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Treatment and Prevention of Hospital Infections (D Vilar-Compte, Section Editor)

Surveillance and Prevention of Surgical Site Infections in Breast Oncologic Surgery with Immediate Reconstruction

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Opinion statement

Surgical site infection (SSI) after immediate breast reconstruction is much more common than would be expected after a clean surgical procedure. Although the SSI rates reported in individual studies are quite variable, there are no obvious explanations for the variation in infection rates between institutions. The microbiology of these SSIs is unusual, with higher proportions of infections caused by atypical *Mycobacterium* species and Gram-negative bacilli than would be expected for this anatomic site. In an effort to prevent SSIs, many surgeons use a variety of different practices including irrigation and soaking of implants with antibiotic solutions and prolonged duration of prophylactic antibiotics, although the literature to support these practices is very sparse. In particular, prolonged use of antibiotics post-discharge is concerning due to the potential for harm, including increased risk of *Clostridium difficile* infection, development of antibiotic-resistant organisms, and drug-related allergic reactions. With higher rates of mastectomy and breast implant reconstruction in women with early-stage breast cancer, including greater utilization of reconstruction in higher-risk individuals, the number of women suffering from

infection after oncologic reconstruction will likely continue to increase. It is imperative that more research be done to identify modifiable factors associated with increased risk of infection. It is also essential that larger studies with rigorous study designs be performed to identify optimal strategies to decrease the risk of SSI in this vulnerable population.

Introduction

An estimated 247,000 women were diagnosed with *in situ* or invasive breast cancer in the USA in 2016, with over 90% of cases categorized as localized or regional disease [1]. In the last decade, women with *in situ* or locally invasive disease, who were likely eligible for breast conservation surgery, increasingly had mastectomy performed [2•, 3]. This translates into approximately 95,000 mastectomy procedures per year performed in women with breast cancer in the USA. Concomitant with increased utilization of mastectomy, the proportion of women choosing to undergo immediate or delayed breast reconstruction increased at least 1.6-fold in the USA and over twofold in England from 2005 to 2014 [4, 5, 6•]. The increase in immediate breast reconstruction is primarily associated with increased use of prosthetic-based reconstruction [4, 7] and increased use of reconstruction in higher-risk women [8••].

One concern with increasing use of immediate reconstruction is the potential for higher incidence of surgical site infection (SSI). Several studies have reported increased risk of SSI associated with breast reconstruction; however, reported SSI rates vary widely depending on the definition used for infection, surveillance method to identify infections, and length of follow-up after operation. Even less information is available to compare the risk of SSI after prosthetic versus autologous reconstruction. Since reconstruction is performed primarily in younger women, the impact of SSI can be long-lasting, with increased hospital length of stay and hospital costs, additional surgical procedures, lower quality of life, and lower satisfaction with the surgical outcome in women with SSI compared to women without infection [9–11].

Incidence of surgical site infection after mastectomy with and without immediate reconstruction

The majority of breast procedures are considered clean operations according to the National Healthcare Safety Network (NHSN), defined as no inflammation encountered during surgery and no exposure to mucous membranes. As such, clean operations have the lowest expected incidence of SSI, typically on the order of 1–2% in the prophylactic antibiotic era. Although this is generally true, investigators have noted that SSI rates within an individual wound class can be highly variable, depending on specific operative and patient characteristics [12]. Mastectomy without immediate reconstruction appears to fit into this category, with SSI rates reported in the past decade from individual studies higher than would be expected for a clean procedure, ranging from approximately 3–18% (Table 1). SSI rates reported from the USA and Japan are lower (2.9–7.7%), while higher rates have been reported from limited resource countries. We speculate that the higher rate of SSI after mastectomy compared to other breast operations, such as reduction mammoplasty, may be due to the longer operative time and large dead space in which lymphatic or serous fluid can accumulate, providing a rich source of nutrients for contaminating bacteria.

As shown in Table 1, numerous investigators have reported SSI rates after mastectomy with immediate implant reconstruction in the surgical literature.

Table 1. Variation in reported SSI rates for mastectomy without reconstruction, mastectomy with implant reconstruction, and mastectomy with autologous flap reconstruction, 2007–2017

Reference	Country	Definition used for SSI	Time period for surveillance	No. SSI/no. persons (%)	No. SSI/no. breasts (%)
Mastectomy without immediate reconstruction					
Felippe (2007) [13]	Brazil	NHSN	30 days	48/272 (17.6)	
Olsen (2008) [9]	US	NHSN	1 year	13/296 (4.4)	
Ashraf (2009) [14]	India	NHSN	30 days	165/927 (17.8)	
Cabaluna (2013) [15]	Philippines	NHSN	30 days	36/254 (14.2)	
Edwards (2014) [16]	US	NHSN	ND	31/425 (7.3)	
Ota (2014) [17]	Japan	Redness, fever, pain, or tenderness	ND	9/308 (2.9)	
Olsen (2015) [18]	US	ICD9 codes	180 days	395/7860 (5.0)	
Carter (2016) [19]	US	ICD9 codes	ND	178/2304 (7.7)	
Mastectomy + implant reconstruction (minimum 250 patients undergoing operation)					
Halvorson (2007) [20] 100% TE	US	Infection plus tissue expander removal	≥1 year	39/2539 (1.5)	
Francis (2009) [21] 100% TE	US	Clinical signs of infection	1 year		49/341 (14.4)
Berry (2010) [22] 100% TE	US	ND	ND		ND/733 (10.1)
Delgado (2010) [23] 100% direct-to-implant	Spain	Infection plus implant removal	ND		4/400 (1.0)
Liu (2011) [24] Most were TE	US	Infection plus IV antibiotics or implant removal	3 months		23/470 (4.9)
Seth (2011) [25][a]	US	Infection plus IV antibiotics or hospital readmission	ND		63/1217 (5.2)
Salzberg (2011) [26] 100% direct-to-implant	US	Infection plus IV antibiotics	Minimum 0.3 months, mean 29 months	1/260 (0.4%)	
Weichman (2012) [27] 100% TE	US	Infection plus antibiotics	ND		74/628 (11.8)
Peled (2012) [28] 100% TE	US	Infection plus antibiotics	Mean 26 months		86/450 (19.1)
Spear (2012) [29] 100% TE	US	ND	ND		23/428 (5.4)

Table 1. (Continued)

Reference	Country	Definition used for SSI	Time period for surveillance	No. SSI/no. persons (%)	No. SSI/no. breasts (%)
Lankiewicz (2012) [30][b] 98% TE	US	NHSN	1 year	54/327 (16.5)	
Butterfield (2013) [31] 95% TE	US	Infection plus antibiotics or implant removal	Minimum 3 months		23/440 (5.2)
Kato (2013) [32] 100% TE	Japan	Infection plus positive culture	1 year	23/539 (4.3)	
Seth (2013) [33][c] 100% TE	US	Infection plus IV antibiotics or surgery	ND		26/369 (7.0)
Reish (2013) [34][a]	US	Erythema plus IV antibiotics or implant removal	At least 1 year	94/1241 (7.6)	
Liu (2014) [35] Most TE	US	NHSN	Median 152 days	43/446 (9.6)	
Frey (2015) [36] 86% TE	US	Infection plus antibiotics	ND		55/1019 (5.4)
Susarla (2015) [37] 71% TE	US	Infection plus antibiotics or surgical treatment	ND		34/582 (5.8)
Gfrerer (2015) [38•] 60% direct-to-implant	US	Infection requiring reoperation	ND		ND/3142 (2.9)
Weichman (2015) [39] 100% TE	US	Infection plus antibiotics	3 months		82/1211 (6.8)
Lovecchio (2015) [40][c] 100% TE	US	Infection plus IV antibiotics	ND		67/1639 (4.1)
Olsen (2015) [18][a]	US	ICD9 codes	180 days	848/8217 (10.3)	
McCullough (2016) [41] 100% TE	US	NHSN	ND	48/378 (12.7)	
Palaia (2015) [42] 100% TE	US	ND	ND		59/603 (9.8)
Woo (2016) [43] 100% TE	Korea	ND	ND		8/397 (2.0)
Viola (2016) [44••] 100% TE	US	NHSN deep infection	1 year	378/3082 (12.3)	
Abedi (2016) [45] 87% TE	Canada	ND	Median 687 days		65/606 (10.7)
Dolen (2016) [46][b] 100% TE	US	Infection plus implant removal	Median 354 days		85/1347 (6.3)

Table 1. (Continued)

Reference	Country	Definition used for SSI	Time period for surveillance	No. SSI/no. persons (%)	No. SSI/no. breasts (%)
Chen (2016) [47] 95% TE	Taiwan	Infection plus tissue expander removal or positive culture	2 years		29/569 (5.1)
Sinha (2017) [48••] 90% TE	US	Infection plus antibiotics, hospitalization, or surgical treatment	1 year	114/1024 (11.1)	
Hunsicker (2017) [49] 100% direct-to-implant	US	Infection plus antibiotics	1 year		48/1584 (3.0)
Mastectomy + autologous flap reconstruction (minimum 100 patients undergoing operation)					
Meretoja (2007) [50] 100% TRAM	Finland	ND	ND	5/151 (3.3)	
Kim (2009) [51] 100% pedicled TRAM	Korea	ND	Minimum 19 months	4/500 (0.8)	
Berry (2010) [22][a]	US	ND	ND		ND/463 (10.5)
Crosby (2011) [52] 59% TRAM, 32% DIEP, 8% SIEA	US	Erythema plus IV antibiotics	Mean 13.2 months		5/284 (1.8)
Llewellyn-Bennett (2012) [53][d] 100% LD	UK	ND	3 months	13/106 (12.3)	
Vargas (2015) [54] 94% DIEP	US	ND	Minimum 5.3 months		55/730 (7.5)
Olsen (2015) [18][a]	US	ICD9 codes	180 days	207/1942 (10.7)	
Abedi (2016) [45] 79% TRAM, 21% DIEP	Canada	ND	Median 594 days		33/395 (8.4)

TE tissue expander; *DIEP* deep inferior epigastric perforator (free flap); *ICD9* International Classification of Diseases, 9th Edition, Clinical Modification; *IV* intravenous; *NHSN* National Healthcare Safety Network; *ND* not described; *TRAM* transverse rectus abdominis myocutaneous flap (pedicled or free); *SIEA* superficial inferior epigastric artery; *LD* latissimus dorsi; *UK* United Kingdom; *US* United States

[a]Did not give breakdown of type of implant or autologous flap reconstructions

[b]Partially overlapping in time period and patient populations, different definitions for SSI

[c]Overlapping patients, but different definitions for SSI

[d]More than 95% were immediate reconstructions

Most often, tissue expanders are used for immediate reconstruction, with subsequent second-stage reconstruction occurring 3–6 months later. More recently, some surgeons have performed direct-to-implant single-stage reconstruction without placement of a tissue expander. As shown in Table 1, the reported SSI rates after immediate implant reconstruction vary dramatically, with some reporting rates lower than for mastectomy without reconstruction (<2%), and others reporting rates >10%. The reason for the wide variation in SSI rates is unknown, but contributing factors may be the variation in definitions used for SSI, aggressiveness of surveillance, and duration of follow-up for infection. In addition, reporting of SSI rates per breast rather than per person makes it difficult to compare many of the results, particularly when a large proportion of the procedures are bilateral operations, which have increased over time [5]. Although the infection rates shown in Table 1 for studies that included only or primarily direct-to-implant reconstruction appear low compared to many of the studies involving tissue expander reconstruction, direct comparison of SSI rates between the two types of implant reconstruction was only performed in two studies, with differing results. Gfrerer [38•] found increased risk of SSI whereas Susarla [37] found no difference in infection rates associated with tissue expander compared to direct-to-implant reconstruction.

Many investigators have reported SSI rates after mastectomy with autologous flap reconstruction, although the majority of these studies are very small (<100 patients) resulting in unstable SSI rates. The studies summarized in Table 1 were restricted to larger series with a minimum of 100 patients. Similar to the findings with immediate implant reconstruction, the reported SSI rates range from <1 to >10%, with no clear reasons for the wide variation.

The American College of Surgeons National Surgical Quality Improvement Program (NSQIP) data has also been used by many investigators to study 30-day SSI rates after mastectomy. Using the 2005–2012 NSQIP data, Butz compared 30-day SSI (superficial or deep incisional) rates in women who underwent mastectomy-only compared to immediate reconstruction (implant or autologous). They reported the same 2.9% SSI rate after both mastectomy-only and mastectomy plus reconstruction in younger women, and slightly higher SSI rates in women aged 65 years and older undergoing immediate reconstruction compared to mastectomy-only (3.6 versus 3.1%) [55]. Most recently, the SSI rate after mastectomy with immediate tissue expander reconstruction reported using the NSQIP database was 3.4% [56, 57]. The SSI rates after immediate autologous reconstruction in the NSQIP database vary depending on the type of flap reconstruction, ranging from 2.8% after pedicled latissimus dorsi (with or without concurrent implant), to 5.5% after microvascular free flap, and 6.0% after pedicled transverse rectus abdominis myocutaneous (TRAM) flap [57]. Silva and colleagues compared the SSI rates after immediate unilateral and bilateral implant versus autologous reconstruction using the 2005–2013 database, and found higher rates after bilateral versus unilateral surgery for both implant (3.6 versus 3.3%, respectively) and autologous reconstruction (5.2 versus 4.3%, respectively) [58].

The SSI rates reported from the NSQIP data are clearly low compared to the majority of studies in the surgical literature, most likely due to the restricted 30-day surveillance for complications in NSQIP. In a cohort of women undergoing mastectomy with immediate implant reconstruction, we found that 48% of SSIs had onset >30 days after operation [30]. Similarly, Weichman [59] and

Chidester [60] reported mean times to SSI of 31 and 35 days, respectively, after implant reconstruction. In a comprehensive analysis of infections after immediate tissue expander reconstruction over a 10-year period, Viola and colleagues found that the median time to SSI was 47 days, with only 30% of the total SSIs identified in the first 30 days after operation [44••]. In our study, which followed patients for 180 days using private insurer claims data, we found that only about one half of SSIs after immediate reconstruction were identified within 30 days [18]. In a recent study reporting results from a multicenter cohort of mastectomy reconstruction patients, 53% of SSIs after direct-to-implant and only 44% of SSIs after tissue expander reconstruction occurred within 30 days after operation [48••]. These results suggest that approximately half of SSIs are missed in studies that restrict surveillance to a short 30-day window after operation, and emphasize the importance of longer follow-up, particularly in patients with implant reconstruction.

Risk factors for SSI after breast surgery

A variety of risk factors have been identified for SSI across reconstructive approaches (including no reconstruction). Risk factors identified repeatedly in multivariate analyses using institutional data or the most recent NSQIP data include obesity or increased body mass index (BMI) [38•, 61–69, 70•, 71, 72], larger breast size [21, 47, 66], diabetes [32, 61, 68, 69, 72, 73] or hyperglycemia [74], smoking [16, 42, 61, 67–69, 72, 73, 75–78], heavy alcohol use [61, 79], older age [16, 62, 74, 78], higher ASA score [57, 69, 79], history of radiotherapy [21, 42, 64, 77], duration of operation (mastectomy-only) [16, 62, 69], bilateral operation [21, 68], and drain duration [47, 80]. In studies that included all operations (with and without immediate reconstruction), implant [68, 77] or autologous flap [68] reconstruction were associated with increased risk of SSI. In a meta-analysis of seven studies, Zhang found that immediate reconstruction was associated with 1.5-fold increased risk of SSI compared to mastectomy-only [81]. Additional factors associated with increased risk of SSI in studies that focused on mastectomy with immediate implant reconstruction included older age [70•], adjuvant radiotherapy [36, 82, 83], longer duration of operation [70•], tissue expander compared to permanent implant [38•], larger breast volume [83], and higher intraoperative expander fill [83]. In two NSQIP studies, pedicled TRAM and microvascular flap were associated with increased risk of SSI compared to immediate implant [71] or latissimus dorsi pedicled flap reconstruction [72].

In the past decade, use of acellular dermal matrix (ADM) as an inferolateral sling in tissue expander and direct-to-implant reconstruction has grown substantially, with routine use reported by 84% of plastic surgeons performing breast reconstruction in a recent survey [84]. Some purported reasons for the increased use of ADM include better pocket control, potential to perform direct-to-implant reconstruction (without the need for tissue expansion) [49], and decreased risk of capsular contracture [85], although the evidence for these benefits in the literature is relatively weak [86].

Synthesizing the literature regarding ADM and SSI risk is difficult for a number of reasons. Some observational studies have not reported significantly increased risk of SSI associated with ADM (compared to non-use), although

due to small sample sizes many of these studies lacked sufficient power to detect a significant difference [87•]. Of the studies that reported significantly increased risk of SSI associated with ADM, different reconstruction procedures were included: three studies included only tissue expander primary reconstruction [27, 88, 89], one had only a small number of direct-to-implant reconstructions [24], and two studies included a mixed population but controlled for increased risk of SSI associated with obesity [63] and with use of a tissue expander [38•]. In a meta-analysis of 17 studies published through 2014, ADM was associated with 1.4-fold increased risk of SSI compared to no use, although significant heterogeneity was noted between studies [90]. In an analysis of immediate tissue expander-based reconstruction from 2005 to 2011 in the NSQIP data, Winecour reported a significantly higher rate of 30-day SSI in procedures with ADM compared to no use (4.5 versus 3.2%, respectively) [70•].

Defining the risk of SSI associated with ADM in tissue expander reconstruction is further complicated by the availability of different products, including matrices of human, bovine, or porcine origin and different degrees of sterility (i.e., terminally sterilized or non-sterile aseptic products) [87•]. Additionally, when tissue expander reconstruction is performed with ADM, a larger volume of saline is typically used for intraoperative inflation of the tissue expander, and the time to final expansion is shortened, which could confound the relationship between ADM use and risk of SSI [87•]. Definitive evidence for the safety of ADM and the risk of SSI in direct-to-implant versus tissue expander primary reconstruction likely will require randomized controlled trials to eliminate the variation in practice patterns and patient selection evident in the existing observational studies.

SSI risk prediction models

Models that can be used to predict SSI risk in women undergoing mastectomy or breast reconstruction have been developed by three groups. Kim and colleagues developed a risk model for SSI after immediate reconstruction using the 2005–2011 NSQIP data. The model contained 11 variables including age, BMI, higher ASA score, bleeding disorder, previous cardiac revascularization, diabetes, active smoking, dyspnea, hypertension, and reconstruction type, and had a c-statistic of 0.678 [71]. Kim subsequently used data self-reported by surgeons in the Tracking Operations and Outcomes for Plastic Surgeons database to develop a second immediate reconstruction SSI risk model. This model contained a smaller set of variables available preoperatively, including age, BMI, former or current smoker, diabetes, higher ASA score, and type of reconstruction, and had a c-statistic of 0.637 [57]. Kato reported a risk score for SSI after immediate or delayed tissue expander or implant reconstruction with 7 variables, including age ≥50 years, diabetes, repeated expander insertion, large expander size, neoadjuvant chemotherapy, nipple-sparing mastectomy, and postoperative hormone use, with a c-statistic of 0.734. The risk score was used to categorize risk into three strata, with progressively higher cumulative incidence rates of SSI [32]. We recently reported a risk prediction model for SSI after mastectomy with or without immediate reconstruction, which included 14 variables (rural residence, rheumatologic disease, depression, diabetes, hypertension, liver disease, obesity, pre-existing pneumonia or urinary tract infection,

smoking, smoking-related diseases, bilateral mastectomy, implant or flap reconstruction, and home healthcare (with lower risk of SSI)) [68]. The c-statistic in a validation population was 0.649. In this risk model, implant and autologous flap reconstruction were both associated with about twofold increased risk of SSI, compared to mastectomy alone. We also created three risk strata based on predicted SSI risk, and found good correlation with the expected and observed infections in the strata. Further work to develop accurate models to predict SSI risk in women eligible for breast reconstruction is needed in order to provide accurate information regarding risk of complications so women can make a truly informed decision regarding immediate reconstruction. These risk prediction models will also enable discussion with the patient of her role in management of underlying conditions to minimize complications.

Microbiology of SSI after mastectomy or breast reconstruction

An interesting feature of SSI after breast reconstruction procedures is the unusual spectrum of bacteria infecting what is generally considered to be a clean surgical site. Numerous reports of SSI caused by nontuberculous Mycobacterial species exist in the literature, most often associated with implant reconstruction [20, 41, 44••, 63, 91, 92]. In addition, the proportion of Gram-negative bacilli isolated from wound cultures in women with SSI after mastectomy is much higher than would be expected from breast specimens, ranging up to 50% in some studies [13, 20, 44••, 59, 60, 77, 82, 93–96]. The presence of nontuberculous Mycobacteria and in particular antibiotic resistant Gram-negative bacilli in infected wounds complicates treatment, since empiric therapy of breast surgical wounds does not usually include antibiotics active against these bacteria. In addition, Spear found that infection with "atypical bacteria," including Gram-negative bacilli and methicillin-resistant *Staphylococcus aureus* (MRSA), was associated with significantly greater implant loss than infection with the more common skin flora [95]. In their comprehensive review of the microbiology of tissue expander infections, Viola found that MRSA or *Pseudomonas* predominated in early SSIs within 30 days after operation [44••]. Clearly, more work is needed to understand the origin of bacteria responsible for these infections and the role of biofilm in implant infections, in order to develop more effective preventive strategies and inform choice of empiric antibiotics in women presenting with infection.

SSI prevention strategies—prophylactic antibiotics

Discontinuation of prophylactic antibiotics within 24 h of surgery is recommended by numerous organizations, including the Society for Healthcare Epidemiology of America and Infectious Diseases Society of America [97, 98]. Despite this recommendation by numerous professional societies, continuation of prophylactic antibiotics post-discharge is very common in breast operations, particularly breast reconstruction. The most recent American Society of Plastic Surgeons practice guidelines for expander/implant breast reconstruction recommends that antibiotics should be discontinued within 24 h after surgery unless drains are present, in which case prophylaxis duration is left to surgeon preference [99]. In a 2009 survey of 650 plastic surgeons, 72% continued

prophylactic antibiotics after discharge in women with immediate breast reconstruction, with cephalexin used in 75% of cases [100]. In a more recent survey of plastic surgeons performing breast reconstruction, 88% continued antibiotics postoperatively, with 32% discontinuing antibiotics within 5 days and 45% continuing for 6 to 10 days postoperatively [84]. These survey results are consistent with a systematic review performed by Phillips of antibiotic utilization in breast reconstruction. In their summary of antibiotic protocols reported in publications from 2005 to 2010, continuation of prophylactic antibiotics until removal of drains was most frequently reported, with prolonged utilization of antibiotics for 4–7 days postoperatively and perioperative use also common [101••]. In a retrospective review of all tissue expander reconstructions during a 10-year time period, Viola and colleagues reported use of postoperative oral prophylactic antibiotics in 78% of cases, with duration ranging from 1 week or until removal of drains [44••].

Despite its pervasive use, there is little evidence to support the use of post-discharge prophylactic antibiotics after mastectomy. In the past decade, 10 studies have been published comparing SSI rates depending on the duration of utilization of prophylactic antibiotics (Table 2). Four of the 10 studies reported significantly lower SSI rates with prolonged utilization of antibiotics, all of which were subject to bias. Edwards et al. reported lower risk of SSI in women undergoing mastectomy without reconstruction who were given prolonged antibiotics after operation [16]. This study is likely subject to confounding bias as procedures were performed by only two surgeons, with one utilizing preoperative antibiotics and the other continuing antibiotics post-discharge until drains were removed. In three studies, high SSI rates prompted a change in the antibiotic prophylaxis protocol, prolonging the duration of antibiotic administration [64, 91, 102]. In these three studies, the SSI rate in the earlier time period was very high, and the lower SSI rate after the change in antibiotic protocol is consistent with "regression to the mean," in which an extreme rate in one period is likely to move back to the normal rate in a subsequent period in the absence of any intervention [103]. In contrast, no difference in SSI rates in patients undergoing mastectomy and/or breast reconstruction depending on the duration of antibiotic prophylaxis was found in the remaining six studies in Table 2, although none had sufficient power to detect a difference unless it was relatively large (more than a twofold decrease in SSI rates). We recently analyzed post-discharge antibiotic utilization in a large cohort of over 12,000 women who underwent mastectomy with or without immediate breast reconstruction using private insurer claims data (Olsen et al., unpublished observations). In procedures with no evidence for complication during the surgical admission, prescription claims for antibiotics within 5 days after hospital discharge were identified after 56% of mastectomy with reconstruction and 23% without immediate reconstruction. Three-quarters of the women prescribed antibiotics in the immediate post-discharge time period were given a cephalosporin. There was no difference in the incidence of SSI in women given post-discharge antibiotics compared to those without antibiotics after mastectomy ($p = 0.18$) or after immediate reconstruction ($p = 0.20$), despite having >80% power to detect a difference in SSI rates if a difference existed.

Phillips recently reviewed SSI rates after reconstruction procedures in which prophylactic antibiotics were given for 24 h or less versus more than 24 h, including most of the studies in Table 2, and found no difference in the

Table 2. Summary of breast surgery studies of prolonged perioperative antibiotic prophylaxis with post hoc power calculations based on detection of 50% reduction in the observed surgical site infection rates

Author (year)	Study population	Antibiotic duration (*n* in each group)	Outcome/SSI rates	Power[a]
Throckmorton (2009) [104]	Breast and/or axillary operations	Pre-op (309) vs. pre + post-op (127)	7.4 vs. 8.7% (NS)	0.47
Clayton (2012) [64]	Immediate breast reconstruction	Pre-op (134) vs. pre-op + drain duration (116)	34.3 vs. 18.1% ($p = 0.004$)	
Liu (2012) [105]	Autologous reconstruction	<24 h (82) vs. >24 h (174)	19.5 vs. 15.5% (NS)	0.51
Mirzabeigi (2012) [102]	Implant reconstruction with prior irradiation	Pre-op + 5–7 days (26) vs. pre-op + 1 month (25)	34.6 vs. 8.0% ($p = 0.04$)	
Avashia (2013) [91]	Tissue expander reconstruction with ADM	≤24 h (19) vs. ≥48 h (119)	31.6 vs. 6.7% ($p = 0.004$)	
Edwards (2014) [16]	Mastectomy-only	Pre-op (157) vs. pre-op + post-op (268)	14.0 vs. 3.4% ($p < 0.001$)	
McCullough (2014) [41]	Immediate tissue expander reconstruction	Pre-op (178) vs. pre-op and post-op (200)	13.5 vs. 12.0% (NS)	0.58
Townley (2015) [106]	Implant reconstruction	Pre-op (94) vs. drain duration (94)	11.7 vs. 9.6% (NS)	0.30
Phillips (2016) [107]	RCT—immediate tissue expander reconstruction	24 h (62) vs. drain duration (50)	19.4 vs. 22% (NS)	0.32
Drury (2016) [108]	Autologous reconstruction	<24 h (659) vs. >24 h (377)	5.0 vs. 2.9% ($p = 0.11$)	0.57

NS not significant, *pre-op* preoperative, *post-op* postoperative, *drain duration* antibiotics continued until drains removed
[a]Power to detect a 50% reduction in observed SSI rates, based on the observed rate with shorter duration of prophylaxis ($\alpha = 0.05$)

summary SSI rates depending on duration of prophylaxis [101••]. Thus, at present, there is no evidence in the literature to support continuation of prophylactic antibiotics beyond 24 h after surgery. There is the potential for harm, however, due to increased risk of infection with *Clostridium difficile*, development of antibiotic-resistant organisms, and other drug-related complications, including allergic reactions. Consistent with these accepted risks, Throckmorton and colleagues found increased drug-related complication rates in breast or axillary surgical patients given postoperative prophylactic antibiotics compared to only a single pre-incision dose of antibiotics [109].

Other SSI prevention strategies

In addition to post-discharge prophylactic antibiotic use, a number of other preventive strategies are used by surgeons to reduce the risk of SSI after reconstructive surgery, including preoperative decolonization, preoperative bathing with chlorhexidine solution, irrigation of the mastectomy pocket with an antibiotic-containing solution, soaking the breast implant

in an antibiotic-containing solution, and perioperative glucose control [110••]. Although decolonization to prevent SSI caused by *S. aureus* has been studied extensively in other operations, only one group analyzed nasopharyngeal colonization in patients undergoing tissue expander reconstruction. Nishibayashi found significantly increased risk of SSI in women colonized with MRSA compared to uncolonized women, suggesting that decolonization with mupirocin may have benefit in this population [111].

In a recent survey of 253 plastic surgeons performing breast implant surgery (80% in private practice), an antiseptic or antibiotic-containing solution was used by 81% for irrigation and by 86% to soak breast implants prior to implantation [112]. In this survey, the most common choices of irrigant were a triple antibiotic solution, followed by povidone-iodine. Similarly, Viola and colleagues found use of triple antibiotic solution for pocket irrigation in more than 85% of tissue expander reconstructions in 3082 patients over a 10-year period at their institution [44••]. Although use of antiseptic or antibiotic-containing solutions for pocket irrigation and soaking breast implants has been recommended in a guideline from the UK [113] to prevent infection and capsular contracture, thought to be caused by subclinical infection, the evidence to support this practice is weak. Only one prior study found decreased incidence of SSI associated with cephalothin-containing irrigant compared to saline alone in women undergoing cosmetic augmentation [114]. This study used a before-after design with over 3 years separating the two time periods studied, and an unusually high SSI rate in the second period when only saline irrigant was used.

Despite this lack of data, use of antiseptic or antibiotic-containing solutions for irrigation and implant soaking is routinely advocated in reviews describing strategies to reduce infection risk in breast implant reconstruction [113, 115, 116]. Khansa and colleagues included irrigation and soaking of implants in a triple antibiotic solution in a standardized protocol to minimize infection risk in tissue expander reconstruction [66]. The protocol also included chlorhexidine bathing the day before and morning of surgery, surgical site antisepsis with chlorhexidine, and prescription of oral antibiotics for prophylaxis post-discharge until drains were removed. They reported a significantly lower SSI rate in the 2-year time period after implementation of the standardized protocol compared to the prior period, although no information was supplied about the prior practices. Optimally, randomized controlled trials to determine the benefit of specific practices, such as antibiotic implant soaking, should be conducted. As this is unlikely, additional studies of standardized infection control interventions are needed to identify specific practices associated with decreased risk of SSI in the breast reconstruction population.

Conclusions

It is clear from a review of the literature that larger multicenter studies are needed to quantify the risk of SSI depending on the type of reconstruction and other operative factors (e.g., ADM, tissue expander versus direct-to-implant, flap type). More data on the baseline risk of SSI after mastectomy without reconstruction are also needed to put the SSI rates associated with breast reconstruction into context. The microbiology of breast SSIs, particularly infections associated with breast implant

reconstruction, also requires further research, including study of the local skin microbiome and the origin of Gram-negative bacilli and other unusual flora in these infections. It is important to learn more about the risk of SSI and develop better preventive strategies to lower rates of infection in this vulnerable population of women diagnosed with breast cancer.

Compliance with Ethical Standards

Conflict of Interest

Dr. Margaret A. Olsen declares consultant fees, advisory board membership, and grant support from Pfizer, as well as grant support from Sanofi Pasteur, outside of the submitted work. Ms. Katelin B. Nickel and Dr. Ida K. Fox declare that they have no conflicts of interest.

Human and Animal Rights and Informed Consent

This article does not contain any studies with human or animal subjects performed by any of the authors.

References and Recommended Reading

Papers of particular interest, published recently, have been highlighted as:

- • Of importance
- •• Of major importance

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2016. CA Cancer J Clin. 2016;66(1):7–30.
2.• Wong SM, Freedman RA, Sagara Y, Aydogan F, Barry WT, Golshan M. Growing use of contralateral prophylactic mastectomy despite no improvement in long-term survival for invasive breast cancer. Ann Surg. 2017;265(3):581–9.

Documents increasing use of bilateral mastectomy in women with early-stage breast cancer, despite no evidence for survival benefit. Women with bilateral mastectomy were also much more likely to undergo immediate breast reconstruction than women with unilateral mastectomy.

3. Rutter CE, Park HS, Killelea BK, Evans SB. Growing use of mastectomy for ductal carcinoma-*in situ* of the breast among young women in the United States. Ann Surg Oncol. 2015;22(7):2378–86.
4. Ilonzo N, Tsang A, Tsantes S, Estabrook A, Thu Ma AM. Breast reconstruction after mastectomy: a ten-year analysis of trends and immediate postoperative outcomes. Breast. 2016;32:7–12.
5. Kummerow KL, Du L, Penson DF, Shyr Y, Hooks MA. Nationwide trends in mastectomy for early-stage breast cancer. JAMA Surg. 2015;150(1):9–16.
6.• Jeevan R, Mennie JC, Mohanna PN, O'Donoghue JM, Rainsbury RM, Cromwell DA. National trends and regional variation in immediate breast reconstruction rates. Br J Surg. 2016;103(9):1147–56.

Documents increasing trend of immediate reconstruction in English National Health Service hospitals from 2000 to 2014, although there was substantial regional variation in utilization.

7. Mennie JC, Mohanna PN, O'Donoghue JM, Rainsbury R, Cromwell DA. National trends in immediate and delayed post-mastectomy reconstruction procedures in England: a seven-year population-based cohort study. Eur J Surg Oncol. 2017;43(1):52–61.
8.•• Albornoz CR, Cordeiro PG, Pusic AL, McCarthy CM, Mehrara BJ, Disa JJ, Matros E. Diminishing relative contraindications for immediate breast reconstruction: a multicenter study. J Am Coll Surg. 2014;219(4):788–95.

Cross-sectional study using that US Nationwide Inpatient Sample showing that increasing trend in immediate breast reconstruction is due to a 2-fold increase in implant reconstruction.

9. Olsen MA, Chu-Ongsakul S, Brandt KE, Dietz JR, Mayfield J, Fraser VJ. Hospital-associated costs due to surgical site infection after breast surgery. Arch Surg. 2008;143(1):53–60.
10. Colakoglu S, Khansa I, Curtis MS, Yueh JH, Ogunleye A, Haewyon C, Tobias AM, Lee BT. Impact of complications on patient satisfaction in breast reconstruction. Plast Reconstr Surg. 2011;127(4):1428–36.
11. Gopie JP, Timman R, Hilhorst MT, Hofer SO, Mureau MA, Tibben A. The short-term psychological impact of

complications after breast reconstruction. Psychooncology. 2013;22(2):290–8.
12. Ferraz EM, Bacelar TS, Aguiar JL, Ferraz AA, Pagnossin G, Batista JE. Wound infection rates in clean surgery: a potentially misleading risk classification. Infect Control Hosp Epidemiol. 1992;13(8):457–62.
13. Felippe WA, Werneck GL, Santoro-Lopes G. Surgical site infection among women discharged with a drain *in situ* after breast cancer surgery. World J Surg. 2007;31(12):2293–9.
14. Ashraf M, Biswas J, Gupta S, Alam N. Determinants of wound infections for breast procedures: assessment of the risk of wound infection posed by an invasive procedure for subsequent operation. Int J Surg. 2009;7(6):543–6.
15. Cabaluna ND, Uy GB, Galicia RM, Cortez SC, Yray MD, Buckley BS. A randomized, double-blinded placebo-controlled clinical trial of the routine use of preoperative antibiotic prophylaxis in modified radical mastectomy. World J Surg. 2013;37(1):59–66.
16. Edwards BL, Stukenborg GJ, Brenin DR, Schroen AT. Use of prophylactic postoperative antibiotics during surgical drain presence following mastectomy. Ann Surg Oncol. 2014;21(10):3249–55.
17. Ota D, Fukuuchi A, Iwahira Y, Kato T, Takeuchi M, Okamoto J, Nishi T. Clinical outcome of reconstruction with tissue expanders for patients with breast cancer and mastectomy. Clin Breast Cancer. 2014;14(5):339–45.
18. Olsen MA, Nickel KB, Fox IK, Margenthaler JA, Ball KE, Mines D, Wallace AE, Fraser VJ. Incidence of surgical site infection following mastectomy with and without immediate reconstruction using private insurer claims data. Infect Control Hosp Epidemiol. 2015;36(8):907–14.
19. Carter SA, Lyons GR, Kuerer HM, Bassett RL Jr, Oates S, Thompson A, Caudle AS, Mittendorf EA, Bedrosian I, Lucci A, et al. Operative and oncologic outcomes in 9861 patients with operable breast cancer: single-institution analysis of breast conservation with oncoplastic reconstruction. Ann Surg Oncol. 2016;23(10):3190–8.
20. Halvorson EG, Disa JJ, Mehrara BJ, Burkey BA, Pusic AL, Cordeiro PG. Outcome following removal of infected tissue expanders in breast reconstruction: a 10-year experience. Ann Plast Surg. 2007;59(2):131–6.
21. Francis SH, Ruberg RL, Stevenson KB, Beck CE, Ruppert AS, Harper JT, Boehmler JH, Miller MJ. Independent risk factors for infection in tissue expander breast reconstruction. Plast Reconstr Surg. 2009;124(6):1790–6.
22. Berry T, Brooks S, Sydow N, Djohan R, Nutter B, Lyons J, Dietz J. Complication rates of radiation on tissue expander and autologous tissue breast reconstruction. Ann Surg Oncol. 2010;17(Suppl 3):202–10.
23. Delgado JF, Garcia-Guilarte RF, Palazuelo MR, Mendez JI, Perez CC. Immediate breast reconstruction with direct, anatomic, gel-cohesive, extra-projection prosthesis: 400 cases. Plast Reconstr Surg. 2010;125(6):1599–605.
24. Liu AS, Kao HK, Reish RG, Hergrueter CA, May JW, Guo L. Post-operative complications in prosthesis-based breast reconstruction using acellular dermal matrix. Plast Reconstr Surg. 2011;127(5):1755–62.
25. Seth AK, Hirsch EM, Fine NA, Dumanian GA, Mustoe TA, Galiano RD, Hansen NM, Kim JY. Additive risk of tumescent technique in patients undergoing mastectomy with immediate reconstruction. Ann Surg Oncol. 2011;18(11):3041–6.
26. Salzberg CA, Ashikari AY, Koch RM, Chabner-Thompson E. An 8-year experience of direct-to-implant immediate breast reconstruction using human acellular dermal matrix (AlloDerm). Plast Reconstr Surg. 2011;127(2):514–24.
27. Weichman KE, Wilson SC, Weinstein AL, Hazen A, Levine JP, Choi M, Karp NS. The use of acellular dermal matrix in immediate two-stage tissue expander breast reconstruction. Plast Reconstr Surg. 2012;129(5):1049–58.
28. Peled AW, Foster RD, Garwood ER, Moore DH, Ewing CA, Alvarado M, Hwang ES, Esserman LJ. The effects of acellular dermal matrix in expander-implant breast reconstruction after total skin-sparing mastectomy: results of a prospective practice improvement study. Plast Reconstr Surg. 2012;129(6):901e–8e.
29. Spear SL, Seruya M, Rao SS, Rottman S, Stolle E, Cohen M, Rose KM, Parikh PM, Nahabedian MY. Two-stage prosthetic breast reconstruction using AlloDerm including outcomes of different timings of radiotherapy. Plast Reconstr Surg. 2012;130(1):1–9.
30. Lankiewicz JD, Yokoe DS, Olsen MA, Onufrak F, Fraser VJ, Stevenson K, Khan Y, Hooper D, Platt R, Huang SS. Beyond 30 days: does limiting the duration of surgical site infection follow-up limit detection? Infect Control Hosp Epidemiol. 2012;33(2):202–4.
31. Butterfield JL. 440 consecutive immediate, implant-based, single-surgeon breast reconstructions in 281 patients: a comparison of early outcomes and costs between SurgiMend fetal bovine and AlloDerm human cadaveric acellular dermal matrices. Plast Reconstr Surg. 2013;131(5):940–51.
32. Kato H, Nakagami G, Iwahira Y, Otani R, Nagase T, Iizaka S, Tamai N, Matsuyama Y, Sanada H. Risk factors and risk scoring tool for infection during tissue expansion in tissue expander and implant breast reconstruction. Breast J. 2013;19(6):618–26.
33. Seth AK, Persing S, Connor CM, Davila A, Hirsch E, Fine NA, Kim JY. A comparative analysis of cryopreserved versus prehydrated human acellular dermal matrices in tissue expander breast reconstruction. Ann Plast Surg. 2013;70(6):632–5.
34. Reish RG, Damjanovic B, Austen WG Jr, Winograd J, Liao EC, Cetrulo CL, Balkin DM, Colwell AS. Infection following implant-based reconstruction in 1952 consecutive breast reconstructions: salvage rates and predictors of success. Plast Reconstr Surg. 2013;131(6):1223–30.

35. Liu DZ, Mathes DW, Neligan PC, Said HK, Louie O. Comparison of outcomes using AlloDerm versus FlexHD for implant-based breast reconstruction. Ann Plast Surg. 2014;72(5):503–7.
36. Frey JD, Alperovich M, Weichman KE, Wilson SC, Hazen A, Saadeh PB, Levine JP, Choi M, Karp NS. Breast reconstruction using contour fenestrated AlloDerm: does improvement in design translate to improved outcomes? Plast Reconstr Surg Glob Open. 2015;3(9):e505.
37. Susarla SM, Ganske I, Helliwell L, Morris D, Eriksson E, Chun YS. Comparison of clinical outcomes and patient satisfaction in immediate single-stage versus two-stage implant-based breast reconstruction. Plast Reconstr Surg. 2015;135(1):1e–8e.
38.• Gfrerer L, Mattos D, Mastroianni M, Weng QY, Ricci JA, Heath MP, Lin A, Specht MC, Haynes AB, Austen WG Jr, et al. Assessment of patient factors, surgeons, and surgeon teams in immediate implant-based breast reconstruction outcomes. Plast Reconstr Surg. 2015;135(2):245e–52e.
Retrospective study of complications after immediate implant reconstruction, including 60% immediate-to-implant and 40% tissue expanders. In multivariable analysis obesity, use of ADM, bilateral surgery, and use of a tissue expander (versus permanent implant) were associated with increased risk of SSI. The findings regarding ADM and tissue expander will be important to confirm, since they are under the control of the operating plastic surgeon.
39. Weichman KE, Clavin NW, Miller HC, McCarthy CM, Pusic AL, Mehrara BJ, Disa JJ. Does the use of biopatch devices at drain sites reduce perioperative infectious complications in patients undergoing immediate tissue expander breast reconstruction? Plast Reconstr Surg. 2015;135(1):9e–17e.
40. Lovecchio F, Jordan SW, Lim S, Fine NA, Kim JY. Risk factors for complications differ between stages of tissue-expander breast reconstruction. Ann Plast Surg. 2015;75(3):275–80.
41. McCullough MC, Chu CK, Duggal CS, Losken A, Carlson GW. Antibiotic prophylaxis and resistance in surgical site infection after immediate tissue expander reconstruction of the breast. Ann Plast Surg. 2016;77(5):501–5.
42. Palaia DA, Arthur KS, Cahan AC, Rosenberg MH. Incidence of seromas and infections using fenestrated versus nonfenestrated acellular dermal matrix in breast reconstructions. Plast Reconstr Surg Glob Open. 2015;3(11):e569.
43. Woo KJ, Paik JM, Mun GH, Pyon JK, Bang SI. Risk factors for complications in immediate expander-implant breast reconstruction for non-obese patients: impact of breast size on complications. Aesthet Plast Surg. 2016;40(1):71–8.
44.•• Viola GM, Baumann DP, Mohan K, Selber J, Garvey P, Reece G, Raad II, Rolston KV, Crosby MA. Improving antimicrobial regimens for the treatment of breast tissue expander-related infections. Plast Reconstr Surg Glob Open. 2016;4(5):e704.
Retrospective review of the microbiology of SSIs in over 3000 patients with immediate tissue expander reconstruction over a 10-year period at a single institution. Found that early infections were more likely to be caused by Gram-negative bacilli or MRSA, and that the majority of SSIs occurred >30 days after operation. In patients with a positive wound culture, 32% of the time the empiric antibiotic regimen would not cover the isolated organism(s).
45. Abedi N, Ho AL, Knox A, Tashakkor Y, Omeis T, Van Laeken N, Lennox P, Macadam SA. Predictors of mastectomy flap necrosis in patients undergoing immediate breast reconstruction: a review of 718 patients. Ann Plast Surg. 2016;76(6):629–34.
46. Dolen UC, Schmidt AC, Um GT, Sharma K, Naughton M, Zoberi I, Margenthaler JM, Myckatyn TM. Impact of neoadjuvant and adjuvant chemotherapy on immediate tissue expander breast reconstruction. Ann Surg Oncol. 2016;23(7):2357–66.
47. Chen CF, Lin SF, Hung CF, Chou P. Risk of infection is associated more with drain duration than daily drainage volume in prosthesis-based breast reconstruction: a cohort study. Medicine (Baltimore). 2016;95(49):e5605.
48.•• Sinha I, Pusic AL, Wilkins EG, Hamill JB, Chen X, Kim HM, Guldbrandsen G, Chun YS. Late surgical-site infection in immediate implant-based breast reconstruction. Plast Reconstr Surg. 2017;139(1):20–8.
Analysed late versus early SSIs in women enrolled in a prospective multicenter cohort of mastectomy reconstruction. Late SSIs (>30 days after operation) occurred in 47% of women with direct-to-implant and 56% of women with tissue expander reconstruction. Late SSIs were associated with higher rates of implant loss. Risk factors for late compared to early SSI included increasing BMI and irradiation after TE placement.
49. Hunsicker LM, Ashikari AY, Berry C, Koch RM, Salzberg CA. Short-term complications associated with acellular dermal matrix-assisted direct-to-implant breast reconstruction. Ann Plast Surg. 2017;78(1):35–40.
50. Meretoja TJ, Rasia S, von Smitten KA, Asko-Seljavaara SL, Kuokkanen HO, Jahkola TA. Late results of skin-sparing mastectomy followed by immediate breast reconstruction. Br J Surg. 2007;94(10):1220–5.
51. Kim EK, Eom JS, Ahn SH, Son BH, Lee TJ. Evolution of the pedicled TRAM flap: a prospective study of 500 consecutive cases by a single surgeon in Asian patients. Ann Plast Surg. 2009;63(4):378–82.
52. Crosby MA, Garvey PB, Selber JC, Adelman DM, Sacks JM, Villa MT, Lin HY, Park SJ, Baumann DP. Reconstructive outcomes in patients undergoing contralateral prophylactic mastectomy. Plast Reconstr Surg. 2011;128(5):1025–33.
53. Llewellyn-Bennett R, Greenwood R, Benson JR, English R, Turner J, Rayter Z, Winters ZE. Randomized clinical trial on the effect of fibrin sealant on latissimus dorsi donor-site seroma formation after breast reconstruction. Br J Surg. 2012;99(10):1381–8.
54. Vargas CR, Koolen PG, Ho OA, Ricci JA, Tobias AM, Lin SJ, Lee BT. Tumescent mastectomy technique in

autologous breast reconstruction. J Surg Res. 2015;198(2):525–9.
55. Butz DR, Lapin B, Yao K, Wang E, Song DH, Johnson D, Sisco M. Advanced age is a predictor of 30-day complications after autologous but not implant-based postmastectomy breast reconstruction. Plast Reconstr Surg. 2015;135(2):253e–61e.
56. Fischer JP, Wes AM, Tuggle CT, Nelson JA, Tchou JC, Serletti JM, Kovach SJ, Wu LC. Mastectomy with or without immediate implant reconstruction has similar 30-day perioperative outcomes. J Plast Reconstr Aesthet Surg. 2014;67(11):1515–22.
57. Kim JY, Mlodinow AS, Khavanin N, Hume KM, Simmons CJ, Weiss MJ, Murphy RX Jr, Gutowski KA. Individualized risk of surgical complications: an application of the Breast Reconstruction Risk Assessment Score. Plast Reconstr Surg Glob Open. 2015;3(5):e405.
58. Silva AK, Lapin B, Yao KA, Song DH, Sisco M. The effect of contralateral prophylactic mastectomy on perioperative complications in women undergoing immediate breast reconstruction: a NSQIP analysis. Ann Surg Oncol. 2015;22(11):3474–80.
59. Weichman KE, Levine SM, Wilson SC, Choi M, Karp NS. Antibiotic selection for the treatment of infectious complications of implant-based breast reconstruction. Ann Plast Surg. 2013;71(2):140–3.
60. Chidester JR, Danci I, Lewis P, Biskup N, Kim H, Gupta S. Antibiogram for periprosthetic infections: a tool for better informed selection of empiric antibiotics for surgical site infections. Ann Plast Surg. 2016;76(Suppl 3):S158–61.
61. Sorensen LT, Horby J, Friis E, Pilsgaard B, Jorgensen T. Smoking as a risk factor for wound healing and infection in breast cancer surgery. Eur J Surg Oncol. 2002;28(8):815–20.
62. Vilar-Compte D, Rosales S, Hernandez-Mello N, Maafs E, Volkow P. Surveillance, control, and prevention of surgical site infections in breast cancer surgery: a 5-year experience. Am J Infect Control. 2009;37(8):674–9.
63. Chun YS, Verma K, Rosen H, Lipsitz S, Morris D, Kenney P, Eriksson E. Implant-based breast reconstruction using acellular dermal matrix and the risk of postoperative complications. Plast Reconstr Surg. 2010;125(2):429–36.
64. Clayton JL, Bazakas A, Lee CN, Hultman CS, Halvorson EG. Once is not enough: withholding postoperative prophylactic antibiotics in prosthetic breast reconstruction is associated with an increased risk of infection. Plast Reconstr Surg. 2012;130(3):495–502.
65. Chang RJ, Kirkpatrick K, De Boer RH, Bruce Mann G. Does immediate breast reconstruction compromise the delivery of adjuvant chemotherapy? Breast. 2013;22(1):64–9.
66. Khansa I, Hendrick RG Jr, Shore A, Meyerson J, Yang M, Boehmler JH. Breast reconstruction with tissue expanders: implementation of a standardized best-practices protocol to reduce infection rates. Plast Reconstr Surg. 2014;134(1):11–8.
67. Rao S, Stolle EC, Sher S, Lin CW, Momen B, Nahabedian MY. A multiple logistic regression analysis of complications following microsurgical breast reconstruction. Gland Surg. 2014;3(4):226–31.
68. Olsen MA, Nickel KB, Margenthaler JA, Fox IK, Ball KE, Mines D, Wallace AE, Colditz GA, Fraser VJ. Development of a risk prediction model to individualize risk factors for surgical site infection after mastectomy. Ann Surg Oncol. 2016;23(8):2471–9.
69. Davis GB, Peric M, Chan LS, Wong AK, Sener SF. Identifying risk factors for surgical site infections in mastectomy patients using the National Surgical Quality Improvement Program database. Am J Surg. 2013;205(2):194–9.
70.• Winocour S, Martinez-Jorge J, Habermann E, Thomsen K, Lemaine V. Early surgical site infection following tissue expander breast reconstruction with or without acellular dermal matrix: national benchmarking using National Surgical Quality Improvement Program. Arch Plast Surg. 2015;42(2):194–200.
Analysis of immediate tissue expander reconstructions using the NSQIP data. Found that ADM was associated with significantly increased risk of SSI, along with older age, obesity, and longer duration of operation.
71. Kim JY, Khavanin N, Jordan SW, ver Halen JP, Mlodinow AS, Bethke KP, Khan SA, Hansen NM, Losken A, Fine NA. Individualized risk of surgical-site infection: an application of the breast reconstruction risk assessment score. Plast Reconstr Surg. 2014;134(3):351e–62e.
72. Gart MS, Smetona JT, Hanwright PJ, Fine NA, Bethke KP, Khan SA, Wang E, Kim JY. Autologous options for postmastectomy breast reconstruction: a comparison of outcomes based on the American College of Surgeons National Surgical Quality Improvement Program. J Am Coll Surg. 2013;216(2):229–38.
73. de Blacam C, Ogunleye AA, Momoh AO, Colakoglu S, Tobias AM, Sharma R, Houlihan MJ, Lee BT. High body mass index and smoking predict morbidity in breast cancer surgery: a multivariate analysis of 26,988 patients from the National Surgical Quality Improvement Program database. Ann Surg. 2012;255(3):551–5.
74. Vilar-Compte D, Alvarez de Iturbe I, Martin-Onraet A, Perez-Amador M, Sanchez-Hernandez C, Volkow P. Hyperglycemia as a risk factor for surgical site infections in patients undergoing mastectomy. Am J Infect Control. 2008;36(3):192–8.
75. Ducic I, Spear SL, Cuoco F, Hannan C. Safety and risk factors for breast reconstruction with pedicled transverse rectus abdominis musculocutaneous flaps: a 10-year analysis. Ann Plast Surg. 2005;55(6):559–64.
76. Selber JC, Kurichi JE, Vega SJ, Sonnad SS, Serletti JM. Risk factors and complications in free TRAM flap breast reconstruction. Ann Plast Surg. 2006;56(5):492–7.
77. Olsen MA, Lefta M, Dietz JR, Brandt KE, Aft R, Matthews R, Mayfield J, Fraser VJ. Risk factors for surgical site infection after major breast operation. J Am Coll Surg. 2008;207(3):326–35.

78. Seth AK, Hirsch EM, Fine NA, Kim JY. Utility of acellular dermis-assisted breast reconstruction in the setting of radiation: a comparative analysis. Plast Reconstr Surg. 2012;130(4):750–8.
79. Nguyen TJ, Costa MA, Vidar EN, Shahabi A, Peric M, Hernandez AM, Chan LS, Sener SF, Wong AK. Effect of immediate reconstruction on postmastectomy surgical site infection. Ann Surg. 2012;256(2):326–33.
80. Hanna KR, Tilt A, Holland M, Colen D, Bowen B, Stovall M, Lee A, Wang J, Drake D, Lin K, et al. Reducing infectious complications in implant based breast reconstruction: impact of early expansion and prolonged drain use. Ann Plast Surg. 2016;76(Suppl 4):S312–5.
81. Zhang P, Li CZ, Wu CT, Jiao GM, Yan F, Zhu HC, Zhang XP. Comparison of immediate breast reconstruction after mastectomy and mastectomy alone for breast cancer: a meta-analysis. Eur J Surg Oncol. 2017;43(2):285–93.
82. Franchelli S, Vassallo F, Porzio C, Mannucci M, Priano V, Schenone E, Leone MS, Canavese G, Santi P, De MA. Breast implant infections after surgical reconstruction in patients with breast cancer: assessment of risk factors and pathogens over extended post-operative observation. Surg Infect. 2012;13(3):154–8.
83. Selber JC, Wren JH, Garvey PB, Zhang H, Erickson C, Clemens MW, Butler CE. Critical evaluation of risk factors and early complications in 564 consecutive two-stage implant-based breast reconstructions using acellular dermal matrix at a single center. Plast Reconstr Surg. 2015;136(1):10–20.
84. Ibrahim AM, Koolen PG, Ashraf AA, Kim K, Mureau MA, Lee BT, Lin SJ. Acellular dermal matrix in reconstructive breast surgery: survey of current practice among plastic surgeons. Plast Reconstr Surg Glob Open. 2015;3(4):e381.
85. Ho G, Nguyen TJ, Shahabi A, Hwang BH, Chan LS, Wong AK. A systematic review and meta-analysis of complications associated with acellular dermal matrix-assisted breast reconstruction. Ann Plast Surg. 2012;68(4):346–56.
86. Nguyen JT, Carey JN, Wong AK. Use of human acellular dermal matrix in implant-based breast reconstruction: evaluating the evidence. J Plast Reconstr Aesthet Surg. 2011;64(12):1553–61.
87.• Cabalag MS, Rostek M, Miller GS, Chae MP, Quinn T, Rozen WM, Hunter-Smith DJ. Alloplastic adjuncts in breast reconstruction. Gland Surg. 2016;5(2):158–73.
Systematic review of ADM use in breast reconstruction. The majority of studies comparing ADM use to no use in two-stage (tissue expander) reconstruction reported worse, although not necessarily significantly different outcomes with ADM. Also gave a good overview of the different types of ADM available in the US and Europe.
88. Lanier ST, Wang ED, Chen JJ, Arora BP, Katz SM, Gelfand MA, Khan SU, Dagum AB, Bui DT. The effect of acellular dermal matrix use on complication rates in tissue expander/implant breast reconstruction. Ann Plast Surg. 2010;64(5):674–8.
89. Brooke S, Mesa J, Uluer M, Michelotti B, Moyer K, Neves RI, Mackay D, Potochny J. Complications in tissue expander breast reconstruction: a comparison of AlloDerm, DermaMatrix, and FlexHD acellular inferior pole dermal slings. Ann Plast Surg. 2012;69(4):347–9.
90. Lee KT, Mun GH. Updated evidence of acellular dermal matrix use for implant-based breast reconstruction: a meta-analysis. Ann Surg Oncol. 2016;23(2):600–10.
91. Avashia YJ, Mohan R, Berhane C, Oeltjen JC. Postoperative antibiotic prophylaxis for implant-based breast reconstruction with acellular dermal matrix. Plast Reconstr Surg. 2013;131(3):453–61.
92. Cicilioni OJ Jr, Foles VB, Sieger B, Musselman K. Mycobacterium fortuitum infection following reconstructive breast surgery: differentiation from classically described red breast syndrome. Plast Reconstr Surg Glob Open. 2013;1(7):e50.
93. Vilar-Compte D, Roldan-Marin R, Robles-Vidal C, Volkow P. Surgical site infection (SSI) rates among patients who underwent mastectomy after the introduction of SSI prevention policies. Infect Control Hosp Epidemiol. 2006;27(8):829–34.
94. Mukhtar RA, Throckmorton AD, Alvarado MD, Ewing CA, Esserman LJ, Chiu C, Hwang ES. Bacteriologic features of surgical site infections following breast surgery. Am J Surg. 2009;198(4):529–31.
95. Spear SL, Seruya M. Management of the infected or exposed breast prosthesis: a single surgeon's 15-year experience with 69 patients. Plast Reconstr Surg. 2010;125(4):1074–84.
96. Klein GM, Phillips BT, Dagum AB, Bui DT, Khan SU. Infectious loss of tissue expanders in breast reconstruction: are we treating the right organisms? Ann Plast Surg. 2017;78(2):149–52.
97. Anderson DJ, Podgorny K, Berrios-Torres SI, Bratzler DW, Dellinger EP, Greene L, Nyquist AC, Saiman L, Yokoe DS, Maragakis LL, et al. Strategies to prevent surgical site infections in acute care hospitals: 2014 update. Infect Control Hosp Epidemiol. 2014;35(Suppl 2):S66–88.
98. Bratzler DW, Dellinger EP, Olsen KM, Perl TM, Auwaerter PG, Bolon MK, Fish DN, Napolitano LM, Sawyer RG, Slain D, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Am J Health Syst Pharm. 2013;70(3):195–283.
99. Alderman A, Gutowski K, Ahuja A, Gray D. ASPS clinical practice guideline summary on breast reconstruction with expanders and implants. Plast Reconstr Surg. 2014;134(4):648e–55e.
100. Phillips BT, Wang ED, Mirrer J, Lanier ST, Khan SU, Dagum AB, Bui DT. Current practice among plastic surgeons of antibiotic prophylaxis and closed-suction drains in breast reconstruction: experience, evidence, and implications for postoperative care. Ann Plast Surg. 2011;66(5):460–5.
101.•• Phillips BT, Halvorson EG. Antibiotic prophylaxis following implant-based breast reconstruction: what

is the evidence? Plast Reconstr Surg. 2016;138(4):751–7.
Review of studies reporting duration of antibiotic prophylaxis and impact on SSI rates in women undergoing immediate implant reconstruction. The review did not provide evidence for benefit of antibiotic prophylaxis beyond 24 hours after surgery.
102. Mirzabeigi MN, Lee M, Smartt JM Jr, Jandali S, Sonnad SS, Serletti JM. Extended trimethoprim/sulfamethoxazole prophylaxis for implant reconstruction in the previously irradiated chest wall. Plast Reconstr Surg. 2012;129(1):37e–45e.
103. Jones HE, Spiegelhalter DJ. Accounting for regression-to-the-mean in tests for recent changes in institutional performance: analysis and power. Stat Med. 2009;28(12):1645–67.
104. Throckmorton AD, Boughey JC, Boostrom SY, Holifield AC, Stobbs MM, Hoskin T, Baddour LM, Degnim AC. Postoperative prophylactic antibiotics and surgical site infection rates in breast surgery patients. Ann Surg Oncol. 2009;16(9):2464–9.
105. Liu DZ, Dubbins JA, Louie O, Said HK, Neligan PC, Mathes DW. Duration of antibiotics after microsurgical breast reconstruction does not change surgical infection rate. Plast Reconstr Surg. 2012;129(2):362–7.
106. Townley WA, Baluch N, Bagher S, Maass SW, O'Neill A, Zhong T, Hofer SO. A single pre-operative antibiotic dose is as effective as continued antibiotic prophylaxis in implant-based breast reconstruction: a matched cohort study. J Plast Reconstr Aesthet Surg. 2015;68(5):673–8.
107. Phillips BT, Fourman MS, Bishawi M, Zegers M, O'Hea BJ, Ganz JC, Huston TL, Dagum AB, Khan SU, Bui DT. Are prophylactic postoperative antibiotics necessary for immediate breast reconstruction? Results of a prospective randomized clinical trial. J Am Coll Surg. 2016;222(6):1116–24.
108. Drury KE, Lanier ST, Khavanin N, Hume KM, Gutowski KA, Thornton BP, Hansen NM, Murphy RX Jr, Fine NA, Kim JY. Impact of postoperative antibiotic prophylaxis duration on surgical site infections in autologous breast reconstruction. Ann Plast Surg. 2016;76(2):174–9.
109. Throckmorton AD, Hoskin T, Boostrom SY, Boughey JC, Holifield AC, Stobbs MM, Baddour LM, Degnim AC. Complications associated with postoperative antibiotic prophylaxis after breast surgery. Am J Surg. 2009;198(4):553–6.
110.•• Ban KA, Minei JP, Laronga C, Harbrecht BG, Jensen EH, Fry DE, Itani KM, Dellinger EP, Ko CY, Duane TM. American College of Surgeons and Surgical Infection Society: surgical site infection guidelines, 2016 update. J Am Coll Surg. 2017;224(1):59–74.
Updated guideline for prevention of SSIs, including after breast operations. Recommends optimal glucose control for all diabetic patients. No recommendations given for duration of antibiotic prophylaxis in breast implant surgery due to lack of definitive data.
111. Nishibayashi A, Tomita K, Sugio Y, Hosokawa K, Yano K. Tissue expander infection in breast reconstruction: importance of nasopharynx screening for methicillin-resistant *Staphylococcus aureus*. Plast Reconstr Surg Glob Open. 2016;4(10):e1076.
112. Chopra K, Gowda AU, McNichols CH, Brown EN, Slezak S, Rasko Y. Antimicrobial prophylaxis practice patterns in breast augmentation: a national survey of current practice. Ann Plast Surg. 2016.
113. Barr SP, Topps AR, Barnes NL, Henderson J, Hignett S, Teasdale RL, McKenna A, Harvey JR, Kirwan CC. Infection prevention in breast implant surgery—a review of the surgical evidence, guidelines and a checklist. Eur J Surg Oncol. 2016;42(5):591–603.
114. Pfeiffer P, Jorgensen S, Kristiansen TB, Jorgensen A, Holmich LR. Protective effect of topical antibiotics in breast augmentation. Plast Reconstr Surg. 2009;124(2):629–34.
115. Craft RO, Damjanovic B, Colwell AS. Evidence-based protocol for infection control in immediate implant-based breast reconstruction. Ann Plast Surg. 2012;69(4):446–50.
116. Ooi A, Song DH. Reducing infection risk in implant-based breast-reconstruction surgery: challenges and solutions. Breast Cancer (Dove Med Press). 2016;8:161–72.