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# Patient reported outcome measures (PROMs) in breast cancer patients after immediate breast reconstruction using the Breast-Q.

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# PART A: PLAGIARISM DECLARATION

I, *Ernst Lodewicus Möller*, hereby declare that the work, on which this dissertation is based, is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

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Signed by candidate

Dr. EL Möllller

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# PART B: FINAL ABSTRACT

## Patient reported outcome measures (PROMs) in breast cancer patients after immediate breast reconstruction using the Breast-Q.


**Background**

Mastectomy is the mainstay of surgical treatment for women with breast cancer in South Africa. The increase in breast reconstruction after a mastectomy has prompted the need to evaluate patient reported outcome measures (PROMs) for this set of operative intervention. This study aimed to assess clinical and patient reported outcome measures in immediate breast reconstruction patients using the BREAST-Q and compare these with international cohorts.

**Methods**

A cross-sectional study was performed on all patients who underwent immediate breast reconstruction between January 2011 and December 2016. This consisted of a retrospective clinical record review of perioperative outcomes, and a quality of life analysis using the BREAST-Q Post-Reconstruction questionnaire. Outcome predictors were identified using Chi-square, Fisher exact, One-way ANOVA, Student t-tests and Kruskal Wallis analysis of variance. A random-effect single arm meta-analysis was performed to compare the BREAST-Q scores with international cohorts.

**Results**

A total of 52 patients were included with a mean age of 43.2 (+/-9.5) years. Eighteen patients (34.6%) developed early complications; of these 8 (44.4%) were major. Thirty-one patients (59.6%) developed late complications; of these 18 (58.1%) were major. Fifteen patients (28.8%) had failed reconstruction. There was a significantly higher risk of failure following a total mastectomy (TM) ($p=0.02$), tissue expander reconstruction (TE) ($p<0.01$) and stage 2 breast cancer ($p=0.01$). Patients who underwent nipple reconstruction and immediate-delayed reconstruction before 12 months, reported higher well-being and satisfaction scores. Compared to international cohorts our BREAST-Q scores were lower but fall within the 95% confidence interval for Sexual Well-Being and Satisfaction with Nipples and Care.


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**Conclusion**

Immediate breast reconstruction poses a high risk of complications and reconstructive failure especially, with TM and TE. Our BREAST-Q scores are comparable to international studies and may be useful in guiding patient consent.

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# PART C: PROTOCOL

# Patient reported outcome measures (PROMs) in breast cancer patients after immediate breast reconstruction using the Breast-Q.

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## I. INTRODUCTION

Breast cancer is the most commonly diagnosed among cancers in South African women. With 21,8% of all new cancers diagnosed attributable to breast cancer and a current lifetime risk of 1:27, makes breast cancer a significant contributor to national health statistics.[1] The average age at which breast cancer is diagnosed, shows to be younger than developed countries[2, 3] and younger women with breast cancer in South Africa is found to have the same clinical and pathological features of women in developed countries, but more advanced in presentation with poorer outcomes.[4]

Mastectomy with or without axillary clearance remains the mainstay of operative management in South Africa, but due to a younger diagnosed population, breast conserving therapy and breast reconstruction after mastectomy, seems a more favourable option due to aesthetics. Very little research exists regarding breast reconstruction in South Africa, and rates and availability differ from health institutions.

Research in the Western Cape has shown that factors other than demographics influence the patient's decision to undergo reconstruction after mastectomy.[5] Primary physician and surgeon's lack of knowledge and ambiguity towards breast reconstruction is inadmissible and

concerning. [6,7] Increasing breast reconstruction rates, varying between 3 to 40% in the U.S.[8-11] has ignited the need for evaluating patient reported outcome measures such as quality of life and patient satisfaction.

The Breast-Q questionnaire jointly developed by Memorial Sloan-Kettering Cancer Center and the University of British Columbia has proved to be a validated and developed tool to assess PROMs. [12-14] It has also been widely utilized by national health systems[15] and other health institutions not only to illustrate the favourable outcome of breast reconstruction compared to mastectomy alone[16], but also comparing different forms of breast reconstruction at different intervals.[17-22]

At Groote Schuur Hospital in the Western Cape South Africa, patients with breast cancer suitable for breast reconstruction are being closely selected and counselled by a combined breast clinic comprising of general surgeons, plastic surgeons and oncologists. Due to limited theatre space and time, general surgeons only perform immediate reconstructive procedures and patients need to comply with the following inclusion criteria:

a. Patient expressed need for immediate breast reconstruction
b. Early Breast Cancer (Stage 0 – 2 disease) but excluding any stage with nodal disease i.e. Stage I B and stages 2A (T0 N1 MO; T1 N1 M0) and 2B (T2 N1 M0).

Immediate reconstructions after mastectomy at Groote Schuur Hospital, entails either expander or implant reconstruction, with expander being favoured by far.

Up to date there is no data available on patient reported quality of life and postoperative satisfaction in South Africa. We therefore defined the dire need to conduct such a research project, to evaluate whether it is achievable in the government health sector of South Africa, and to evaluate whether our practice of immediate reconstruction is acceptable according to patient reported outcomes and comparable to international statistics.

## II. AIM OF THE STUDY

### Primary Aim:

1. To evaluate patient reported outcome measures (HR-QOL and patient satisfaction) in breast cancer patients who received immediate breast reconstruction after mastectomy

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by the Department of Surgery, Endocrine Oncologic Unit, Grootte Schuur Hospital, utilizing the Breast-Q© questionnaire.

**Secondary Aim:**

2. To conduct an audit of all breast reconstruction patients during our selected period and determine if there is any statistical correlation between PROMs and their demographics, tumour pathology, procedure of immediate reconstruction, complications of surgery and postoperative care.
3. To compare our findings with international statistics and research
4. To determine whether PROMs evaluation and research is feasible in South African Government hospitals with breast reconstruction options available.

## III. METHODOLOGY

Study population:

All female patients who underwent immediate implant or tissue expander reconstruction after mastectomy during 1 January 2011 to 31 December 2016 by the Department of General Surgery, Endocrine Oncologic Unit, Groote Schuur Hospital.

Study design:

Cross-sectional study involving two components:

a. **Retrospective patient folder review to obtain the following data** *(Appendix A)*:
    i. Age
    ii. Presenting complaint (Pain; Lump; Nipple discharge; Skin changes)
    iii. Breast affected (Right or Left)
    iv. Mode of Diagnosis (Mammography; Ultrasound; FNA; Histology)
    v. Type of Breast Cancer (DCIS; Ductal; Lobular etc.) including BRCA ½ positive patients due to their high lifetime risk for breast cancer
    vi. Receptor status of Breast Cancer (ER; PR; HER-2)
    vii. Stage of Breast Cancer (TNM)
    viii. Mastectomy type and laterality (Unilateral therapeutic; Bilateral therapeutic etc.)

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ix. Reconstruction procedure (Expander/Implant/Autologous) and (Unilateral/Bilateral)

x. Post-reconstruction therapy (Radiation; Chemotherapy; Hormonal)

xi. Post-reconstruction complications (Early complications i.e. hematoma; sepsis; seroma)

xii. Post-operative complications (Late complications i.e Contracture of expander or implant capsule etc.)

xiii. Re-operate or Re-reconstruction

**b. Real time Completion of the Breast-Q© Postoperative Reconstruction module by the identified patients**

i. Patients will be contacted personally to counsel regarding the research project and determine if the patient is willing to form part of the research. All patients must complete the questionnaire at least 1 year since their implant based or autologous reconstruction procedure.

ii. Means of participation is offered to the patient as follows (in English / Afrikaans/ Xhosa):

- Personally completing the questionnaire at GSH on a selected date. Patients in need of transportation costs will be subsidized in this regard
- Receiving a posted letter with consent and questionnaire to be completed and prepaid envelope to return to GSH.
- Receiving an email containing the brochure, consent and questionnaire to complete and return to the following address ernstmoller10@gmail.com.

iii. Informed consent will be obtained before completing the questionnaire.

iv. After completion of the questionnaire (Sections 1-6 & 11-14 only) all data will be kept anonymously and captured on the Breast-Q© pre-configured Microsoft Excel© database.

v. The pre-configured database will be electronically submitted to the QScore© analysis program provided by the developers of the Breast-Q© questionnaire, to calculate appropriate quality of life and patient satisfaction scores.

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**c. Consent to Utilize the Breast-Q© as research tool**

i. All correspondence regarding utilization of Breast-Q©, application form and prerequisite guidelines as explained in the Breast-Q© User Manual will be completed

**d. Interpretation of Breast-Q© scores as calculated by QScore©**

*(As described in the Breast-Q© User Manual)*

i. "All Breast-Q© scores range from 0-100. The scores are computed from the responses to the separate questions by adding them together and converting the score to a scale from 0 to 100 (like conversion into a percentage). A higher score means high satisfaction or better health-related quality of life."

ii. "The clinical meaning of BREAST-Q© scores and the smallest clinically significant differences are not yet defined (research is ongoing). However, the interpretation of the clinical significance of BREAST-Q© scores is facilitated by the recently available data from a study of 2000 patients at Memorial Sloan-Kettering Cancer Center in New York (USA). The mean values of QL scores in the general population are indicated with an arrow on the printout to serve as a rough guide for the severity of the limitations or symptoms. A study of the subjective significance to the patients of changes in QL scores suggests that a mean change of 5 to 10 on the multi-item scales is perceived as 'a little' change, 10 to 20 as 'a moderate' change and greater than 20 as 'very much' change."

## IV. STATISTICAL ANALYSIS

1. All data from patient folders will be captured on a Microsoft Excel© spreadsheet via a Google Docs© preconfigured template.
2. All data from the questionnaires will be analyzed using the QScore program and captured on an additional spreadsheet
3. All data will then be submitted for statistical analysis.

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## V. ETHICS

The protocol will be submitted to the two following ethical bodies for approval:

1. DRC – Reviewed and Approved
2. Human Research Ethics Committee

Note: During the entire research, all patient information will be kept anonymous and confidential. Groote Schuur Folder numbers will be used as patient identifiers during data capturing and questionnaire completion.

## VI. LIMITATIONS

Possible limitations can be expected:

1. Poor participation in questionnaire completion due to socio-economic, accessibility and communication factors
2. Language barrier with English format of questionnaire
3. Potential patient data shortcomings from folders

## VII. FUNDING


- Department of General Surgery Research Fund for patient transportation costs and stationary for questionnaires.


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7. Lord Jesus Christ my Saviour for my strength and all my blessings

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# PART E: ABBREVIATIONS

| | | |
|---|---|---|
| 1. | PROMs: | Patient reported outcome measures |
| 2. | DRC: | Departmental Research Committee |
| 3. | HREC: | Human Ethics Research Committee |
| 4. | GSH: | Groote Schuur Hospital |
| 5. | HRQoL: | Health Related Quality of Life |
| 6. | QL: | Quality of Life |
| 7. | BSE: | Breast Self-Examination |
| 8. | FNA: | Fine Needle Aspiration |
| 9. | ER: | Estrogen Receptor |
| 10. | HER-2: | Human Epidermal Growth Factor Receptor 2 |
| 11. | NSM: | Nipple Sparing Mastectomy |
| 12. | SSM: | Skin Sparing Mastectomy |
| 13. | TM: | Total Mastectomy |
| 14. | TE | Tissue Expander |
| 15. | DTI | Direct-to-implant |
| 16. | LD | Latissimus dorsi |
| 17. | TRAM | Transverse rectus abdominis myocutaneous |
| 18. | DIEP | Deep inferior epigastric artery perforator |
| 19. | BMI | Body mass index ($kg/m^2$) |
| 20. | SSI | Surgical site infection |
| 21. | Et al. | And others |
| 22. | ANOVA | Analysis of Variance |

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# PART F: LIST OF APPENDICES

1. 1.1 University of Cape Town (UCT) HREC Approval letter
   1.2 Amendment of Ethics Approval letter
2. World Journal of Surgery Author Guidelines

# PART G: STRUCTURED LITERATURE REVIEW

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# 1. Objectives and Aims

Objective of the Literature Review

a. Assess the burden of breast cancer in South Africa
b. Explore breast reconstruction research in South Africa
c. Explore the history, forms and outcomes of breast reconstruction techniques
d. Define and examine the need for objective patient reported outcome measures
e. Identify a PROMs tool for example the Breast-Q and evaluate its utilization

Aim of the Study

a. To evaluate patient reported outcome measures (HRQoL and patient satisfaction) in breast cancer patients who received immediate breast reconstruction after mastectomy
b. To determine if there is any statistical correlation between PROMs and their demographics, tumour pathology, procedure of immediate reconstruction, complications of surgery and postoperative care and identify predictors of QoL
c. To compare our findings with international literature

# 2. Literature Search Methods

a. Pubmed, Medline, Google Scholar and PRIMO search engine via the UCT online library website were used to acquire the relevant articles. Only English articles were used.
b. Search words/phrases used:
    i. Breast cancer epidemiology
    ii. South Africa
    iii. Breast reconstruction
    iv. Autologous
    v. Implant based, prosthesis based
    vi. Delayed, Immediate, Immediate-delayed
    vii. Health related quality of life questionnaire
    viii. Patient satisfaction
    ix. Breast-Q
    x. Complications, Outcomes, Predictors
c. Related citations by search engines were used
d. References cited in acquired journal articles were used to broaden search and literature review

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## 3. Interpretation of Literature

### a. Introduction and Epidemiology of Breast Cancer

Breast cancer is the most commonly diagnosed cancer in South African women. According to the National Cancer Registry, breast cancer represents 21,8% of all cancers diagnosed in South African women, roughly 8230 cases per year, making breast cancer a significant contributor to national health statistics.[1] The current lifetime risk for women developing breast cancer is 1:27[1] and has increased from 1:39 in 1993-1995.[2] This might be due to the previous segregated and political fragmented public healthcare system, which excluded large portions of the population from adequate health care and health-related record keeping.[3]

Although the incidence of breast cancer in South Africa has risen, possibly due to improvements in screening, detection and reporting, there is still low breast cancer awareness in many provinces[4]. To date, there is still no official breast cancer screening and prevention programs in South Africa and individual health institutions mostly drive any interventions.[5] Breast self-examination (BSE) was only performed in 9.7- 24% of patients in recent studies[6, 7], which further contributes to lack of breast cancer detection and may impact negatively on the accuracy of incidence data for breast cancer in South Africa.[8]

As a developing country, the burden of disease related to cancer in South Africa will prove to be significant in the coming decades. Fregene et al. estimated a more than two-thirds cancer incidence increase by the year 2020, with the most significant number of female cancers attributable to breast cancer.[9] The average age at which breast cancer is diagnosed has been shown to be younger than developed countries[10, 11], with an age-standardized incidence rate of 33.4 per 100000 women in Southern Africa.[12] Younger women with breast cancer in South Africa have been found to have the same clinical and pathological features of women in developed countries, but more advanced in presentation and poorer outcomes.[13] These facts are concerning for a country burdened by poverty and poor economic growth as treatment according to international evidence-based standards may be challenging.

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## b. Breast Reconstruction in South Africa and Internationally

Throughout South Africa, both in the Private and Public health sector, mastectomy with or without axillary clearance is the mainstay of operative management. With a younger diagnosed population, Breast Conserving Therapy and or Breast Reconstruction after mastectomy are important surgical options for patients.

In South Africa, very little published research exists regarding breast reconstruction surgery. Reconstructive surgery rates and availability differ from institutions and provinces in South Africa. Nel et al. were the first to mention mastectomy as an acceptable form of operative management in 1985. They also concluded that 80% of their post-mastectomy patients were satisfied with their postoperative physical outcome and most women had no further need for breast reconstruction as time progressed.[14]

A prospective study conducted by Panieri et al. in the Western Cape, identified 135 breast cancer patients for loco-regional surgery. Eighty-three of these patients were considered suitable for mastectomy with reconstruction and 51 patients (61%), declined mastectomy and reconstruction with reasons not relating to their age, race, employment or marital status. Only 34 patients (24%) underwent mastectomy with breast reconstruction.[15] Therefore there is a need for South African health institutions in investigating the factors influencing breast reconstruction and providing satisfactory patient-reported outcomes after breast reconstruction.

Breast reconstruction after a mastectomy has become a more prominent means of operative management in the last two decades. Research in the U.S. has shown reconstruction rates increasing from 3.4% to 8.3% over a ten year period[16], but variations from 13.5 to 40% in breast reconstruction rates are common.[17-19] Studies also revealed breast reconstruction is not just influenced by patient factors (i.e. age, race, marital status, ethnicity etc.), but also their breast and plastic surgeon's role in their treatment.[20, 21] Patient factors are usually non-modifiable[22], while referring or primary treating surgeons' lack of knowledge and ambiguity regarding breast reconstruction options, is inadmissible and concerning.[22,23]

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## c. Forms of Breast Reconstruction

Breast reconstruction after a mastectomy has evolved over decades, with multiple advances and improvements in technique and technology. Breast reconstruction in the modern day can either be autologous or implant-based (tissue expander or permanent implant), immediate or delayed.

### i. Implant-based reconstruction

The introduction of the silicone implant in 1963 by Cronin and Gerow, revolutionized not only cosmetic breast surgery but also post-mastectomy breast reconstruction.[24] The procedure involved a delayed insertion of the implant underneath the healed mastectomy flaps. It was only in 1971 when Snyderman and Guthrie successfully inserted a silicone implant under the remaining chest wall skin following mastectomy when immediate breast reconstruction took flight and prevailed for the following decade.[25] Even though silicone implants initiated the modern era of breast reconstruction, it certainly didn't come without its problems. A patient with a more extensive skin deficit after mastectomy, would not benefit from this reconstruction, therefore requiring additional techniques and technology to be developed.

Improving on these basics of silicone implants, Radovan successfully published his results with skin tissue expanders in 1982.[26] His technique involved the gradual expansion of breast skin over six weeks, to accommodate a permanent silicone implant and adequately match the contralateral breast dome. Tissue expanders have dramatically evolved over the last two decades with newer generation tissue expanders being texturized, anatomical in shape, including tabs to secure the expander to the chest wall and integrated ports to improve the ease and comfortability of the expansion process. In 1984, Becker introduced a dual-chamber tissue expander as part of the implant-based reconstruction armamentarium.[27] The expander consisted of an outer shell of silicone with a saline inflatable inner shell. This eliminated the need for a second procedure and concurrently expanded the breast gradually with adequate symmetry.

The advent of the skin-sparing mastectomy (SSM) technique by Toth and Lappert in 1991 escalated the popularity of immediate implant-based or better known as direct-to-implant (DTI) reconstruction tremendously.[28] By preserving skin with the SSM technique, without influencing the oncological safety, a sufficient breast envelope is created that can accommodate an implant with fewer complications and improved patient health-related quality of life and satisfaction.[29] In South Africa, Serrurier et al. successfully performed 488 immediate direct-to-

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implant reconstructions after skin-sparing or wise pattern skin-reducing mastectomies without the use of an acellular dermal matrix.[30] Their overall major complication rate was less than 5%, and only two patients had local recurrences. These findings emphasize why implant-based reconstruction is still the most popular form of reconstruction not just in South Africa, but worldwide.

ii. Autologous Reconstruction

Even though various techniques on autologous breast reconstruction was published as early as the 19th century, the first modern day reconstruction was considered in the late 1970s when the pedicled latissimus dorsi (LD) myocutaneous flap was reintroduced.[31,32] Even though this flap allowed single staged reconstruction procedures, there was the concern that the LD flap is of inadequate volume, thus requiring an implant underneath. To enhance the LD flap's volume for reconstruction, Hokin and Silfverskiold described the extended LD flap in 1987, incorporating more of the subcutaneous fat overlying the LD muscle to achieve a better breast mound, but with a higher incidence of fat necrosis.[33] Although the LD flap underwent various tweaks and improvements with or without an underlying implant and satisfactory results, the donor site morbidity, for example, large scars on the back and prolonged seromas, was significant.

As with implant-based reconstruction, skin sparing mastectomies eliminated large skin defects after mastectomy which led to various autologous harvesting techniques, with fewer donor site morbidity. In 1979, Robbins described the vertical rectus abdominis myocutaneous flap to reconstruct the breast and even though there were various adaptations of the flap, the versatility of abdominal flaps was discovered for breast reconstruction.[34] The Transverse rectus abdominis myocutaneous (TRAM) flap, described in 1982 by Hartrampf and colleagues, became a real workhorse in pedicled autologous breast reconstruction for decades to follow.[35] Its advantages included an autologous tissue reconstruction with adequate volume for symmetrisation leaving an acceptable scar after harvest and concurrently an abdominoplasty. Although early disadvantages of possible arterial and blood supply problems and abdominal weakness were reported, they have become negligible with Taylor's suggestion of strategic delay of the pedicle two weeks before surgery and the used of mesh reconstruction for the abdominal defect.[36,37]

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Free tissue transfer for breast reconstruction has become increasingly popular in the last 2 decades, especially for immediate reconstruction, where fresh recipient vessels can be dissected out for microsurgical anastomosis. Holmstrom was the first to utilize discarded abdominoplasty flaps for the reconstruction of a breast in 1979.[38] After that, authors like Grotting and Arnez published a series of successful breast reconstruction using a free TRAM flap.[39,40] Grotting et al. also concluded that the free TRAM flap had less abdominal complications and fewer flap necrosis due to the limited muscle harvested. Refinements in the free TRAM techniques surfaced which led to the muscle-sparing TRAM (MS-TRAM) being utilized more often, to limit further abdominal morbidity. Even though the MS-TRAM had negligible abdominal donor site morbidity, Allen and Treece refined the technique even more by completely retaining the rectus abdominis muscle at the donor site, thereby giving birth to the deep inferior epigastric artery perforator (DIEP) flap.[41] Other alternatives to the free TRAM includes the superficial inferior epigastric artery (SIEA) flap, superior gluteal artery perforator (S-GAP) flap and the transverse upper gracillis myocutaneous (TUG) flap.[42-44]

iii. Implant-based and Autologous Breast Reconstruction Outcomes

Both implant-based and autologous reconstruction after mastectomy, especially skin-sparing mastectomies remains safe. Whether one option is more reliable than the other, is still controversial and no level 1 evidence exists. For implant-based reconstruction, Mc Carthy et al. stratified risk factors in determining perioperative complications.[45] They found that obesity, smoking, hypertension and age of older than 65 years, were all independent risk factors for complications. Smoking, obesity and hypertension were also associated with a higher risk for reconstructive failure. In autologous reconstruction, Greco et al. found obesity (BMI>30), to be the determining risk factor for infectious and non-infectious complications post-operatively.[46] Frey et al. found that more reconstructive complications occur with direct-to-implant and autologous reconstruction compared to tissue expansion.[47] On the contrary, a systematic review and meta-analysis by Tsoi et al. revealed that implant-based reconstruction has a higher risk of reconstructive failures and surgical site infections (SSI) compared to autologous tissue.[48] More comparative studies will be required to have adequate evidence-based protocols; therefore it is crucial that breast reconstruction units evaluate their outcomes.

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## d. Patient Reported Outcome Measures after breast reconstruction

It is well known that mastectomy for breast cancer is a major psychological stress for patients[49] and that offering breast reconstruction has improved not only physical, but also emotional well-being.[50, 51] In addition, recent studies have shown that post-mastectomy breast reconstruction, whether implant or autologous tissue reconstruction, is oncologically safe[52-54], which makes post-mastectomy reconstruction even more attractive. Patient reported outcome measures (PROMs) have therefore become an extremely valuable tool for assessing patients' perception of quality of surgical care.[55]

The patient reported outcome measures could be regarded as a patient's perception of their surgical outcome. With the increased effort of both breast and plastic surgeons to provide patients with adequate guidance and statistics regarding breast reconstruction, measuring surgical outcome, for example: complications, morbidity and mortality, is no longer adequate.[56] More comprehensive measures are needed, which includes objective patient outcomes.[57]

The Memorial Sloan-Kettering Cancer Centre evaluated 229 quality of life measurement tools. Of the 229, inclusion and exclusion criteria removed 220, including ad hoc, generic, education, oncologic and non-English questionnaires. Some of the major critics with regarding the excluded questionnaires were the lack of validity, reliability and responsiveness concerning psychometric properties. Of the remaining seven questionnaires, six had no proper development invalidity and development with the last questionnaire suffering from significant content limitations. They concluded that a breast surgery questionnaire, should not just undergo full development and validation, but implement measuring tools for the different types of surgery as well.[56]

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## e. The Breast-Q questionnaire and its utilization

A questionnaire, that has proven to be extensively researched, validated and developed to assist in the increasing demand of PRO instruments, is the BREAST-Q©. [55,58,59] The fact that the Breast-Q© incorporates the clinical information of a patient's outcome, makes the Breast-Q© an attractive questionnaire to utilize in clinical trials and improves the communication of patient related issues.[60]

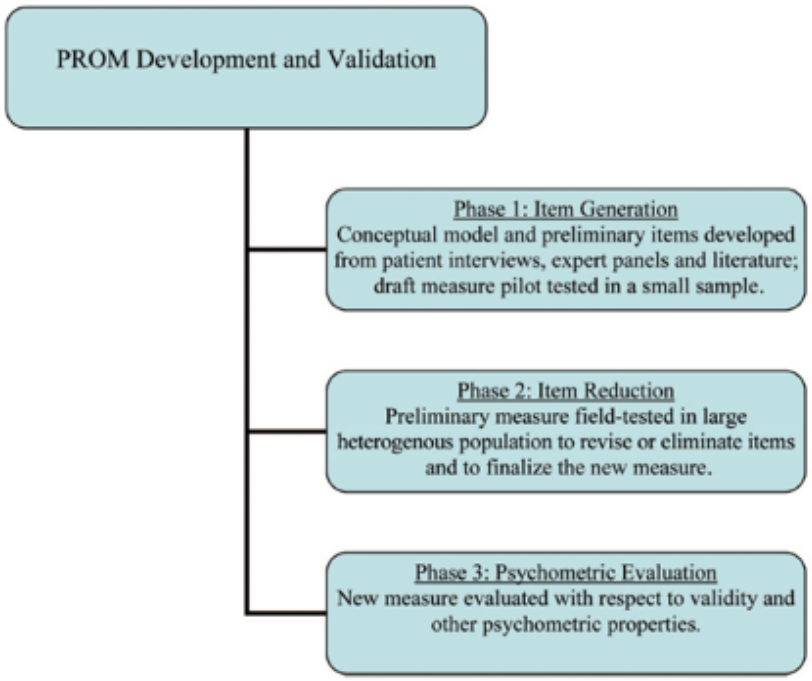


Figure 1: Three-stage approach to patient-reported outcome measure development. (From: Cano S, Klassen A, Pusic A. The Science behind Quality-of-Life Measurement: A Primer for Plastic Surgeons. Plast Reconstr Surg 2009; 123: 98e-106e)

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The Breast-Q© is a patient reported outcome instrument, developed jointly by Memorial Sloan-Kettering Cancer Center and the University of British Columbia. At present, there are 4 BREAST-Q© modules (Augmentation, Reduction, Mastectomy, Reconstruction) each of which comprises multiple scales. A fifth module (the BREAST-Q©: Breast Conserving Therapy module) is currently in development for women undergoing lumpectomy with and without radiation for the treatment of breast cancer.

The overall framework of the BREAST-Q© comprise the following two head domains: HR-QOL (Health related quality of life) and patient satisfaction.

HR-QOL consists of 3 subdomains: physical, psychosocial, and sexual well-being. Patient satisfaction also consists of 3 subdomains: satisfaction with breast, satisfaction with overall outcome and satisfaction with care.[60]

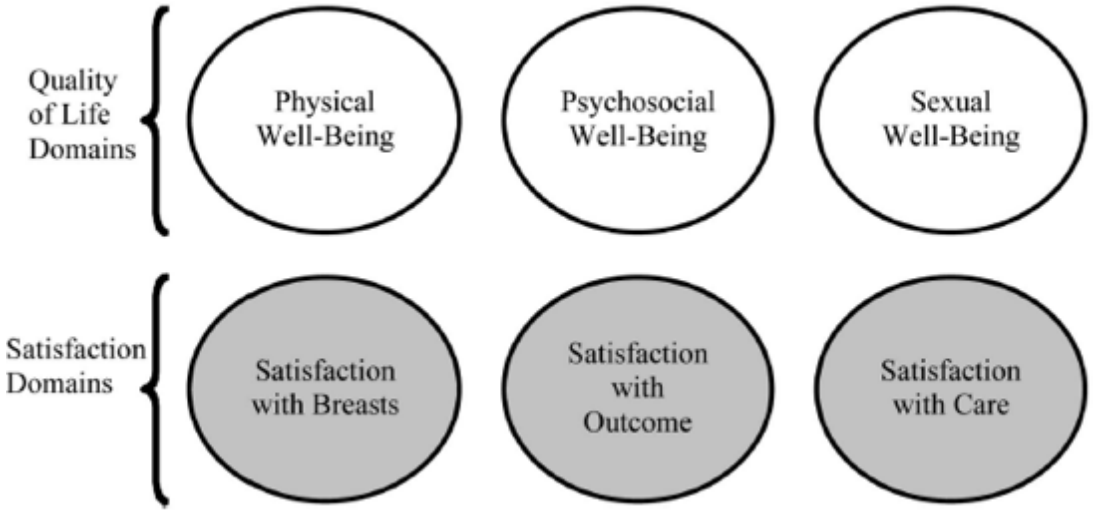


Figure 2. Breast-Q©: Conceptual Framework (From: Pusic A, Klassen A, Scott A, et al. Development of a new patient reported outcome measure for breast surgery: the BREAST-Q©. Plast Reconstr Surg 2009; 124:345–53)

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This well researched and developed conceptual framework of the Breast-Q© has made it a favourite research tool in recent publications.

The UK's National Mastectomy and Breast Reconstruction Audit published in 2011, has been the hallmark of research evaluating PROM's utilizing the Breast-Q©. [61] 150 NHS trusts and 114 independent hospitals in England, as well as six other trusts from Wales and Scotland, submitted data regarding mastectomy and breast reconstruction during the period 1 January 2008 to 31 March 2009. Although the data submission regarding PROM's research was variable, more than 8000 women received a 3- and 18-months post-mastectomy questionnaire. There was an excellent response rate of over 80% at both time intervals. 31% of the study population underwent breast reconstruction, either immediate (21%) or delayed (10%). These national audit results showed that the overall experience of mastectomy and breast reconstruction in the NHS was excellent. It also proved that breast reconstruction had a positive effect on the quality of life when comparing PROM's of mastectomy alone with these of immediate and delayed breast reconstruction in this cohort of patients.[62]

Eltahir et al. found the same results in the Netherlands when they compared women undergoing mastectomy alone with women who underwent breast reconstruction. They found that women

undergoing successful reconstruction, were significantly more satisfied with the appearance of their breasts, fared better psychosocially, sexually and physically, and had been less pain and fewer limitations on physical activity. They also concluded that the Breast-Q© added a large amount of strength to their research as a condition-specific instrument. [63]

Rosson et al. utilized the Breast-Q© questionnaire to evaluate the pre-operative quality of life before immediate, delayed or revision reconstruction. They have found a statistical difference in the quality of life when comparing the revision group to the immediate and delayed group. Therefore, illustrating the magnitude of the effect of unsatisfactory breast reconstruction on the psychological functioning of patients.[64]

The Breast-Q© has also proven to be a valuable tool in assessing the post-operative quality of life when comparing autologous to implant/ expander-based breast reconstruction. A cross-sectional survey by Hu et al. evaluated 219 patients who underwent breast reconstruction during 1988 – 2006. Of the 110 who had implant/expander reconstruction, 92% had saline implants and 90% of the autologous reconstruction group were pedicle flaps. Despite the autologous reconstruction group having a significantly more advanced Stage of Breast Cancer, patient-reported satisfaction seemed to be higher in the more extended post-reconstructive groups (6 – 8 & 8 ≥ years). [65] (Figure 3)

This finding of greater satisfaction with autologous reconstruction has been echoed in studies not utilizing the Breast-Q©. Clough et al. conducted two prospective studies looking at cosmetic outcome after five years in implant and autologous breast reconstruction using a 5-point global scale. Patients who underwent implant reconstruction, independent of which type, had a decreased patient-reported outcome of 86% at two years, to 54% after 5 years. [66] Autologous TRAM reconstructions proved to have a more acceptable patient-reported satisfaction rate with 96.4% at two years and 94.2% at five years. [67] The 5-point global scale is more straightforward than the Breast-Q© but in this instance generated similar results, highlighting the fact that more patient-reported outcome instruments should be researched. However, the Breast-Q©, as patient-reported outcome instrument seems to be gaining universal acceptance.

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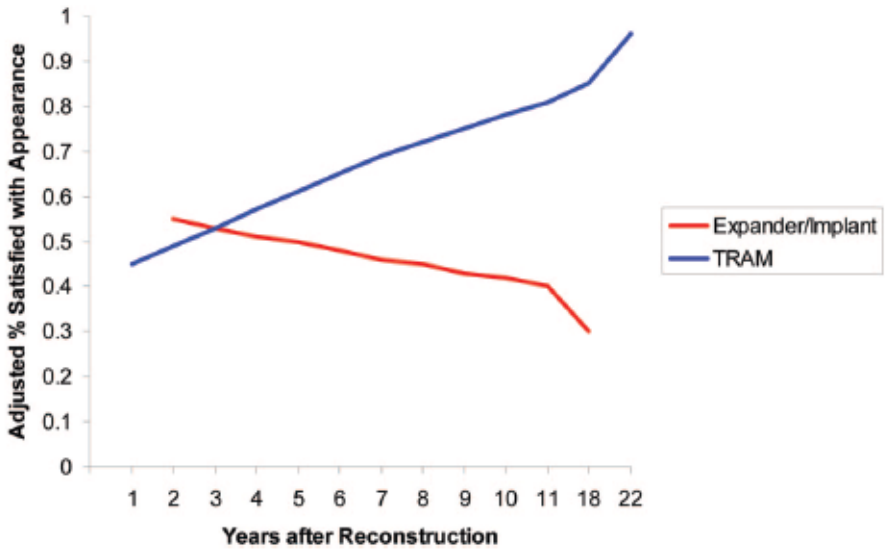


Figure 3: Cross-sectional graph of percentage of satisfaction with reconstructed breast appearance over time, adjusted for age, stage, radiation, unilateral or bilateral procedure, nipple reconstruction and symmetry procedure. (From: Hu et al. Patient-Reported Aesthetic Satisfaction with Breast Reconstruction during the Long-Term Survivorship Period. Past Reconstr Surg 2009: 124: 1-8)

Implant-based reconstruction has been extensively evaluated employing the Breast-Q©, specifically assessing the impact on patient satisfaction of silicone vs saline implants. Macadam et al. conducted a cross-sectional study evaluating 145 responders to the Breast-Q© and EORTC QLQC30 questionnaires evaluating the patient satisfaction after silicon (75 women) and saline (68 women) implants. Mean scores of silicon vs saline using the Breast-Q© was compared and statistical significance even after multivariate linear regression, showed higher satisfaction scores in 4 subscales after silicone implants. The EORTC QLQC30, on the other hand, has shown no statistical difference in the global health when comparing saline and silicone implants.[68] McCarthy et al. found similar findings in their multicentre cross-sectional survey but has also proven as earlier mentioned[66], that patients had decreased satisfaction as time progressed after implant reconstruction. [69]

Zhong et al. utilized the Breast-Q© to evaluate the quality of life post autologous breast reconstruction. Fifty-one women completed the Breast-Q© after DIEP and MS-TRAM flap reconstruction. Results have shown statistically significant satisfaction and clinical meaningful

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reconstruction rates as early as three weeks post-operatively but has demontrated deterioration in abdominal donor site during the first 3 postoperative months.[70]

Reviewing all abovementioned research utilizing the Breast-Q©, its additive value to a Breast Cancer Unit is unquestionable. The fact that all this research was conducted in developed countries with well-organized Breast Cancer Units and adequate funding brings into question the possible utility of PROMs like the Breast-Q© in resource constrained developing countries. It is further not clear what the impact of socio-economic and patient factors i.e. level of education, accessibility to tertiary oncologic care, income etc. might also inhibit or influence the evaluation of the quality of post-operative care in developing countries.

## 4. Conclusion

South Africa has an increased breast cancer burden which is mainly due to improved access to diagnostic services among other factors. With increasing numbers of mastectomies being performed, whether modified radical or skin sparing, there is an increasing need for adequate breast reconstruction modalities, both implant-based and autologous. Although units are performing successful breast reconstructions after mastectomy, there is no data available on patient reported quality of life and postoperative satisfaction in South Africa. We, therefore, identified the need to conduct a research project to evaluate whether PROM tools such as the Breast Q could be used in the public health sector in South Africa and to assess patient satisfaction levels with their breast reconstruction and compare these to international outcomes.

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# Tables

Table 1: Review of International Literature

| Study | Year | Type of Reconstruction | Participants | Psychosocial Well-Being | Sexual Well-Being | Physical Well-Being | Satisfaction with Breast | Satisfaction with Nipples | Satisfaction with Outcome | Satisfaction with Information | Satisfaction with Surgeon | Satisfaction with Medical Team | Satisfaction with Office |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Sugrue et al.[61]** | 2013 | PIBR; TEBR; ABR (Combined) | 30 | - | - | 81 (+/- 13) | - | 92 (+/- 10) | - | 76 (+/- 19) | 83 (+/- 21) | 89 (+/- 19) | 94 (+/- 12) |
| **Eltahir et al.[63]** | 2013 | PIBR; TEBR; ABR (Combined) | 92 | 75.5 (+/- 17.9) | 61.1 (+/- 22.4) | 74.6 (+/- 16.3) | 70.5 (+/- 17.9) | 64.6 (+/- 30.3) | 78.4 (+/- 19.1) | 71 (+/- 15.1) | 90.4 (+/- 15.3) | 86.7 (+/-20.1) | 86 (+/-19.2) |
| **Liu et al.[71]** | 2014 | PIBR; TEBR<br>ABR | 48<br>26 | 75.5 (+/- 17.1)<br>86.1 (+/- 17.4) | 52.1 (+/- 18.6)<br>64.8 (+/- 20.9) | 78.7 (+/- 12.9)<br>79.1 (+/- 15.6) | 64.2 (+/- 12.6)<br>73.5 (+/- 20.8) | -<br>- | 63.3 (+/- 22.1)<br>79.2 (+/- 21.5) | 67.4 (+/- 18.8)<br>80.4 (+/-13.6) | 82.4 (+/- 20.4)<br>95.9 (+/- 10.8) | -<br>- | - |
| **Dean et al.[72]** | 2016 | PIBR; TEBR; ABR (Combined) | 53 (Immediate cohort only) | 73.6 | 56.7 | 73.9 | 66.1 | - | - | - | - | - | - |
| **Pirro et al.[73]** | 2017 | PIBR; TEBR<br>ABR | 34<br>31 | 67.6 (+/- 20.5)<br>73.5 (+/- 10) | 52.7 (+/- 18.5)<br>51.7 (+/- 6.8) | 75.1 (+/- 13.4)<br>67.5 (+/- 9.5) | 59.3 (+/- 11.8)<br>69.1 (+/- 6.2) | 57.5 (+/- 25.6)<br>69.0 (+/- 21.4) | 75.5 (+/- 16.6)<br>91.5 (+/- 10.8) | 66.8 (+/- 16.1)<br>72.1 (+/- 16.5) | 86.9 (+/- 16.8)<br>95.5 (+/- 7.6) | 92.9 (+/ 14.5)<br>80.8 (+/- 20.1) | 90.1 (+/- 16.6)<br>81.5 (+/- 18.0) |
| **Aguiar et al.[74]** | 2017 | PIBR; TEBR | 57 (Recon group) | - | 52 | 77 | 75 | - | - | - | 100 | 100 | - |
| **Pusic et al.[75]** | 2017 | PIBR; TEBR<br>ABR | ~783<br>~383 | 71.8 (+/- 19)<br>74.7 (+/- 19.2) | 53 (+/- 21.2)<br>55.4 (+/- 19.8) | 76.7 (+/- 14.5)<br>74.9 (+/- 15.1) | 64.0 (+/- 16.8)<br>67.8 (+/- 17.2) | - | - | - | - | - | - |
| **Santosa et al.[76]** | 2018 | PIBR; TEBR<br>ABR | 1490<br>523 (at 1 year) | 71.8 (+/- 19.3)<br>74.7 (19.3) | 52.7 (+/- 21.1)<br>55.5 (+/- 20.6) | 76.0 (+/- 14.6)<br>74.9 (+/- 15.1) | 63.1 (+/- 17.4)<br>68.6 (+/-17) | - | - | - | - | - | - |
| **Cereijo-Garea et al.[77]** | 2018 | PIBR; TEBR; ABR (Combined | 101 | 75.3 (+/- 19.5) | 63.4 (+/- 23.7) | 70.4 (+/- 16.8) | 60.8 (+/- 18.8) | 71.3 (+/- 24.4) | 75.3 (+/- 20.2) | 74 (+/- 19.1) | 95.0 (+/- 10.4) | 96.3 (+/- 10.8) | 97.5 (+/- 7.8) |
| **Yoon et al.[78]** | 2018 | PIBR; TEBR; ABR (Combined | ~1056 (Immediate cohort only) | 74.4 (+/- 19) | 54.8 (+/- 21.4) | 76.3 (+/- 14.8) | 65.1 (+/- 18.1) | - | - | - | - | - | - |

Abbreviations: PIBR= Permanent implant breast reconstruction; TEBR= Tissue expander breast reconstruction; ABR= Autologous breast reconstruction

# PART H: JOURNAL ARTICLE

## Patient reported outcome measures (PROMs) in breast cancer patients after immediate breast reconstruction using the Breast-Q.


| | |
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**Abstract**

**Background**

Mastectomy is the mainstay of surgical treatment for women with breast cancer in South Africa. The increase in breast reconstruction after a mastectomy has prompted the need to evaluate patient reported outcome measures (PROMs) for this set of operative intervention. This study aimed to assess clinical and patient reported outcome measures in immediate breast reconstruction patients using the BREAST-Q and compare these with international cohorts.

**Methods**

A cross-sectional study was performed on all patients who underwent immediate breast reconstruction between January 2011 and December 2016. This consisted of a retrospective clinical record review of perioperative outcomes, and a quality of life analysis using the BREAST-Q Post-Reconstruction questionnaire. Outcome predictors were identified using Chi-square, Fisher exact, One-way ANOVA, Student t-tests and Kruskal Wallis analysis of variance. A random-effect single arm meta-analysis was performed to compare the BREAST-Q scores with international cohorts.

**Results**

A total of 52 patients were included with a mean age of 43.2 (+/-9.5) years. Eighteen patients (34.6%) developed early complications; of these 8 (44.4%) were major. Thirty-one patients (59.6%) developed late complications; of these 18 (58.1%) were major. Fifteen patients (28.8%) had failed reconstruction. There was a significantly higher risk of failure following a total mastectomy (TM) ($p=0.02$), tissue expander reconstruction (TE) ($p<0.01$) and stage 2 breast cancer ($p=0.01$). Patients who underwent nipple reconstruction and immediate-delayed

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reconstruction before 12 months, reported higher well-being and satisfaction scores. Compared to international cohorts our BREAST-Q scores were lower but fall within the 95% confidence interval for Sexual Well-Being and Satisfaction with Nipples and Care.

**Conclusion**

Immediate breast reconstruction poses a high risk of complications and reconstructive failure especially, with TM and TE. Our BREAST-Q scores are comparable to international studies and may be useful in guiding patient consent.

**Introduction**

Breast cancer is the most common cancer among South African women [1]. As in other developing countries [2, 3], South African women with breast cancer present at an earlier age and with more advanced disease [4]. Mastectomy, whether total, skin-sparing or nipple sparing, with or without axillary clearance, remains the mainstay of surgical treatment in South Africa. While breast reconstruction is performed in both the private health sector and to a lesser extent, the public health sector, there is limited published data on breast reconstruction after breast cancer surgery in South Africa. In 2003, Panieri et al. showed that factors other than demographics influence the patient's decision to undergo reconstruction after mastectomy, some of these include the choice of a more straightforward procedure, religious reasons, old age and regarding breast appearance as unimportant [5]. Primary physician and surgeon's lack of knowledge and ambiguity towards breast reconstruction have also been identified as important factors in patient selection for breast reconstruction [6, 7].

Internationally, with increasing numbers of bilateral mastectomies, breast reconstruction rates, in particular, implant-based reconstruction, are rising [8]. This has prompted the

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development of tools to objectively evaluate clinical and patient reported outcome measures such as post-operative complications, quality of life and patient satisfaction [9, 10]. While many tools and questionnaires have been developed [11], the BREAST-Q questionnaire jointly developed by Memorial Sloan-Kettering Cancer Centre and the University of British Columbia has been widely utilized by national health systems and health institutions not only to illustrate the favourable outcome of breast reconstruction compared to mastectomy alone, but also comparing different forms of breast reconstruction at different intervals [12-19].

In South Africa, while access to breast reconstruction is limited, large tertiary centre breast units have a careful multidisciplinary team selection process to identify suitable patients. As surgical resources are under tremendous pressure, this selection process is critical to ensure the best possible use of surgical services. Quality of life (QoL) and satisfaction after breast reconstruction data should be part of this process, but to date, there is no published data on patient reported outcome measures in South Africa.

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**Material and Methods**

Inclusion Criteria:

A cross-sectional study was conducted consisting of a retrospective clinical record review of all patients (aged 18 and above) who underwent a mastectomy with immediate breast reconstruction between 1 January 2011 to 31 December 2016. The patients were all managed by a single surgical unit, based at Groote Schuur Hospital, a large teaching, tertiary referral hospital, in Cape Town, South Africa, serving primarily uninsured patients. All patient information were included in the retrospective record review and only the patients who completed the BREAST-Q was included in the BREAST-Q analysis. Patients also had to be at least 1 year after their final reconstruction surgery.

Exclusion Criteria:

Patients with incomplete data sets or whom rejected informed consent, were excluded from the study.

The following data were collected: demographics, presenting complaint, mode of diagnosis, type (total, skin sparing or nipple sparing) and laterality of mastectomy with or without nodal clearance, type of reconstruction, tumour characteristics, staging of breast cancer, adjuvant therapy, complications, re-operations, the outcome of final reconstruction and survival. Complications were divided in early (<2weeks) and late complications (>2weeks), as well as minor (not requiring admission or surgery i.e. surgical site infection requiring antibiotics) and major (requiring admission or surgery, i.e. skin flap necrosis requiring debridement or explant of the prosthesis). Reconstructive failure included implant or expander explant without re-insertion or complete autologous flap necrosis/loss.

The BREAST-Q Post-Reconstruction questionnaire was then administered to all patients in the cohort either in person or by email. The BREAST-Q Post-Reconstruction Module, measures health-related quality of life (HRQoL) after breast reconstruction following mastectomy within 6 domains: (1) psychosocial well-being, (2) physical well-being, (3) sexual well-being, (4) satisfaction with breasts, (5) satisfaction with outcome, and (6) satisfaction with care. BREAST-Q questionnaire responses were entered into a preconfigured Excel spreadsheet and converted to a score of 0 – 100, using Qscore which was developed according to the Rasch model. The higher the score, the higher the HRQoL. As a comparator for these scores, we reviewed ten comparable studies which reported PROMs for an implant or autologous breast reconstruction using the BREAST-Q Post-Reconstruction module. The mean BREAST-Q scores for each domain reported was tabled for comparison.

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**Statistical Analysis**

The demographic, clinical variables and clinical outcomes were reported using mean (±Standard Deviation) for numerical variables and proportions for the categorical variables. Outcomes of Quality of Life (QoL) numerical variables were reported as mean (±Standard Deviation) since they were normally distributed for the different clinical characteristics. The group differences in categorical variables were tested using Chi-square tests, or Fisher exact tests when group numbers were small (expected frequency <5 in any cell) and the large number assumption for Chi-square tests were not met. Analysis of variance (One-way ANOVA) or Student t-tests (equal/unequal variance) was used for continuous, normally distributed variables. Kruskal Wallis analysis of variance; a non-parametric test, was used for variables that were not normally distributed. To test the strength of association between numerical variables, Pearson correlation coefficients/coefficient of determination ($r/r^2$) were reported. A p-value of ≤0.05 was used as the threshold for statistical significance. To compare the BREAST-Q means of our study with international literature, we conducted a random-effect single arm meta-analysis of the mean scores.

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**Ethics**

Approval was obtained from the Human Research Ethics Committee of the Faculty of Health Sciences of the University of Cape Town. HREC 528/2014.

**Results**

**Baseline Characteristics**

Fifty-four patients underwent immediate breast reconstruction after mastectomy from 1 January 2011 to 31 December 2016 (Table 1). Two patients were excluded due to lack of data. The mean age of patients was 43.2 (+/-9.5) years. Twenty-six patients (50%) had total

mastectomies (TM), 26 (50%) had skin-sparing mastectomies (SSM) and none had nipple sparing mastectomies (NSM). Thirty-three patients (63.5%) had tissue expander (TE) reconstruction, 15 patients (28.8%) had immediate implant reconstruction and 4 patients (7.7%) had autologous reconstruction. Only 13 patients (25%) had nipple-areola reconstruction. The majority of patients presented with invasive ductal carcinoma (73.1%); 77% of these were in earlier stages (Stage 0 – 2). Adjuvant treatment consisted of radiotherapy in 22 (42.3%), chemotherapy in 32 (61.5%) and hormonal therapy in 30 (57.7%) patients respectively. All Stage 3 patients received neoadjuvant chemotherapy. 82.7% of the patients are alive free of disease, 7.7% are documented to have a recurrence and 9.6% died. Of the 5 patients whom died, one had stage 2 and four had stage 3 disease and all deaths were breast cancer related.

**Post-Reconstruction Complications**

Eighteen patients (34.6%) developed early complications; of these 8 (44.4%) were major. Thirty-one patients (59.6%) presented with late complications; of these 18 (58.1%) were major. Of the patients with major late complications, 12/18 (66.7%) had no early complications, 4/18 (22.2%) had minor early complications and only 2/18 (11.1%) had early major complications. There was no statistical significance between the early complication groups for all variables. There was however a higher distribution of major early complications with unilateral mastectomy (87.5%), TE reconstruction (62.5%), Stage 1 breast cancer (37.5%) and chemotherapy (62.5%) (Table 2a).

There was a statistically significant difference (p=0.03) for late complications groups when a unilateral mastectomy was performed. There was a higher distribution of major late complications with unilateral mastectomy (61.1%), TM (66.7%), TE reconstruction (72.2%),

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absence of contralateral procedure (61.1%), Stage 2 breast cancer (55.6%), Chemotherapy (55.6%) and Hormonal Therapy (66.7%), though these did not reach statistical significance (Table 2b).

**Final Outcome of Reconstruction** (Table 2c)

Fifteen patients (28.8%) had failed post-mastectomy breast reconstruction. Most of these (12/15 -80%) resulted from major late complications. The primary reason for reconstruction failure was wound dehiscence in 7 patients, infections in 6, cancer recurrence in 1, and mechanical failure in one further case.. There was a statistically significant higher risk for reconstructive failure associated with TM ($p=0.02$), expander reconstruction ($p<0.01$) and stage 2 breast cancer ($p=0.01$). There was also a higher distribution of failed reconstructions for unilateral mastectomy (60%), nodal clearance (53.3%), the absence of contralateral procedure (66.7%), radiotherapy (66.7%), chemotherapy (73.3%) and hormonal therapy (60%). Of the patients who died, four out of five had expander reconstructions and one autologous reconstruction. All four expander reconstructions failed.

**BREAST-Q response distribution, predictors of HRQoL and meta-analysis**

Thirty-six patients completed the BREAST-Q post-reconstruction module (response rate of 75%), excluding five cancer related deaths. Sixteen patients completed the Breast-Q via email and twenty patients completed it in person. The mean scores for each domain are depicted in Fig.1. The BREAST-Q responses correlating to the clinical variables are depicted in Table 3. Predictors for better Psychosocial Well-Being included nipple reconstruction ($p=0.05$) and the absence of hormonal therapy ($p=0.01$). Predictors for better Sexual Well-Being included SSM ($p=0.03$), absence of nodal clearance ($p=<0.01$), nipple reconstruction ($p=0.05$), earlier stage breast cancer ($p=0.04$), absence of radiotherapy ($p=0.01$) and

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hormonal therapy (p<0.01), and immediate-delayed breast reconstruction within 12 months (p=0.01). Unilateral mastectomy with prophylactic contralateral mastectomy was the only predictor for better Physical Well-Being (p=0.03). Predictors for higher Satisfaction with Breast was nipple reconstruction (p=0.04) and predictors for higher Satisfaction with Outcome was the absence of early complications (p=0.04) and immediate-delayed breast reconstruction within 12 months (p=<0.01).

Table 4 outlines the BREAST-Q scores of 11 studies, ours included, assessing implant-based and autologous breast reconstruction either combined or independently. Only three studies including ours assessed all domains of the BREAST-Q. When compared to the meta-analysis model, our scores are slightly lower for each domain but fall within the 95% CI for Sexual Well Being, Satisfaction with Nipples, Satisfaction with Information and Satisfaction with Office personnel (Fig. 2).

**Discussion**

Mastectomy, whether total, skin sparing or nipple sparing, has a major psychological impact on a patient's life [20]. Breast reconstruction following mastectomy improves not only physical, but also emotional well-being [21]. Recent studies confirmed that post-mastectomy breast reconstruction, whether autologous or implant-based, is oncologically safe. This has led to a significant increase in breast reconstruction worldwide [22]. However, although breast reconstruction may improve patients' HRQoL, outcomes are variable and major complications are common.

With the increasing effort of both breast and plastic surgeons to provide patients with adequate guidance and statistics regarding breast reconstruction, only measuring surgical

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outcomes (complications, morbidity and mortality), is no longer adequate [11]. More comprehensive measures are needed, including objective patient outcome assessments [23]. By evaluating these PROMs, predictors of QoL can be identified and communicated to patients, to assist in their post-mastectomy reconstructive plan.

Implant-based reconstruction with tissue expander as preferred method remains the most common form of breast reconstruction in the USA [24]. This finding is confirmed in our study with 63.5% of patients undergoing TE. Although implant-based reconstruction is relatively simple, with no donor site morbidity and more rapid recovery, major complications have been reported in up to 46% of patients [25]. In our study population, 15.7% and 36.4% respectively developed major early and late complications. Of concern to us was the fact that 66.7% of patients with major late complications, had no early complications, which could be due to underreporting or missed early complications and needs to be addressed in our post-operative care.

Although early complications (<2 weeks) are usually indicative of possible technical challenges during surgery, major late complications (>2 weeks) remains the primary predictor of reconstructive failure as seen in our cohort. Contradictory to Roostaien et al. our tissue expander patients presented with more major complications compared to immediate implants [26]. This could be attributed to higher rates of nodal clearance, perioperative chemotherapy and hormonal therapy in the TM patients in our cohort. While multiple studies found no overall differences in complications when it came to the type of mastectomy and perioperative chemotherapy, our research proves otherwise [27, 28]. Regarding nodal clearance and perioperative hormonal therapy (Tamoxifen), our study confirms an increased risk of complications as shown in other studies [29, 30]. Interestingly, unilateral vs bilateral

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mastectomy was the only variable which predicted an increased risk of late complications (p=0.03) A single other study by Jagsi et al. has shown an increased risk for infections in the first two years for patients undergoing unilateral mastectomy and reconstruction [31].

Complications increase morbidity throughout the reconstruction process, but the outcome of the final reconstruction rests on implant success or failure. In our study, fifteen patients (28.8%%) had failed breast reconstruction post-mastectomy of which 12 were TE and three immediate implants. Even though this is higher than the 20% reported by Momoh et al. [32], one patient had tissue expander mechanical failure and elected not to proceed further while another had tissue expander explant due to recurrence. The majority of our patients had explants due to infection or wound-related complications, which is in keeping with other studies [33, 34]. TE reconstruction (p<0.01), TM (p=0.02) and Stage 2 breast cancer (p=0.02) were statistically significant predictors for implant failure. A smaller skin envelope and thinner mastectomy flaps with TM may raise the risk for infectious and wound complications and thereby implant failure [35]. Furthermore, the fact that our cohort mortalities had a higher stage disease and failed reconstruction was associated only with expanders, either delayed, or no reconstruction should rather be offered. Worth reporting, although not statistically significant is the presence of perioperative radiotherapy in 66.7% of our failed reconstruction patients, as radiation significantly increases failure rates in implant-based reconstruction [36].

The overall response rate for the completion of the BREAST-Q was 75% which is lower than other studies which reported over 80% response rates [16, 37]. This may be due to the overall poor clinical follow up, prohibitive transport costs for patients and difficulty making contact telephonically or via email in a resource-constrained health context. Very few studies have

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identified clear predictors for QoL after breast reconstruction. Matthews et al. determined the type of reconstruction as a predictor for Satisfaction with Outcome with DIEP reconstruction being favoured and psychological well-being a key predictor for Satisfaction with Breast [38]. In contrast, our study found that only nipple reconstruction increased Satisfaction with Breast appearance, an association which has been reported in other studies [39]. The absence of early complications and TE reconstruction completed within 12 months had the highest Satisfaction with Outcome in our research. As waiting times are exceptionally long in our clinical service, a correlation of satisfaction with earlier reconstruction may assist in motivating for earlier surgical dates.

When evaluating well-being as a domain for HRQoL after breast reconstruction, Cereija-Garea et al. provided a comprehensive study of associations with multiple variables [40]. The variables associated with the worst quality of life for Physical Well-Being was SSM and lymphedema, while immunotherapy accounted for the worst scores on Sexual and Psychosocial Well-Being. In our study, bilateral risk-reducing mastectomies predicted worst Physical Well-being scores regardless of the type of mastectomy. TM, nodal clearance, the absence of nipple reconstruction, later stage breast cancer, perioperative radiotherapy and failed reconstruction, resulted in lower Sexual Well-Being scores. Our finding of poorer Sexual Well-Being scores for patients who had undergone nodal clearance and perioperative radiotherapy coincides with other literature [40, 41]. However, hormonal therapy, which predicted poor Sexual and Psychosocial Well-Being in our study was found to have little impact on QoL by Schover et al. [42].

To date, only one meta-analysis using the BREAST-Q has been performed, comparing autologous versus implant-based reconstruction [43]. In this meta-analysis, Basta et al.

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concluded that both options have high scores for satisfaction and well-being, but autologous breast reconstruction demonstrated significantly higher scores. As we conducted a single arm meta-analysis model combining both implant-based and autologous reconstruction, we cannot comment on the difference between them, but confirm that our model's BREAST-Q scores are similar to other studies [14, 37, 40, 44-50].

**Limitations and Weaknesses**

The size of this cohort is a significant limitation and has impacted on the significance of some of the findings. This small size is due to difficult access to theatre time to perform larger numbers of reconstructions and also due to unobtainable and incomplete clinical records limiting the number of patients included. Although some patients completed the BREAST-Q by email and not in person, validity studies has shown no bias in the completion method [10]. The BREAST-Q questionnaire has not specifically been validated in our socioeconomic context and was not translated for this study which may have influenced the responses. There are also substantially more implant-based reconstructions, than autologous, which will skew the BREAST-Q score analysis.

**Conclusion**

Immediate breast reconstruction post-mastectomy, while desirable for many patients, carries a high risk of major complications and implant failure. Tissue expander reconstruction remains the mainstay of implant-based reconstruction but is associated with higher major complications rates and reconstructive failure especially with TM, later staged breast cancers and perioperative radiotherapy. This has influenced our unit's selection criteria for immediate reconstruction by selecting younger patients with early stage breast cancer and without the need for perioperative radiotherapy. The BREAST-Q has potential as a tool to evaluate HRQoL

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and predictors of improved outcomes which can be used to guide patients in their decision making. Comparable BREAST-Q scores with international cohorts confirm the feasibility of these studies in developing countries. However further robust prospective research evaluating HRQoL in South African breast reconstruction patients is necessitated, especially evaluating autologous and implant-based reconstruction independently and in comparison with greater cohort numbers.

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## Tables and Figures

**Table 1.** Baseline characteristics of the study population (N=52)

| Characteristic | Distribution |
|---|---|
| Age at surgery (years), mean (±SD) | 43.2 (9.5) |
| Presenting Complaint, n (%) | |
| Lump | 46 (88.6) |
| BRCA 1/2 mutation | 2 (3.8) |
| Nipple discharge | 2 (3.8) |
| Skin changes | 2 (3.8) |
| Breast Affected, n (%) | |
| Left | 26 (50) |
| Right | 24 (46.2) |
| Bilateral | 2 (3.8) |
| Mode of Diagnosis (Imaging), n (%) | |
| Mammogram | 28 (53.9) |
| Mammogram / Ultrasound | 24 (46.1) |
| Mode of Diagnosis (Laboratory), n (%) | |
| FNA | 2 (3.9) |
| FNA/Core Biopsy | 31 (59.6) |
| Incisional/Excisional biopsy | 2 (3.8) |
| Core Biopsy | 15 (28.8) |
| N/A | 2 (3.9) |
| Laterality of Mastectomy, n (%) | |
| Bilateral risk reducing | 2 (3.8) |
| Unilateral | 38 (73.1) |
| Unilateral therapeutic and contralateral prophylactic | 12 (23.1) |
| Type of Mastectomy, n (%) | |
| Total | 26 (50) |
| Skin sparing | 26 (50) |
| Nipple sparing | 0 (0) |
| Axillary Nodal Clearance, n (%) | 25 (48.1) |
| Type of Reconstruction, n (%) | |
| Expander | 33 (63.5) |
| Implant | 15 (28.8) |
| Autologous | 4 (7.7) |
| Contralateral Symmetrizing Procedure, n (%) | |
| Reduction/Mastopexy | 19 (36.5) |
| None | 33 (63.5) |

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| | |
|---|---|
| Nipple Reconstruction, n (%) | 13 (25) |
| Histological Type of Breast Cancer, n (%) | |
| DCIS/ LCIS/ Paget's | 10 (19.2) |
| Invasive Ductal | 40 (77) |
| N/A (BRCA patients) | 2 (3.8) |
| Estrogen Receptor, n (%) | |
| ER Positive | 32 (61.5) |
| ER Negative | 18 (34.6) |
| N/A | 2 (3.9) |
| HER2 Receptor, n (%) | |
| HER2 Positive | 21 (40.4) |
| HER2 Negative | 29 (55.7) |
| N/A | 2 (3.9) |
| Tumour Stage, n (%) | |
| T0 (BRCA patients) | 2 (3.8) |
| Tis | 10 (19.2) |
| T1 | 13 (25) |
| T2 | 21 (40.4) |
| T3 | 2 (3.9) |
| T4 | 4 (7.7) |
| Nodal Stage, n (%) | |
| N0 | 27 (51.9) |
| N1 | 17 (32.7) |
| N2 | 3 (5.7) |
| N3 | 5 (9.6) |
| Metastasis Stage (M0), n (%) | 52 (100) |
| Anatomic Stage of Breast Cancer, n (%) | |
| Stage 0 | 12 (23.1) |
| Stage 1 | 8 (15.4) |
| Stage 2 | 20 (38.4) |
| Stage 3 | 12 (23.1) |
| Radiotherapy, n (%) | 22 (42.3) |
| Chemotherapy, n (%) | 32 (61.5) |
| Hormonal Therapy, n (%) | 30 (57.7) |
| Early Complications (<2 weeks), n (%) | |
| Major | 8 (15.4) |
| Minor | 10 (19.2) |
| None | 34 (65.4) |

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| | |
|---|---|
| Late complications (>2 weeks), n (%) | |
| Major | 18 (34.6) |
| Minor | 13 (25) |
| None | 21 (40.4) |
| Reoperations, n (%) | |
| None | 8 (15.4) |
| 1-2 operations | 38 (73.1) |
| >2 operations | 6 (11.5) |
| Outcome of Final Reconstruction, n (%) | |
| Failed | 15 (28.9) |
| Immediate | 14 (26.9) |
| Immediate delayed (<12 months) | 5 (9.6) |
| Immediate delayed (>12 months) | 18 (34.6) |
| Survival / Recurrence, n (%) | |
| Alive/ Recurrence | 4 (7.7) |
| Alive/ Remission | 43 (82.7) |
| Died | 5 (9.6) |

Abbreviations: BRCA= Breast cancer gene; DCIS / LCIS= Ductal / Lobular carcinoma in situ; ER= Estrogen receptor; PR= Progesterone receptor; HER= Human epidermal growth factor

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**Table 2a.** Distribution of early complications in study population **(n=52)**

| Characteristic | None (n=34) | Minor (n=10) | Major (n=8) | p-value |
|---|---|---|---|---|
| Age at Surgery (years), mean (±SD) | 42.3 (9) | 43 (11.6) | 47.4 (8.7) | 0.40 |
| Laterality of Mastectomy, n (%) | | | | |
| Bilateral risk reducing | 1 (2.9) | 0 | 1 (12.5) | 0.28 |
| Unilateral | 23 (67.7) | 8 (80) | 7 (87.5) | |
| Unilateral therapeutic and contralateral prophylactic | 10 (29.4) | 2 (20) | 0 | |
| Type of Mastectomy, n (%) | | | | |
| Modified radical | 17 (50) | 5 (50) | 4 (50) | 1.00 |
| Skin sparing | 17 (50) | 5 (50) | 4 (50) | |
| Axillary Nodal Clearance, n (%) | 16 (47.1) | 7 (70) | 2 (25) | 0.19 |
| Type of Reconstruction, n (%) | | | | |
| Expander | 22 (64.7) | 6 (60) | 5 (62.5) | 0.98 |
| Implant | 9 (26.5) | 3 (30) | 3 (37.5) | |
| Autologous | 3 (8.8) | 1 (10) | 0 | |
| Contralateral Symmetrizing Procedure, n (%) | | | | |
| Reduction/Mastopexy | 9 (26.5) | 6 (60) | 4 (50) | 0.10 |
| None | 25 (73.5) | 4 (40) | 4 (50) | |
| Anatomic Stage of Breast Cancer, n (%) | | | | |
| Stage 0 | 9 (26.5) | 1 (10) | 2 (25) | 0.50 |
| Stage 1 | 4 (11.8) | 1 (10) | 3 (37.5) | |
| Stage 2 | 14 (41.2) | 4 (40) | 2 (25) | |
| Stage 3 | 7 (20.6) | 4 (40) | 1 (12.5) | |
| Radiotherapy, n (%) | 15 (44.1) | 5 (50) | 2 (25) | 0.53 |
| Chemotherapy, n (%) | 20 (58.8) | 7 (70) | 5 (62.5) | 0.81 |
| Hormonal Therapy, n (%) | 18 (52.9) | 8 (80) | 4 (50) | 0.28 |

*Statistically significant differences ($p<0.05$)

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**Table 2b.** Distribution of late complications in study population **(n=52)**

| Characteristic | None (n=21) | Minor (n=13) | Major (n=18) | p-value |
|---|---|---|---|---|
| Age at Surgery (years), mean (±SD) | 45.2 (10.2) | 42.1 (8.3) | 41.7 (9.5) | 0.45 |
| Laterality of Mastectomy, n (%) | | | | |
| Bilateral risk reducing | 0 | 2 (15.4) | 0 | ***0.03**** |
| Unilateral | 19 (90.5) | 8 (61.5) | 11 (61.1) | |
| Unilateral therapeutic and contralateral prophylactic | 2 (9.5) | 3 (23.1) | 7 (38.9) | |
| Type of Mastectomy, n (%) | | | | |
| Modified radical | 9 (42.9) | 5 (38.5) | 12 (66.7) | 0.22 |
| Skin sparing | 12 (57.1) | 8 (61.5) | 6 (33.3) | |
| Axillary Nodal Clearance, n (%) | 9 (42.9) | 7 (53.9) | 9 (50) | 0.81 |
| Type of Reconstruction, n (%) | | | | |
| Expander | 14 (66.7) | 6 (46.2) | 13 (72.2) | 0.24 |
| Implant | 6 (28.6) | 4 (30.8) | 5 (27.8) | |
| Autologous | 1 (4.8) | 3 (23.1) | 0 | |
| Contralateral Symmetrizing Procedure, n (%) | | | | |
| Reduction/Mastopexy | 9 (42.9) | 3 (23.1) | 7 (38.9) | 0.51 |
| None | 12 (57.1) | 10 (76.9) | 11 (61.1) | |
| Anatomic Stage of Breast Cancer, n (%) | | | | |
| Stage 0 | 5 (23.8) | 4 (30.8) | 3 (16.7) | 0.53 |
| Stage 1 | 5 (23.8) | 1 (7.7) | 2 (11.1) | |
| Stage 2 | 5 (23.8) | 5 (38.5) | 10 (55.6) | |
| Stage 3 | 6 (28.6) | 3 (23.1) | 3 (16.7) | |
| Radiotherapy, n (%) | 7 (33.3) | 7 (53.9) | 8 (44.4) | 0.49 |
| Chemotherapy, n (%) | 16 (76.2) | 6 (46.2) | 10 (55.6) | 0.18 |
| Hormonal Therapy, n (%) | 9 (42.9) | 9 (69.2) | 12 (66.7) | 0.20 |

*Statistically significant differences ($p<0.05$)

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**Table 2c.** Distribution of Outcome of Final Reconstruction in study population **(n=52)**

| Characteristic | Failed (n=15) | Immediate (n=14) | Immediate delay <12 months (n=5) | Immediate delay >12 months (n=18) | p-value |
|---|---|---|---|---|---|
| Age at Surgery (years), mean (±SD) | 40.2 (10.9) | 43.6 (10.1) | 44.8 (4.1) | 44.9 (8.8) | 0.53 |
| Laterality of Mastectomy, n (%) | | | | | |
| Bilateral risk reducing | 0 | 2 (14.3) | 0 | 0 | 0.11 |
| Unilateral | 9 (60) | 11 (78.6) | 5 (100) | 13 (72.2) | |
| Unilateral therapeutic and contralateral | 6 (40) | 1 (7.1) | 0 | 5 (27.8) | |
| Type of Mastectomy, n (%) | | | | | |
| Modified radical | 11 (73.3) | 3 (21.4) | 4 (80) | 8 (44.4) | ***0.02**** |
| Skin sparing | 4 (26.7) | 11 (78.6) | 1 (20) | 10 (55.6) | |
| Type of Reconstruction, n (%) | | | | | |
| Expander | 12 (80) | 0 | 5 (100) | 16 (88.9) | ***<0.01**** |
| Implant | 3 (20) | 10 (71.4) | 0 | 2 (11.1) | |
| Autologous | 0 | 4 (28.6) | 0 | 0 | |
| Axillary Nodal Clearance, n (%) | 8 (53.3) | 3 (21.4) | 3 (60) | 11 (61.1) | 0.13 |
| Contralateral Symmetrizing Procedure, n (%) | | | | | |
| Reduction/Mastopexy | 5 (33.3) | 6 (42.9) | 2 (40) | 6 (33.3) | 0.95 |
| None | 10 (66.7) | 8 (57.1) | 3 (60) | 12 (66.7) | |
| Anatomic Stage of Breast Cancer, n (%) | | | | | |
| Stage 0 | 3 (20) | 7 (50) | 0 | 2 (11.1) | ***0.01**** |
| Stage 1 | 1 (6.7) | 4 (28.6) | 1 (20) | 2 (11.1) | |
| Stage 2 | 6 (40) | 0 | 2 (40) | 12 (66.7) | |
| Stage 3 | 5 (33.3) | 3 (21.4) | 2 (40) | 2 (11.1) | |
| Radiotherapy, n (%) | 10 (66.7) | 3 (21.4) | 2 (40) | 7 (38.9) | 0.10 |
| Chemotherapy, n (%) | 11 (73.3) | 5 (35.7) | 4 (80) | 12 (66.7) | 0.57 |
| Hormonal Therapy, n (%) | 9 (60) | 6 (42.9) | 2 (40) | 13 (72.2) | 0.32 |

*Statistically significant differences ($p<0.05$)

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**Table 3.** Distribution of BREAST-Q outcomes and study population characteristics (N=36)

| | WBPsy | | WBS | | WBPhy | | SBreast | | SOut | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | p-value | | p-value | | p-value | | p-value | | p-value |
| Age at Surgery, $r^2$ (%) | 0.4 | 0.72 | 0.04 | 0.89 | 2.3 | 0.37 | 4.4 | 0.22 | 1.0 | 0.58 |
| Laterality of Mastectomy, mean (±SD) | | | | | | | | | | |
| Bilateral risk reducing | 88 (17) | 0.18 | 90 (0) | 0.12 | 55 (31.1) | ***0.03**** | 45.5 (0.7) | 0.23 | 68 (9.9) | 0.79 |
| Unilateral | 67 (20) | | 53.1 (21) | | 65.6 (15.4) | | 58.3 (18.3) | | 67.7 (29) | |
| Unilateral therapeutic and contralateral prophylactic | 80 (25.2) | | 48 (34.1) | | 83 (15.8) | | 68.6 (19.5) | | 75.7 (20.9) | |
| Type of Mastectomy, mean (±SD) | | | | | | | | | | |
| Modified radical | 69.5 (22.9) | 0.78 | 43.4 (24.7) | ***0.03**** | 70.3 (18.6) | 0.56 | 59.9 (22.3) | 0.93 | 66.9 (34.9) | 0.64 |
| Skin sparing | 71.6 (20.7) | | 62.7 (24.5) | | 66.8 (16.9) | | 59.3 (15.4) | | 71.3 (18.5) | |
| Axillary Nodal Clearance, mean (±SD) | | | | | | | | | | |
| Yes | 68.7 (22.4) | 0.67 | 39.1 (23.4) | ***<0.01**** | 69.3 (19.1) | 0.80 | 58.6 (21.7) | 0.80 | 63.8 (34.2) | 0.33 |
| No | 71.9 (21.3) | | 63.7 (23.5) | | 67.8 (16.9) | | 60.2 (16.6) | | 72.9 (20.7) | |
| Type of Reconstruction, mean (±SD) | | | | | | | | | | |
| Expander | 66.7 (19.6) | 0.27 | 51.2 (21.8) | 0.15 | 67.5 (16.7) | 0.60 | 62.1 (18.1) | 0.54 | 72.4 (27.1) | 0.21 |
| Implant | 75.7 (24.7) | | 64.6 (30) | | 71.8 (20.2) | | 55.7 (17.1) | | 68.6 (19.3) | |
| Autologous | 88 (17) | | 30 (42.4) | | 59 (12.7) | | 51.5 (37.5) | | 37.5 (53) | |
| Contralateral Symmetrizing Proce, mean (±SD) | | | | | | | | | | |
| Reduction/ Mastectomy | 67 (23.4) | 0.42 | 54.8 (27.5) | 0.91 | 62.4 (15.9) | 0.11 | 61 (16.7) | 0.71 | 66.6 (21.6) | 0.64 |
| None | 73 (20.4) | | 53.7 (25.8) | | 72.1 (17.8) | | 58.6 (19.9) | | 71 (29.9) | |

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|---|---|---|---|---|---|---|---|---|---|---|
| Nipple Reconstruction, mean (±SD) | | | | | | | | | | |
| Yes | 79.5 (18.3) | 0.06 | 65.5 (27.2) | ***0.05**** | 70.4 (19.4) | 0.61 | 67.8 (15) | ***0.04**** | 83.1 (16.3) | 0.06 |
| No | 65.7 (21.8) | | 47.7 (25.7) | | 67.2 (16.7) | | 54.9 (18.9) | | 61.6 (28.6) | |
| Anatomic Stage of Breast Cancer, mean (±SD) | | | | | | | | | | |
| Stage 0 | 80.4 (18.9) | 0.34 | 72.1 (20.1) | ***0.04**** | 62 (20.2) | 0.57 | 59.7 (11.9) | 0.21 | 75 (12.3) | 0.27 |
| Stage 1 | 62.1 (26.1) | | 55.7 (28.3) | | 71.3 (16.8) | | 57.6 (21.7) | | 69 (27.9) | |
| Stage 2 | 71.1 (18) | | 50.3 (21.6) | | 72 (18.5) | | 65.9 (17.1) | | 75.4 (19.8) | |
| Stage 3 | 64.8 (26) | | 34.3 (29.1) | | 66 (11.8) | | 46.8 (22.9) | | 47 (45.2) | |
| Radiotherapy, mean (±SD) | | | | | | | | | | |
| Yes | 62.6 (19.2) | 0.07 | 39.7 (20.7) | ***0.01**** | 64.8 (14.6) | 0.34 | 58.1 (19.1) | 0.72 | 64 (26.4) | 0.35 |
| No | 75.8 (21.6) | | 63.3 (25.3) | | 70.6 (19.1) | | 60.5 (18.5) | | 72.7 (26.9) | |
| Chemotherapy, mean (±SD) | | | | | | | | | | |
| Yes | 69.8 (22.2) | 0.78 | 49.8 (25.2) | 0.24 | 67.2 (14.9) | 0.64 | 60.1 (19.7) | 0.83 | 70.3 (27.1) | 0.80 |
| No | 71.9 (21) | | 60.2 (26.9) | | 70 (21.1) | | 58.7 (17.3) | | 68 (27.1) | |
| Hormonal Therapy, mean (±SD) | | | | | | | | | | |
| Yes | 64.4 (20.7) | ***0.01**** | 45.3 (24.3) | ***<0.01**** | 69.9 (17.7) | 0.47 | 57.8 (20.7) | 0.43 | 64 (29.9) | 0.13 |
| No | 83.3 (17.5) | | 71.8 (20.4) | | 65.3 (17.4) | | 63.1 (13.2) | | 80.1 (14.3) | |
| Early Complications (<2 weeks), mean (±SD) | | | | | | | | | | |
| Major | 61.6 (21.1) | 0.29 | 59.3 (25.3) | 0.16 | 61 (20.6) | 0.09 | 51.6 (20.2) | 0.08 | 57.9 (33.4) | ***0.04**** |
| Minor | 67.8 (25.5) | | 38.6 (32.8) | | 61.4 (12.3) | | 50.4 (25) | | 53.3 (31.2) | |
| None | 75.5 (19.6) | | 58.3 (22.1) | | 74.1 (16.6) | | 66.4 (11.7) | | 80.4 (15.8) | |

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| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Late complications (>2 weeks), mean (±SD) | | | | | | | | | | |
| Major | 71.1 (24.7) | 0.92 | 45.5 (25.1) | 0.47 | 76 (20.9) | 0.17 | 61 (21.1) | 0.92 | 64.7 (25.2) | 0.76 |
| Minor | 72.7 (18.7) | | 56.2 (27.8) | | 69.5 (19.2) | | 57.6 (18.9) | | 68.4 (26.8) | |
| None | 69.1 (22.2) | | 58.3 (25.9) | | 62.9 (12.7) | | 59.9 (17.6) | | 72.8 (28.7) | |
| Reoperations, mean (±SD) | | | | | | | | | | |
| None | 65.3 (24.6) | 0.85 | 36.3 (27.6) | 0.36 | 67.8 (14.3) | 0.44 | 49.8 (16.9) | 0.37 | 60.5 (42.7) | 0.73 |
| 1-2 operations | 71.7 (20.1) | | 56.3 (25.8) | | 66.7 (17.7) | | 59.6 (18.7) | | 69.6 (24.7) | |
| >2 operations | 69.4 (30) | | 56.8 (26.3) | | 77.8 (18.9) | | 67.4 (18.1) | | 74.8 (28.2) | |
| Outcome of Final Reconstruction, mean (±SD) | | | | | | | | | | |
| Failed | 65.8 (26.6) | 0.29 | 34.5 (26.3) | 0.06 | 72 (18) | 0.85 | 50 (23.2) | 0.28 | 46.4 (25.6) | ***0.01**** |
| Immediate | 81.5 (20.5) | | 65 (32.3) | | 64.6 (17.9) | | 58 (18.2) | | 68.1 (26.3) | |
| Immediate delayed (<12 months) | 71.8 (10.4) | | 66.3 (17) | | 70 (15) | | 69 (12.5) | | 93.8 (12.5) | |
| Immediate delayed (>12 months) | 65.4 (20.2) | | 54.1 (17.2) | | 68.5 (18.9) | | 63.4 (16.2) | | 76.4 (22.1) | |

Abbreviations: WBPsy= Psychosocial Well-Being; WBS= Sexual Well-Being; WBPhy= Physical Well-Being; SBreast= Satisfaction with Breasts; SOut= Satisfaction with Outcome

*Statistically significant differences ($p<0.05$)

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**Table 4.** Review of International Literature

| Study | Year | Type of Reconstruction | Participants | Psychosocial Well-Being | Sexual Well-Being | Physical Well-Being | Satisfaction with Breast | Satisfaction with Nipples | Satisfaction with Outcome | Satisfaction with Information | Satisfaction with Surgeon | Satisfaction with Medical Team | Satisfaction with Office |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Sugrue et al.[37]** | 2013 | PIBR; TEBR; ABR (Combined) | 30 | - | - | 81 (+/- 13) | - | 92 (+/- 10) | - | 76 (+/- 19) | 83 (+/- 21) | 89 (+/- 19) | 94 (+/- 12) |
| **Eltahir et al.[14]** | 2013 | PIBR; TEBR; ABR (Combined) | 92 | 75.5 (+/- 17.9) | 61.1 (+/- 22.4) | 74.6 (+/- 16.3) | 70.5 (+/- 17.9) | 64.6 (+/- 30.3) | 78.4 (+/- 19.1) | 71 (+/- 15.1) | 90.4 (+/- 15.3) | 86.7 (+/-20.1) | 86 (+/-19.2) |
| **Liu et al.[46]** | 2014 | PIBR; TEBR<br>ABR | 48<br>26 | 75.5 (+/- 17.1)<br>86.1 (+/- 17.4) | 52.1 (+/- 18.6)<br>64.8 (+/- 20.9) | 78.7 (+/- 12.9)<br>79.1 (+/- 15.6) | 64.2 (+/- 12.6)<br>73.5 (+/- 20.8) | -<br>- | 63.3 (+/- 22.1)<br>79.2 (+/- 21.5) | 67.4 (+/- 18.8)<br>80.4 (+/-13.6) | 82.4 (+/- 20.4)<br>95.9 (+/- 10.8) | -<br>- | - |
| **Dean et al.[45]** | 2016 | PIBR; TEBR; ABR (Combined) | 53 (Immediate cohort only) | 73.6 | 56.7 | 73.9 | 66.1 | - | - | - | - | - | - |
| **Pirro et al.[47]** | 2017 | PIBR; TEBR<br>ABR | 34<br>31 | 67.6 (+/- 20.5)<br>73.5 (+/- 10) | 52.7 (+/- 18.5)<br>51.7 (+/- 6.8) | 75.1 (+/- 13.4)<br>67.5 (+/- 9.5) | 59.3 (+/- 11.8)<br>69.1 (+/- 6.2) | 57.5 (+/- 25.6)<br>69.0 (+/- 21.4) | 75.5 (+/- 16.6)<br>91.5 (+/- 10.8) | 66.8 (+/- 16.1)<br>72.1 (+/- 16.5) | 86.9 (+/- 16.8)<br>95.5 (+/- 7.6) | 92.9 (+/ 14.5)<br>80.8 (+/- 20.1) | 90.1 (+/- 16.6)<br>81.5 (+/- 18.0) |
| **Aguiar et al.[44]** | 2017 | PIBR; TEBR | 57 (Recon group) | - | 52 | 77 | 75 | - | - | - | 100 | 100 | - |
| **Pusic et al.[48]** | 2017 | PIBR; TEBR<br>ABR | ~783<br>~383 | 71.8 (+/- 19)<br>74.7 (+/- 19.2) | 53 (+/- 21.2)<br>55.4 (+/- 19.8) | 76.7 (+/- 14.5)<br>74.9 (+/- 15.1) | 64.0 (+/- 16.8)<br>67.8 (+/- 17.2) | - | - | - | - | - | - |
| **Santosa et al.[49]** | 2018 | PIBR; TEBR<br>ABR | 1490<br>523 (at 1 year) | 71.8 (+/- 19.3)<br>74.7 (19.3) | 52.7 (+/- 21.1)<br>55.5 (+/- 20.6) | 76.0 (+/- 14.6)<br>74.9 (+/- 15.1) | 63.1 (+/- 17.4)<br>68.6 (+/-17) | - | - | - | - | - | - |
| **Cereijo-Garea et al.[40]** | 2018 | PIBR; TEBR; ABR (Combined) | 101 | 75.3 (+/- 19.5) | 63.4 (+/- 23.7) | 70.4 (+/- 16.8) | 60.8 (+/- 18.8) | 71.3 (+/- 24.4) | 75.3 (+/- 20.2) | 74 (+/- 19.1) | 95.0 (+/- 10.4) | 96.3 (+/- 10.8) | 97.5 (+/- 7.8) |
| **Yoon et al.[50]** | 2018 | PIBR; TEBR; ABR (Combined | ~1056 (Immediate cohort only) | 74.4 (+/- 19) | 54.8 (+/- 21.4) | 76.3 (+/- 14.8) | 65.1 (+/- 18.1) | - | - | - | - | - | - |
| **Möller et al.** | 2018 | PIBR; TEBR; ABR (Combined) | 36 | 70.7 (+/- 21.5) | 54.1 (+/- 26.1) | 68.4 (+/-17.5) | 59.6 (+/-18.5) | 69 (+/- 28.1) | 69.3 (+/- 26.7) | 65.9 (+/- 23.4) | 85.1 (+/- 22,2) | 88.7 (+/- 17.8) | 88.6 (+/- 19.2 |

*Abbreviations: PIBR= Permanent Implant Breast Reconstruction; TEBR= Tissue expander breast reconstruction; ABR=Autologous breast reconstruction

**Fig 1.** Mean and Range of BREAST-Q Scores (N=36)

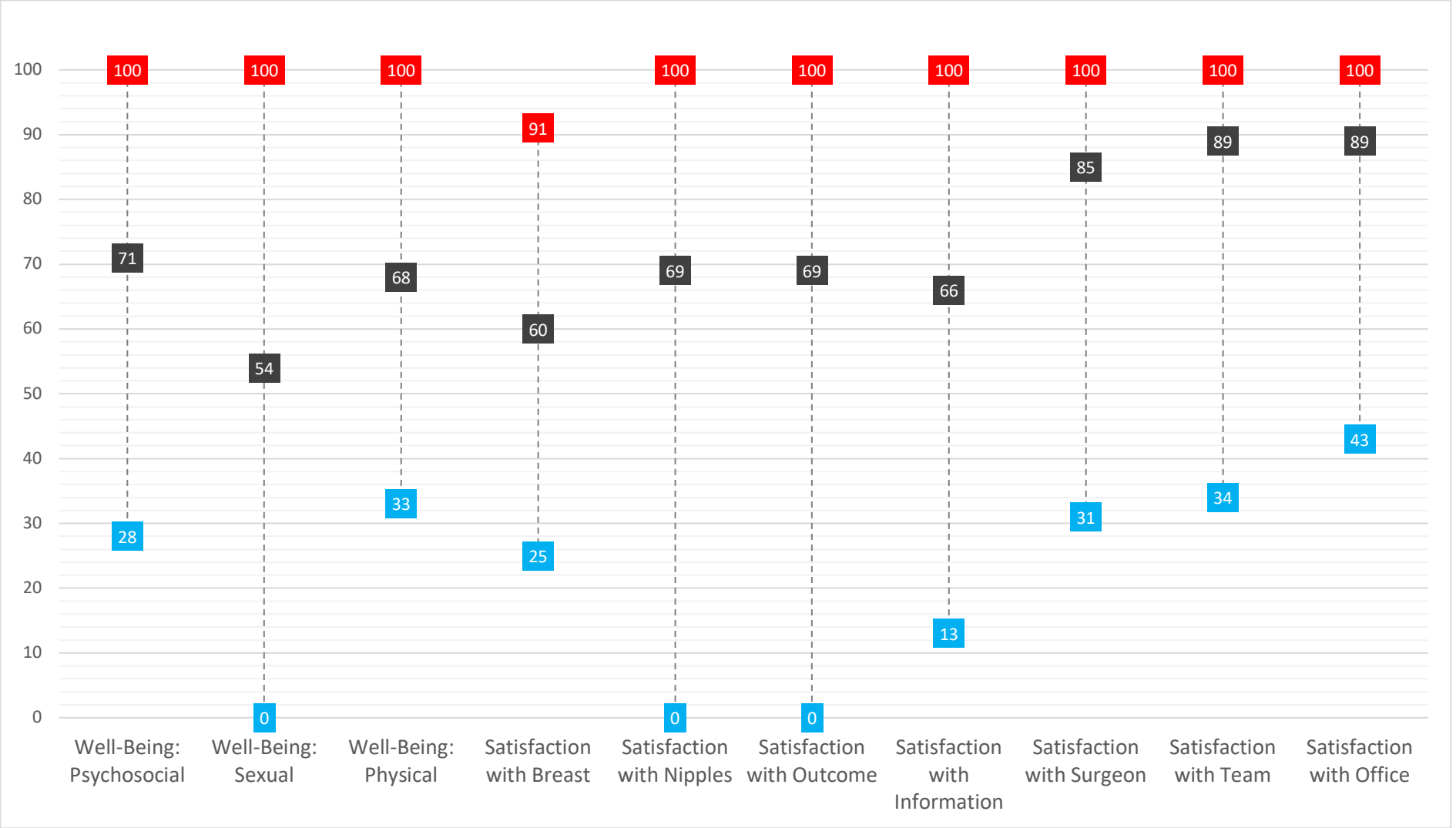
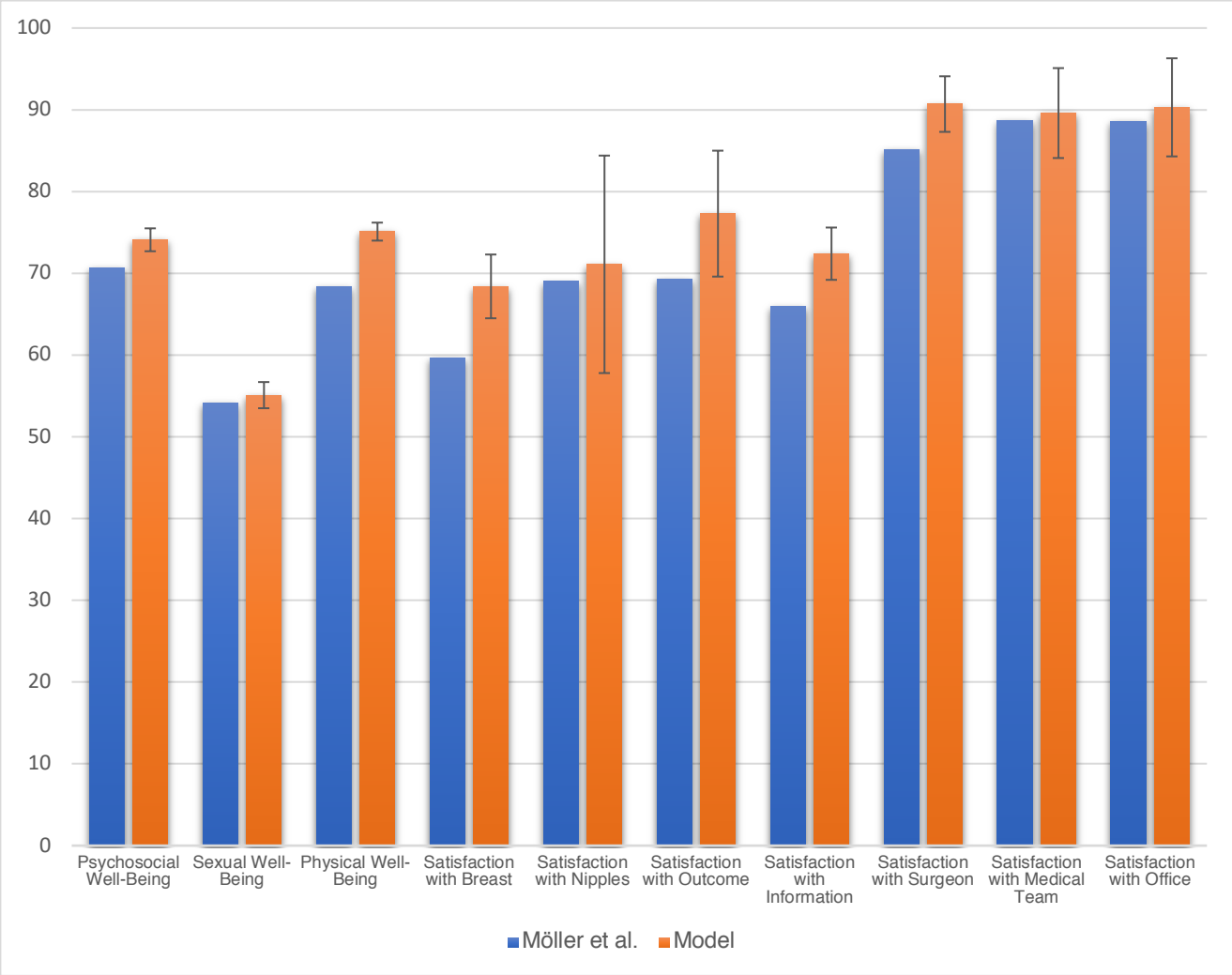


**Fig 2.** Comparison of Mean BREAST-Q scores with the Meta-Analysis Model




The error bars represent the 95% Confidence intervals

# PART I: APPENDICES

## 1.1 UCT HREC Approval letter

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room E52-24 Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6492 • Facsimile [021] 406 6411
Email: Sumayah.arlefdien@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

**04 August 2014**

**HREC/REF: 528/2014**

**Dr L Cairncross**
General Surgery
J –floor
OMB

Dear Dr Cairncross

**Project Title: PATIENT REPORTED OUTCOME MEASURES (PROM's) IN BREAST CANCER PATIENTS AFTER IMMEDIATE BREAST RECONSTRUCTION USING THE BREAST-Q (MMed candidate- Ernst L Moller)**

Thank you for your response letter dated 31 July 2014, addressing the issues raised by the Human Research Ethics Committee (HREC).

It is a pleasure to inform you that the HREC has **formally approved** the above mentioned study.

**Approval is granted for one year until the 30 August 2015.**

Please submit a progress form, using the standardised Annual Report Form, if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.

***We acknowledge that the following student- Dr E Moller is also involved in this study.***

Please note that the on-going ethical conduct of the study remains the responsibility of the principal investigator.

**Please quote the HREC REF in all your correspondence.**

Yours sincerely

Signature Removed

**PROFESSOR M BLOCKMAN**
**CHAIRPERSON, HSF HUMAN ETHICS**

Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938

**Hrec/ref:528/2014**

## 1.2 Amendment of Ethics Approval letter

UNIVERSITY OF CAPE TOWN

HUMAN RESEARCH ETHICS COMMITTEE
18 APR 2018
HEALTH SCIENCES FACULTY
UNIVERSITY OF CAPE TOWN

FACULTY OF HEALTH SCIENCES
Human Research Ethics Committee

### FHS016: Annual Progress Report / Renewal

| HREC office use only (FWA00001637; IRB00001938) This serves as notification of annual approval, including any documentation described below. | | | |
|---|---|---|---|
| ☑ Approved | Annual progress report | Approved until/next renewal date | 30.4.2019 |
| ☐ Not approved | See attached comments | | |
| Signature Chairperson of the HREC | Signature Removed | Date Signed | 12/5/2018 |

| Comments to PI from the HREC |
|---|
| |

**Principal Investigator to complete the following:**

**1. Protocol information**

| | | | |
|---|---|---|---|
| Date (when submitting this form) | 17/04/2018 | | |
| HREC REF Number | 528/2014 | Current Ethics Approval was granted until | 30/08/2015 |
| Protocol title | Patient related outcome measures in breast cancer patients after immediate breast reconstruction using the Breast-Q. | | |
| Protocol number (if applicable) | | | |
| Are there any sub-studies linked to this study? | ☐ Yes ■ No | | |
| If yes, could you please provde the HREC Ref's for all sub-studies? Note: A separate FHS016 must be submitted for each sub-study. | | | |
| Principal Investigator | Dr Lydia Cairncross | | |
| Department / Office Internal Mail Address | Department of General Surgery | | |



(Note: Please complete the Closure form (FHS010) if the study is completed within the approval period)

2. World Journal of Surgery Author Guidelines

# *WORLD JOURNAL OF SURGERY* INSTRUCTIONS FOR AUTHORS

## GENERAL

*World Journal of Surgery* (*WJS*) publishes original articles that offer significant contributions to knowledge in the broad fields of clinical surgery, innovative developments in surgery, global surgical practice and economics, surgical education, rural surgery and surgical history. *WJS* welcomes predominantly human research, including clinical research, outcomes, and health service research. Laboratory research will be published only if it is highly significant and with clear and immediate translational potential to surgical care. *WJS* has an international circulation and is designed to serve as a medium for rapid dissemination of new and important information about the science and art of surgery throughout the world. In the interests of a wide international readership, use of the English language is required. Articles that are accepted for publication are done so with the understanding that they, or their substantive contents, have not been and will not be submitted to any other publication.

## TYPES OF MANUSCRIPTS

**PLEASE NOTE: *World Journal of Surgery* does not accept Case Reports and Book Reviews for review or publication.** *WJS* will consider publication without prior invitation the following types of manuscripts:

**Original Scientific Reports**: Original Scientific Reports are full-length reports of original basic or clinical investigations. Original Scientific Reports must adhere to a 2,500 word limit (not including the title page, abstract, references, tables, and figures). The final word count should be included in the title page of the manuscript. All clinical trials must be registered through a public trials registry that is acceptable to the International Committee of Medical Journals Editors (ICMJE). For information on ICMJE's statement to register clinical trials, please go to http://www.icmje.org/publishing_10register.html. The trial registration number and agency should be listed on the title page and at the end of the abstract. Randomized clinical trials should be reported following the CONSORT criteria and provide a completed checklist and flow diagram upon manuscript submission. For information on CONSORT and to download the CONSORT checklist and flow diagram, please go to http://www.consort-statement.org/.

**Brief Original Scientific Reports**: Brief communications describing an original observation or new technique. All efforts will be made to expedite review and publication of noteworthy brief reports. Brief Original Scientific Reports must adhere to a 1,500 word limit (not including the title page, abstract, references, tables and figures). The final word count should be included in the title page of the manuscript.

**Innovative Techniques in Surgery around the World:** The WJS in interested in publishing high quality descriptions of innovative surgical techniques that have the potential to improve the quality or efficiency of care. While techniques with universal appeal are most sought after, novel techniques that allow broader access to care in resource challenged environments are also desirable. The successful manuscript will contain a detailed description of the technique and be richly illustrated with figures, and/or video. Line drawings are much superior to intraoperative photos, generally. A brief description of the authors experience with the technique should also be included, if possible. Qualifying manuscripts should be less than 1250 words, have no more than 3 authors, have no more than 5 references, and no more than 8 figures/video segments. A brief unstructured abstract is also required. Please see our instructions for submitting streaming video, below.

**Papers Presented at ISW Congress**: Includes manuscripts presented at an International Surgical Week (ISW) World Congress or at an Integrated Society meeting.

**Multimedia Scientific Reports**: *WJS* seeks manuscripts that contain brief video clips of surgical techniques or operative findings. Please see the "**MULTIMEDIA MANUSCRIPT SUBMISSION**" below for submitting video augmented manuscripts.

**Surgery in Rural Settings and Low and Middle Income Countries**: *WJS* seeks high quality manuscripts describing the unique problems and unique solutions facing surgeons in rural and impoverished settings, globally. *WJS* requires that manuscripts that use primary data from a low- or middle-income country should include one or more local co-authors. A local co-author is defined as a national of that country who is living and working in their home country. All other author requirements need to be met for the author(s) from the low and middle income country. The editors understand that there may be extenuating circumstances in which this requirement cannot be met. In such cases, a cover letter should explain why a local co-author is not included. Further details on this editorial policy can be found at: World J Surg (2011) 35:2367–2368.

**Letter to the Editor**: Letters should pertain to material previously published in *WJS*. Letters should not exceed 500 words with no more than five references, the first of which should be the article on which you wish to comment.

*WJS* will also consider for publication the following types of manuscripts by invitation only:

- Editorial Perspective
- Invited Scientific Review
- Invited Symposium Papers
- Reply to Letter to the Editor
- Invited Commentary
- Surgical History

## MANUSCRIPT SUBMISSION GUIDELINES AND REQUIREMENTS

All manuscripts must be submitted online to *WJS* via the ScholarOne Manuscripts website (formerly Manuscript Central). Please login directly onto the site at http://mc.manuscriptcentral.com/*WJS* and upload your manuscripts following the instructions given on the screen. Authors should keep copies of all manuscript files. WJS accepts no responsibility for files that are lost or destroyed due to electronic problems. Upon manuscript submission, the Editorial Office will review all manuscript files to verify that guidelines and policies stated in this document are adhered to. Your manuscript will be unsubmitted if it does not meet the proper submission requirements.

Authors entering the ScholarOne Manuscripts website can either create a new account or use an existing one. If you have an existing account, please use it for all your submissions and you can track their status on the same page. If you are unsure about whether or not you have an account, or have forgotten your password, enter your e-mail address into the "Password Help" section. You will then receive an automatic e-mail with a new password which you will be prompted to change after logging in. Otherwise please create a new account and then follow the instructions given on the screen. Once you have logged into your account, ScholarOne Manuscripts will lead you through the submission process in a step-by-step orderly process. If you cannot finish your submission in one visit, you can save a draft and re-enter the process at the same point for that manuscript. At any point during this process, there are Help buttons available to see common questions and a support link to ask a specific question via email. After submission, you may return periodically and monitor the progress of your submission through the review process. Authors should go to https://mc.manuscriptcentral.com/wjs and click on "System Requirements" for the most updated list of system and browser requirements that should be used with ScholarOne Manuscripts.

Upon manuscript submission in the ScholarOne Manuscripts website, authors will be required to enter the following information:

- Selection of the appropriate manuscript type
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- Structured abstract (up to 250 words)
- Selection of the appropriate keywords associated with the manuscript
- Names and details of all contributing authors [i.e., e-mail, first name, middle initial(s), surname, degree(s); the departmental and institutional affiliation(s); complete street or mailing address for each affiliation, including the city, state or province, and country where the work was performed]. **NOTE: Fellowships are**

**not included in the Journal and NO MORE THAN 6 AUTHORS will be accepted for all manuscripts without a letter detailing explicit contribution to all 3 phases of authorship as stated in the "Consensus Guideline on Surgery Journal Authorship" published in World J Surg. 2006; 30:1135-1136. Individual contributors who have not reached this level of contribution should be acknowledged at the end of the manuscript text.**

- Copyright Transfer Statement signed and dated by the corresponding author on behalf of all authors must be uploaded with each manuscript submission. To download the form, please go to www.springer.com/00268 and click on "Copyright Transfer Statement".

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John G. Hunter, MD, Editor-in-Chief
*World Journal of Surgery* Editorial Office
Department of Surgery
Oregon Health & Science University
3181 S.W. Sam Jackson Park Road, L223
Portland, Oregon 97239-3098
Tel: (971) 275-2918
Fax: (503) 274-9433
E-mail: **worldjsurg@ohsu.edu**

## MANUSCRIPT PREPARATION AND ORGANIZATION

**General instructions**:

- Use a normal, plain font (e.g., 10-12 point Times Roman or Arial) for text
- Double-space the text
- Use italics for emphasis
- Use the automatic page numbering function to number the pages
- Do not use field functions
- Use tab stops or other commands for indents, not the space bar
- Use the table function, not spreadsheets, to make tables

**Manuscript style and text formatting**: Styling and text formatting refers to the use of special effects to enhance the appearance of the published article. Please make note of the following "Dos and Don'ts" regarding styling:

- **DO** enter all lists as single column lists.
- **DO** use your word processing features to indicate bold, italic, superscript, and subscript text within a
- paragraph or heading.
- **DO NOT** center text for headings. All text should be justified left, with ragged (unjustified) right margins.
- **DO NOT** use italic, underline, or other type effects for the entire text of a heading.
- **DO NOT** use all capital letters for a heading; use initial caps instead.
- **DO NOT** use multiple spaces to set up columns or tables; use tabs instead.
- **DO NOT** use carriage returns at the end of each line of text (use the word wrap feature).

**Manuscript organization**: Manuscripts should be organized and follow the sequence as indicated below:

**TITLE PAGE**: The title page should include:

- A concise and informative title

- The name(s) of the author(s) including the affiliation(s) and address(es) of each author. The complete name and address of the author to whom correspondence should be sent, as well as his/her phone number, fax number, and email address.
- A short title for use as a running head.
- Keywords: 2-3 keywords relevant to the manuscript
- Trial registration number for randomized clinical trials (see "Types of Manuscripts: Original Scientific Reports" above)
- Grant support for the research reported
- Potential and real conflicts of interest
- Manuscript word count

**ABSTRACT (if applicable)**: The abstract must appear between the title page and the Introduction section of the manuscript, even if it has been uploaded separately. Manuscripts should contain a structured abstract of not more than 250 words. It should be a factual description of the study performed organized with the headings of *Background* (includes aims, hypotheses, or objectives), *Methods* (includes patient population, procedures, and data analysis), *Results*, and *Conclusions*. The abstract should contain the data to support the key findings or conclusions of the study. The trial registration number for randomized clinical trials must be included at the end of the abstract. The first time an abbreviated term is used, spell it out in full and follow with the abbreviation in parentheses – for example: ultrasound (US).

**TEXT**: Original Scientific Reports should be arranged in sections titled Introduction, Material and Methods, Results, and Discussion.

1. Introduction: conveys the background and purpose of the report
2. Material and Methods
3. Results & Discussion

When required by the nature of the report, manuscripts that do not follow this specific format may be accepted.

**ACKNOWLEDGEMENTS**: A brief statement should acknowledge individuals, other than authors, who were of direct help in the reported work or if the work was supported by a federal or commercial grant. All acknowledged persons should give their written consent to being named in the manuscript. This consent is to be uploaded upon manuscript submission.

**REFERENCES**: Reference citations in the text should be identified by numbers in brackets (e.g. [4]). Number the references in order of their first appearance in the text (not alphabetically). Once a reference is cited, all subsequent citations should be to the original number. References may not appear in your Reference List unless they have been cited in the text or tables. Manuscripts that have been accepted for publication or are in press may be listed as references, but the Journal does not reference unpublished data and personal communications. Use the form for references adopted by the U.S. National Library of Medicine, as in Index Medicus. For each reference, show inclusive page ranges (e.g., 7-19).

In references to journal articles, please include (1) surname and initials (without periods) of the first three authors and et al for all others, (2) the year in parentheses, (3) title of article. (4) abbreviated Journal name, (5) volume number, and (6) inclusive page numbers, in that order. An example follows:

1. Honda T, Nozaki M, Isono N, et al (2001) Endoscope-assisted facial fracture repair. World J Surg 25:1075-1083

In references to books, please include (1) surname and initials (without periods) of the first three authors and et al. for all others, (2) chapter title, if any, (2) chapter title, if any, (3) the year in parentheses, (4) editor(s), if any, (5) title of book, (6) publisher, (6) city of publication, and (7) inclusive page numbers. Volume and edition numbers, and name of translator should be included when appropriate. Examples follow:

1. Harlan BJ, Starr A, Harwin FM, Anesthesia for cardiac surgery (1996) In: Illustrated Handbook of Cardiac Surgery, Springer-Verlag, New York, p. 6-12

2. Jones MC, Smith RB, Treatment of gastric cancer (1976) In: Ford TL (ed) Cancer of the Digestive System, Springer-Verlag, Berlin, p. 140-154

**TABLES:**

- All tables are to be numbered using Arabic numerals
- Tables should always be cited in text in consecutive numerical order
- For each table, please supply a table heading
- The table title should explain clearly and concisely the components of the table
- Identify any previously published material by giving the original source in the form of a reference at the end of the table caption
- Footnotes to tables should be indicated by superscript lower-case letters (or asterisks for significance values and other statistical data) and included beneath the table body

**ARTWORK:**

**Electronic Figure Submission**

- Supply all figures electronically
- Indicate what graphics program was used to create the artwork
- For vector graphics, the preferred format is EPS; for halftones, please use TIFF format. MS Office files are also acceptable.
- Vector graphics containing fonts must have the fonts embedded in the files
- Save and name your figure files with "Fig" and the figure number (e.g., Fig1.eps)

**Line Art**

- Definition: Black and white graphic with no shading
- Do not use faint lines and/or lettering and check that all lines and lettering within the figures are legible at final size
- All lines should be at least 0.1 mm (0.3 pt) wide
- Scanned line drawings and line drawings in bitmap format should have a minimum resolution of 1200 dpi

**Halftone Art**

- Definition: Photographs, drawing, or paintings with fine shading, etc.
- If any magnification is used in the photographs, indicate this by using scale bars within the figures themselves.
- Halftones should have a minimum resolution of 300 dpi

**Combination Art**

- Definition: a combination of halftone and line art (e.g., halftones containing line drawing, extensive lettering, color diagrams, etc.)
- Combination artwork should have a minimum resolution of 600 dpi

**Color Art**

- Color art is free of charge for online publication
- If black and white will be shown in the print version, make sure that the main information will still be visible. Many colors are not distinguishable from one another when converted to black and white. A simple way to check this is to make a xerographic copy to see if the necessary distinctions between the different colors are still apparent.
- If the figures will be printed in black and white, do not refer to color in the captions.
- Color artwork should be submitted as RGP (8 bits per channel).

**Figure Lettering**

- To add lettering, it is best to use Helvetica or Arial (san serif fonts)
- Keep lettering consistently sized throughout your final-sized artwork, usually about 2-3mm (8-12 pt).
- Variance of type size within an illustration should be minimal, e.g., do not use 8-pt type on an axis and 20-pt type for the axis label.
- Avoid effects such as shading, outline letters, etc.
- Do not include titles or captions into your illustrations

**Figure Numbering**

- All figures are to be numbered using Arabic numerals
- Figure parts should be denoted by lowercase letters (a, b, c, etc.)
- Figures should always be cited in text in consecutive numerical order
- If an appendix appears in your manuscript and it contains one or more figures, continue the consecutive numbering of the main text. Do not number the appendix figures, "A1, A2, A3, etc." Figures in online appendices (Electronic Supplementary Material) should, however, be numbered separately.

**Figure Captions**

- Each figure should have a concise caption describing accurately what the figure depicts. Include the captions in the text file of the manuscript, not in the figure file.
- Figure captions begin with the term Fig. in bold type, followed by the figure number, also in bold type.
- No punctuation is to be included after the number, nor is any punctuation to be placed at the end of the caption.
- Identify all elements found in the figure in the figure caption; and use boxes, circles, etc., as coordinate points in graphs.
- Identify previously published material by giving the original source in the form of a reference citation at the end of the figure caption

**Figure Placement and Size**

- When preparing your figures, size figures to fit in the column width.
- For most journals the figures should be 39 mm, 84 mm, 129 mm, or 174 mm wide and not higher than 234 mm.

**Accessibility (in order to give people of all abilities and disabilities access to the content of your figures, please make sure of the following)**

- All figures have descriptive captions (blind users could then use a text-to-speech software or a text-to-Braille hardware)
- Patterns are used instead or in addition to colors for conveying information (color-blind users would then be able to distinguish the visual elements)
- All figure lettering has a contrast ratio of at least 4.5:1

**MULTIMEDIA MANUSCRIPT SUBMISSION:**

- A Multimedia manuscript is an article with imbedded video material. Up to 3 videos per manuscript submission will be accepted. All standard instructions for Audio, Video, and Animations should be followed for Multimedia Manuscript Submissions.
- The content of these files must be identical to that reviewed and accepted by the editors of *World Journal of Surgery*
- All narration should be in English.
- Generally, the video clip is used to support the technique description. Additional data regarding the results of the procedure described should be included with the manuscript.

**ELECTRONIC SUPPLEMENTARY MATERIAL:**

**Submission**

- Supply all supplementary material in standard file formats.
- Please include in each file the following information: article title, journal name, author names; affiliation and e-mail address of the corresponding author.
- To accommodate user downloads, please keep in mind that larger-sized files may require very long download times and that some users may experience other problems during downloading.

**Audio, Video, and Animations**

- Resolution: 16:9 or 4:3
- Maximum file size: 25 GB
- Minimum video duration: 1 sec
- Supported file formats: avi, wmv, mp4, mov, m2p, mp2, mpg, mpeg, flv, mxf, mts, m4v, 3gp

**Text and Presentations**

- Submit your material in PDF format; .doc or .ppt files are not suitable for long-term viability.
- A collection of figures may also be combined in a PDF file.

**Spreadsheets**

- Spreadsheets should be converted to PDF if no interaction with the data is intended.
- If the readers should be encouraged to make their own calculations, spreadsheets should be submitted as .xls files (MS Excel).

**Specialized Formats**

- Specialized formats such as .pdb (chemical), .wrl (VRML), .nb (Mathematica notebook), and .tex can also be supplied.

**Collecting Multiple Files**

- It is possible to collect multiple files in a .zip or .gz file.

**Numbering**

- If supplying any supplementary material, the text must make specific mention of the material as a citation, similar to that of figures and tables.
- Refer to the supplementary files as "Online Resource", e.g., "... as shown in the animation (Online Resource 3)", "... additional data are given in Online Resource 4".
- Name the files consecutively, e.g. "ESM_3.mpg", "ESM_4.pdf".

**Captions**

- For each supplementary material, please supply a concise caption describing the content of the file.

**Processing of supplementary files**

- Electronic supplementary material will be published as received from the author without any conversion, editing, or reformatting.

**Accessibility**

In order to give people of all abilities and disabilities access to the content of your supplementary files, please make sure that

- The manuscript contain a descriptive caption for each supplementary material
- Video files do not contain anything that flashes more than three times per second (so that users prone to seizures caused by such effects are not put at risk)

**ABBREVIATIONS, DRUG AND PRODUCT NAMES, DIGITS:** Please use the standard abbreviations and units listed in Scientific Style and Format: The CBE Manual for Authors, Editors, and Publishers, Sixth Edition (Reston, Va., Council

of Biology Editors, 1994). The first time an abbreviated term is used, spell it out in full and follow with the abbreviation in parentheses – for example: ultrasound (US).

Generic names for drugs and chemicals should be used the first time the drug or chemical is mentioned in the text and, preferably, thereafter. The first reference to a drug or chemical in the text should be followed by the manufacturer name, city, state or province, and country – and, if you wish, the trade name – in parentheses.

Please express digits as numerals except when they are the first word in a sentence. Decimals should be written in North American format. Express units of measurement in the metric system whenever possible, and abbreviate them when used with numbers.

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Conflict of Interest: http://www.springer.com/authors?SGWID=0-111-6-791531-0
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Statement of Human and Animal Rights: http://www.springer.com/authors?SGWID=0-111-6-608309-0

## REVIEW AND ACTION

The editorial staff will examine the manuscripts and will customarily send them to appropriate experts. Authors will be notified as to the acceptability of a manuscript as rapidly as possible. All manuscripts will be put through iThenticate, an online plagiarism detection tool comparing the manuscript against previously published scientific work in other journals. If any misconduct is detected, the editorial office will contact the author(s) concerning next steps and actions.

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## CONSENSUS STATEMENT ON SUBMISSION AND PUBLICATION OF MANUSCRIPTS

(Published in the June 2001 issue of *World Journal of Surgery*, page A7)

Increasing problems of duplicate and fraudulent submissions and publications have prompted the editors of surgical journals, including *World Journal of Surgery*, to support these overall principles of publication:

**Duplicate Submission and Publication**

In general, if a manuscript has been peer-reviewed and published, any subsequent publication is duplication. Exceptions to this general rule may be:

a) Prior publication in meeting program abstract booklets or expanded abstracts such as those published by the Surgical Forum of the American College of Surgeons or Transplantation Proceedings. However, these must be referenced in the final manuscript.

b) A manuscript which extends an original database (a good rule might be expansion by 50% or more) or which analyzes the original database in a different way in order to prove or disprove a different hypothesis. Previous manuscripts reporting the original database must, however, be referenced.

c) Manuscripts which have been published originally in non-English language journals, provided that the prior publication is clearly indicated on the English language submission and referenced in the manuscript. In some circumstances, permission to publish may need to be obtained from the non- English language journal.

For example, any submission duplicating material previously published in full in "Proceedings" or book chapters is considered duplicate unless the exceptions in (a) above apply. Similarly, manuscripts dealing with subgroups of data (i.e., patients) that have previously been analyzed, discussed and published as a larger group are considered duplicate unless (b) above applies.

The Internet raises special concerns. If data have previously appeared on the Internet, submission of those data for publication is considered duplication. If Internet publication follows journal publication, the journal publication should be clearly referenced. Some journals may provide early Internet publication of accepted peer reviewed papers which are subsequently published in that journal. This does not constitute duplication if both manuscripts are identical and covered by the same single copyright.

**Fraudulent Publication**

The following activities are examples of fraudulent publication practices:

a) Willful and knowing submissions of false data for publication.
b) Submission of data from sources not the author's (or authors') own.
c) Falsely certifying that the submitted work is original and has not been submitted to, or accepted by, another journal.
d) Sponsoring or vouching for a manuscript containing data over which the sponsor has no control or knowledge.
e) Allowing one's name to appear as an author without having contributed significantly to the study.
f) Adding an author's name to a manuscript to which he/she has not contributed, or reviewed or agreed to in its current form.
g) Flagrant omission of reference to the work of other investigators which established their priority.
h) Falsification of any item on the copyright form.
i) Failure to disclose potential conflict of interest with a sponsoring agency.

While not intended as an all-inclusive document, these examples and guidelines should alert authors to potential problems that should be avoided when they are considering submission of a manuscript to a peer-reviewed journal.

**Surgery Journal Editors Group Consensus Statement on the Adoption of the COPE Guidelines**

We, the undersigned member journals of the Surgery Journal Editors Group (SJEG), in the furtherance of integrity in surgical and scientific publication, agree to adopt the guidelines established by the Committee on Publication Ethics (COPE)[1]. The COPE guidelines represent a means of addressing a variety of ethical concerns, including duplicate publication and authorship misconduct issues, which have, unfortunately, become more prevalent.
This statement is being simultaneously published in the respective journals of the members of the Surgery Journal Editors Group, as follows:

*American Journal of Surgery*
Kirby I Bland, MD
*Annals of Surgery*
Layton F Rikkers, MD, Keith D Lillemoe, MD
*Annals of Surgical Oncology*
Charles M Balch, MD
*Annals of Thoracic Surgery*
L Henry Edmunds Jr, MD
*Archives of Surgery*
Julie Freischlag, MD
*BJS*
Derek Alderson, MD, Jonothan J Earnshaw, MD
*Burns*
Steven E Wolf, MD
*Canadian Journal of Surgery*
Edward J Harvey, MD, Garth L Warnock, MD
*Der Chirurg*
JR Siewert, MD
*Digestive Surgery*
Markus W Büchler, MD, John P Neoptolemos, MD
*Diseases of the Colon and Rectum*
Robert D Madoff, MD
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*Female Pelvic Medicine & Reconstructive Surgery*
Alfred E Bent, MD
*HPB*
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*Journal of the American College of Surgeons*
Timothy J Eberlein, MD
*Journal of Burn Care and Research*
Richard Gamelli, MD
*Journal of Gastrointestinal Surgery*
Charles Yeo, MD, Jeffrey Matthews, MD
*Journal of Hepato-Biliary-Pancreatic Sciences*
Tadahiro Takada, MD
*Journal of Laparoendoscopic & Advanced Surgical Techniques,* C Daniel Smith, MD
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Jay L Grosfeld, MD
*Journal of Surgical Education*
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*Journal of Surgical Research*
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Lawrence H Cohn, MD
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Basil A Pruitt Jr, MD
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Maurice E Arregui, MD, Carol Scott-Conner, MD, PhD

*The American Surgeon*
J David Richardson, MD
*World Journal of Surgery*

John G Hunter, MD
*Zentralblatt für Chirurgie*
Hans Lippert, MD, Ulrich Hopt, MD, Karl-Walter Jauch, MD

[1]*COPE Committee on Publication Ethics.* http://publicationethics.org/guidelines

## CONSENSUS STATEMENT ON SURGERY JOURNAL AUTHORSHIP – 2006

In the majority of clinical and research studies submitted to surgery journals for possible publication, many individuals participate in the conception, execution, and documentation of each of those works. However, recognition of work in the form of authorship has varied widely. This consensus statement is being issued to clarify and define the criteria for surgical journal authorship.

The following guidelines should be used to identify individuals whose work qualifies them as authors as distinct from those who are contributors to the work under consideration. All persons designated as authors should qualify for authorship, and all those who qualify should be so credited.

### A. Authorship Criteria

Individuals claiming authorship should meet all of the following 3 conditions:

1. Authors make substantial contributions to conception and design, and/or acquisition of data, and/or analysis and interpretation of data;
2. Authors participate in drafting the article or revising it critically for important intellectual content; and
3. Authors give final approval of the version to be submitted and any revised version to be published.

Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content. Allowing one's name to appear as an author without having contributed significantly to the study or adding the name of an individual who has not contributed or who has not agreed to the work in its current form is considered a breach of appropriate authorship.

Acquisition of funding, collection of data, contributing cases, or general supervision of the research group, of itself, or just being the Chair of the department does not justify authorship if the above criteria are not fulfilled.

### B. Order of Authors

The order of authorship on the byline should be a joint decision of the co-authors. Authors should be prepared to explain the order in which authors are listed.

### C. Multi-Center Studies

When a large, multi-center group has conducted the work, the group should identify the individuals who accept direct responsibility for the manuscript. These individuals should fully meet the criteria for authorship defined above and editors will ask these individuals to complete journal-specific author and conflict of interest disclosure forms. When submitting a group-author manuscript, the corresponding author should clearly indicate the preferred citation and should clearly identify all individual authors as well as the group name.

### D. Contributors Listed in Acknowledgments

All contributors who do not meet the criteria for authorship should be listed in an acknowledgments section. Examples of those who might be acknowledged include: individuals who allowed their clinical experience (i.e., cases) to be included, a person who provided purely technical help, writing assistance, or a department Chair who provided only general support. Financial and material support should also be acknowledged.

Groups of persons who have contributed materially to the paper but whose contributions do not justify authorship may be listed under a heading such as "clinical investigators" or "participating investigators," and their function or contribution should be described - for example, "served as scientific advisors," "critically reviewed the study proposal," "collected data," or "provided and cared for study patients."

Because readers may infer their endorsement of the data and conclusions, all persons listed as contributors must give written permission to be acknowledged.

**E. In Conclusion**

This consensus statement is intended as a basic guide for authors. In the interest of promoting the highest ethics in surgical publishing and the surgical sciences, we ask that authors take these criteria into careful consideration when submitting a manuscript to a peer-reviewed surgical journal. This statement is being simultaneously published in the respective journals of the members of the Surgical Journal Editors Group, as follows:

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*The American Surgeon*
Talmadge A. Bowden, Jr. MD
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Charles M. Balch. MD
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L. Henry Edmunds, Jr., MD
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*Canadian Journal of Surgery*
Garth L. Warnock, MD, James P. Waddell, MD
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*Digestive Surgery*
Markus Büchler, MD, John Neoptolemos, MD
*Diseases of the Colon & Rectum*
Victor Fazio, MD
*Journal of the American College of Surgeons*
Timothy J. Eberlein, MD
*Journal of Burn Care and Research*
Richard Gamelli, MD
*Journal of Gastrointestinal Surgery*
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*Surgical Laparoscopy, Endoscopy & Percutaneous Techniques*
Maurice E. Arregui, MD, Carol Scott-Conner, MD
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