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## Impact of Neoadjuvant Chemotherapy on Wound Complications after Breast Surgery

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### Abstract

**Background**—Use of neoadjuvant chemotherapy for breast cancer is increasing. The objective was to examine risk of post-operative wound complications in patients receiving neoadjuvant chemotherapy for breast cancer.

**Methods**—Patients undergoing breast surgery from 2005–2010 were selected from the American College of Surgeons National Surgical Quality Improvement Program database. Patients were included if pre-operative diagnosis suggested malignancy and an axillary procedure was performed. A stepwise multivariable regression analysis of predictors of post-operative wound complications, overall and stratified by breast surgery type, was performed. Our primary variable of interest was receipt of neoadjuvant chemotherapy.

**Results**—Of 44,533 patients, 4.5% received neoadjuvant chemotherapy. Wound complications were infrequent with or without neoadjuvant chemotherapy (3.4% vs. 3.1%,  $p=0.4$ ). Smoking, functional dependence, obesity, diabetes, hypertension and mastectomy were associated with wound complications. No association with neoadjuvant chemotherapy was seen (OR 1.01 [CI 0.78–1.32]). However, a trend towards increased complications in neoadjuvant patients undergoing mastectomy with immediate reconstruction (OR 1.58 [CI 0.98–2.58]) was observed.

**Conclusion**—Breast post-operative wound complications are infrequent and not associated with neoadjuvant chemotherapy. However, given the trend towards increased complications in patients undergoing mastectomy with immediate reconstruction, neoadjuvant chemotherapy should be one of many factors considered when making multidisciplinary treatment decisions.

### Keywords

breast cancer; neoadjuvant chemotherapy; post-operative complications; wound infection

### Background

Indications for neoadjuvant chemotherapy in the treatment of breast cancer are expanding <sup>(1)</sup>. Neoadjuvant chemotherapy provides the advantages of monitoring the *in situ* breast tumor for treatment response and the potential for breast conserving surgery (BCS) in patients with locally advanced breast cancer who otherwise may not have been candidates <sup>(2)</sup>. Given that both overall and disease-free survival are equivalent after neoadjuvant and adjuvant chemotherapy, neoadjuvant chemotherapy can be considered as a treatment option for any patient who is expected to require systemic treatment <sup>(3–5)</sup>.

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Therefore there is a need to improve understanding of the potential for post-operative complications in recipients of neoadjuvant chemotherapy.

A recent study assessing post-operative morbidity following breast cancer surgery demonstrated that the most frequent complication was wound infection<sup>(6)</sup>. Given that neutropenia is a common side effect of breast cancer chemotherapeutics<sup>(7)</sup>, this has raised concern that patients treated with neoadjuvant chemotherapy may be at increased risk for post-operative complications. This has been examined in several single institution series that have focused primarily on mastectomy with or without immediate reconstruction; in these studies, no increase in post-operative complications in patients treated with neoadjuvant chemotherapy was identified<sup>(8–11)</sup>. However, the conclusions of these retrospective studies conducted primarily at academic centers are limited by small sample size, exclusion of patients undergoing breast conservation, and lack of generalizability to community settings.

The objective of our study was to examine the risk of post-operative wound complications in patients receiving neoadjuvant chemotherapy for breast cancer using the American College of Surgeons – National Surgical Quality Improvement Program (ACS-NSQIP) database<sup>(12)</sup>. By using this prospectively collected multi-institutional dataset, we were able to examine the relationship between receipt of neoadjuvant chemotherapy and post-operative wound complications, stratified by type of surgical procedure, across multiple institutions reflecting a variety of settings. These results have the potential to influence the choice and sequencing of the multidisciplinary components of breast cancer treatment.

## Methods

### Data

The ACS-NSQIP is a quality improvement program that provides risk-adjusted surgical outcomes data to participating hospitals. In 2010, the ACS-NSQIP database included data contributed by 258 academic and community hospitals throughout the United States. Operative cases are selected using a systematic sampling process to minimize bias in case selection; in any 8-day sampling cycle, case selection is limited to no more than 3 breast lumpectomies. Pre-operative and intra-operative variables are collected via chart abstraction and other methods by a trained Surgical Clinical Reviewer. Thirty-day post-operative outcomes include complications, mortality, re-operation, and length of stay. A full description of the ACS-NSQIP program is available online<sup>(12)</sup>.

### Patient Cohort

We selected a cohort of patients who underwent 1) BCS (CPT codes: 19162, 19301, 19160, 19300, 19140, 19120, 19125, 19126), 2) mastectomy (CPT codes: 19307, 19306, 19305, 19302, 19240, 19220, 19200, 19304, 19303, 19182, 19180), or 3) mastectomy and reconstruction (CPT code: 19340 or codes for mastectomy plus 19340, 19342, 15734, 19350, 19357, 19360, 19361, 19364, 19366, 19367, 19368, or 19369) from the 2005–2010 ACS-NSQIP Participant Use Files. Patients were included if their pre-operative diagnoses included malignant neoplasm of the breast (ICD-9 diagnosis codes: 174.0 – 174.9), neoplasm of the breast (239.3), personal history of breast cancer (v.10.3), secondary breast cancer (198.81), ductal carcinoma in situ (233.0), breast lump or mass (611.72), or inflammatory breast disease (611.0).

To further limit our cohort to patients likely to have malignant disease (thereby eligible for neoadjuvant chemotherapy), patients were also required to have undergone either a sentinel lymph node biopsy (CPT codes: 38500, 38505, or 38525), or an axillary lymph node dissection (CPT codes: 38740, 38745 or codes for modified radical or radical mastectomy); patients who did not undergo an axillary staging procedure at the time of their breast

procedure were excluded. Finally, we excluded male breast cancer patients and any patients with metastatic cancer at the time of their breast cancer surgery.

## Outcomes

The primary outcome was wound complication. Wound complications were categorized as superficial surgical site infection, deep infection (including deep surgical site infection and organ space infection), and dehiscence. Although re-operation is considered a complication by the ACS-NSQIP, we excluded it from our study, as it is impossible to differentiate re-operation for positive margins or a positive sentinel lymph node from a true complication that requires return to the operating room.

## Variables

Our primary explanatory variable was receipt of neoadjuvant chemotherapy within 30 days of the operation. We also evaluated a number of preoperative factors including demographics (age, race), co-morbidities (diabetes mellitus, hypertension, congestive heart failure, chronic obstructive pulmonary disease, steroid use, bleeding disorder, history of cardiac surgery, history of stroke or transient ischemic event, open or infected wound), laboratory values (white blood cell count, hematocrit, platelets) and other factors (smoking, alcohol use, functional status, body mass index). Breast surgical procedure was categorized as BCS, mastectomy, or mastectomy with immediate reconstruction. Axillary surgery was categorized as either axillary lymph node dissection or sentinel lymph node biopsy; patients undergoing both procedures were included in the axillary lymph node dissection group.

## Data analysis

General summary statistics were generated to describe our cohort. A univariate analysis compared demographics, pre-operative, and operative variables between patients who did and did not receive neoadjuvant chemotherapy. The Mantel-Haenszel Chi-squared test and the Fisher's exact test were used to examine the relationship between the variables and the two chemotherapy groups. Variables having  $p \leq 0.1$  were considered for inclusion into a multivariable logistic regression model to further explore the association between chemotherapy and wound complications while adjusting for other factors. Multivariable models were built for the overall cohort, as well as stratified by type of breast surgery. All statistical analyses were performed using SAS v.9.2 (Cary, NC, USA).

## Results

A cohort of 44,533 patients was identified. Of these, 2,006 (4.5%) received neoadjuvant chemotherapy. Patient demographics, pre-operative and operative characteristics are presented in Table 1. Patients treated with neoadjuvant chemotherapy were younger and had less co-morbidities. However, they were more likely to smoke and to be overweight or obese. Additionally, neoadjuvant patients had more frequent steroid use and hematologic laboratory abnormalities.

Patients undergoing BCS were less likely to have been treated with neoadjuvant chemotherapy than those undergoing mastectomy (1.6% vs. 5.8%,  $p < 0.001$ ). Additionally, in those patients undergoing mastectomy, patients treated with neoadjuvant chemotherapy were less likely to receive immediate reconstruction (21.3% vs. 29.3%,  $p < 0.001$ ). Axillary lymph node dissections were more common in the neoadjuvant patient cohort (85.7% versus 48.2%,  $p < 0.001$ ).

As expected, short-term survival for patients was excellent, with an overall 30-day mortality of 0.06% (Table 2). 30-day morbidity was slightly lower in those patients receiving

neoadjuvant chemotherapy (5.6 vs. 7.0%,  $p = 0.01$ ). However, the wound complication rate was comparable between the two groups (3.4% vs. 3.1%,  $p = 0.4$ ), with a slightly higher rate of dehiscence in the neoadjuvant chemotherapy cohort (0.7% vs. 0.3%,  $p = 0.009$ ).

In the multivariable analysis, factors predictive of wound complications included smoking, functional dependence, being overweight or obese, diabetes, hypertension, and mastectomy (Table 3). Neoadjuvant chemotherapy was not significantly associated with wound complication on multivariable analysis (odds ratio 1.01, 95% confidence interval 0.78–1.32,  $p = 0.9$ ).

Because we anticipated that factors associated with wound complications would differ dramatically based on the surgical procedure performed, we performed a stratified analysis (Table 4). Patients undergoing BCS had a wound complication rate of 1.9%. In these patients, being overweight or obese, being functionally dependent, and undergoing an axillary lymph node dissection was associated with wound complications. Compared to patients undergoing BCS, patients undergoing mastectomy had a higher rate of wound complications (3.50% without reconstruction and 3.95% with immediate reconstruction). Factors associated with an increased risk of wound complications included smoking, being overweight or obese, and diabetes. For patients not undergoing immediate reconstruction, functional dependence and hypertension were also associated with increased risk of wound complication. Receipt of neoadjuvant chemotherapy was not significantly associated with an increased risk of wound complications regardless of surgery received. However, a trend towards increased wound complications was seen in those patients undergoing mastectomy with immediate reconstruction but this did not reach statistical significance (odds ratio 1.58, 95% confidence interval 0.98–2.58,  $p = 0.06$ ).

## Discussion

In this analysis of the ACS-NSQIP database, we confirmed the findings from prior studies demonstrating that wound complications after breast cancer surgery are infrequent (4%). Wound complication rates do vary by type of surgical procedure performed, with the lowest rates observed after BCS (1.9%) and the highest after mastectomy with reconstruction (4.0%). As expected, factors associated with wound complications also varied by type of surgical procedure. For patients undergoing BCS, age, obesity, functional dependence, and undergoing a concurrent axillary lymph node dissection were associated with increased risk. For patients undergoing mastectomy, factors differed. Some of the observed factors, such as obesity, smoking, and hypertension, have been noted in prior studies<sup>(6, 13)</sup>. However, we also identified functional dependence and diabetes as increasing risk; these factors have not previously been reported. However, regardless of type of surgery received, use of neoadjuvant chemotherapy did not significantly increase the risk of wound complications.

Concern regarding the theoretical increased risk of wound complications after the receipt of neoadjuvant chemotherapy has existed within the breast surgery community for some time. In response to early concerns, MD Anderson Cancer Center developed a protocol regarding timing of surgery for recipients of pre-operative chemotherapy. Under their “strict operative criteria”, all patients treated with neoadjuvant chemotherapy had to have a resectable tumor, white blood cell count greater than 2500 cells/mm<sup>3</sup>, and platelet count greater than 50,000 cells/mm<sup>3</sup> prior to mastectomy<sup>(9)</sup>. This early single-institution study demonstrated that post-mastectomy morbidity in patients who received pre-operative chemotherapy was no different from patients who did not have pre-operative chemotherapy. Since that time, several studies have reported similar findings<sup>(8–11, 14)</sup>; in these studies, “strict operative criteria” as reported by the MD Anderson group were not required. The findings of our study further corroborate the conclusions of these single-institution, retrospective studies.

Recently, there has been growing interest in outcomes after neoadjuvant chemotherapy and mastectomy with immediate reconstruction. Two single institution studies of patients who underwent mastectomy and immediate reconstruction found no significant difference in complication rates between patients who received neoadjuvant chemotherapy and those who did not<sup>(8, 11)</sup>. Although we did not identify a statistically significant association between receipt of neoadjuvant chemotherapy and wound complications after mastectomy with immediate reconstruction, a trend was observed. This is noteworthy given the selection bias apparent in our patients undergoing immediate reconstruction after neoadjuvant chemotherapy. Patients selected for immediate reconstruction after neoadjuvant chemotherapy were younger and overall “healthier” than those who underwent mastectomy alone. Despite this, a trend towards increased wound complications after neoadjuvant chemotherapy and immediate reconstruction was noted. This may be a direct result of the chemotherapy received. However, other clinical data unavailable in the ACS-NSQIP dataset, including cancer stage and receipt of post-mastectomy radiation, may also impact patients’ risk of wound complications. Given the available data, we cannot conclude that expanding the use of immediate reconstruction to all patients who undergo neoadjuvant chemotherapy would be acceptable. However, our data does support the conclusion that neoadjuvant chemotherapy recipients selected by their surgeons to be a good candidate for immediate reconstruction can be expected to have good post-operative outcomes.

Several limitations exist for our study. First, patients in our study were not randomized to either timing of chemotherapy or to type of surgery performed, and as a result selection bias inevitably exists. Differences between the patient groups were evident for a number of factors, including age and co-morbidities, and multivariable logistic regression was used to adjust for this. Other variables relevant to patient selection, such as cancer stage, were not available in our dataset and remain unaccounted for in this analysis.

Additionally, the sampling strategy utilized by the NSQIP under-samples patients undergoing BCS compared to mastectomy; this is reflected in our BCS rate of 31%, which is lower than what has been reported for the United States population<sup>(15, 16)</sup>. However, because we are not reporting on rates of surgery, but rather complications according to surgery type, this difference should not impact the conclusions of our study. Similarly, our reported rates of wound complications are lower than complication rates reported in other series<sup>(8, 10)</sup> especially after breast reconstruction; this likely relates to the definitions of complications used. As the ACS-NSQIP is a quality improvement program largely designed to evaluate outcomes after general and vascular surgery, disease specific complications that would be relevant to breast cancer surgery (such as seroma aspiration or delay of chemotherapy) are not collected. This likely explains the difference between the rates reported in our study and other single-institution series.

Next, it is possible that our cohort of neoadjuvant chemotherapy recipients is incomplete. In the ACS-NSQIP, chemotherapy received in the 30 days prior to surgery is recorded and this variable was used to define our neoadjuvant cohort. It is possible that some neoadjuvant patients had a longer interval between the end of chemotherapy and surgery, and therefore may have been misclassified. Currently, no standard exists for the optimal interval between chemotherapy and surgery. However, one recently published randomized controlled trial described surgery between 14 and 28 days after chemotherapy<sup>(2)</sup> and another study reported a median 27 day interval<sup>(9)</sup>. This suggests that the majority of our cohort was appropriately categorized.

Finally, we were underpowered to detect small differences in wound complication rates; over 60,000 neoadjuvant chemotherapy patients would have been required to achieve a power of 80%. However, wound complication rates were low, even for the group who

underwent mastectomy with reconstruction. We therefore believe that a clinically meaningful difference is unlikely to be observed with additional patients.

Although limitations exist to our study, these results currently represent the most comprehensive evaluation of neoadjuvant chemotherapy and post-operative wound complications following the surgical treatment of local-regional breast cancer. By using the ACS-NSQIP database, we were able to examine the outcomes from a multi-institutional cohort representing a range of community and academic surgical practices. Additionally, we had the benefit of prospectively collected and validated pre-operative and operative variables; this allowed us to control for both previously described risk factors for wound complications (including obesity, smoking, axillary dissection, and mastectomy) (6, 13, 17, 18) as well as other unique factors. One of the greatest strengths of our study, however, is the rigorous methodology applied to collection of post-operative complications by the ACS-NSQIP. This increases the reliability and validity of our conclusions.

## Conclusions

In conclusion, we demonstrated that the rate of wound complications for breast cancer patients undergoing neoadjuvant chemotherapy is low, at 3.4%. In our multivariable model, a number of previously identified factors, including smoking, hypertension, and obesity were associated with an increased risk of wound complications for patients undergoing mastectomy. However, receipt of neoadjuvant chemotherapy was not associated with an increased risk of wound complications.

Although it did not reach statistical significance, a trend towards increased risk of wound complications after mastectomy and immediate reconstruction for patients who received neoadjuvant chemotherapy was observed. This was observed despite the evident selection bias in patients who were chosen to undergo immediate reconstruction. Although the association between neoadjuvant chemotherapy and post-operative wound complications was much less strong than that observed for other clinical factors (especially obesity), it represents one of many factors that must be considered by surgeons when making recommendations for immediate reconstruction in patients who have received neoadjuvant chemotherapy.

## References

1. Kaufmann M, von Minckwitz G, Bear HD, Buzdar A, McGale P, Bonnefoi H, et al. Recommendations from an international expert panel on the use of neoadjuvant (primary) systemic treatment of operable breast cancer: new perspectives 2006. *Ann Oncol.* 2007 Dec 1; 18(12):1927–34. [PubMed: 17998286]
2. Loibl S, von Minckwitz G, Raab G, Blohmer J-U, Dan Costa S, Gerber B, et al. Surgical procedures after neoadjuvant chemotherapy in operable breast cancer: results of the GEPAR DUO trial. *Ann Surg Oncol.* 2006 Nov 1; 13(11):1434–42. [PubMed: 16983592]
3. Rastogi P, Anderson SJ, Bear HD, Geyer CE, Kahlenberg MS, Robidoux A, et al. Preoperative chemotherapy: updates of National Surgical Adjuvant Breast and Bowel Project Protocols B-18 and B-27. *J Clin Oncol.* 2008 Feb 10; 26(5):778–85. [PubMed: 18258986]
4. Waljee JF, Newman LA. Neoadjuvant systemic therapy and the surgical management of breast cancer. *Surg Clin North Am.* 2007 Apr 1; 87(2):399–415. ix. [PubMed: 17498534]
5. Mauri D, Polyzos NP, Salanti G, Pavlidis N, Ioannidis JPA. Multiple-treatments meta-analysis of chemotherapy and targeted therapies in advanced breast cancer. *J Natl Cancer Inst.* 2008 Dec 17; 100(24):1780–91. [PubMed: 19066278]
6. El-Tamer MB, Ward BM, Schiffner T, Neumayer L, Khuri S, Henderson W. Morbidity and mortality following breast cancer surgery in women: national benchmarks for standards of care. *Ann Surg.* 2007 May 1; 245(5):665–71. [PubMed: 17457156]

7. Bear HD, Anderson S, Brown A, Smith R, Mamounas EP, Fisher B, et al. The effect on tumor response of adding sequential preoperative docetaxel to preoperative doxorubicin and cyclophosphamide: preliminary results from National Surgical Adjuvant Breast and Bowel Project Protocol B-27. *J Clin Oncol*. 2003 Nov 15; 21(22):4165–74. [PubMed: 14559892]
8. Warren Peled A, Itakura K, Foster RD, Hamolsky D, Tanaka J, Ewing C, et al. Impact of chemotherapy on postoperative complications after mastectomy and immediate breast reconstruction. *Arch Surg*. 2010 Sep 1; 145(9):880–5. [PubMed: 20855759]
9. Broadwater JR, Edwards MJ, Kuglen C, Hortobagyi GN, Ames FC, Balch CM. Mastectomy following preoperative chemotherapy. Strict operative criteria control operative morbidity. *Ann Surg*. 1991 Feb 1; 213(2):126–9. [PubMed: 1992938]
10. Hu Y-Y, Weeks CM, In H, Dodgion CM, Golshan M, Chun YS, et al. Impact of neoadjuvant chemotherapy on breast reconstruction. *Cancer*. 2011 Jul 1; 117(13):2833–41. [PubMed: 21264833]
11. Azzawi K, Ismail A, Earl H, Forouhi P, Malata CM. Influence of neoadjuvant chemotherapy on outcomes of immediate breast reconstruction. *Plast Reconstr Surg*. 2010 Jul 1; 126(1):1–11. [PubMed: 20595827]
12. American College of Surgeons. [Accessed December 31, 2011] National Surgical Quality Improvement Initiative. [database on the Internet]. [cited December 2011]. Available from: <http://www.acsnsqip.org>
13. McCarthy CM, Mehrara BJ, Riedel E, Davidge K, Hinson A, Disa JJ, et al. Predicting complications following expander/implant breast reconstruction: an outcomes analysis based on preoperative clinical risk. *Plast Reconstr Surg*. 2008 Jun 1; 121(6):1886–92. [PubMed: 18520873]
14. Deutsch MF, Smith M, Wang B, Ainsle N, Schusterman MA. Immediate breast reconstruction with the TRAM flap after neoadjuvant therapy. *Ann Plast Surg*. 1999 Mar 1; 42(3):240–4. [PubMed: 10096612]
15. Greenberg CC, Lipsitz SR, Hughes ME, Edge SB, Theriault R, Wilson JL, et al. Institutional variation in the surgical treatment of breast cancer: a study of the NCCN. *Ann Surg*. 2011 Aug 1; 254(2):339–45. [PubMed: 21725233]
16. Morrow M, Jagsi R, Alderman AK, Griggs JJ, Hawley ST, Hamilton AS, et al. Surgeon recommendations and receipt of mastectomy for treatment of breast cancer. *JAMA: The Journal of the American Medical Association*. 2009 Oct 14; 302(14):1551–6. [PubMed: 19826024]
17. Khansa I, Colakoglu S, Curtis MS, Yueh JH, Ogunleye A, Tobias AM, et al. Postmastectomy breast reconstruction after previous lumpectomy and radiation therapy: analysis of complications and satisfaction. *Ann Plast Surg*. 2011 May 1; 66(5):444–51. [PubMed: 21451371]
18. Nahabedian MY, Tsangaris T, Momen B, Manson PN. Infectious complications following breast reconstruction with expanders and implants. *Plast Reconstr Surg*. 2003 Aug 1; 112(2):467–76. [PubMed: 12900604]

**Table 1**

Patient Demographic Pre-operative and Operative Characteristics

Variable	Neoadjuvant Chemotherapy (N=2006)		No Neoadjuvant Chemotherapy (N=42527)		P value
	N	%	N	%	
<b>Demographics</b>					
Age in years [mean (SD)]	52.1 (12.0)		59.63 (13.1)		<0.0001
Race/ethnicity					
White	1362	67.9	30663	72.1	<0.0001
Black	256	12.8	4314	10.1	
Other	224	11.2	3874	9.1	
Missing	164	8.2	3676	8.6	
<b>Preoperative health and co-morbidities</b>					
Current smoker	323	16.1	6114	14.4	0.032
Alcohol use (>2 drinks per day)	13	0.7	636	1.5	0.002
Functional status: partial/fully dependent	22	1.1	582	1.4	0.304
Body Mass Index classification					
Normal weight	596	29.7	13842	32.6	0.001
Underweight	41	2.0	998	2.4	
Overweight/Obese	1367	68.2	27536	64.8	
Diabetes Mellitus	111	5.5	3726	8.8	<0.0001
Chronic Obstructive Pulmonary Disease	24	1.2	1133	2.7	<0.0001
Previous cardiac surgery	13	0.7	768	1.8	0.0001
Congestive heart failure	8	0.4	77	0.2	0.029
Hypertension (requiring medication)	602	30.0	18209	42.8	<0.0001
History of transient ischemic attack	15	0.8	773	1.8	0.0004
Steroid use	79	3.9	515	1.2	<0.0001
Bleeding disorder	55	2.7	675	1.6	<0.0001
Open or infected wound	31	1.6	272	0.6	<0.0001
<b>Preoperative Lab Values</b>					



Variable	Neoadjuvant Chemotherapy (N=2006)		No Neoadjuvant Chemotherapy (N=42527)		P value
	N	%	N	%	
White Blood Cell count >11 or <4.5	650	32.4	4387	10.3	<0.0001
Missing	141	7.0	7513	17.7	
Hematocrit <38	1473	73.4	11128	26.2	<0.0001
Missing	115	5.7	6707	15.8	
Platelet count <150 or >400	226	11.3	2258	5.3	<0.0001
Missing	146	7.3	7565	17.8	
<b>Operative Variables</b>					
American Society of Anesthesiologists class					
No disturbance	48	2.4	3029	7.1	<0.0001
Mild disturbance	1234	61.5	26898	63.3	
Severe disturbance	706	35.2	12057	28.4	
Life-threatening disturbance	16	0.8	499	1.2	0.003
Blood transfusion	15	0.8	112	0.3	
Wound Class					
Clean	1930	96.2	41574	97.8	<0.0001
Clean-contaminated/dirty/infected	76	3.8	953	2.2	
<b>Type of Surgery</b>					
Breast Conserving surgery	220	11.0	13571	31.9	<0.0001
Mastectomy	1406	70.1	20482	48.2	
Mastectomy with Immediate Reconstruction	380	18.9	8474	19.9	
Axillary lymph node dissection	1720	85.7	20477	48.2	<0.0001
Sentinel lymph node biopsy	286	14.3	22050	51.9	

**Table 2**

Frequency of post-operative complications, with and without neoadjuvant chemotherapy

Outcome variable	Neoadjuvant Chemotherapy		No Neoadjuvant chemotherapy		P value
	N = 2006	%	N = 42527	%	
30-day Mortality	4	0.20	23	0.05	0.032
30-day Morbidity	112	5.6	2989	7.0	0.013
Overall wound complication	60*	3.4	1304*	3.1	0.413
Superficial infection	37	1.8	851	2.0	0.624
Dehiscence	13	0.65	119	0.28	0.009
Deep infection/abscess	20	1.0	376	0.88	0.544

\* Some patients experienced more than one type of wound complication.

**Table 3**

Multivariable model of factors associated with wound complications in patients undergoing breast cancer surgery

Factor	N (%)N = 44533	Adjusted Odds Ratio	95% Confidence Interval	P value
Neoadjuvant chemotherapy	2006 (4.5%)	1.00	0.77 – 1.31	0.973
Age		1.00	0.99–1.00	0.252
<i>Race</i>				
White	32025 (71.9%)	1.00	Reference	
Black	4570 (10.3%)	0.82	0.65–0.98	0.431
Other	4098 (9.2%)	0.80	0.65–0.98	0.229
Smoker	6437 (14.5%)	1.56	1.35–1.80	<0.0001
Partial/fully dependent	604 (1.4%)	2.02	1.43–2.88	<0.0001
Overweight/obese	28903 (64.9%)	2.16	1.87–2.50	<0.0001
Diabetes mellitus	3837 (8.6%)	1.57	1.33–1.85	<0.0001
Hypertension	18811 (42.2%)	1.25	1.10–1.43	0.001
<i>Type of Breast Surgery</i>				
Breast conserving surgery	13791 (31.0%)	1.00	Reference	
Mastectomy	21888 (49.2%)	1.82	1.54–2.16	0.034
Mastectomy + reconstruction	8854 (19.9%)	2.51	2.09–3.02	<0.0001
Axillary lymph node dissection *	22197 (49.8%)	1.00	0.88–1.14	0.945

\* Analysis performed using sentinel lymph node biopsy as the reference

**Table 4**

Stratified Multivariable model of factors associated with wound complications in patients undergoing breast cancer surgery

<b>4a. Breast Conserving Surgery</b>				
<b>Factor</b>	<b>N (%) N=13791</b>	<b>Adjusted Odds Ratio</b>	<b>95% Confidence Interval</b>	<b>P value</b>
Neoadjuvant Chemotherapy	220 (1.6%)	0.43	0.10–1.75	0.236
Age	-	0.99	0.98–1.00	0.032
<i>Race</i>				
White	10232 (74.2%)	1.00	Reference	
Black	1320 (9.6%)	1.22	0.84–1.78	0.363
Other	1047 (7.6%)	1.02	0.64–1.63	0.739
Smoker	1849 (13.4%)	1.12	0.78–1.61	0.536
Partial/fully dependent	98 (0.7%)	3.16	1.25–7.95	0.015
Overweight/obese	9299 (67.4%)	2.14	1.51–3.01	<0.0001
Diabetes mellitus	1107 (8.0%)	1.33	0.89–2.00	0.167
Hypertension	6202 (45.0%)	1.14	0.85–1.53	0.398
Axillary lymph node dissection*	1663(12.1%)	1.56	1.10–2.20	0.012
<b>4b. Mastectomy</b>				
<b>Factor</b>	<b>N (%) N=21888</b>	<b>Adjusted Odds Ratio</b>	<b>95% Confidence Interval</b>	<b>P value</b>
Neoadjuvant Chemotherapy	1406 (6.4%)	0.94	0.68–1.30	0.706
Age	-	1.00	0.99–1.00	0.242
<i>Race</i>				
White	15124 (69.1%)	1.00	Reference	
Black	2620 (12.0%)	0.74	0.59–0.94	0.254
Other	2317 (10.6%)	0.74	0.56–0.97	0.285
Smoker	3368 (15.4%)	1.68	1.39–2.02	<0.0001
Partial/fully dependent	481 (2.2%)	2.01	1.37–2.97	0.0004
Overweight/obese	14737 (67.3%)	1.86	1.53–2.26	<0.0001
Diabetes mellitus	2401 (11.0%)	1.60	1.30–1.96	<0.0001
Hypertension	10483 (47.9%)	1.32	1.11–1.58	0.002
Axillary lymph node dissection*	15992 (73.1%)	0.90	0.76–1.58	0.245
<b>4c. Mastectomy with Immediate Reconstruction</b>				
<b>Factor</b>	<b>N (%) N=8854</b>	<b>Adjusted Odds Ratio</b>	<b>95% Confidence Interval</b>	<b>P value</b>
Neoadjuvant Chemotherapy	380 (4.3%)	1.58	0.98–2.58	0.062
Age	-	1.01	1.00–1.02	0.209
<i>Race</i>				
White	6669 (75.3%)	1.00	Reference	
Black	630 (7.1%)	0.76	0.51–1.15	0.510
Other	734 (8.3%)	0.78	0.51–1.21	0.652
Smoker	1220 (13.8%)	1.60	1.21–2.14	0.001

<b>4a. Breast Conserving Surgery</b>				
<b>Factor</b>	<b>N (%) N=13791</b>	<b>Adjusted Odds Ratio</b>	<b>95% Confidence Interval</b>	<b>P value</b>
Partial/fully dependent	25 (0.3%)	0.90	0.12–6.94	0.921
Overweight/obese	4867 (55.0%)	2.86	2.17–3.77	<0.0001
Diabetes mellitus	329 (3.7%)	1.86	1.22–2.84	0.004
Hypertension	2126 (24.0%)	1.16	0.89–1.52	0.263
Axillary lymph node dissection *	4542 (51.3%)	1.01	0.80–1.26	0.949

\* Analysis performed using sentinel lymph node biopsy as the reference