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Post-Discharge Prophylactic Antibiotics Following Mastectomy With and Without Breast Reconstruction

David K. Warren, MD, MPH[1], **Kate M. Peacock, MPH**[1], **Katelin B. Nickel, MPH**[1], **Victoria J. Fraser, MD**[1], **Margaret A. Olsen, PhD, MPH**[1,2],

CDC Prevention Epicenter Program

[1]Division of Infectious Diseases, Washington University School of Medicine, St. Louis, MO, USA

[2]Division of Public Health Sciences, Washington University School of Medicine, St. Louis, MO, USA

Abstract

Background: Prophylactic antibiotics are commonly prescribed at discharge for mastectomy, despite guidelines recommending against this practice. We investigated factors associated with post-discharge prophylactic antibiotic use after mastectomy with and without immediate reconstruction (IR) and the impact on surgical site infection (SSI).

Study Design: We studied a cohort of women aged 18–64 years undergoing mastectomy between 1/1/2010–6/30/2015 using the MarketScan Commercial Database. Patients with non-surgical perioperative infections were excluded. Post-discharge oral antibiotics were identified from outpatient drug claims. SSI was defined using ICD-9-CM diagnosis codes. Generalized linear models were performed to determine factors associated with post-discharge prophylactic antibiotic use and SSI.

Results: The cohort included 38,793 procedures; 24,818 (64%) with immediate reconstruction. Prophylactic antibiotics were prescribed post-discharge after 2,688 (19.2%) mastectomy only and 17,807 (71.8%) mastectomies with IR. The 90-day incidence of SSI was 3.5% after mastectomy only and 8.8% after mastectomy with IR. Antibiotics with anti-methicillin-sensitive *Staphylococcus aureus* (MSSA) activity were associated with decreased SSI risk after mastectomy only (adjusted relative risk [aRR], 0.74; 95% confidence interval [CI], 0.55, 0.99) and mastectomy with IR (aRR, 0.80; 95% CI, 0.73, 0.88), respectively. The number needed to treat (NNT) to prevent one additional SSI was 107 and 48, respectively.

Conclusion: Post-discharge prophylactic antibiotics were common after mastectomy. Anti-MSSA antibiotics were associated with decreased risk of SSI for mastectomy only and mastectomy with IR patients. The high NTTs suggest that potential benefits of post-discharge antibiotics should be weighed against potential harm associated with antibiotic over-use.

PRECIS

Corresponding author: Margaret A. Olsen, PhD, MPH, Washington University School of Medicine, Division of Infectious Diseases, 4523 Clayton Ave. Campus Box 8051, St. Louis, MO 63110. molsen@wustl.edu. Phone: (314) 454-8320. Fax: (314) 454-5392.

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Post-discharge anti-MSSA prophylactic antibiotics were associated with slightly decreased risk of surgical site infection after mastectomy with and without immediate reconstruction. The high number needed to treat to prevent one infection suggests the need to balance the small apparent benefit of continuing antibiotics against the harms of overuse.

Keywords

Mastectomy; breast reconstruction; surgical site infection; prophylactic antibiotics; post-discharge antibiotics; risk factors

INTRODUCTION

Surgical site infections (SSIs) are among the most common healthcare-associated infections in the U.S.[1] The Centers for Disease Control and Prevention SSI guidelines recommend against the use of prophylactic antibiotics in clean surgeries after the surgical incision is closed, even in the presence of surgical drains, due to lack of evidence for benefit.[2] In contrast, the American Society of Plastic Surgeons guidelines for breast implant reconstruction recommend that prolonged antibiotic prophylaxis be left to surgeon preference when surgical drains are present.[3] In practice, up to 70% of plastic surgeons continue prophylactic antibiotics post-discharge after mastectomy with breast reconstruction.[4, 5]

While post-discharge prophylactic antibiotics are common after mastectomy with breast reconstruction, there is conflicting evidence for its effectiveness in preventing SSI. Several studies have reported decreased risk of SSI with post-discharge prophylactic antibiotic use after mastectomy with[6–9] and without[10] immediate breast reconstruction. However, these studies have limitations, including data from single surgeons, comparing two surgeons with differing prescribing practices, and regression to the mean due to high SSI rates prior to change in antibiotic use.[11] Conversely, numerous studies demonstrated no effect of post-discharge antibiotics on SSI following mastectomy, although many of these studies lacked sufficient power to detect an association with only a moderate effect.[12–21]

Exposure of patients to prolonged antibiotic regimens results in higher costs, selection of antibiotic-resistant organisms and increased risk of *Clostridioides difficile* infection.[22–26] The importance of outpatient antibiotic stewardship is increasingly recognized, since outpatient antibiotic prescriptions constitute the majority of antibiotic use. Therefore, outpatient stewardship interventions may have greater potential to decrease the prevalence of antibiotic resistant organisms than inpatient efforts.[27]

To better understand the impact of prolonged prophylactic antibiotics, we aimed to determine 1) the prevalence and factors associated with post-discharge prophylactic antibiotic use and 2) whether post-discharge prophylactic antibiotic use was associated with decreased SSI risk after mastectomy with and without immediate breast reconstruction using a large database of U.S. commercially insured persons.

METHODS

We established a cohort of adult women aged 18–64 years who underwent mastectomy from 1/1/2010–6/30/2015 using the IBM® MarketScan® Commercial Database. The 2010–2015 Commercial Database includes medical and outpatient pharmacy claims for over 100 million persons covered by employer-sponsored and commercial health plans. This study was considered exempt from oversight by the Washington University Human Research Protection Office.

Women undergoing mastectomy were identified based on a Current Procedural Terminology or *International Classification of Diseases, 9th edition, Clinical Modification* (ICD-9-CM) procedure code for mastectomy (Appendix Table 1). We implemented additional measures to verify that mastectomy was performed and to identify the date of the procedure (see Appendix), as described previously.[28]

We applied additional exclusions for complicated admissions, procedures in which post-discharge antibiotics were not possible or could have been used for therapeutic indications (Figure 1). Exclusions during the index surgical admission included death and additional surgery other than mastectomy, using the National Healthcare Safety Network (NHSN) procedure list.[29] To exclude patients who may have received antibiotics due to a recent or current infection, mastectomies were excluded in women with an ICD-9-CM diagnosis code for a systemic or serious (i.e., septicemia) or minor (e.g. upper respiratory) infection (Appendix Table 2).

The population was restricted to women with known U.S. region of residence and continuous medical and prescription drug insurance enrollment from 365 days before through 90 days after mastectomy to assess comorbidities, complications, and post-discharge antibiotic use.

Identification of Exposures, Outcomes, and Covariates

The primary exposure of interest was post-discharge prophylactic antibiotic, defined as a paid prescription filled between 15 days before the mastectomy encounter through 2 days post-discharge (Appendix Table 3). Prescriptions filled in the 15 days prior to mastectomy were considered prophylactic, based on the median time of 15 days between the last plastic surgeon clinic encounter and mastectomy admission. If a patient had an antibiotic prescription in the timeframe for prophylactic antibiotics that was the same as a filled antibiotic prescription in the 30 to 16 days prior to the mastectomy encounter, it was not considered prophylactic. We analyzed both any use and category based on antibiotic activity (Appendix Table 3).

Comorbidities were identified in the year before surgery, primarily based on the Elixhauser classification, with calculation of the 30-day readmission score.[30, 31] Prescription drug claims were used to increase the sensitivity of identification of diabetes and smoking (Appendix Table 1). Prior antibiotics included paid prescriptions filled in the 16–30 days prior to the mastectomy admission.

All analyses were stratified by reconstruction because of differences in the patient populations and SSI risk. The primary outcome of interest was SSI from 2 to 90 days after mastectomy, identified using ICD-9-CM diagnosis codes during inpatient and/or non-diagnostic outpatient encounters (Appendix Table 4). Censoring was implemented for subsequent surgical procedures within 90 days using codes defined by the 2015 NHSN procedure list.[29] Censoring was not performed if the subsequent procedure was a breast surgery coded for SSI, or if the SSI was coded using a breast-specific code (e.g., implant infection).[28]

Statistical Analyses

Bivariate comparisons were performed using Chi-square tests for binary and Mann-Whitney U or Kruskal-Wallis tests for continuous variables. Independent factors associated with post-discharge prophylactic antibiotics and for SSI were identified with generalized linear models, with calculation of relative risks and robust standard errors. Variables with $p < 0.2$ in bivariate analysis or with clinical/biologic plausibility were included in the initial models, with the exception of post-discharge prophylactic antibiotics (primary exposure in the SSI model). Variables were removed in a backwards stepwise manner with $p < 0.1$ the threshold for retention. Potential multicollinearity of independent variables was assessed using variance inflation factors and model discrimination with the c statistic.[32]

To assess the clinical impact and robustness of associations between post-discharge prophylactic antibiotics and SSI risk, we calculated the number needed to treat and E-value, respectively. The E-value is the minimum relative risk that a potentially unmeasured confounder would have to have with both the outcome and primary exposure, after controlling for covariates, to account for the observed association between the primary exposure with the outcome.[33] All statistical analyses were performed in SAS version 9.4 (Cary, NC), with $p < 0.05$ considered statistically significant. Post-hoc tests to determine the power to detect a 50% and 25% difference in SSI incidence depending on utilization of post discharge oral antibiotics were performed using Power Analysis and Sample Size 14 software (Kaysville, Utah).

RESULTS

A total of 80,692 mastectomy procedures were identified among women 18–64 years old between January 1, 2010 and June 30, 2015. After excluding 41,899 surgical encounters (Figure 1), the final study cohort included 38,793 mastectomies, of which 24,818 (64.0%) included immediate breast reconstruction (Table 1). Approximately 88% of breast reconstruction procedures involved a breast implant (n=21,755). Among mastectomy plus immediate reconstruction, the median age was 50 years and 9.7% resided in a rural area. Among mastectomy only encounters, the median age of patients was 55 years and 18.4% resided in a rural area.

Prophylactic antibiotics were prescribed post-discharge after 2,688 (19.2%) mastectomy only procedures and 17,807 (71.8%) mastectomy plus reconstruction (Table 1). Post-discharge prophylactic antibiotic use ranged from 18.9% in 2013 to 19.7% in 2015 after mastectomy only and 68.2% in 2010 to 74.4% in 2015 after mastectomy plus reconstruction.

Antibiotics with anti-methicillin sensitive *Staphylococcus aureus* (MSSA) activity were most common, accounting for 70.3% and 72.8% among those with post-discharge prophylactic antibiotics after mastectomy only and mastectomy plus reconstruction, respectively. The most commonly prescribed post-discharge prophylactic antibiotics were cephalexin (56.8%), ciprofloxacin (8.0%), and sulfamethoxazole/trimethoprim (7.4%) after mastectomy only and cephalexin (57.9%), cefadroxil (10.6%), and clindamycin (8.2%) after mastectomy plus reconstruction (Appendix Table 3).

Results of bivariate analyses for factors associated with post-discharge prophylactic antibiotic receipt stratified by immediate reconstruction are shown in Appendix Table 5. In multivariable analysis, the risk of a filled prescription for a post-discharge prophylactic antibiotic after mastectomy only was significantly higher for women with diabetes, prior *S. aureus* infection, neoadjuvant chemotherapy, and those with a surgical complication during the index admission (Table 2). Women living in a rural area, with neurological disorders, and older age were significantly less likely to fill a post-discharge prophylactic antibiotic prescription. Among mastectomy plus reconstruction, implant-based surgery was independently associated with 44% increased risk of a post-discharge prophylactic antibiotic prescription (Table 3). Other independent risk factors for prophylactic post-discharge antibiotic after mastectomy plus reconstruction were residing in the Northeast or West U.S., valvular heart disease, and more recent years of surgery. Women who smoked, lived in a rural area, with neurological disorder, depression, or pulmonary circulation disease were significantly less likely to fill a post-discharge prophylactic antibiotic prescription.

The 90-day incidence of SSI was 3.5% after mastectomy only and 8.8% after mastectomy plus immediate reconstruction (Table 1). Among mastectomy only, the incidence of SSI was 3.2% among women filling a prescription post-discharge compared to 3.6% among women who did not fill a prophylactic antibiotic prescription post-discharge ($p = 0.334$). Among mastectomy plus immediate reconstruction, the incidence of SSI was 8.3% among women filling a prescription post-discharge compared to 9.9% among women who did not fill a post-discharge prophylactic antibiotic prescription ($p < 0.001$). The lowest SSI incidence after both mastectomy only and mastectomy plus reconstruction was in women who filled a prescription for an anti-MSSA antibiotic post-discharge (2.7% and 7.8%, respectively).

The results of bivariate analyses for factors associated with SSI are shown in Appendix Tables 5 and 6. In multivariable analysis, post-discharge anti-MSSA prophylactic antibiotics were independently associated with decreased SSI risk after mastectomy only (relative risk [RR], 0.74; 95% confidence interval [CI], 0.55, 0.99; Table 4). Prophylactic anti-MRSA antibiotics and quinolones were not associated with SSI risk. Independent risk factors for SSI after mastectomy only included diabetes, psychoses, and obesity. For the observed adjusted RR of 0.74 for anti-MSSA prophylactic antibiotics, the E-value was 2.04 for the point estimate, with a lower limit of 1.11. Based on the adjusted RR of 0.74, 107 women would need to be treated with an anti-MSSA antibiotic post-discharge after mastectomy only to prevent one additional SSI.

In multivariable analysis, post-discharge prophylactic antibiotics with anti-MSSA activity were independently associated with decreased SSI risk after mastectomy plus immediate

reconstruction (RR, 0.80; 95% CI, 0.73, 0.88; Table 5). Prophylactic anti-MRSA antibiotics and quinolones were not associated with decreased SSI risk. Other independent risk factors for SSI after mastectomy plus reconstruction included diabetes, psychoses, obesity, and smoking. For the observed adjusted RR of 0.80 for anti-MSSA prophylactic antibiotics, the E-value was 1.81 for the point estimate and 1.53 for the lower bound. Based on these results, 48 women would need to be treated with anti-MSSA post-discharge prophylactic antibiotics after mastectomy plus reconstruction to prevent one additional woman from developing an SSI.

DISCUSSION

In this analysis of commercially insured women, we found that post-discharge prophylactic antibiotics were used in over 70% of women with immediate reconstruction and in 19% after mastectomy only. Factors associated with utilization after mastectomy only included history of *S. aureus* infection, neoadjuvant chemotherapy, and a noninfectious wound complication during the mastectomy admission. In the reconstruction population the most influential factor associated with utilization of prophylactic post-discharge antibiotics was implant reconstruction, with slightly increased antibiotic use over the study period. In multivariable analyses slightly decreased risk of SSI was found in women who filled a prescription for a prophylactic antibiotic with anti-MSSA activity after both mastectomy only and mastectomy plus reconstruction.

The utilization of continued oral prophylactic antibiotics we report is consistent with the results of our prior multicenter study in which 35% of women after mastectomy only and 85% after mastectomy plus reconstruction were given an antibiotic prescription at discharge in the absence of evidence for infection.[17] The variation in prophylactic antibiotic utilization in our prior study was largely driven by individual surgeons and by study site, rather than by patient factors.[17] In our current study, prolonged prophylactic antibiotic utilization was also likely driven largely by individual surgeons and institutions, since the discriminative ability of the multivariable models to identify patient-level factors associated with post-discharge prophylactic antibiotics use was poor. Since no facility or provider information is available in the MarketScan database, we were unable to directly assess associations with individual providers.

Most prior studies of continued prophylactic antibiotics after mastectomy plus immediate reconstruction showed no decreased risk of SSI, although the single-center studies in the literature and our prior multicenter study were underpowered to address risk of SSI specifically.[11, 17] More recently, two adequately powered studies using administrative claims data showed no association of continued prophylactic antibiotics with decreased SSI risk after mastectomy plus reconstruction.[18, 19]

Only two prior studies have evaluated post-discharge prophylactic antibiotic use in the mastectomy only population. The study by Edwards *et al.* is subject to confounding bias as surgery was performed by two surgeons, with one utilizing only preoperative antibiotics and the other continuing antibiotics post-discharge.[10] The other study was our prior multicenter study in which we did not find evidence for benefit of post-discharge

prophylactic antibiotics, although it was underpowered to detect an association with SSI (power = 0.28).[17]

In contrast to prior studies, our current study focused on SSI risk associated with specific categories of prophylactic antibiotics. Although MRSA is a relatively uncommon etiology in post-mastectomy breast infections, the majority of organisms isolated from breast infections, particularly after implant reconstruction, are resistant to first-generation cephalosporins and similar narrow-spectrum anti-MSSA antibiotics.[34, 35] In a recent study comparing the microbiology of SSIs after mastectomy with tissue expander reconstruction in women treated with post-discharge prophylactic antibiotics vs only perioperative antibiotics, Monroig *et al.* found no difference in the incidence of SSI, but more diverse etiology in women treated with post-discharge prophylaxis, including more Gram-negative bacteria and fewer *S. aureus* infections.[36] The authors caution that while there is no evidence for benefit of prolonged post-discharge antibiotics, prolonged oral therapy may be associated with harm due to selection of antibiotic resistant bacteria.[36]

Interestingly, we found decreased SSI risk among women who filled a prescription for antibiotics with anti-MSSA activity, but not with anti-MRSA antibiotics or quinolones. In the mastectomy plus reconstruction population we had > 80% power to detect a 25% decrease in SSI risk for all three categories of post-discharge antibiotics, but we lacked sufficient power in the mastectomy only population (power = 0.21 for anti-MRSA antibiotics and 0.17 for quinolones). Although in multivariable analysis anti-MSSA antibiotics were associated with decreased risk of SSI compared to no post-discharge antibiotics, the lower bounds of the E-value were only 1.11 (mastectomy only) and 1.53 (mastectomy plus reconstruction). The E-value represents the relative risk of an unmeasured confounder that would explain away the treatment-outcome result (i.e., reduced risk of SSI associated with anti-MSSA post-discharge antibiotics). The lower bound of the E-value represents the relative risk of an unmeasured confounder that would negate the significance of the adjusted treatment-outcome result. For mastectomy only an unmeasured confounder with a RR of 1.11 would alter the findings such that anti-MSSA prophylactic antibiotic therapy would no longer be significantly associated with decreased SSI risk. Similarly, an unmeasured confounder with a RR of 1.53 would result in a non-significant association of anti-MSSA antibiotics with decreased SSI risk after mastectomy plus reconstruction. Given the inability to identify some important predictors of SSI (e.g., glucose control), or accurately capture others (e.g., obesity, smoking) with claims data, such unmeasured confounders may exist which could account for the slightly decreased risk of SSI associated with anti-MSSA antibiotics.

We found that 107 women would need to be treated with an anti-MSSA antibiotic post-discharge to prevent one additional SSI after mastectomy only, while 48 women would need to be treated after mastectomy plus reconstruction to prevent one additional infection. The relatively small benefit associated with post-discharge anti-MSSA antibiotics needs to be balanced against the harms of unnecessary antibiotic utilization, given the substantial numbers needed to be treated. Antibiotics with anti-MSSA activity are associated with moderate risk of *C. difficile* infection,[37] and other adverse events, ranging from more

common minor (e.g., rash) to more rare serious complications (e.g., anaphylaxis, acute renal failure).[38]

Limitations of our study include the potential for both unmeasured confounding and incomplete capture of some risk factors, as described above. We attempted to mitigate the incomplete capture of obesity and smoking by requiring only a single diagnosis code, which increases the sensitivity of identification of these conditions.[39] When possible we used medications in addition to diagnosis codes to improve the sensitivity of detection of other important risk factors.[39–42] Other variables, such as prior *S aureus* infection, might be underestimated by coding data. There was a possibility of misclassification of therapeutic antibiotics as prophylactic if an infectious diagnosis was not recorded at the time of the prescription. However, we used strict criteria including exclusion for a variety of perioperative infections within 30 days of surgery to mitigate this misclassification. Lastly, our study was limited to non-elderly privately insured women, so may not be generalizable to the uninsured, Medicaid, or Medicare populations.

Advantages of our study include the very large size of the cohort, which resulted in more than 90% power to detect a 25% difference in SSI incidence with use of post-discharge prophylactic antibiotics. We used a detailed methodologic approach combining careful patient selection and follow-up with rigorous statistical analyses to determine the effect of post-discharge prophylactic antibiotics on risk of SSI. We studied the use and impact of specific categories of commonly used oral antibiotics, which allowed us to separate the effects of antibiotics based on microbial activity.

We used a large commercial claims database to determine factors associated with use of post-discharge prophylactic antibiotics in non-elderly women after mastectomy only and mastectomy plus immediate reconstruction and 90-day SSI risk. Use of post-discharge antibiotics did not appear to be driven by patient risk factors, but rather likely by physician preference. Antibiotics with anti-MSSA activity were associated with a small but significantly decreased risk of 90-day SSI after both mastectomy only and mastectomy plus reconstruction. The small apparent benefit of post-discharge oral antibiotics should be balanced with the risks associated with over-use of antibiotics, particularly given the relatively large number of women who would need to be treated in order to prevent one infection.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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CONFLICTS OF INTEREST

MAO reports consultant work and grant funding from Pfizer outside the submitted manuscript. VJF reports her spouse is the Chief Clinical Officer at Cigna Corporation. DKW reports consultant work with Centene Corp., PDI Inc., Pursuit Vascular, and Homburg & Partner and is a sub-investigator for a Pfizer-sponsored study for work outside the submitted manuscript. No other authors report competing interests.

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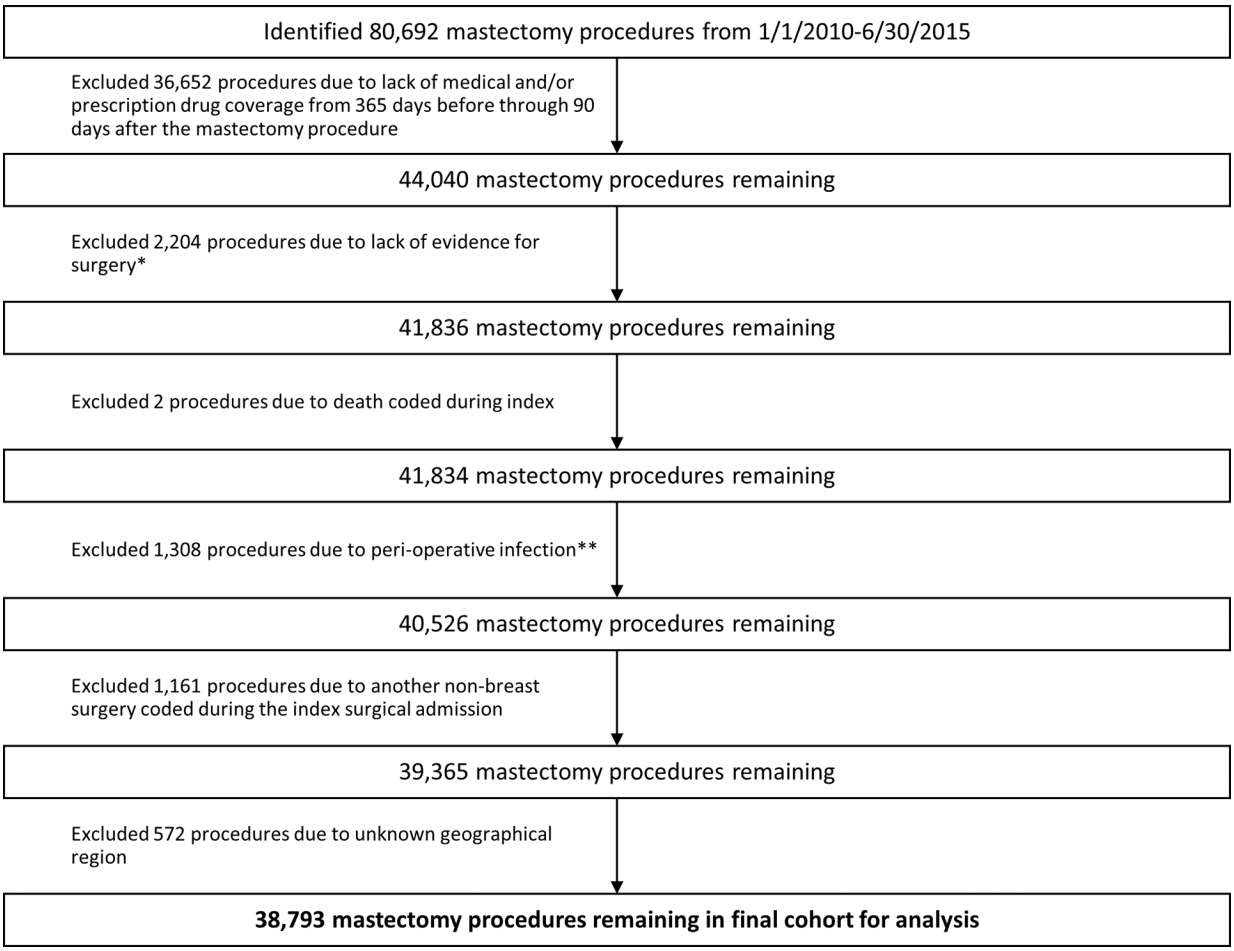

Figure 1.

Flow Diagram With Exclusion Criteria to Establish Population of Mastectomy Procedures among Women Aged 18–64 Years From January 2010 Through June 2015 in the MarketScan Commercial Database

* Excluded procedures lacking claims from both a surgeon and facility, if also without supporting evidence for surgery (i.e., operating room services, pathology, breast reconstruction, anesthesiology claims), procedures only coded by a provider in outpatient surgery encounter if no facility claims within +/− 1 day, and procedures without evidence of performance in a hospital (inpatient or outpatient surgery) or ambulatory surgical center.

** Excluded for major infection coded in the 30 days prior through 2 days post-discharge and minor infection coded in the 14 days prior through 2 days post-discharge.

Table 1.

Characteristics of the Commercially Insured Mastectomy Population

Characteristic	Mastectomy only n (%) N = 13,975	Mastectomy with immediate reconstruction n (%) N = 24,818
Age in years, median (interquartile range)	55 (48, 60)	50 (43, 56)
Patient residence, region		
Northeast	1,659 (11.9%)	4,628 (18.7%)
North Central	3,421 (24.5%)	5,745 (23.2%)
South	5,998 (42.9%)	9,865 (39.8%)
West	2,897 (20.7%)	4,580 (18.5%)
Rural residence[a]	2,575 (18.4%)	2,405 (9.7%)
Implant reconstruction	N/A	21,755 (87.7%)
Inpatient mastectomy	5,233 (37.5%)	16,282 (65.6%)
Modified radical mastectomy	7,101 (50.8%)	7,954 (32.1%)
Reason for mastectomy		
Invasive Cancer	12,014 (86.0%)	18,858 (76.0%)
Ductal carcinoma in situ	1,404 (10.1%)	4,066 (16.4%)
Prophylactic	557 (4.0%)	1,894 (7.6%)
Post-discharge prophylactic antibiotic use		
Anti-methicillin-resistant *Staphylococcus aureus*	461 (3.3%)	3,482 (14.0%)
Anti-methicillin-susceptible *Staphylococcus aureus*	1,890 (13.5%)	12,954 (52.2%)
Quinolone	337 (2.4%)	1,371 (5.5%)
No antibiotic use	11,287 (80.8%)	7,011 (28.2%)
Surgical site infection within 90 days of procedure	490 (3.5%)	2,173 (8.8%)
Year of surgery		
2010	2,976 (21.3%)	4,056 (16.3%)
2011	2,698 (19.3%)	4,399 (17.7%)
2012	2,947 (21.1%)	5,166 (20.8%)
2013	2,327 (16.7%)	4,435 (17.9%)
2014	2,125 (15.2%)	4,676 (18.8%)
2015	902 (6.4%)	2,086 (8.4%)

[a]Rural residence was defined as residing outside of a metropolitan statistical area.

Table 2.

Patient and Operative Factors Independently Associated with Receipt of Post-discharge Prophylactic Oral Antibiotics after Mastectomy Only in Multivariable Analysis

Variable	RR (95% CI)[a]
Demographics and comorbidities	
Rural residence[b]	0.90 (0.83, 0.99)
Diabetes	1.14 (1.04, 1.26)
Staphylococcus aureus infection in prior year	2.04 (1.48, 2.81)
Neoadjuvant chemotherapy prior 60 days	1.11 (1.02, 1.20)
Other neurological disorders	0.66 (0.47, 0.95)
Operative factors	
Surgical complication during mastectomy admission (hemorrhage, hematoma, dehiscence)	1.39 (1.17, 1.67)

[a]Also adjusted for age as a continuous variable. Variables entered into model, but not retained: fluid and electrolyte disorders, psychoses.

[b]Rural residence was defined as residing outside of a metropolitan statistical area.

C-statistic = 0.54

Abbreviations. CI, confidence interval; RR, relative risk.

Table 3.

Patient and Operative Factors Independently Associated with Receipt of Post-discharge Prophylactic Oral Antibiotics after Mastectomy plus Immediate Reconstruction in Multivariable Analysis

Variable	RR (95% CI)[a]
Demographics and comorbidities	
Patient residence, region	
Northeast	1.09 (1.07, 1.12)
North central	Reference
South	0.98 (0.96, 1.00)
West	1.04 (1.02, 1.07)
Rural residence[b]	0.96 (0.93, 0.99)
Depression	0.96 (0.93, 1.00)
Other neurological disorders	0.91 (0.84, 0.98)
Psychoses	1.04 (1.00, 1.08)
Pulmonary circulation disease	0.77 (0.62, 0.95)
Smoking	0.97 (0.95, 1.00)
Valvular disease	1.05 (1.00, 1.11)
Operative factors	
Implant reconstruction	1.44 (1.39, 1.49)
Year of surgery	
2010	Reference
2011	1.04 (1.02, 1.07)
2012	1.03 (1.00, 1.06)
2013	1.06 (1.04, 1.09)
2014	1.09 (1.06, 1.11)
2015	1.09 (1.06, 1.13)

[a]Also adjusted for age using a spline (3 knots). Variables entered into model, but not retained: smoking proxy, obesity, *Staphylococcus aureus* infection prior year, neoadjuvant chemotherapy prior 60 days, anemia prior 30 days, chronic blood loss anemia, hypertension

[b]Rural residence was defined as residing outside of a metropolitan statistical area.

C-statistic = 0.61

Abbreviations. CI, confidence interval; RR, relative risk.

Table 4.

Patient and Operative Factors Independently Associated with Surgical Site Infection after Mastectomy Only in Multivariable Analysis

Variable	RR (95% CI)[a]
Post-discharge prophylactic antibiotic category	
Anti-methicillin-resistant *Staphylococcus aureus*	0.98 (0.61, 1.56)
Anti-methicillin-susceptible *Staphylococcus aureus*	0.74 (0.55, 0.99)
Quinolone	1.41 (0.91, 2.20)
No antibiotic use	Reference
Demographics and comorbidities	
Rural residence[b]	1.23 (1.00, 1.52)
Depression	1.33 (0.96, 1.84)
Diabetes	1.85 (1.50, 2.28)
Hypertension	1.20 (0.98, 1.46)
Hypothyroidism	1.32 (1.02, 1.73)
Obesity	1.27 (1.02, 1.59)
Psychoses	2.01 (1.43, 2.81)
Smoking	1.23 (0.98, 1.55)
Smoking proxy	1.39 (0.97, 1.99)
Weight loss	1.77 (1.03, 3.05)

[a]Also adjusted for age using a spline (3 knots). Variables entered into model, but not retained: anemia prior 30 days, index complication, rheumatoid arthritis/collagen vascular disease, year of surgery

[b]Rural residence was defined as residing outside of a metropolitan statistical area.

C-statistic = 0.63

Abbreviations. CI, confidence interval; RR, relative risk.

Table 5.

Patient and Operative Factors Independently Associated with Surgical Site Infection after Mastectomy with Immediate Reconstruction in Multivariable Analysis

Variable	RR (95% CI)[a]
Post-discharge prophylactic antibiotic category	
Anti-methicillin-resistant *Staphylococcus aureus*	0.90 (0.80, 1.03)
Anti-methicillin-susceptible *Staphylococcus aureus*	0.80 (0.73, 0.88)
Quinolone	1.08 (0.91, 1.27)
No antibiotic use	Reference
Demographics and comorbidities	
Rural residence[b]	1.16 (1.03, 1.32)
Depression	1.13 (0.98, 1.31)
Diabetes	1.31 (1.15, 1.51)
Hypertension	1.20 (1.08, 1.32)
Obesity	1.63 (1.46, 1.83)
Psychoses	1.45 (1.22, 1.74)
Rheumatoid arthritis/collagen vascular disease	1.26 (0.97, 1.64)
Smoking	1.29 (1.15, 1.43)
Smoking proxy	1.33 (1.04, 1.71)
Operative factors	
Implant reconstruction	1.22 (1.07, 1.38)
Modified radical mastectomy	1.13 (1.04, 1.23)
Year of surgery	
2010	reference
2011	0.88 (0.77, 1.00)
2012	0.84 (0.74, 0.96)
2013	0.91 (0.80, 1.04)
2014	0.87 (0.76, 0.99)
2015	0.78 (0.66, 0.93)

[*] Also adjusted for age using a spline (5 knots). Variables entered into model, but not retained: index complication, patient residence region, hypothyroidism, liver disease, other neurological disorders, peripheral vascular disease, pulmonary circulation disease, valvular disease

[b] Rural residence was defined as residing outside of a metropolitan statistical area.

C-statistic = 0.60

Abbreviations. CI, confidence interval; RR, relative risk.