

Forskningsrapport



Huvudsökande:

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Frågeställning:

Livskvalitet och hälsoekonomi för kvinnor som genomgått mastektomi - ur ett långtidsperspektiv.

Tre frågor till Maria:

Hur kan resultatet av er forskning hjälpa patienterna, rent konkret?

Bröstcancer är den vanligaste cancerdiagnosen hos kvinnor i Sverige. En kombination av nya behandlingsalternativ, bättre diagnostik och tidigare upptäckt har bidragit till förbättrad överlevnad efter bröstcancer och idag är förväntad 10 års överlevnad över 80%.

Mortaliteten vid bröstcancer minskar vilket innebär att fler kvinnor överlever genomgången bröstcancerkirurgi och lever med dess eventuella eftersviter under en längre period. Detta medför att beslut gällande bröstrekonstruktion även bör sättas i perspektivet av patientupplevd hälsorelaterad livskvalité över tid.

Kvinnor som genomgår bröstrekonstruktion efter mastektomi har visats ha en bättre skattad hälsorelaterad livskvalité än de kvinnor som inte genomgår bröstrekonstruktion, dock kan bröstets betydelse för kroppsuppfattningen variera mellan kvinnor. Studier som jämför olika rekonstruktionsmetoder och tidpunkt för rekonstruktion avseende patientnöjdhet, kosmetik och onkologisk säkerhet kan hjälpa vården att förstå var vi ska lägga resurser.

Hur viktigt har stödet från Bröstcancerförbundet varit för er forskning?

Stödet från Bröstcancerförbundet har varit avgörande för genomförandet av projektet.

Vad vill du hälsa alla Bröstcancerförbundets givare?

Genom att ge ett bidrag till Bröstcancerförbundet hjälper du till att säkerställa att vi kan fortsätta forskningen, inte bara kring bröstcancer i sig, utan även det omhändertagande och den vård vi vill ge kvinnor efter att deras cancer är färdigbehandlad.

Marias populärvetenskapliga rapport finns att läsa på efterföljande sidor.

Populärvetenskaplig sammanfattning

Nationell utvärdering av kvinnor som genomgått mastektomi - livskvalitet och hälsoekonomi ur ett långtidsperspektiv

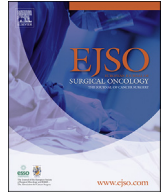
Bröstcancer är den vanligaste cancerdiagnosen hos kvinnor i Sverige. En kombination av nya behandlingsalternativ, bättre diagnostik och tidigare upptäckt har bidragit till förbättrad överlevnad efter bröstcancer och idag är förväntad 10 års överlevnad över 80%. Kirurgiska alternativ vid tumörresektion kan allmänt delas in i bröstbevarandetekniker eller mastektomi, där hela bröstparenkymet tas bort. Kirurgiska framsteg har lett till en ökad andel kvinnor som opereras med bröstbevarandetekniker och andelen kvinnor som genomgår mastektomi har minskat från 40% till 30% på riksnivå mellan 2008 och 2021 (NKBC). Samtliga kvinnor som genomgår mastektomi bör informeras om möjligheten till bröstrekonstruktion, antingen i samband med mastektomin, sk direkt rekonstruktion, eller vid ett senare tillfälle, sk sen rekonstruktion. Målet vid bröstrekonstruktion är att återforma bröstets form och volym vilket kan ske med implantat, kroppsegenvävnad (autolog) eller en kombination av dessa metoder. Faktorer som t.ex lokoregional strålbehandling, adjuvant cytostatika, kroppsbyggnad, övriga sjukdomar och tidigare kirurgi påverkar valet av rekonstruktionsmetod.

Mortaliteten vid bröstcancer minskar vilket innebär att fler kvinnor överlever genomgången bröstcancerkirurgi och lever med dess eventuella eftersviter under en längre period. Detta medför att beslut gällande bröstrekonstruktion bör även sättas i perspektivet av patientupplevd hälsorelaterad livskvalité över tid.

Kvinnor som genomgår bröstrekonstruktion efter mastektomi har visats ha en bättre skattad hälsorelaterad livskvalité än de kvinnor som inte genomgår bröstrekonstruktion, dock kan bröstets betydelse för kroppsuppfattningen variera mellan kvinnor. Studier som jämför olika rekonstruktionsmetoder och tidpunkt för rekonstruktion avseende patientnöjdhet, kosmetik och onkologisk säkerhet är få.

Swedish Breast Reconstruction Outcome Study (SweBRO) är en nationell enkät- och registerstudie som utfördes 2016 där samtliga kvinnor i Sverige som hade genomgått en mastektomi åren 2000, 2005, och 2010 identifierades via nationella cancerregistret erbjöds att delta. Deltagarna besvarade internationellt validerade patientenkäter relaterade till både allmän hälsorelaterad och specifik bröstcancerrelaterad livskvalitet, inklusive EQ-5D, EORTC QLQ-30, BREAST-Q och EORTC BRR 23. Cancerdata från deltagarna samlades in från regionala register och matchades på individuell patientnivå, likaså data från dödsregistret. Det övergripande syftet med studien är att utvärdera patientupplevd livskvalitet på lång sikt för patienter som genomgått mastektomi, med eller utan bröstrekonstruktion, på nationell nivå. Av de 5853 kvinnorna som tillfrågades valde 2904 att delta i studien (svarsfrekvens 50%). 31% av deltagarna hade genomgått bröstrekonstruktion. Det första delprojektet från SweBRO undersökte geografiska variationer av förekomsten av bröstrekonstruktion i Sverige och hur detta har ändrats under tiden (Unukovych et al1).

SweBRO studien är unik i litteraturen med fokus på patientupplevd livskvalité hos kvinnor efter mastektomi, med eller utan bröstrekonstruktion. Studien innefattar en nationell kohort som har besvarat validerade patientenkäter, har en hög svarsfrekvens och därmed deltagarantal, och har en lång uppföljningstid (5-15 år efter cancerbehandling). Kvinnor som har besvarat enkäten har samtliga överlevt eller lever med sin bröstcancer vid inklusionstillfället och deras svar speglar hur det är att leva med sviterna av cancerbehandlingen, med fokus på lokal kirurgiskbehandling och eventuell rekonstruktion.



Breast reconstruction patterns from a Swedish nation-wide survey

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ABSTRACT

Objectives: The overall aim of the Swedish Breast Reconstruction Outcome Study was to investigate national long-term outcomes after mastectomy with or without breast reconstruction. The current report evaluates breast reconstruction (BR) patterns in Sweden over time.

Materials and methods: This is a cross-sectional, registry-based study where all women operated with mastectomy 2000, 2005, 2010 were identified (N = 5853). Geographical differences in type of BR were investigated using heatmaps. Distribution of continuous variables were compared using the Mann-Whitney U test, categorical variables were compared using the chi-square test.

Results: Mean age at survey was 69 years (SD=±11.4) and response rate was 50%, responders were on average six years younger than the non-responders and had a more favourable tumor stage (both $p < 0.01$). Of the 2904 responders, 31% (895/2904) had received a BR: implant-based in 58% (516/895) autologous in 31% (281/895). BR was immediate in 20% (176/895) and delayed in 80% (719/895) women. Women with BR were on average one year older, more often had a normal BMI, reported to be married or had a partner, had a higher educational level and a higher annual income when compared to those without BR (all $p < 0.001$). The independent factors of not receiving BR were older age and given radiotherapy.

Conclusions: To our knowledge, this is the first national long-term follow-up study on women undergoing mastectomy with and without BR. Around 30% of the survey responders have had a BR with a significant geographical variation highlighting the importance of information, availability and standardisation of indications for BR.

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Introduction

Breast cancer (BC) is the most common cancer among women worldwide. The annual incidence of BC in Sweden is around 9000 cases today; incidence rates have been increasing with 6 377, 7 005,

7 977, and 9 382 new cases diagnosed in 2000, 2005, 2010, and 2015, respectively [1]. A population-based national mammography screening program was initiated in 1989 and implemented thereafter in the early 90s. Early diagnosis combined with advances in the multi-modal treatment resulted in the 10-year survival for BC at

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80%, implying that nearly 90 000 women with a personal history of BC live in Sweden today [1].

Breast-conserving surgery is the first-choice alternative for unifocal tumors, whereas mastectomy may be recommended due to the oncological or medical reasons, or may be chosen by woman herself, where the information and recommendations from medical providers play a role [2,3]. Predictors of post-mastectomy breast reconstruction (BR) are multidimensional and include socio-demographical (e.g. patient educational level, awareness, lifestyle, age), medical (e.g. comorbidity, adjuvant treatment, cancer stage and biology) and geographical factors (e.g. distance to department providing reconstruction, local traditions) [4,5]. Immediate BR has been shown to have some advantages over delayed reconstruction [6–8] and is usually offered to women with breast carcinoma in situ or early stage BC with low risk of recurrence.

Long-term health related quality of life (HRQoL) and satisfaction with treatment outcomes are important considerations for women choosing BC treatment modality [9]. Likewise, these outcomes are essential to health-care providers for treatment planning and health economics. Several studies report on short-term outcomes of BR [10–13]. Long-term HRQoL data as well as reconstruction patterns covering an entire nation, however, are lacking for BC patients.

The overall aim of the Swedish Breast Reconstruction Outcome (SweBRO) study is to investigate national long-term outcomes after mastectomy with or without BR on a national level. This first report evaluates response patterns and geographic variations, as well as the BR evolution over time.

Methods

Study design

This is a cross-sectional, national study combining register-based medical and oncological data with the survey on patient-reported outcomes.

Patient identification and registry data

At study initiation in 2015, all women diagnosed with BC in Sweden in 2000, 2005 and 2010 were selected, so that the follow-up period would reach 15, 10 and 5 years, respectively.

Women were identified through the National Breast Cancer Registry [1], where all diagnosed BC cases are reported nationwide since 1999 [14]. The target population comprised women diagnosed with BC and treated by total mastectomy with or without BR. Women who underwent breast-conserving procedure as a definitive surgery were not eligible.

Personal identity number and name, date of birth, home address, date of BC diagnosis (*date of mastectomy for the South region), and side of mastectomy (right/left/bilateral) were requested from all six regional cancer centres in Sweden (Stockholm-Gotland, Uppsala-Örebro, Southeast, South, West, North). All potential study participants were checked against the National Cause of Death Registry; only women alive at the time of study initiation comprised the survey population. A total of 5 853 women were eligible: 1 259, 1 976, and 2 618 in the years 2000, 2005, and 2010, respectively. Oncological data on tumor size, lymph node status, distant metastases, and adjuvant or neoadjuvant treatment for the eligible patients were collected.

Survey administration and management

The survey was conducted over a period of five months, from April 20th 2016 to September 22nd 2016.

A letter of invitation was sent via post to all 5853 eligible women, also including information on the two different ways of responding to the questionnaires: on paper or online. Survey questions addressed different patient-related outcome measures (PROMs) including health-related quality of life, satisfaction with appearance, experience with provided health care as well as socio-demographic characteristics and health economics. These results will be presented in a separate article.

The EQ-5D [15], the EORTC QLQ-C30, the EORTC BR23, the EORTC BRR24 [16,17] and the BREAST-Q [18] questionnaires were used. Study-specific questions assessing socio-demographic characteristics and history of received health care were added due to the fact that neither existing PROMs nor cancer register data covered them.

A commercial survey provider was responsible for survey management and data collection. Each woman was assigned a unique random identification number to be used on paper or for log in online. A study coordinator, ready to answer queries about the study or take note of those who did not want to participate, was available via telephone or e-mail throughout the whole study period.

Four weeks after the invitation letter, a second one was sent out to those women who had not answered the questionnaires online, but now also included a set of paper-based questionnaires and a prepaid return envelope. Finally, two reminders were sent to those who had not yet answered the survey neither online or via post after four (reminder 1) or eight (reminder 2) weeks.

Only a very few number of women contacted the study coordinator to actively decline from taking part in the questionnaires referring to low interest, no time or inability to participate in the survey, a few of them ($n < 5$) also wished to opt out from the clinical data analyses and were excluded accordingly. The majority of non-responders did not reply to the letters or logged in online and that is why no information regarding their reported outcomes or BR data is available.

Completed paper-based questionnaires were digitally scanned and transferred into the study database. Answers given in such a way that digital scanning failed (e.g. double answer, incomplete filling of box) were manually read and transcribed into the database.

Statistical analyses

Tables of demographics and characteristics were produced, distinguishing between responders and non-responders as well as calendar years. This was done in order to identify possible selection mechanisms. Heatmaps were used to describe geographical distribution of responders as well as differences in timing and type of BR. Descriptive tables of reconstruction by year and region of residence were also produced, along with comparisons between timing and type of reconstruction. Geographical differences in timing and type of reconstruction were investigated using heatmaps. Survey response as a dichotomous outcome was modeled by logistic regression to compare factors which may influence the likelihood of responding. Logistic regression models were also employed to identify factors associated with the occurrence, timing and type of reconstruction. These factors included patient age, tumour size, nodal status, radiotherapy, chemotherapy, and endocrine therapy. Distribution of continuous variables were compared using mean and standard deviation (SD) or median and quartiles, and the Mann-Whitney *U* test; categorical variables were compared using the chi-square test and proportions were compared using the methods described by Newcombe [19,20]. All tests were two-sided with a significance level of $\alpha = 5\%$. R version 3.4.4 (R Foundation for Statistical Computing, Vienna, Austria) was used for all analyses.

Table 1
Patients characteristics among survey responders with or without breast reconstruction.

	Total (%)	Reconstruction (%)	No reconstruction (%)	p-value
Total	2904 (100)	895 (100)	2009 (100)	
Mode				<0.001
Paper	1713 (59)	425 (47)	1288 (64)	
Web	1191 (41)	470 (53)	721 (36)	
Age at selection, yr				<0.001
Median (IQR)	60 (50–69)	60 (51–68)	59 (49–69)	
<50	1411 (24)	359 (20)	1052 (26)	
50–59	1505 (26)	508 (28)	997 (25)	
60–69	1582 (27)	525 (29)	1057 (26)	
>69	1355 (23)	399 (22)	956 (24)	
Body Mass Index (BMI)				<0.001
<25	1470 (51)	510 (57)	960 (48)	
25–30	944 (33)	295 (33)	649 (32)	
>30	429 (15)	81 (9)	348 (17)	
Missing data	61 (2)	9 (1)	52 (3)	
Marital status				<0.001
Married	1538 (53)	515 (58)	1023 (51)	
Partner	320 (11)	133 (15)	187 (9)	
Widow	405 (14)	43 (5)	362 (18)	
Single	512 (18)	157 (18)	355 (18)	
Other	116 (4)	44 (5)	72 (4)	
Missing data	13 (0)	3 (0)	10 (0)	
No. of children				0.07
1	489 (17)	159 (18)	330 (16)	
2	1290 (44)	430 (48)	860 (43)	
3	562 (19)	186 (21)	376 (19)	
4 or more	185 (6)	44 (5)	141 (7)	
0/Missing data	378 (13)	76 (8)	302 (15)	
Educational level				<0.001
Elementary school	729 (25)	111 (12)	618 (31)	
High school	922 (32)	326 (36)	596 (30)	
University	1120 (39)	447 (50)	673 (33)	
Missing data	133 (5)	11 (1)	122 (6)	
Yearly income, SEK				<0.001
<100 000	294 (10)	36 (4)	258 (13)	
100 000–250 000	1195 (41)	223 (25)	972 (48)	
250 000–400 000	733 (25)	381 (43)	352 (18)	
>400 000	357 (12)	207 (23)	150 (7)	
Missing data	325 (11)	48 (5)	277 (14)	
Smoking status				<0.001
Non-smoker	1372 (47)	381 (43)	991 (49)	
Former smoker	1179 (41)	413 (46)	766 (38)	
Current smoker	240 (8)	78 (9)	162 (8)	
Missing data	113 (4)	23 (3)	90 (4)	

Ethical approval

The study was approved by the Regional Research Ethical Review Board in Uppsala (Dnr 2014:354 and Dnr 2014:354/1).

Results

Response rate and responder's characteristics

The overall response ratio was 50% (2904/5853); it increased in the later cohorts with 47% year 2000 (593/1259), 48% year 2005 (943/1976) and 52% year 2010 (1368/2618). Women from the year 2010 were overrepresented both in the original study cohort (45%, 2618/5853) and among responders (47%<L). Response patterns during the survey period, stratified for region of residence, year of diagnosis, age, and questionnaire modality (paper vs. online) are presented in [Supplementary Table 1](#) and [Supplementary Figs. 5a–d](#).

Mean age (\pm SD) at survey completion was 69 (\pm 11.4) years. Responders were on average six years younger than the non-responders. This trend was also seen on a group level where women of 60 years or older responded less often. Significant regional differences in the proportion of responding women were

found ($p < 0.001$); the highest response rate was obtained in the Stockholm-Gotland and Uppsala-Örebro regions (both 53%) and the lowest rate in the West region (43%) as shown in [Supplementary Fig. 1](#).

Tumour and treatment characteristics are presented in [Supplementary Table 2](#). Responders more often had a favourable tumour stage ($p < 0.001$) than non-responders and more often received radiotherapy (38% vs. 31%) or chemotherapy (29% vs. 21%), both $p < 0.001$.

In univariable analyses, participation in the survey was associated with node-positivity (OR: 1.21; 95% CI 1.05–1.40), receiving radiotherapy (OR: 1.37; 95% CI 1.23–1.52) and chemotherapy (OR: 1.56; 95% CI 1.39–1.74). In the multivariable model, chemotherapy (OR: 1.23; 95% CI (1.08–1.41) and tumor size (OR: 0.86; 95% CI 0.77–0.97) were associated with survey participation ([Table 2](#), left). Older women (>50 years) were less likely to participate in the study ([Table 2](#), left bottom).

Breast reconstruction patterns

Out of 2904 responders, 31% ($n = 895$) had received a BR. Overall, the rate of BR nationwide increased over time from 29% to 30% and to 32% in years 2000, 2005 and 2010, respectively. The

Table 2
Logistic regression models for survey participation (left) and breast reconstruction (right).

	Survey participation				Breast Reconstruction			
	Univariable		Multivariable		Univariable		Multivariable	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
T2+ vs. <T2	0.91	(0.82–1.02)	0.86	(0.77–0.97)	1.09	(0.93–1.29)	1.07	(0.88–1.29)
N+ vs. N0	1.21	(1.05–1.40)	1.08	(0.92–1.27)	0.90	(0.72–1.12)	0.79	(0.61–1.03)
RT+ vs. RT-	1.37	(1.23–1.52)	1.13	(1.00–1.29)	1.02	(0.87–1.20)	0.76	(0.62–0.94)
ET+ vs. ET-	0.95	(0.86–1.05)	1.01	(0.90–1.12)	0.87	(0.74–1.02)	1.03	(0.86–1.23)
CT+ vs. CT-	1.56	(1.39–1.76)	1.23	(1.08–1.41)	1.43	(1.21–1.70)	1.16	(0.95–1.41)
Age at selection, yr								
<50	1.00	(Ref.)	1.00	(Ref.)	1.00	(Ref.)	1.00	(Ref.)
50–59	1.13	(0.98–1.31)	1.16	(1.00–1.35)	0.40	(0.33–0.49)	0.40	(0.33–0.49)
60–69	0.82	(0.71–0.94)	0.85	(0.73–0.98)	0.13	(0.10–0.17)	0.13	(0.10–0.16)
>69	0.33	(0.28–0.39)	0.36	(0.31–0.43)	0.03	(0.02–0.05)	0.03	(0.02–0.05)

T2+ = tumors larger than 5 cm, T2 = tumors > 2 cm but ≤ 5 cm, N = nodal status, RT = Radiotherapy, ET = Endocrine therapy, CT = Chemotherapy, OR = odds ratio, CI = confidence interval.

overall BR rate was the highest in the Stockholm-Gotland region (44%), followed by the West (32%), Uppsala-Örebro (27%), South and South-East (both 26%), and the lowest in the Northern region (22%), [Supplementary Fig. 2](#).

Factors associated with breast reconstruction

Women with BR were on average one year older, more often had a normal body-mass index (BMI, 57% vs. 48%), reported to be married or had a partner at the time of survey completion (72% vs. 60%), had a higher educational level (i.e. high school or university, 86% vs. 63%) and a higher annual income when compared to those without BR (all $p < 0.001$, [Table 1](#)).

Chemotherapy was associated with BR in the univariable analysis (OR: 1.43; 95% CI 1.21–1.70), but when adjusted for age, tumour size, nodal status and other adjuvant therapies in the multivariable analyses, the independent factors of not receiving BR was radiotherapy (OR: 0.76; 95% CI 0.62–0.94) and older age of the patient ([Table 3](#), right).

Timing and type of breast reconstruction

The timing of BR was immediate in 20% (176/895) and delayed in 80% (719/895) women ([Supplementary Table 3](#)). Reported rates of immediate BR varied among the regions, being 2% in the North versus 41% in Stockholm-Gotland region ([Supplementary Fig. 3](#)).

Implant-based techniques were used in 58% (516/895), autologous in 31% (281/895) women, a combination of techniques in 2% and unknown in 9% of all reconstructed women ([Supplementary Table 3](#)). Regional variations of BR method (autologous vs. implant-based) are presented in [Supplementary Fig. 4](#).

Radiotherapy and older age of the patients were associated with delayed BR (vs. immediate) in both univariable and multivariable

analyses ([Table 3](#), left). These factors were also negatively associated with autologous reconstruction (vs. implant-based) ([Table 3](#), right).

Discussion

Sweden is a relatively sparsely populated country with approximately ten million inhabitants. The healthcare system is largely tax-funded and aims to provide equal access to health care services in all regions, covering mammography screening, BC diagnostics and treatment. According to the current Swedish National BC Guidelines all women planned for mastectomy should be informed about the possibility of BR [14]. Data on, to what extent BR has been offered and performed, on a national level are currently not available.

The current report is the first within the SweBRO study focusing on survey participation, geographical patterns and evolution of breast reconstruction in Sweden during the last two decades. This report indicates that despite best efforts to offer patients equal health care, there are remarkable geographical differences in BR rate, timing and technique in the country. These differences cannot be explained based on oncological or surgical differences between patients, and are more likely to be driven by socio-economic patient factors affecting BR rate, as well as access to breast reconstruction surgical know-how.

These results should be interpreted in the context of the response rate and subsequent selection bias created by responders versus non-responders. Therefore, a thorough evaluation of the response rate was performed.

About half of the eligible women who underwent mastectomy in 2000, 2005 or 2010 participated in the study by completing the questionnaires. Survey responders were younger than non-responders and had been treated for less advanced tumors. This

Table 3
Logistic regression models for breast reconstruction timing and technique.

	Immediate reconstruction*				Autologous reconstruction#			
	Univariable		Multivariable		Univariable		Multivariable	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
RT+ vs. RT-	0.70	(0.51–0.98)	0.57	(0.41–0.80)	0.44	(0.35–0.55)	0.33	(0.26–0.41)
Age at selection, yr								
<50	1.00	(Ref.)	1.00	(Ref.)	1.00	(Ref.)	1.00	(Ref.)
50–59	0.61	(0.43–0.86)	0.59	(0.42–0.83)	0.51	(0.41–0.63)	0.46	(0.36–0.58)
60–69	0.25	(0.15–0.39)	0.23	(0.14–0.36)	0.22	(0.17–0.29)	0.18	(0.14–0.24)
>69	0.02	(0.00–0.14)	0.02	(0.00–0.13)	0.05	(0.03–0.10)	0.04	(0.02–0.08)

RT = Radiotherapy, OR = odds ratio, CI = confidence interval. * immediate vs. delayed, # autologous vs. implant-based

could possibly be related to better general health status and activity level in a younger patient population, with a higher willingness to participate in studies and contribute to breast cancer research. There was no way to assess whether the women were medically and mentally fit to answer the questionnaire as all women alive at the survey initiation were eligible and invited to participate with no age constraints, but this may be an explanation why the elderly patients were less likely to participate in the study.

As the higher response rate among young women was stable through the study period as well as between regions, this selection bias would not have affected the results indicating geographical differences in delivery of care. The response rate might mirror the rate of BR as seen in Complementary Figure 2, probably due to larger interest in responding to questionnaires concerning BR among women who have undergone this procedure.

Overall, the rate of BR after mastectomy had increased nationwide from 29% reported in group 2000 to 32% in 2010. The optimal rate of postmastectomy BR in general is hard to determine; available data on the national rates of BR in other countries for the similar time period have been reported as follows: Australia: 14% (1999–2006) [24], Denmark: 10% (1982–2000) [25], England: 16.5% (2006–2009) [26], USA: 16.5% (1998–2002) in the Surveillance, Epidemiology and End Results (SEER) database [27] and 23% in the later National Cancer Database (1998–2007) [28]. These rates and their variation are difficult to interpret due to differences in health-care systems and national guidelines for breast surgery and reconstruction, where patient selection and resources might play a role. Moreover, the cited studies are not directly comparable with each other as the data were obtained retrospectively from the mixed sources, i.e. population-based or hospital-based. For example, one of the most exploited and representative for BC databases in the US, the SEER captures only immediate reconstructions [27].

In the current study, breast reconstruction rate was the highest in the capital region (Stockholm-Gotland, 44%) and the lowest in the north (Northern region, 2%). The difference most likely reflects access to specialist care and the women's possibility and willingness to travel to centres where BR is offered [29]; the Northern region is also less densely populated than the capital region.

Similar regional differences were found in other studies evaluating BR rates in different areas of the countries: USA (range 7.7–48.7%) [27,28], Canada (range 4.3–10%) [30], and England (range 8.4–13.9%) [26].

The geographical variability should be further studied in order to make sure that the women are provided with adequate information and access to equal care. Local routines, availability of plastic and breast oncoplastic surgeons, surgeon's preference and woman's choice may also have played a role. Only 20% of all BRs in the current study were immediate with great variability in the country (from 1% to 41%). In fact, the capital differs from the rest of the country as immediate BR has been offered for more than 20 years even to women with more advanced tumor stage and treatment with chemo and radiotherapy [6]. Recent Swedish studies on oncological safety of BR using implants or autologous tissue might have contributed to a wider acceptance of BR by the medical community and patients [6,31,32].

Our results nevertheless indicate that the information of and access to care might not have been equally provided in Sweden. In a lower volume centres the availability of reconstructive plastic surgeons could have been limited, especially in the earlier time period (i.e. 2000–2005). Some of the centres, however, have had trained breast oncoplastic surgeons who perform immediate implant-based BRs.

In addition, all breast cancer patients have right to choose health-care provider elsewhere in the country and may be referred

to another center with a reconstructive expertise. Although it is hard to investigate this pathway in a systematic manner, it might have been underused and there are presumably more women who may be referred for and benefit from BR.

Socio-economic status, including income and education were associated with BR in this study which is also supported by other studies [4,33]. Active smoking and overweight are known risk factors for surgical complications [34,35] and are by many considered contraindications for BR. The current study only includes data on BMI and smoking at the time of the survey (i.e. years after the mastectomy) and the impact of those factors on the initial decision for BR is therefore uncertain.

In the current survey, implant-based reconstructions were more frequent than the autologous BR (58 vs. 31%), which may be due to the fact that implant techniques are offered by a larger number of hospitals and are traditionally performed by both plastic and breast surgeons, whereas autologous microsurgical techniques are commonly offered at the departments of plastic surgery at university hospitals. The choice of BR method and timing may also depend on factors such as local traditions and availability of reconstructive expertise at the time of mastectomy or at a later stage [4,36].

The strengths of the study include a national coverage where women were identified through the National Breast Cancer Registry and new data collected from PROMs as well as the National Registry to provide long-term outcome data. The PROM instruments used have previously been validated in BC populations and women in this study were offered to answer either online or on paper and this data will be reported elsewhere.

Limitations of this study include the moderate response rate. The most probable explanation for this is the long follow-up design of the survey with women asked 5–15 years after their BC diagnosis and treatment. Efforts were made to improve response rate including reminding letters and an available contact person. This however had fairly low impact on the response rate (Supplemental Figs. 5a–b) Supplementary NOT Supplementary. Unfortunately, the socio-demographic characteristics of the non-responders were not available since these data were retrieved from the survey questionnaires. Clinical and oncological data were however available and analysed to better define the responders in the context of the entire study population.

In conclusion, in this nationwide study around 30% of women who had a mastectomy 5–15 years ago have had a BR, with a significant geographical variation. Patients' age and socioeconomic factors, as well as treatment-related characteristics, were shown to play a role, thus highlighting the importance of information, availability and standardisation of indications for BR. Further development of national guidelines for management of BC including recommendations on to whom, how and when to offer BR may contribute to further harmonization of care according to best standards. Equally, patient involvement and collaboration with patient advocacy organisations may be of importance to increase awareness regarding BR possibilities.

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Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent

The study was performed according to the ethical approval given by the Regional Research Ethical Review Board in Uppsala prior to study initiation. As such consent to use the new and collected data from the questionnaires was gathered from each patient at the time of filling out the questionnaires (on line or hard copy) through the patient information forms. For the non-responders no intervention was performed and no new data collected. The data used to define non-responders was gathered on group level from previously collected data of the Swedish cancer registry with no individual data included/presented.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRedit authorship contribution statement

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ejso.2020.04.030>.

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