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Choice of implant filler in breast reconstruction: A study of the cost-effectiveness of saline and silicone implants

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Abstract

Breast reconstruction following mastectomy is increasing and implant-based breast reconstruction is the most common surgical approach. Saline and silicone implants have different cost and complication profiles and it is unclear which is the more cost-effective option. A systematic review of the literature was undertaken to summarize the quality of life data in breast reconstruction, specifically, previously published health state utility values relevant to breast reconstruction. In addition, a cost-utility analysis was undertaken from the perspective of the third-party payer, accounting for the most common complications associated with saline and silicone implants. This demonstrated that despite the increased initial cost of silicone implants, they are cost-effective with a willingness-to-pay threshold of $50,000 (ICUR $52.26/QALY). Overall, silicone implants provide improved quality of life with a marginal cost increase.

Key Words

Saline-filled implant, silicone implant, implant-based breast reconstruction, cost-utility analysis, economic analysis, health state utility values, systematic review

Co-Authorship Statement

Chapter 1	Kathleen Nelligan – Sole author
Chapter 2	Kathleen Nelligan – Study design, data collection, manuscript preparation
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List of Abbreviations

ADM	Acellular dermal matrix
BIA-ALCL	Breast implant-associated anaplastic large cell lymphoma
CCI	Canadian Classification of Health Interventions
CCO	Cancer Care Ontario
CEA	Cost-effectiveness analysis
CHEERS	Consolidated Health Economic Evaluation Reporting Standards
CT	Computed tomography
CUA	Cost-utility analysis
DIEP Flap	Deep inferior epigastric flap
EQ-5D	Euro-Qol 5D
FDA	Food and Drug Administration
GDP	Gross domestic product
HMMS	Healthcare Materials Management Service
HSUV	Health state utility value
ICER	Incremental cost-effectiveness ratio
ICUR	Incremental cost-utility ratio
LHSC	London Health Sciences Centre
MOHLTC	Ministry of Health and Long-Term Care
MRI	Magnetic resonance imaging
NICE	National Institute for Health and Care Excellence
OHIP	Ontario Health Insurance Plan
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
QALY	Quality-adjusted life year
QBP	Quality-Based Procedure
RCT	Randomized controlled trial
SG	Standard gamble
SJHC	St. Joseph's Health Care, London
TRAM Flap	Transverse rectus abdominis myocutaneous flap
TTO	Time trade-off
VAS	Visual analogue scale
WTP	Willingness-to-pay

1. Chapter 1: Introduction

Overview

The purpose of this thesis is to compare silicone and saline implants in terms of cost-effectiveness in the context of breast reconstruction. This chapter reviews the clinical context of increasing demand for reconstructive breast surgery and the available surgical options. In addition, a brief overview of the existing cost-effectiveness analyses in breast reconstruction will be undertaken, highlighting the gaps in the literature on comparison of implant types. Finally, the regulatory climate and the present challenges in health care spending and planning will provide a framework for the rationale for this project.

1.1. Clinical Context: Breast Cancer and The Increasing Rate of Mastectomy

Breast cancer is the most common cancer among Canadian women, affecting 1 in 8 women over their lifetime.(1) Although breast cancer continues to represent 13 percent of cancer deaths among Canadian women, the mortality rate has declined over the past three decades likely due to the increased use of screening mammography and improved breast cancer treatments.(1,2)

Treatment goals and pathways are dictated by the stage of breast cancer at the time of presentation and typically consist of surgical resection of the primary tumour with or without chemotherapy and radiation. Surgical ablation of the primary tumour can be in the form of either lumpectomy (i.e., breast conserving therapy) or mastectomy. In early stage breast cancer (Stage I or II), lumpectomy followed by radiation is comparable to

mastectomy in overall survival, although mastectomy is associated with a decreased rate of local recurrence.(3–5)

Despite the more invasive nature of mastectomy, recent literature has shown that more women are choosing mastectomy over breast conserving therapy.(6) Prophylactic mastectomy is also increasing in frequency. Contralateral prophylactic mastectomy reduces the relative risk of contralateral breast cancer by 95 percent in women who have had breast cancer, reflecting an absolute risk reduction of approximately 20 to 25%.(7,8) From 1998 to 2003, rates of contralateral prophylactic mastectomy increased approximately 150 percent in women with invasive breast cancer.(9) The same trend has been identified among women with ductal carcinoma in situ.(10) In addition, with the widespread availability of testing for BRCA genetic mutations over the past two decades, bilateral prophylactic mastectomy as a risk reducing strategy is increasingly chosen.(11) The choice of mastectomy and or contralateral prophylactic mastectomy over breast conserving therapy or unilateral mastectomy alone is multifactorial; however, women who choose the former tend to be younger and of Caucasian race and to have private insurance coverage, larger tumours and family histories of breast or ovarian cancer.(6,8,9,12) The rationale behind the choice of surgical resection is incompletely understood; however, fear of developing a cancer in the contralateral breast in addition to the desire for a more symmetric reconstruction have been cited.(13)

1.2. Overview of Breast Reconstruction

1.2.1. Need for Breast Reconstruction Surgery

The combination of early detection, improved treatment and patient preference for mastectomy has contributed to a greater number of women surviving breast cancer with significant mastectomy defects. Breast scars and deformities due to mastectomy can decrease quality of life.(14–16) It is generally accepted that breast reconstruction improves body image in women after mastectomy although factors such as personality traits and body mass index may influence the degree of improvement in quality of life.(17,18) Nonetheless, although many factors influence a woman's decision to undergo reconstructive breast surgery, it is likely that these elements have contributed to the increased demand for breast reconstruction in recent years.

Breast reconstruction rates have increased in the past 20 years in both Canada and the United States.(19,20) This has paralleled an increase in the rate of contralateral prophylactic mastectomy since women undergoing bilateral mastectomies tend to have higher rates of reconstruction.(21) An analysis of the United States Nationwide Inpatient Sample between 1998 and 2008 revealed that 60 percent of women who had contralateral prophylactic mastectomies underwent reconstruction while 81 percent of women undergoing bilateral prophylactic mastectomy underwent immediate reconstruction.(21) Additionally, the rate of reconstruction among women who had contralateral prophylactic mastectomies rose by 3 percent per year during the study period. Not only have rates of breast reconstruction increased, but the rate of implant-based reconstruction has also increased by 11 percent per year from 1998 to 2008 in the United States.(19)

In Ontario, the breast reconstruction rate increased from 19.3 percent in 2002 to 27.9 percent in 2008.(20) Unfortunately, there remains a significant geographic disparity across the province in immediate breast reconstruction rates, which may be attributed to access to a plastic surgeon.(20) In 2016, in an effort to increase access to breast reconstruction, Cancer Care Ontario (CCO) recommended that all women undergoing mastectomy be offered a consultation with a plastic surgeon to discuss breast reconstruction.(22) In addition, dedicated hospital funding to support breast reconstruction has been available since 2016 when CCO designated breast reconstruction as a Quality-Based Procedure.(23) Although it is too early to assess the effects of these changes, it is reasonable to expect rates of breast reconstruction to increase as a result.

1.2.2. Breast Reconstruction Options

Multiple techniques for breast reconstruction have been developed over the years and can broadly be categorized into autologous breast reconstruction and implant-based reconstruction. Both autologous and implant-based reconstructions can be performed as immediate (i.e., completed at the same time as mastectomy) or delayed procedures. Timing is influenced by a number of factors including tumour stage at presentation, requirement for adjuvant treatment, plastic surgeon availability and patient preference.

1.2.2.1. Autologous Reconstruction

Autologous breast reconstruction involves use of a patient's own tissues to reconstruct the breast mound. It is especially helpful for patients who have undergone radiation as implant-based reconstruction can be challenging in a radiated tissue bed.(24) Tissue can be harvested either regionally with pedicled flaps or from distant sites requiring

microvascular anastomosis at the recipient site. The abdomen is the most common donor site for autologous breast reconstruction because an adequate volume of tissue is typically available and is of similar skin colour and consistency to breast tissue. Further, for large pendulous breasts, abdominal tissue is easily molded to match the contralateral breast shape. The transverse rectus abdominis (TRAM) myocutaneous flap has been a workhorse flap for autologous breast reconstruction. It results in good quality tissue for reconstruction of the breast mound and has the benefit of reducing redundant abdominal tissue, if desired. However, it is associated with donor site morbidity in the form of abdominal bulging and hernias due to weakening of the abdominal wall musculature.(25,26) The deep inferior epigastric (DIEP) flap avoids the donor site morbidity of the TRAM flap by preserving the rectus abdominis muscle and as such does not result in abdominal wall weakness.(26) Conversely, it may increase the frequency of complications at the breast recipient site including fat necrosis and partial or complete flap loss.(27) Other common flaps include the pedicled latissimus dorsi flap, which may be considered in women without sufficient abdominal tissue for reconstruction.(28) It may be used alone or in conjunction with implant-based reconstruction.

1.2.2.2. Implant-Based Reconstruction

Although autologous breast reconstruction has been found to be more cost-effective than implant-based reconstruction,(29) not all patients desire or are candidates for autologous reconstruction due to body habitus or personal choice. Implant-based breast reconstruction utilizes a synthetic implant to reconstruct the breast mound and, as for autologous reconstruction, can be either immediate or delayed. For either, the reconstruction may be performed as a single-stage or two-stage procedure. In a single-

stage procedure, the implant pocket is developed and a permanent implant is placed. A two-stage procedure involves the initial placement of a tissue expander which acts to stretch the skin and soft tissues to accommodate a permanent implant which is placed at a later surgery following several months of serial expansion. Breast implants available in North America must be approved by the Food and Drug Administration (FDA) in the United States or Health Canada in Canada. Implants can be categorized by their shape, texture and content.

1.2.2.3. Types of Breast Implants

Breast implants available in North America are made with two types of fillers: silicone and saline. Silicone gel breast implants were developed by Dow Corning in 1962.(30) The evolution of breast implants is complex and can be confusing because of the nomenclature of "generations" of implants which describe the various types. The first generation of breast implants was characterized by a thick outer shell, firm interior gel, anatomic shape and a Dacron patch which was sutured to the chest wall to keep the implant in position.(31) Beginning in 1970, these were replaced by the second generation of implants which featured a round shape, a smooth, thin outer shell and a less viscous gel filler. An initial positive experience with these implants was characterized by a more natural shape and feel. However, longer term follow-up demonstrated gel "bleed" (i.e., slow passage of silicone gel through an intact outer shell) and, more importantly, an extremely high rate of implant rupture.(32) The third generation of implants attempted to resolve these issues with a more cohesive gel filler and a thicker, low-bleed shell. These implants, first introduced in 1982, also featured a textured surface option. The fourth generation of implants was first introduced in 1993 and featured a more strongly cohesive

gel filler within the same low-bleed shell of the third-generation devices but was developed under strict regulatory control by the FDA with the intention of eventual re-introduction into the market.(33) The fifth generation of implants was first developed in 1993 and was characterized by a highly cohesive, form-stable gel. Like the fourth-generation implants, these are available in smooth and textured surfaces with the same low-bleed shell; however, these are also available as anatomic implants in addition to round varieties.(31,33,34)

Saline implants were developed in the 1950s but early versions were limited by high rates of deflation.(33) Eventually these were popularized in North America during the 1990s when silicone implants were removed from the market due to safety concerns, which included implant rupture, an association with connective tissue diseases and increased risk of breast cancer.(35) After numerous studies concluded that the latter two concerns were invalid, silicone implants were reintroduced in both Canada and the United States following the standard premarket approval processes.(36,37) Saline implants continue to be used but have higher complications rates including visible rippling, firm consistency and greater potential for noticeable deflation and resultant re-operation.(38,39) Conversely, potential advantages of saline implants include an ability to fill to volumes larger than those offered with silicone implants, a lower cost and an alternative for women who have inherent concerns about silicone gel implants.

The two principle classes of implant shape are round and anatomic (“tear drop”). The theoretical advantage of an anatomic implant is the creation of a more naturally shaped breast mound with decreased upper pole fullness relative to round implants. Importantly,

the extent to which an implant holds its shape under the influence of gravity is influenced by the filler. Therefore, anatomic implants with more highly cohesive gel filler tend to maintain their upper pole shape against gravity. A recent study demonstrated that in the breast reconstruction population, patients who received round implants were more likely to undergo revision symmetry procedures than those who received anatomic implants.(40) Despite this theoretical advantage, numerous other studies have been unable to demonstrate a difference in appearance or quality of life between anatomic and round implants.(34,41) Further, the use of anatomic implants can be complicated by implant malposition, such as implant malrotation, and require subsequent reoperation for correction.(31)

Both saline and silicone implants in current use have silicone elastomer shells that vary in surface characteristics. Broadly, these surface qualities are characterized as “smooth” and “texturized,” although textured implants have variable surface morphology based on patented designs by device manufacturers. While all implants will result in capsule formation, capsular contracture is less common with textured implants. (42) The textured surface is particularly common in anatomically-shaped implants as the surface texture helps maintain the implant position within the implant cavity. However, there are some drawbacks to the textured surface, namely the evolving body of literature suggesting an association with breast implant-associated anaplastic large cell lymphoma (BIA-ALCL).(43,44) While the understanding of this disease is still developing and the reported incidence is low, rates reported in the literature are rising.(45) Rates of BIA-ALCL may rise over the coming years with increased awareness and surveillance.

1.2.3. Summary of Clinical Problem

Saline and silicone-filled implants are used in both the breast augmentation and reconstruction populations with good results. While silicone implants have been associated with higher rates of capsular contracture,(46) they have also been associated with improved patient satisfaction compared to patients with saline implants.(47) In Canada, the cost of silicone implants may be twice the price of saline implants.(30) Since satisfaction and rates of complications requiring reoperation differ between patients with saline versus silicone implants, it would be useful to determine the option that is most effective taking into account clinical outcomes, quality of life and cost.

1.3. Economic Context: Decision-Making in a Publicly-Funded Health Care System

In Canada, health care spending is among the highest internationally and is on the rise.(48) In 2015, health expenditure reflected 10.4 percent of the gross domestic product (GDP) and is expected to rise to 11.5 percent in 2017.(48) In a resource-constrained system, it is important to consider the value for money achieved with health care expenditures since spending in one area removes resources in other areas.

Economic analyses are decision-making tools used to inform choice and funding of therapies or interventions with the goal of choosing the most economically effective options.(49) There are multiple forms of economic analysis, differentiated by the number and unit of measure of health outcomes (Table 1.1). Cost-minimization analysis compares cost when patient outcomes are equal. Cost-benefit analysis examines the monetary value of multiple patient outcomes. However, it is often challenging to assess the value of a health state in monetary terms. Cost-effectiveness analysis measures cost against a single

health outcome measured in natural units (e.g., life years gained). While this is a useful method of analysis, it can be challenging to compare analyses measured in different natural units (e.g., life years gained versus premature births avoided). Cost-utility analysis measures patient outcomes using a common denominator: healthy years (e.g., quality adjusted life years).(49)

Table 1.1 Economic Analyses

Method	Assumption	Number of Outcomes	Unit of Outcome
Cost-minimization analysis	Patient outcomes equal	None	None
Cost-benefit analysis	Patient outcomes not equal	Many	Monetary
Cost-effectiveness analysis	Patient outcomes not equal	One	Natural Units
Cost-utility analysis	Patient outcomes not equal	One	Quality of Life

1.3.1. Cost-Utility Analysis in Breast Reconstruction

Cost-effectiveness analysis (CEA) is a type of economic evaluation that is used to determine the value for money of various treatments and interventions.(49) A subtype of CEA is cost-utility analysis (CUA), whereby cost is measured against health status, most commonly expressed in quality-adjusted life-years (QALYs).(50,51) The advantage of using a cost-utility analysis is that it facilitates comparisons of different interventions and health states through a common denominator, the QALY. Comparisons may be made across disease groups for which outcomes measured in natural units may not be directly comparable (e.g., hip fractures avoided versus life years gained).

There are increasing numbers of cost-utility analyses examining breast reconstruction options. Several have compared autologous and implant-based reconstruction (29,52–54)

while others have examined adjuncts to surgery and surgical materials such as CT angiography and acellular dermal matrix.(55,56) Overall, there is evidence to support greater cost-effectiveness with autologous reconstruction. Unfortunately, not all women are candidates for autologous reconstruction due to body habitus, comorbidities and patient preference. In terms of implant-based reconstruction, no cost-utility analysis has compared saline and silicone implants which are associated with different costs and quality of life. There is a clear clinical demand for implant-based breast reconstruction. However, given resource constraints, health care providers may be asked to justify use of devices seen as more costly. A cost-utility analysis of saline and silicone implants would provide helpful information to physicians, hospitals and policymakers when purchasing implants for breast reconstruction.

A secondary consideration from the existing cost-utility analyses is choice of health state utilities. Often CUAs estimate new utility values for the health states included in the analysis. Although generating new health state utility values may allow for more accurate assessment of the specific health state description used in a model, repeatedly surveying physicians and patients is time-consuming and costly. Given the need for cost-effectiveness analyses in resource-limited systems and the increasing rate of breast reconstruction, understanding the existing published health state utility values and the methods used to evaluate them is essential. Furthermore, developing strong estimates of health state utility values is paramount to enhancing the external validity of a CUA model.

1.4. Rationale for Cost-Utility Analysis in Implant-Based Breast Reconstruction

Breast reconstruction is a recognized component of the cancer treatment pathway and rates are increasing in both the United States and Canada.(20) Further, implant-based reconstruction increased by 11 percent between 1998 to 2008 in the United States and continues to be the most common type of breast reconstruction in North America.(19) There is a clear clinical demand for implant-based breast reconstruction; however, there are a wide variety of implant designs to choose from with varying advantages and disadvantages. In a resource constrained health care system, whether publicly- or privately-funded, it is essential to consider the cost-effectiveness of these treatment options. An important element of implant-based breast reconstruction is implant choice. Saline and silicone implants have different quality of life, safety and cost profiles. It is essential to find cost-effective alternatives that continue to provide women seeking breast reconstruction a high quality of life in the survivorship period. Further, outlining the cost-effectiveness of implant alternatives may help health care providers justify the use of interventions that are more costly but associated with improvements in quality of life. Therefore, the first component of this study is an examination of the existing health state utility values in breast reconstruction through a systematic review of the literature. The second component of this study is a cost-utility analysis of saline and silicone implants for immediate, unilateral, implant-based breast reconstruction.

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2. Chapter 2: A Systematic Review of Utility Measurements in Breast Reconstruction

Overview

This chapter reviews approaches to health status assessment and utility generation. In addition, a systematic review of health state utility values in breast reconstruction explores the existing literature supporting this component of economic analysis in the breast reconstruction population. Utilities are summarized in a quantitative analysis and methods of health status assessment in this field are compared to existing guidelines. The results of this analysis can serve as a reference for utility values for future cost-utility analyses in breast reconstruction.[1]

2.1. Introduction

Breast reconstruction is an integral component of the breast cancer treatment pathway and rates are increasing in both the United States and Canada.(1,2) However, there are a wide variety of approaches ranging from autologous to implant-based options. Factors which may determine the best option for an individual woman include medical comorbidities, body habitus, breast cancer characteristics and personal preferences. Within these domains, there are a number of variables that can influence cost and quality of life associated with the procedure, including the use of venous couplers, acellular dermal matrices and implant type.(3–5) In a resource constrained health care system, it is essential to consider the cost-effectiveness of these and other treatment options.

[1] A portion of the work covered in Chapter 1 is included here as part of the Integrated Article Format.

2.1.1. Cost-Utility Analysis

Cost-effectiveness analysis (CEA) is a type of economic evaluation that is used to determine the value for money of treatments and interventions.(6) A subtype of CEA is cost-utility analysis (CUA), whereby cost is measured against health status, most commonly expressed in quality-adjusted life-years (QALYs).(7,8) The advantage of using a cost-utility analysis is that it facilitates comparisons of different interventions and health states through a common denominator, the QALY. This allows for comparisons across disease groups for which outcomes measured in natural units may not be directly comparable (e.g., hip fractures avoided versus life years gained). QALYs can be calculated by multiplying the value and duration of a given health state.(8) The value of a health state, known as the health state utility value (HSUV) or single index score, ranges from zero (death) to 1 (perfect health).(8) States worse than death can have a value less than zero. Thus, one QALY equates to one year of life lived in perfect health.

$$QALY = HSUV * Duration\ of\ health\ state\ (years)$$

$$1\ QALY = 1 * 1\ year$$

2.1.2. Health Status Assessment

Health state utility values can be generated through direct elicitation or indirect health status assessment.(9) Direct elicitation methods include techniques such as visual analogue scale (VAS), time trade-off (TTO) and standard gamble (SG) (Table 2.1).(8,9)

Table 2.1 Direct Elicitation Methods

Method	Description
Visual Analogue Scale	Respondents rank health states along a line with well-defined end points (e.g., perfect health and death) according to desirability. The utility of the impaired health state is the fractional distance along the continuous scale.(8)
Time Trade-Off	Respondents choose between two alternatives: living *x* years in an impaired health state or living in perfect health for *y* years (a shorter period of time). The time period is varied until respondent finds the two choices equivalent. Then the utility of the impaired health state is x/y.(9)
Standard Gamble	Respondents choose between remaining in an impaired health state or taking a gamble, in which they may return to full health or die. The probability of death is varied until the respondent finds the certainty and gamble equivalent. The utility of the impaired health state is the probability of returning to full health at the point of indifference.(9)

When using a VAS, individuals are asked to rank health states along a scale from best to worst imaginable health or from perfect health to death.(8) Although attractive in its simplicity, this method is limited by inconsistent anchors, context bias (i.e., where valuation depends on number of states presented at the same time), scaling bias (i.e., reluctance to rate health states at extremes of the scale) and emphasis on rating rather than choice, which does not have grounding in economic theory.(8,10) Time trade-off and standard gamble both involve an element of choice and as such have stronger grounding in economic theory. The time trade-off method asks respondents to choose between living in an impaired health state for a period of time, *x,* and living in perfect health for a shorter period of time, *y*. The time of x or y is then varied until the respondent finds the choices equivalent. The utility is then *y/x*.(8,9) Standard gamble also presents a choice to respondents, asking them to choose between staying in a state of impaired health or taking a gamble in which they either return to full health or die. The probability of returning to full health is then varied until the respondent is indifferent at which point the probability is the utility of the impaired health state.(8,9)

Indirect health status assessment is performed through administration of questionnaires that address multiple domains of quality of life such as pain, physical functioning and emotional well-being.(8) Questionnaires can either be generic, assessing a broad scope of domains relevant to health in general, or specific to a given disease population.(9) Generic tools allow for comparison across multiple disease groups but can be insensitive to domains that are specific to particular disease populations.(11) For instance, breast reconstruction impacts multiple domains such as body image and sexual functioning, but these are not directly addressed in generic tools such as the Euro-Qol 5D (EQ-5D).(12,13) However, condition-specific measures of quality of life decrease the comparability of results across diseases. Because of this, disease-specific measures must be mapped to a generic measure prior to being used in economic evaluations.(9)

Health status questionnaires can be classified as either preference-based or non-preference-based measures. Non-preference-based measures ask respondents to depict their health in different domains of quality of life and, in doing so, describe a health state.(14) Preference-based measures capture the desirability of a health state.(9) The latter, also referred to as multi-attribute utility scales, generate specific health states for which a single index score (i.e., health state utility value) is calculated using preference weights developed through direct elicitation surveys of the general population.(8) Importantly, preference-based questionnaires can be used to generate utilities. Scores from non-preference-based measures cannot be used directly to generate utilities; instead they must be mapped using a statistical function.(8)

Health state utility values (HSUVs) are commonly estimated by surveying patients, but they can also be assessed by surveying experts (e.g., physicians) or the general population. Importantly, each of these groups tend to value health states differently and there are limitations with surveying each of these populations. While the general population, comprised mainly of healthy individuals, tends to underestimate the utility of diseased health states, patients who have experienced those states and have become accustomed to them may place a higher value on those states.(9) Medical and surgical experts may have greater knowledge of diseased states than the general population but may be biased by their personal opinions of interventions and emotional connection with patients.(15)

2.1.3. Existing CUAs in Breast Reconstruction

There are increasing numbers of cost-utility analyses examining breast reconstruction options. Often these CUAs generate new utility values for the health states included in the analysis. Although generating new health state utility values may allow for more accurate assessment of the specific health state descriptions used in a model, repeatedly surveying physicians and patients is time-consuming and costly. Given the need for cost-effectiveness analyses in resource limited systems and the increasing rate of breast reconstruction, understanding the existing published health state utility values and the methods used to evaluate them is essential. Furthermore, developing strong estimates of health state utility values is important to enhancing the external validity of CUA models.(16)

Thus, the purpose of this systematic review of utility measurements in breast reconstruction was twofold. The first aim was to describe the metrics used to generate utilities in the breast reconstruction literature and the second was to summarize the values reported for common early and late postoperative complications for implant-based and autologous breast reconstruction.

2.2. Methods

2.2.1. General

A systematic review was conducted to identify previously reported utility values and quality of life outcomes generated through validated questionnaires in breast reconstruction for either therapeutic or prophylactic mastectomy. The main objective was to identify utility values for all health states relevant to breast reconstruction that can be used in future cost-utility analyses.

2.2.2. Data Sources

An electronic search of English-language literature was performed of MEDLINE® and Embase® databases for relevant articles published prior to November 2017. The search strategy was designed with assistance from a librarian experienced in systematic reviews (Table 2.2). In addition, reference lists of accepted papers and relevant review articles were manually reviewed to identify additional articles.

Table 2.2 Search Strategy

No.	Search
1	exp mammaplasty/ or (mammaplast$ or mammoplast$ or mastoplast$).mp. or (breast$ adj5 reconstruct$).mp. (16795)
2	exp "Costs and Cost Analysis"/ (225003)
3	(economic value of life or economics, medical or economics, pharmaceutical or models, economic or markov chains or monte carlo method or uncertainty).sh. (68649)
4	economics.fs. (407092)
5	(quality of life or quality-adjusted life years).sh. (180352)
6	((econom$ or cost or costly or costing or costed or prices or pricing or discount or discounts or discounted or discounting or budget$ or afford$ or pharmacoeconomic$ or pharmaco) adj1 economic$).ti,ab. (228130)
7	(decision adj1 (tree$ or analy$ or model$)).ti,ab. (15477)
8	((value or values or valuation) adj2 (money or monetary or life or lives)).ti,ab. (4665)
9	(QOL or QOLY or QOLYs or HRQOL or QALY or QALYs).ti,ab. or (quality$ adj2 life$).tw. (243759)
10	((((quality adj1 life) or (willingness adj1 pay) or (quality adj1 adjusted life year$) or sensitivity) adj analys?s) or quality adjusted life expectanc$).ti,ab. (27847)
11	economics.sh. (27494)
12	(Economic Impact or Economic Value or Pharmacoeconomics or Health Care Cost or Economic Factors or Economics or Cost Analysis or Cost or Economic Analysis or Cost-Effectiveness or Costs or "Quality of Life" or Health Care Cost or Cost Savings or Cost-Benefit Analysis or Hospital Costs or Medical Costs or Quality-of-Life).mp. (892619)
13	exp Economic Evaluation/ or exp Pharmacoeconomics/ or Quality Adjusted Life Year.sh. or exp Quality of Life/ (245192)
14	or/2-13 (1285636)
15	1 and 14 (1387)
16	limit 15 to english language (1285)
17	16 not (exp Animals/ not (Human/ and exp Animals/)) (1283)
18	meta analysis.mp,pt. or MEDLINE.tw. or systematic review.tw. (256532)
19	17 and 16 (1283)
20	limit 17 to "review articles" (161)
21	17 not 20 (1122)
22	19 or 21 (1283)
23	case report.ti. (213167)
24	22 not 23 (1281)

2.2.3. Literature Screen

After removal of duplicates, all citations were screened in two stages by two independent reviewers (Table 2.3). In the first stage, title and abstract were reviewed with the following exclusion criteria: abstract only, non-English language articles, case reports, letters, commentaries, non-systematic reviews, animal studies and in vitro studies. Since it was anticipated that there would be few reports of utility values and that this may be challenging to elicit from title and abstract alone, inclusion criteria were intentionally made broad for the first stage of screening. Articles were included if they met the following criteria: the study examined women undergoing breast reconstruction for either therapeutic or prophylactic mastectomy and the study had the potential to report utility values (i.e., was a possible economic analysis (i.e., referred to as cost-utility analysis, cost-analysis, economic analysis, cost effectiveness analysis in title or abstract), reported health state utility values (e.g., a report of independent utility generation, systematic review or meta-analysis of utilities) or reported on quality of life using a validated tool that could be used to generate utilities). If it was unclear whether a citation met the inclusion criteria based on title and abstract alone, it was included for full-text review.

Table 2.3 Systematic Review Inclusion and Exclusion Criteria

	Inclusion Criteria	Exclusion Criteria
First Stage	Population • breast reconstruction for therapeutic or prophylactic mastectomy) Design • economic analysis • utility generation report or validated patient-reported outcome measure • systematic review/meta-analysis	Incorrect population Design • conference abstract • non-English language articles • case reports • letters • commentaries • non-systematic reviews • laboratory (animal or in vitro) studies
Second Stage	Design • cost-utility analysis • utility generation report	Design • patient-reported outcome measure without utility values for specific postoperative health states

In the second stage, the full text of articles that met inclusion criteria were reviewed in addition to those studies for which a determination could not be made based on title and abstract alone. A study was included after the second stage if it reported utilities (i.e. was a cost-utility analysis or if it generated or reported utility values without a formal economic analysis). Exclusion criteria at the second stage included incorrect study design (i.e. did not report utilities), with the addition of cost-analysis, cost-effectiveness analysis, cost-minimization analysis and cost-benefit analysis to the exclusion criteria. Studies that reported validated health status measures but did not report utility values for specific post-operative health states (e.g., complication states) were also excluded since the value reported was an aggregate of successful, unsuccessful and complicated procedures.

2.2.4. Data Abstraction

Data was abstracted from included studies encompassing the following details: author, journal, publication year, study design, study population (e.g., breast reconstruction,

implant-based breast reconstruction, autologous reconstruction etc.), intervention (e.g., subtype of implant-based or autologous reconstruction, use of acellular dermal matrix etc.), population and number of individuals surveyed to generate utility values, utility metrics, health states, health state definitions and utility values reported.

2.2.5. Analysis

Included studies were discussed in a narrative fashion. There is a lack of consensus on reporting methodology for HSUV studies; however, generic criteria have been published by Papaioannou et al. and used in other systematic reviews of HSUVs.(16,17) Others abide by the National Institute for Health and Clinical Excellence Guide to the Methods of Technology Appraisal or CHEERS reporting guidelines.(18,19) Study quality was described narratively with respect to these criteria. Studies that reported original utility values and the number of individuals surveyed for utility generation were included in a quantitative analysis in which weighted averages and standard deviations of reported values were calculated with weights based on number of individuals surveyed (Appendix 1).(20) Since none of the articles reported confidence intervals or standard deviations for the health state utility values a formal meta-analysis could not be performed. All statistics were calculated using Microsoft® Excel®.

2.3. Results

2.3.1. Search Results

The systematic review process is outlined in the PRISMA flow chart (Figure 2.1). The literature search yielded 3060 records through MEDLINE and Embase of which 2279 remained after duplicates were removed. In addition to 4 records identified through cross-referencing, a total of 2283 records were screened. Of these, 2249 records were excluded based on title and abstract. Full-text review was done for 219 citations and 200 were excluded at this stage. Of the excluded citations, 17 were published in abstract format only, 9 were cost-analyses, 3 were not specific to breast reconstruction (i.e., were studies of women with breast cancer without specific assessment of reconstruction), 1 was a cost-effectiveness analysis, 1 was a preference model that did not generate utilities and 169 used non-preference-weighted quality of life measures. Of the full-text articles reviewed 19 met inclusion criteria and only 10 of these published original utility values (i.e., not obtained from a synthesis of the literature) that could be incorporated into a pooled analysis.

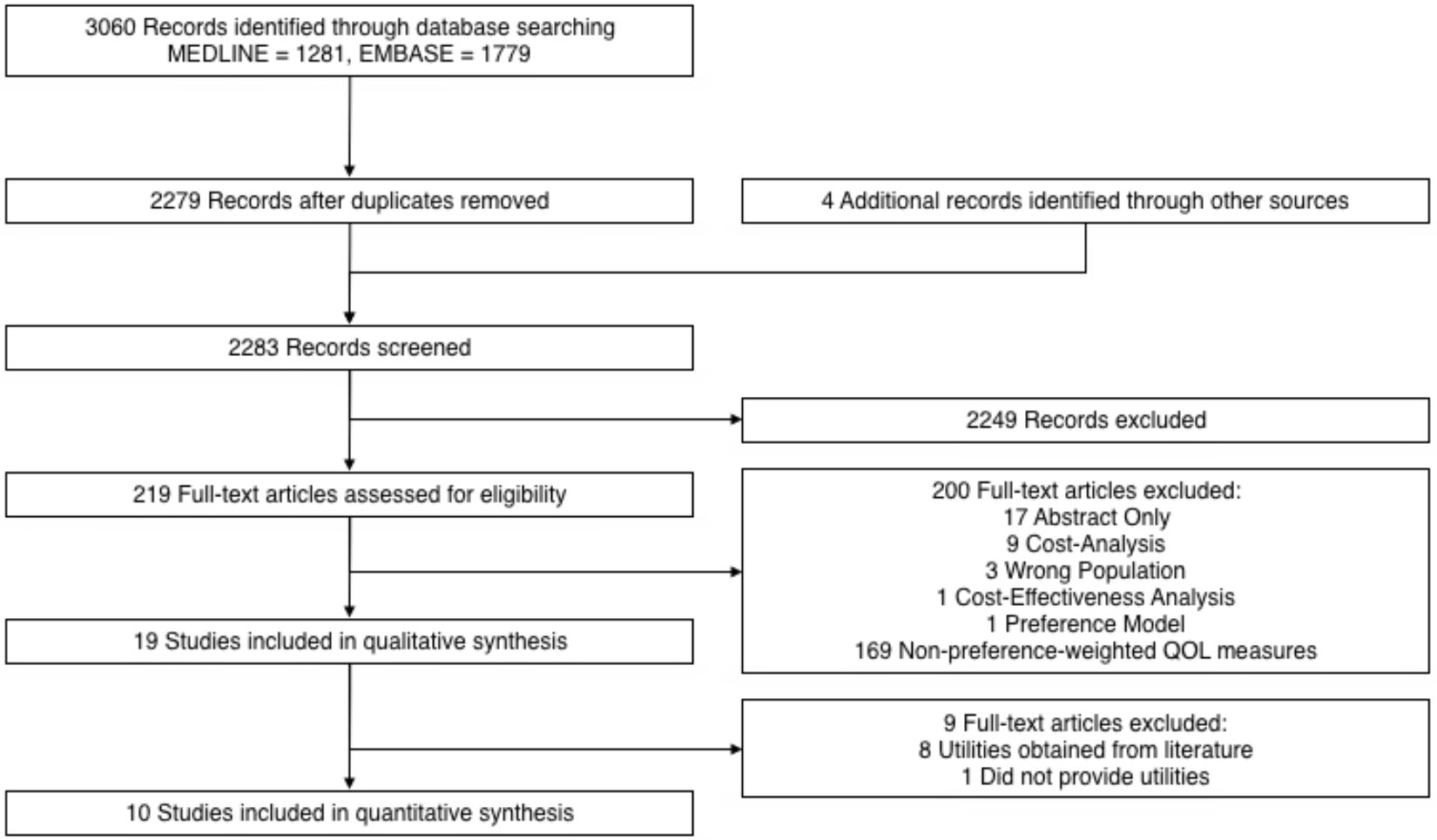

Figure 2.1 PRISMA Search Strategy Flow Diagram Utilities

2.3.2. Study Design

Of the articles included following full-text review, 17 were cost-utility analyses and 2 were utility generation reports related to breast cancer and reconstruction (Table 2.4). Of the cost-utility analyses, 9 assessed the relative costs and benefits of autologous reconstruction, 6 assessed those of implant-based reconstruction and 4 did not specify the reconstructive modality used but compared all reconstruction techniques to mastectomy alone. Of the included studies, only one specified unilateral or bilateral reconstruction. Further, only 5 studies specified timing of reconstruction as either immediate or delayed.

Table 2.4 Characteristics of Included Studies

Author	Design	CUA Model			Utility Generation			Contribution to Pooled Estimate
		Population	Intervention	Reconstruction Methods	Population	Utility Metric	Number Surveyed	
Chatterjee et al. 2013(21)	CUA	Free Autologous Reconstruction	Laser-Assisted Indocyanine Green Angiography	Free Flap	Expert Opinion	TTO VAS	10	Included
Grover et al. 2013(22)	CUA	Breast Reconstruction	Reconstruction Method	Direct to implant, expander-implant, pedicled flap, free flap, pedicled latissimus dorsi flap with implant	Expert Opinion	VAS	9	Included
Hummelink et al. 2017(23)	CUA	Free Autologous Reconstruction	3D Planning with CT Angiography	DIEP Flap	Literature Review(21)		N/A	Included[2]
Ibrahim et al. 2015(24)	Utility Report	Breast Reconstruction	N/A	Breast reconstruction without nipple reconstruction	General Population	TTO VAS SG	103	Included
Keskey et al. 2017(25)	CUA	Breast Cancer	Unilateral Mastectomy vs. Contralateral Prophylactic Mastectomy	With or without reconstruction	Literature Review(26–29)		N/A	Excluded

[2] Values were obtained from literature but Hummelink et al. report a value that was not reported in source article so it was included to incorporate this additional HSUV.

Table 2.4 Characteristics of Included Studies

Author	Design	CUA Model			Utility Generation			Contribution to Pooled Estimate
		Population	Intervention	Reconstruction Methods	Population	Utility Metric	Number Surveyed	
Krishnan et al. 2014(30)	CUA	Implant-Based Reconstruction	Acellular Dermal Matrix (ADM)	Expander-implant immediate with or without ADM	Expert Opinion	TTO VAS	5	Included
Krishnan et al. 2013(31)	CUA	Implant-Based Reconstruction	Acellular Dermal Matrix (ADM) vs Autologous Dermal Flaps	Single-stage, implant-based immediate with ADM or autologous dermal flap	Expert Opinion	TTO VAS	10	Included
Krishnan et al. 2015(32)	CUA	Free Autologous Reconstruction	Reconstruction Method	DIEP, muscle sparing TRAM	Literature Review(33)		N/A	Excluded
Krishnan et al. 2016(34)	CUA	Implant-Based Reconstruction	Reconstruction Method	Single-stage, expander implant	Expert Opinion	VAS	15	Included[3]
Malin et al. 2002(35)	CUA	Breast Cancer	N/A	Unspecified	Literature Review(36)		N/A	Excluded
Matros et al. 2015(37)	CUA	Breast Reconstruction	Reconstruction Method	Implant-based, autologous perforator flaps	Patients	BREASTQ	526	Excluded[4]

[3] Utilities not reported by Krishnan et al. so were derived based on QALYs and health state duration for use in this study.

[4] Utilities not reported and could not be derived based on reported health state information.

Table 2.4 Characteristics of Included Studies

Author	Design	CUA Model			Utility Generation			Contribution to Pooled Estimate
		Population	Intervention	Reconstruction Methods	Population	Utility Metric	Number Surveyed	
Offodile et al. 2015(38)	CUA	Free Autologous Reconstruction	Preoperative CT Angiography	Free flap	Expert Opinion	TTO VAS	Not Reported	Excluded
Peasgood et al. 2010(26)	Utility Report	Breast Cancer	N/A	Unspecified	Literature Review		N/A	Excluded
Preminger et al. 2008(39)	CUA	Breast Reconstruction	Reconstruction Method	Implant-based, free TRAM	Literature Review, Author Assumption		N/A	Excluded
Razdan et al. 2016(40)	CUA	Locally-Advanced Breast Cancer	Reconstruction Method	Mastectomy alone, immediate expander-implant, delayed autologous	Patients	BREASTQ	343	Included[5]
Roberts et al. 2014(27)	CUA	Breast Cancer	Unilateral Mastectomy vs. Contralateral Prophylactic Mastectomy	Expander-implant	Literature Review		N/A	Excluded
Thoma et al. 2008(41)	CUA	Free Autologous Reconstruction	Reconstruction Method	DIEP, SIEA	Literature (Thoma et al. 2004)		N/A	Excluded
Thoma et al. 2003(42)	CUA	Breast Reconstruction	Reconstruction Method	Free TRAM, pedicled TRAM	Expert Opinion	VAS	33	Included

[5] Included because utilities were reported for successful surgery. However, utilities were not reported for complication health states and could not be derived based on reported health state information.

Table 2.4 Characteristics of Included Studies

Author	Design	CUA Model			Utility Generation			Contribution to Pooled Estimate
		Population	Intervention	Reconstruction Methods	Population	Utility Metric	Number Surveyed	
Thoma et al. 2004(33)	CUA	Breast Reconstruction	Reconstruction Method	DIEP, free TRAM	Expert Opinion	VAS	32	Included

2.3.3. Utility Generation

Utilities were generated through expert opinion surveys in 7 studies, through literature review in 9 studies, through patient questionnaires in 2 studies and through a survey of the general population in 1 study. Of the studies that generated utilities from expert opinion, 4 administered time trade-off surveys or visual analogue scales to experts depending on respondent familiarity with each tool while 4 administered visual analogue scales alone. Only 1 study used standard gamble to generate utilities. Of the 2 articles that surveyed patients to generate utilities, both used the BREAST-Q™, a validated, patient-reported outcome measure which has been widely used.(43) Of the cost-utility analyses that obtained utilities from the literature, 4 cited articles that generated utilities through expert opinion (TTO or VAS),(23,32,35,38) one cited a value generated for an "absent breast" health state using the Health and Activity Limitation Index(39) and the remainder were unspecified.

2.3.4. Health States

Overall, the 19 included articles reported utility values for 35 distinct health states of which 17 were related to breast reconstruction. However, definitions and durations of health states varied by study and were inconsistently reported.

2.3.5. Utility Values

Only the 10 studies that generated original utility values were included in the pooled estimates (Table 2.5). Successful surgery (i.e., without complications) was reported by 8 studies of which 4 studies reported utilities for multiple reconstructive techniques resulting in 15 observations that contributed to the pooled estimate of 0.73 (95%CI 0.59-

0.87). Successful autologous breast reconstruction had a higher average utility than successful implant-based breast reconstruction. Complication states varied widely, with total flap loss associated with the lowest utility (0.55 95%CI 0.40-0.71), which was worse than the utility of mastectomy alone (0.60 95%CI 0.51-0.68). The utility for hematoma (0.73 95%CI 0.59-0.87) approached that of successful surgery; however, this may be explained by the higher utilities ascribed to the hematoma health state following autologous reconstruction and the heavier weighting of these studies due to the greater number of individuals surveyed for utility generation. Only 3 studies reported utility values for explantation or capsular contracture health states.

Table 2.5 Pooled Health State Utility Values

Health State	Mean Utility[a]	SD[a]	N[b]	References[c]
Successful Breast Reconstruction	0.73	0.07	15	(21,22,30,31,33,34,40,42)
Implant-Based Breast Reconstruction	0.70	0.02	8	(22,30,31,34,40)
Autologous Breast Reconstruction	0.79	0.09	6	(21,22,33,40,42)
Total Flap Loss	0.55	0.07	6	(21,22,33,42)
Partial Flap Necrosis	0.72	0.02	8	(21,22,33,42)
Mastectomy Skin Necrosis	0.68	0.04	5	(21,30,31,42)
Hematoma	0.73	0.07	9	(21,30,31,33,34,42)
Infection	0.67	0.09	9	(21,22,30,31,34,42)
Explantation	0.613	0.04	3	(30,31)
Capsular Contracture Grade III/IV	0.59	0.01	4	(30,34)
Revision	0.62	0.01	2	(34)
Nipple Deformity	0.89	N/A	3	(24)
Mastectomy Alone	0.60	0.04	2	(22,40)

[a] Weighted mean and SD, [b] Number of observations, [c] discrepancies between number of observations and number of references is due to some citations reporting utilities for multiple reconstructive techniques

2.3.6. Methodological Quality

Overall, none of the studies met all of the requirements for the NICE reference case. Only two studies surveyed the patient population for health status assessment. Both of these used the BREAST-Q which is a validated condition-specific instrument.(37,40) However, at the time of the analysis, the BREAST-Q did not have preference weighting available so an average of the domain scores was used.(37,40) Neither of these studies report demographic information for the respondents of the BREAST-Q so it is not possible to know if the population sampled is representative of the population modelled. Likewise, response rates and attrition are not reported. The CHEERS guidelines recommend mapping for non-preference weighted instruments.(19) This was not performed in either of the aforementioned cost-utility analyses. Further, the method by which the authors generated utilities for specific health states based on the temporal association to survey completion is unclear.

The remainder of the studies that generated unique utility values solicited expert opinion using direct elicitation methods. This methodology is not recommended by either the NICE guidelines or the CHEERs guidelines.

2.3.7. Heterogeneity

None of the articles reported confidence intervals for the health state utility values so neither a formal meta-analysis nor a quantitative assessment of heterogeneity could be performed.

2.4. Discussion

Cost-utility analyses have an increasingly important role in resource planning given the anticipated increased demand for health care services required by an aging population.(44) To conduct high-quality analyses, the estimates of health state utility values must reflect the perceptions of society at large.(45) In the breast reconstruction literature, a number of CUAs have been conducted. These have used health state utility values from a variety of sources. This systematic review attempted to catalogue the methods of developing or choosing HSUVs in breast reconstruction-related CUAs and aggregate published values into pooled estimates.

The results of this systematic review show that 50% of CUAs in breast reconstruction select utility values previously reported in the literature, whether from single sources or published meta-analyses. The remainder generated utility values independently, the majority through direct elicitation surveys of physicians with only two studies obtaining utility values by direct patient survey. There is considerable debate over the best group to survey in health state utility value generation.(9,46) Proponents of patient valuation of health states argue that patients know their own health and disease status best. However, reported values may be higher due to the tendency of patients to adapt to their existing health state over time. This may result in smaller than expected improvements in quality of life with new interventions.(9) Others advocate for health status assessment by the general population since economic analyses are meant to reflect values held by individuals from diverse perspectives to be representative of a broader, societal perspective.(47) Population-derived utilities are preferred for economic evaluations designed to inform public policy decision-making since these utilities may be more

representative of values held by the general population.

While use of generic health status measures is recommended in cost-utility analyses, none of the included studies used such a measure, favouring instead direct-elicitation techniques. Although there are many published studies that use generic health status measures, these are limited by poor sensitivity to changes in health status in the post-surgical breast reconstruction population. In breast surgery, and breast reconstruction in particular, many of the generic patient outcome measures are not sensitive to changes in quality of life associated with early and late post-operative health states.(48) As such, other scales have been developed to evaluate quality of life in these situations, such as the BREAST-Q and the BRECON-31.(43,49) However, these measures do not yet have preference-weighting and, therefore, are limited in their use with respect to utility generation.

The majority of cost-utility analyses included in the quantitative analysis used direct elicitation techniques, typically administered to medical experts. Although 3 studies did report using time trade-off to generate utilities, 7 studies reported using visual analogue scales for utility generation. Visual analogue scale is advantageous in that it is easy to administer and understand. However, it is limited by multiple sources of bias and has poor grounding in economic theory.(8,10) Recognition of these limitations is important when borrowing values from the literature for utility estimates.

This systematic review has several strengths. It provides a summary of published cost-utility analyses in breast reconstruction with an emphasis on the method of utility

generation. In addition, the quantitative analysis summarizes the published utilities as weighted averages which can be used in future cost-utility analyses. Unfortunately, the available studies included in the systematic review did not publish confidence intervals for utility values. Therefore, a formal meta-analysis and quantitative assessment of heterogeneity could not be performed. However, possible sources of heterogeneity among reported utility values include variability in definition of health states, duration of health states and method of health status assessment (i.e., direct versus indirect elicitation, generic or diseases specific measures, preference-weighted or non-preference weighted measures). Despite these limitations, this review contextualizes the existing literature on economic analyses in breast reconstruction and highlights discrepancies between commonly used methods for health status assessment and existing guidelines.

2.5. Conclusions

Utility values in breast reconstruction are variable and affected by surgical technique and post-operative outcomes. The most commonly used methods of health status assessment in the breast reconstruction literature are the VAS and TTO. This analysis can serve as a reference for utilities and health states for future CUAs in breast reconstruction.

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3. Chapter 3: A Cost-Utility Analysis of Saline and Silicone Implants in Breast Reconstruction

Overview

This chapter outlines considerations and parameters in designing cost-utility-analyses. A cost-utility analysis examining saline and silicone implants in the context of immediate, unilateral, implant-based breast reconstruction is described. Results demonstrate silicone implants to be cost-effective despite higher baseline costs. This analysis supports ongoing funding of silicone implants due to associated quality of life improvements.[6]

3.1. Introduction

Breast reconstruction is a recognized component of the breast cancer treatment pathway. As breast cancer mortality has decreased, management has increasingly focused on interventions that result in improved quality of life in the survivorship period. There are many approaches and adjuncts to breast reconstruction with diverse cost and complication profiles.

In the context of breast reconstruction, adjuncts such as the use of CT angiography and acellular dermal matrix have been demonstrated to be cost-effective in the American health care system.(1,2) However, there remain a number of other parameters that are unaccounted for in the existing cost-effectiveness literature. For instance, implant options

[6]A portion of the work covered in Chapters 1 and 2 is included here as part of the Integrated Article Format.

are highly heterogeneous in terms of both cost and outcome profiles. One cross-sectional survey of patients undergoing breast reconstruction showed higher quality of life among patients who received silicone implants as compared to saline implants.(3) However, saline implants can offer a significant cost savings. Further, rates of complications such as capsular contracture and implant rupture may result in downstream costs to the patient and health care system. These variations are not accounted for in the existing cost-effectiveness literature; thus, it is important to delineate which is truly the cost-effective option.

Cost-utility analysis facilitates integration of these outcomes, describing costs in monetary units and outcomes in terms of health-related quality of life. This form of economic analysis provides useful insights into efficient allocation of limited healthcare resources. Although there are many factors that influence health-care spending decisions including disease burden, social consensus, inequality and rule of rescue (i.e. perceived duty to save lives in danger), cost-effectiveness analysis can be used to identify effective treatments within resource constraints. (4)

Constructing a cost-effectiveness analysis requires identification of costs and effects for all relevant stakeholders. To develop such a model, perspective (i.e., relevant stakeholders) must be considered in addition to health states and associated probabilities, utilities and costs.

3.1.1. Considerations in Designing Cost-Utility Analyses

3.1.1.1. Perspective

The perspective of the cost-utility analysis determines which costs and outcomes should be included. Decision-makers in health care include patients, clinics, hospitals, insurers and public funders of health care. The societal perspective examines all costs and outcomes relevant to society at large.(5) In practice, this can be challenging to measure as documentation of patient costs requires patient enrollment and logging of incurred costs. In the plastic surgery literature, the perspective of the hospital or third-party payer is commonly adopted as these organizations bear the majority of costs relating to surgical procedures. This is consistent with the recommendations from the Second Panel on Cost-Effectiveness in Health and Medicine which recommends the health care perspective as the reference case.(6)

3.1.1.2. Health States, Probabilities and Utilities

Individual states of health are termed “health states.” These include individual well and unwell conditions that collectively comprise a person’s health status. Health states include concrete health outcomes, such as death, as well as more nuanced improvements or deteriorations such as recovery of extremity function, ability to walk or chronic pain.(7) In breast reconstruction, health states are related to technique and outcome. For instance, abdominal morbidity can be associated with the use of abdominal-based flaps while capsular contracture can occur after implant insertion. To determine the net cost-effectiveness of different types of implants in breast reconstruction, all relevant health states must be identified in addition to the associated probabilities, costs and quality of life of each health state.

3.1.1.3. Costs

There are varying levels of precision in estimating costs incurred by hospitals (Table 3.1). Types of costs can be broken down into direct and indirect costs. Direct costs include costs related to patient care (e.g., nursing, medications, investigations, etc.). Indirect costs are those not directly related to patient care but that are nonetheless required to support the patient, hospital, organization (e.g., health records, administration, maintenance, patient out-of-pocket costs etc.). Costs can be calculated through multiple approaches. The most accurate method of costing is micro-costing which accounts for all resources used (e.g., medications, laboratory tests, length of stay in a particular ward, etc.).(8) Unfortunately, it is challenging to do this outside of a prospective clinical study whereby costs incurred can be tracked reliably. Average daily costs are the least accurate in which total cost to the hospital per day is averaged over all categories of patients.(8) This method does not allow for differentiation between patients that use more services than others, such as patients in an intensive care unit as compared to those on low-acuity wards. Other approaches include calculating average costs for case-mix groups, disease-specific per diem costs and generic per diem costs. These are ultimately influenced by how specifically cases and diseases are defined (e.g., patients undergoing mastectomy with immediate reconstruction versus patients undergoing oncologic surgery in general).

Table 3.1 Costing Methods

Method	Description
Micro-costing	All resources used are estimated and the costs for each are summed.
Case-mix costing	Patients are divided into clinically-meaningful groups based on type of case and length of stay.
Per diem costing	Total resource use and expenditure are divided by number of days of service provided to generate average daily cost.

3.1.2. Rationale and Hypothesis

Given the increasing rate of implant-based reconstruction it is essential to delineate the cost-effectiveness of alternative implant-based treatments. The cost-effectiveness of different implant types has not yet been analyzed; however, saline and silicone implants vary in complication rates, costs and associated quality of life. This study examined the cost-utility of saline and silicone implants in the context of immediate, unilateral, implant-based breast reconstruction.

3.2. Methods

3.2.1. Perspective

The perspective of a third-party payer was adopted for this analysis, specifically the Ontario Ministry of Health and Long-Term Care (MOHLTC). Relevant costs included operating room expenses, clinic costs and physician costs. Home care costs were not accounted for in this analysis. It was not possible to obtain the cost to the patient in terms of productivity losses and out-of-pocket expenses since secondary data were used for this analysis. As a result, a societal perspective was not considered.

3.2.2. Population

The population was assumed to be women with stage I or II breast cancer seeking unilateral mastectomy with implant-based reconstruction in the immediate setting. The age of the cohort was assumed to be 52.5 years based on average age at diagnosis of breast cancer in Canada.(9) Life-expectancy was assumed to be 83.9 years, derived from Canadian census data, since life-expectancy of stage I and II breast cancer survivors approaches that of age-matched controls.(10,11)

3.2.3. Time Horizon

The time horizon for the analysis was assumed to be 31.4 years based on difference between life-expectancy and age at diagnosis.

3.2.4. Health States

A review of the surgical literature was conducted to identify relevant complications associated with implant type following implant-based breast reconstruction. These complications included capsular contracture, implant rupture, unplanned revision and explantation. Complications related to implant use but unrelated to implant filler type (e.g., breast-implant associated anaplastic large cell lymphoma, hematoma, etc.) were not included. The complications were defined as distinct health states (Table 3.2) with associated probabilities, costs and utilities. Assumptions regarding duration of health states and treatment course were based on institutional practice patterns.

Table 3.2 Health State Descriptions

Health State	Description and Assumptions
Successful Surgery	Initial pre-surgical consultation with plastic surgeon, followed by outpatient surgery. Surgery assumed to be 2.5 h duration. Patient returns for follow-up visit at 1 week, 2 weeks, 6 weeks and 6 months.
Capsular Contracture Grade III/IV	Patient develops significant capsular contracture requiring surgical capsulotomy as outpatient. Patient keeps original implants. In addition to costs of successful surgery, patient requires repeat clinic visit to discuss problem prior to surgical intervention. Surgery assumed to be 2 h duration. Patient returns for follow-up visit at 2 weeks, 6 weeks and 6 months. Duration of health state assumed to be 1 year followed by a return to successful surgery health state.
Explantation	Patient develops problem requiring or preferring implant removal without replacement. In addition to costs of successful surgery, patient requires repeat clinic visit to discuss problem prior to surgical intervention. Surgery assumed to be 1 h duration as outpatient. Patient returns for follow-up visit at 2 weeks, 6 weeks and 6 months. Duration of health state assumed to be 1 year followed by return to mastectomy defect health state.
Unplanned Revision	Patient develops clinical problem related to implant-based reconstruction. In addition to costs of successful surgery, patient requires repeat clinic visit to discuss problem prior to surgical intervention. Surgery assumed to be 2 h duration as outpatient. Patient returns for follow-up visit at 2 weeks, 6 weeks and 6 months. Duration of health state assumed to be 1 year followed by return to successful surgery health state.
Saline Implant Rupture	Patient develops clinically evident deflation seeking implant replacement. In addition to costs of successful surgery, patient requires repeat clinic visit to discuss problem prior to surgical intervention. Surgery assumed to be 2 h duration as outpatient. Patient returns for follow-up visit at 2 weeks, 6 weeks and 6 months. Duration of health state assumed to be 1 year followed by return to successful surgery health state.
Silicone Implant Rupture	Concern for rupture triggers presentation to plastic surgeon. Workup includes MRI followed by surgery for implant exchange. In addition to costs of successful surgery, patient requires repeat clinic visit to discuss problem prior to surgical intervention. Surgery assumed to be 2.5 h duration as outpatient. Patient returns for follow-up visit at 2 weeks, 6 weeks and 6 months. Duration of health state assumed to be 1 year followed by return to successful surgery health state.

3.2.5. Costs

The costs for implant-based reconstruction were based on values obtained from the Case-Costing Centre at St. Joseph's Health Care (SJHC) London. SJHC is a predominantly ambulatory care hospital with outpatient surgical facilities and an inpatient surgical ward. The Surgical Case Costing Centre at SJHC performs micro-costing for surgical procedures that are designated as Quality-Based Procedures by the Ontario MOHLTC. Quality-Based Procedures reflect clusters of clinically-related patients, diagnoses and

treatments that are used to direct improvements in health services and can be refined based on Canadian Classification of Health Intervention (CCI) codes.(12) Breast cancer surgeries, including both ablation and reconstruction, have been identified as Quality-Based Procedures since 2016.(13) CCI codes were used to identify relevant procedures (Table 3.3) The cost estimates from the Case Costing Centre include all direct and indirect costs incurred during day surgery except physician costs. This includes operating room supplies, nursing, administrative overhead, pharmaceuticals, imaging and laboratory investigations for operating room supplies including implants, and acellular dermal matrix (Appendix 2). Overhead and operating room labour is estimated based on staffing and converted into a cost per minute of operating room time. The average cost of relevant CCI codes was used as the base cost for complication health states. Billing codes under the "Schedule of Benefits: Physician Services Under the Health Insurance Act" were used to estimate physician costs (Table 3.4).(14)

Costs for implants were obtained from the Healthcare Materials Management Service (HMMS). HMMS works with both SJHC and London Health Sciences Centre (LHSC) to facilitate purchasing and inventory management through competitive bidding agreements. Costs for individual implant models are confidential and protected under the competitive bidding agreements so average prices of saline and silicone implants were used (Appendix 3).

Costs for breast MRIs were obtained from the institutional radiology department. Breast MRI procedural costs, including supplies, technologists and storage, are $130 per exam. The cost of the MRI machine is approximately $2.5 million which is depreciated over 7

years at SJHC. Costs for radiologist reads of an MRI were obtained from the "Schedule of Benefits". All costs were reported in 2017 Canadian Dollars (Appendix 4, Appendix 5).

Table 3.3 CCI Codes for Implant-Based Breast Reconstruction

CCI Code	Description
1YM90LAPM	Excision total with reconstruction, breast simple mastectomy with no node dissection without tissue with implantation of breast prosthesis
1YM90LAPME	Excision total with reconstruction, breast simple mastectomy with no node dissection using local flap with implantation of breast prosthesis
1YM90LAPMK	Excision total with reconstruction, breast using homograft with implantation of breast prosthesis
1YM90LAQF	Excision total with reconstruction, breast simple mastectomy with no node dissection without tissue with implantation of prosthesis and expander
1YM90LAQFE	Excision total with reconstruction, breast simple mastectomy with no node dissection using local flap with implantation of prosthesis and expander
1YM90LATP	Excision total with reconstruction, breast simple mastectomy with no node dissection without tissue with implantation of tissue expander
1YM90LATPE	Excision total with reconstruction, breast using local flap with implantation of tissue expander
1YM90LATPK	Excision total with reconstruction, breast using homograft with implantation of tissue expander
1YM92LAPME	Excision radical with reconstruction, breast modified or NOS using local flap with implantation of breast prosthesis
1YM92LAPMK	Excision radical with reconstruction, breast modified or NOS using homograft with implantation of.breast prosthesis
1YM92LAQFE	Excision radical with reconstruction, breast modified or NOS using local flap with implantation of prosthesis and expander
1YM92LATPE	Excision radical with reconstruction, breast modified or NOS using local flap with implantation of tissue expander
1YM92LATPK	Excision radical with reconstruction, breast modified or NOS using homograft with implantation of tissue expander
1YM92TRPME	Excision radical with reconstruction, breast extended [Urban] using local flap with implantation of breast prosthesis
1YM92TRPMK	Excision radical with reconstruction, breast extended.[Urban] using homograft with implantation of breast prosthesis
1YM92TRQFE	Excision radical with reconstruction, breast extended [Urban] using local flap with implantation of prosthesis and expander
1YM92TRTPE	Excision radical with reconstruction, breast extended [Urban] using local flap with implantation of tissue expander
1YM92TRTPK	Excision radical with reconstruction, breast extended.[Urban] using homograft with implantation of tissue expander
1YM92WPPME	Excision radical with reconstruction, breast super [Wangensteen] using local flap with implantation of breast prosthesis
1YM92WPPMK	Excision radical with reconstruction, breast super [Wangensteen] using homograft with implantation of breast prosthesis
1YM92WPQFE	Excision radical with reconstruction, breast super [Wangensteen] using local flap with implantation of prosthesis and expander
1YM92WPTPE	Excision radical with reconstruction, breast super [Wangensteen] using local flap with implantation of tissue expander

1YM92WPTPK	Excision radical with reconstruction, breast super [Wangensteen] using homograft with implantation of tissue expander
1YM90LAPM	Excision total with reconstruction, breast simple mastectomy with no node dissection without tissue with implantation of breast prosthesis
1YM91LAXXQ	Excision radical, breast using combined sources of tissue [e.g., local flap and tissue expander] modified or NOS
1YM91LAPM	Excision radical, breast with implantation of breast prosthesis modified or NOS
1YM91LATP	Excision (modified) radical, breast with implantation of tissue expander
1YM88LAPM	Excision partial with reconstruction, breast without tissue with implantation of prosthesis
1YM88LAPME	Excision partial with reconstruction, breast with local flap with implantation of prosthesis
1YM88LAPMK	Excision partial with reconstruction, breast using homograft with implantation of prosthesis
1YM88LAQF	Excision partial with reconstruction, breast without tissue with implantation of prosthesis and expander
1YM88LAQFE	Excision partial with reconstruction, breast with local flap with implantation of prosthesis and expander
1YM88LATP	Excision partial with reconstruction, breast without tissue with implantation of tissue expander
1YM88LATPE	Excision partial with reconstruction, breast with local flap with tissue expander
1YM88LATPK	Excision partial with reconstruction, breast using homograft with implantation of tissue expander

Table 3.4 OHIP Billing Codes for Implant-Based Breast Reconstruction and Related Procedures

Code	Description
R119	Breast mound creation by prosthesis as sole procedure
R114	Revision of breast mound
Z135	Open capsulotomy with or without replacement of breast prosthesis
Z142	Removal of breast prosthesis
Z182	Breast capsulectomy
A085	Consultation
A935	Special surgical consultation
A086	Repeat consultation
A083	Specific assessment
A084	Partial assessment
X446	Breast MRI unilateral or bilateral multi-slice sequence

3.2.6. Probabilities

The probabilities associated with clinically relevant health states for implant-based breast reconstruction with saline and silicone implants were obtained from a review of the literature. An electronic search of English-language articles published prior to November 2017 was conducted. The search strategy was developed with assistance from a librarian familiar with systematic reviews. The search strategy included terms relevant to implant-based breast reconstruction (Table 3.5). Results were screened for articles that examined saline versus silicone implants in the context of implant-based reconstruction and reported post-operative outcomes (Table 3.6). Citations were screened in two-stages. The first stage involved a review of title and abstract. Articles that met inclusion criteria or for which a determination could not be made were reviewed in the second stage in full text. Parameter estimates were extracted from relevant articles and weighted averages were calculated as appropriate.

Table 3.5 Search Strategy

No.	Search
1	Breast Implantation/ or Breast Implants/ or (breast$ and (implant$ or prosthes$)).mp. (13358)
2	exp *Breast/su and exp *"Prostheses and Implants"/ (846)
3	or/1-2 (13374)
4	follow-up studies.sh. or (follow-up or followup or follow$).mp. (3502738)
5	3 and 4 (4030)
6	Reoperation/ or (revision$ or re-vision$ or (repeat$ adj3 surg$) or re-operat$ or reoperat$ or re-construct$ or reconstruct$ or mastectom$ or mammectom$).mp. or exp prosthesis failure/ or prosthesis-related infections/ or Implant Capsular Contracture/ or contracture$.mp. or exp treatment outcome/ or complication$.mp. or outcome$.tw. or (ae or co).fs. or incidence.sh. or incidence$.tw. or infect$.tw. (7255071)
7	Comparative Study/ or (vs$1 or vs or versus or compar$).tw. or ((silicone$ or textured$ or round) and saline$).tw. or ((augmentation$ and ((revision$ or re-vision$) adj3 augmentation$)) or ((re-construct$ or reconstruct$) and ((revision$ or re-vision$) adj3 reconstruct$))).tw. or (different$ adj2 types$).tw. or (two adj2 different$).tw. or ((textured or rough) and smooth$).tw. (6570586)
8	3 and 4 and 6 and 7 (1351)
9	*Breast Implantation/ or *Breast Implants/ or (breast$.tw. and (implant$ or prosthes$).ti.) (6140)
10	(re-construct$ or reconstruct$ or mastectom$ or mammectom$).tw. (282471)
11	7 and 9 and 10 (774)
12	8 or 11 (1685)
13	limit 12 to english language (1582)
14	13 not (exp Animals/ not (Human/ and exp Animals/)) (1537)
15	meta analysis.mp
16	14 and 15 (80)
17	limit 14 to "review articles" (121)
18	14 not 17 (1416)
19	16 or 18 (1475)
20	case report.ti. (213628)
21	19 not 20 (1467)

Table 3.6 Systematic Review Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
Population • implant-based breast reconstruction for therapeutic or prophylactic mastectomy) Design • RCT, retrospective or prospective cohort study, observational study • exposure: comparisons of saline versus silicone implants • outcomes: postoperative complications (immediate and delayed)	Population • autologous reconstruction • reconstruction for non-oncologic entities (e.g., congenital/traumatic breast anomalies) Design • conference abstract • non-English language articles • case reports • letters • commentaries • non-systematic reviews • laboratory (animal or in vitro) studies

The systematic review yielded 2185 records. The 1267 records which remained after duplicates were removed were screened by title and abstract. Of these, 23 records were reviewed in full text (Figure 3.1). There was a paucity of studies directly comparing saline versus silicone implants in implant-based breast reconstruction. Due to heterogeneity in study design and reported outcomes, none of the studies reported data useful for meta-analysis. Overall, there were a large number of retrospective and prospective non-randomized studies examining saline and silicone implants. However, few undertook direct comparisons between saline and silicone implants. At present, the best prospective data for saline and silicone implants comes from the post-market approval analyses of saline implants and silicone implant Core studies.(15–18) The silicone implant Core studies examined the fourth and fifth generation silicone implants most commonly used today. Ultimately, parameter estimates for this analysis were extracted from relevant Core studies and post-market approval data.

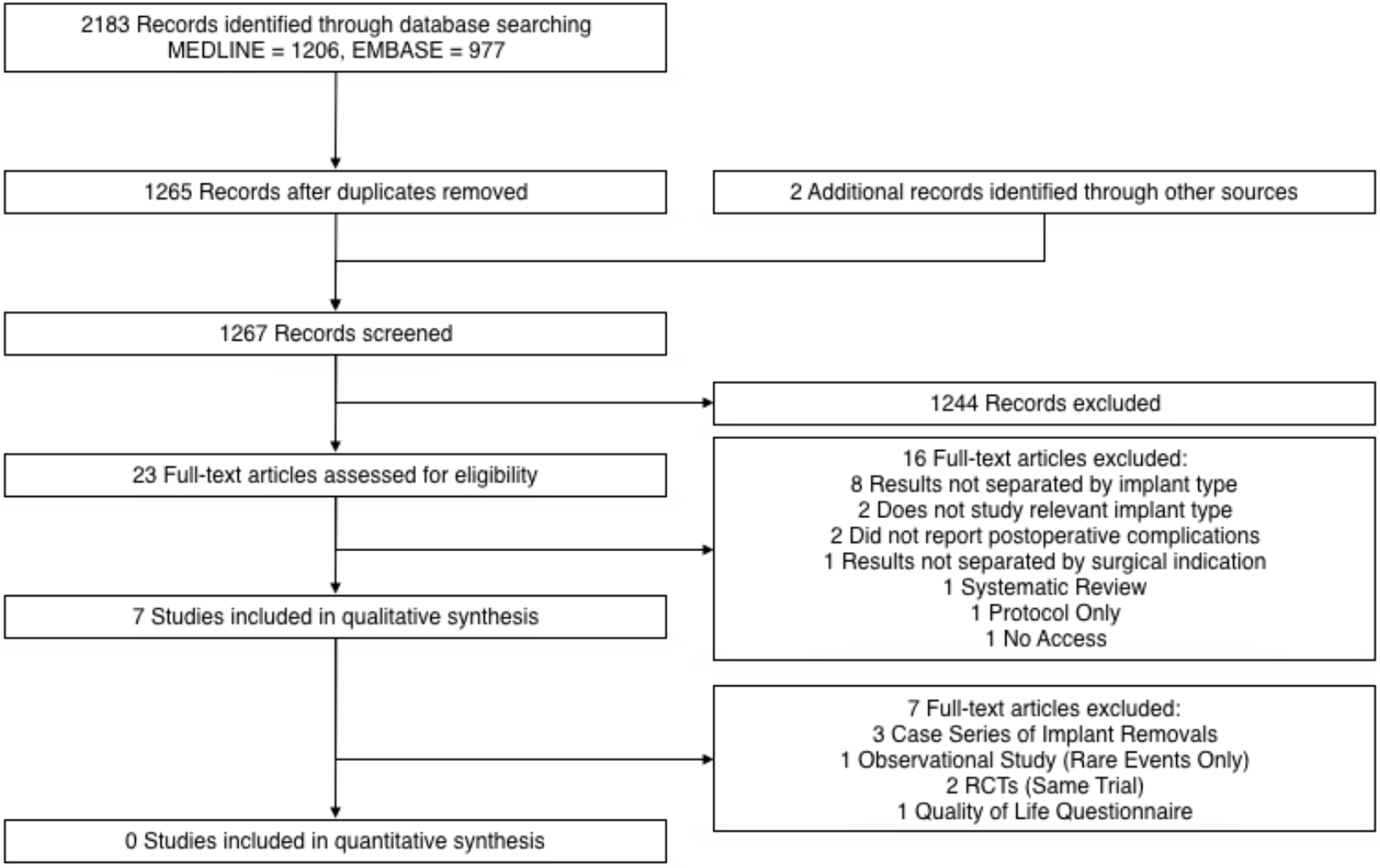

Figure 3.1 PRISMA Search Strategy Flow Diagram Probability Estimates

3.2.7. Utilities

Utility values for clinically relevant health states were derived from a systematic review of the literature (Chapter 2). An electronic search of English-language articles published prior to November 2017 was conducted. The search strategy was conducted with assistance from a librarian familiar with systematic reviews. The search strategy included terms relevant to implant-based breast reconstruction and economic analysis (Table 2.2). Articles which generated unique utility values and reported number of individuals surveyed were included in a quantitative synthesis in which pooled estimates were generated. Weighted averages and standard deviations were calculated with weights based on study size. Additional values were generated from published quality of life data as appropriate.(3)

Utilities were converted into quality adjusted life years by multiplying the utility by the duration of the health state and adding it to remaining life years multiplied by the utility of a successful surgery. The average age of women in the cohort was assumed to be 52.5 based on average age at diagnosis of breast cancer.(9) Life-expectancy was assumed to be 83.9 years, derived from Canadian census data since life-expectancy of stage I and II breast cancer survivors approaches that of age-matched controls.(10,11)

3.2.8. Analysis

A decision tree model was designed using TreeAge Pro 2017 © (Figure 3.1). Costs, QALYs and probabilities of each health state were incorporated into the model (Table 3.7). Expected values for costs and outcomes were derived by the roll-back method and summed to generate the expected cost and utility of breast reconstruction with saline or

silicone implants. Costs and utilities were discounted at a rate of 3 percent per year. Onset of complications was assumed to be 10 years based on follow-up data from silicone implant Core studies and post-market approval data for saline implants.(15–18) The incremental cost-utility ratio (ICUR) was calculated using the following formula:

$$ICUR = \frac{Expected\ cost\ of\ silicone\ implant - Expected\ cost\ of\ saline\ implant}{Expected\ QALY\ of\ silicone\ implant - Expected\ QALY\ of\ saline\ implant}$$

An intervention is considered cost-effective if the ICUR is less than the willingness-to-pay (WTP) threshold for an additional quality-adjusted life year. The willingness-to-pay threshold was set at $50,000/QALY, as a conservative boundary and to be consistent with current literature.(19)

One-way sensitivity analysis was performed to determine if the baseline decision analysis was robust by varying the complication rate of saline implants from 0 to 1 in increments of 0.02 and observing how this affected the ICUR. Other sensitivity analyses were conducted to examine different rates of capsular contracture, implant rupture and discounting rates.

Table 3.7 Health State Costs, Probabilities and Utilities

Health State	Cost SJHC ($)	Cost LHSC ($)	Probability (citation)	Range[1]	Utility[2] (citation)	Range	Duration (Years)	QALYs[3]
Silicone								
Successful Surgery	6988.12	5788.12	0.472 (15,16)	(0.285, 0.545)	0.77 (3)	(0.544, 0.933)	31.4	16.47
Complication States			0.528					
Capsular Contracture Grade III/IV	5946.71	4747.51	0.075 (15,16)	(0.092, 0.067)	0.59	(0.58, 0.6)	0.5	16.34
Explantation	5750.66	4551.46	0.136 (15)		0.61	(0.585, 0.655)	0.5	14.34
Unplanned Revision	5981.06	47.81.86	0.260 (15)		0.62	(0.61, 0.62)	0.5	16.36
Implant Rupture	6948.81	5675.46	0.057 (15,16)	(0.076, 0.049)	0.62[4]		0.5	16.36
Saline								
Successful Surgery	6765.52	5468.32	0.446 (17,18)	(0.44, 0.454)	0.72 (3)	(0.476, 0.923)	31.4	15.40
Complication States			0.554					
Capsular Contracture Grade III/IV	5946.71	4747.51	0.146 (17,18)	(0.127, 0.161)	0.59	(0.58, 0.6)	0.5	15.31
Explantation	5750.66	4781.86	0.079 (17)		0.61	(0.585, 0.655)	0.5	13.90
Unplanned Revision	5981.06	4551.46	0.226 (17)		0.62	(0.61, 0.62)	0.5	15.33
Implant Rupture	6461.71	5164.51	0.103 (17,18)	(0.099, 0.105)	0.61[5]		0.5	15.33

[1]Range refers to highest and lowest reported values for a probability or utility. [2]All utilities were generated from a systematic review of published utilities (Chapter 2, Table 2.5) except those for successful surgery which were generated from published BREAST-Q data.(3) [3]QALYs discounted at 3% per year. [4]Utility for implant rupture silicone adapted from unplanned revision since rupture is typically asymptomatic. [5]Utility for implant rupture saline adapted from explantation since deflation results in temporary explantation-like deformity

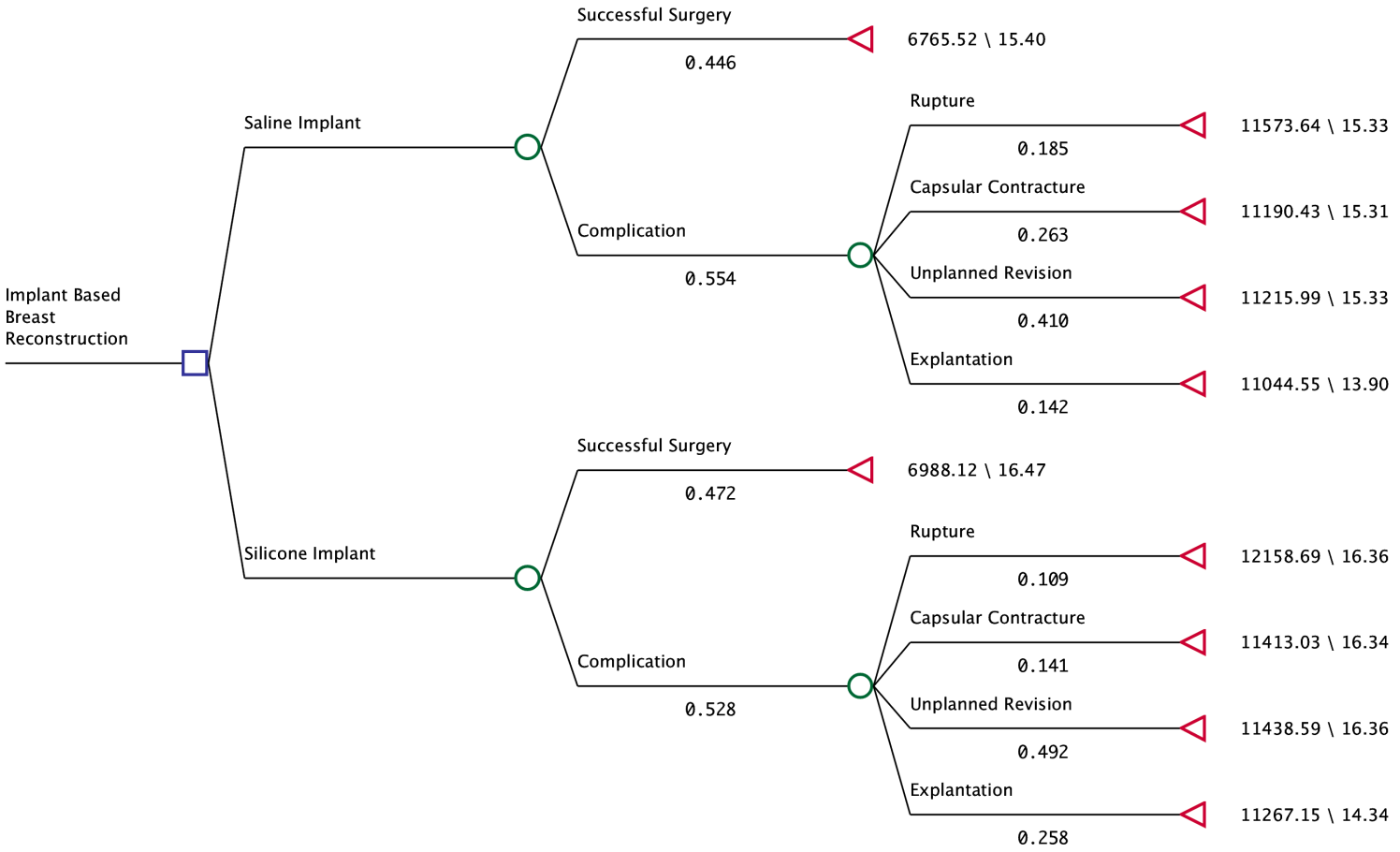

Figure 3.2 Decision model used in cost-utility analysis for saline versus silicone implants in breast reconstruction (SJHC Data). Probabilities displayed below branches. Costs and QALYs displayed to the right of terminal branches.

3.3. Results

The cost-utility analysis revealed an incremental cost increase of $103.63 associated with the use of silicone implants and a gain of 0.89 QALYs. The incremental cost-utility ratio was $116.51 per QALY for silicone implants (Table 3.8) . Overall, silicone implants are cost-effective as the ICUR was less than the WTP threshold. The analysis was also repeated with cost data from London Health Sciences Centre (LHSC) (Appendix 5, Appendix 6), a partner organization in HMMS. Despite a slightly lower base cost for saline implants at LHSC, silicone implants were still cost-effective within a WTP threshold of $50,000/QALY (Table 3.8). Sensitivity analyses were conducted with discounting rates of 1.5% and 5%. When discounted at a rate of 1.5%, the ICUR was $79.14.

Table 3.8 Results of Cost-Utility Analysis of Implant Type in Breast Reconstruction

Strategy	Cost ($)	Incremental Cost ($)	Effect (QALYs)	Incremental Effect (QALYs)	ICUR ($/QALY)
3% Discounting Rate					
SJHC					
Saline Implant	9250.52		15.25		
Silicone Implant	9354.15	103.63	16.14	0.89	116.51
LHSC					
Saline Implant	7451.51		15.25		
Silicone Implant	7679.83	228.33	16.14	0.89	256.71
1.5% Discounting Rate					
SJHC					
Saline Implant	9643.18		18.71		
Silicone Implant	9728.01	84.83	19.79	1.07	79.14
5% Discounting Rate					
SJHC					
Saline Implant	8815.77		11.99		
Silicone Implant	8940.21	124.44	12.70	0.72	173.74

One-way sensitivity analysis of SJHC data revealed that silicone implants were cost-effective at any complication rate associated with saline implants using a WTP threshold of $50,000/QALY. Saline implants became more costly and less effective than silicone implants at a complication rate of 0.58. (Figure 3.3). The sensitivity analysis was repeated for the LHSC data with similar results. Saline implants were more costly and less effective than silicone implants at a complication rate of 0.62 (Figure 3.4). One-way sensitivity analysis varying the probability of saline implant rupture demonstrated that silicone implants were cost-effective at any rate of saline implant rupture (SJHC Data). Silicone implants were more effective and less costly when the probability of saline implant rupture reached 0.66 (Figure 3.5). One-way sensitivity analysis was also performed varying the probability of saline implant capsular contracture. This demonstrated that silicone implants were cost-effective at any probability of saline capsular contracture within the $50,000/QALY WTP threshold (Figure 3.6). However, with increasing probability of capsular contracture, the ICUR for silicone implants increased. This was because capsular contracture was a less costly health state compared to two of the remaining complication health states (i.e., implant rupture and unplanned revision). This sensitivity analysis was repeated varying the rate of silicone implant capsular contracture. With increasing probability of capsular contracture, the ICUR for silicone implants decreased consistent with the capsular contracture health state being less costly than the remaining complication health states as described above. Silicone implants were cost-effective at any rate of capsular contracture within a WTP threshold of $50,000/QALY (Figure 3.7).

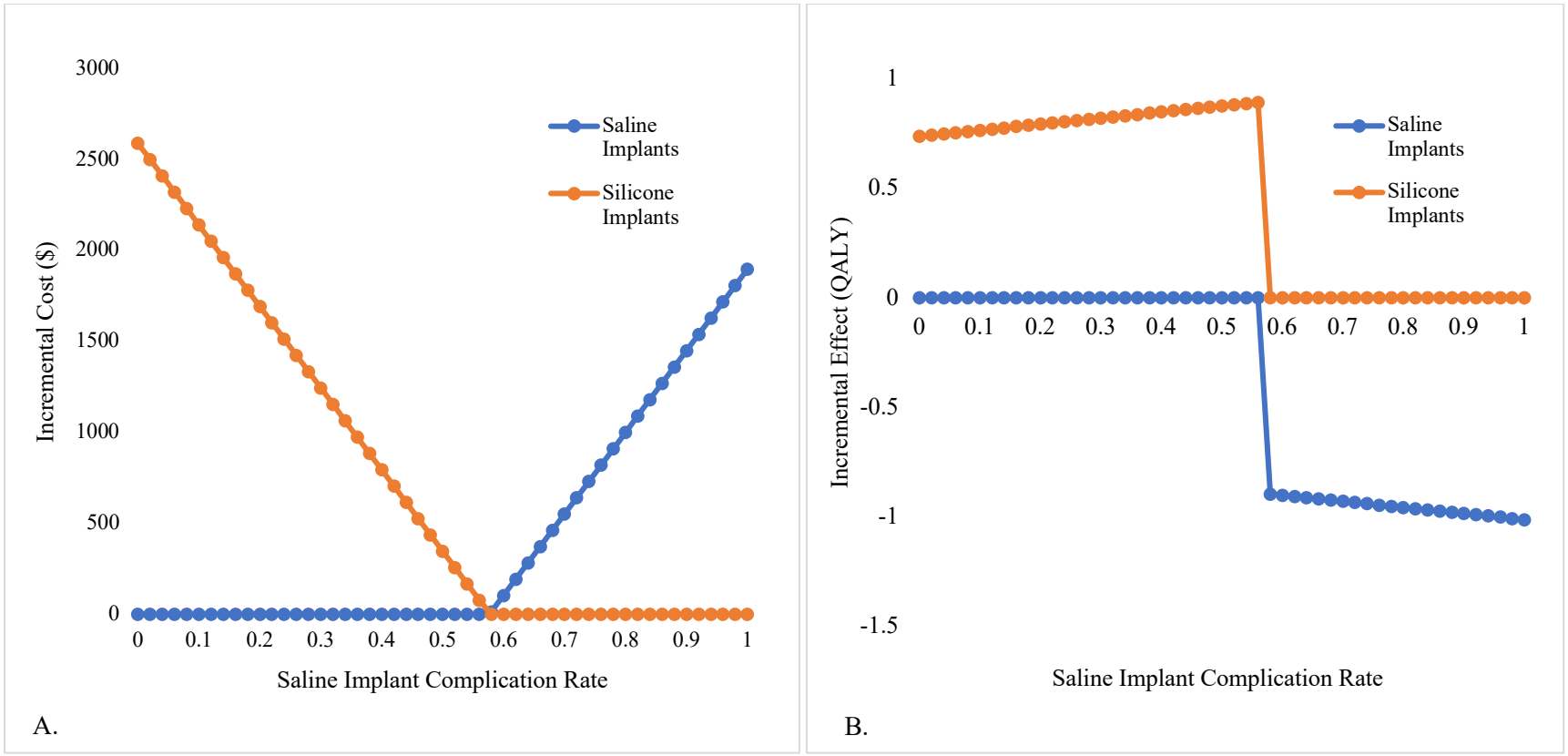

Figure 3.3 One-way sensitivity analysis varying complication rate of saline implants (SJHC Data).
A. Incremental cost of saline and saline implants as a function of saline implant complication rate. B. Incremental effect of saline and silicone implants as a function of saline implant complication rate. Up to a saline implant complication rate of 0.58 it is more effective but also more costly to use silicone implants. After this it is cheaper and more effective to use silicone implants.

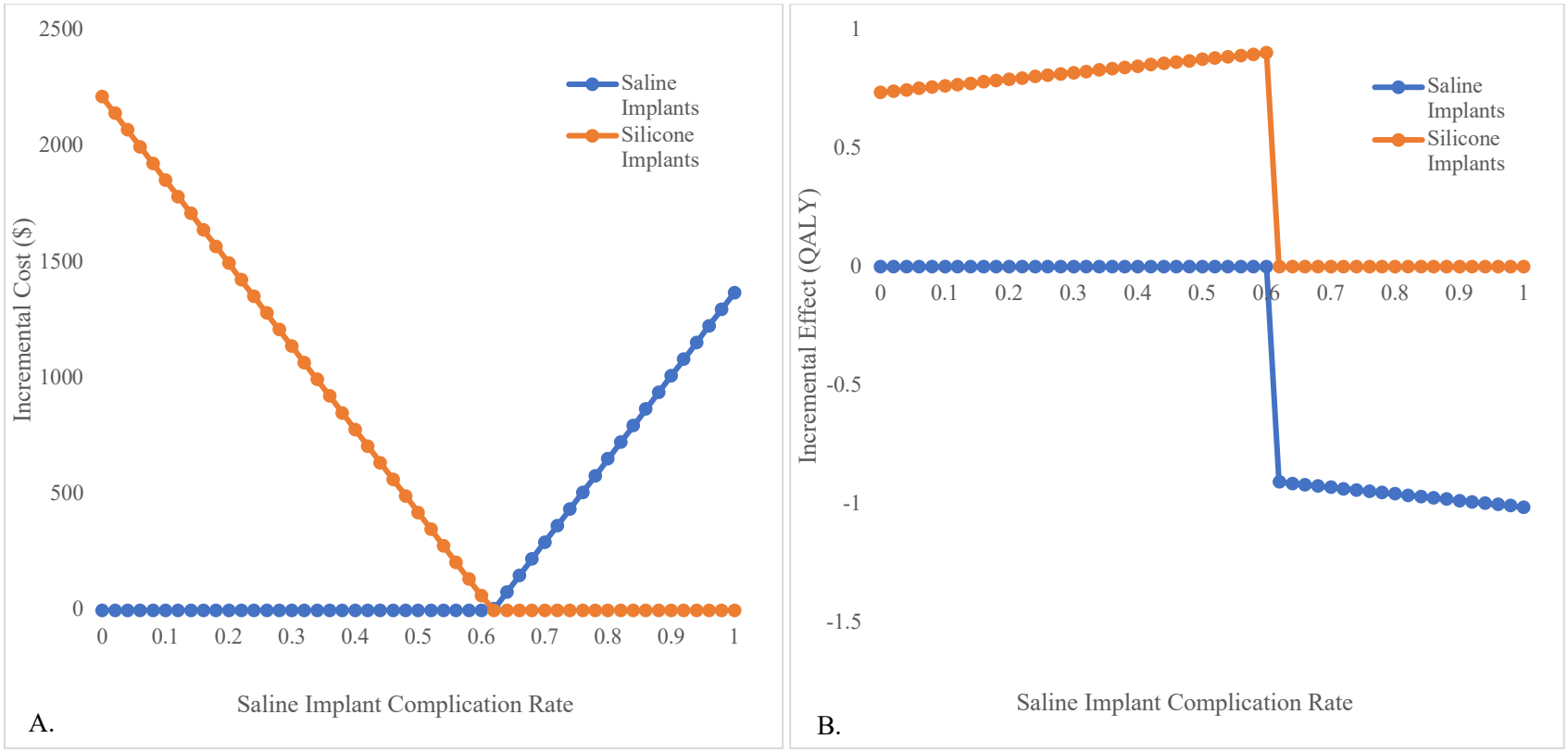

Figure 3.4 One-way sensitivity analysis varying complication rate of saline implants (LHSC Data).
A. Incremental cost of saline and saline implants as a function of saline implant complication rate. B. Incremental effect of saline and silicone implants as a function of saline implant complication rate. Up to a saline implant complication rate of 0.62 it is more effective but also more costly to use silicone implants. After this it is cheaper and more effective to use silicone implants.

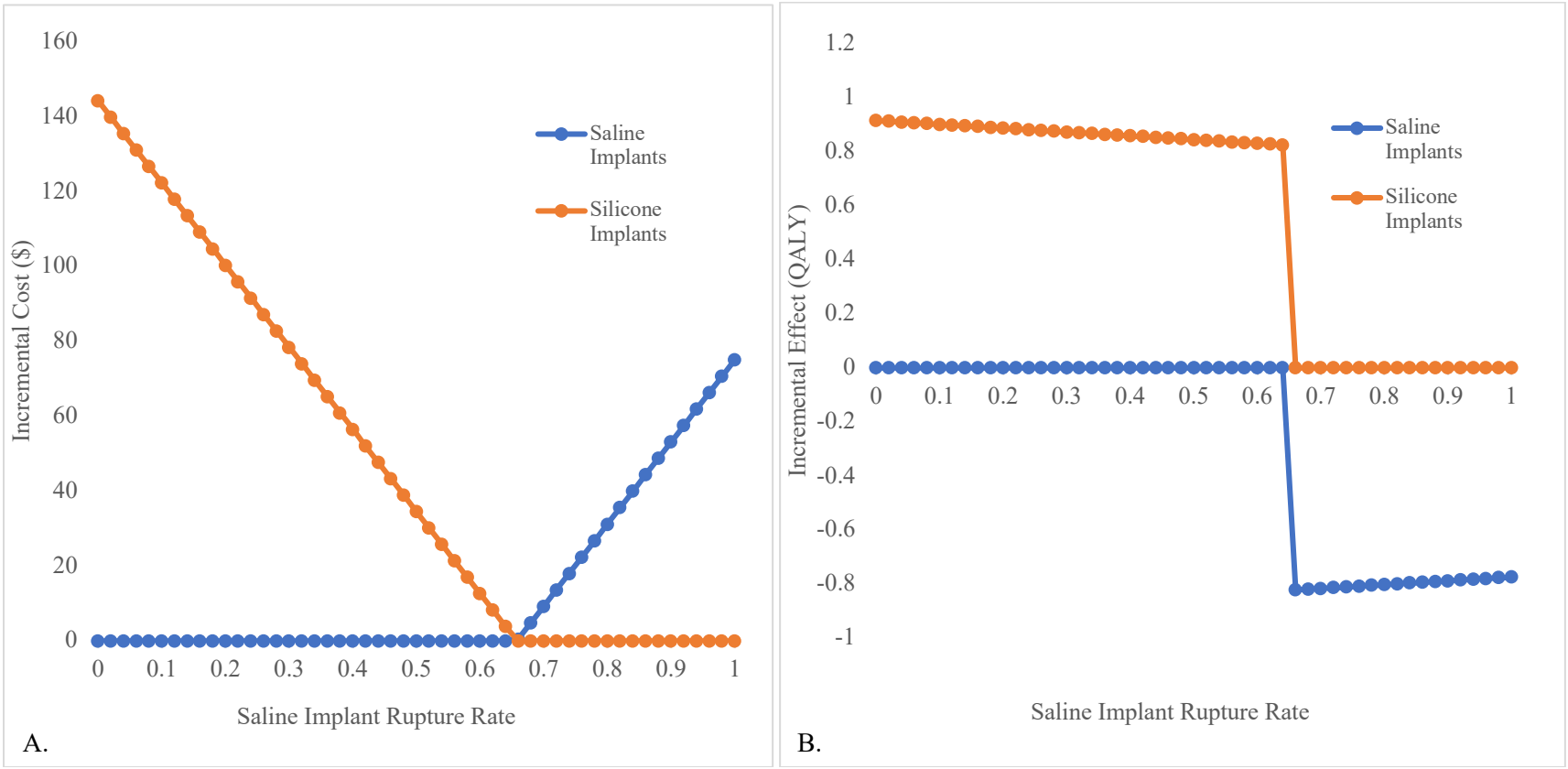

Figure 3.5 One-way sensitivity analysis varying probability saline implant rupture (SJHC Data).
A. Incremental cost of saline and saline implants as a function of saline implant rupture rate. B. Incremental effect of saline and silicone implants as a function of saline implant rupture rate. Up to a saline implant rupture rate of 0.66 it is more effective but also more costly to use silicone implants. After this it is cheaper and more effective to use silicone implants.

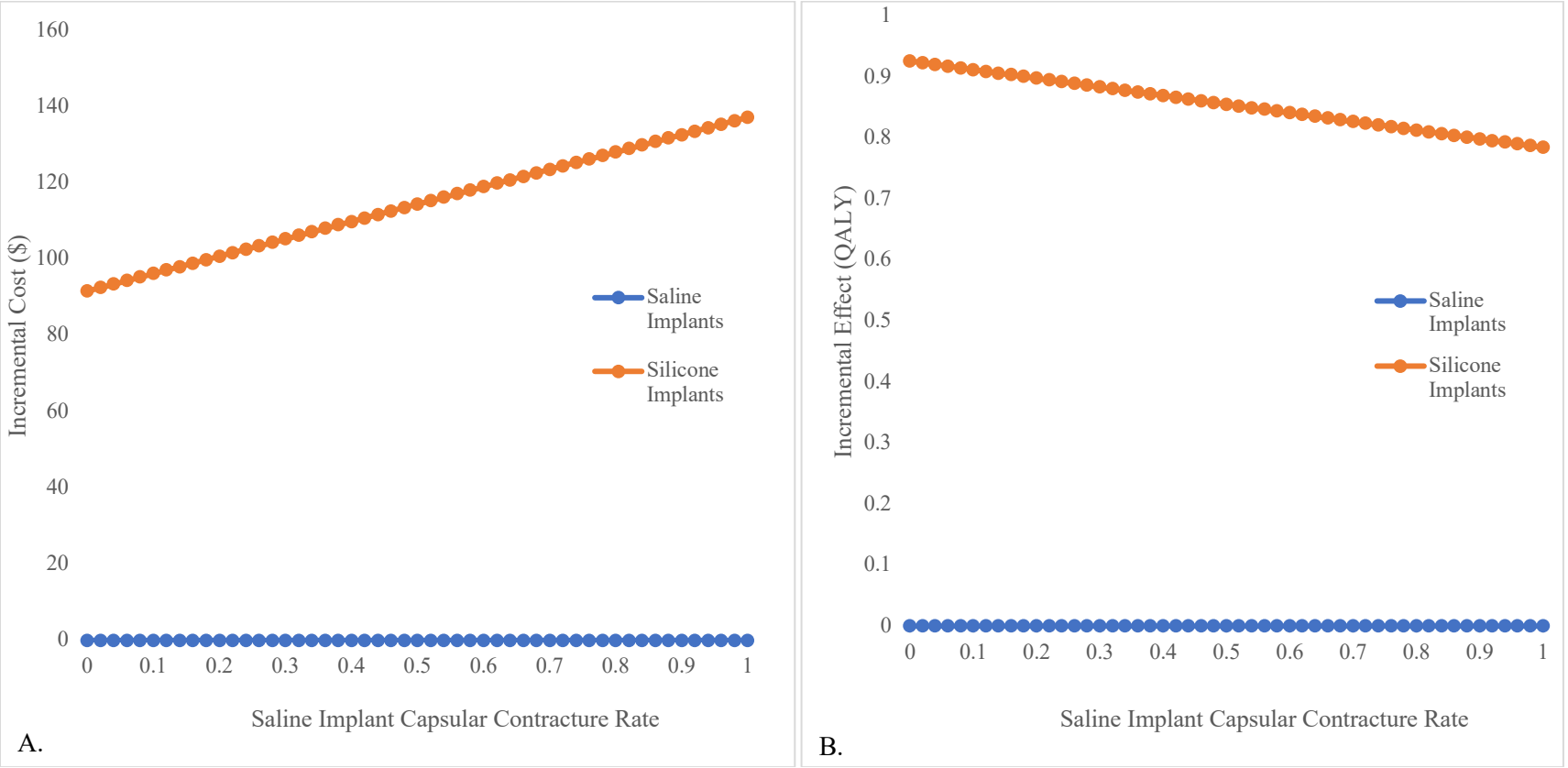

Figure 3.6 One-way sensitivity analysis varying probability of saline implant capsular contracture (SJHC Data).
A. Incremental cost of saline and saline implants as a function of saline implant capsular contracture rate. B. Incremental effect of saline and silicone implants as a function of saline implant capsular contracture rate. As saline implant capsular contracture rate increases the incremental cost of silicone implants increases and incremental effect decreases. This was because capsular contracture was a less costly health state compared to two of the remaining complication health states (i.e., implant rupture and unplanned revision).

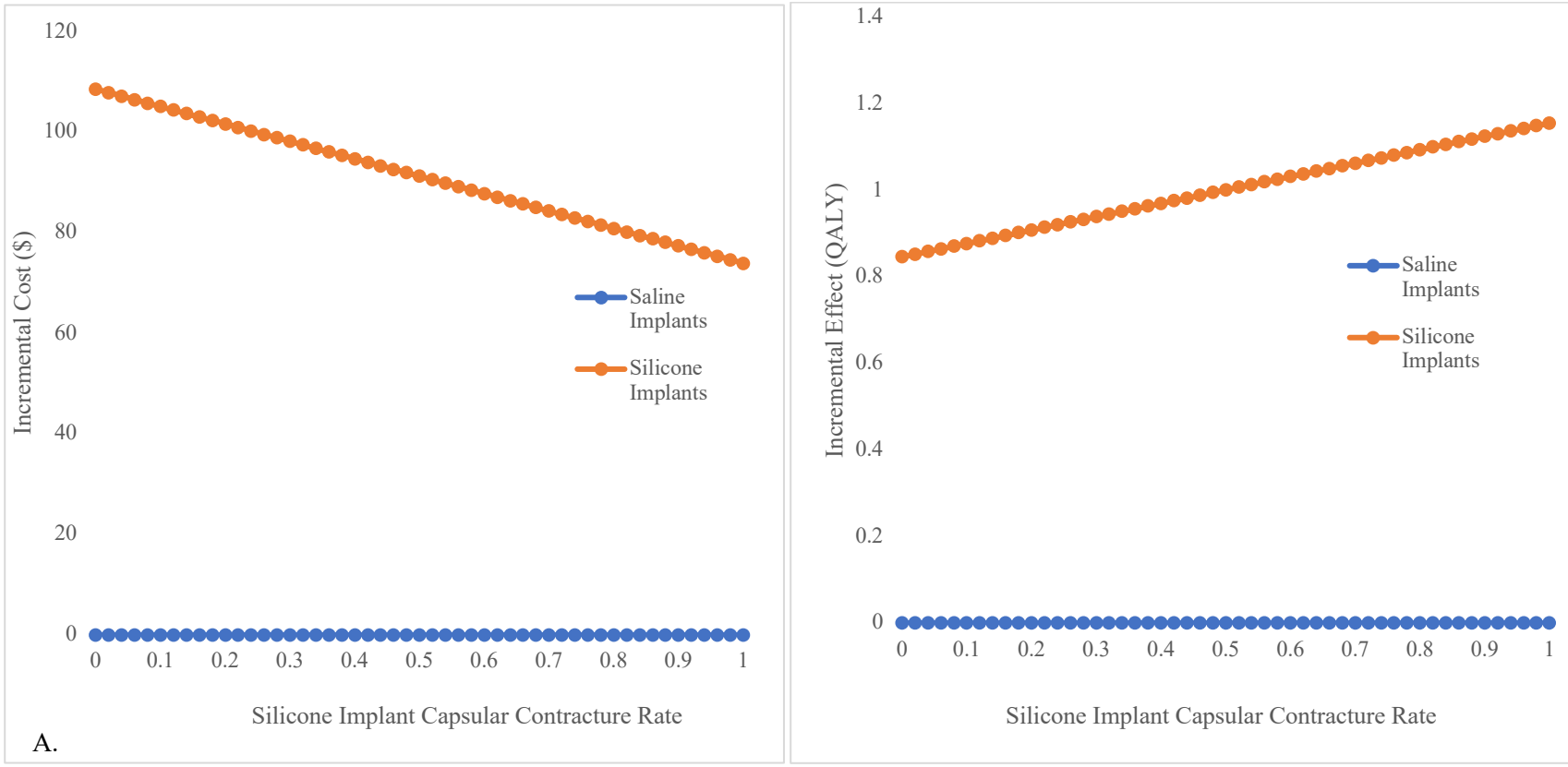

Figure 3.7 One-way sensitivity analysis varying probability of silicone implant capsular contracture (SJHC Data).
A. Incremental cost of saline and saline implants as a function of silicone implant capsular contracture rate. B. Incremental effect of saline and silicone implants as a function of silicone implant capsular contracture rate. As silicone implant capsular contracture rate increases the incremental cost of silicone implants decreases and incremental effect increases. This was because capsular contracture was a less costly health state compared to two of the remaining complication health states (i.e., implant rupture and unplanned revision).

3.4. Discussion

Breast reconstruction is becoming increasingly common following both therapeutic and prophylactic mastectomy and is important to quality of life in the survivorship period. Identifying cost-savings is imperative in resource-limited systems. However, more costly interventions must be contextualized in terms of their associated quality of life improvement.

This cost-utility analysis compares the two most commonly used types of implants in North America, saline-filled and silicone gel implants, in the context of breast reconstruction. The results suggest that both saline-filled and silicone implants are cost-effective within a willingness-to-pay threshold of $50,000/QALY. Further, increasing saline-filled implant complication rates beyond 0.58 in a one-way sensitivity analysis results in silicone implants being less costly and more effective (i.e. dominant strategy).

This model focused on the unilateral, immediate, one-stage implant-based breast reconstruction population. Women included in the model were assumed to have early stage (I or II) breast cancer as these women are eligible for immediate breast reconstruction. Typically, women with more advanced breast cancer (locally advanced or metastatic) are not eligible for this form of reconstruction due to higher risk of recurrence, anticipated requirement for adjuvant radiation and altered life-expectancy. Further, women with early stage breast reconstruction who survive the first three years following diagnosis return to life-expectancy of age-matched controls.(11) For this reason, the general population life-expectancy was used in this analysis. This analysis focused on unilateral reconstruction. Although contralateral prophylactic mastectomy is

increasing, unilateral mastectomy continues to be more common. Although a lower percentage of women undergoing unilateral mastectomy undergo reconstruction (27.4% versus 56% bilateral), this still constitutes a greater total number of unilateral reconstructions than bilateral reconstructions.(20) Patients undergoing unilateral implant-based reconstruction are different from those undergoing bilateral reconstructions in that patients undergoing contralateral prophylactic mastectomy tend to be younger, of Caucasian race, with private insurance coverage and family histories of breast and ovarian cancer.(21–23) They are also different in terms of expected outcomes such as symmetry and cosmesis which tend to be better with bilateral reconstructions. Because of this, the results of this analysis may not be generalizable to the bilateral reconstruction population. However, implant filler is not expected to confer a difference in outcomes between unilateral and bilateral reconstructions. This analysis also focused on immediate reconstruction since more women are opting for immediate reconstruction in both Canada and the United States.(20,24)

The perspective used for this analysis was that of the Ministry of Health and Long-Term Care (MOHLTC). Costs relevant to the MOHLTC include operating room costs, surgeon and anesthetist billing costs, clinic costs and community care costs. Operating room costs were obtained through the institutional case costing centre. The “Schedule of Benefits for Physician Services under the Health Insurance Act” was used the surgeon, anesthetist and radiologist billing codes for both operating room and clinic-related costs.(14) Patients who undergo implant-based breast reconstruction often require community care for drains for approximately one week. These costs were not included in this analysis and as such this constitutes a gap in the costs from the MOHLTC perspective.

Health states were defined based on a review of the literature. The most common complications associated with implant filler type were used to determine relevant health states. Psychological impacts of different implant filler options were assumed to be accounted for by the health state utility value. Duration of each health state was an approximation based on surgeon practice patterns. Given typical wait times for repeat consultation and surgery, these were felt to be conservative estimates. Certain elements of the health state definitions, including surgery duration, influenced costs, such as estimates of anesthesiology billing since these billing codes are based on time units.

This model used utilities obtained from the literature. Although this analysis focused on women undergoing unilateral reconstruction, none of the included utilities specified whether utilities were specific to unilateral or bilateral reconstruction. Conversely, the majority of utilities reported in the context of implant-based reconstruction examined the immediate implant-based reconstruction scenario.(1,25–28) This suggests that the utilities used here may prevent the results of this analysis from being extrapolated to delayed reconstruction. It is challenging to know how the utilities used would be influenced by unilateral or bilateral reconstruction. Bilateral reconstruction is associated with improved symmetry compared to unilateral reconstruction. However, the population of individuals undergoing bilateral mastectomy and reconstruction may be different from the unilateral population in terms of their expectations of post-operative outcomes. Nonetheless, it is not expected that implant filler would influence quality of life based on unilateral versus bilateral reconstruction.

Varying complication rates influence the relative cost-effectiveness of saline and silicone implants. This analysis is unfortunately limited by a lack of high-quality data directly comparing saline and silicone implants. A recent Cochrane systematic review was published on this topic concluding that it was not possible to delineate differences between saline and silicone implants based on existing trials.(29) However, the review was limited in several ways. Firstly, there are few randomized controlled trials (RCTs) directly comparing saline and silicone implants. Secondly, the RCTs that are published do not reflect the currently available implants, particularly with regard to the later generations of silicone implants. Some of the largest prospective studies of saline and silicone implants come from the Core Studies required for FDA approval. The Core Studies are industry-funded, prospective, non-randomized studies in which women receiving breast implants for augmentation or reconstruction were followed for 10 years. Although there are myriad retrospective and prospective cohort studies of women undergoing implant-based breast reconstruction, few provide independent analysis of complication rates based on implant type.

Costs for this analysis were obtained from multiple sources of secondary data. Estimates of direct and indirect costs of implant-based breast reconstruction were obtained through the institutional Case-Costing Centre. This Centre does case-costing for QBPs in breast reconstruction through micro-costing initiatives which have the potential to provide accurate cost estimates of all resources used. These costs were ultimately aggregated to provide average costs for patients undergoing implant-based breast reconstruction. Costs for individual implant models are confidential and protected under the competitive bidding agreements so average prices of saline and silicone implants available through

HMMS were used. Although these costs may be lower than catalogue prices, they may be a better reflection of implant costs incurred at centres with competitive bidding agreements. However, because local costs were used here, this model may not be generalizable to institutions without competitive bidding agreements or other provinces with different fee structures for physician and procedure billing.

A decision-tree model was used to perform the cost-utility analysis. Other types of models, such as Markov models, can account for repeated events in time. Use of a Markov model requires probability estimates of successful surgery, complications as well as movement between each well and unwell health state. These models have the advantage of being able to account for repeated events in time, such as requiring multiple revision surgeries or developing multiple complications. Although conceptually it is understood that certain events predispose to further complications (e.g., infection leading to higher risk of capsular contracture), transition probabilities are not available in the current literature. Given the limitations of the literature, the most appropriate model was the decision-tree. Deterministic sensitivity analyses were conducted to determine if the baseline decision analysis was robust. Varying overall probability of complications in addition to probability of implant rupture and capsular contracture demonstrated that silicone implants remained cost-effective within a WTP threshold of $50,000/QALY.

There are increasing numbers of cost-utility analyses examining breast reconstruction options. Several have compared autologous and implant-based reconstruction.(27,28,30,31) Overall, there is evidence to support cost-effectiveness of autologous reconstruction. For instance, Matros et al. found DIEP flap reconstruction to

be cost-effective relative to implant-based reconstruction with an ICER of $11,941/Breast-QALY.(31) Another CUA found both pedicled and free autologous reconstruction to be cost-effective within a WTP threshold of $100,000/QALY relative to the do-nothing alternative.(27) Interestingly, that study found implant-based reconstruction was not cost-effective as all implant-based reconstructive options exceeded the WTP threshold. Importantly, marginal changes in utility may influence relative cost-effectiveness.(30) Other CUAs have examined adjuncts to surgery and surgical materials such as CT angiography and acellular dermal matrix, both of which have been found to be cost-effective.(1,32) In terms of timing for reconstructive surgery, single-stage, direct-to-implant reconstruction has been found to be cost effective.(26) Thus far, no cost-utility analysis has compared saline and silicone implants. This cost-utility analysis provides important information to physicians, hospitals and policymakers when purchasing implants for breast reconstruction.

Overall, silicone implants are cost-effective for implant-based breast reconstruction. Given the improved quality of life-associated with silicone implants and only a marginal increase in cost, this analysis supports continued use of silicone implants despite higher initial cost.

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4. Chapter 4: General Discussion and Conclusions

Overview

This chapter reviews the results and implications of the systematic review of health state utility values in breast reconstruction (Chapter 2) and the cost-utility analysis comparing saline and silicone implants in breast reconstruction (Chapter 3). These analyses add to the existing literature on utility measurement and economic analysis in breast reconstruction by contextualizing existing health state utility values based on methodology and by demonstrating cost-effectiveness of silicone implants in implant-based breast reconstruction. [7]

4.1. General Discussion

The purpose of this paper was to analyze the relative cost-effectiveness of saline and silicone implants in the immediate breast reconstruction population. The rationale behind this study is that the Canadian health care system is facing increasing fiscal limitations in the setting of increasing demand for resources related to, among other things, the aging population. Due to improvements in treatment and earlier detection, more women are diagnosed with breast cancer and transitioning into the survivorship period with breast deformities related to lumpectomy and mastectomy.

[7]A portion of the work covered in Chapters 1 and 2 is included here as part of the Integrated Article Format.

Mastectomy in particular has increased in frequency over the years, and with it the demand for post-mastectomy reconstructive surgery. Breast reconstruction does not prolong life but is associated with improvement in quality of life for women in the survivorship period.(1) Implant-based reconstruction is the most common surgical approach.(2) Examining the quality of life changes associated with different approaches to implant-based breast reconstruction can help find economic efficiencies as well as justify treatments that offer significant improvements in quality of life.

This project was undertaken in two parts. First, a systematic review of the literature was conducted to identify health state utility values (HSUVs) published in the breast reconstruction literature. Methodological strengths of this review include the use of multiple databases, a search strategy developed with librarian assistance and screening undertaken by two independent reviewers. Further strengths of this analysis include a narrative description of current methodology used to generate HSUVs in breast reconstruction. This allows readers to better contextualize existing utilities in breast reconstruction, especially when comparing to other illnesses. Specifically, the results served to highlight limitations in the existing literature and discrepancies between the most common methodology and current guidelines on HSUV generation. Finally, the results of the quantitative analysis can serve as a reference for postoperative HSUVs in breast reconstruction. This is one of few systematic reviews and meta-analyses on HSUVs in breast reconstruction and is unique in its focus on values relating to post-operative complication health states.

Results of the systematic review demonstrated that the majority of reported utilities were

generated in the context of cost-utility analyses, most commonly by surveying medical experts (i.e., plastic surgeons) with visual analogue scales (VAS). As discussed in Chapter 2, the VAS has some inherent bias.(3,4) Time trade-off (TTO) and standard gamble (SG) have greater grounding in economic theory but can be more challenging to administer.(3)

Debate exists over whether to survey experts, patients or the general public in health state utility evaluation. It is thought that patients become accustomed to states of impaired health and, as such, ascribed higher value to those states than healthy individuals would ascribe. One study included in the systematic review examined HSUVs related to breast reconstruction without nipple reconstruction (i.e., nipple deformity) by surveying the general population and medical students.(5) These individuals ascribed a higher utility to nipple deformity than experts ascribed to successful implant-based or autologous reconstruction in other articles.(6–13) This study evaluated the health state using TTO, SG and VAS with the VAS scores being slightly lower, although this difference was not statistically significant.(5) This is consistent with estimates derived using the VAS since these can be influenced by scaling bias, resulting in values closer to the midpoint than with other direct elicitation techniques. Further, they found that higher medical education influenced utility scores. Although this study is an isolated example of differences that may be related to population surveyed and type of direct valuation technique, it is nonetheless important to remember that these factors influence HSUVs when interpreting or borrowing from the literature.

The systematic review of utilities was large, returning 2249 citations. Although the majority could be excluded based on predetermined criteria after a review of title and abstract, there were a large number of studies that described quality of life data by patient report. Unfortunately, the majority of these studies used ad hoc surveys and non-preference-based health status measures, preventing this quality of life data from being used to generate utilities in our analysis. Further, few studies reported quality of life data with respect to complication states. Post-surgical complication states are typically of short duration with patients returning to baseline quality of life over a period of weeks to months. However, this limits the useful information available to translate into utility measures. Finally, there is significant variability in the use of generic and disease-specific health status measures. Generic tools, whether preference-based or not, allow for comparison across different disease populations.(3) However, these can be insensitive to changes in quality of life in surgical patients which may be temporary or based on body image, psychosocial and sexual well-being in addition to physical well-being.(14) Disease-specific measures tend to be better able to delineate these nuances. However, few have passed through rigorous psychometric testing in the breast reconstruction population resulting in poor internal and external validity.(14)

The BREAST-Q is a disease-specific, patient-reported outcome measure that was developed using the Rasch psychometric method and provides interval level measurement.(15) The BREAST-Q has six subscales including satisfaction with breasts, satisfaction with outcome, psychosocial well-being, sexual well-being, chest well-being and abdominal wall physical well-being. Items are summed for each domain and transformed into a score ranging from 0-100. It is becoming more commonly used as a

patient-reported quality of life metric in clinical studies and has been used for utility generation in two cost-utility analyses.(11,16) Unfortunately, preference-rating has not been done for the BREAST-Q. Studies that use utilities derived from BREAST-Q data use the average score from the subscales. Utilities based on BREAST-Q scores were included in both the quantitative analysis of utilities (Chapter 2) and the cost-utility analysis (Chapter 3) since there is reported data on quality of life with saline and silicone implants using this measure. Within these limitations these values constitute the best quality of life data regarding saline and silicone implants. Because BREAST-Q-derived utilities are based on patient opinions, the estimates may be higher than those derived from the general population. However, because preference-weighting has not been done for the BREAST-Q, scores do not reflect relative importance of each domain and as such may not accurately reflect health status. This is a limitation of using BREAST-Q data to derive utility estimates.

The results of the systematic review provide information on health state utility values relevant to post-surgical health states in breast reconstruction. Although there are several limitations to the validity of these HSUVs, until such time that preference weighting and mapping functions are available for disease-specific questionnaires, they reflect the best available quality of life data for implant-based breast reconstruction. Further, despite these limitations, the aggregate data reported here provide a better estimate than each individual study and can be used as more accurate estimates of HSUVs in future CUAs.

The second stage of the project involved a cost-utility analysis of saline and silicone implants in the context of outpatient, immediate, unilateral implant-based breast

reconstruction. Data from this analysis came from multiple sources. Utilities were obtained from a review of the literature. Operative costing data was obtained from the institutional case costing centre. This centre does micro-costing for Quality-Based Procedure (QBP) groups, including reconstructive breast surgery. Micro-costing data is used to generate average costs for QBPs which can be subdivided based on Case-Costing Initiative (CCI) codes. The average cost for all relevant CCI codes was used as the base operative cost. Average costs of saline and silicone implants were obtained from the institutional purchasing centre, Healthcare Materials Management Services (HMMS). Relevant billing codes were used to estimate surgeon and anesthesia costs.

Micro-costing involves estimation of all resource costs. In this scenario micro-costs have been aggregated by CCI codes. Unfortunately, immediate breast reconstruction procedures have the potential to be categorized under multiple CCI codes and, as such, a broad scope of codes were used in an attempt to capture all relevant procedures. In doing this, it is possible that micro-costing data from procedures not strictly immediate, implant-based breast reconstruction were included. Further, since immediate breast reconstruction by definition occurs during the same operation as the mastectomy, a component of the cost estimate accounts for the surgical ablation. Since this base cost was used as an estimate of operative costs for subsequent procedures (due to similar operating room supplies and duration), this may constitute an over-estimation of operative costs for subsequent procedures related to complication states. However, this potential overestimation is applied to both saline and silicone arms of the analysis.

Implant costs were obtained from HMMS which is responsible for coordinating

competitive bidding agreements with industry suppliers. Costs for individual implants at St. Joseph's Health Care (SJHC), London are protected under confidentiality agreements so average costs of saline and silicone implants were used. Use of pricing under competitive bidding agreements has the potential to underestimate implant-related costs; thus, the results of this cost-utility analysis may not accurately reflect costs at institutions without such agreements. Indeed, between London Health Sciences Centre (LHSC) and SJHC, there were differences in the average costs of saline and silicone implants purchased, mainly related to lower cost of saline implants (Appendix 2). Unfortunately, because of the aforementioned confidentiality agreements, implant model type and numbers purchased were not available, so it is unknown if the cost discrepancy was related to the choice of implant subtype, numbers used or differences in the competitive bidding agreements. Overall, cost-savings are expected to be similar for both saline and silicone implants; however, small changes in implant cost may influence the degree to which silicone implants are considered cost-effective (i.e., through changes in the ICUR).

Health state parameter estimates were obtained from the literature, specifically the silicone Core studies and the 10-year post-market approval data for saline-filled implants from Mentor and Allergan.(17–20) These are large, population-based, prospective studies and provide some of the best quality data on implants and related complications. These studies have several limitations including industry-sponsorship and the non-randomized study design which are potential sources of bias. Unfortunately, a systematic review of the literature on implant-related complications (Chapter 3) revealed that there are few randomized-controlled trials and prospective, non-randomized trials directly comparing saline and silicone implants. This is consistent with a recent Cochrane Systematic Review

on the topic.(21) The few published randomized controlled trials were done on earlier generations of implants and likely do not reflect the complication profile of implants in use today.(22,23) Nonetheless, the fact that only a few studies were used to develop parameter estimates is an inherent limitation of this analysis, which stems from the limitations of the available literature.

Cost-utility analyses are becoming more common as stakeholders in healthcare funding attempt to provide of high-quality services with limited resources. Several cost-utility analyses have been published regarding breast reconstruction options. These include comparisons of autologous and alloplastic techniques as well as adjuncts to surgery. Within the realm of autologous reconstruction, several studies have found free tissue transfer to be cost-effective relative to pedicled techniques. Thoma et al. found that free TRAM was cost-effective relative to pedicled TRAM and that DIEP flap reconstruction was cost-effective relative to TRAM flap reconstruction.(12,13) Conversely, a cost-utility analysis done by Grover et al. found both pedicled and free autologous reconstruction to be cost-effective with pedicled options being favoured slightly due to lower costs.(7) This same study found implant-based reconstruction was not cost-effective relative to the do-nothing alternative, as it exceeded a willingness-to-pay threshold of $100,000. However, this study was unusual in that they found only small improvements in quality-adjusted life years for each type of approach relative to the do-nothing option. Other studies have found autologous reconstruction to be cost-effective relative to implant-based reconstruction. For instance, Matros et al. performed a cost-utility analysis with utilities derived from BREAST-Q data and found that DIEP flap reconstruction was cost-effective within a WTP threshold of $50,000, with an incremental cost-effectiveness ratio (ICER)

of $11,941/Breast-QALY relative to implant-based reconstruction.(16) However, even small differences in utility and cost can result in large changes in the ICUR, as demonstrated by a Markov model developed by Preminger et al. in which cost and utility of implant-based reconstruction and TRAM flap reconstruction were varied.(24) Unfortunately, a significant limitation of that model was that it did not generate health state utility values specific to each reconstructive modality and instead assumed a baseline utility of 0.7 for both TRAM flap and implant-based reconstruction, which was then varied in a sensitivity analysis. Nonetheless, a marginal increase in the utility of implant-based reconstruction from 0.7 to 0.704 made implant-based reconstruction cost-effective within a WTP threshold of $50,000/QALY.

Adjuncts to breast reconstruction have also been demonstrated to be cost-effective, such as the use of CT angiography and laser-assisted indocyanine green angiography in autologous reconstruction.(6,25) Adjuncts to implant-based reconstruction including acellular dermal matrix may be cost-effective. One study demonstrated that acellular dermal matrix (ADM) is cost-effective relative to staged expander-implant reconstruction; however, another analysis suggested that autologous dermal flaps should be used when available since these are significantly less costly than ADM with minimal difference in quality of life.(8,9) Finally, direct-to implant reconstruction dominates staged expander-implant reconstruction.(10)

There are no previously published cost-utility analyses comparing saline and silicone implants in the context of breast reconstruction. Saline implants offer an initial cost-savings relative to silicone implants amounting to approximately $226.60 at SJHC,

although this is variable based on hospital and competitive bidding agreements (Appendix 2). It can be challenging to justify devices with higher initial costs if quality of life is not considered. When such information is taken into consideration, silicone implants are cost-effective. Institutional variation in cost does influence the degree to which silicone implants are cost-effective, as seen with the change in ICUR between LHSC and SJHC data (Table 3.8). It is possible that other institutions may find variable incremental cost-effectiveness of silicone implants due to different base price relative to the cost of saline implants and other perioperative costs. Ultimately, silicone implants provide improved quality of life at a marginal increase in cost relative to saline implants. This analysis may be useful to physicians, policy-makers and hospital administrators when justifying choice of implant in the context of breast reconstruction.

4.2. References

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5. Appendices

Appendix 1. Sample Calculations

Example: Weighted Average of Utility for Successful Surgery

Table A1. Values for Calculation of Utility of Successful Surgery

Article	Successful Surgery Qualifier	Utility (x)	Weight (w)[1]	x*w
Chatterjee et al. 2013	Free Autologous	0.85	10	8.50
Grover et al. 2013	Alloplastic Two-Stage	0.71	9	6.39
	Alloplastic One-Stage	0.74	9	6.66
	Pedicled Autologous	0.83	9	7.47
	Free Autologous	0.85	9	7.65
	Latissimus Dorsi Flap with Implant	0.74	9	6.66
Krishnan et al. 2014	Immediate Alloplastic Two-Stage with ADM	0.7	5	3.50
	Immediate Alloplastic Two-Stage without ADM	0.66	10	6.60
Krishnan et al. 2013	Immediate Alloplastic One-Stage	0.74	10	7.40
Krishnan et al. 2016	Immediate Alloplastic One-Stage	0.69	15	10.35
	Immediate Alloplastic Two-Stage	0.66	15	9.90
Razdan et al. 2016	Immediate Alloplastic Two-Stage	0.698	196	136.81
	Delayed Autologous	0.692	76	52.59
Thoma et al. 2003	Autologous	0.87	33	28.71
Thoma et al. 2004	Autologous	0.87	32	27.84
Sum			447	327.03
Weighted Average Utility		=	327.03/447	0.73

[1]Weights are equal to number of individuals surveyed

Worked Example – Weighted Average

$$\bar{x}_{wt} = \frac{\sum_{i=1}^{n} x_i w_i}{\sum_{i=1}^{n} w_i}$$

$$\bar{x}_{wt} = \frac{0.85*10+0.71*9+0.74*9+0.83*9+0.85*9+0.74*9+0.7*5+0.66*10+0.74*10+0.69*15+0.66*15+0.698*196+0.692*76+0.87*33+0.87*32}{10+9+9+9+9+9+5+10+10+15+15+196+76+33+32}$$

$$\bar{x}_{wt} = \frac{327.03}{447}$$

$\bar{x}_{wt} = 0.73$

Worked Example – Weighted Standard Deviation

$$SD_{wt} = \sqrt{\frac{\left(\frac{\sum_{i=1}^{n} w_i x_i^2}{\bar{w}} - n * \bar{x}_{wt}^2\right)}{n-1}}$$

Where $\bar{w} = \frac{\sum_{i=1}^{n} w_i}{n}$ and $\bar{x}_{wt} = \frac{\sum_{i=1}^{n} x_i w_i}{\sum_{i=1}^{n} w_i}$

$$SD_{wt} = \sqrt{\frac{\left(\frac{241.362948}{29.8} - 15 * 0.73161^2\right)}{14}}$$

$$SD_{wt} = \sqrt{0.005}$$

$$SD_{wt} = 0.071$$

Table A1.2 Values for Calculation of Utility of Successful Implant-Based Reconstruction

Article	Health State Qualifier	Utility (x)	Weight (w)[1]	x*w
Grover et al. 2013	Alloplastic Two-Stage	0.71	9	6.39
	Alloplastic One-Stage	0.74	9	6.66
Krishnan et al. 2014	Immediate Alloplastic Two-Stage with ADM	0.7	5	3.50
	Immediate Alloplastic Two-Stage without ADM	0.66	10	6.60
Krishnan et al. 2013	Immediate Alloplastic One-Stage	0.74	10	7.40
Krishnan et al. 2016	Immediate Alloplastic One-Stage	0.69	15	10.35
	Immediate Alloplastic Two-Stage	0.66	15	9.90
Razdan et al. 2016	Immediate Alloplastic Two-Stage	0.698	196	136.81
Sum			269	187.61
Weighted Utility		=	187.61/269	0.70

[1]Weights are equal to number of individuals surveyed

Table A1.3 Values for Calculation of Utility of Successful Autologous Reconstruction

Article	Health State Qualifier	Utility (x)	Weight (w)[1]	x*w
Chatterjee et al. 2013	Free Autologous	0.85	10	8.50
Grover et al. 2013	Pedicled Autologous	0.83	9	7.47
	Free Autologous	0.85	9	7.65
Razdan et al. 2016	Delayed Autologous	0.692	76	52.59
Thoma et al. 2003	Autologous	0.87	33	28.71
Thoma et al. 2004	Autologous	0.87	32	27.84
Sum			169	132.76
Weighted Utility		=	132.76/169	0.79

[1]Weights are equal to number of individuals surveyed

Table A1.4 Values for Calculation of Utility of Total Flap Loss

Article	Health State Qualifier	Utility (x)	Weight (w)[1]	x*w
Chatterjee et al. 2013	Free Autologous	0.53	10	5.30
Grover et al. 2013	Pedicled Autologous	0.58	9	5.22
	Free Autologous	0.53	9	4.77
Thoma et al. 2003	Debridement and Salvage with Tissue Expander	0.61	33	20.13
	Debredment	0.44	33	14.52
Thoma et al. 2004	Autologous	0.61	32	19.52
Sum			126	69.46
Weighted Utility		=	69.46/126	0.55

[1]Weights are equal to number of individuals surveyed

Table A1.5 Values for Calculation of Utility of Partial Flap Necrosis

Article	Health State Qualifier	Utility (x)	Weight (w)[1]	x*w
Chatterjee et al. 2013	Free Autologous	0.77	10	7.70
Grover et al. 2013	Pedicled Autologous	0.74	9	6.66
	Free Autologous	0.77	9	6.93
Thoma et al. 2003	Partial Skin Necrosis	0.71	33	23.43
	Fat Necrosis Resolves Spontaneously	0.74	33	24.42
	Fat Necrosis w/ Debridement or Drain	0.69	33	22.77
Thoma et al. 2004	Partial Skin Necrosis	0.71	32	22.72
	Fat Necrosis Resolves Spontaneously	0.74	32	23.68
Sum			191	138.31
Weighted Utility		=	138.31/191	0.72

[1]Weights are equal to number of individuals surveyed

Table A1.6 Values for Calculation of Utility of Mastectomy Skin Necrosis

Article	Health State Qualifier	Utility (x)	Weight (w)[1]	x*w
Chatterjee et al. 2013	Free Autologous	0.7	10	7.00
Krishnan et al. 2014	Immediate Alloplastic Two-Stage with ADM	0.614	5	3.07
	Immediate Alloplastic Two-Stage without ADM	0.6	10	6.00
Krishnan et al. 2013	Immediate Alloplastic One-Stage	0.67	10	6.70
Thoma et al. 2004	Autologous	0.71	33	23.43
Sum			68	46.20
Weighted Utility		=	46.20/68	0.68

[1]Weights are equal to number of individuals surveyed

Table A1.7 Values for Calculation of Utility of Hematoma

Article	Health State Qualifier	Utility (x)	Weight (w)[1]	x*w
Chatterjee et al. 2013	Free Autologous	0.77	10	7.70
Krishnan et al. 2014	Immediate Alloplastic Two-Stage with ADM	0.636	5	3.18
	Immediate Alloplastic Two-Stage without ADM	0.61	10	6.10
Krishnan et al. 2013	Immediate Alloplastic One-Stage	0.69	10	6.90
Krishnan et al. 2016	Immediate Alloplastic One-Stage	0.64	15	9.60
	Immediate Alloplastic Two-Stage	0.6356	15	9.53
Thoma et al. 2003	Drainage Required	0.77	33	25.41
	No Drainage	0.79	33	26.07
Thoma et al. 2004	Autologous	0.77	32	24.64
Sum			163	119.13
Weighted Utility		=	119.13/163	0.73

[1]Weights are equal to number of individuals surveyed

Table A1.8 Values for Calculation of Utility of Infection

Article	Health State Qualifier	Utility (x)	Weight (w)[1]	x*w	
Chatterjee et al. 2013	Free Autologous	0.75	10		7.50
Grover et al. 2013	Pedicled Autologous	0.72	9		6.48
	Free Autologous	0.75	9		6.75
Krishnan et al. 2014	Immediate Alloplastic Two-Stage with ADM	0.605	5		3.03
	Immediate Alloplastic Two-Stage without ADM	0.595	10		5.95
Krishnan et al. 2013	Immediate Alloplastic One-Stage	0.675	10		6.75
Krishnan et al. 2016	Immediate Alloplastic One-Stage	0.5802	15		8.70
	Immediate Alloplastic Two-Stage	0.538	15		8.07
Thoma et al. 2003	Autologous	0.745	33		24.59
Sum			116	77.81	
Weighted Utility			=	77.81/116	0.67

[1]Weights are equal to number of individuals surveyed

Table A1.9 Values for Calculation of Utility of Explantation

Article	Health State Qualifier	Utility (x)	Weight (w)[1]	x*w	
Krishnan et al. 2014	Immediate Alloplastic Two-Stage with ADM	0.585	5		2.93
	Immediate Alloplastic Two-Stage without ADM	0.585	10		5.85
Krishnan et al. 2013	Immediate Alloplastic One-Stage	0.655	10		6.55
Sum			25	15.33	
Weighted Utility			=	15.33/25	0.61

[1]Weights are equal to number of individuals surveyed

Table A1.10 Values for Calculation of Utility of Capsular Contracture Grade III/IV

Article	Health State Qualifier	Utility (x)	Weight (w)[1]	x*w	
Krishnan et al. 2014	Immediate Alloplastic Two-Stage with ADM	0.592	5		2.96
	Immediate Alloplastic Two-Stage without ADM	0.6	10		6.00
Krishnan et al. 2016	Immediate Alloplastic One-Stage	0.59	15		8.85
	Immediate Alloplastic Two-Stage	0.58	15		8.70
Sum			45	26.51	
Weighted Utility			= 26.51/45		0.59

[1]Weights are equal to number of individuals surveyed

Table A1.11 Values for Calculation of Utility of Revision

Article	Health State Qualifier	Utility (x)	Weight (w)[1]	x*w	
Krishnan et al. 2016	Immediate Alloplastic One-Stage	0.61	15		9.15
	Immediate Alloplastic Two-Stage	0.62	15		9.30
Sum			30	18.45	
Weighted Utility			= 18.45/30		0.62

[1]Weights are equal to number of individuals surveyed

Table A1.12 Values for Calculation of Utility of Nipple Deformity

Article	Health State Qualifier	Utility (x)	Weight (w)[1]	x*w	
Ibrahim et al. 2015	VAS	0.84	103		86.52
	TTO	0.92	103		94.76
	SG	0.92	103		94.76
Sum			309	276.04	
Weighted Utility			= 276.04/309		0.89

[1]Weights are equal to number of individuals surveyed

Table A1.13 Values for Calculation of Utility of Mastectomy Alone

Article	Health State Qualifier	Utility (x)	Weight (w)[1]	x*w	
Grover et al. 2013		0.68	9		6.12
Razdan et al. 2016		0.586	71		41.61
Sum			80	47.73	
Weighted Utility			= 47.73/80		0.60

[1]Weights are equal to number of individuals surveyed

Appendix 2. Costs Included in Case Costing Centre Procedure Estimate[1]

Cost Category	Included Components
Direct Labour	Variable Direct Labour Variable Direct Other Labour (Contracted-Out)
Direct Supply	Variable Direct Material - General Supplies Variable Direct Material - Patient Specific Supplies
Direct Other	Fixed Direct Other - Sundry Fixed Direct Labour - Management/Operations Fixed Direct Building, Equipment and Grounds - Equipment Expense (including amortization), undistributed building and grounds) Fixed Direct Labour Administration - Labour Components of the administration departments Fixed Direct Other - Sundry Administration - Other components of the administration department
Fixed Indirect	Variable Indirect - Variable operating expenses from overhead functional centres Fixed Indirect - Fixed operating expenses from overhead functional centres

[1]Source SJHC Case Costing Centre. [2]Labour cost estimated based on cost/min of operating time.

Appendix 3. Institutional Implant Costs

Institution	Average Implant Cost ($)[1]			
	All Implants	**Saline Implants**	**Silicone Implants**	**Difference**
St. Joseph's	713.82	515	737.6	222.6
LHSC	640.38	417	736.8	319.8
Average	666.34	494	737.56	243.56

[1]Source HMMS April 2017 - November 2017

Appendix 4. SJHC Cost Data

Health State	Silicone Successful	Silicone Rupture	Silicone Capsular Contracture	Silicone Unplanned Revision	Silicone Explantation	Saline Successful	Saline Rupture	Saline Capsular Contracture	Saline Unplanned Revision	Saline Explantation
Items										
Day Surgery SJHC	6004	6004	5266.4	5266.4	5266.4	5781.4	5781.4	5266.4	5266.4	5266.4
Procedure R119	350					350				
Anesthesia R119	405.27					405.27				
Preoperative Consult	81.10	47.95	47.95	47.95	47.95	81.10	47.95	47.95	47.95	47.95
First Postoperative Follow-up Visit	41.55	41.55	41.55	41.55	41.55	41.55	41.55	41.55	41.55	41.55
Subsequent Postoperative Follow-up Visit	106.2	79.65	79.65	79.65	79.65	106.2	79.65	79.65	79.65	79.65
Procedure Z135		195.95	195.95				195.95	195.95		
Anesthesia Z135		315.21	315.21				315.21	315.21		
Cost MRI Breast		191.15							0	
Procedure R114				230.30					230.30	
Anesthesia R114				315.21					315.21	
Procedure Z142					150					150
Anesthesia Z142					165.11					165.11
MRI Breast Read		73.35								
Total State Cost	6988.12	6948.81	5946.71	5981.06	5750.66	6765.52	6461.71	5946.71	5981.06	5750.66
Total Net Cost	6988.12	13936.93	12934.83	12969.18	12738.78	6765.52	13227.23	12712.23	12746.58	12516.18

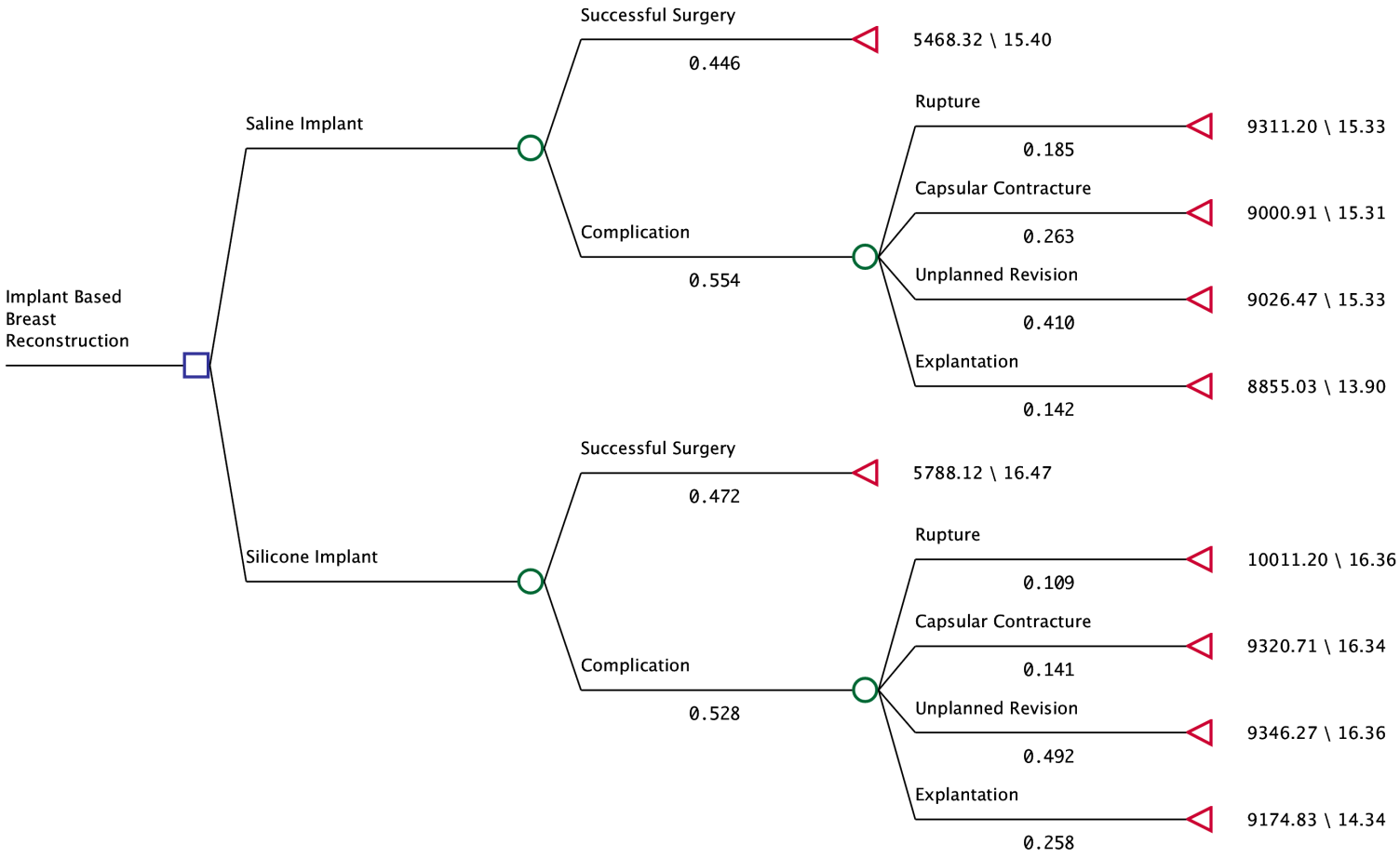
Total Net Cost 3% Discount	N/A	12158.69	11413.03	11438.59	11267.15	N/A	11573.64	11190.43	11215.99	11044.55
Total Net Cost 1.5% Discount	N/A	12975.68	12112.21	12141.80	11943.28	N/A	12333.36	11889.61	11919.20	11720.68
Total Net Cost 5% Discount	N/A	11254.09	10638.88	10659.97	10518.53	N/A	10732.45	10416.28	10437.37	10295.93

Appendix 5. LHSC Cost Data

Health State	Silicone Successful	Silicone Rupture	Silicone Capsular Contracture	Silicone Unplanned Revision	Silicone Explantation	Saline Successful	Saline Rupture	Saline Capsular Contracture	Saline Unplanned Revision	Saline Explantation
Items										
Day Surgery LHSC	4804	4804	4067.2	4067.2	4067.2	4484.2	4484.2	4067.2	4067.2	4067.2
Procedure R119	350					350				
Anesthesia R119	405.27					405.27				
Preoperative Consult	81.10	47.95	47.95	47.95	47.95	81.10	47.95	47.95	47.95	47.95
First Postoperative Follow-up Visit	41.55	41.55	41.55	41.55	41.55	41.55	41.55	41.55	41.55	41.55
Subsequent Postoperative Follow-up Visit	106.2	79.65	79.65	79.65	79.65	106.2	79.65	79.65	79.65	79.65
Procedure Z135		195.95	195.95				195.95	195.95		
Anesthesia Z135		315.21	315.21				315.21	315.21		
Cost MRI Breast		191.15							0	
Procedure R114				230.30					230.30	
Anesthesia R114				315.21					315.21	
Procedure Z142					150					150
Anesthesia Z142					165.11					165.11
MRI Breast Read		73.35								
Total State Cost	5788.12	5675.46	4747.51	4781.86	4551.46	5468.32	5164.51	4747.51	4781.86	4551.46
Total Net Cost	5788.12	11463.58	10535.63	10569.98	10339.58	5468.32	10632.83	10215.83	10250.18	10019.78

Total Net Cost 3% Discount	10011.20	9320.71	9346.27	9174.83	9311.20	9000.91	9026.47	8855.03
Total Net Cost 1.5% Discount	10678.48	9878.89	9908.49	9709.96	9918.41	9559.09	9588.69	9390.16
Total Net Cost 5% Discount	9272.36	8702.68	8723.77	8582.32	8638.88	8382.88	8403.97	8262.52

Appendix 6. Decision Tree for LHSC Data



6. Curriculum Vitae

Kathleen Nelligan

Post-Secondary Education and Degrees

Plastic and Reconstructive Surgery Resident, Western University	2016-present
Master of Surgery, Western University (Candidate)	2017-present
Doctor of Medicine, Western University	2012-2016
Bachelor of Sciences (Honours), University of Toronto	2008-2012

Honours and Awards

Certificate of Merit, Surgery Clerkship Rotation, University of Western Ontario	2015
Kenneth Colling Award in Medicine, University of Western Ontario	2014
Summer Undergraduate Research Program Funding, Institute of Medical Sciences, University of Toronto	2013
First Place Poster, Department of Paediatrics Research Day, Hospital for Sick Children	2012
Chancellor's Award, Trinity College, University of Toronto	2011

Publications

Wong P, McIvar J, **Nelligan K**, Bleakley J, McCartney C. Factors influencing the choice of anesthetic technique in primary hip and knee arthroplasties. *Pain Management* 2016;6(3):297-311.

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