Title: Variation in Opioid Prescribing after Outpatient Breast Surgery: Time for a Streamlined Approach?

Authors: J. La MD, MESc (1), A. Alqaydi MD (1), X. Wei MSc (2), G.C. Digby MD, MSc(HQ) (3), S.B. Brogly PhD (4), MSc, S.J. Merchant MSc, MHSc, MD (1,4)

Affiliations:

(1) Division of General Surgery and Surgical Oncology, Queen's University, Kingston, ON, Canada
(2) ICES Queen's, Kingston, ON, Canada
(3) Department of Medicine, Queen's University, Kingston, ON, Canada
(4) Department of Surgery, Queen's University, Kingston, ON, Canada

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Corresponding Author:

Dr. Shaila J. Merchant MSc, MHSc, MD

Associate Professor

Division of General Surgery and Surgical Oncology

Queen's University, Kingston, ON, Canada

shaila.merchant@kingstonhsc.ca

Abstract

Background: Opioids are frequently prescribed for pain management after surgery but can lead to misuse, diversion, and inappropriate disposal. We describe opioid prescribing and predictors of higher dose prescriptions in patients undergoing outpatient breast surgery in Ontario, Canada.

Methods: Patients ≥18 years undergoing outpatient breast surgery without reconstruction from 2012-2020 were identified using linked administrative health data. Procedure types were categorized: P±axilla, T±axilla and R±axilla (P=partial excision, T=total excision, R=radical excision, axilla=axillary intervention). Primary outcome was filling an opioid prescription within seven days of surgery. Secondary outcomes were total oral morphine equivalents (OME) filled (milligrams, mg) and filling >1 prescription within seven days of surgery. Associations (risk ratios, RR and 95% confidence intervals, CI) between patient and clinical variables and outcomes were estimated in multivariate models.

Results: 84,369 patients underwent outpatient breast surgery. Patients were mostly female (98%), healthy (Charlson comorbidity index, CCI 0-1, 91%), and resided in an urban location (89%). Over half (56%) underwent surgery for malignant disease, mostly P±axilla (90%). Of the cohort, 72% (n=60,620) filled an opioid prescription. Mean OMEs prescribed increased with invasiveness of the procedure (P±axilla=163±400 mg; T±axilla=180±307 mg; R±axilla=208±255 mg, p<0.0001). For all procedures, opioid prescribing decreased over the study period from 185±344 mg in 2012 to 106±384 mg in

2020. Factors associated with filling >1 opioid prescription were bilateral versus unilateral surgery (RR 1.64, 95% CI 1.42, 1.89), CCI 2+ versus 0-1 (RR 1.68, 95% CI 1.49, 1.90), male sex (RR 1.43, 95% CI 1.11, 1.85), malignant disease (RR 1.21, 95% CI 1.10, 1.33) and increased invasiveness (RR 2.07, 95% CI 1.79, 2.40 for R±axilla vs P±axilla).

Interpretation: Most patients undergoing outpatient breast surgery fill an opioid prescription within seven days. Dosing varied by surgical procedure and patient factors. More streamlined opioid prescribing for outpatient breast surgery may be warranted in some patients.

Introduction

The rising use and misuse of opioids is a national and international crisis contributing significantly to opioid-related deaths, particularly in young adults (1, 2). In Canada, between January 2016 and June 2019, there were greater than 13,900 apparent opioid-related deaths and 17,000 opioid-related hospitalizations (3). In North America, physicians prescribe higher quantities of opioids compared to other countries (4, 5) and the amount prescribed is greater than what is needed, evidenced by large numbers of unused opioids (6, 7). This may lead to long-term use in opioid naïve patients (8, 9), misuse by others in the household (10, 11), and diversion (12). Opioids are commonly prescribed by surgeons to treat acute post-operative pain. In the United States, despite writing only 1.8% of all medication prescriptions, surgeons accounted for 9.8% of all opioid prescriptions (13).

Breast surgery is commonly used to treat benign and malignant conditions. Breast cancer is the most common cancer in Canadian women, occurring in 1:8 females with 27,000 new cases in 2019 (14). Post-operative pain management practices in breast surgery are variable amongst United States surgeons (15, 16) with high rates of opioid over-prescription (5), despite recent literature suggesting that the appropriate length of time that opioids should be prescribed for breast surgery, if prescribed at all, is only five days (17). In fact, a recent Canadian study demonstrated that patients undergoing breast surgery can achieve adequate pain control with minimal to no post-operative opioids (18).

The Ontario Ministry of Health and Long-Term Care mandated data collection on opioid prescribing in 2012 (19), allowing for detailed evaluation of prescribing practices. Given the high volumes of breast surgery in Canada, the lack of detailed population-based

data on prescribing, and recent evidence from single institution studies suggesting that lower prescribing can be achieved, we sought to evaluate post-operative opioid prescribing in patients undergoing outpatient breast surgery in Ontario, Canada.

Methods

Study Cohort and Setting

We conducted a retrospective population-based cohort study of patients at least 18 years of age in Ontario, Canada undergoing outpatient breast surgery from July 1, 2012 to June 30, 2020. Ontario has a population of ~14 million people which represents nearly 38.8% of the Canadian population (20). Ontario has a universal health insurance plan which covers basic healthcare services (i.e. costs associated with physician visits, inpatient hospitalizations, etc.). Patients at least 18 years of age undergoing outpatient breast surgery, with or without axillary intervention were identified. Patients were excluded if they had concomitant breast reconstructive surgery (anticipated higher pain levels), died within 30 days of surgery, or were less than 18 years of age. We captured the first breast surgery per patient during the study period and subsequent breast surgery for the same patient was included only if at least 6 months had passed from initial breast surgery **(Figure 1)**.

Administrative Databases

We used the linked administrative databases housed at ICES (formerly known as the Institute for Clinical Evaluative Sciences). Outpatient surgery was captured using the

Canadian Institute for Health Information (CIHI) Same Day Surgery (SDS) database, which are mandatory submissions from hospitals to the Ministry of Health. Codes for partial breast excision (P) (i.e. lumpectomy, excisional biopsy), total breast excision (T) (i.e. mastectomy), radical breast excision (R) (i.e. mastectomy with removal of axillary lymph nodes) and simultaneous axillary intervention (axilla) were selected from the Canadian Classification of Health Interventions **(Appendix)**. International Classification of Diseases, 10th revision (ICD-10), diagnostic codes were used to identify malignant diagnoses, with the remainder classified as benign **(Appendix)**. Opioid prescriptions were identified from the Narcotics Monitoring System (NMS) database. Established in July 2012 through the Ontario Narcotics Strategy, the NMS records information on controlled drug prescriptions issued to Ontario residents, regardless of payment method. Categorization of opioids, including combinations, was performed (codeine, tramadol, oxycodone, morphine, hydromorphone, methadone, other) **(Appendix).** Demographic characteristics including age and sex were captured in the Registered Persons Database (RPDB). CIHI discharge abstract database which are mandatory submissions from hospitals to the Ministry of Health, was used to capture patient comorbidity. These datasets were linked using unique encoded identifiers and analyzed at ICES. Data were reported in accordance with recommendations from the RECORD statement (21).

Variables

We characterized patients by sex (male, female), age (18-29, 30-39, 40-49, 50-59, 60-69, 70-79, 80+ years) and Charlson Comorbidity Index (CCI 0-1, 2+) in five years prior to the index breast surgery. CCI categorizes ICD diagnosis codes into pre-defined

comorbid conditions and assigns a weight based on disease burden and its relative importance to patient prognosis (22). Postal codes linked to the postal code conversion file (PCCF) were used to assign area-level income quintiles, where quintile 1 represents the lowest incomes. Residence was defined as either rural (community size <10,000) or urban using PCCF. Institutions were defined as those providing instruction to medical students (teaching hospitals) and those that do not (small [<100 beds] and community [≥100 beds] hospitals). Diagnoses were categorized as benign or malignant. Procedure types were categorized as follows: P±axilla, T±axilla, R±axilla. Those receiving bilateral surgery were classified into the most invasive procedure using the following hierarchy: P±axilla<T±axilla<R±axilla where P±axilla is considered least invasive. The number of surgeries per patient in the study period was categorized (1, 2, 3+).

Outcomes

The primary outcome was filling an opioid prescription within seven days of surgery (days 0-7) where day 0 was day of surgery. Secondary outcomes were total oral morphine equivalents (OME) filled (milligrams, mg) and more than 1 prescription filled within seven days of surgery.

Statistical Analyses and Ethics Approval

Patient characteristics, procedure type, year of surgery and institution classification were compared by opioid prescription filled using the standardized difference where a difference ≥0.10 indicates a statistically significant difference between groups (23). Associations (risk ratios, RR and 95% confidence intervals, CI) between the above

covariates and outcomes (filling of any opioid prescription, filling of more than 1 opioid prescription) were estimated in multivariate models using modified Poisson regression. Models of >1 opioid prescriptions were restricted to those patients who filled at least one prescription. Differences in mean and median OME dose were examined by procedure, institution, and year of surgery using ANOVA and Kruskal-Wallis tests as appropriate. Because the dose may better indicate extent of opioid exposure and potential for subsequent harm, sensitivity analyses were performed to estimate associations between our covariates and higher filling, pre-determined as $\geq 75^{th}$ percentile. This study was approved by the Health Sciences and Affiliated Teaching Hospitals Research Ethics Board at Queen's University.

Results

A total of 109,352 outpatient breast surgeries were performed from July 1, 2012 through June 30, 2019. After exclusions were applied, 84,369 patients comprised the study cohort **(Figure 1)**. Most patients (72%, n=60,620) filled an opioid prescription, with the majority (96%) not filling additional prescriptions within seven days of surgery. Few patients filled additional prescriptions (1 additional=2%; 2 additional=0.2%; 3+ additional=0.1%).

Patients in the cohort were mostly female (98%), with median age of 57±15 years. The majority had a CCI of 0-1 (91%, indicating low comorbidity based on hospital encounters in the prior 5 years) and resided in an urban setting (89%). Surgery was most often performed in a community hospital (69%), and less often in teaching (27%), small (0.7%), and pediatric (0.2%) hospitals. Over half (56%) of patients had malignancy. Types

of procedures were P±axilla (90%), T±axilla (7%), and R±axilla (4%). Few (4%) underwent bilateral surgery. Most patients underwent one surgery during the study period (96%); a minority of patients underwent two (3%) or three or more (0.2%). The number of patients undergoing surgery per study year was similar except for 2012 and 2020 where data for only six months was captured **(Table 1)**.

Oral morphine equivalents filled by procedure type, hospital type, and year of surgery is summarized in **Table 2** for n=60,547 patients as data for 73 patients could not be converted using the ICES macro. The mean OME (±standard deviation) filled within seven days of surgery increased with greater invasiveness of the procedure (P±axilla=163±400 mg; T±axilla=180±307 mg; R±axilla=208±255 mg, p<0.0001). Mean OMEs filled did not vary significantly between teaching (173±496 mg) and community (164±339 mg) hospitals (p=0.054), even when examined by procedure type (data not shown). For all procedures, opioid filling decreased over the study period from 185±344 mg in 2012 to 106±384 mg in 2020 (p<0.0001).

Figure 2 illustrates the most common opioid prescriptions filled. Codeine was the most common (39%), followed by oxycodone (23%), tramadol (22%), hydromorphone (12%), morphine (2%), methadone (0.7%) and others (0.5%).

Table 3 summarizes factors associated with prescriptions filled within seven days of breast surgery among all patents in the cohort. In adjusted models, factors associated with filling an opioid prescription were bilateral surgery (RR 1.08, 95% CI 1.06, 1.10), malignant diagnosis (RR 1.16, 95% CI 1.15, 1.17), and increased invasiveness of the procedure (RR 1.10, 95% CI 1.09, 1.12 for R±axilla versus P±axilla). Factors associated with a decreased likelihood of filling an opioid prescription include: age 80+ (RR 0.80,

95% CI 0.78, 0.83 versus age 18-29), age 70-79 (RR 0.89, 95% CI 0.87, 0.91 versus age 18-29), age 60-69 (RR 0.93, 95% CI 0.91, 0.95, versus age 18-29), CCI 2+ (RR 0.90, 95% CI 0.89, 0.92 versus CCI 0-1), all non-community hospitals [i.e. pediatric hospital (RR 0.57, 95% CI 0.46, 0.70 versus community hospital)], and surgery in 2020 (RR 0.96, 95% CI 0.94, 0.99 versus 2012).

Table 4 summarizes factors associated with filling more than one opioid prescription within seven days of surgery among the 60,620 patients who filled at least one prescription. In the adjusted models, factors significantly associated with filling more than one prescription were ages 30-39 (RR 1.87, 95% CI 1.46, 2.40 versus age 18-29), 40-49 (RR 1.51, 95% CI 1.20, 1.92 versus age 18-29), 50-59 (RR 1.30, 95% CI 1.03, 1.64 versus age 18-29), bilateral surgery (RR 1.64, 95% CI 1.42, 1.89), malignant diagnosis (RR 1.21, 95% CI 1.10, 1.33) CCI 2+ (RR 1.68, 95% CI 1.49, 1.90 versus CCI 0-1), small hospital (RR 1.89, 95% CI 1.26, 2.85 versus community hospital), male sex (RR 1.43, 95% CI 1.11, 1.85), and increased invasiveness of surgery (RR 2.07, 95% CI 1.79, 2.40 R±axilla versus P±axilla).

In the sensitivity analysis among the 60,620 patients who filled at least one prescription, factors associated with higher (≥75th percentile) prescription filling were similar to those observed for filling more than 1 prescription **(Appendix)**. Age 30-39 (RR 1.33, 95% CI 1.24, 1.44 versus age 18-29), age 40-49 (RR 1.37, 95% CI 1.27, 1.46 versus age 18-29), age 50 – 59 (RR 1.36, 95% CI 1.27, 1.46 versus age 18-29), bilateral surgery (RR 1.35, 95% CI 1.29, 1.41), malignant diagnosis (RR 1.18, 95% CI 1.15, 1.21), CCI 2+ (RR 1.11, 95% CI 1.07, 1.16 versus CCI 0-1), small hospital (RR 1.34, 95% CI 1.16, 1.56 versus community), urban residence (RR 1.17, 95% CI 1.12, 1.21 versus rural), male sex

(RR 1.22, 95% CI 1.12, 1.32) and increased invasiveness of surgery (RR 1.45, 95% CI 1.39, 1.52 R±axilla versus P±axilla) were associated with higher prescription filling. In the same model, factors associated with reduced prescription filling were age 80+ (RR 0.89, 95% CI 0.81, 0.98 versus age 18-29), and surgery in more recent years (RR 0.22, 95% CI 0.20, 0.25 for 2020 versus 2012). There was significant overlap between patients that filled >1 prescription and those in the ≥75th percentile of filled opioids, as among 2,240 patients who filled >1 prescription, 1907 (85%) of patients filled ≥75th percentile of opioids.

Interpretation

We describe opioid prescribing in patients undergoing outpatient breast surgery without reconstructive procedures in the province of Ontario. Most patients (72%) filled a prescription for opioid medication, with variability in the agent and amount prescribed. While there is a trend in decreased opioid filling in more recent years, certain patient and clinical factors were associated with higher filling.

Despite recent small studies showing that opioids can be successfully eliminated in breast surgery, most patients in Ontario undergoing outpatient breast surgery filled an opioid prescription. Moo et al. (24) showed that routine opioid prescriptions were not necessary after excisional biopsy or lumpectomy if patients were encouraged to use non-steroidal anti-inflammatory agents. Rojas et al. (25) reported similar pain scores in patients undergoing lumpectomy who received opioids compared to those who did not and were encouraged to take acetaminophen and ibuprofen. While these studies were limited to patients undergoing lumpectomy, the majority (90%) of patients in our cohort also

underwent partial excision, suggesting that if an opioid-sparing approach was developed for these patients, then opioid prescribing would be significantly reduced.

However, while elimination of opioids in this population may be a desirable goal, there are factors that signal appropriate need for opioid medications. As anticipated, the amount of opioid filled correlated with increased invasiveness of breast surgery, with those undergoing total or radical resection most likely to fill an opioid prescription and require more than one opioid prescription. Similarly, Murphy et al. (26) reported that patients undergoing breast resection and concomitant reconstructive procedures were most likely to seek additional opioid prescriptions. Park et al. (16) also reported that higher OME were prescribed and used with increased invasiveness of surgery and was highest in patients undergoing concomitant reconstructive procedures. We also report that patients aged 30-59, males, those with malignancy, greater comorbidities, undergoing bilateral surgery, and receiving care in small hospitals were more likely to require additional opioid medication within seven days of surgery. Kulkarni et al. (27) similarly found that that younger age, bilateral procedures, as well as severity of preoperative pain, anxiety and depression were associated with more severe post-operative pain following breast reconstruction. Younger women may desire or require more extensive breast surgery which may increase the need for opioid medications (28, 29). It is possible that the need for more than one prescription in males is related to differences in pain perception between the sexes, although data in this domain is controversial (30). Patients with malignancy require more extensive surgery (i.e. margins, axillary surgery for staging or disease removal), which may contribute to increased pain.

The observation of higher prescribing in small hospitals is interesting. Community and teaching hospitals may be more likely to have enhanced awareness and protocols pertaining to opioids, leading to decreased likelihood of over-prescribing. Those with greater comorbidities may have higher opioid requirements for reasons other than breast surgery. For example, Cronin et al. (31) reported that comorbid mood disorders such as depression and anxiety resulted in increased opioid use postoperatively in patients undergoing rotator cuff repair. These studies suggest that while opioids can potentially be eliminated in less invasive breast surgery such as lumpectomy, other factors such as age, sex, malignancy, presence of comorbidities and extent of surgery may require healthcare providers to be aware of higher pain needs. Being aware of such factors preoperatively is important so that expectations can be managed, education can be provided, and the patient can be offered an individualized approach to pain management (32).

While flexibility in prescribing is important to accommodate individual needs, we show variability in the type and amount of agent prescribed in Ontario. We demonstrate large standard deviations in the amounts prescribed for each type of procedure, ranging from 255 to 400 mgs. Even larger variations in prescribing have been observed in Ontario patients undergoing otologic surgery (33). The variation in agent prescribed is also noteworthy as some patients in our cohort received powerful narcotics such as oxycodone, hydromorphone and morphine, known to contribute to opioid-related deaths in Ontario (34). A more streamlined approach to narcotic prescribing can be successfully introduced and implemented in healthcare institutions. For example, Hartford et al. (18) found that a multipronged initiative that streamlined opioid prescribing in patients undergoing outpatient breast surgery did not impact the average pain reported.

In more recent years of the study, we observed a decreased likelihood of filling higher quantities (i.e. ≥75th percentile) of opioid medications. This has also been observed in patients undergoing pediatric (35), dental (36) and general surgical procedures (37) and may be due to increasing provider awareness pertaining to the opioid crisis (38), national efforts to address the crisis (39, 40) and awareness of interventions to reduce prescribing (41, 42). Surgeons are interested in interventions that reduce prescribing (43) and studies suggest that such interventions can be successfully implemented. Hill et al. (41) educated surgeons and residents about the number of pills patients need for post-operative pain control after five general surgical operations. They subsequently observed that the number of opioids initially prescribed decreased by more than half. In a systematic review, Zhang et al. (42) identified behavioral interventions that resulted in a statistically significant decrease in the amount of opioid prescribed after surgery without negatively impacting pain control. This behooves institutions to carefully examine opioid prescribing practices within specific populations with a plan to implement strategies to effect change.

While our study provides new and detailed data on opioid prescribing after outpatient breast surgery in Canada, there are limitations. We captured opioid prescribing by filling of the prescription, but this may not capture actual patient opioid consumption. Studies have shown that some patients consume less than what is prescribed (7). We did not identify those who may have an opioid use disorder. Provider prescribing may be different in patients with opioid use disorder and may influence the type of agent and amount prescribed. Prescriptions for methadone and other agents were filled by a minority of patients in the cohort and therefore this likely has little effect on our overall conclusions. Patient-reported outcomes such as pain scores and satisfaction with pain management are

critical in understanding the patient pain experience. These data are not available in the health administrative database and therefore prescribing could not be correlated with these important outcomes. The pain experience may also be affected by patient race/ethnicity (27), which was not available in our dataset. There likely was some miscoding of procedure types, as radical resection implies simultaneous removal of axillary lymph nodes; however, a very small percentage of our patients underwent axillary intervention coded separately from radical resection.

In conclusion, most patients undergoing outpatient breast surgery in Ontario, Canada, filled an opioid prescription to manage post-operative pain, contrary to recent literature suggesting that opioids can be significantly reduced, if not eliminated. While the amount of opioid filled post-operatively has decreased in recent years, there remains significant variability in prescribing. Further efforts to anticipate patient pain needs and to streamline prescribing may be warranted.

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Figures and Tables

Figure 1 – Cohort creation flowchart for patients undergoing outpatient breast surgery in Ontario, Canada during the study period.

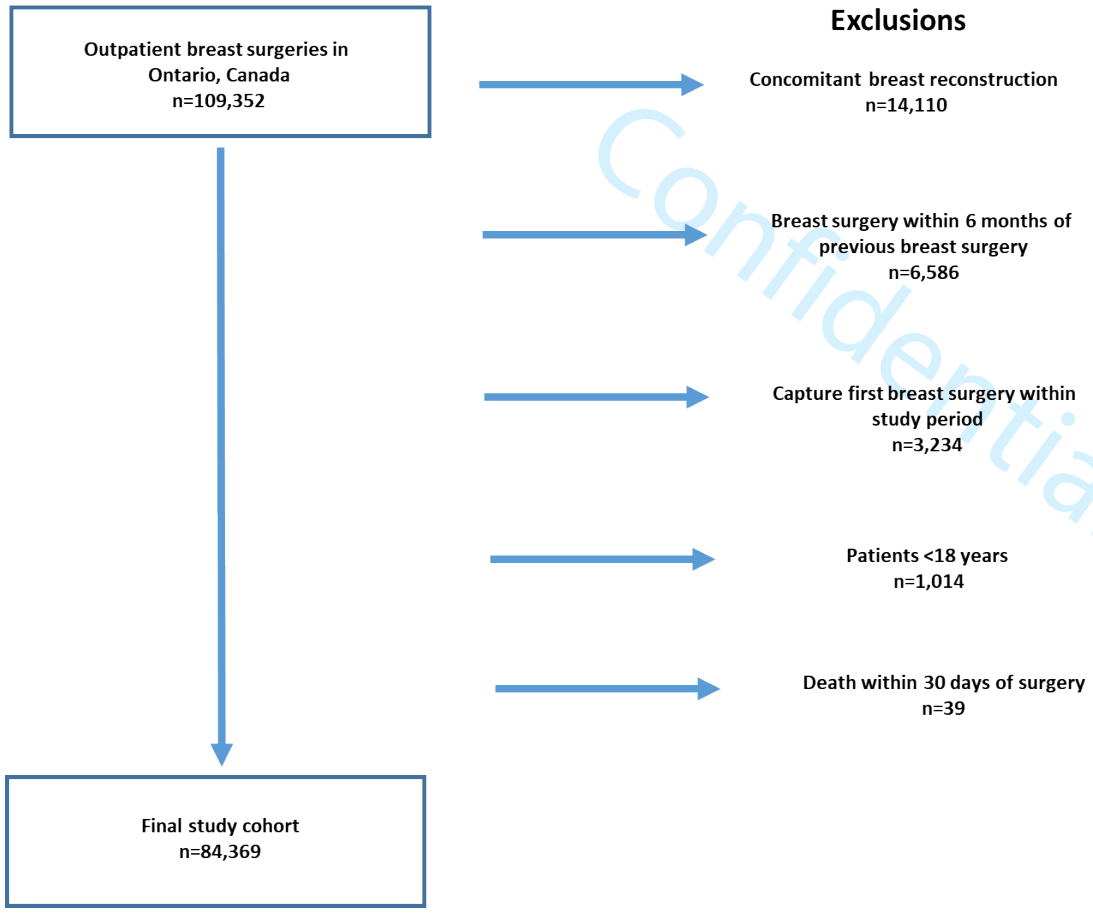

Figure 2 – Categorization of opioids filled by patients within seven days of outpatient breast surgery during the study period.

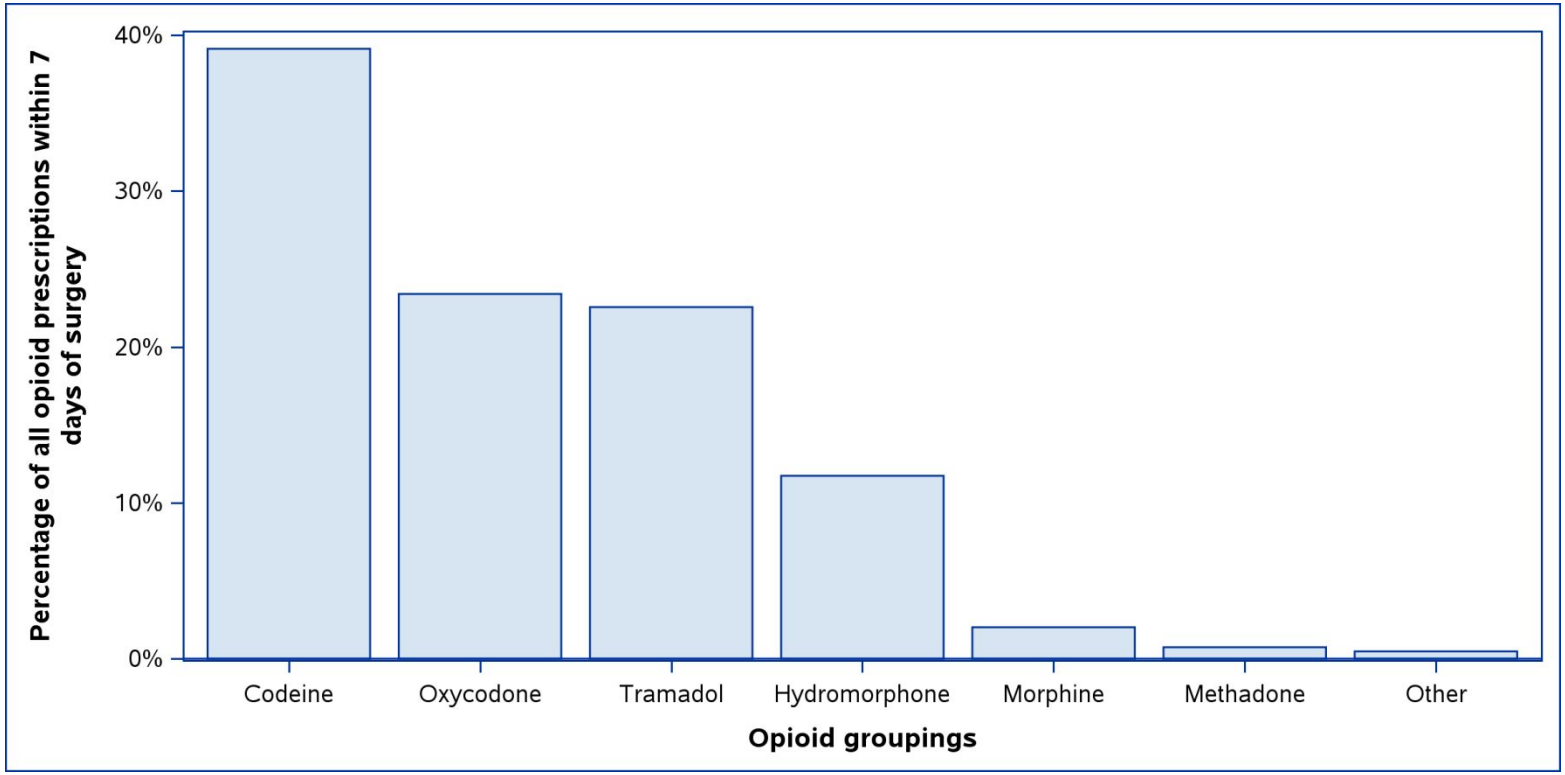

Table 1- Characteristics of patients undergoing outpatient breast surgery in Ontario, Canada during the study period, categorized by filling of opioid prescriptions within seven days of surgery date with standardized difference (n=84,369).

Variable	n (%)	Filled opioid prescription days 0-7	Did not fill opioid prescription	All patients	Standardized Difference
Any opioid prescription filled up to 7 days after surgery		n=60,620 (71.9%)	n=23,749 (28.1%)	n=84,369	
Sex	Female	59,627 (71.9%)	23,319 (28.1%)	82,946 (98.3%)	0.013
	Male	993 (69.8%)	430 (30.2%)	1,423 (1.7%)	0.013
Age at first surgery date (years)	Mean +/-standard deviation	56.9 (14.9)	57.9 (15.8)	57.2 (15.2)	0.068
Age (years)	18-29	3,230 (71.0%)	1,320 (29.0%)	4,550 (5.4%)	0.01
	30-39	4,146 (71.3%)	1,669 (28.7%)	5,815 (6.9%)	0.007
	40-49	10,158 (73.5%)	3,656 (26.5%)	13,814 (16.4%)	0.037
	50-59	15,411 (73.9%)	5,429 (26.1%)	20,840 (24.7%)	0.06
	60-69	14,992 (72.1%)	5,793 (27.9%)	20,785 (24.6%)	0.008
	70-79	9,471 (69.8%)	4,091 (30.2%)	13,562 (16.1%)	0.043
	80+	3,212 (64.2%)	1,791 (35.8%)	5,003 (5.9%)	0.092
Charlson comorbidity status	0-1	55,764 (72.5%)	21,175 (27.5%)	76,939 (91.2%)	0.097
	2+	4,856 (65.4%)	2,574 (34.6%)	7,430 (8.8%)	0.097
Socioeconomic status (quintiles)	1	10,490 (69.9%)	4,509 (30.1%)	14,999 (17.8%)	0.044
	2	11,932 (72.1%)	4,626 (27.9%)	16,558 (19.6%)	0.005

	3	12,265 (72.4%)	4,665 (27.6%)	16,930 (20.1%)	0.015
	4	12,599 (72.4%)	4,809 (27.6%)	17,408 (20.6%)	0.013
	5	13,334 (72.2%)	5,140 (27.8%)	18,474 (21.9%)	0.009
Location of residence	Missing	80 (62.0%)	49 (38.0%)	129 (0.2%)	0.018
	Rural	6,519 (69.9%)	2,808 (30.1%)	9,327 (11.1%)	0.034
	Urban	54,021 (72.1%)	20,892 (27.9%)	74,913 (88.8%)	0.036
Hospital Type	Missing	1,966 (65.0%)	1,059 (35.0%)	3,025 (3.6%)	0.063
	Community	43,018 (74.3%)	14,852 (25.7%)	57,870 (68.6%)	0.18
	Pediatric	54 (40.3%)	80 (59.7%)	134 (0.2%)	0.054
	Small	299 (51.3%)	284 (48.7%)	583 (0.7%)	0.077
	Teaching	15,283 (67.2%)	7,474 (32.8%)	22,757 (27.0%)	0.139
Breast cancer diagnosis	No	24,735 (67.0%)	12,172 (33.0%)	36,907 (43.7%)	0.211
	Yes	35,885 (75.6%)	11,577 (24.4%)	47,462 (56.3%)	0.211
Type of procedure	Excision partial breast +/-axillary intervention	53,679 (70.8%)	22,152 (29.2%)	75,831 (89.9%)	0.165
	Excision total breast +/- axillary intervention	4,417 (80.6%)	1,066 (19.4%)	5,483 (6.5%)	0.119
	Excision radical breast +/- axillary intervention	2,524 (82.6%)	531 (17.4%)	3,055 (3.6%)	0.11
Any bilateral surgery	No	57,728 (71.5%)	22,965 (28.5%)	80,693 (95.6%)	0.075

	Yes	2,892 (78.7%)	784 (21.3%)	3,676 (4.4%)	0.075
Number of surgeries per patient	1	58,394 (71.8%)	22,954 (28.2%)	81,348 (96.4%)	0.018
	2	2,129 (73.9%)	753 (26.1%)	2,882 (3.4%)	0.019
	3+	97 (69.8%)	42 (30.2%)	139 (0.2%)	0.004
Patients filling a subsequent opioid prescription within 7 days of surgery	0 additional	58,380 (100.0%)	0 (0.0%)	58,380 (69.2%)	7.22
	1 additional	1,948 (100.0%)	0 (0.0%)	1,948 (2.3%)	0.258
	2 additional	187 (100.0%)	0 (0.0%)	187 (0.2%)	0.079
	3+ additional	105 (100.0%)	0 (0.0%)	105 (0.1%)	0.059
Patients filling a subsequent opioid prescription within 30 days of surgery	0 additional	54,184 (97.6%)	1,352 (2.4%)	55,536 (65.8%)	3.07
	1 additional	4,722 (95.2%)	239 (4.8%)	4,961 (5.9%)	0.335
	2 additional	1,005 (95.0%)	53 (5.0%)	1,058 (1.3%)	0.149
	3+ additional	709 (97.8%)	16 (2.2%)	725 (0.9%)	0.141
Year of surgery	2012	3,959 (69.3%)	1,751 (30.7%)	5,710 (6.8%)	0.033
	2013	8,052 (73.1%)	2,956 (26.9%)	11,008 (13.0%)	0.025
	2014	8,604 (73.7%)	3,065 (26.3%)	11,669 (13.8%)	0.038
	2015	8,237 (74.1%)	2,879 (25.9%)	11,116 (13.2%)	0.044
	2016	8,029 (74.5%)	2,748 (25.5%)	10,777 (12.8%)	0.051
	2017	7,322 (71.4%)	2,938 (28.6%)	10,260 (12.2%)	0.009
	2018	6,923 (70.0%)	2,961 (30.0%)	9,884 (11.7%)	0.032

	2019	6,774 (68.1%)	3,171 (31.9%)	9,945 (11.8%)	0.066
	2020	2,720 (68.0%)	1,280 (32.0%)	4,000 (4.7%)	0.042

Table 2 – Mean and median oral morphine equivalents (OME) (milligrams, mg) filled within seven days of surgery in the cohort by procedure, institution and year of surgery during the study period. OME data not available for n=73 patients as data could not be converted with the ICES macro (n=60,547).
SD= standard deviation
IQR=interquartile range

Variable	Value	n	Mean (SD), mg	P-value for Mean	Median (95% IQR), mg	P-value for Median
Overall		60,547	166.3 (389.3)		135 (90-180)	
Type of procedure	Excision partial breast +/- axillary intervention	53,618	163.2 (400.3)	<.0001	135 (90-180)	<.0001
	Excision total breast +/- axillary intervention	4,409	179.8 (307.4)		135 (100-225)	
	Excision radical breast +/- axillary intervention	2,520	208.4 (255.3)		150 (113-225)	
Hospital type	Teaching	15,272	173.3 (495.5)	0.0543	135 (90-180)	0.8377
	Community	42,961	164.4 (338.7)		135 (90-180)	
	Small	296	169.3 (164.8)		135 (75-200)	
	Pediatric	54	233.3 (358.1)		113 (68-225)	
Year of surgery	2012	3,950	185.3 (344.2)	<.0001	135 (113-225)	<.0001
	2013	8,044	184.9 (396.7)		135 (113-225)	

	2014	8,596	192.3 (490.9)		135 (113-225)	
	2015	8,223	187.3 (563.2)		135 (113-225)	
	2016	8,016	179.0 (334.0)		135 (113-225)	
	2017	7,317	171.4 (343.6)		135 (100-180)	
	2018	6,916	141.2 (235.9)		113 (75-150)	
	2019	6,767	104.1 (156.2)		75 (50-113)	
	2020	2,718	106.2 (384.3)		75 (50-113)	

Table 3 – Unadjusted and adjusted analyses of factors associated with filling of opioid prescription within seven days of outpatient breast surgery (n=84,369).
CI = confidence interval

Variable	Value	Unadjusted RR (95% CI)	Adjusted RR (95% CI)
Age (years)	30-39	1.00 (0.98 - 1.03)	0.97 (0.95 - 1.00)
	40-49	1.04 (1.01 - 1.06)	0.97 (0.95 - 1.00)
	50-59	1.04 (1.02 - 1.06)	0.96 (0.94 - 0.99)
	60-69	1.02 (1.00 - 1.04)	0.93 (0.91 - 0.95)
	70-79	0.98 (0.96 - 1.01)	0.89 (0.87 - 0.91)
	80+	0.90 (0.88 - 0.93)	0.80 (0.78 - 0.83)
	18-29	Ref	Ref
Any bilateral surgery	1	1.10 (1.08 - 1.12)	1.08 (1.06 - 1.10)
	0	Ref	Ref
Breast cancer diagnosis	1	1.13 (1.12 - 1.14)	1.16 (1.15 - 1.17)
	0	Ref	Ref
Charlson comorbidity status	2+	0.90 (0.89 - 0.92)	0.90 (0.89 - 0.92)
	0-1	Ref	Ref
Hospital Type	Missing	0.87 (0.85 - 0.90)	0.87 (0.85 - 0.89)
	Pediatric	0.54 (0.44 - 0.67)	0.57 (0.46 - 0.70)
	Small	0.69 (0.64 - 0.75)	0.72 (0.66 - 0.78)
	Teaching	0.90 (0.89 - 0.91)	0.90 (0.89 - 0.91)
	Community	Ref	Ref
Location of residence	Missing	0.89 (0.77 - 1.02)	0.92 (0.80 - 1.05)
	Urban	1.03 (1.02 - 1.05)	1.02 (1.00 - 1.03)
	Rural	Ref	Ref
Sex	Male	0.97 (0.94 - 1.00)	0.98 (0.95 - 1.02)
	Female	Ref	Ref
Socioeconomic status (quintiles)	2	1.03 (1.02 - 1.05)	1.02 (1.01 - 1.04)

	3	1.04 (1.02 - 1.05)	1.03 (1.01 - 1.04)
	4	1.03 (1.02 - 1.05)	1.02 (1.01 - 1.04)
	5	1.03 (1.02 - 1.05)	1.03 (1.01 - 1.04)
	1	Ref	Ref
Type of procedure	Excision total breast +/ axillary intervention	1.14 (1.12 - 1.15)	1.12 (1.10 - 1.13)
	Excision radical breast +/- axillary intervention	1.17 (1.15 - 1.19)	1.10 (1.09 - 1.12)
	Excision partial breast +/- axillary intervention	Ref	Ref
Year of surgery	2013	1.05 (1.03 - 1.08)	1.05 (1.03 - 1.07)
	2014	1.06 (1.04 - 1.09)	1.06 (1.04 - 1.08)
	2015	1.07 (1.05 - 1.09)	1.06 (1.04 - 1.09)
	2016	1.07 (1.05 - 1.10)	1.07 (1.05 - 1.09)
	2017	1.03 (1.01 - 1.05)	1.02 (1.00 - 1.04)
	2018	1.01 (0.99 - 1.03)	1.01 (0.98 - 1.03)
	2019	0.98 (0.96 - 1.00)	0.97 (0.95 - 1.00)
	2020	0.98 (0.95 - 1.01)	0.96 (0.94 - 0.99)
	2012	Ref	Ref

Table 4 – Unadjusted and adjusted analyses of factors associated with filling more than 1 opioid prescription within seven days of outpatient breast surgery (n=60,620).
CI = confidence interval

Variable	Value	Unadjusted RR (95% CI)	Adjusted RR (95% CI)
Age (years)	30-39	1.98 (1.56 - 2.53)	1.87 (1.46 - 2.40)
	40-49	1.63 (1.30 - 2.04)	1.51 (1.20 - 1.92)
	50-59	1.42 (1.14 - 1.77)	1.30 (1.03 - 1.64)
	60-69	1.19 (0.95 - 1.49)	1.04 (0.82 - 1.32)
	70-79	1.08 (0.85 - 1.37)	0.89 (0.69 - 1.15)
	80+	1.31 (1.00 - 1.73)	0.99 (0.74 - 1.32)
	18-29	Ref	Ref
Any bilateral surgery	1	2.22 (1.94 - 2.53)	1.64 (1.42 - 1.89)
	0	Ref	Ref
Breast cancer diagnosis	1	1.24 (1.14 - 1.35)	1.21 (1.10 - 1.33)
	0	Ref	Ref
Charlson comorbidity status	2+	1.83 (1.63 - 2.06)	1.68 (1.49 - 1.90)
	0-1	Ref	Ref
Hospital Type	Missing	0.85 (0.65 - 1.09)	0.87 (0.67 - 1.14)
	Pediatric	2.12 (0.83 - 5.46)	1.83 (0.73 - 4.55)
	Small	2.20 (1.48 - 3.28)	1.89 (1.26 - 2.85)
	Teaching	1.23 (1.12 - 1.34)	1.16 (1.06 - 1.27)
	Community	Ref	Ref
Location of residence	Missing	1.11 (0.42 - 2.90)	1.02 (0.39 - 2.64)
	Urban	0.80 (0.71 - 0.90)	0.81 (0.72 - 0.92)
	Rural	Ref	Ref
Sex	Male	1.74 (1.36 - 2.21)	1.43 (1.11 - 1.85)
	Female	Ref	Ref
Socioeconomic status (quintiles)	2	0.83 (0.73 - 0.94)	0.85 (0.75 - 0.96)

	3	0.75 (0.66 - 0.86)	0.77 (0.68 - 0.88)
	4	0.79 (0.70 - 0.89)	0.81 (0.71 - 0.92)
	5	0.74 (0.65 - 0.84)	0.77 (0.68 - 0.88)
	1	Ref	Ref
Type of procedure	Excision total breast +/ axillary intervention	2.05 (1.81 - 2.31)	1.74 (1.52 - 1.98)
	Excision radical breast +/- axillary intervention	2.62 (2.29 - 3.01)	2.07 (1.79 - 2.40)
	Excision partial breast +/- axillary intervention	Ref	Ref
Year of surgery	2013	1.02 (0.83 - 1.24)	1.04 (0.85 - 1.27)
	2014	1.14 (0.94 - 1.38)	1.15 (0.95 - 1.40)
	2015	1.04 (0.85 - 1.26)	1.07 (0.88 - 1.30)
	2016	1.05 (0.86 - 1.28)	1.10 (0.90 - 1.34)
	2017	1.04 (0.85 - 1.27)	1.08 (0.89 - 1.32)
	2018	1.09 (0.89 - 1.33)	1.13 (0.92 - 1.38)
	2019	0.91 (0.74 - 1.12)	0.94 (0.76 - 1.16)
	2020	1.31 (1.03 - 1.66)	1.24 (0.97 - 1.57)
	2012	Ref	Ref

Appendix

Canadian Classification of Health Interventions codes for breast and axillary procedures

Excision Partial Breast

1YK87LA	Excision partial, nipple using open excisional approach	1YK87	Excision partial, nipple
1YK89LA	Excision total, nipple using open approach	1YK89	Excision total, nipple

1YL87LA	Excision partial, lactiferous duct using open approach	1YL87	Excision partial, lactiferous duct
1YL89LA	Excision total, lactiferous duct using open approach	1YL89	Excision total, lactiferous duct

1YM87DA	Excision partial, breast using endoscopic approach with simple apposition	1YM87	Excision partial, breast
1YM87GB	Excision partial, breast using endoscopic guide wire (or needle hook) excision technique with simple apposition of tissue	1YM87	Excision partial, breast
1YM87LA	Excision partial, breast using open approach with simple apposition of tissue (e.g. suturing)	1YM87	Excision partial, breast
1YM87UT	Excision partial, breast using open guide wire (or needle hook) excision technique and simple apposition of tissue	1YM87	Excision partial, breast

Excision Total Breast

1YM89LA	Excision total, breast using open approach	1YM89	Excision total, breast

Excision Radical Breast

1YM91LA	Excision (modified) radical, breast without tissue	1YM91	Excision radical, breast
1YM91TR	Excision extended radical, breast without tissue	1YM91	Excision radical, breast
1YM91WP	Excision super radical, breast without tissue	1YM91	Excision radical, breast

Excision partial lymph nodes, axillary

1MD87LA	Excision partial, lymph node(s), axillary using open approach	1MD87	Excision partial, lymph node(s), axillary

Excision total lymph nodes, axillary

1MD89LA	Excision total, lymph node(s), axillary using open approach	1MD89	Excision total, lymph node(s), axillary
1MD89LAXXA	Excision total, lymph node(s), axillary using open approach with full thickness graft	1MD89	Excision total, lymph node(s), axillary
1MD89LAXXE	Excision total, lymph node(s), axillary using open approach with local flap	1MD89	Excision total, lymph node(s), axillary
1MD89LAXXF	Excision total, lymph node(s), axillary using open approach with free distant flap	1MD89	Excision total, lymph node(s), axillary
1MD89LAXXG	Excision total, lymph node(s), axillary using open approach with pedicled distant flap	1MD89	Excision total, lymph node(s), axillary
1MD89LAXXN	Excision total, lymph node(s), axillary using open approach with synthetic tissue	1MD89	Excision total, lymph node(s), axillary

Biopsy axillary lymph nodes

2MD71HA	Biopsy, axillary lymph nodes using percutaneous (needle) approach	2MD71	Biopsy, axillary lymph nodes
2MD71LA	Biopsy, axillary lymph nodes using open approach	2MD71	Biopsy, axillary lymph nodes

International Classification of Diseases 10th Edition codes used to identify malignant breast disease

C5000	Malignant neoplasm of right nipple and areola
C5001	Malignant neoplasm of left nipple and areola
C5009	Malignant neoplasm of nipple and areola, unspecified side
C5010	Malignant neoplasm of central portion of right breast
C5011	Malignant neoplasm of central portion of left breast
C5019	Malignant neoplasm of central portion of breast, unspecified side
C5020	Malignant neoplasm of upper-inner quadrant of right breast
C5021	Malignant neoplasm of upper-inner quadrant of left breast
C5029	Malignant neoplasm of upper-inner quadrant of breast, unspecified side
C5030	Malignant neoplasm of lower-inner quadrant of right breast
C5031	Malignant neoplasm of lower-inner quadrant of left breast
C5039	Malignant neoplasm of lower-inner quadrant of breast, unspecified side
C5040	Malignant neoplasm of upper-outer quadrant of right breast
C5041	Malignant neoplasm of upper-outer quadrant of left breast
C5049	Malignant neoplasm of upper-outer quadrant of breast, unspecified side
C5050	Malignant neoplasm of lower-outer quadrant of right breast
C5051	Malignant neoplasm of lower-outer quadrant of left breast
C5059	Malignant neoplasm of lower-outer quadrant of breast, unspecified side

C5060	Malignant neoplasm of axillary tail of right breast
C5061	Malignant neoplasm of axillary tail of left breast
C5069	Malignant neoplasm of axillary tail of breast, unspecified side
C5080	Overlapping malignant lesion of right breast
C5081	Overlapping malignant lesion of left breast
C5089	Overlapping malignant lesion of breast, unspecified side
C5090	Malignant neoplasm of right breast, part unspecified
C5091	Malignant neoplasm of left breast, part unspecified
C5099	Malignant neoplasm of breast, part unspecified, unspecified side

Categorization of opioids received and filled by patients undergoing outpatient breast surgery

Codeine including combinations
ACETAMINOPHEN & CAFFEINE & CODEINE PHOSPHATE
CODEINE PHOSPHATE
ACETAMINOPHEN & CAFFEINE CITRATE & CODEINE PHOSPHATE
CODEINE SULFATE
ACETAMINOPHEN & CODEINE PHOSPHATE
ACETYLSALICYLIC ACID & BUTALBITAL & CAFFEINE & CODEINE PHOSPHATE
ACETYLSALICYLIC ACID & CAFFEINE CITRATE & CODEINE PHOSPHATE
ACETYLSALICYLIC ACID & CODEINE PHOSPHATE & METHOCARBAMOL
ACETYLSALICYLIC ACID & CAFFEINE & CODEINE PHOSPHATE
CODEINE PHOSPHATE & PSEUDOEPHEDRINE HCL & TRIPROLIDINE HCL

Tramadol including combinations
ACETAMINOPHEN & TRAMADOL
TRAMADOL HCL
ACETAMINOPHEN & TRAMADOL HCL
TRAMADOL

Oxycodone including combinations
ACETAMINOPHEN & OXYCODONE HCL
OXYCODONE HCL
ACETYLSALICYLIC ACID & OXYCODONE HCL

Morphine
MORPHINE SULFATE

Hydromorphone
HYDROMORPHONE HCL
HYDROMORPHONE

Methadone
METHADONE HCL
METHADONE

Other
MEPERIDINE HCL
BUPRENORPHINE HCL & NALOXONE HCL
FENTANYL CITRATE
PENTAZOCINE HCL
HYDROCODONE BITARTRATE

NALOXONE HCL & OXYCODONE HCL
TAPENTADOL HCL
BUPRENORPHINE
BUTORPHANOL TARTRATE

Unadjusted and adjusted analyses of factors associated with ≥75th percentile of opioid prescribing (n=60,620).
CI = confidence interval

Variable	Value	Unadjusted RR (95% CI)	Adjusted RR (95% CI)
Age (years)	30-39	1.40 (1.30 - 1.52)	1.33 (1.24 - 1.44)
	40-49	1.47 (1.37 - 1.58)	1.37 (1.27 - 1.46)
	50-59	1.47 (1.37 - 1.57)	1.36 (1.27 - 1.46)
	60-69	1.35 (1.26 - 1.44)	1.25 (1.17 - 1.34)
	70-79	1.26 (1.17 - 1.35)	1.16 (1.08 - 1.25)
	80+	1.02 (0.93 - 1.12)	0.89 (0.81 - 0.98)
	18-29	Ref	Ref
Any bilateral surgery	1	1.46 (1.40 - 1.52)	1.35 (1.29 - 1.41)
	0	Ref	Ref
Breast cancer diagnosis	1	1.17 (1.14 - 1.20)	1.18 (1.15 - 1.21)
	0	Ref	Ref
Charlson comorbidity status	2+	1.12 (1.07 - 1.17)	1.11 (1.07 - 1.16)
	0-1	Ref	Ref
Hospital Type	Missing	0.70 (0.64 - 0.77)	0.81 (0.74 - 0.88)
	Pediatric	1.12 (0.77 - 1.64)	0.96 (0.67 - 1.37)
	Small	1.17 (1.00 - 1.37)	1.34 (1.16 - 1.56)
	Teaching	1.08 (1.05 - 1.11)	1.02 (0.99 - 1.05)
	Community	Ref	Ref
Location of residence	Missing	1.12 (0.80 - 1.57)	1.18 (0.85 - 1.64)

	Urban	1.14 (1.09 - 1.18)	1.17 (1.12 - 1.21)
	Rural	Ref	Ref
Sex	Male	1.22 (1.13 - 1.33)	1.22 (1.12 - 1.32)
	Female	Ref	Ref
Socioeconomic status (quintiles)	2	0.94 (0.90 - 0.98)	0.95 (0.91 - 0.98)
	3	0.92 (0.89 - 0.96)	0.92 (0.89 - 0.96)
	4	0.92 (0.89 - 0.96)	0.92 (0.89 - 0.96)
	5	0.90 (0.86 - 0.93)	0.91 (0.87 - 0.94)
	1	Ref	Ref
Type of procedure	Excision total breast +/- axillary intervention	1.32 (1.26 - 1.37)	1.30 (1.25 - 1.36)
	Excision radical breast +/- axillary intervention	1.68 (1.60 - 1.75)	1.45 (1.39 - 1.52)
	Excision partial breast +/- axillary intervention	Ref	Ref
Year of surgery	2013	0.96 (0.91 - 1.00)	0.96 (0.92 - 1.01)
	2014	1.02 (0.97 - 1.07)	1.02 (0.97 - 1.07)
	2015	0.97 (0.92 - 1.02)	0.98 (0.93 - 1.03)
	2016	0.94 (0.89 - 0.98)	0.95 (0.90 - 1.00)
	2017	0.75 (0.71 - 0.79)	0.76 (0.73 - 0.81)
	2018	0.54 (0.50 - 0.57)	0.55 (0.51 - 0.58)
	2019	0.28 (0.25 - 0.30)	0.28 (0.26 - 0.30)
	2020	0.23 (0.20 - 0.26)	0.22 (0.20 - 0.25)
	2012	Ref	Ref