Δ, mean change in SF-36 score from preoperative to 12 months postoperative; MCS, Mental Component Summary; N, number of participants; n/a, not applicable; PCS, Physical Component Summary; SF-36, Short Form-36.

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Appendix B. Ethics extension approval for study 118.056

Content removed due to privacy reasons.

Appendix C. Ethics approval for study 73.17

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Appendix D. Short Form-36 (SF-36)

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Appendix E. Multidimensional Body-Self Relations Questionnaire (MBSRQ)

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Appendix F. Surgical Complications Checklist

BILATERAL BREAST REDUCTION RESEARCH Complications Checklist

DOCTORS:
PLEASE TICK ANY RELEVANT COMPLICATIONS AND TREATMENTS REQUIRED

Research Code: B____
Date: _____

Timeframe post BBR surgery (circle): 4 wks 3 m 6m 12m 18m Other:_____
Date:

On the day of this assessment has the patient any of the following (please tick):	**Y/N**	**Treatment(s) (as per code list below)**	**Comments**
2= Incomplete wound healing (wound not yet epithelised completely)			
3= Scar issues eg hypertrophic/hypersensitive			
7= Asymmetry (noticable by patient AND Dr)			
8= Altered nipple sensation (total numbness or changes to the extent that it is causing patient distress)			
9= Skin necrosis due to loss of blood supply (greater than 2cm squared> otherwise tick "2"))			
13= Dog ears requiring further surgery (**only tick once listed for surgery)			

Since last assessed, has this patient had any of the following:	**Y/N**	**Treatment(s)**	**Comments**
1= Wound infection requiring antibiotics			
4= Thrombo-embolic event eg PE, DVT			
5= Breast Haematoma - palpable mass requiring aspiration or surgery (do not count simple brusing)			
6= Chest infection/pneumonia within the first 4/52 post surgery			
10= Reaction to anaesthetic			
11= Constipation due to analgesic use			
12= Other- comment			

Treatment codes for complications:
0= Not applicable/no treatment
1 = Antibiotics
2= Return to theatre (eg skin graft, washout, debridement, evacuation of haematoma)
3= Dressings
4= Other- comment
5= Revisional surgery (eg dog ears, scar revision, re-reduction) ** only code once listed for surgery

Appendix G. Ethics approval for study 7848

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Appendix H. Pre-operative BREAST-Q Reduction module

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Appendix I. Post-operative BREAST-Q Reduction module

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Appendix J. Data Usage Agreement

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Appendix K. Descriptive statistics and internal consistency of normative BREAST-Q scores

Item responses	N	Mean	SD	Min	Max	% floor	% ceiling	Cronbach's alpha
Satisfaction with Breasts	**513**	**51.9**	**17.3**	**0**	**100**	**0.2%**	**4.1%**	**0.92**
1. With your breasts in mind, in the past 2 weeks, how satisfied or dissatisfied have you been with:								
a. How your breasts look in clothes?	513	2.96	0.80	1	4	5.3%	24.8%	
b. How your breast size matches the rest of your body?	513	2.96	0.87	1	4	7.0%	28.3%	
c. The size of your breasts?	513	2.86	0.88	1	4	7.4%	25.2%	
d. The shape of your breasts when you are wearing a bra?	513	3.05	0.78	1	4	3.9%	29.6%	
e. How equal in size your breasts are to each other?	513	3.12	0.81	1	4	4.5%	34.9%	
f. How comfortably your bras fit?	513	2.81	0.84	1	4	6.8%	20.9%	
g. The shape of your breasts when you are not wearing a bra?	513	2.43	0.95	1	4	18.9%	13.5%	
h. How you look in the mirror clothed?	513	2.86	0.83	1	4	7.0%	20.9%	
i. How your breasts sit/hang on your chest?	513	2.56	0.91	1	4	13.8%	15.2%	
j. How normal your breasts look?	513	3.01	0.79	1	4	5.5%	25.9%	
k. How you look in the mirror unclothed?	513	2.29	0.94	1	4	23.0%	10.5%	
Psychosocial Wellbeing	**513**	**55.0**	**21.8**	**0**	**100**	**1.9%**	**6.2%**	**0.97**
2. With your breasts in mind, in the past 2 weeks, how often have you felt:								
a. Confident in a social setting?	513	3.62	1.06	1	5	4.1%	20.7%	
b. Of equal worth to other women?	513	3.66	1.19	1	5	6.6%	28.9%	
c. Good about yourself?	513	3.51	1.12	1	5	5.5%	19.3%	
d. Self-assured?	513	3.41	1.13	1	5	7.0%	16.6%	
e. Confident in your clothes?	513	3.39	1.19	1	5	8.0%	18.3%	
f. Accepting of your body?	513	3.3	1.22	1	5	9.9%	17.4%	
g. That your appearance matches who you are inside?	513	3.28	1.27	1	5	12.3%	17.5%	
h. Confident about your body?	513	3.08	1.25	1	5	14.6%	12.7%	
i. Attractive?	513	2.91	1.18	1	5	15.6%	9.0%	

Item responses	N	Mean	SD	Min	Max	% floor	% ceiling	Cronbach's alpha
Sexual Wellbeing	**473**	**48.5**	**24**	**0**	**100**	**8.2%**	**4.2%**	**0.92**
3. Thinking of your sexuality, how often do you generally feel:								
a. Comfortable/at ease during sexual activity?	405	3.34	1.25	1	5	11.4%	18.3%	
b. Confident sexually?	435	3.23	1.24	1	5	12.2%	15.9%	
c. Satisfied with your sex life?	410	3.26	1.28	1	5	12.2%	18.1%	
d. Sexually attractive in your clothes?	464	2.93	1.22	1	5	15.9%	9.3%	
e. Sexy when unclothed?	458	2.5	1.31	1	5	31.4%	8.1%	
Physical Wellbeing	**513**	**71.2**	**13.1**	**0**	**100**	**0.2%**	**4.1%**	**0.89**
4. In the past 2 weeks, how often have you experienced:								
a. Headaches?	513	2.12	1.00	1	5	32.2%	2.0%	
b. Pain in your breast area?	513	1.42	0.75	1	5	71.0%	0.6%	
c. Lack of energy?	513	2.72	1.08	1	5	11.7%	7.2%	
d. Difficulty doing vigorous physical activities (e.g. running or exercising)?	513	2.64	1.33	1	5	25.2%	11.3%	
e. Feeling physically unbalanced?	513	2.24	1.19	1	5	36.5%	4.3%	
f. Shoulder pain?	513	1.89	1.11	1	5	52.4%	2.5%	
g. Difficulty sleeping because of discomfort in your breast area?	513	1.3	0.71	1	5	80.7%	1.0%	
h. Neck pain?	513	1.99	1.11	1	5	45.2%	2.9%	
i. Painful gouges or grooves in your shoulders from your bra straps?	513	1.73	1.08	1	5	61.2%	3.1%	
j. Feeling physically uncomfortable?	513	2.14	1.08	1	5	34.9%	3.1%	
k. Rashes under your breasts?	513	1.58	0.97	1	5	67.1%	2.0%	
l. Back pain?	513	2.26	1.24	1	5	37.2%	5.5%	
m. Arm pain?	513	1.49	0.87	1	5	69.8%	1.6%	
n. Pain, numbness or tingling in your hands because of your breast size?	513	1.2	0.61	1	5	88.1%	0.4%	

Appendix L. BREAST-Q scores for each of the four scales stratified by socio-demographic characteristics for Australian and United States populations

Sociodemographic variable	Australia			United States		
	n	Mean	SD	n	Mean	SD
Satisfaction with Breasts						
Age						
18–24	62	49.8	13.7	6	63.8	22.7
25–34	99	50.2	16.1	93	57.1	16.2
35–44	88	48.8	18.4	171	55.9	16
45–54	87	49.7	16.1	241	56.7	13.6
55–64	75	56.6	18.1	402	56.8	17.6
65+	102	56.1	18.6	289	56.5	16.6
BMI						
< 30 kg/m^2	356	54.0	16.7	912	58.7	16.4
≥ 30 kg/m^2	157	47.4	17.8	287	50	14
Bra cup size						
< D cup	283	52.8	17.0	719	59.3	16.1
≥ D cup	230	50.9	17.6	487	52.7	15.7
Chronic health condition?						
Yes	148	48.6	17.0	595	56.4	16.5
No	365	53.3	17.3	606	56.9	16.1
Employment status						
Full-time	119	52.9	17.1	511	57.1	15.8
Part-time	143	50.8	17.8	168	56.5	17.2
Voluntary work	3	58.7	11.0	33	59.6	14.2
Homemaker	84	51.0	19.2	85	54.6	15.4
Student	26	49.7	10.6	16	60.4	15.8
Retired	85	56.1	17.3	326	56.8	16.9
Unable to work or disabled	21	48.0	18.0	12	50.9	18.5
Unemployed	24	45.8	13.0	19	50.4	15.3
Other	8	55.5	12.6	32	55.8	15.9
All participants	**513**	**51.9**	**17.3**	**1206**	**56.7**	**16.3**

Sociodemographic variable	Australia			United States		
	n	Mean	SD	n	Mean	SD
Psychosocial Wellbeing						
Age						
18–24	62	50.0	19.8	6	61.0	27.5
25–34	99	51.9	19.9	93	62.7	18.6
35–44	88	49.1	21.6	171	61.5	21.2
45–54	87	52.0	22.3	241	67.2	17.0
55–64	75	59.9	21.3	402	68.9	19.3
65+	102	64.8	21.6	289	70.7	17.8
BMI						
< 30 kg/m^2	356	57.7	21.3	912	70.4	17.8
≥ 30 kg/m^2	157	48.6	21.7	287	58.1	19.4
Bra cup size						
< D cup	283	55.8	21.8	719	69.9	18.3
≥ D cup	230	53.9	21.9	487	63.8	19.5
Chronic health condition?						
Yes	148	49.4	23.0	596	66.8	19.2
No	365	57.2	21.0	606	68.1	18.8
Employment status						
Full-time	119	55.0	23.2	511	66.6	19.1
Part-time	143	54.8	20.0	168	68.0	18.3
Voluntary work	3	61.3	27.7	33	70.5	19.6
Homemaker	84	50.8	22.7	85	61.5	20.7
Student	26	51.8	17.4	16	61.1	21.5
Retired	85	64.6	19.6	326	70.4	18.1
Unable to work or disabled	21	45.4	24.1	12	54.8	11.3
Unemployed	24	45.5	23.5	19	61.0	21.5
Other	8	60.8	13.5	32	72.2	18.1
All participants	**513**	**55.0**	**21.8**	**1206**	**67.5**	**19.0**

Sociodemographic variable	Australia			United States		
	n	Mean	SD	n	Mean	SD
Sexual Wellbeing						
Age						
18–24	56	50.0	24.1	5	53.6	13.3
25–34	98	50.9	23.1	88	55.7	16.7
35–44	84	43.7	23.6	157	54.9	19.9
45–54	83	47.5	23.4	226	56.9	18.2
55–64	68	50.5	24.8	345	55.8	20.0
65+	84	49.0	25.0	200	52.5	20.3
BMI						
< 30 kg/m^2	336	51.4	23.4	778	57.5	19.0
≥ 30 kg/m^2	137	41.4	23.9	240	47.8	18.9
Bra cup size						
< D cup	258	50.1	24.2	602	57.2	19.2
≥ D cup	215	46.7	23.6	423	52.4	19.2
Chronic health condition?						
Yes	131	39.6	25.0	492	54.1	20.3
No	342	51.9	22.7	529	56.3	18.5
Employment status						
Full-time	118	48.9	23.1	461	55.9	18.4
Part-time	135	50.8	23.2	151	58.0	18.0
Voluntary work	3	49.7	18.3	29	51.5	16.1
Homemaker	83	48.3	24.5	80	53.6	22.0
Student	19	44.2	24.1	14	54.5	18.5
Retired	69	50.5	25.1	233	54.2	21.1
Unable to work or disabled	20	33.0	25.0	12	39.7	19.3
Unemployed	20	44.7	25.4	16	51.1	24.2
Other	6	50.0	22.6	25	55.5	18.2
All participants	**473**	**48.5**	**24.0**	**1025**	**55.2**	**19.4**

Sociodemographic variable	Australia			United States		
	n	Mean	SD	n	Mean	SD
Physical Wellbeing						
Age						
18–24	62	70.0	12.6	6	68.7	13.9
25–34	99	68.9	13.7	93	74.7	11.3
35–44	88	70.3	12.8	171	75.4	10.7
45–54	87	70.5	12.8	241	75.5	10.1
55–64	75	74.4	12.7	402	75.5	11.4
65+	102	73.2	13.0	289	76.9	10.7
BMI						
< 30 kg/m^2	356	73.0	12.9	912	77.6	10.2
≥ 30 kg/m^2	157	67.2	12.5	287	69.8	11.0
Bra cup size						
< D cup	283	72.9	13.0	719	78.1	9.8
≥ D cup	230	69.2	12.9	487	72.2	11.4
Chronic health condition?						
Yes	148	66.6	11.7	596	73.9	10.8
No	365	73.1	13.1	606	77.5	10.7
Employment status						
Full-time	119	71.2	14.1	511	75.8	10.8
Part-time	143	71.2	13.2	168	75.7	9.8
Voluntary work	3	67.7	4.2	33	80.2	9.7
Homemaker	84	71.9	13.4	85	74.9	11.1
Student	26	71.2	11.0	16	77.7	12
Retired	85	73.6	11.1	326	76.4	10.2
Unable to work or disabled	21	63.9	12.1	12	62.7	12.5
Unemployed	24	67.6	14.1	19	68.7	20.6
Other	8	70.4	14.4	32	74.3	11
All participants	**513**	**71.2**	**13.1**	**1206**	**75.7**	**10.9**

Appendix M. Plastic and Reconstructive Surgery journal published article

Crittenden TA, Watson DI, Ratcliffe J, Griffin PA, Dean NR. Outcomes of Breast Reduction Surgery Using the BREAST-Q: A Prospective Study and Comparison with Normative Data. *Plast Reconstr Surg*. 2019;144(5):1034-1044.

Removed due to copyright restriction. Can be accessed at:

https://journals.lww.com/plasreconsurg/Abstract/2019/11000/Outcomes_of_Breast_Reduction_Surgery_Using_the.3.aspx

Appendix N. Ethics approval for study 299.18

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Appendix O. Letter of invitation for study 299.18

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Appendix P. Participant information sheet for study 299.18

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Appendix Q. Patient Health Questionnaire

MR288A-5

Patient Health Questionnaire

Government of South Australia
SA Health

☐ Verify name, DOB and address with patient / family

Information	
Date form completed: ..... Who completed the form: ..... Height: ..... Weight: ..... Body Mass Index (BMI):	Patient Label

Answer all questions and tick boxes on all of the 4 pages ***Please tick***

Anaesthesia	
Have you had an anaesthetic before? If yes, list most recent and/or major operation(s):	☐ Yes ☐ No
Have you or any **blood relative** ever had any **problems with anaesthetics**? Details:	☐ Yes ☐ No
How far can you walk without stopping? ☐ round the house only ☐ 1–2 blocks ☐ regular walking and exercise What stops you from walking further? ☐ Shortness of breath ☐ Joint Pain ☐ Chest Pain ☐ Leg Pain ☐ Other:	
Do you have: ☐ Loose Teeth ☐ Chipped Teeth ☐ Capped / Crowned Teeth?	☐ Yes ☐ No
Do you have dentures? Upper: ☐ Partial ☐ Full Lower: ☐ Partial ☐ Full	☐ Yes ☐ No
☐ Do you have any neck stiffness? or ☐ Difficulty opening your mouth?	☐ Yes ☐ No
☐ Heartburn ☐ Reflux ☐ Indigestion ☐ Hiatus hernia ☐ Stomach Ulcers	☐ Yes ☐ No
☐ Gastric band ☐ Weight loss surgery Date:	☐ Yes ☐ No
Have you had steroids such as Prednisolone, Cortisone or Hydrocortisone in a tablet or through your vein in the last 3 months? When? What for?	☐ Yes ☐ No
In the last two weeks have you had: ☐ Cold ☐ Flu ☐ Sore Throat ☐ Chest Infection	☐ Yes ☐ No
Females, is there any possibility you may be pregnant?	☐ Yes ☐ No
Females, are you breastfeeding?	☐ Yes ☐ No
Do you have any questions or concerns about the anaesthetic, procedure or operation that you would like to discuss? For example: needle phobia, anxiety. Details:	☐ Yes ☐ No
Allergies / Sensitivity	
Do you have a known **allergy / sensitivity** to latex or rubber? What reaction?	☐ Yes ☐ No
Do you have any allergies / sensitivities to medications, foods, or skin sensitivities? Please list:	☐ Yes ☐ No
Alcohol, Tobacco and Drugs	
Do you drink alcohol? How many days a week? How many glasses a day on average?	☐ Yes ☐ No
Do you smoke cigarettes? If yes, how many per day?	☐ Yes ☐ No
Thinking of quitting?	☐ Yes ☐ No

Answer all questions and tick boxes on all of the 4 pages	***Please tick***
Have you ever smoked in the past? If yes, how many cigarettes/day? For how many years? When did you quit?	☐ Yes ☐ No
Do you use recreational drugs? For example Marijuana, Ecstasy, Cocaine What? How often? When last used?	☐ Yes ☐ No
Cardiac	
Do you have high blood pressure?	☐ Yes ☐ No
☐ Heart failure ☐ AF (Atrial fibrillation) ☐ Rheumatic Fever ☐ Heart Murmur	☐ Yes ☐ No
☐ Chest Pain or Angina ☐ Chest Tightness ☐ Palpitations How often? What triggers it?	☐ Yes ☐ No
A heart attack? When?	☐ Yes ☐ No
Have you ever had heart surgery? Details:	☐ Yes ☐ No
Do you have: ☐ Pacemaker ☐ Implantable Defibrillator ☐ Heart Stent/s When inserted? Type: (Bring information card if available)	☐ Yes ☐ No
Any heart investigations (ie: Echocardiogram, Angiogram) in the last 3 years? What? Where? When?	☐ Yes ☐ No
Do you attend a heart clinic or see a Cardiologist? Where? Who? Last appointment date:	☐ Yes ☐ No
Respiratory	
Do you have troublesome shortness of breath? When?	☐ Yes ☐ No
☐ Chronic bronchitis ☐ Emphysema ☐ Tuberculosis ☐ Persistent cough ☐ COPD	☐ Yes ☐ No
Do you have Asthma? How often? What triggers it?	☐ Yes ☐ No
Do you use a puffer, inhaler, nebulizer (eg. Ventolin)? What? How often?	☐ Yes ☐ No
Have you ever been in hospital for your Asthma? Where? When?	☐ Yes ☐ No
☐ Snore loudly? ☐ Have you been observed to stop breathing while asleep? ☐ Fall asleep easily during the day while sitting/driving?	☐ Yes ☐ No
☐ Sleep Apnoea ☐ Use CPAP ☐ Sleep studies Where? When? **Bring CPAP machine into hospital when you are admitted**	☐ Yes ☐ No
Neurological	
Have you had? ☐ Strokes ☐ Mini Strokes (TIAs) ☐ Blackouts ☐ Funny Turns ☐ Seizures How often? When was your last one?	☐ Yes ☐ No
☐ Muscular Dystrophy ☐ Myotonic Dystrophy ☐ Multiple Sclerosis	☐ Yes ☐ No
Do you have pain? ☐ Acute ☐ Chronic Details:	☐ Yes ☐ No
Mental Health	
Do you have Mental Health problems? ☐ Anxiety ☐ Depression ☐ Bi-polar ☐ Other:	☐ Yes ☐ No
☐ Dementia ☐ Alzheimer's Disease ☐ Short Term Memory Loss	☐ Yes ☐ No
Intellectual Disability? Details:	☐ Yes ☐ No
Can you sign your own consent? If no, who can?	☐ Yes ☐ No

Answer all questions and tick boxes on all of the 4 pages	***Please tick***
Cognition / Perception / Psychosocial	
Do we need to book an interpreter? Language:	☐ Yes ☐ No
Do you have? ☐ Hearing Problem ☐ Vision Problems Details: **Bring your hearing aids and glasses to hospital on admission**	☐ Yes ☐ No
Do you have any cultural / spiritual issues that we need to know about? Describe:	☐ Yes ☐ No
Do you have an Advance Care Directive? (If yes, please bring it to the hospital with you)	☐ Yes ☐ No
Endocrine / Organ Function	
Do you have Diabetes? ☐ Insulin ☐ Tablets ☐ Diet-controlled Most recent HbA1c value? What are your usual blood sugar levels?	☐ Yes ☐ No
Do you require a specific diet? If yes, what type of diet?	☐ Yes ☐ No
☐ Kidney Disease? ☐ Thyroid Disease? Details:	☐ Yes ☐ No
Liver disease or jaundice? Details:	☐ Yes ☐ No
Do you have any existing pressure areas? ☐ Pressure Wounds ☐ Dermatitis	☐ Yes ☐ No
Painful areas on your skin? Describe:	☐ Yes ☐ No
Pressure Injury Risk Assessment. Nurse only to complete Braden Score: ☐	
Connective Tissue / Mobility	
Do you have Arthritis? ☐ Osteoarthritis ☐ Rheumatoid Which joints?	☐ Yes ☐ No
Muscular disease or weakness in the arms or legs? Details:	☐ Yes ☐ No
☐ Artificial joints ☐ Implants Details:	☐ Yes ☐ No
Do you use a: ☐ Walking Frame ☐ Stick ☐ Wheelchair **Bring your walking aids into hospital when you are admitted**	☐ Yes ☐ No
Have you had any falls in the last 6 months? Details:	☐ Yes ☐ No
Falls Risk Assessment required? Nurse only to complete on admission ☐ Yes ☐ No	
Haematology / Other	
Do you have Anaemia? Are you Anaemic at the moment? ☐ Yes ☐ No	☐ Yes ☐ No
Excessive bleeding or bruising (or family member with this problem)? Details:	☐ Yes ☐ No
Other blood disorders (eg. Thalassemia, Sickle Cell)? Details:	☐ Yes ☐ No
Blood transfusion? If yes, when:	☐ Yes ☐ No
Blood clots? ☐ Deep Vein Thrombosis (DVT) ☐ Clot in Lung ☐ Other:	☐ Yes ☐ No
Do you have any other serious illnesses or hereditary diseases not mentioned above (eg. Cancer, Polio, Cerebral Palsy, Dwarfism)? Details:	☐ Yes ☐ No
Have you had a hospital admission for any health problems (excluding operations) in the last 3 years? Details:	☐ Yes ☐ No
Infectious Diseases	
Do you have? ☐ HIV ☐ AIDS ☐ Hepatitis B ☐ Hepatitis C ☐ Other Hepatitis:	☐ Yes ☐ No
Have you ever been told that you have: ☐ MRSA ☐ VRE ☐ Other: If yes, informed by: Where and when:	☐ Yes ☐ No

Answer all questions and tick boxes on all of the 4 pages ***Please tick***

Medications / Drugs	
Do you take any medications/drugs? List ALL regular and occasional medications and tablets or attach an up to date drug list from your pharmacist or GP. **Bring your medications to hospital on day of admission in chemist pack or original bottles/boxes.**	☐ Yes ☐ No
Do you take any blood thinners (ie. Aspirin, Warfarin, Clopidogrel), Anti-inflammatories or Herbal medicines? **NOTE: All herbal medications and nonessential medications (for example: Fish oil, Krill oil, Glucosamine, Garlic, Ginger) should be stopped at least one week before surgery.**	☐ Yes ☐ No
Do you use a pill box? If yes, who fills it?	☐ Yes ☐ No

REGULAR MEDICATIONS (Please copy name and dose from packet)	Strength (eg: per tablet)	How many at each time of day?			
		Morning	Midday	Evening	Night

LIST OCCASIONAL MEDICATIONS

Write any questions or comments

Additional Information
Your contact phone number between 3pm and 7pm of the business day before your surgery
Mobile: **Home:** **Work:**
Do you require a sick certificate? ☐ Yes ☐ No ☐ Centrelink ☐ Workcover ☐ Other:
All the above information is correct to the best of my knowledge. **Signature:** (Person completing form)

Day Surgery Patients Only
If you are having day surgery you cannot drive for 24 hours after your anaesthetic. You must have a responsible adult to accompany you home and stay with you for the first 24 hours following anaesthesia.
Responsible adult name: Phone number:
I certify that: will escort me home and will be with me for 24 hours following anaesthesia.
Patient Signature: Date: (If patient unable to sign include carer name and signature)

Last reviewed April 2014 Next review April 2016

Appendix R. Australasian Journal of Plastic Surgery original article

AUSTRALASIAN JOURNAL OF Plastic Surgery

AJOPS | ORIGINAL ARTICLE
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Measuring breast volume in hypertrophy: laser scanning or water displacement?

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Abstract

Background: The accurate determination of intact breast volume facilitates preoperative planning for a range of plastic surgical breast procedures. In women with breast hypertrophy, volumetric assessment assists in planning the amount of tissue to be removed during breast reduction surgery to achieve breast symmetry. Further, in jurisdictions where restrictive surgical guidelines exist, measurement of intact breast volume is essential in order to justify breast reduction surgery. Not all practitioners have access to magnetic resonance imaging (MRI) or three dimensional (3D) laser scanning facilities, so the purpose of this study was to determine whether water displacement of the intact breast is an effective substitute method of measurement in women with breast hypertrophy.

Methods: A prospective cohort study was undertaken to measure breast volume using water displacement and 3D laser scanning in breast hypertrophy patients. The volume of a total of 322 breasts were determined using both measurement techniques; 194 preoperatively and 128 at 12 months following breast reduction surgery. Pearson correlations, linear regression and Bland-Altman analyses were used to compare the methods of breast volume assessment.

Results: The mean breast volume according to 3D laser scan was 1440 millilitres (SD = 588 millilitres) and for water displacement was 1419 millilitres (SD = 811 millilitres). There was a strong linear association between breast volumes as measured using water displacement and 3D laser scanning using a Pearson correlation ($r = 0.89$, $p < 0.001$). However, using the Bland-Altman analysis, the two methods were found not to be in agreement, with water displacement values consistently larger than 3D scan values.

Conclusions While a strong linear association was found between breast volume measurements made using the water displacement technique and 3D laser scanning, the two methods did not have a high level of equivalence. Water displacement of the intact breast is not an accurate enough tool to be used as a substitute for 3D laser scanning, and therefore not an optimal method of breast volume measurement in women with breast hypertrophy.

Key words: breast volume, water displacement, 3D laser scan, breast hypertrophy, breast reduction

Introduction

Breast hypertrophy is for some women a cause of considerable physical and psychosocial impairment, and adversely affects quality of life. Physical symptoms may include: chronic back, neck, shoulder and breast pain; skin rashes; headaches; shoulder grooving from the constant pressure of bra straps; a reduced capacity for carrying out daily activities and exercise; and numbness or tingling in hands/fingers.[1] Psychosocially, women with breast hypertrophy often display low self-esteem and poor body image, reduced psychosexual function, anxiety and depression.[2]

Breast reduction surgery is widely known to be the most effective treatment for breast hypertrophy.[3] Surgery provides almost immediate symptomatic relief in most cases, and considerably improves the health-related quality of life and wellbeing in women suffering from the functional symptoms of breast hypertrophy.[4,5] Despite these proven benefits, an increase in the prevalence of breast hypertrophy, and hence in demand for breast reductions, has led to restrictions being placed on surgery by healthcare funders and third-party providers in many jurisdictions. Arbitrary restrictions on either the minimum amount of breast tissue required to be removed at surgery or a body mass index cut-off point have been introduced in many institutions and countries worldwide.[6]

Measurement of breast volume plays an important role in breast reduction, reconstruction, developmental asymmetry and augmentation. In women with breast hypertrophy it is important for preoperative planning, in intraoperative decision-making regarding the amount of tissue to be taken from each breast to achieve symmetry, and where removal of a minimum amount of breast tissue is required to justify surgery.[17-21] Accurate estimation of breast volume and predicted tissue resection weight also promotes improved counsel to the patient and provides a valuable guide to training surgeons.

A variety of techniques are described in the literature to meet the need for accurate and objective measurement of breast volumes in the clinical setting including magnetic resonance imaging (MRI), mammography, plaster casting, Grossman-Roudner plastic cups, water displacement, anthropometric measurement and 3D surface imaging.[7-16]

In a situation where a woman is undergoing post-mastectomy breast reconstruction, the gold standard for measuring the breast tissue volume for reconstruction is the Archimedes method of water displacement of the mastectomy specimen.[22] When measuring breast tissue volume in the intact state, such as in candidates for breast reduction surgery, MRI is reported as being the most accurate.[23] However, MRI is expensive and not always accessible. Three-dimensional laser scanning has also been demonstrated as a valid method of breast volume measurement,[11,12,22] but some centres lack access to this technology. Water displacement of the intact breast has been used in some centres since 1970, but has not previously been validated against more recent methods.[24]

The purpose of this study is to assess the validity of measuring breast tissue volume using water displacement of the intact breast and to compare this measurement technique with 3D laser scan measurement.

Methods

Patient selection and measurement

A prospective cohort study was performed at Flinders Medical Centre in Adelaide, Australia. All women aged 18 years and above with breast hypertrophy who were eligible to be placed on a waiting list for bilateral breast reduction surgery between March 2007 and February 2016 were informed of the study. Women who met the

eligibility criteria were invited to voluntarily participate in the study and were provided with a letter and information sheet further outlining the study. Women who were unable to complete written questionnaires, had impaired cognitive capacity, or refused to participate, were excluded from the study. Approval was obtained for this study from the local Southern Adelaide Clinical Human Research Ethics Committee (SAC HREC approval 118.056).

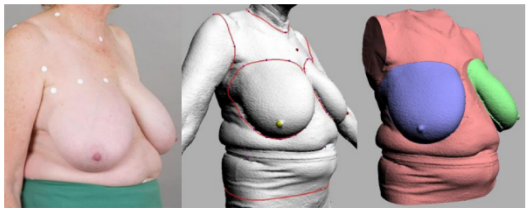
Bilateral breast volumes were obtained preoperatively and/or at 12 months postoperatively by two different techniques—3D laser scanning and water displacement. Patients proceeded immediately from measurement by water displacement to the 3D scanning within the same appointment to allow direct comparison. Some participants had breast volume measurements taken at both the preoperative and 12 months postoperative times, while other participants were measured once as additional measurement was considered onerous for some patients.

Three-dimensional laser body scanning was performed using a Cyberware WBX scanner (Cyberware, Monterey, USA) and Cyslice software (Headus Pty Ltd, Perth, Australia). The Cyberware WBX scanner has four sets of laser heads and cameras that move vertically to scan the surface anatomy of subjects in the upright position. Prior to scanning, the assessor placed 'landmarks' on subjects using palpation to demarcate selected anatomical areas and the breast perimeter. Breast volume was measured according to the validated protocol described by Veitch et al[25] and Yip et al.[22] Figure 2 illustrates the application of landmarks on a large-breasted woman to section the breast from the torso for volume analysis.

Water displacement measurements based on Archimedes' principle was performed on each breast to determine the volume, as described by Schultz et al.[7] A large calibrated container was filled with warm water and the patient asked to individually immerse each breast into the container, using a specially modified surgical bed and ensuring that the superior and lateral edges of the breast were at water level (Figure 1). Individual breast volumes were then determined by the amount of water displaced.

Figure 1: Water displacement technique

Figure 2: Volumetric analysis of the breast with Cyberware WBX 3D scan and CySlice software



A **B** **C**

A=Photograph showing landmark placement following determination of breast borders by palpation B=Scan image with outline of breast and torso boundary C=CySlice image to section the breast portion of the scan from the torso

Statistical analysis

Data was entered into a spreadsheet and statistical analysis performed using SPSS v23.0 statistical software (IBM Corp, Armonk, New York). Pearson coefficients were calculated to assess the linear association between the two measurement techniques.

The strength of any correlation between the two techniques was then determined with a Bland-Altman analysis.[26] This analysis plots the mean breast volume measurements for both techniques against their differences. If the two methods are comparable and in agreement, then the differences should be small and the mean of the differences should be close to zero. The 95% limits of agreement were formed using the mean difference in volumes ±1.96 standard deviation (SD) of the differences

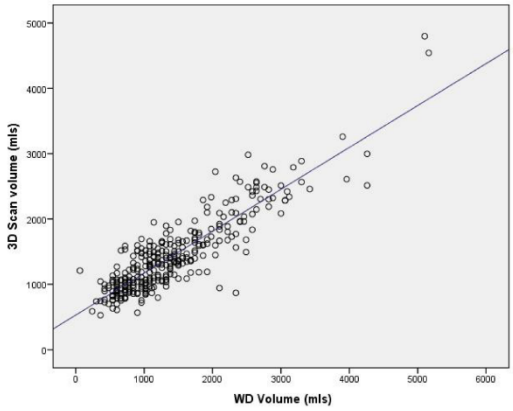
in volumes. Linear regression analysis was performed to assess proportional bias between the two measurement techniques.

Results

A total of 322 breasts were measured in the study using both 3D laser scanner and water displacement techniques—194 breasts (97 women) were measured preoperatively and 128 breasts (64 women) were measured postoperatively. The mean breast volume according to 3D laser scan was 1440 millilitres (SD = 588 millilitres) and using water displacement was 1419 millilitres (SD = 811 millilitres).

In comparing the breast volumes obtained from 3D laser scanning and water displacement, a Pearson correlation demonstrated a strong positive linear association between the two methods ($r = 0.89$, $p < 0.001$) (Figure 3).

Figure 3: Pearson correlation of breast volume measurement—water displacement mean volume versus 3D laser scan mean volume

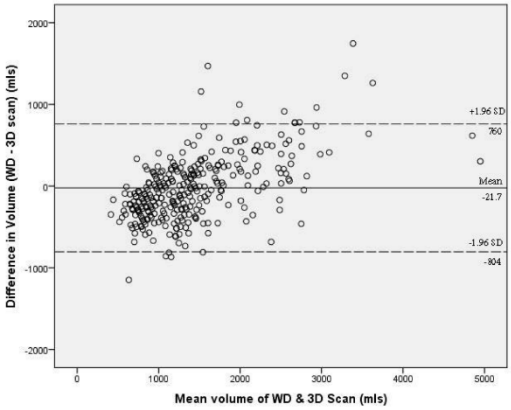


There is a linear association between the two methods

Figure 4 shows the results of the Bland-Altman plot showing the differences between the two techniques plotted against the averages of the two techniques. A mean difference of -21.7 millilitres with a standard deviation of 399 millilitres was found between the two techniques. While most values were within the 95 percent limits of agreement (a lower limit of -804 millilitres and an upper limit of 760 millilitres), the majority of the data points are widely spread across this range and do not lie close to zero, which would have been the case if there was good agreement between the measured values.

Linear regression analysis confirmed a degree of proportional bias, meaning that one method gave values that were consistently higher or lower than those of the other method. In this instance, the breast volumes obtained from water displacement tended to be larger than those from the 3D scanner, and the difference between the two methods increased as the mean volume increased. This is evident from the plot where there was a discernable trend for more points to be above the line of mean difference in volume as the mean volume increased (Figure 4).

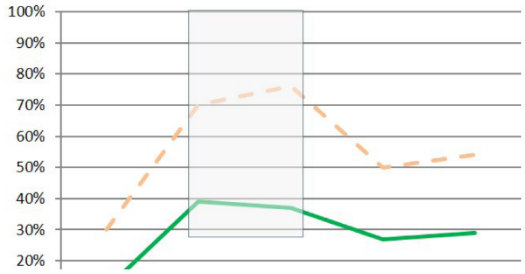
Figure 4: Bland-Altman plot showing mean breast volume versus difference in mean breast volume as measured by water displacement and 3D scanning techniques



While most values lie within the 95% limits of agreement on the plot (±1.96 x SD), there is a large difference in measurement of breast volume using the two methods

The statistical analyses therefore suggest that despite a strong linear correlation between the two methods of breast volume measurement, the measures have low agreement on actual values. The water displacement values were consistently larger than the 3D scan values. The greatest agreement in breast volume measurement between the two methods (within 10 percent) was seen for volumes between 1000 and 2000 millilitres (Figure 5). The findings of this study are in contrast to previous studies conducted in our unit that demonstrated equivalence between 3D laser scanner and direct water displacement of mastectomy specimens, and also between the 3D laser scanner and MRI.

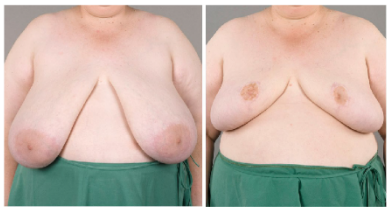
Figure 5: The level of agreement between the two methods



Solid green line indicates volumes within 10% agreement and orange dashed line indicates volumes within 20% agreement. Shaded area highlights the range of breast volumes with the highest level of agreement.

Figure 6 demonstrates the breast volumes measured using water displacement and 3D laser scanning in a single patient both preoperatively and postoperatively at 12 months. The amount of breast tissue removed from each breast was 1444 grams, totalling 2888 grams. The patient's body weight remained relatively stable during this period—127 kilograms prior to surgery and 125.3 kilograms at the postoperative time point.

Figure 6. Breast volumes measured using water displacement and 3D laser scanning in a single patient both preoperatively and postoperatively at 12 months



Measurement type	Pre-operative			Post-operative		
	Right	Left	Total	Right	Left	Total
WD (ml)	4260	3900	8160	1920	1920	3840
3D Scan (ml)	2997	3259	6256	1623	1684	3307
TRW (g)	*1444*	*1444*				

Discussion

A large number of techniques for the objective measurement of breast volume have been described in the literature. However, these techniques often vary in accuracy and reliability and some are limited in their application to large-breasted patients. Many studies specifically on women with breast hypertrophy aim to develop a formula for estimating breast reduction weight in reduction mammoplasty rather than the assessment of breast volumes both before and after surgery.[27-32] This is most likely driven by restrictions placed on breast reduction surgery by healthcare providers or insurance companies which often require surgeons to predict a minimum weight of resected breast tissue. Although a formula to predict tissue resection weight is clinically useful, there remains a need for the accurate determination of absolute breast volumes both in planning breast surgery and in assessing outcomes following surgery.

The use of 3D scanning in the specialty of plastic and reconstructive surgery has increased in recent times. It provides a valuable and non-invasive assessment of the breast for the surgeon, describing the volume, shape, contour, projection and symmetry. This information can not only be useful in the preoperative phase but in the assessment of postoperative outcomes and symmetry. The accurate and objective measurement of breast volume is particularly important in the complex field of breast reconstruction, such as in assessing outcomes following autologous fat grafting techniques[11] and preoperatively for unilateral reduction or augmentation for asymmetry.[33,34] Three-dimensional scanning technology has also been employed in other areas of plastic surgery including facial symmetrisation [35,36] and for the preoperative planning of nasal surgery.[37]

The Cyberware WBX laser scanner and CySlice software used in this study have previously been validated against water displacement in measuring mastectomy specimens with a strong correlation demonstrated.[22] The same 3D laser scanner and protocol were also found to be strongly equivalent to non-contrast MRI for the assessment of breast volume.[11]

The most accurate metric of true breast tissue volume is water displacement of mastectomy specimens, however, this is not applicable other than in post-mastectomy reconstruction scenarios.[15,22,38] Additionally, volume measurement of the intact breast has proven to be more variable due to the challenge of correctly differentiating breast tissue from the chest wall.

This study aimed to determine whether water displacement is a valid lower-cost method of breast volume measurement in women with breast hypertrophy compared to 3D laser scanning. Our measurement of 322 breasts by both 3D laser scan and water displacement showed a close association between the two techniques but the water displacement method had a clear tendency to estimate a larger volume than the 3D scan. A possible explanation for the difference between techniques is that measurement using water displacement requires the patient to be in a prone position, which may change the form of the breast and add axillary or abdominal fat to the breast measurement. In contrast, patients are in the upright position for measurement with the 3D scanner.

The water displacement technique is also highly dependent on the positioning of the patient. Alternative devices for the water displacement technique have been described to address the disadvantages of the immersion technique used in this study.[39] Our study supports previous findings that, although water displacement is easily accessible and a low-cost option, the technique has relatively low accuracy for measurement of the intact breast due to poor reproducibility.[13,40] Three-dimensional scanning and MRI display the highest level of accuracy and reliability and provide a comprehensive assessment of volume and shape for breasts in situ. However, these techniques can be cost-prohibitive. Linear anthropometric measurements are less accurate, however, the costs are negligible, they are fast and they have been shown to provide a reliable estimate of breast volume in the clinical setting.[9,10,14,41]

Another source of difference is that 3D scanning technology allows for a curved cut plane at the back of the breast where it can digitally follow the curved chest wall, while water displacement has by definition a flat cut plane at the water level. The manual positioning of landmarks prior to 3D scanning using palpation to accurately identify the margins of the breast base, and relying on these points later in the scan image, helps to control for potential location error.

Key advantages of this study are its large sample size and that the data was collected prospectively. One limitation of this study is that not all participants had breast volume measurements taken at both the preoperative and 12 months postoperative times. It was decided that additional measurement was too onerous for some patients given the commitments associated with voluntarily participating in the study. As a result, both of these techniques were performed on discrete subsets of patients at each time point.

Future extensions to this work would be to incorporate the results of comprehensive anthropometric body shape assessment that was also conducted pre- and postoperatively as part of this study. Analysis of patient-reported outcome measures data collected during the study would also further enhance our understanding of surgery outcomes and of the overall satisfaction in women with reduction in breast volume through surgery.

Conclusion

This study found a strong linear association between the measurement of breast volumes using water displacement and 3D laser scanning techniques in women with breast hypertrophy but the methods have low agreement on actual values. While water displacement may be more convenient and accessible in clinical practice, 3D scanning remains preferable as it has been proven to be a more accurate and reliable technique for the determination of intact breast volume.

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Disclosure

The authors have no financial or commercial conflicts of interest to disclose.

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Appendix S. Anthropometric measurements

Surgery = ☐ BBR ☐ ABDO
Timeframe = ☐ Pre surgery
☐ 3 mo post surgery
☐ 6 mo post surgery
☐ 12 mo post surgery

Research Code =_____

Date:_____

Measurer:_____

AFESA – Breast Reduction Measurement Chart

- **Measure in millimetres**
- Tape measure to be firm but not tight
- Tape measure and anthropometer to be horizontal at all times
- Patients to "stand tall" and **without shoes**
- Zero end of tape measure to be below the number end of the tape measure so that the graduation lines meet.

Tape Measurements

Measurement chart	Description	Measurement (mm)
Bra size	**Own bra size =** **Post surg bra size =**	
Unisex chest	• **Mark** the sternomanubrial point by feel (or 5-6cm below the jugular notch or run fingers between 1st and 2nd intercostal spaces to sternum) • Arms out and place across the lower section of the scapulars • Lower arms to side and measure using the cross over hand technique	
Bust Girth	• Eye ball apex of breast and measure circumferentially around breast and body • Repeat measurement lower down until highest measurement is achieved • Put **land marks** on for bust point to bust point on the apex of the breast	
Under Bust Girth	• Place tape measure in the crease where the bra ends on the pts back • Bring the tape measure together along the bra line on the front	
Intermammary Fold Girth	• Ask patient to lift breasts. Measure circumference in intermammary fold.	
Waist girth /circumference	• Tie elastic around the person well above the waist • Ask the patient to put the elastic at their waist then ask them to put their hands on their waist • Index fingers of person should line up with elastic- adjust as necessary and **mark** centre back, front, left and right. Measure this circumference around markings	
Hip girth/ Maximum hip	• Find widest aspect of hips and **mark** right and left sides • Measure horizontal circumference	
Bust width- bust point to bust point	• Measure between the **land marks**. This may or may not be the nipple	
Nipple to Nipple	• Ask patient to point to nipples and measure between this point	
Height (Stature)	• Using anthropometer measure height from **behind**.Ask pt to stand up straight, remove shoes. • Ensure head is looking forward and eye level is horizontal with ear hole	
Suprasternale (Jugular notch) to ground	• **Mark** the jugular notch • Line up point of anthropometer to jugular notch and take reading ensuring anth. Is vertical	
Pubic symphysis to ground	• Ask patient to feel for pubic bone. They should feel soft, then a hard point. • **Mark** this point with a dot and measure from here to the ground	
Bi-Acromial Shoulder width	• Palpate for shoulder point. Release pressure and remeasure to ensure the soft tissue point is horizontal with the bony point. **Mark** the shoulder point once established • Using the sliding calliper measure **bony** points from **behind.**	
Bi-iliac Hip width	• Measure from the **front**. Palpate for iliac crest with flat palms. You may need to work your way out to lateral aspect of hip bone • Slide finger up over hip bone to find ridge of hip. Ensure this point is horizontal by feeling several times. **Mark** each hip with a dot. • Using calliper measure between each **bony** point	

Weight and Volumes

Item	Description	Measurement
Weight (kg)	• Zero machine. • **Remove shoes** and heavy clothing/objects	(kg)
Water displacement LEFT	• Shoulder touching the bucket with arm by their side • Ensure all of breast immersed in warm water • Measure distance from water level to top of the bucket in **mm**	(mm)
Water displacement RIGHT		(mm)
Scanner LEFT breast volume	• Record segmented volume	(ml)
Scanner RIGHT breast volume	• Record segmented volume	(ml)
Scanner Torso volume (ml)		(ml)
Scanner TOTAL BODY vol (ml)		(ml)
Data Extraction	By:_____(name) Scan # Used_____ Date Extracted:_____	