

# Breast Hypertrophy and outcome of Breast Reduction Surgery

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Ineko AB

To my family  
Karina  
Julia  
Agnes



# ABSTRACT

**Aim:** The overall aim of this thesis was to improve our knowledge of breast hypertrophy in women, its associated problems, and the outcome of breast reduction.

**Patients and methods:** **I.** Five hundred and twelve woman were studied retrospectively for prevalence of and risk factors for complications. **II.** The study included 325 women, either randomized to prophylactic antibiotics or not. **III.** The Breast Evaluation Questionnaire (BEQ) for women with breast hypertrophy and breast reduction was validated. Two hundred and twenty-five women who had had breast reduction surgery and 216 controls were included. **IV.** Three hundred and forty-eight women were evaluated for gain in health-related quality of life (HRQL) after breast reduction surgery in this prospective, longitudinal paired study. **Results:** **I.** A long suprasternal notch to nipple distance increased the risk of infection and necrosis of the nipple. High BMI increased the risk of wound infection. A larger weight of resection increased the risk of delayed wound healing and fat necrosis. Smokers have twice the risk of getting a postoperative infection and diabetics are at higher risk of nipple necrosis. **II.** The incidence of postoperative infections was not significantly different between the groups. **III.** The modified BEQ is valid and shows good reliability. **IV.** Breast hypertrophy is associated with low HRQL, and breast reduction surgery increases HRQL. **Conclusions:** **I.** Sternal notch to nipple distance, BMI, resection weight, diabetes mellitus, and smoking are independent risk factors for complications after breast reduction surgery. **II.** One prophylactic dose of 2 g intravenous Cloxacillin or 600 mg Clindamycin did not reduce the incidence of postoperative infections. **III.** The BEQ has proven to be valid and to have good stability after being modified (mBEQ), when used before and after breast reduction surgery. **IV.** Women with breast hypertrophy have reduced quality of life and the HRQL is strongly increased or normalized after breast reduction surgery when SF-36, mBEQ, BRSQ, and BREAST-Q are analyzed. Those with a higher body mass index, a longer sternal notch to nipple distance, a larger preoperative breast volume, or large volume of breast resection enjoy gains in health-related quality of life that are similar to, although probably not greater than, other women.

**Keywords:** Breast, hypertrophy, breast reduction, mammoplasty, complication, prophylactic, antibiotic, infection, validation, reliability, quality of life, questionnaire

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## SAMMANFATTNING PÅ SVENSKA

**Bakgrund:** Brösthypertrofi innebär att bröstet är större än normalt och de kvinnor som söker sjukvård har associerade, fysiska, psykiska eller psykosociala problem med detta. Vilken volym ett normalt bröst har är svårt att definiera även om man uppskattat det till ca 300-400 ml. Storleken varierar dock med kroppsvikt och eftersom den generella kroppsvikten ökar i västvärlden ökar sannolikt även bröstvolymen. **Material och metod:** I den första artikeln har vi gått igenom journaler ifrån 512 patienter som har genomgått en bröstförminskande operation för att klarlägga vilka komplikationer som förekommer och huruvida dessa kan förutsägas av annan sjuklighet eller livsstil som exv. diabetes, övervikt och rökning eller mätbara observationer i bröstens utseende. I den andra artikeln har vi prospektivt och slumpmässigt, låtit hälften av ca 320 kvinnor som genomgått bröstförminskande kirurgi få en dos med s.k. förebyggande antibiotika för att se om detta kan minska de infektioner som drabbar ca 11-16% av kvinnorna efter operationen. I artikel III har vi bedömt validitet och reliabilitet hos enkäten ”Breast Evaluation Questionnaire” (BEQ) för att undersöka huruvida den är tillförlitlig till att bedöma psykosociala besvär vid förstörd byst och vilken effekt bröstförminskande kirurgi har. I den fjärde artikeln använder vi fyra olika enkäter, BREAST-Q, modifierad BEQ, SF-36 och Breast Related Symptom Questionnaire (BRSQ) för att bedöma livskvaliteten, i olika perspektiv, hos kvinnor som söker sjukvård till följd av stor byst och vilken livskvalitetsförändring dessa kvinnor upplever efter sin bröstförminskande operation. **Resultat:** Studierna visar att kvinnor med stor byst upplever nedsatt fysisk, psykisk och psykosocial livskvalitet och att en bröstförminskande operation har en mycket positiv inverkan på kvinnans förmåga till att vara fysiskt aktiva, slippa smärta och vara psykosocialt mer bekväma med sin byst, trots att komplikationerna efter en bröstförminskande operation är vanliga och där infektioner inte kan minskas genom förebyggande antibiotika givet i en dos preoperativt. De faktorer som påverkar komplikationer är storleken på bysten, hur mycket bröstet hänger, hur mycket vävnad som tas bort under operationen, om man lider av Diabetes mellitus och om man röker, vilket dramatiskt ökar risken för infektioner. **Konklusion:** Kvinnor med problem av brösthypertrofi upplever sänkt livskvalitet. Bröstförminskande operationer är en mycket effektiv metod för att normalisera eller minska de fysiska, psykiska och psykosociala problem kvinnor med stor byst ibland upplever trots att komplikationer är vanliga och där förebyggande antibiotika, givet enligt rådande rekommendationer, inte minskar andelen infektioner efter operationen.

## LIST OF PAPERS

This thesis is based on the following studies, referred to in the text by their Roman numerals.

- I. Lewin R, Göransson M, Elander A, Thorarinsson A, Lundberg J, Lidén M. Risk factors for complications after breast reduction surgery. *J Plast Surg Hand Surg.* 2014; 48:10-14.
- II. Lewin R, Elander A, Thorarinsson A, Kölby L, Sahlin P-E, Lundberg J, Panczel A, Lidén M. A Randomized Prospective Study of Prophylactic Cloxacillin in Breast Reduction Surgery. *Annals of Plastic Surgery* 2015; Jan; 74(1): 17-21.
- III. Lewin R, Elander A, Lundberg J, Thorarinsson A, Claudelin M, Bladh H, Lidén M. Validation of the Breast Evaluation Questionnaire for women subjected to breast reduction surgery. Submitted 2016.
- IV. Lewin R, Lidén M, Selvaggi G, Lundberg J, Thorarinsson A, Elander A. Prospective evaluation of health after breast-reduction surgery using BREAST-Q, SF-36, BRSQ and modified BEQ. Manuscript.

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## ABBREVIATIONS

ASA	American Association of Anesthesiology
BDI	Beck Depression Inventory
BEQ	Breast Evaluation Questionnaire
BMI	Body Mass Index
BRSQ	Breast Related Symptoms Questionnaire
HRQL	Health Related Quality of Life
IMF	Inframammary fold
JM	Distance between jugulum and mammilae = Sternal-notch to nipple distance
MBC	Minimal Bactericidal Concentration
mBEQ	Modified Breast Evaluation Questionnaire
MIC	Minimal Inhibitory Concentration
NAC	Nipple Areola Complex
PRO	Patient Reported Outcome
QALY	Quality Adjusted Life Years
QoL	Quality of Life
SF-36	Short Form-36
SSI	Surgical Site Infection
WHO	World Health Organization

## DEFINITIONS IN SHORT

Bottoming out	Gradual descent of breast parenchyma below the original location of the inframammary fold location with the result that the NAC appears to be displaced superiorly.
“Dog-ears”	Lump of skin, usually in the beginning or end of a scar when sutured.
Fat Necrosis	A cell injury which results in premature death of fat cells due to inadequate blood supply.
Hypertrophic scars	A raised scar, often with a reddish colour, that do not grow beyond the boundaries of the original wound.
Inframammary fold	The fold where the breast starts inferiorly from the chest wall.
Keloidic scars	Raised scar formation that grows beyond the wound boundaries.
MIC	The lowest concentration of an antimicrobial that will inhibit the visible growth of a microorganism after overnight incubation.
Skin Necrosis	A cell injury that results in premature death of epithelium and dermal tissue due to inadequate blood supply.
Tactile hyperesthesia	Pain resulting from a stimulus that not normally provoke pain.
Seroma	Collection of fluid that sometimes appear within the operated tissue after surgery.
Wound Dehiscence	In these studies a wound measuring at least one cm <sup>2</sup> for at least two weeks.



# 1 INTRODUCTION

## 1.1 The cultural history of the breast

For thousands of years, the female breast has been a symbol of sexuality, motherhood, and nurture, and at times it has even been used as a metaphor for the collective responsibility of the nation, as during the French Revolution. At the dawn of human history, the ability to breast-feed was the difference between life and death for newborn babies, as there was no substitute for mother's milk. The so-called Venus figurines—ancient figures of women made of clay, bone, or stone, unearthed and dated to tens of thousands years ago—often have large breasts, bellies, and buttocks. All of them are believed to have been symbols of fertility. Ever since, the symbolism of motherhood and breast-feeding has gone hand in hand throughout history and religion, especially in art.

In the Renaissance, there was a transition in the visual arts from the sacred breast to the more erotic breast. These two forms of symbolism existed in parallel until the early nineteenth century, when, combined, the maternal breast with erotic overtones was used to serve national interests. Witness the bloody uprising in 1830, as painted by Delacroix (Fig. 1).

During the First and Second World Wars, pictures of terrorized women, their breasts bared, were used in the recruiting propaganda for the US Army. In the 1960s and 1970s, the women's liberation movement ushered in a 'bra-burning' era, and to this day groups of women use their naked breasts to make political statements.<sup>1</sup>



Figure 1. Eugène Delacroix (1830)  
La Liberté Guidant le peuple

## 1.2 The history of breast reduction

The general intention in breast reduction surgery is to reduce the negative effects of large breasts on physical function, but also to reduce the negative psychological and psychosocial effects. Breast reduction was first described in the sixth century AD. The first step in the history of breast reduction was to reduce breast size and manage healing. In the sixteenth century, Hans Schaller undertook what is thought to have been the first successful breast amputation, and in 1848 Johann Friedrich Dieffenbach conducted a breast resection via the inframammary fold. Variants on the resection of the breast have been conducted over the years.<sup>2</sup>

The second step was to create a new but smaller breast, with the preservation of the nipple. Hippolyte Morestin did the first transposition of the areola in the early twentieth century. Max Thorek popularized

mastectomies and free nipple grafting in 1922. The third step came when Victor Aubert described in 1923 how to reduce vascular complications of the nipple by making a flap, enabling the transposition of the nipple–areola complex with preserved blood circulation. In 1925, Raymond Passot duly described the technique of translocating the nipple to a position further up on the chest, and in 1930 Emil Schwarzmann suggested the superomedial dermal pedicle as a way of preserving circulation to the nipple (Fig. 2). A variety of techniques for breast reduction followed, and Hermann Biesenberger was the first to remove the skin in favour of an inverted T, even though his technique often led to necrosis.

In the 1950s, the development of new techniques for breast reduction accelerated. Thus in 1956, the Wise ‘keyhole pattern’ was developed for skin resection and became the basis of our modern breast reduction technique. Strömbeck further developed Schwarzmann’s ideas about a

Schwarzmann

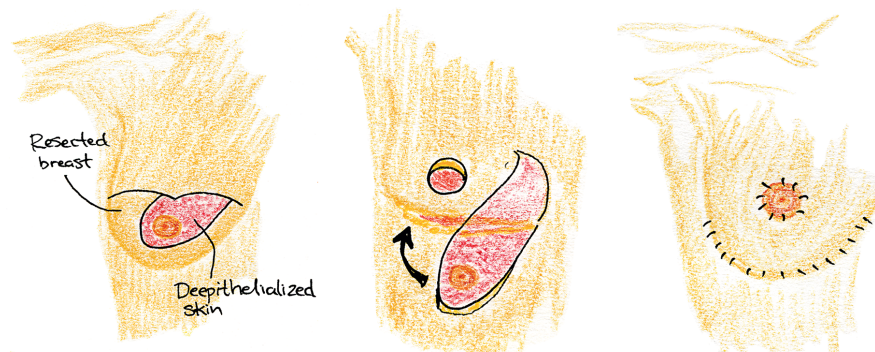


Figure 2 Schwarzmann

dermoglandular flap in 1960, publishing his horizontal 'dermoglandular bipedicle flap'.<sup>4</sup> In 1963, Skoog published 'A technique of breast reduction, transposition of the nipple on a cutaneous vascular pedicle', which described a superolateral flap.<sup>5</sup> In 1972, McKissock modified Strömbeck's technique by creating a thin 'vertical bipedicle flap'.<sup>6</sup>

During the 1960s, both Pitanguy and Weiner used superior pedicle techniques in combination with keyhole resection of the skin,<sup>7,8</sup> whereas Ribeiro, Robbins, and others developed the inferior dermoglandular pedicle technique in the 1970s to improve circulation and sensory function in the nipple-areola complex (NAC).<sup>9,10</sup> The common problem with many techniques was bottoming out, so in an attempt to reduce this Orlando and Guthrie (1975) tried to make superomedial pedicles that would preserve the volume and resist gravity<sup>11</sup>. In Europe and South America, surgeons such as Lassus, LeJour, and Benelli tried different short-scar techniques,<sup>12-15</sup> which became popular in order to avoid long horizontal scars and the attendant risk of becoming hypertrophic. These ideas also spread to the US and inspired Hammond to develop short-scar periareolar inferior pedicle reduction (SPAIR) mammoplasty<sup>16</sup> and Hall-Finday<sup>17,18</sup> to develop the LeJour technique further. In 1985, Hester described 'the mound technique', in which the circulation of the areola was based on a central block of breast tissue

attached to the pectoralis major.<sup>19</sup> In 1990, Blomqvist et al. published 'Nipple-areola transposition by the superolateral-rotation pedicle technique in reduction mammoplasty: surgical description', which describes the dominant technique used at Sahlgrenska today.<sup>20</sup>

### 1.3 Epidemiology

Breast hypertrophy is a common condition. Every year in Sweden some 1,500 women undergo a breast reduction surgery procedure. It is difficult to define normal breast size. Studies that attempt to determine the normal breast size have concluded that it is about 300!400 ml.<sup>21</sup> Since average body weight is gradually increasing in the Western world, the same probably goes for what can be defined as being a normal breast size. Many women who have large breasts do not experience the problems of back pain, neck pain, and other stress symptoms that those who seek help suffer from, although they may have difficulty in finding clothes, and in working and moving freely. Despite this, for various reasons many women with problems do not seek treatment for breast hypertrophy.

### 1.4 Breast embryology

The breast develops in the fourth week from two ectodermal thickenings called mammary ridges, or milk lines, that run from the future axilla down to the future inguinal region and medial thigh (Fig. 3). These ridges normally disappear except at the sites of the breasts, in women, where the ridge develops into primary buds in the fifth week. The buds grow down into the underlying dermis, and in the tenth week they begin to branch to form secondary buds in the twelfth week. At birth, the mammary gland consists of 15!20 lactiferous ducts that open into the mammary pit. Within a few weeks of birth, this converts into a nipple, and later forms milk-producing passageways in the fully developed breast.<sup>22</sup>



Figure 3. Milk lines



## 1.5 Breast anatomy

In young adult women, the breast is a rounded eminence lying within the superficial fascia. The base of the breast, where it attaches to the surface, overlies the deep pectoral fascia, which in turn overlies the pectoralis major muscle, the serratus muscle, and the oblique externus abdominis muscle. It's boundaries vertically is, from the second or third rib to the sixth rib, and in the transverse plane from the sternal edge, medially, to near the mid-axillary line laterally. A part of the breast in the superolateral quadrant extends through the fascia to the axilla, the so-called tail of Spence. Between the breast and the deep fascia, there is loose connective tissue that allows the breast some movement.

The breast is organized internally from epithelial glandular tissue, fibrous connective tissue (stroma) surrounding the glandular tissue, and interlobular adipose tissue. The gland is stabilized by stromal tissue from the ducts to the dermis and also by the suspensory, so-called Cooper's, ligaments that anchor the breast to the pectoralis major muscle (fig 4). In a breast without ptosis in young women, the areola is usually positioned in the fourth intercostal space above the submammary fold, just lateral to the mid-clavicular line.<sup>23</sup>

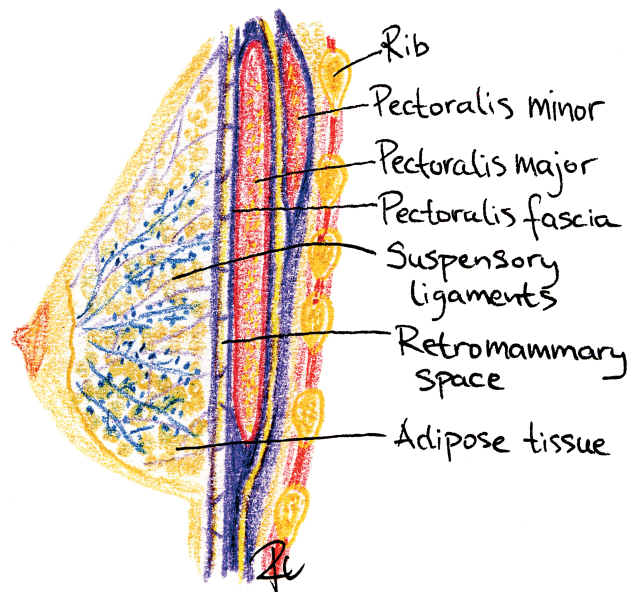


Figure 4. Breast Anatomy

The blood supplies to the breasts consist of branches from the axillary artery, the internal thoracic artery, and some intercostal arteries (fig 5). The axillary artery supplies blood via the superior thoracic artery, the pectoral branches of thoracoacromial artery, the lateral thoracic artery and the subscapular artery. The internal mammary artery, mostly from the second to the fifth perforator, gives perforating branches to the anteromedial part of the breast and the second to the fourth intercostal arteries give perforators to the more lateral part of the breast.

The main blood supply to the NAC, approximately 60%, comes from medial perforators, which run more superficially than the lateral, deeper-coming perforators, which can account for about 30% of the blood supply to the NAC.

Around the NAC, there is a venous plexus which!together with veins from glandular tissue!drains blood to the deep veins that accompany the arterial blood supply.<sup>24-26</sup>

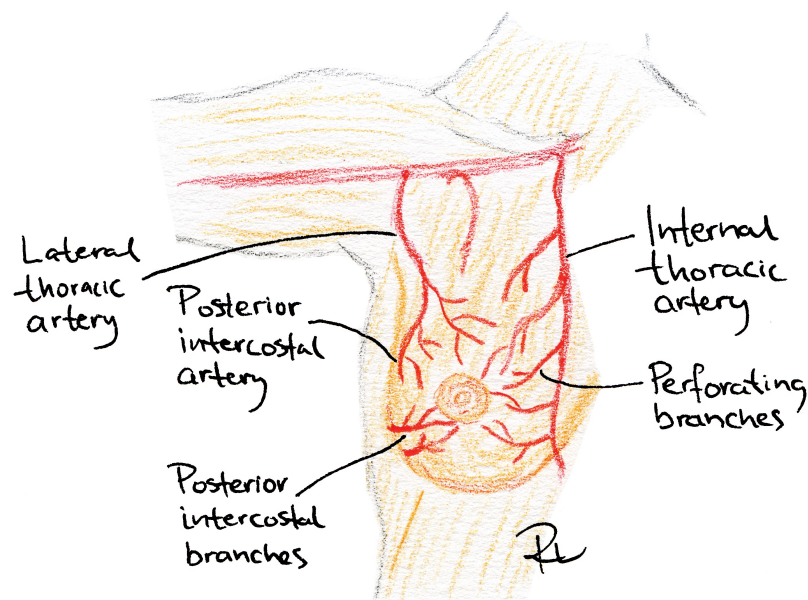


Figure 5. Anatomy of the main vascular structures

The intercostal nerve from the second to the sixth rib gives the breast innervation, of which the lateral innervation comes from the third to the sixth rib and the medial innervation comes from the second to the sixth rib (fig 6). Sensory innervation to the nipple-areola complex comes from both the lateral and the medial cutaneous branches of the third to the fifth intercostal nerves. The fourth nerve may be the main sensory nerve to the nipple, and enters the breast along the lateral border.<sup>24,27</sup>

The lymphatic system of the breast is composed of deep and superficial lymph vessels that communicate with each other and also from one breast to the other. Lymph vessels course laterally around the margin of the pectoralis major muscle and drain to pectoral lymph nodes that accompany the lateral thoracic vessels, and further to axillary lymph nodes. Another lymphatic route passes through the pectoralis major muscle and through the intercostal space, and ends up in parasternal lymph nodes along the internal mammary vessels and also in infra-clavicular lymph nodes. The third lymph vessel route is the intramuscular drainage, which passes directly through the pectoralis muscle to the

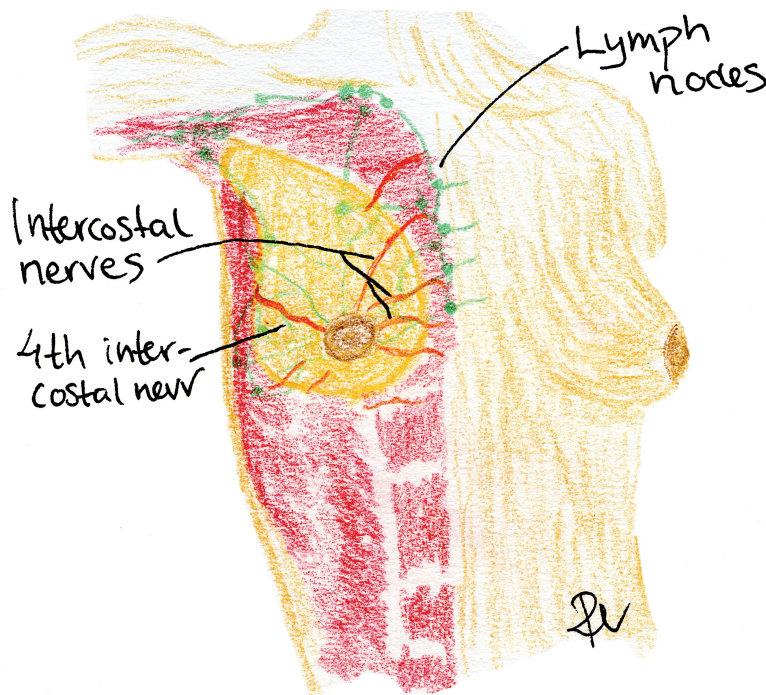


Figure 6. Anatomy of the nerval structures

## 1.6 Breast aesthetics

During the mid-1950s, Penn et al.<sup>29</sup> tried to define the perfect breast and wrote the article “Breast reduction” in which they examined a number of women between 18 and 39 years of age and concluded that the distance should be an equilateral triangle between the nipples and the sternal notch with a distance of 20.63 cm in an attractive breast. This work has been very important for the planning of transposition of the nipples to the distance of usually 19-22 cm (fig 7). In 2012 Mallucci et al<sup>30</sup> wrote the study “Concepts in aesthetic breast dimensions: Analysis of the ideal breast” where they studied pictures of 100 topless women published in tabloid paper “The Sun” and came to the conclusion that the perfect breast should have a 45:55 ratio between the upper and lower pole of the breast. Two years later they did another study confirming these results.<sup>31</sup>

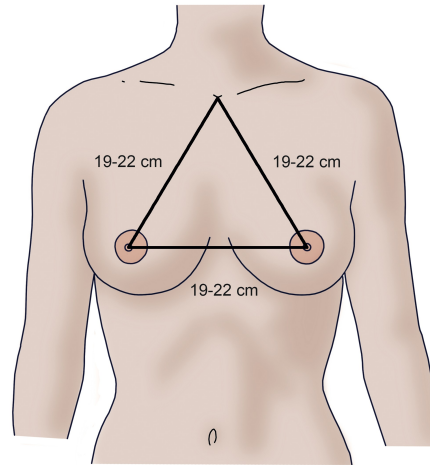


Figure 7. The ideal breast

## 1.7 Physiology of the normal breast

The breast undergoes major changes in life, and especially during puberty when the growth of the stroma and glandular breast tissue increases. Later, in the menopause, there is a transition from glandular tissue to more in-growth of fat and less vascularized tissue. Growth of the breast usually ends in late adolescence or soon after, although further growth during the latter part of life can occur as a gain in weight. During pregnancy, the ducts and lobules proliferate and the blood flow increases. After pregnancy, the ducts and lobules undergo involution when lactation ceases, but the breast never returns completely to its pre-pregnancy state. Many women find that their breasts change after pregnancy and lactation, often with reduced volume

and more ptosis, whereas some women may find that after the end of lactation, their breasts increase in size.<sup>2,32</sup>

After the menopause, there is progressive atrophy of lobules and ducts with fatty replacement of breast tissue; the stroma becomes less cellular and the collagenous fibers decrease in number. Many women at this age experience that their breast volume has become reduced, while some women instead experience increased volume and ptosis of the breasts - and associated breast hypertrophy problems.<sup>23</sup>

## 1.8 Gigantomastia

Gigantomastia is defined as a breast weight of more than 3% of the total body weight or a breast in need of a reduction of at least 1 500 g per side.<sup>33</sup> The etiology of this condition is in most cases idiopathic with normal hormone levels, but sometimes an imbalance of endogenous hormone production and excessive release of oestrogen or prolactin, during puberty or pregnancy is found. A rare etiology is drug-induced gigantomastia.<sup>34-37</sup>

## 1.9 Symptoms of breast hypertrophy

The women seeking help for their large breasts have physical symptoms, psychosocial problems, and practical concerns. Many of these women have tried to reduce their breast size for a long time through weight-loss, exercise, and physical therapy before seeking medical care.<sup>38,39</sup>

### Physical symptoms

Many women report **pain from the breasts, neck and back as well as pain and numbness in arms and hands.**

**Headaches** due to tense muscles.<sup>40</sup>

**Grooves in the shoulders** due to the bra strap; the grooves can be painful and hyper-pigmented.

**Eczema and fungal growth** under the breasts where the contact between the breast-skin and the skin of the upper abdomen is tight.

The experience of **heavier breathing.**<sup>41</sup>

**Restrictions in physical activity**<sup>42</sup> due to hindered movements or movements making activities painful when the breasts pendulate.

Many women report that they have to use 2-3 **different bras at the**

**same time** to reduce breast movement.

### Psychosocial and psychological symptoms

It is **difficult to find clothes** that fit over a large bust, and sleeves will not fit in length when one is forced to go up in size. Many also feel that they look more obese than they really are when they are wearing clothes that fit the breasts. Large bras need to be purchased in specialty stores and they are more expensive than normal bras.

**Feeling of discomfort and embarrassment in social situations** where too much emphasis is perceived to be on the breasts.

**Contributing to eating disorders**<sup>43,44</sup> as disproportionate upper body may lead to over eating in an attempt to camouflage their large breasts or may restrict eating as to reduce the breast size.

**Being uncomfortable in intimate situations** and unwilling to expose the breasts in front of their partner.

**Feeling of sexual unattractiveness** with too large breasts.<sup>45</sup>

**Lower self-esteem** and insecurity in social settings and concerning their body.<sup>46</sup>

**Feeling depressed and anxious due to their dissatisfaction with their breasts.**<sup>47</sup>

## 1.10 Swedish national guidelines

The Swedish national guidelines for breast reduction were presented in 2008.<sup>48</sup> In this work, it was suggested that a breast volume over 800 cm<sup>3</sup> (depending also on the size of the woman) should be considered to be hypertrophic, and that this size in combination with symptoms from the neck and back, long sternal notch to nipple distance, and/or psychosocial problems, should be the indication for breast reduction surgery. To be offered breast reduction, BMI criteria were described, referring to less surgical complications in non-obese women. It was therefore suggested that the BMI must be < 25 if the patient is less than 50 years of age, and < 27 if the patient is over 50 years of age. Smoking is prohibited 4 weeks before and 4 weeks after surgery, due to higher complication rates in smokers.

## 1.1.1 Surgical techniques

### 1.1.1.1 General aspects of breast reduction techniques

Many different surgical techniques have been described over the years, but they all have four basic concepts in common. **Firstly**, the vascular supply to the nipple-areola complex (NAC) must be adequate; **secondly**, there is removal of breast parenchyma and fat; **thirdly**, there is removal of excess skin; and **lastly**, there is shaping of the breast.<sup>49</sup>

The vascular supply of the NAC is complex and comes from different main arteries, ensuring blood supply from different directions and different depths. This complex vascularity makes it possible to base the pedicle from any direction, if it is done in a proper way with consideration of the vascular anatomy. Common variations of the pedicle are; superior pedicle, superiolateral pedicle, superiomedial pedicle, medial pedicle, lateral pedicle, inferior pedicle, central pedicle, and vertical and horizontal bipedicles.

Removal of the breast tissue is done either before the pedicle is formed or after it has been formed, depending on the surgical plan. As the breast is reduced in volume, the skin envelope must be adjusted to the new breast

volume and therefore also reduced. Different patterns of skin removal have been described, but the classical method is the inverted-T scar.

As the patients often have scarring as the top three complaints after surgery, there have been techniques (such as short scars) to limit the length of the scar. Shaping of the breast has always been a challenge for surgeons, and it is done with the breast parenchyma and is not only shaped using skin draping. The post-operative result often changes the shape of the NAC, and sometimes the breast is stretched too much in the lower part of the breast, i.e. "bottoming out". Many techniques for breast reduction have been used to try to address these problems by having internal sutures, using the pectoralis major muscle, and even having a different supportive mesh framework. However, to my knowledge there are no techniques for breast reduction that are superior to other techniques, as different patients have different anatomical conditions. It is therefore important to consider different surgical strategies to achieve full patient satisfaction—with the best possible aesthetic result.

### 1.1.1.2 Liposuction

This is a technology that may be an option for women who want a very small reduction, and do not want to risk unsightly scars or have a tendency to keloid formation. However,



it is only possible if the breast has a significant amount of fatty tissue. More common is liposuction laterally coupled to a more traditional reduction surgery.<sup>2</sup>

### 1.11.3 Wise-pattern design

#### Inferior pedicle technique

The name of the technique implies that the blood supply is from the inferior pedicle, which is not entirely true. A more appropriate description would be the “inferior segment technique.”<sup>50</sup> The new nipple position is marked using bimanual palpation of the inframammary fold (IMF). The distance from the sternal notch to the nipple is usually 21-25 cm. An inverted V with 4.5- to 7-cm limbs or the keyhole pattern is drawn onto the breast skin. Horizontal lines from the inferior end-points of the vertical lines are drawn to the medial and lateral lines of the IMF. The inferior pedicle is 8!10 cm at its base, and is de-epithelialized. A horseshoe-shaped resection is done, but leaving a layer of tissue over the pectoralis fascia to preserve vessels and nerves that enter the pedicle. The skin is tailored around the pedicle, which can be anchored with sutures to the surrounding tissue and the pectoralis fascia.<sup>3</sup>

#### Strömbeck horizontal bipedicle technique

This technique uses a dermal flap for preservation of the NAC (fig 8). The flap is attached both medially and

laterally, and resection is done mainly inferiorly but also cranially. Problems in relocating the NAC to its new inset and lack of feeling in the NAC postoperatively were common.<sup>4,51</sup>



Figure 8. Strömbeck horizontal bipedicle technique

### **McKissock vertical bipedicle technique**

This breast reduction technique uses a dermoglandular pedicle going from the inferior to superior in a vertical direction. In the superior part of the pedicle, above the nipple, there is a dermal-only component, that easily could be folded when relocated to the new NAC position.<sup>6</sup>

### **Medial or superomedial pedicle technique**

This breast reduction technique can be used for all degrees of size reduction, as the vascular supply to the NAC is dominated from the medial vessels and the pedicle can be done thin and still have good vascular supply. A wise-pattern design is used, and depending on the length of the planned elevation of the nipple, it can be designed to be a medial or superomedial pedicle. If the distance is short, a medial pedicle will not easily rotate into the correct position. This technique tends to conserve the breast volume medially and the resection is mostly inferior and lateral where the need for resection often is most important. After glandular resection, the NAC is rotated into the correct position and sutured, and the skin flaps are put together and stitched in the inverted-T shape.<sup>49</sup>

### **Superolateral pedicle technique**

This is exactly the same technique as described above for the superomedial pedicle technique, but the vascular supply is from the lateral and deeper

vessels from branches of the axillary arteries, i.e. the lateral thoracic arteries (fig 9). Resection is done predominantly from the inferior part of the breast, including the medial and lateral parts. The resection from the lateral part should be larger than on the medial side, as there is often underestimation of the lateral volume.<sup>20</sup>

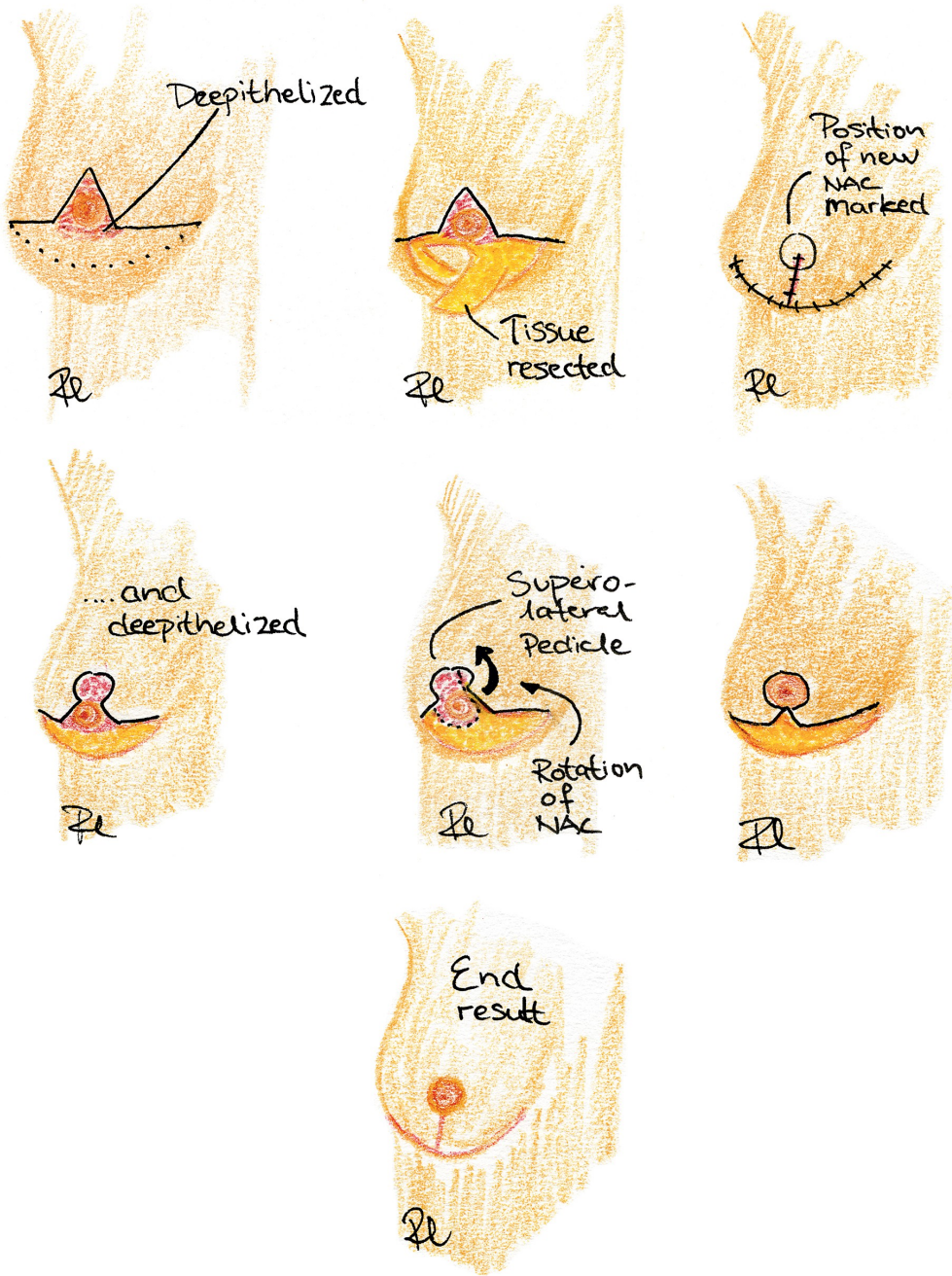


Figure 9. Superolateral pedicle technique

### **Superior pedicle technique**

This is same technique as described for the superomedial pedicle technique, but the NAC slides cranially to the new position. The de-epithelialized area around the NAC is incised medially and laterally to enhance the sliding, and if necessary the dermis can be divided 1 cm inferior to the NAC. The skin is managed as previously described for Wise pattern i.e. the inverted-T pattern.

### **Central mound pedicle technique**

The technique is based on a glandular blood supply to the nipple through the pectoralis muscle. A Wise pattern is drawn, and the skin together with subcutaneous fat is separated entirely from the gland to which the NAC is attached. An inferiorly de-epithelialized dermal flap of about 4 cm can be used. To preserve vessels and nerves, 3–4 cm of tissue over the pectoralis fascia is spared. The gland can be resected tangentially, modified, and anchored to the chest wall, and the skin is re-draped over the gland.<sup>52</sup>

## **1.11.4 Short-Scar techniques**

### **The short scar periareolar inferior pedicle reduction mammoplasty (SPAIR)**

This technique is useful in medium-to-large resections. An inferior pedicle is sutured to the upper pole for breast fullness, and down to the pectoralis muscle fascia to stabilize the breast. The skin envelope is sutured to the NAC with periareolar purse string technique using non-absorbed sutures combined with vertical scar technique, where the inferior dog-ear is handled by de-epithelialization of the medial part of the skin border and shaping of the scar to a J-form going laterally.<sup>16,53</sup>

### **L-shaped short-scar breast reduction**

This is used in small-to-moderate breast reductions with the goal of reducing scar length compared to the more classical inverted-T pattern. The preoperative drawing and planning is based on chest measurements and distances from the mid-sternal line. The incision is located 1 cm above the IMF, and the breast is extensively undermined at the level of pectoralis fascia. Resection is done inferiorly, the remaining pillars are sutured together, and the skin is closed in an L-shape going laterally.<sup>52,54</sup>

### 1.11.5 Vertical mammoplasty

#### Lassus Technique

This is best used in small-to-moderate breast reductions, and may give more projection than a horizontal resection—with avoidance of horizontal scars. A circular area between the top of the new NAC position and a point 4–5 cm above the submammary fold is de-epithelialized, and a central wedge resection is done without any undermining of the gland.<sup>12</sup> The skin is sutured together at the end of surgery. The shape is like the “nose of the Concorde”, which will settle after some time and give good results without the problem of bottoming out. Hall-Findlay has modified the technique, among others, using a superomedial pedicle.<sup>17</sup>

#### Vertical reduction with a short horizontal scar

The technique is similar to the Lassus reduction but with a few modifications, such as undermining underneath the NAC and to the upper part of the breast. A 2-0 stich is placed from the fascia of the pectoralis major muscle in the upper limit of undermining to the area under the central pedicle, just above the NAC position. The medial pillars are stitched together, the skin is closed, and the remaining dog-ear is excised inferiorly.

### 1.11.6 Periareolar reduction

#### Benelli mastopexi and reduction

This is used in moderate breast hypertrophy, as there is a risk of enlargement of the NAC and also of the scar. The technique uses de-epithelialization around the NAC, and from this zone one gains access to the gland, which can be resected in different directions depending on the need. The rest of the gland is modelled with stiches to achieve a good breast shape and the wound is closed with round block cerclage stiches.<sup>15</sup>

#### Curcumvertical reduction technique

This technique of breast reduction combines periareolar skin removal with the vertical scar method. It is possible to use this technique for large resections, but a 400- to 700-g resection is ideal. The new desired nipple position is marked, and the area to be de-epithelialized has the form of an inverted drop where the sharp angle is located 2–4 cm above the IMF. The gland is detached from the skin (and 1 cm of subcutaneous fat) inferiorly and excised in a W-shaped resection. The pillars are sutured together and also anchored to the pectoralis fascia. A stitch divides the wound into circular and vertical ones. The periareolar wound is closed using cinching sutures or interlocking sutures. One never lets

the vertical suture line go under the IMF.<sup>49</sup>

### **1.11.7 No vertical-scar breast reduction**

This technique is especially useful in large and ptotic breasts. The pedicle is inferiorly based and the resection is done around and above the pedicle. Instead of opening the skin in a Wise pattern, the skin is pulled down to the IMF like a blind and a button-hole for the NAC is made. The NAC is sutured, and also the IMF. Some problems with flattening of the breast mound can be seen.<sup>55</sup>

### **1.11.8 Breast amputation and free nipple graft**

In women with very large breasts where the pedicle will be too long to be supplied with sufficient blood or when the patient wants to have really small breasts and the size of a pedicle would make this impossible, a breast amputation using the Wise pattern can be used together with the NAC transplanted as a free graft. The free grafting can also be a solution in a situation with a devascularized nipple intraoperatively. A problem when using this technique is, of course, the risk of necrosis of the NAC—and sometimes depigmentation<sup>2,49</sup>

## 1.12 Complications

### 1.12.1 Early complications - within 30 days

**Haematoma** is an early complication, and in some cases a reoperation is needed for active bleeding or if large amounts of blood clots (but not active bleeding) impair capillary refill to the NAC.

**Seroma** is exudate that may occur postoperatively and in exceptional cases, it may have to be drained.

**Infections** are common, but they are difficult to define. Classic signs such as redness, swelling, heat gain, and pain along with pus would indicate an infection! hopefully complemented with positive culture results. Several different definitions have been presented over the years but without any consensus emerging.

**Skin necrosis** means that the blood circulation to the affected skin is inadequate.

**Fat necrosis** means that circulation to the fat tissue is inadequate. Fat tissue is more sensitive to this than skin.

**Nipple loss** is one of the more tedious complications of this kind of surgery, and it is usually divided into three different categories where the first is epidermolysis, which means that the upper layer of the skin

sloughs off. The others are partial necrosis, which is total necrosis in part of areola, and total necrosis, which means that the whole NAC is affected (fig 10).



Figure 10. Necrosis of the NAC

### 1.12.2 Late complications - after 30 days

**Nipple numbness** affects some patients. There is either total absence of sensory function or the sensory system has deteriorated.

**Hypertrophic scars** can affect patients, which is usually perceived as being cosmetically very distracting and sometimes even functionally disturbing! with itching and tingling, especially in keloids. Inframammary scarring is perceived as

being aesthetically disturbing, especially by younger women.

**Asymmetry** often occurs. However, as this is common in the general population (without any breast surgery), it is not so disturbing.

**Inadequate reduction** can occur, where the end result does not come up to the patient's expectations.

**Over-reduction** can occur, and once again there is a discrepancy between expectations and result.

**"Boxy" breast deformity and lateral fullness** are cosmetic deviations that are said to be more common with some breast reduction techniques.

**Recurrent enlargement** can occur when surgery is performed before the breast has stopped growing, or in gigantomasti.

**Inability to breast-feed** is reported in the literature to be about 30%, but this is difficult to evaluate, and it might be different depending on the breast reduction technique. However, all women are not able to breast-feed, and especially those with large breasts are said to have more problems than those with smaller ones, which is why the cause of inability to breast-feed postoperatively is difficult to evaluate.

**"Dog-ears"** are protrusions of extra skin, and if they give functional

problems or are aesthetically disturbing, they can be excised after 1 year.

**Tactile hyperesthesia** may present in rare occasions, and is described as a sharp sensation of pain to the touch. This causes great morbidity for the affected woman.

**"Bottoming out"** is a problem seen in most types of breast reduction techniques.<sup>56</sup>



## 1.13 Surgical site infection (SSI)

### 1.13.1 Background

Over the centuries, before late 1860 when Joseph Lister introduced the principles of antisepsis, surgical patients often got postoperative infections and sepsis, which was frequently fatal. When the skin barrier is broken (as in surgery) there is always a risk of contamination with bacteria—and sometimes a postoperative infection.<sup>57</sup> Postoperative infection is the second most common nosocomial infection in Sweden, causing unnecessary costs for society, and great morbidity for the patient.<sup>58</sup> In most cases, it is the patient's own bacteria that contaminate the wound, e.g. skin flora that grow in the wound and later cause a clinical infection.<sup>57,59</sup> Microbial contamination of the surgical site is a necessary precursor to SSI. The risk of SSI can be expressed according to the following equation:

$$\text{The risk of surgical site infection} = \frac{\text{(dose of bacterial contamination} \times \text{virulence)}}{\text{resistance of the host (i.e. patient)}}^{57}$$

The bacteria in the ducts of the breasts are predominantly *Staphylococcus epidermidis*<sup>60</sup>, but the most common bacterium in postoperative infections after breast reduction surgery is *Staphylococcus aureus*.<sup>57,59,61-63</sup>

### 1.13.2 Criteria for defining SSI

There are no universal criteria for an infection, as it often involves interpretation of clinical symptoms and laboratory findings.<sup>64,65</sup> The Centers for Disease Control (CDC) have tried to define SSI by dividing the infections into three different categories:<sup>57,62,66,67</sup>

1. Superficial incisional SSI, arising within 30 days of surgery and involving only skin or subcutaneous tissue
2. Deep incisional SSI, arising within 30 days of surgery if no implant is left in place or within 1 year if an implant is in place, and involving deep soft tissue such as the fascia and muscle layers.
3. Organ/space SSI, arising within 30 days of surgery if no implant is left in place or within 1 year if an implant is in place, and involving any part of the anatomy.

The criteria for superficial SSI from the CDC are about purulent drainage, organisms isolated, clinical signs, or diagnosis of SSI by the surgeon or attending physician.

We found this scale to be too subjective, as did Tanner et al.<sup>68</sup>, which is why we developed a simpler objective scale, which is described in Materials and methods and later on in the Discussion.

### 1.13.3 Prophylactic antibiotics

The main reason for using antibiotics prophylactically is to prevent postoperative infection. With the rise of bacterial resistance, driven by inadequate use of antibiotics, it is also very important to reduce the need for postoperative antibiotic treatment. Also with increasing resistance antibiotic postoperative treatment will become less effective.

Prophylactic antibiotic in e.g. gut surgery<sup>69,70</sup>, vascular surgery<sup>71,72</sup>, abdominoplasty<sup>73</sup>, orthopedic surgery<sup>74</sup>, and also in breast cancer surgery<sup>75</sup>, have reduced the postoperative infections.<sup>76</sup> In other kinds of surgery, though the scientific evidence for the effectiveness of prophylactic antibiotics is weak. There is still a need for well-designed prospective studies that evaluate timing, dosage, and type of antibiotics regarding postoperative infections. In breast reduction surgery there have been controversies about the effectiveness of prophylactic antibiotics, as the few studies that have been done have led to different conclusions.<sup>61,67,76-80</sup>

The concentration of antibiotic in serum depends on the speed of absorption and the bioavailability. Water-soluble antibiotics such as beta-lactam antibiotics, glycosides or aminoglycosides are mostly distributed in the extracellular compartments which makes concentration in

tissue low. Antibiotics that are fat-soluble, such as clindamycin, have the capability of intracellular penetration, which makes the concentration in tissue high—sometimes even higher than in serum. When using antibiotics, the pharmacokinetics in relation to the minimum inhibitory concentration (MIC) for the specific bacterium to be treated always must be considered.<sup>81</sup> With regard to prophylactic antibiotic the timing to surgery is crucial, if it is given too early or too late in relation to initiating surgery, the effect against bacteria will be suboptimal. The optimal time frame for intravenous administration is believed to be 30–120 min before surgery.<sup>82,83</sup> In this aspect there have been very few high-quality studies in the field of plastic surgery.

Beta-lactam antibiotics mainly has a bactericidal effect, and its mechanism of action is to interfere with the cell wall synthesis of the bacteria. After an intravenous dose of 2 g cloxacillin, which is effective against methicillin sensible *Staphylococcus aureus* and *Streptococcus* group A, C, and G, a concentration in serum above the MIC of these bacteria is achieved.

Clindamycin has a bacteriostatic effect, which generally, at least in Sweden, is effective against bacteria such as *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Streptococcus viridans*,

and also some anaerobic bacteria. It uses the mechanism of binding to the bacterial ribosome, thus inhibiting protein synthesis. The maximum concentration in serum is reached after 45 min when administered intravenously.

## 1.14 Patient Reported Outcomes and HRQL

Quality of life is a broad term that can include the more general well-being of individuals—such as economic, social, and environmental well-being — and it is not only related to health. It is often associated with happiness and satisfaction with life. The World Health Organization (WHO) has defined health as “a complete state of physical, mental, and social well-being, not merely absence of disease”. There is no consensus about what should be included in the term “quality of life”, and in clinical medicine and clinical trials the focus is on diseases and their consequences. To distinguish between the broader quality of life and the narrow concept relating to diseases, the term “health-related quality of life” (HRQL) is used. There are many aspects of this that can be included, such as general health, physical function, physical symptoms, emotional functioning, cognitive functioning, role functioning, social well-being, psychosocial well-being, sexual functioning, toxicity, and existential issues.<sup>84</sup>

Patient-reported outcome (PRO) means that the patients themselves judge their own state of mind and quality of life without interference or interpretation from clinicians, relatives, or other people. Several studies have shown that patients’ own

evaluation of their lives differs from estimates done by people around the patient. PRO can be measured using open or semi-structured interviews or questionnaires. The reasons for measuring HRQL are several. Many diseases are incurable or chronic, and when a new treatment or therapy is considered there must be a weighting of the positive clinical effect against potential loss of HRQL.<sup>85</sup>

By using questionnaires/instruments, most often self-administered, for evaluation of HRQL, it is possible to gain information about disease, surgery, or other interventions. If questionnaires are used, it is important that they measure what they are intended to measure and that they are stable enough to measure a real state of quality of life—and also sensitive enough to detect the mood and changes in quality of life. Most often, it is also of great importance that the questionnaire has been validated for the intended population, especially when a specific disease is being evaluated.

There are several different types of HRQL instruments<sup>84-86</sup>

**Generic instruments** e.g. SF-36 are used to measure general health, irrespective of disease, and it is also possible to use them in healthy populations. An advantage is that comparisons may be done between populations, but they may also be insensitive to the disease condition and to

the specific problems and disabilities that are associated with them.

**Population-specific instruments** are designed to be appropriate to particular demographic groups, e.g. studies of children in general or elderly people in general.

**The diagnosis-/disease-specific instruments** e.g. BREAST-Q, are more sensitive to specific problems of the disease studied, and measure the patient's perceptions of a specific disease or health problem and the clinical effect of an intervention. The instrument only contains items relevant to the actual disease and the acceptability to respond among patients is often high.

**Dimension-specific instruments** assess one particular aspect of health status such as the presence of depression, psychosocial behaviour, or sexual activity e.g. mBEQ and BDI.

**Individualized instruments** allow the respondents to choose the content of the instrument and/or rate the importance of individual items. This gives a very high content validity, but they often need to be administered by interviewing to achieve a high response rate.

**Utility measures** e.g. EQ-5D, attach values, derived from general population surveys, to individual health states and express them as a single index. The index can be used in comparisons between treatments,

and also for evaluation of cost-utility analysis—but it can also be broad in focus, and may therefore not be sensitive enough to reflect the disease of interest.

**Summary items** try to reflect a certain health status by using a single item or very few items. As the questions are few they are easy for respondents to fill in, but the problem is often that they are not sensitive enough to capture small, clinically important changes.<sup>86</sup>

## 2 AIM

The overall aim of this thesis was to improve the knowledge about women with breast hypertrophy and the outcome of breast reduction.

### 2.1 Specific aims

**To identify** risk factors for complications after breast reduction surgery.

**To evaluate** the effect of prophylactic antibiotics in breast reduction surgery given according to standard recommendations.

**To evaluate** the validity and reliability of the Breast Evaluation Questionnaire (BEQ).

**To analyze** the impact of breast hypertrophy on both general and breast related health.

**To evaluate** health effects of breast reduction surgery.

**To evaluate** the correlation between BMI, sternal notch to nipple distance, breast volume, and resection weight and health gain.

## 3 PATIENTS AND METHODS

### 3.1 Statistical methods Paper I - IV

#### 3.1.1 General

The distribution of variables is given as the mean, SD, median, and range (minimum and maximum) for continuous variables and as the number and percentage for categorical variables. All significance tests were two-sided and conducted at the 5% significance level. All statistical analyses were performed using SAS Version 9, SAS Institute, Cary, NC, USA. See table 1.

#### 3.1.2 Paper I

Modelling of complications by various predictors was done by first performing univariable logistic regression for each predictor. The result from the logistic regression was given as Odds Ratios (OR) with 95% confidence intervals, p-values, and area under the ROC curve. Area under ROC curve was calculated for description of goodness of predictors. In order to identify independent predictors, all univariable significant predictors were entered into a stepwise multiple logistic regression analysis. Final models were then calculated by multiple logistic regressions using the predictors select-

ed in the stepwise model. The result from the multiple logistic regression was given as adjusted Odds Ratios (OR) with 95% confidence intervals, adjusted p-values, and area under the ROC curve.

#### 3.1.3 Paper II

For comparison between the two randomized study groups, Fisher exact test was used for dichotomous variables, the Mantel-Haenszel  $\chi^2$  test was used for ordered categorical variables, and the Mann-Whitney U-test was used for continuous variables. For comparison between dichotomous outcome variables between the two randomized study groups Relative Risk (RR) with 95% confidence interval and risk difference with 95% confidence interval were calculated. For primary outcome exact 95% confidence intervals were calculated for the proportions.

#### 3.1.4 Paper III

An exploratory factor analysis of all the items of the BEQ was performed to analyze the correlations among the items and how they clustered together to represent underlying factors. The scales obtained from this factor analysis were validated both internally and externally. In order to investigate whether the data were suitable for an exploratory factor analysis, the Kaiser-Meyer-Olkin (KMO) measure of sample adequacy was calculated and Bartlett's test of sphericity was performed. The KMO statistic measures

the relationship between the correlations and the partial correlations. Bartlett's test of sphericity is used to test whether or not there is a correlation between the variables. In order to perform an exploratory factor analysis, KMO should be  $> 0.5$  and Bartlett's test should be highly significant. The number of latent factors (subscales) was chosen based on scree plots, and an orthogonal rotation varimax was used. Only items with factor loadings  $> 0.5$  were included in the latent factors.

### **Validity**

Internal consistency of subscales was analysed by Cronbach's alpha, multitrait-scaling analyses (for item-convergent validity and item-discriminate validity), and for the external validation (for convergent validity and discriminate validity) against "Social Functioning" and "Role Emotional" of the SF-36 and questions no. 1-3 of the BREAST-Q (reduction). Item-convergent validity and item-discriminate validity are both considered subtypes of construct validity. Convergent validity refers to the degree to which two subscales that should theoretically be related are in fact related. To test external convergent validity, a strong but incomplete correlation to the BREAST-Q (reduction) was expected. In contrast, external discriminate validity tests whether items that are supposed to be unrelated or vaguely related are in fact unrelated or vaguely related. To test external discriminate validity, a weak-to-

moderate correlation to the SF-36 was expected.

### **Internal validity**

Cronbach's alpha values from 0.70 and higher were aimed for; scales with alpha values of less than 0.60 were considered unacceptable. Correlation between each item and its own scale corrected for overlap, item convergent validity, was accepted if  $> 0.40$ . Item discriminant validity was assessed from correlations between the items in the investigated scale and in the other scales. A scaling success was counted if the item was significantly higher correlated to its own scale (corrected for overlap) than to all other subscales in the same modified BEQ questionnaire. The subscales were calculated from the mean of the items included and transformed linear to a 0-100 scale.

### **External validity**

#### **Convergent validity**

Convergent validity was established by comparing the observed Pearson correlation coefficient ( $r$ ) between the subscales of BEQ and variables in the BREAST-Q reduction module with the high theoretical correlations expected between BEQ and BREAST-Q.

#### **Discriminant validity**

Discriminant validity was established by comparing the observed Pearson correlation coefficient ( $r$ ) between the subscales of BEQ and



SF-36 dimensions with the low theoretical correlations expected between BEQ and SF-36.

Pitman's non-parametric permutation test was used for significance testing of the correlations.<sup>87</sup>

### **Known-groups validation**

Sensitivity analyses were performed by known-groups analysis, comparing patients waiting for breast reduction surgery and controls (women not having any breast surgery) using Mann-Whitney U-test. Cohen's effect size (ES) between the two groups was also calculated.

### **Reliability**

A subsample of 36 patients was selected for a retest of the modified BEQ at 2-4 weeks after the first test. Reliability of test-retest analysis was assessed with the distribution of the change, intra-individual SD (sw), and intraclass correlation coefficient (ICC) for the subscales. Wilcoxon's signed-rank test was used for analysis of systematic changes between test and retest for subscales. In 95% of the observations, the true value will be within  $1.96 \times sw$  of the measured value.

## **Responsiveness**

We evaluated the ability of the questionnaire to detect change over time. A second modified BEQ was sent to a subsample of 27 patients one year postoperatively. The distributions are given for before surgery, for 1 year after surgery, and for change from before surgery to 1 year after surgery. Wilcoxon's signed-rank test was used to analyze the change from preoperatively to postoperatively. Standardized response mean (SRM) and Effect size (ES) were also calculated.

### **3.1.5 Paper IV**

For comparison between two groups, the Mann-Whitney U-test was used for continuous variables, the Mantel-Haenszel Chi-square test for ordered categorical variables, and Fisher's exact test for dichotomous variables. For comparison of change over time, the Wilcoxon signed rank test was used for continuous variables and Sign test for ordered categorical variables. Spearman's rank correlation coefficient was used for all correlation analyses.

**Table 1. Statistical methods paper I-IV**

Statistical methods	Paper			
	I	II	III	IV
<b>Descriptiv Statistics</b>				
Mean, SD, Median, Minimum and maximum for continuous variables	X	X	X	X
Number and % for categorical variables	X	X	X	X
<b>Statistical Analysis</b>				
For comparison between two groups:				
" Mann-Whitney U-test for continuous variables	X	X	X	X
" Mantel-Haenzsel Chi-Square test for ordered categorical variables		X		X
" Fisher's exact test for dichotomous variables		X		X
For changes over time:				
" Wilcoxon Signed Rank Test for continuous variables				X
" Sign test for ordered categorical variables				X
Standardized response mean (SRM) and Effect size (ES)			X	
Relative Risk with 95% Confidence Interval and Risk Difference with 95% Confidence Interval		X		
Univariable logistic regression analysis with Odds ratio with 95% Confidence Interval	X			
Stepwise multiple logistic regression analysis, OR with 95% CI and calculation of area under the ROC-curve	X			
Spearman rank correlation coefficient				X
Exploratory Factor Analysis, Kaiser-Meyer-Olkin measure of sample adequacy, Bartlett's test and Varimax rotation			X	
Internal Validity: Cronbach's alpha, correlation item to scale corrected for overlap, Item discriminant analysis			X	
External Validity: Pearson correlation coefficient, Pitman's non-parametric permutation test.			X	
Reliability: Test – retest: Distribution of changes, intra-individual SD, intra-class correlation coefficient for subscales and Weighted Kappa and percent agreement for single items			X	

## 3.2 Patients

### 3.2.1 Study I

Medical records of 512 consecutive women mean ages 40 years, who underwent bilateral breast reduction surgery were included in this retrospective study.

### 3.2.2 Study II

Altogether, 345 women were candidates for this randomized and prospective study. Sixteen were excluded due to previous breast surgery, three were lost to follow-up, and one patient had been randomized to the control group, but received prophylactic antibiotics by mistake. Three hundred and twenty-five women met the criteria according to the protocol. One hundred and sixty-three mean age 40 years were randomized to the control group and 162, mean age 40 years were randomized to the intervention group.

### 3.2.3 Study III

Two hundred and twenty-five women, mean ages 40 years, undergoing breast reduction were consecutively included in this validation study. For the control population, 1,000 women aged between 18 and 70 years old and living in the western region of Sweden were sent a letter and the mBEQ. Two hundred and sixteen women (22 %), mean ages 43 years returned the questionnaires.

### 3.2.4 Study IV

Three hundred and forty-eight consecutive women were potential candidates for this prospective study. One hundred and fifty-nine, mean ages 44 years, answered both the preoperative and the postoperative questionnaires (46%). One hundred and twenty-nine women answered either the preoperative questionnaire or the postoperative questionnaire (37%). Sixty women did not answer any questionnaire (17%). The mean ages of those who did not answer either questionnaire or only one was 38 years.

## 3.3 Methods of data collection

### 3.3.1 Study I

Medical charts were reviewed retrospectively for patients who underwent bilateral breast reduction surgery between 2001 and 2007. Five hundred and twelve women were identified. Complications were registered and when it comes to accessing infections, an infection scale was used.

### 3.3.2 Study II and IV

Women referred to the Department of Plastic Surgery at Sahlgrenska University Hospital, were asked to participate in both studies. They were to be randomized to prophylactic antibiotics or as controls. The randomization was done using a, Microsoft Office Access 2008, balancing mean of age, BMI, breast volume and sternal notch to nipple distance.

Questionnaires for study IV, SF-36, BRSQ, mBEQ and BREAST-Q, were sent home to the patients before surgery. One year after breast reduction another letter with an internet-key were sent to the patients so they could fill in the questionnaires using a computer. If no response a reminder letter was sent and if still no response a letter with questionnaires were sent.

### 3.3.3 Study III

The patients were asked to answer mBEQ, SF-36, and BREAST-Q (reduction) preoperatively and 1 year postoperatively. For further analysis, a subgroup of the participants completed one more mBEQ 2-4 weeks after the first questionnaire was completed. A control group was built by sending the BEQ to 1000 randomly selected women, from a Swedish register, which had not been subjected to breast surgery, between 18-70 years of age, living in the region of western Sweden. The register contains all Swedish citizens and is called "*SPAR, Statens Personadressregister*". These women were representing the normal population. Exclusion criteria for the control group were women who had undergone breast surgery or had returned incomplete questionnaires.

## 3.4 Questionnaires

### 3.4.1 Study III and IV

The **Breast Evaluation Questionnaire (BEQ)** was initially developed to evaluate the psychosocial effect of breast augmentation.<sup>88</sup> It has since been modified (to the mBEQ), has been validated, and proven to be reliable for the breast hypertrophy population, a study that is presented in this thesis (Study III). The questionnaire has four dimensions: Breast, Clothes, Naked, and Family. The last question in the fourth dimension was deleted from the original version after psychometric analysis, analysis of missing items, expert opinions, and field-testing. The score is between 1 (very dissatisfied/uncomfortable) and 5 (very satisfied/comfortable).

The **Short Form 36 (SF-36)** is a generic questionnaire with good reliability and validity in Swedish.<sup>89-91</sup> It is designed for measurement of health-related quality of life (HRQL) with a recall period of 4 weeks. This instrument contains 36 items in 8 domains: Physical Functioning (PF, 10 items), Role limitations due to Physical problems (RP, 4 items), Bodily Pain (BP, 2 items), General Health (GH, 5 items), Vitality (VT, 4 items), Social Functioning (SF, 2 items), Role limitations due to Emotional problems (RE, 3 items), and Mental Health (MH, 5 items). A score for each domain is calculated using a standardized scoring system. The scoring is between 0 (worst

possible HRQL) and 100 (best possible)

HRQL). From these domains Mental and Physical Composite can be obtained.

The **BREAST-Q**<sup>92,93</sup> (reduction) questionnaire is specific for the condition of breast hypertrophy and was developed through patient interviews, focus groups, expert panels, and literature reviews. It has been tested for both reliability and validity. BREAST-Q has three QoL domains (Physical well-being, Psychosocial well-being, and Sexual well-being) and three satisfaction domains (Satisfaction with breasts, Outcome, and Care). Four domains (Satisfaction with breasts, Psychosocial well-being, Sexual well-being, and Physical well-being) were evaluated pre- and postoperatively, and therefore these could be used for assessment of changes after surgery.

### 3.4.2 Study IV

The **Breast-Related Symptoms Questionnaire (BRSQ)** (table 2) was developed for evaluation of the population of women who undergo breast reduction surgery. It has been validated and tested for reliability.<sup>94-</sup>

<sup>97</sup> A 13 item scale containing questions concerning breast-related symptoms. Scoring is between 1 (problems all the time) and 5 (no problems at all). Two scores can be obtained; Breast symptoms summary score (BSS-score) which is the mean of the thirteen items and the score of physical symptoms that contains seven of the items.

**Table 2. Breast Related Symptoms Questionnaire (BRSQ)**

1-5 (1 =All the time and 5=None of the time)	
1. My breast size causes upper back pain	8. My breast size makes it difficult for me to participate in sports
2. Because of my breast size I have difficulty in finding bras and clothes to fit	9. My breast size causes neck pain
3. Due to my breast size I have headaches	10. My breast size causes shoulder pain
4. I have breast pain	11. I have a hard time running because of my breast size
5. My breast size causes lower back pain	12. Because of my breast size I have pain in my hands or feel numb
6. Rashes or itching develop under my breasts	13. My breast size causes arm pain
7. I have a painful bra strap grooves	

### 3.5 Infection scale

There is no universal definition of an infection and several different classification systems have been proposed in the literature,<sup>62,65,73,98</sup> but there is no consensus regarding the optimal evaluation methodology. A positive bacterial culture or swab from the wound is sometimes regarded as indicating an infection. The classical symptoms of infection are heat, pain, swelling, redness, purulent drainage, and induration. However, many of the symptoms can also be seen after a soft tissue necrosis and inflammatory reaction. Treatment with antibiotics can also be regarded as an indication of an infection, but it is well known that prescription of antibiotics differs depending on tradition in different countries!and probably also on the experience of the prescriber.

We used classical symptoms of infections and created an “infection scale” which made evaluation of the symptoms more homogenous and also possible to compare with other studies (table 3). The grading was from 1, which was not necessarily an infection, to 4, which was much more likely to be an infection. This made the scale more useful, as it was possible to evaluate whether antibiotic treatment was initiated without strong symptoms of an infection (i.e. grade 1).

**Table 3. Definition and grading of wound infection**

Grading	Definition
1	Wound exudate
2	Redness, swelling, heat, and exudate
3	Redness, swelling, and heat + purulent drainage or induration
4	Grade 3 + fever and/or septicaemia

## **3.6 Ethics**

All the studies were conducted in accordance with the declaration of Helsinki and were approved by the Regional Ethical Review Board in Gothenburg, Sweden (entry no. 036-09).



## 4 RESULTS

### 4.1 Study I

Altogether, 512 records were reviewed and 216 complications were seen in 162 women within 30 days of the breast reduction surgery, giving an overall complication rate of 32%. The surgical dermoglandular pedicle techniques used were the superolateral technique (82%), the sliding nipple technique (10%), the superomedial technique (1.6%), the inferior technique (Robbins) (0.6%) and LeJour (0.2%).

#### 4.1.1 Univariable predictors

**Age** was significantly correlated to *fat necrosis* (OR 1.06 95% CI=1.01-1.10,  $p=0.012$ ), *delayed wound healing* (OR 0.98 95% CI=0.96-1.00,  $p=0.034$ ), and to *necrosis of the areola* (OR 1.04 95% CI=1.01-1.08,  $p=0.022$ ).

**BMI** was significantly correlated to *wound infection* (OR 1.24 95% CI=1.11-1.38),  $p<0.001$  and *fat necrosis* (OR 1.43 95% CI=1.17-1.75),  $p<0.001$ .

The **specimen weight** of the removed breast tissue was significantly correlated to *wound infections* (OR 1.17 95% CI=1.06-1.28,  $p=0.001$ ), *fat necrosis* (OR 1.28 95% CI=1.11-1.48,  $p<0.001$ ), *delayed wound healing* (OR 1.13 95% CI=1.02-1.25,  $p=0.021$ ) and *necrosis of the areola*,

(OR 1.21 95% CI=1.06-1.37,  $p=0.004$ ).

Preoperative **breast volume** was significantly correlated to all of the complications *wound infection*, (OR 1.14 95% CI=1.04-1.24,  $p=0.005$ ) *fat necrosis*, (OR 1.23 95% CI=1.06-1.42,  $p=0.006$ ), *delayed wound healing* (OR 1.12 95% CI=1.02-1.24,  $p=0.24$ ) and *necrosis of the areola* (OR 1.21 95% CI=1.06-1.39,  $p=0.005$ ).

**Sternal notch to nipple distance** (JM) was significantly correlated to *wound infection* (OR 1.17 95% CI=1.08-1.27,  $p<0.001$ ), *fat necrosis* (OR 1.38 95% CI=1.17-1.62,  $p<0.001$ ) and *necrosis of the areola* (OR 1.38 95% CI=1.20-1.60,  $p<0.001$ ).

**ASA classification** I vs. II was significantly correlated to *wound infections* (OR 1.88 95% CI=1.10-3.22,  $p=0.021$ ).

**Smoking** was significantly correlated to *wound infection* (OR 2.35 95% CI=1.31-4.20,  $p=0.004$ ).

**Diabetes mellitus** was significantly correlated to *necrosis of the areola* (OR 8.22 95% CI=2.09-32.34,  $p=0.003$ ).

### 4.1.2 Independent predictors and strongest univariable predictors

The strongest independent predictors to *wound infection* were **sternal notch to nipple distance (JM)** (adjusted OR: 1.14 95% CI 1.04-1.26,  $p=0.008$ ), **smoker** (adjusted OR: 2.89 95% CI 1.54-5.44,  $p=0.001$ ) and **BMI** (adjusted OR: 1.15 95% CI 1.02-1.30,  $p=0.027$ ), area under the ROC curve = 0.69 (fig 11).

The strongest predictor to *fat necrosis* was **specimen weight** of the removed breast tissue (OR 1.28 95% CI=1.11-1.48,  $p<0.001$ ), area under the ROC curve = 0.74. Due to the small number of fat necrosis ( $n=13$ ) no multivariable analysis could be performed.

The strongest predictor to *delayed wound healing* was **specimen weight** of the removed breast tissue (OR 1.13 95% CI=1.02-1.25,  $p=0.021$ ), area under the ROC curve = 0.58.

The strongest independent predictors to *necrosis of the areola* were **sternal notch to nipple distance (JM)** (adjusted OR: 1.37 95% CI 1.18-1.59,  $p<0.0001$ ) and **diabetes** (adjusted OR: 5.11 95% CI 1.09-24.1,  $p=0.039$ ), area under the ROC curve = 0.81.

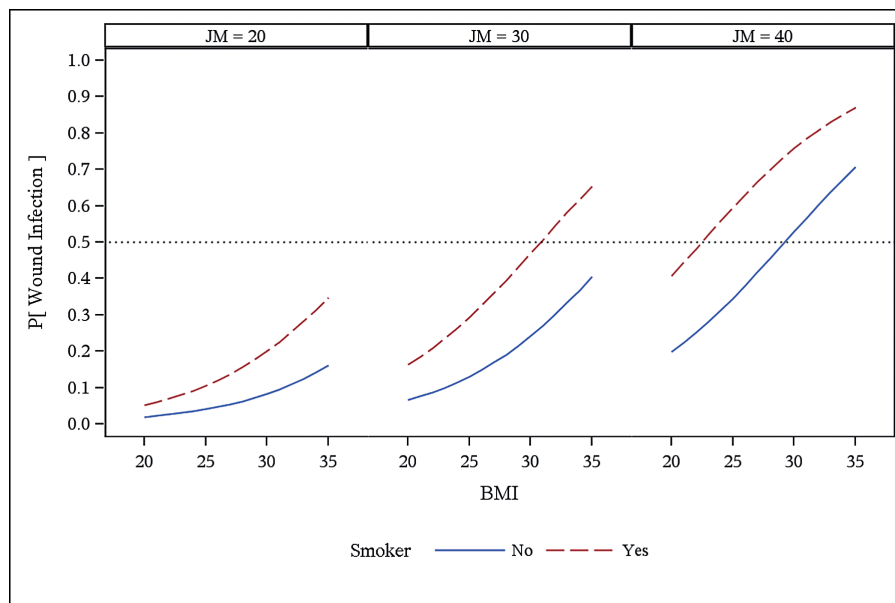


Figure 11. Prediction of wound infection by sternal-notch to nipple distance, smoking and BMI

## 4.2 Study II

One hundred sixty-two patients were assigned to the intervention group, which received preoperative antibiotic prophylaxis, and 163 patients to the control group. There were no significant differences between the two groups, preoperatively, concerning; age, BMI, preoperative breast volume, sternal notch to nipple distance, ASA classification or smoking.

Fifty-eight patients had postoperative antibiotic treatment due to suspected postoperative infection in the breast. Twenty-six of those (16.0%) were in the intervention group and 32 (19.6%) were controls. No significant difference was found between the groups (RR=0.82; 95% CI=0.51-1.31, p=0.49).

Twelve (7.4%) patients from the intervention group had a suspected infection, graded between 2 and 4,

and in the control group 15 patients (9.2%) were having a suspected infection graded between 2 to 4. No statistical difference was found between the groups (RR 0.80; 95% CI=0.39-1.66, p=0.69).

The duration of operation is generally considered to be a risk factor for SSI.<sup>59,62,64,99</sup> In our study there was a significant difference in duration of surgery between patients who had a postoperative antibiotic treatment due to suspected SSI and those who did not have postoperative antibiotic treatment (table 4).

Infections after different times of antibiotic administration were compared. The prophylactic antibiotics were supposed to be given between 30-90min prior surgery but due to logistic reasons this was not always achieved, why we analysed and concluded that the infection rate was not related to when the prophylactic antibiotic was administered (table 5).

**Table 4. Duration of surgery in patients treated with antibiotics postoperatively, due to suspected infection and those who not had a suspected infection**

Variable	No postop. antibiotic treatment (n=267)	Postoperative antibiotic treatment within 30 days from operation. (n=58)	p-value
Operation time (min)	110.1 (37.6) 103.5 (38.0; 240.0) n=258	129.0 (46.4) 123.0 (60.0; 240.0) n=58	0.0067
For continuous variables Mean (SD) / Median (Min; Max) / n= is presented. For comparison between groups the Mann-Whitney U-test was used for continuous variables.			

**Table 5. Infections correlated to time between administration of antibiotics prophylaxis and skin incision**

Variable	<30 min (n=35)	30-90- min (n=77)	>90 min (n=47)	Test between groups p-value		
				<30 min vs 30-90- min	<30 min vs >90 min	30-90- min vs >90 min
Postoperative antibiotic treatment within 30 days from operation.	4 (11.4%)	14 (18.2%)	7 (14.9%)	0.5436	0.9085	0.8311
Infection grading 1-4 within 30 days from operation						
No infection	32 (91.4%)	65 (84.4%)	40 (87.0%)			
Grade 1	1 (2.9%)	6 (7.8%)	2 (4.3%)			
Grade 2	2 (5.7%)	5 (6.5%)	1 (2.2%)			
Grade 3	0 (0.0%)	1 (1.3%)	2 (4.3%)			
Grade 4	0 (0.0%)	0 (0.0%)	1 (2.2%)	0.4986	0.3862	0.7102
Infection grading within 30 days from operation: No infection + Grade1 vs. Grade2-4						
No infection+Grade1	33 (94.3%)	71 (92.2%)	42 (91.3%)			
Grade 2 - Grade 4	2 (5.7%)	6 (7.8%)	4 (8.7%)	1.0000	0.9517	1.0000
For categorical variables n (%) is presented.						
For pairwise comparison between groups Fisher's Exact test was used						
For dichotomous variables and the Mantel-Haenszel Chi Square Exact test was used for ordered categorical variables.						

## 4.3 Study III

### 4.3.1 Translation of the Breast Evaluation questionnaire

Translation and back-translation was performed and field-testing of how the questionnaire was perceived after translation was successfully done.

### 4.3.2 Content validity of the Breast Evaluation questionnaire

Five patients were interviewed about the questions, their meaning and how long it would take filling it in. The board of plastic surgeons and the field test both concluded that all but the last question of the BEQ were relevant and important to the population of women with breast hypertrophy. The last question “How important is the size of your breast to following people in your life?” was deleted and the modified BEQ (mBEQ) resulted. The validation and reliability testing continued with mBEQ.

### 4.3.3 Psychometric analysis

**Acceptability-** Two hundred out of 225 patients (89%) answered the questionnaires and in each item, less than 8% were missing.

**Exploratory factor analysis-** The Kaiser–Meyer–Olkin measures of sample adequacy were 0.88 and Bartlett’s test of sphericity was significant with  $p < 0.0001$ , which indicates no objections against explorative factor analysis.

The scree plot in exploratory factor analysis indicated four dimensions. To evaluate the construct validity within the mBEQ we found the following dimensions; *Breast attributes*; *Clothes*; *Naked* and *Family*. The four-dimension model explained 63.9 percent of the variance. After the orthogonal rotation varimax the first 3 dimension appeared exactly as we defined. The fourth dimension excluded the first sub question (item) regarding question nr 3.1 (you, yourself) (factor loading  $< 0.40$ ).

**Internal consistency** was excellent for the four dimensions. Using Cronbach’s alpha, the dimensions ranged between 0.90 – 0.97. Item convergent validity was very good. All correlations with own scales corrected for overlap  $\geq 0.49$ . The scaling success was 100% in three of the dimensions and 96% in the dimension *clothes*.

**Test-retest-** intraclass correlation coefficient (ICC) ranged from 0.70-0.84 in the four dimensions between test and retest scores, and thus acceptable.

**Convergent validity-** the correlation between the subscales of the modified BEQ and the BREAST-Q (re-

duction) was significant correlated in eleven out of twelve, and as expected graded strong to very strong in nine of them. ( $r_s=0.45-0.7$ ).

***Discriminate validity-*** Role Emotional and Social Functioning in SF-36 was significant correlated to mBEQ in four out of eight dimensions, but as expected there was a weak to moderate correlation ( $r_s=0.15-0.22$ ).

***Known-groups validation-*** Two-hundred and sixteen women out of one-thousand (22%) sent back a complete mBEQ. The scoring was compared to the preoperative scoring of the 225 patients who was subjected to breast reduction. There was a significant difference between groups in all four dimensions.  $P<0.0001$ .

***Responsiveness-*** A subsample of 27 patients received a second modified BEQ at one year postoperatively. All the 27 patients responded. The patients that were followed up one year postoperatively showed significant improvement in all four dimensions

<i>Breast</i>	57.1	(SD29.0)	$p<0.0001$
<i>Clothes</i>	49.9	(SD28.7)	$p<0.0001$
<i>Naked</i>	48.5	(SD28.4)	$p<0.0001$
<i>Family</i>	28.9	(SD27.1)	$p<0.0001$ .

The effect size varied between 1.07 (*Family*) and 1.97 (*Breast*), which indicates good responsiveness.

## 4.4 Study IV

### 4.4.1 Demographic data

Three hundred forty-eight patients, who were subjected to breast reduction surgery, were enrolled in the study. In total, 284 patients (83%) answered questionnaires either preoperatively, postoperatively, or both. The demographic data were compared between patients who answered both questionnaires (159) and those who answered only one (pre- or postoperatively) or none of the questionnaires (189). A significant difference was found regarding mean age (44.1 years (SD16.1) vs. 37.7 years (SD 14.8); ( $p < 0.0001$ ), ASA classification ( $p = 0.015$ ), and mean suprasternal notch to nipple distance (27.5 cm (SD 2.8) vs. 28.3 cm (SD 3.0); ( $p = 0.021$ ), between those who answered both questionnaires and those who did not.

### 4.4.2 SF-36

The breast hypertrophy patients had significantly lower scores preoperatively than the matched normal population regarding all dimensions of SF-36. The differences in score from the normal population varied from 8 to 29. After breast reduction, five domains (Role Physical, Bodily Pain, Vitality, Social Function, and Role Emotional) were significantly improved compared to the preoperative score, by 11–32 points, and all of those but Vitality was normal, i.e. not significantly different from the normal population. Also Physical composite was significantly improved ( $p = 0.0001$ ). However, the three dimensions General Health, Physical Function, and Mental Health were not affected by the surgical intervention. Neither was Mental composite ( $p = 0.14$ ). (fig 12)

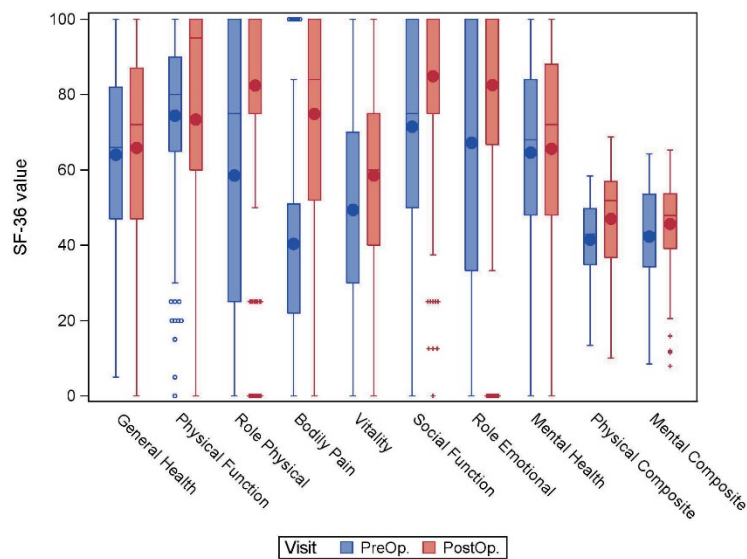


Figure 12. SF-36 before and after breast reduction surgery

### 4.4.3 Breast-Related Symptoms Questionnaire (BRSQ)

The improvements in scores (pre-operatively to postoperatively) were significant in all thirteen items. The summary score improved from 38.6 (SD 15.7) to 85.7 (SD 18.5) ( $p < 0.0001$ ). A value of five (purple in the graf) is the best and a value of one (blue in the graf) is the worst possible. The item with least improvement (38.5%) was “The size of my breasts causes pain and numbness in my hands” and the item with most improvement (92.5%) was “The size of my breasts makes it difficult to find bras and clothes that fit” (fig 13).

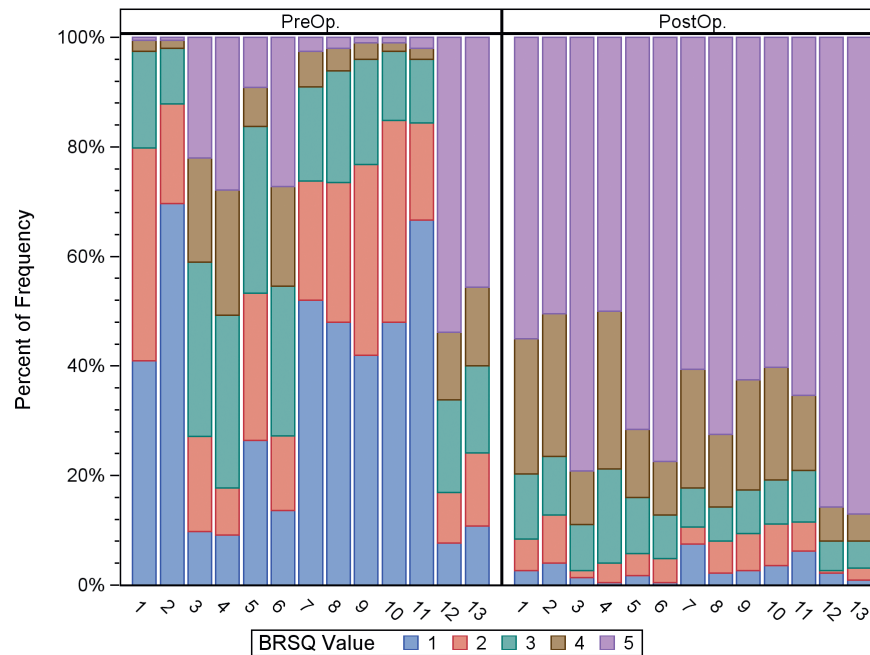


Figure 13. BRSQ before and after surgery



#### 4.4.4 mBEQ

The preoperative scores of all four domains “Breast”, “Clothes”, “Naked”, and “Family” in the modified Breast Evaluation Questionnaire (*mBEQ*) were significantly lower than for a Swedish normal population ( $n = 216$ ) ( $p < 0.0001$ ). After breast-reduction surgery, there were significant improvements in all four dimensions!significantly exceeding the score of the normal population (fig 14).

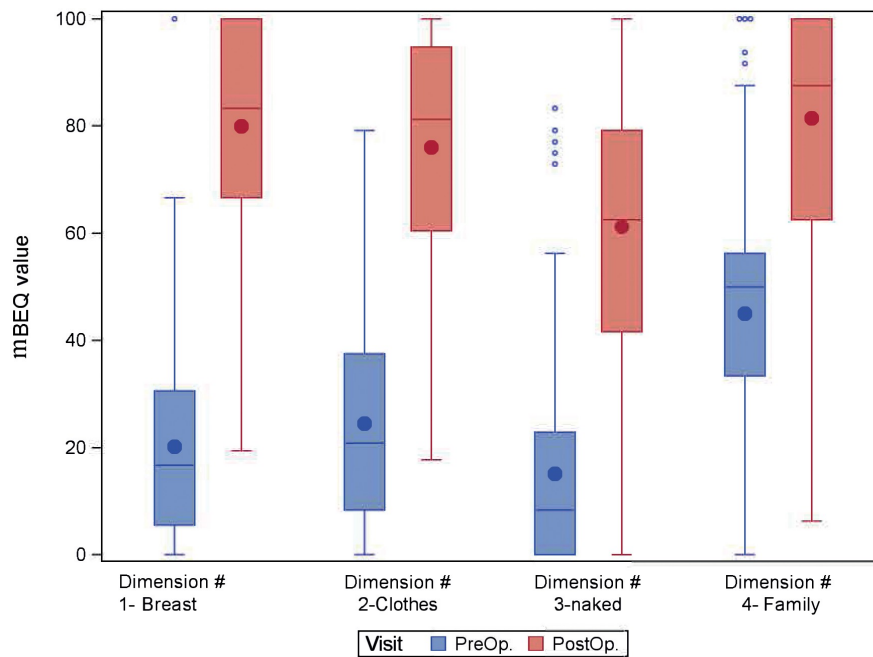


Figure 14. mBEQ before and after breast reduction surgery

#### 4.4.5 BREAST-Q

All four categories "Satisfaction with breasts", "Psychosocial well-being", "Sexual well-being", and "Physical well-being" in BREAST-Q were significantly improved ( $p < 0.0001$ ). The improvements in score varied from 24 to 43 (fig 15). The "Satisfaction with breasts" concerns breast appearance (e.g. size, symmetry, softness, cleavage), and satisfaction with breasts in relation to how a bra fits and how the breasts look when clothed or unclothed. Eighty three % of the women answered preoperatively "very dissatisfied" or "somewhat dissatisfied" to the question "How your breasts look in clothes?" and postoperatively 93 % answered "somewhat satisfied" or "very satisfied".

Nintyseven percent answered "dissatisfied or somewhat dissatisfied" to the question about the "How satisfied have you been with the size of your breasts?" and postoperatively 88 % answered "somewhat satisfied or very satisfied". To the question "How satisfied are you with breast shape not wearing a bra?" 94% answered preoperatively "very dissatisfied or somewhat dissatisfied" compared to postoperative answers from 81 % who were somewhat satisfied or very satisfied.

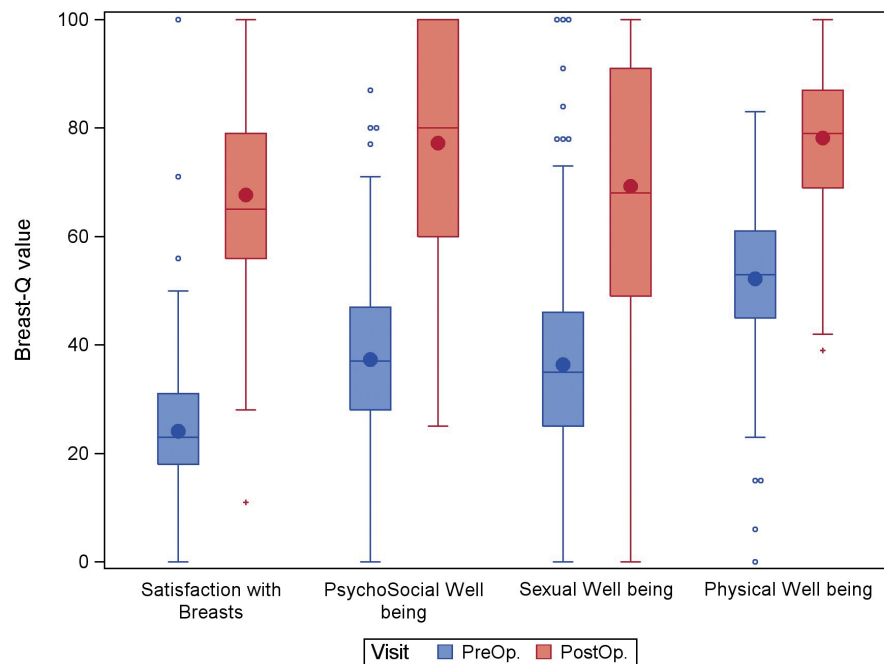


Figure 15. BREAST-Q before and after breast reduction surgery

#### 4.4.6 Correlation analysis

Correlation analyses were performed to investigate whether preoperative **BMI, breast volume, sternal notch to nipple distance, or resection weight** would affect the preoperative symptoms presented and the degree of gain in quality of life after breast reduction surgery. All significant correlations were weak.

##### Preoperatively

The *General Health* in SF-36 was significant, but weak, correlated to **BMI** i.e. higher BMI correlated to less general health ( $r_s = -0.14$ ;  $p = 0.0436$ ).

Preoperative "*satisfaction with breast appearance*" in BREAST-Q was significant, but weak, correlated to **breast volume** and **sternal notch to nipple distance** i.e. women with larger breast with more ptosis were less satisfied with their breasts ( $r_s = 0.20$ ;  $p = 0.0078$ ) and ( $r_s = 0.20$ ;  $p = 0.0085$ ), respectively.

##### Postoperatively

The only significant correlation regarding **BMI** ( $r_s = -0.25$ ;  $p = 0.0025$ ) was between low preoperative BMI and a greater reduction in *Bodily Pain* in the SF-36.

Regarding preoperative **breast volume**, we found a significant correlation with postoperative "*Satisfaction with breast appearance*" in the

BREAST-Q ( $r_s = 0.21$ ;  $p < 0.024$ ), i.e. the larger breast preoperatively, the greater the satisfaction with breast appearance postoperatively. No significant correlation was found between pre-op breast volume and physical symptoms.

A significant correlation was found between a longer preoperative **sternal notch to nipple distance** on the one hand and a higher score in *Bodily Pain* ( $r_s = -0.19$ ;  $p = 0.024$ ) and *Social Function* ( $r_s = -0.23$ ;  $p = 0.0063$ ) in the SF-36 i.e. women having long sternal notch to nipple distance tend to be less satisfied with Bodily Pain and Social Function. A longer sternal notch to nipple distance also correlates to "Satisfaction with breast appearance" in the BREAST-Q ( $r_s = 0.20$ ;  $p = 0.025$ ) i.e. Longer sternal notch to nipple distance resulted in higher satisfaction with the breast appearance.

No significant correlations were found between mean weight of resection or proportion of breast resection (specimen weight / breast volume) to any parameter in the postoperative questionnaires.

## 5 DISCUSSION

### 5.1 Discussion of the findings

**Almost no woman regrets having the operation; on the contrary, women who have their breast reduction midlife often regret that they did not have the surgery earlier.**

For some women, breast hypertrophy is a condition that has significant physical and mental impact, not only on the psychosocial level but also in their daily lives. Many women have to stop or avoid certain activities such as running and horseback riding, and many feel restricted in their social lives.<sup>40,46,95,100-103</sup>

Health-related quality of life (HRQL) is a central aspect of breast reduction surgery because the procedure, rather than save lives, is designed to improve lives. It is unfortunately rare in medicine to be able to cure a disease, and what is usually called for is help in relieving pain or making life less problematic and hopefully more worth living. This is why evaluations of QOL and HRQL attract so much attention and are more frequently used as the endpoint of medical studies. Breast reduction surgery is one of those procedures that can make a difference in the lives of the women affected, enabling them to live their lives without

being hampered by the size of their breasts.

Breast reduction is a common surgical procedure, performed on both medical and aesthetic indications. The discrepancy in indications, whether medical or aesthetic, has an impact on whether the reduction surgery should be provided by the public health service, as is the case for medical indications, or paid for by the individual where the reasons are aesthetic. It is therefore important to clarify when breast size is considered hypertrophic and which symptoms can be related to breast volume, meaning the weight of the breasts. Thus, the symptoms related to breast hypertrophy are both objective and subjective in character.

The size of the breasts must also be evaluated in relation to body composition and height. It is likely that many women with large breasts never experience any symptoms, and of those who do, many of those symptoms do not correspond to the risk of surgery. Yet the opposite is also true, where women whose breasts do not meet the Swedish national guidelines to be accepted for surgery nevertheless perceive them as large and heavy. The composition of the breasts may also affect the weight of the breasts, since glandular tissue weighs more than fat, which may be significant for young women, who generally have more glandular tissue than postmenopausal women, who have a larger amount of fat.<sup>23</sup> In

medical practice, objective parameters have been preferred in recent decades. This means that it is the medical professional who set the indications for a certain procedure on the basis of objective findings.

Thus when the Swedish national medical indications<sup>48</sup> were described for breast hypertrophy in 2008, the main indication was the size of the measured breast volume and not what the women experienced. This thinking was mainly based on a lack of knowledge about how to distinguish between women with medical problems from those with purely aesthetic issues. The aim of this thesis is thus to improve our knowledge of women with breast hypertrophy and the outcome of breast reduction surgery.

The physical symptoms of women with breast hypertrophy are described in the introduction to this thesis and are well documented in the literature.<sup>38,95,102,104,105</sup> Study IV evaluates these women's HRQL, and in an SF-36 they score significantly lower in all eight sections than the matched normal population, as also found by Blomqvist et al<sup>106</sup> and Carreto et al.<sup>44</sup> Also, when the mBEQ score was analysed and compared to the normal population there were significantly lower scores in all four sections concerning psychosocial satisfaction. The impact of breast hypertrophy on the psychosocial well-being is previously presented by Klassen et al.<sup>107</sup> in a qualitative

study. There is no Swedish normal material for the Breast-Related Symptoms Questionnaire (BRSQ) and BREAST-Q, so it is difficult to evaluate the preoperative score for Swedish conditions. Thoma et al. concluded that living with breast hypertrophy is associated with a lower HRQL, measured by use of BRSQ, than the matched Canadian population and a similar HRQL to those living with moderate angina or a kidney transplant.<sup>102</sup>

If breast reduction surgery were possible without scars and complications it would be an almost perfect operation; however, it is a fact that complications after breast reduction surgery are common.

First, we retrospectively studied the complications after breast reduction surgery to see if we could find any risk factors for complications. All early complications within thirty days were registered. Infections were described and categorized according to the infection scale, which is based on signs of infection.<sup>108</sup> Our results show a total complication rate of 32 per cent, which is quite high for a procedure categorized as clean surgery<sup>57</sup>, but fully comparable to findings in other studies.<sup>63,109-112</sup> The most common complication is post-operative infection, which is 16 per cent if graded 1–4 on the infection scale, and 11 per cent if graded 2–4. The first grading with wound exudate is not an infection, but in some cases might go on to become so.

Grading 2–4 is more likely to be an infection, so the actual incidence of post-operative infections probably lies somewhere between 11 and 16 per cent. In the literature, the incidence of post-operative infections varies between 0 and 34 per cent. One of the reasons for this variance is the lack of uniform criteria for superficial surgical site infections (SSI).<sup>62,65,68</sup> The definition of SSI from the Centre for Disease Control (USA) is in our opinion too subjective, which demonstrates through the last stated SSI-criteria “diagnose of an infection by surgeon or attending physician”.<sup>66</sup> Our infection scale based on symptoms probably makes the results comparable to others if so wished, although it needs to be validated and tested for intra- and inter-rater reliability.

The most important findings in Study I were that the sternal notch to nipple distance, BMI, weight of resection, diabetes mellitus, and smoking were identified as independent risk factors for complications. This means that the potential risk factors that show a significant correlation with complications are stronger than the others. Sternal notch to nipple distance was independently significantly correlated to both necrosis of the NAC and post-operative infections. This would seem logical, as the vascular supply to the nipple is reduced when the length of the pedicle increases, which is probably the case when the distance from the sternal notch to the nipple increases.

The circulation also has to be able to withstand infections. BMI was also an independent risk factor for wound infection, as has previously, together with other complications, been proven for many kinds of surgery including breast reduction,<sup>113-117</sup> e.g. Setälä et al.<sup>112</sup> presented more areola necrosis in obese patients but no increase of infections. The amount of resected breast was independently correlated to delayed wound-healing and fat necrosis. Cunningham et al.<sup>110</sup> also presented significant more complications and delayed healing correlated to the resection weight. One explanation might be more perforators resected and inadequate blood supply. Diabetes mellitus affects small vessels and this might explain the correlation with necrosis in the NAC. Similar results can also be seen in immediate breast reconstruction.<sup>118</sup> Smoking is well known to inhibit the oxygenation of tissue, which has the same effect as reducing blood flow and makes the tissue more susceptible to infection; like others, our results show a double risk of post-operative infection among smokers. This result is well documented in the literature.<sup>119,120</sup> It is of great importance that the women who undergo to breast reduction surgery are well informed about the complications and the importance of not smoking several weeks before and after surgery to reduce the risk of complications after surgery.

Other factors as surgical technique used and the experience of the sur-

geon also affects the complication rate.<sup>57,121</sup> This is true for how the dermoglandular pedicle is dissected, the relation between the remaining breast volume and the skin envelope, and how tense it is at the junction between the horizontal and vertical scars. All these factors may affect the ability to heal, as poor circulation in tense tissue carries a higher risk of necrosis and infection.<sup>57,118</sup> There may also be fat necrosis and necrosis of the nipple–areola complex (NAC), depending on the choice of pedicle<sup>25</sup> and, even more so, the skill of the surgeon. We have not addressed these issues in our studies.

As the incidence of post-operative infections after breast reduction surgery is 11–16 per cent, even though this surgery is categorized as ‘clean’—which means that it is a uninfected operative wound in which no inflammation is encountered and the respiratory, alimentary, genital, or uninfected urinary tract is not entered<sup>62</sup>—it is of paramount importance to reduce this high incidence. Antibiotic treatment of post-operative infections brings the risk of potential allergic reactions and can drive the emergence of resistant organisms as Methicillin-resistant *Staphylococcus aureus* (MRSA). The natural bacterial flora can also be suppressed and secondary infections can follow—*Clostridium difficile* infections, in other words.<sup>61</sup> The finding in Study II was that 2 g of prophylactic, one-dose Cloxacillin (or 600 mg of prophylactic, one-dose

Clindamycin in case of penicillin allergy) did not significantly reduce the incidence of post-operative infections.

Previous studies of the effect of prophylactic antibiotics in breast reduction surgery have been inconclusive because of mixed types of surgery—for example, mastopexy and breast reduction—non-randomized methodology, and also insufficient power. Platt et al. and Veiga-Filho et al. found decreased postoperative breast infection when using prophylactic antibiotics, whereas Serletti et al. and Ahmadi et al. did not.<sup>61,67,76–80</sup> The preventive effect of prophylactic antibiotics in breast reduction surgery is dependent on the chosen drug being effective against *Staphylococcus aureus*, as this is the dominant bacteria in surgical site infections<sup>57,60</sup> (SSI), and that the concentration in serum is sufficient when surgery starts. Therefore the administration, absorption, and time to surgery are important.<sup>57,81,82</sup> Intravenously given, Cloxacillin and Clindamycin have a peak concentration within an hour—a concentration well over the therapeutic doses needed—which is maintained for hours. Study II we analysed the time between the administration of antibiotics and the incidence of post-operative infection without finding any significant difference between those who received one dose of antibiotic less than 30 minutes prior to the start of surgery, those who received it 30–90 minutes

before surgery, and those who received one dose of prophylactic antibiotic more than 90 minutes before start of surgery. In order to reduce the incidence of post-operative infections after breast reduction surgery, other measures than prophylactic Cloxacillin or Clindamycin must be taken. There are several other factors in the care of the patient that it has been suggested will affect the incidence of SSI. An optimal use of preoperative antiseptic showers and sterile conditions in the operating theatre, while ensuring that patients are normothermic during surgery, that they are non-smoking, and that operations are conducted with skilful surgical techniques might all prevent some SSI.<sup>57</sup> In Study II, all of these aspects were optimized, as they were mandatory in the hospital in question. However, in this study we could show that surgical time had a significant effect on the incidence of postoperative infections, as well documented in literature<sup>57,121</sup>. For planning of future breast reduction surgery it seems as it is of importance to keep surgery time short.

Over the years, many studies of HRQL have been performed, but mostly using generic questionnaires or non-validated questionnaires.<sup>122</sup> We wanted to evaluate different dimensions of HRQL including the psychosocial aspects of this specific population. At the time, only the BRSQ was proven to be valid<sup>122</sup> for our population, and this questionnaire did not include psychosocial

issues. As we could not find a validated questionnaire for a psychosocial evaluation, we started the process of validating<sup>123,124</sup> the Breast Evaluation Questionnaire<sup>88</sup> (BEQ), originally developed to evaluate psychosocial aspects after breast augmentation surgery, but for which the suggestion was that it might prove useful when canvassing the population of women undergoing breast reduction surgery. That suggestion was strongly criticized because it was not properly validated and reliability-tested for the population.<sup>125</sup> During the work of validating BEQ, the BREAST-Q<sup>92,126</sup> was launched, so we went through the translation process from English to Swedish for this questionnaire too, and used it for the tests of convergent validity in the validation of the BEQ. The main finding in Study III was that the BEQ, when modified, is valid and reliable for the evaluation of women with breast hypertrophy who undergo breast reduction surgery.<sup>127</sup>

The most important finding in Study IV was that the HRQL strongly and significantly increased one year after breast reduction surgery. Another important finding was that the correlations between the BMI, preoperative breast volume, sternal notch to nipple distance, resection weight, and HRQL gain measured using the SF-36, BRSQ, mBEQ, and BREAST-Q were weak.



Studies have come to the same conclusion about the effectiveness of breast reduction surgery in improving HRQL.<sup>47,128-132</sup> Study IV is the first to use mBEQ to evaluate the women's psychosocial satisfaction with their breasts and the first we know of to use BREAST-Q for pre- and post-operatively matched women. The generic SF-36 questionnaire was used because it is much used in different fields of medicine, which offers the possibility of comparing data. We also used the BRSQ<sup>94,96,122</sup>, which before BREAST-Q and the validation of the mBEQ was the only questionnaire in the field of breast reduction that was properly validated and reliability tested, and proven to be stable and valid. It has been suggested that a clinically valuable change in a 100-point quality of life scale is a ten-point change.<sup>102</sup>

Breast reduction surgery evidently improves the lives of the women, physical, mentally, and psychosocially, as the health gain in BRSQ, mBEQ, and BREAST-Q was significant for all of these dimensions. The improvement in SF-36 was significant in five out of eight sections (Role Physical, Bodily Pain, Vitality, Social Function, and Role Emotional) and we had at least ten-point changes in four out of those five sections that also were normalized in compared to the matched normal population (Role Physical, Bodily Pain, Social Function, and Role Emotional). These results both resemble and differ from others' re-

sults with the SF-36 questionnaire after breast reduction surgery, largely because the literature is inconclusive, probably due to the weakness of generic questionnaires that lack the sensitivity for specific diseases such as breast hypertrophy and for post-breast reduction surgery.<sup>47</sup> Freire et al. presented significant improvement in all dimensions, but General Health, after six months. Miller et al.<sup>133</sup> presents a normalization of all eight dimensions without any significant differences except for Social Function, which significant exceeded the age-matched normal population in Canada.<sup>133</sup> The result from the BRSQ is strong and shows a positive effect mainly on pain, but also on the ability to engage in physical activities. Valtonen et al.<sup>134</sup> showed the same result, but also presented better improvement in BSS Score in obese women and in women with long sternal notch to nipple distance, which we did not find. Thoma et al.<sup>102</sup> presented a preoperative breast symptom summary score (BSS score) of 52.6 compared to our 38.5, and a post-operative BSS score of 96.2 compared to our 92.6. Similarly, the BREAST-Q showed a strong improvement in all areas, which included both physical aspects and psychosocial and mental issues. So far, only one study has previously been published on the subject, and while they could not pair their patients as we did, their results confirm ours.<sup>135</sup> Collins et al.<sup>97</sup> have studied surgical and non-surgical interven-

tions in the treatment of breast hypertrophy, reporting an improvement in pain symptoms, but conservative treatments did not bring any permanent relief of symptoms.

Correlation analyses were performed to investigate whether preoperative BMI, preoperative breast volume, sternal notch to nipple distance, or resection weight would affect the degree of gain in quality of life. The significant correlations were weak and contradictory, and there is a strong suspicion they were chance outcomes.

**BMI** is one of the factors in the Swedish national guidelines<sup>48</sup> that must be met if the patient is to be accepted for surgery by the health service. This is because it is believed that a higher BMI leads to more complications. In our study of normal-weight or slightly obese women, a higher BMI was not correlated to more symptoms from breast hypertrophy.

Postoperatively a preoperative BMI weakly correlated with the dimension of bodily pain in SF-36: a low preoperative BMI gave significantly more pain relief post-operatively, but the same effect was not seen in the condition-specific BRSQ and was not described by Thoma et al.<sup>102</sup>, Iwuagwu et al.<sup>100</sup>, or Valtonen who did not find any correlation between BMI and SF-36.

**Preoperative breast volume** appears logically connected to the amount of back pain, as it more heavily compresses the neck and back; however, the preoperative breast volume was not correlated to preoperative pain, i.e. larger breast did not correlate to more pain. Kerrigan et al. presents similar results.<sup>95</sup>

Postoperatively preoperative breast volume only weakly correlated to ‘satisfaction with breast’ in BREAST-Q—the larger the breasts, the more satisfied with breast aesthetics—but not in mBEQ. Furthermore, there was no correlation between preoperative breast volume and postoperative pain relief in either SF-36 or the BRSQ, i.e. those with a larger breast volume enjoy gains in HRQL that are similar to, although not greater than, other women.

**Sternal notch to nipple distance** is also described in the national Swedish guidelines as a factor to consider, as it is believed to correlate with problems associated with breast hypertrophy. Preoperatively it weakly correlated to “appearance of breast” in BREAST-Q, i.e. a long sternal notch to nipple distance the more unsatisfied with breast aesthetics.

Postoperative the sternal notch to nipple distance was found to weakly correlate to Social Functioning in SF-36 and also to bodily pain, but it was not correlated to the mBEQ or to the BRSQ. There was also a simi-

larly weak correlation between sternal notch to nipple distance and 'satisfaction with breast' in BREAST-Q.

**Resection weight** has been debated for many years, as some insurance companies in the US used to demand a certain amount of resection in order to qualify for reimbursement.<sup>136,137</sup> There is also a certain logic to thinking that you have to reduce the breast more than a little in order get the health effect of relieving pain. Resection weight was not correlated to any factor in any of the four questionnaires, and others have showed similar results.<sup>97,105,138,139</sup>

## 5.2 Methodological considerations

If one is to measure quality of life, it is important to be certain what being measured exactly, and that the chosen instruments really will measure just that. Generic instruments such as SF-36s have been much used for many different populations, but, as with similar tools, the risk is that they are insufficiently sensitive to fully capture all the issues associated with the disease or condition in question; here, for example, they are not sensitive enough to note the changes that occur after breast reduction surgery.<sup>45,92,102,122</sup> Once the BEQ had undergone validation and reliability tests, with minor changes it was found to be valid, offering good reliability for use with the population of women with breast hypertrophy who undergo breast reduction. If an instrument is not validated and reliability-tested for the population being studied, it is impossible to be certain that the results are reliable. Furthermore, any measure would be best if it highlighted the studied condition or disease *in toto*, as BREAST-Q does, yet not even this questionnaire is comprehensive. The dimension-specific questionnaire mBEQ has a greater number of questions about psychosocial issues than the BREAST-Q does, and might be a useful complement.

The infection scale has thus far not been validated, nor yet tested for inter- and intra-reliability. However, it has anyway been useful, in the first study, as a template, to define and organize the infections found in the medical charts. Also in the second study, the infection scale was useful to evaluate different symptoms of infection and the antibiotic treatment, even if it was a secondary outcome variable.

## 6 REGARDING FUTURE INDICATIONS FOR BREAST REDUCTION SURGERY

In an ideal world with limitless resources, the public health service would try to resolve all problems associated with breast hypertrophy, whether physical, psychosocial, or mental. Indeed, in that scenario, all of these factors would be of equal importance. This would probably lead to an increase of patients. However, with things as they are, it behoves us to find a fair way to apply the same criteria throughout Sweden when selecting the women who are in greatest need of a breast reduction.

The only way to avoid all complications is to not do any surgery in the first place. That said, the findings in this thesis indicate that one should only operate on healthy, young, non-smoking, women with a normal BMI, a short distance between the sternal notch and the nipple, small breasts, and only in need of small resections. Impossible, of course, but even so one has to optimize as much as feasibly possible to reduce complications and maximize patient outcomes.

The BMI criterion calls for a normal weight (BMI 18.5–24.9, plus 1–2 BMI units for breast weight), as it possibly reduces the incidence of wound infections and, crucially, body weight is a factor that can be adjusted, unlike, say, sternal notch to nipple distance.

However, BMI is not an exact measure of obesity, and perhaps it would be better to measure body fat percentage (%BF) instead, as studies have indicated its use when correlated to SSI.<sup>140-142</sup> On the other hand, we found that women with a higher BMI had just as good a health gain as the women with lower BMI one year after breast reduction surgery, so why should we not include those women? Other studies of HRQL in women who were more obese than the patients in our studies concludes much the same,<sup>143</sup> and the only reason for these women not to have surgery at public expense is the extra cost of a greater number of visits due to minor complications.

Sternal notch to nipple distance should not be used as an indication for surgery in the public health service, because no particular effect of pain relief is proven. Neither is preoperative breast volume a good measure, as women differ in height, habitus, and muscle. There might be occasions when it is useful to weigh the breast, as some are heavier than others even though their volume is smaller. Gland tissue weighs more than water and less than fat. One

consequence is that the Swedish national guidelines tend to discriminate against women whose breasts are predominantly gland tissue, which more often than not means young women. For breasts with predominantly gland tissue, the volume should perhaps be measured and then multiplied by 1.2, as gland tissue is heavier than water. This would extend the indications to include women with less volume than 800 ml but with heavy breasts. More studies about the correlation between breast weight and HRQL gain are needed if we are to understand the factors at work for these women.

The strongest criterion that is proven and unchanged is the non-smoking requirement.

**If summarized, the proposed indications for breast reduction are as follows:**

1	Either BMI < <b>27</b> for all women or %BF < 31
2	Either breast weight > <b>800ml</b> per breast or <b>volume x 1.2</b> if predominantly gland tissue in breast
3	<b>No smoking</b>
4	All in combination with <b>physical, psychological, and/or psycho-social</b> issues

## 7 STRENGTH & LIMITATIONS

### 7.1 Study I

The strength of the first study is the large population size and the infection scale, which enables a reliable grading of infections.

Retrospective design is always a limitation when data is retrieved from medical records, especially regarding the patients' history of smoking, the registration of infections, and patient follow-up. The infection scale is non-validated and has not been tested for inter-rater reliability.

### 7.2 Study II

The main strength of the second study was its prospective and randomized design with a sufficient number of patients to be valid. To avoid the effect of outliers in terms of age, BMI, and breast volume we used a randomization program that automatically adjusted for these parameters. All the surgeons were experienced in breast reduction surgery.

One limitation of the study was the lack of a valid methodology for the estimation of infection rates. There is no consensus on how exactly to define an SSI. The infection scale is non-validated. However, we believe

that by using a graded infection scale, with well-defined grades, together with an analysis of post-operative treatment with antibiotics, we can minimize this problem. The study was not performed blind using a placebo for the control group, which may prove to be a limitation; however, the evaluation of the outcome was as objective as possible, using an infection scale, and the evaluators were unaware of which patient belonged to which group. Cultures from wounds were not always taken, which may have strengthened the diagnosis of infection.

Postoperative visits were scheduled for one and two weeks, with close contact with the clinic in the eventuality of any infection or other complication. This may have meant that patients infected later but within the 30 days slipped through the net.

### 7.3 Study III

The main strength of the third study was the extensive validation statistics performed. One of its limitations, however, seems likely to have been the weak response rate in the control group. Only one letter was sent, without reminders. Medical students with a special interest in these matters conducted the in-depth interviews in the field test. It is possible that experts would have obtained slightly different results. However, the medical students' find-

ings were in line with the opinion of the expert evaluation group, and they were also supported by the low proportion of missing responses to each separate question in the modified BEQ. to nipple distance (28.3 cm versus 27.5 cm).

## 7.4 Study IV

The main strengths of the fourth study were a comparatively high number of patients and its prospective longitudinal paired design, with the same patients followed preoperatively and post-operatively using BREAST-Q and mBEQ.

A weakness of the study, meanwhile, was the low response rate from women who answered both the preoperative and post-operative questionnaires (45 per cent). One reason might be that most of the patients were young and healthy, and even though they agreed to participate in the study their interest in completing the questionnaire once they had had the operation was limited. There could also be a fear of being exposed, especially when some of the questions were intimate. The burden of having four different questionnaires might also have been too great. More than 80 per cent of the women answered either the preoperative questionnaire or the post-operative questionnaire, and these women only differed to the women who answered both questionnaires in mean age (38 as opposed to 44), ASA classification, and sternal notch



## 8 CONCLUSIONS

### 8.1 Study I

Complications after breast reduction surgery are common, and the sternal notch to nipple distance is an independent risk factor for post-operative wound infection and necrosis of the nipple–areola complex (NAC). BMI is also an independent risk factor for wound infection. The amount of resection is an independent risk factor for fat necrosis and delayed wound-healing. Diabetes is an independent risk factor for necrosis of the NAC, and smokers have twice the risk of getting a post-operative infection. Breast volume is not an independent risk factor for complications following breast reduction surgery.

### 8.2 Study II

Infections after breast reduction surgery are common, and intravenous Cloxacillin, 2 g (or Clindamycin, 600 mg, in case of allergy) given as one dose 30–90 minutes before the start of surgery, did not significantly reduce the incidence of post-operative infections within 30 days.

### 8.3 Study III

The Breast Evaluation Questionnaire (BEQ), originally developed for breast-augmented women, is also proven to be valid, offering good

reliability once it has been adjusted (modified BEQ, with the last question deleted) when used for the population of women with breast hypertrophy and who undergo breast reduction surgery.

### 8.4 Study IV

Women with breast hypertrophy who qualify for surgery under the Swedish national guidelines have a reduced quality of life when their SF-36 and mBEQ scores are compared those of the normal population. Women's health-related quality of life (HRQL) is strongly increased or normalized *after* breast reduction surgery measured using the questionnaires SF-36, mBEQ, BRSQ and BREAST-Q.

Correlation analysis shows no certain connection between women who have a high BMI, a long sternal notch to nipple distance, a large pre-operative breast volume, or large resections on the one hand and HRQL on the other.

## 9 FUTURE PERSPECTIVES

Much is now known and is readily available about breast reduction, and in this thesis I go further in understanding breast hypertrophy and breast reduction surgery. Yet still some thorny issues remain.

### **Who benefits from breast reduction surgery?**

As we have shown, women operated on for breast hypertrophy tend to benefit a great deal, and no one group of women enjoy a greater benefit from surgery than any other. Could every woman who thinks that her breast size is an encumbrance, a drawback in her daily life, benefit from this surgery? Should it be funded by the taxpayer? Sweden still lacks studies of these issues and the related questions of health economics.

### **QALY and Cost calculations**

Sweden as yet has no full studies of quality-adjusted life year (QALY) calculations. It is important to evaluate such calculations, as there is a steady discussion of indications for breast reduction and mastopexy surgery within the public health service.

### **Sick leave**

We do not know if women with breast hypertrophy have more days of sick leave each year compared to the general population, and whether this can be reduced by breast reduction surgery.

### **Breast aesthetics**

There is a lack of objective templates for preferred post-operative aesthetic results, and this will have to be remedied before any technical advances to improve the women's sense of aesthetic satisfaction are likely. There might also be certain details in the post-operative results—the NAC, say—that are more important in determining overall patient satisfaction with the aesthetic results. So far these details have not been studied.

### **Body habitus and muscle**

We do not know why some women with breast hypertrophy suffer from physical pain and some do not. Are there any differences in the muscle and/or skeletal composition between these women?

### **Post-operative infections**

Is it possible to reduce the incidence of post-operative infections by adding antibiotics to Klein's solution infiltrated to the breast before the

surgery begins, or using sutures soaked in antibiotic?

**Bottoming out**

Is it possible to reduce bottoming out by using acellular dermal matrix (ADM) or synthetic mesh to better define and stabilize the inframammary fold (IMF)?

**Outcome and age**

Is each woman's satisfaction with her breasts dependent on her age?

**Breast weight**

Do the physical symptoms caused by breast hypertrophy correlate to breast weight?

**Percent Body Fat (%BF)**

Is %BF a better measurement with which to anticipate the risk of infection?

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