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### Surgeon Choice in the Use of Post-Discharge Antibiotics for Prophylaxis Following Mastectomy With and Without Breast Reconstruction

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#### Abstract

Multiple guidelines recommend discontinuation of prophylactic antibiotics < 24 hours after surgery. In a multicenter, retrospective cohort of 2,954 mastectomy patients  $\pm$  immediate breast reconstruction, we found that utilization of prophylactic-post discharge antibiotics varied dramatically at the surgeon-level among general surgeons, and was virtually universal among plastic surgeons.

The Centers for Disease Control and Prevention guidelines for prevention of surgical site infections (SSIs) recommend discontinuation of prophylactic antibiotics in clean surgeries after the surgical incision is closed.<sup>1</sup> In contrast, the American Society of Plastic Surgeons guidelines for implant breast reconstruction recommend that prolonged antibiotic

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Conflicts of interest

MAO reports consultant work with Pfizer and grant funding through Pfizer, Merck, and Sanofi Pasteur for work 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, Homburg & Partner, and Carefusion/BD and is a sub-investigator for a Pfizer-sponsored study for work outside the submitted manuscript. JHH reports that the present work was conducted during her affiliation with the University of Pennsylvania. JHH is currently an employee of, and holds shares in, the GSK group of companies. No other authors report conflicts of interest relevant to this article.

prophylaxis when surgical drains are present be left to surgeon preference.<sup>2</sup> In practice, postdischarge prophylactic antibiotic use is common after mastectomy with reconstruction.<sup>3,4</sup>

We determined the prevalence of post-discharge prophylactic antibiotic use and patient, operative, and surgeon factors associated with use among women undergoing mastectomy with and without immediate breast reconstruction at six hospitals from three academically affiliated sites.

#### METHODS

We conducted a retrospective cohort study using electronic health record (EHR), manual record review, and billing data from 6 hospitals at 3 U.S. sites. Site 1 included one academic and one community hospital, site 2 one academic hospital and site 3 one academic and two community hospitals.

We identified mastectomy admissions among women aged 18 years from 7/1/2011 to 6/30/2015 using International Classification of Diseases, 9<sup>th</sup> Revision, Clinical Modification (ICD-9-CM) procedure codes 85.33–85.36 and 85.41–85.48. Mastectomy was verified using physician Current Procedural Terminology coding for mastectomy (19303–19307, one site) and by review of surgeon description and anesthesia duration (two sites).

We excluded admissions likely to have antibiotics prescribed at discharge for therapeutic indications, based on ICD-9-CM diagnosis codes during the mastectomy admission (e.g, SSI, pneumonia) or intravenous antibiotic at discharge (Appendix Table 1). We also excluded admissions lacking ICD-9-CM diagnosis codes, with length of stay (LOS) >90 days, or ending in death.

Prophylactic antibiotics were defined as oral antibiotics prescribed at surgical discharge in the absence of an infectious diagnosis (Appendix Table 2). If the patient was admitted on oral antibiotic therapy and the same antibiotic was prescribed at discharge, it was not considered prophylactic.

Factors associated with prophylactic antibiotic use included patient (e.g., comorbidities), operative, and surgeon factors with clinical plausibility for antibiotic use and/or SSI risk (Appendix Table 3). Comorbidities were defined by ICD-9-CM diagnosis codes<sup>5</sup> and operative factors by diagnosis and procedure codes (Appendix Table 4). Surgeon specialty was determined using the institution and Medicare physician directories. Low, medium, and high volume surgeons were defined by the annual number of cases per surgeon, per specialty (Figure 1).

Potential SSIs were identified using diagnosis and procedure codes suggestive of infection for encounters within 90 days after mastectomy (Appendix Table 5), and verified using the 2015 National Healthcare Safety Network criteria.<sup>6</sup>

#### **Statistical Analyses:**

Univariate analyses were performed using Chi-square and Mann-Whitney U tests, as appropriate. We used a modified Poisson regression model to estimate adjusted relative risks

of prophylactic antibiotic utilization with backward selection using p < 0.1 in univariate analysis for entry and p < 0.05 for retention. REDCap and SAS v9.4 (SAS Institute Inc., Cary, NC) were used for data management and analysis. The study was approved by the local Human Research Protection Offices.

#### RESULTS

We initially identified 3,164 mastectomy admissions. Thirty-one admissions were excluded due to infection coded during admission, 157 with no evidence for mastectomy, 18 due to conflicting information regarding breast reconstruction, 3 with no information on discharge antibiotics, and one due to intravenous antibiotics at discharge. The final cohort included 2,954 mastectomy admissions: 1,546 (52.3%) at site 1, 846 (28.6%) at site 2, and 562 (19.0%) at site 3.

Prophylactic antibiotics were prescribed after 85.3% and 36.2% of mastectomy admissions with and without breast reconstruction, respectively. The utilization of prophylactic antibiotics and type of antibiotics prescribed varied by site (Table 1).

Prophylactic discharge antibiotic prescribing was more common after procedures performed by plastic (85.9%) versus general surgeons (27.7%, *P*<0.001; Figure 1). Practice variation in prescribing was evident, with two high-volume general surgeons using post-discharge prophylactic antibiotics in >85% of their cases (Figure 1). In contrast, 11 of 12 medium to high volume plastic surgeons prescribed post-discharge prophylactic antibiotics in >75% of their cases.

Overall, 103 (3.5%) SSIs were identified; 21 (2.0%) after mastectomy alone and 82 (4.3%) after mastectomy with reconstruction. Seventy-four SSIs (72%) were classified as deep/ organ-space infection. Seventy-six of 80 SSIs were culture positive, including 5 patients with MRSA. Post-discharge prophylactic antibiotic use was not associated with SSI following mastectomy alone (7/373 (1.9%) SSIs with versus 14/657 (2.1%) SSI without post discharge antibiotics, p = 0.781) or mastectomy with reconstruction (69/1,641 (4.2%) SSI with versus 13/283 (4.6%) SSI without post discharge antibiotics, p = 0.765).

In multivariable analysis, study site (relative risk [RR], 1.40; 95% confidence interval [CI], 1.30–1.51 site 2; RR, 0.62; 95% CI, 0.52–0.73 site 3 versus site 1), LOS (RR, 0.88; 95% CI, 0.83–0.93 for 3–4 days; RR, 0.74; 95% CI, 0.68–0.80 for 5–6 days; RR, 0.55; 95% CI, 0.45–0.66 for 7 days versus 1–2 days), intraoperative antibiotic type (RR, 0.75; 95% CI, 0.60–0.94 any vancomycin; RR, 1.42; 95% CI, 1.16–1.75 single antibiotic besides vancomycin, cefazolin, or clindamycin or >1 antibiotic; RR, 0.56; 95% CI, 0.35–0.89 no antibiotic documented, versus cefazolin-only or clindamycin-only), and neoadjuvant chemotherapy (RR 1.05; 95% CI 1.00–1.09) were associated with prophylactic post-discharge antibiotic use among mastectomy with reconstruction patients. Among mastectomy only patients, LOS >2 days (RR, 1.36; 95% CI, 1.15–1.62) and surgery 90 minutes (RR, 1.51; 95% CI, 1.23–1.86) were the only factors associated with prophylactic post-discharge antibiotics in multivariable analysis.

#### DISCUSSION

We demonstrated that post-discharge prophylactic antibiotic utilization was 36.2% among mastectomy without reconstruction and 85.3% for mastectomy with reconstruction patients, consistent with prior plastic surgeon surveys.<sup>3,4</sup> Post-discharge prophylactic antibiotic use varied considerably by study site, ranging from 30.4–43.8% after mastectomy alone, and 52.5–95.4% after mastectomy with reconstruction. There was substantial prescribing variation amongst general surgeons; plastic surgeons had consistently high utilization of post discharge prophylactic antibiotics.

Factors associated with post-discharge prophylactic antibiotic use included intraoperative antibiotic type, study site, receipt of neoadjuvant chemotherapy, and short LOS after mastectomy with reconstruction, and longer LOS and surgery duration after mastectomy without reconstruction. Comorbidities (e.g., morbid obesity, smoking, diabetes) known to be associated with SSI risk were not associated with post-discharge antibiotics. We demonstrated variability in the type of antibiotics prescribed by study site. These findings suggest that factors other than underlying comorbidities influenced post-discharge prophylactic antibiotic prescribing practices.

Our study has several limitations. Our study sites may not reflect all community practices, particularly in non-academically affiliated hospitals. We did not have power to detect differences in SSI rates by post-discharge antibiotic use; a larger-scale study to assess SSI rates and adverse events is warranted. Antibiotic prescribing was identified in the EHR, therefore, surgeon rationale could not be determined, and we cannot rule out assessment of patient SSI risk in the decision-making process.

Evidence in the literature is lacking for benefit of post-discharge prophylactic antibiotics after surgery,<sup>2,7</sup> and potential for harm due to unnecessary antibiotic use.<sup>8,9</sup> We showed that prophylactic antibiotics were commonly prescribed after discharge in mastectomy patients with and without reconstruction. Given the variation in discharge antibiotic prescribing by individual physicians, improved communication between infection prevention and surgeons as part of a stewardship intervention to improve antibiotic prescribing is important to prevent the development of antimicrobial resistance and adverse events from unnecessary antibiotic use.<sup>10</sup>

#### **Supplementary Material**

Refer to Web version on PubMed Central for supplementary material.

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Figure 1. Proportion of individual surgeon's mastectomy patients prescribed prophylactic postdischarge antibiotics stratified by surgeon volume and specialty (plastic surgeon [A] versus general surgeon [B]).

The dashed line represents the overall proportion of post-discharge antibiotics among procedures overseen by a plastic and general surgeon, respectively. Plastic and general surgeon annual volume thresholds were based on the distribution of annual volume within the surgeon specialty and are displayed in the x axes of the plots..

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# Table 1.

Proportion of Mastectomy Admissions with Prophylactic Discharge Antibiotics and Top Antibiotic Choices by Immediate Reconstruction and Study Site

	Mastectomy v	vith reconstru	iction			Mastectomy	vithout reco	onstruction		
	Total	Site 1	Site 2	Site 3	$P^{I}$	Total	Site 1	Site 2	Site 3	$P^{I}$
Mastectomy admissions, n	1,924	1,009	732	183		1,030	537	114	379	
Prophylactic discharge antibiotics, n (%)	1,641 (85.3)	847 (83.9)	698 (95.4)	96 (52.5)	<0.001	373 (36.2)	163 (30.4)	44 (38.6)	166 (43.8)	<0.001
Top 4 prophylactic discharge antibiotics among mastectomy admissions, n (%) $^2$					<0.001					<0.001
Cefadroxil	552 (33.2)	2 (0.2)	535 (76.2)	15 (14.4)		33 (8.7)	0 (0.0)	33 (73.3)	0 (0.0)	
Cephalexin	287 (17.3)	242 (28.3)	8 (1.1)	37 (35.6)		246 (65.1)	114 (69.5)	2 (4.4)	130 (76.9)	
Clindamycin	133 (8.0)	32 (3.7)	90 (12.8)	11 (10.6)		27 (7.1)	9 (5.5)	4 (8.9)	14 (8.3)	
Trimethoprim/ sulfamethoxazole	644 (38.8)	554 (64.8)	54 (7.7)	36 (34.6)		60 (15.9)	36 (22.0)	3 (6.7)	21 (12.4)	
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Pper chi-square test.

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<sup>2</sup> A total of 1,661 antibiotics were prescribed at discharge without evidence of infection following 1,641 mastectomy with reconstruction admissions with discharge antibiotics; a total of 378 antibiotics were prescribed at discharge without evidence of infection following 373 mastectomy without reconstruction admissions with discharge antibiotics. Column percentages do not add up to 100% as only utilization of the top 4 antibiotics are shown.