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Trends in immediate breast reconstruction and radiation after mastectomy: A population study

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Abstract

Introduction: In the last decade, there has been an increase in women undergoing immediate breast reconstruction (IBR) at the time of mastectomy. Recent literature suggests a shift in practice: surgeons are becoming more comfortable with IBR in the setting of possible post-operative adjuvant radiotherapy, despite the known complications. This study sought to investigate, at a population level, the patient and surgeon characteristics associated with the use of IBR and which of these factors were predictive of adjuvant radiotherapy.

Methods: This retrospective population-based cohort study included all adult women who underwent mastectomy in the province of Ontario from 2007 to 2014. The Canadian Institute for Health Information (CIHI) administrative database was used to generate patient demographic and clinical data. The Ontario Health Insurance Plan (OHIP) database was used to elicit surgeon characteristics including clinical experience and volume of practice dedicated to breast surgery. Outcome variables included reconstruction concurrent with mastectomy, alloplastic versus autologous reconstruction, and use of radiation.

Results: 25, 861 patients underwent mastectomy and 2,972 had IBR (11.5%). The rate of IBR after mastectomy increased over time from 7.2% in 2007 to 17.2% in 2014 ($p < 0.001$). There was also an increase in the proportion of patients with IBR who received radiation over the time period; from 19.4% in 2007 to 28.2% in 2014 ($p = 0.003$). In the first regression analysis, IBR was associated with younger patient age, residing in closer proximity to cancer clinics, absence of malignant breast disease (i.e. prophylactic mastectomy), having a younger surgeon performing the mastectomy, and receiving care at a teaching hospital. A second analysis showed that patient variables predictive of radiation after IBR were a younger age and a more advanced cancer stage and no variables specific to surgeon or institution were predictive of radiation in patients with IBR.

Conclusions: A significant increase in the rate of IBR as well as the use of radiation occurred over the seven-year study period. Multiple patient and surgeon factors were associated with IBR. Variables associated with radiation in IBR were harder to predict. Given the increase in the use of radiation in IBR, further research is needed to look at long-term outcomes in these patients at the population level.

Introduction

A significant shift in breast reconstruction following mastectomy has occurred in the last decade with an increase in the number of women undergoing mastectomy and immediate implant-based reconstruction; this is particularly occurring in younger women[1-8]. One of the challenges with implant-based reconstruction is the potential need for adjuvant radiation therapy and the subsequent risk of complications, such as reconstruction failure, capsular contracture, infection, implant exposure, and mastectomy flap necrosis[5, 9-17]. Krueger et al. demonstrated that the combination of IBR followed by radiation resulted in 68% of patients suffering a complication (including 37% with total reconstruction failure) in comparison to a 31% complication rate when radiation is not used (8% with total reconstruction failure)[15]. This has been re-demonstrated in newer literature in a recent publication from the Cleveland clinic by Manyam et al.[16]

Recently, there have been studies demonstrating increased use of implants during IBR in the setting of radiation despite its known complication profile[10]. At present, there is limited literature examining whether the increase in implant-based IBR is associated with an increase in complications and poor outcomes due to a need for adjuvant radiotherapy. Indeed, it is not established that the more liberal use of implant-based IBR has resulted in more of these women being treated with radiation.

The primary objective of this study was to review women undergoing immediate, implant-based breast reconstruction over a seven-year period and determine the frequency of post-operative adjuvant radiotherapy, whether there was a change in this frequency over the study period, and to determine whether there are factors which predict the use of radiation. In addition, we aimed to update the population-based trends and predictive factors for undergoing IBR following mastectomy.

Methods

Study design and data sources

This retrospective population-based cohort study included all adult women who underwent a mastectomy in the province of Ontario, Canada (population approximately 13 million)[18], from January 1, 2007 to December 31, 2014. We excluded patients who were not Ontario residents, did not have a physician billing record for the mastectomy, or for whom we were unable to determine age, sex, or mastectomy

laterality. We also excluded patients who had undergone prior mastectomy or radiation or if more than one surgical approach was identified for the procedure (i.e. both with and without IBR). The number of patients excluded at each step of the cohort build is presented in Figure 1.

Health care delivery in Ontario is intended to provide universal access to care, which allows capture of hospital and physician-based health care encounters through administrative databases. Databases used in this study to obtain diagnostic and procedural data include the CIHI Discharge Abstract Database, Same Day Surgery, and National Ambulatory Care Reporting System databases, and the OHIP database. Cancer diagnostic data was captured from the Ontario Cancer Registry (OCR), whereas the Activity Level Reporting (ALR) database was used to identify the provision of radiotherapy. Additional patient and physician characteristics were acquired from the Registered Persons Database and the Institute for Clinical Evaluative Sciences (ICES) Physician Database, respectively. These datasets were linked using unique encoded identifiers and analyzed at ICES. Ethics approval for this study was obtained from the Sunnybrook Health Sciences Centre Research Ethics Board. Reporting of this study follows the RECORD statement (see Table S1)[19].

Variable definitions

Canadian Classification of Health Interventions (CCI) codes were used to define mastectomies as occurring with or without immediate reconstruction (see Table S2 for a complete list of codes used for this study). These same codes were also used to define the reconstruction approach as implant-based, flap-based, or a combination of the two.

The primary outcome was adjuvant radiotherapy, which was defined as radiation administered within one year of mastectomy to account for any delays in the commencement of post-operative radiotherapy due to adjuvant chemotherapy (captured in the ALR database). Radiation delivered more than one year after the index surgery was presumed to represent treatment of a recurrence rather than treatment of the primary disease. As part of the Ontario Cancer Registry, the ALR database captures radiation and systemic therapy services and outpatient oncology clinic visits for every patient diagnosed with a malignant neoplasm in Ontario[20].

The following characteristics were recorded for each patient: age, rural residence, neighbourhood income quintile (adjusted for household size and housing costs), expected resource utilization (surrogate variable for patient comorbidity), history of radiotherapy within one-year of prior lumpectomy (to indicate prior ipsilateral breast cancer treatment), immigration status (immigration within the prior 10-years represents 'recent' immigration), current breast cancer diagnosis (diagnosis within one-year before mastectomy),

cancer stage, and year of the procedure. Expected resource utilization was derived from the Johns Hopkins University Adjusted Clinical Group® case-mix system's Resource Utilization Bands (RUB[20] and summarized as low (RUB= 0-3), moderate (RUB=4), and high (RUB=5) expected resource utilization. We also captured characteristics of the surgeons who performed the mastectomy and the reconstruction, including age, experience (years since medical school graduation), annual total surgical volume (based on OHIP billings), and the proportion of their practice devoted to breast-related care (proportion of all surgical consultations related to a breast diagnosis, presented in quintiles). Lower annual surgical volumes and higher devotion of their practice to breast could be considered surrogates for being a breast subspecialist. Since surgeon age and years since graduation (surrogate variable for experience) are highly correlated, in keeping with other large administrative database publications, we elected to present data for the surgeon age as the surrogate for surgeon experience. Additional baseline variables included institution teaching status (academic vs community), distance from the patient's residence to the nearest cancer centre, and whether or not the mastectomy was performed in a city with a cancer clinic.

Statistical Analysis

Differences in baseline characteristics between those with and without IBR at the time of mastectomy were evaluated using standardized differences (SD). A SD greater than 0.10 was interpreted as a potentially meaningful difference[22]. Trends across the study period were assessed using the Cochran-Armitage test for trend. We investigated potential predictors of IBR using unadjusted and adjusted modified Poisson regression analysis[23]. This approach was also used to explore associations between baseline predictor variables and receipt of radiotherapy within the subgroup of patients with cancer (with known cancer stage) who underwent IBR at the time of mastectomy. The following predictors for that analysis were considered: patient age, distance from home to the nearest cancer centre, institution teaching status, breast cancer diagnosis, prior lumpectomy and radiotherapy (implying that mastectomy represents recurrence rather than new primary cancer), experience of the mastectomy surgeon and the plastic surgeon, type of reconstruction, and year of the procedure. The linearity of continuous predictors was assessed using restricted cubic splines[24]. Continuous variables that demonstrated a non-linear association with the dependent variable were categorized prior to modeling.

Subgroup analyses were conducted to explore predictors of IBR within the subgroup of breast cancer patients and within that subgroup, based on age ≤65 vs >65 years (sensitivity analysis to evaluate potential impact of treatment decisions for older patients on variables predicting delivery of radiation in the entire post-mastectomy reconstruction cohort). A subgroup analysis was also conducted to investigate associations with receipt of radiotherapy among breast cancer patients with immediate implant-based

reconstruction. For all analyses, reported p-values are from 2-tailed tests where a value of < 0.05 was considered statistically significant. All analyses were performed using SAS EG version 7.1 (SAS Institute, Cary, NC, USA).

Results

Between January 1, 2007 and December 31, 2014, a total of 25, 861 patients in Ontario underwent mastectomy, 2,972 (11.5%) of which had IBR (Table 1). Of those with IBR, 734 (24.7%) received flap-based reconstruction, 1922 (64.7%) received implant reconstruction, and 316 (10.6%) received an implant plus flap. IBR patients tended to be younger, were less likely to have a breast cancer diagnosis, and more likely to have a history of prior lumpectomy and radiotherapy (where a new cancer diagnosis will not typically be eligible for further radiation). Finally, patients were more likely to undergo IBR if they lived closer to a cancer clinic, resided in higher income neighbourhoods, were treated in a teaching hospital or were treated by a younger mastectomy surgeon, a mastectomy surgeon with lower annual surgical volumes and a mastectomy surgeon with higher breast devotion (Table 1).

Figure 2 outlines year-after-year IBR rates. IBR increased each year from 7.2% in 2007 to 17.2% in 2014 ($p < 0.001$). Implant-based reconstruction consistently represented approximately 75% of all reconstruction procedures.

Poisson regression modeling (Table 2) revealed the following to be predictive of undergoing IBR after mastectomy: younger age, distance less than 50 km to a cancer centre, prior lumpectomy and radiation, treatment at a teaching institution, not currently having a cancer diagnosis, and a younger mastectomy surgeon. Having a cancer diagnosis predicted against receiving IBR with a relative risk of 0.33. On the contrary, undergoing treatment at a teaching institution strongly predicted IBR (RR = 2.36). Subgroup analyses based on patient age (≤65 vs >65 years) and among patients with breast cancer revealed the same predictors of IBR as within the overall population (data for age-based subgroup analyses not reported).

Among patients with breast cancer and IBR, 492 (25.7%) received radiotherapy within one-year of mastectomy, increasing significantly over the study period from 19.4% in 2007 to 28.2% in 2014 ($p = 0.003$) (Table 3). Table 4 presents the Poisson Regression Model identifying variables predictive of administration of radiation in the setting of IBR for patients with a cancer diagnosis and known cancer stage. Younger patients and those with more advanced cancer stage predicted adjuvant radiotherapy. Cancer stage of III or IV strongly predicted radiation (RR 7.02, $p < 0.001$) while prior lumpectomy plus radiation predicted against radiation (RR 0.24, $p < 0.001$). There was a trend toward implant-based reconstruction being more likely to receive radiotherapy than those with flap-based reconstruction,

although this difference did not reach significance (RR 1.22, p = 0.055). Distance to the nearest cancer centre or having surgery at a teaching institution did not predict radiation administration. No mastectomy surgeon or plastic surgeon factors (age/experience, breast devotion or total annual surgical volume) predicted for which patients were more likely to receive post-reconstruction radiation (data not shown). Similar results were obtained from a subgroup analysis restricted to patients with implant only-based reconstruction (Table 4).

Discussion

Immediate breast reconstruction in Ontario steadily increased over the study period, and implant-based reconstruction continues to comprise approximately 75% of reconstructions. This is consistent with previously reported trends in the United States and Canada[2-5, 25-27]. Regression analysis demonstrated that younger patients were significantly more likely to receive immediate breast reconstruction, which is consistent with previous literature[1-8,28]. Patients with a cancer diagnosis were also less likely to receive IBR. This was seen in other studies in which IBR was more common in patients where radiation was not anticipated (in situ disease, earlier stage cancer patients or prophylactic cases)[2,3,9,28]. Coroneos et al. also found that surgical oncologists, plastic surgeons, and radiation oncologists did not support IBR in more advanced disease[29]. The results of the current study may suggest the same; that plastic surgeons are cautious in offering IBR to patients with more advanced cancers that may require post-mastectomy radiation. Similar to that shown by Zhong et al the age and experience of the mastectomy surgeon was correlated with IBR; that is, older surgeons were not involved with IBR as frequently as younger mastectomy surgeons[26]. Similarly, mastectomy surgeons with high surgical volume practices and a smaller devotion of their practice to breast are less likely to offer and arrange IBR for their patients.

As expected, we found that radiation therapy was strongly correlated with increasing cancer stage. The benefits of post-mastectomy radiotherapy for invasive breast cancer patients with four or more positive lymph nodes has been accepted as a modality to reduce loco-regional recurrence, breast cancer specific recurrence, and breast cancer specific mortality; however, controversy remains about the benefits in patients with 1-3 positive lymph nodes[30,31]. Current recommendations continue to support the consideration of post-mastectomy radiation for 1-3 lymph node positive patients despite a SEER data study evaluating patients from 1998-2008 that found no survival benefit in patients post-mastectomy who received radiation for 1 positive lymph node[30-34]. Since the vast majority of patients for whom IBR is offered are early stage and clinically node negative, those who are found to be pathologically node positive are typically in the 1-3 node positive category, and the benefits of radiation to these patients should outweigh the potential toxicity and the implications for successful reconstruction[31].

Discussions around possible post-mastectomy radiation avoidance in IBR patients fits with an evolving trend to choose wisely with adjuvant treatments such as radiation in patients aged 65 years or older, where radiation (at least in breast conserving surgery for early stage disease) can be safely avoided without adversely impacting overall survival[35]. It is unclear whether this finding can be generalized to post-mastectomy patients, but oncologists should weigh these decisions against the potential morbidity of treatments in patients where a clear survival benefit is lacking[33]. Given the relatively low numbers of post-reconstruction patients identified in this study who do receive adjuvant radiation (approximately 100 patients in Ontario per year), population-level research should be undertaken to examine the outcomes for these patients compared to age and stage-matched patients who do not receive radiation, both in terms of treatment-related toxicity and recurrence and mortality data.

Mastectomy surgeons associated with higher rates of reconstruction also are more likely to work at academic centres in proximity to cancer centres. This may be a reflection of a more multidisciplinary approach where active discussions with radiation oncologists about the risks versus benefits of post-mastectomy radiation in reconstructed patients can be undertaken. Cancer Care Ontario (CCO) Breast Cancer Pathway was designed to reflect this more current, multidisciplinary approach to cancer care, and expects every mastectomy patient to be referred to a plastic surgeon to discuss the potential for breast reconstruction[36]. Higher rates of reconstruction may also simply reflect a greater availability of reconstructive plastic surgeons at academic centres as well. Platt et al found that there was a strong correlation between rates of breast reconstruction and the presence of a plastic surgeon in the hospital where mastectomy was done[37].

Consideration of IBR in the setting of advanced cancer stage or anticipated adjuvant radiation therapy varies between centres and is modified by a patient's tolerance for risk if implant-based reconstruction is considered. In general, reconstructive surgeons have avoided implant-based surgery if radiation is known to be required. However, our data demonstrates that a significant number (25.7%) of women undergoing IBR receive adjuvant radiotherapy and that this rate increased significantly over the study period. Certainly many women, and their surgeons, will have been "caught" with an unexpected need for radiotherapy after IBR. The fact that the rates are as high as they are, and increasing significantly, suggests that mastectomy and reconstructive surgeons may be becoming more comfortable completing IBR in women with a possible requirement for radiotherapy. Multiple technical modifications in reconstructive surgery have been developed to enhance the safety and outcomes of IBR followed by radiation. These include so-called "delayed-immediate reconstruction" (in which a tissue expander is placed at the time of mastectomy and inflated prior to beginning of radiotherapy with later permanent implant placement), the use of acellular dermal matrix (ADM), autologous fat grafting and others. In

addition, new, individualized techniques of radiotherapy delivery are being developed to avoid unnecessary radiation to the implant[13].

Limitations of this study include inherent challenges with any large database research. Although CIHI codes allowed for identification of patients with procedures specific to the cohort of interest, it is possible that some misclassification during the coding process could occur. Although a limitation of the OCR database is its potential misclassification of Stage 0 patients into Stage 1, it is unlikely for this to have had an impact on the findings of this study. The database was unable to distinguish immediate one-stage implant-based reconstruction with immediate two-stage reconstruction with placement of a tissue expander followed by delayed definitive implant placement. Strengths of this study include data on a population level which, because of a single, universal health care system in the province of Ontario is able to capture virtually all patient care and thereby provide a large sample size. This allows for the identification of cohorts of uncommon clinical scenarios such as IBR patients receiving adjuvant radiation. Another limitation of this study is that the data is only available up until 2014. Due to the nature of the process required for permission to access to these large databases, there can be a time delay in data collection and data analysis.

Conclusion

While IBR rates have increased 2.5 fold during the seven-year period of this large, population-based study, less than one fifth of all mastectomy patients are receiving IBR. Since the majority of these early stage breast cancer patients will not require radiation post-mastectomy, it is likely that many women are still not being offered the option when it would be appropriate. Given that patients are more likely to receive IBR when treated by a specialized mastectomy surgeon affiliated with a cancer centre, multidisciplinary teams and consultations with plastic surgeons should be encouraged on a broader basis. This study has shown increasing rates of radiation and IBR. In this trend of moving away from avoiding IBR in any patients who might require postmastectomy radiation, surgical teams who do high volumes of IBR are adapting their techniques to accommodate potential radiation toxicity. Further work is needed on large cohorts to determine the safety profile as well as the effects on recurrence and mortality rates of this approach.

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Figure 1: Cohort build results.

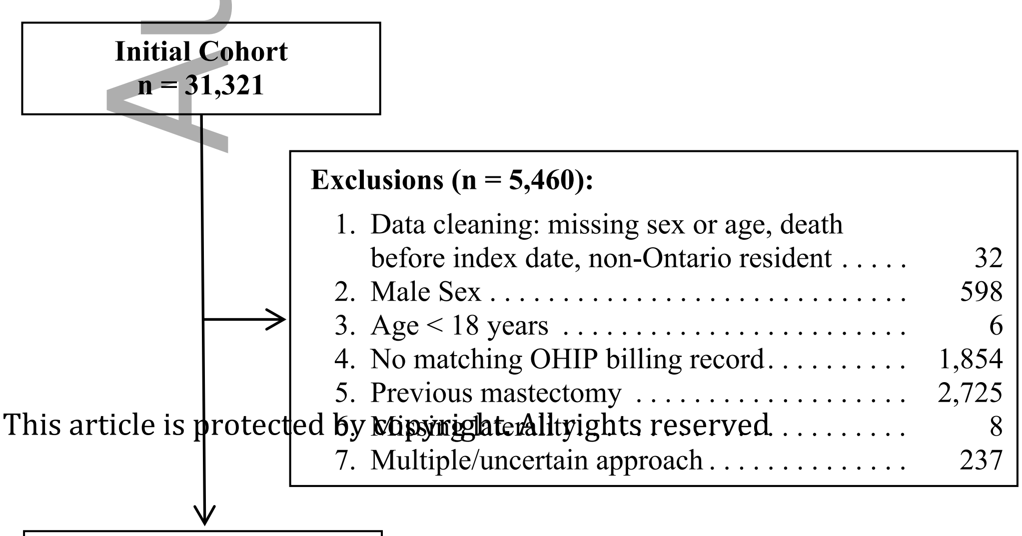

Table 1: Baseline variables, overall and by immediate reconstruction status.

Variable	Overall n = 25,861	No Immediate Reconstruction n = 22,889	Immediate Reconstruction n = 2,972	SD	p-value
Age*	60.3 ± 14.5	61.8 ± 14.3	48.8 ± 10.4	1.04	<0.001
Current cancer diagnosis	21,153 (81.8%)	19,589 (85.6%)	1,564 (52.6%)	0.76	<0.001
Cancer stage†					
Stage 0	108 (0.5%)	77 (0.4%)	31 (1.6%)	0.12	<0.001
Stage I	5,600 (24.3%)	4,777 (22.6%)	823 (41.8%)	0.42	
Stage II	8,590 (37.2%)	8,014 (38.0%)	576 (29.3%)	0.19	
Stage III	5,510 (23.9%)	5,338 (25.3%)	172 (8.7%)	0.45	
Stage IV	503 (2.2%)	490 (2.3%)	13 (0.7%)	0.14	
Stage NA	2,756 (11.9%)	2,402 (11.4%)	354 (18.0%)	0.19	
Expected Resource Utilization					
Low utilization	7,806 (30.2%)	7,031 (30.7%)	775 (26.1%)	0.10	0.051
Moderate utilization	9,950 (38.5%)	8,641 (37.8%)	1,309 (44.0%)	0.13	
High utilization	8,105 (31.3%)	7,217 (31.5%)	888 (29.9%)	0.04	
Rural residence	3,669 (14.2%)	3,408 (14.9%)	261 (8.8%)	0.19	<0.001
Immigration status					
Non-immigrant	23,429 (90.6%)	20,742 (90.6%)	2,687 (90.4%)	0.01	0.523
Recent immigrant	1,004 (3.9%)	878 (3.8%)	126 (4.2%)	0.02	
Long-term resident	1,428 (5.5%)	1,269 (5.5%)	159 (5.3%)	0.01	
Neighbourhood income‡					
Quintile 1	4,442 (17.2%)	4,111 (18.0%)	331 (11.1%)	0.19	<0.001
Quintile 2	5,033 (19.5%)	4,555 (19.9%)	478 (16.1%)	0.10	
Quintile 3	5,018 (19.4%)	4,482 (19.6%)	536 (18.0%)	0.04	
Quintile 4	5,587 (21.6%)	4,833 (21.1%)	754 (25.4%)	0.10	
Quintile 5	5,720 (22.1%)	4,854 (21.2%)	866 (29.1%)	0.18	
Distance (km) to cancer clinic*	35.0 ± 61.3	36.3 ± 62.9	24.9 ± 45.6	0.21	<0.001
Cancer clinic within city	19,480 (75.3%)	16,689 (72.9%)	2,791 (93.9%)	0.59	<0.001
Teaching hospital	8,466 (32.7%)	6,587 (28.8%)	1,879 (63.2%)	0.74	<0.001
Prior lumpectomy and RT	2,464 (9.5%)	1,860 (8.1%)	604 (20.3%)	0.35	<0.001
Mastectomy Surgeon Specific Variables					
Surgeon Age*	48.7 ± 9.3	48.9 ± 9.4	47.1 ± 8.7	0.19	<0.001
Surgeons annual volume*	850.1 ± 484.9	881.5 ± 487.5	608.8 ± 387.0	0.62	<0.001

Surgeons breast devotion*	22.3 ± 23.8	20.2 ± 22.6	38.8 ± 26.4	0.76	<0.001

*Mean ± SD; †Restricted to patients with a cancer diagnosis; ‡Missing data for 61 patients; RT = Radiotherapy, SD = Standardized Difference.

Figure 2: Trends in type and overall use of immediate reconstruction over the study period.

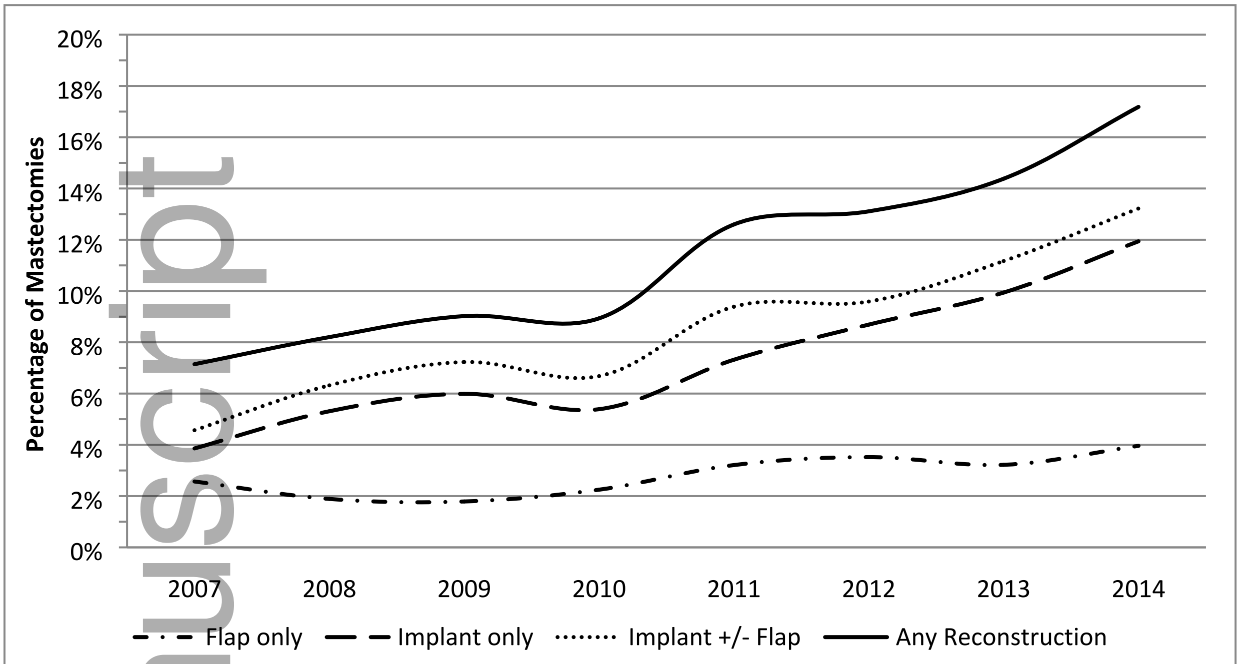

Table 2: Poisson regression model predicting immediate breast reconstruction post-mastectomy, both in the overall cohort and in a subgroup of patients with a current cancer diagnosis.

Variable	Overall Cohort (n = 25,861)		Cancer Subgroup (n = 21,153)	
	RR (95% CI)	p-value	RR (95% CI)	p-value
Patient age*	0.60 (0.58-0.61)	<.0001	0.58 (0.56-0.60)	<.0001
Distance to cancer centre (>50km vs <50km)	0.74 (0.67-0.82)	<.0001	0.67 (0.57-0.78)	<.0001
Teaching institution	2.36 (2.21-2.53)	<.0001	2.64 (2.39-2.91)	<.0001
Current cancer diagnosis†	0.33 (0.31-0.35)	<.0001	--	--
Prior lumpectomy and radiotherapy	1.47 (1.36-1.59)	<.0001	2.80 (2.47-3.17)	<.0001
Mastectomy surgeons experience (age)*	0.85 (0.82-0.88)	<.0001	0.78 (0.75-0.82)	<.0001

*Estimate represents a 10-year/unit increase; †'Type of reconstruction' not included in subgroup analysis; RR = Relative Risk, CI = Confidence Interval.

Table 3: Trends in the number (%) of patients who receive radiotherapy among patients with a current cancer diagnosis and either immediate reconstruction, immediate implant-based reconstruction or no immediate reconstruction.

Year	Immediate Reconstruction (n = 1564)	Immediate Implant-based Reconstruction (n = 1,039)	No Immediate Reconstruction (n = 19,589)
2007	21 (19.4%)	12 (19.1%)	844 (35.7%)
2008	21 (18.1%)	15 (19.5%)	910 (38.8%)
2009	32 (24.8%)	21 (23.6%)	968 (42.8%)
2010	31 (22.1%)	21 (23.9%)	982 (42.4%)
2011	52 (23.9%)	28 (22.8%)	1,126 (43.4%)
2012	70 (28.8%)	47 (28.7%)	1,221 (47.1%)
2013	79 (29.4%)	58 (29.9%)	1,221 (47.4%)
2014	96 (28.2%)	71 (29.5%)	1,277 (50.4%)
Overall	402 (25.7%)	273 (26.3%)	8,549 (43.6%)
p-value	0.0029	0.0043	<0.001

Table 4: Poisson regression model predicting radiotherapy in patients with a current cancer diagnosis and either any type of immediate breast reconstruction or within a subgroup of patients with implant-based reconstruction.

Variable	Any Type of Reconstruction (n = 1,126)		Implant Subgroup (n = 828)	
	RR (95% CI)	**p-value**	**RR (95% CI)**	**p-value**
Patient age*	0.87 (0.80-0.95)	0.0016	0.85 (0.77-0.94)	0.0015
Distance to nearest cancer centre*	1.00 (0.99-1.00)	0.0995	1.00 (0.99-1.00)	0.0581
Teaching institution	1.08 (0.89-1.30)	0.4383	1.01 (0.80-1.27)	0.9672
Cancer stage (II vs 0/I)	3.67 (2.82-4.78)	<.0001	3.02 (2.24-4.08)	<.0001
Cancer stage (III/IV vs 0/I)	7.02 (5.49-8.99)	<.0001	6.58 (4.98-8.68)	<.0001
Prior lumpectomy and radiotherapy	0.24 (0.13-0.45)	<.0001	0.39 (0.21-0.75)	0.0049
Mastectomy surgeon experience (age)*	1.05 (0.96-1.14)	0.263	1.04 (0.94-1.16)	0.4186
Plastic surgeon experience (age)*	1.04 (0.95-1.15)	0.4053	0.99 (0.88-1.12)	0.8692
Type of reconstruction (implant vs. flap) †	1.22 (1.00-1.49)	0.0554	--	--

*Estimate represents a 10-year increase; †'Cancer diagnosis' not included in subgroup analysis; RR = Relative Risk, CI = Confidence Interval.