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## Postoperative Outcomes After Staged vs. Coordinated Breast Surgery and Bilateral Salpingo-oophorectomy

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## Abstract

**Background/Objective:** The objective of this study was to compare postoperative complication rates and healthcare charges between patients who underwent coordinated versus staged breast surgery and bilateral salpingo-oophorectomy (BSO).

**Methods:** The MarketScan<sup>®</sup> administrative database was used to identify adult female patients with invasive breast cancer or BRCA1/BRCA2 mutations who underwent BSO and breast surgery (lumpectomy or mastectomy with or without reconstruction) between 2010 and 2015. Patients were assigned to the coordinated group if a breast operation and BSO were performed simultaneously or the staged group if BSO was performed separately. Primary outcomes were (1) incidence of 90-day postoperative complications and (2) 2-year aggregate perioperative healthcare

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charges. Fisher's exact tests, Wilcoxon Rank-Sum tests, and multivariable regression analyses were performed.

**Results:** Of the 4228 patients who underwent breast surgery and BSO, 412 (9.7%) were in the coordinated group and 3816 (90.3%) were in the staged group. The coordinated group had a higher incidence of postoperative complications (24.0% vs. 17.7%; p<0.01), higher risk-adjusted odds of postoperative complications (OR 1.37, 95% CI 1.06-1.76; p=0.02), and similar aggregate healthcare charges before (median charges: \$106,500 vs. \$101,555; p=0.96) and after risk-adjustment (IRR 1.00; 95% CI 0.93-1.07; p=0.95). In a subgroup analysis, incidence of postoperative complications (12.9% for coordinated operations vs. 11.7% for staged operations; p=0.73) was similar in patients whose breast operation was a lumpectomy.

**Conclusions:** While costs were similar, coordinating breast surgery with BSO was associated with more complications in patients who underwent mastectomy but not in patients who underwent lumpectomy. These data should inform shared decision-making in high-risk patients.

#### **Keywords**

Risk-reducing surgery; mastectomy; salpingo-oophorectomy; coordinated surgery

## Introduction:

In patients with pathogenic BRCA 1 and 2 mutations, risk-reducing bilateral salpingooophorectomy (BSO) is recommended between the ages of 35-45, and may decrease the lifetime risk of ovarian cancer by up to 96%<sup>1</sup>. Similarly, risk-reducing bilateral mastectomy may also be offered to these high-risk women with or without breast cancer and may decrease their lifetime risk of new or recurrent breast cancer by up to 95%<sup>2</sup>. Having both breast and gynecologic procedures results in an estimated 1.1-to 4.2-year increase in life expectancy<sup>3-9</sup>. Furthermore, prior studies suggest an association of risk-reducing BSO with improved survival<sup>10</sup>, mitigation of risk for in-breast tumor recurrence<sup>11</sup>, and reduced risk of contralateral breast cancer<sup>12</sup> in patients with pathogenic mutations and invasive breast cancer who choose to undergo breast conserving surgery as a definitive oncologic operation. Given the health consequences of risk-reducing BSO, which include early menopause, the possible desire for future fertility, and patient concern for surgical complications, patients may elect to stage breast operations and BSO, while others choose to undergo both surgeries in a single, coordinated operation.

Coordinated procedures offer the benefits of fewer operative and anesthetic events as well as a single, consolidated recovery period<sup>13</sup>. However, prior studies investigating postoperative outcomes after coordinated breast and gynecologic operations have published mixed results, with some suggesting higher complication rates while others reporting similar rates<sup>14-17</sup>. Moreover, the impact of coordinating breast and gynecologic operations on cost is not well understood. Using the MarketScan<sup>®</sup> database, we therefore sought to: (1) evaluate postoperative outcomes in patients who underwent coordinated breast surgery and BSO versus staged operations and (2) compare total healthcare charges between these two groups.

## Methods:

#### Data Source:

International Classification of Diseases–9 (ICD-9) diagnostic codes were used to identify adult female patients within the MarketScan<sup>®</sup> database with a diagnosis of invasive breast cancer or BRCA1 or BRCA2 mutation who underwent BSO and either lumpectomy or mastectomy between 2010 and 2015. MarketScan<sup>®</sup> contains approximately 215 million unique individuals in the United States who have different forms of employer-based insurance and captures longitudinal data from inpatient admissions, outpatient services, pharmaceutical claims, and annual enrollment. All data obtained from the MarketScan<sup>®</sup> for this purpose were de-identified and thus, this work was exempt from Institutional Review Board review.

#### **Study Procedures:**

Patients were assigned to the coordinated group if a simultaneous double-site surgery was performed. A double-site surgery was defined as a coordinated single-day operation including BSO with either mastectomy, delayed post-mastectomy breast reconstruction, lumpectomy, or delayed post-lumpectomy breast reconstruction. Patients were assigned to the staged group if the BSO was performed without a concurrent breast operation. Common Procedural Terminology (CPT) codes from the primary or secondary procedures were used to identify patients undergoing mastectomy, post-mastectomy breast reconstruction, lumpectomy, post-lumpectomy breast reconstruction, and BSO. In administrative datasets such as MarketScan<sup>®</sup>, the service and admission dates associated with billing codes may not reflect the actual date of the procedure. Thus we included patients in the coordinated group if the BSO and breast surgery procedure codes were within 7 days of each other under that assumption that two elective procedures performed within a 7-day span were more likely to have been coordinated procedures.

## Evaluation of postoperative complications:

Demographic, clinical, and treatment factors collected from the MarketScan<sup>®</sup> database included age (18-45, 45-55, >55), region of surgery (Northeast, North-central, South, and West), year of surgery (2010-2015), diagnosis of breast cancer within the year preceding surgery, type of reconstruction (none, post-lumpectomy breast reconstruction, immediate implant placement, delayed implant placement, autologous tissue-based reconstruction, and unspecified reconstruction, surgical approach for BSO (laparoscopic vs. open), concurrent hysterectomy, concurrent axillary lymph node dissection, administration of neoadjuvant or adjuvant chemotherapy, use of adjuvant endocrine therapy, and Elixhauser comorbidity index. Race and ethnicity data were not readily available for all patients in the MarketScan<sup>®</sup> database and thus could not be reliably reported here. The primary outcome was presence of any of the following postoperative complications within 90 days of surgery: surgical site infections of either the breast or abdomen, postoperative seroma, hematoma, wound dehiscence, implant removal, blood transfusion, postoperative ileus, cardiac adverse events, pulmonary adverse events, and venous thromboembolic events. A list of all procedural and diagnostic codes used in this study is included in Appendix A. For the staged group,

complications were tracked for 90 days from each operation for a total follow up time of up to 180 days. If there were fewer than 90 days between the first and second operation, the time period during which complications were measured was the entire duration between the first and second operation and 90 days after the second operation.

#### Evaluation of perioperative costs:

Aggregate healthcare charges over the span of 2 years were compiled using the MarketScan<sup>®</sup> inpatient and outpatient billing databases. For both the staged and coordinated groups, the two-year period began on the date of the first operation and was inclusive of both the mastectomy and BSO events. Patients were excluded from this analysis if they did not have two full years of postoperative follow-up data available in this MarketScan<sup>®</sup> dataset. The overall outcome for perioperative costs was the sum of all inpatient, outpatient, and prescription drug charges during the measurement period.

#### **Statistical Analysis:**

Baseline demographic and clinical factors for each group were compared using chi-squared tests. Incidence of postoperative complications were compared using Fisher's exact tests and a multivariable logistic regression was fit to estimate the adjusted odds ratio [OR] of experiencing a postoperative complication while controlling for age, region of surgery, breast cancer diagnosis, year of surgery, reconstruction type, surgical approach for BSO, concurrent hysterectomy, concurrent axillary lymphadenectomy, systemic therapy receipt, and comorbidity index. Total healthcare charges, which had a nonparametric distribution, were compared using the Wilcoxon rank-sum test. Finally, while treating dollars as count data<sup>18</sup>, a negative binomial regression was fit to estimate the incidence rate ratio of healthcare charges while controlling for the same criteria described above. All statistical analyses were performed using SAS (SAS Institute, Cary, NC, USA). All tests were two-tailed; the threshold for statistical significance was p<0.05.

## Results:

#### **Demographic and Clinical Factors:**

A total of 4228 patients with invasive breast cancer or BRCA 1 or 2 mutation who underwent both a breast operation and BSO between 2010 and 2015 were identified within the MarketScan<sup>®</sup> database. Of these patients, 412 patients (9.7%) had coordinated operations, while 3816 (90.3%) had staged operations. Demographic and clinical factors stratified between the two groups are shown in Table 1. The two groups were similar in terms of age and region of surgery, Elixhauser Comorbidity Index score, and proportions receiving laparoscopic BSO, axillary lymphadenectomy, adjuvant chemotherapy, and adjuvant endocrine therapy. Compared to the coordinated group, the staged group had higher proportions of patients: with a breast cancer diagnosis (98.7% vs. 97.1%; p<0.02), whose operation was performed prior to 2013 (66.5% vs 61%; p<0.01), who received a lumpectomy (34.8% vs 20.6%; p<0.01), who had no breast reconstruction operation (53.1% vs 32.3%; p<0.01), and who had a concurrent hysterectomy with BSO (55% vs 34%; p<0.01). A higher proportion of patients in the coordinated group received neoadjuvant chemotherapy (16.5% vs 11.5%; p=0.02).

After excluding 1365 patients without two years of follow up data, a total of 2863 patients were included in the cost analysis, 321 (11.2%) in the coordinated group and 2542 (88.8%) in the staged group. Demographic and clinical factors stratified between the two groups in the sub-analysis are shown in Table 2. The two groups were similar in terms of age, year and region of surgery, Elixhauser comorbidity score, and proportions receiving lumpectomy, laparoscopic BSO, concurrent hysterectomy with BSO, axillary lymphadenectomy, adjuvant chemotherapy, and adjuvant endocrine therapy. Compared to the coordinated group, the staged group had higher proportions of patients with a breast cancer diagnosis (98.9% vs. 97.2%; p=0.03), who received a lumpectomy (33.9% vs 19.3%; p<0.01), who had no breast reconstruction operation (45.7% vs 33%; p<0.01), and who had a concurrent hysterectomy with BSO (52.5% vs 32.7%; p<0.01). A higher proportion of patients in the coordinated group received neoadjuvant chemotherapy (26.5% vs 15.1%; p<0.01).

#### **Postoperative Complications:**

When lumpectomy and mastectomy patients were analyzed together, total complication rates were higher in those who underwent coordinated rather than staged procedures (24.0% vs. 17.7%; p<0.01). When stratified by complication type, the coordinated group had a higher rate of surgical site infections of the breast or abdomen (10.9% vs 6.5%; p<0.01), postoperative seroma formation (8.0% vs 5.5%; p=0.045) and venous thromboembolic events (2.4% vs 1.0%; p=0.02) compared to the staged group. The rates of hematoma, wound dehiscence, implant removal, blood transfusion, postoperative ileus, and major cardiac or pulmonary adverse events were similar between cohorts, as shown in Table 3.

Among all patients, post-mastectomy breast reconstruction with autologous tissue (OR 1.93, 95% confidence interval [CI] 1.36-2.75; p<0.01) or with a delayed implant (OR 1.27, 95% CI 1.02-1.57; p=0.03), post-lumpectomy reconstruction (OR 1.62, 95% CI 1.05-2.50; p=0.03), and concurrent hysterectomy (OR 1.22, 95% CI 1.03-1.45; p=0.02) were associated with a higher risk of complications, along with Elixhauser comorbidity score >3 (OR 1.73, 95% CI 1.45-2.07; p<0.01) and adjuvant chemotherapy receipt (OR 1.21, 95% CI 1.02-1.44; p=0.03). When controlling for these factors along with age, year and region of surgery, breast surgery type, BSO approach, and endocrine therapy receipt, coordinated procedures were associated with a higher rate of complications (OR 1.37, 95% CI 1.06-1.76; p=0.02), as shown in Appendix B.

A subgroup analysis stratified by breast surgery (lumpectomy vs. mastectomy) is shown in Table 4. Complication rates were similar among the 1,413 lumpectomy patients undergoing coordinated (12.9%) vs. staged procedures (11.7%). Importantly, lumpectomy receipt (OR 0.55, 95% CI 0.43-0.70; p<0.01) was associated with a lower adjusted odds of complications in the multivariable regression. Among the 2,815 who received mastectomy, complication rates were significantly higher in the coordinated group (26.9% vs. 20.9%, p=0.01).

#### Perioperative and postoperative costs:

Median healthcare charges across this period were \$106,500 (interquartile range [IQR] \$59,738-\$166,289) for the coordinated group and \$101,555 (IQR \$65,950-162,980) for the staged group (p=0.96), as shown in Table 5. When looking at factors that influenced

healthcare charges, comorbidity index >3 (rate ratio [RR] 1.10, 95% CI 1.04-1.16; p<0.01), breast cancer diagnosis (RR 1.27, 95% CI 1.05-1.53; p=0.01), axillary node dissection (RR 1.16, 95% CI 1.11-1.22; p<0.01), adjuvant chemotherapy receipt (RR 1.82, 95% CI 1.74-1.91; p<0.01), and adjuvant endocrine therapy receipt (RR 113, 95% CI 1.07-1.21; p<0.01) were associated with higher perioperative healthcare charges. Furthermore, post-lumpectomy breast reconstruction (RR 1.26, 95% CI 1.13-1.40; p<0.01) and post-mastectomy breast reconstruction with autologous tissue (RR 1.52, 95% CI 1.38-1.69; p<0.001), delayed implant placement (RR 1.18, 95% CI 1.10-1.25; p<0.01) or immediate implant placement (RR 1.10, 95% CI 1.00-1.21; p=0.047) were associated with increased healthcare charges compared to no breast reconstruction. Conversely, a laparoscopic approach to BSO (RR 0.92, 95% CI 0.87-0.97; p<0.01) was associated with decreased healthcare charges. Adjusting for these factors along with age, year and region of surgery, breast surgery type, and hysterectomy receipt, the perioperative healthcare charges associated with staged vs. coordinated operations were similar (RR 1.00, 95% CI 0.93-1.07; p=0.95), as shown in Appendix C.

## **Discussion:**

In this retrospective review of a large claims database of patients with pathogenic genetic mutations or breast cancer diagnoses, we compared 90-day complication rates between patients receiving coordinated vs. staged approaches to combined breast surgery and risk-reducing BSO. We found that among all patients or those undergoing mastectomy, complication rates were higher in those undergoing coordinated procedures, but complication rates appeared to be similar in those undergoing coordinated or staged lumpectomy with BSO. Notably, both approaches were similar in cost. In an era of expanded genetic testing and fertility preservation options, these data are important to consider during preoperative shared decision-making, particularly in patients with breast cancer requiring adjuvant therapy, with comorbid conditions, or who plan to undergo concurrent hysterectomy or breast reconstruction.

Several prior studies have evaluated the safety of coordinated breast and gynecologic operations. In a retrospective review of 73 patients who underwent concurrent breast and gynecologic operations, Ma et al reported that 37% of patients had a postoperative complication within 30 days of surgery and 7% of patients had a postoperative complication beyond 30 days after surgery<sup>19</sup>. In another review of 464 patients who underwent free flap breast reconstruction, Del Corral et al did not find any differences in incidence of postoperative complications in 42 patients who had undergone a concurrent gynecologic operation with breast reconstruction compared to 422 patients who had breast reconstruction alone<sup>16</sup>. Furthermore, in a review of 537 patients who underwent breast reconstruction, Jayraman et al found that there were no differences in rate of complications between 39 patients who had mastectomy and implant-based reconstruction performed in conjunction with a gynecologic procedure compared to the 498 patients who underwent mastectomy and implant-based reconstruction alone<sup>15</sup>. More recently, Elmi et al published a retrospective analysis of 5470 patients within the NSQIP database who underwent risk-reducing mastectomy and demonstrated similar rates of 30-day morbidity and postoperative infections in the 149 patients who had a concurrent BSO compared to the group that had mastectomy

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alone both on univariate and multivariable analyses<sup>17</sup>. However, these cohort studies contained fewer patients with coordinated operations than our analysis. A larger review of 77,154 patients in the NSQIP database who underwent breast surgery showed a 2-fold increase in complications associated with coordinated breast, plastic, and gynecologic surgeries compared to single-site breast operations<sup>14</sup>.

Most of the existing literature has compared coordinated breast and gynecologic operations to single-site breast operations rather than staged breast and gynecologic operations. These studies may not account for risk of complications encountered during a second operation, second anesthesia induction event, and second recovery period. We identified one previous study directly comparing coordinated and staged breast and gynecologic surgeries in 62 patients with breast cancer and BRCA mutations. Chapman et al found similar rates of complications including ileus, surgical site infection, and blood transfusion between coordinated and staged breast and gynecologic surgeries (OR 4.76; 95% CI, 0.56-40.6)<sup>20</sup>. However, this study was likely underpowered to detect differences in dichotomous outcomes between the two groups. Our analysis captures a larger nationwide sample which demonstrated increased rates of surgical site infections and venous thromboembolic events after coordinated breast and gynecologic operations.

Interestingly, the increased rate of postoperative complications in the coordinated group of our cohort was most evident in patients whose breast operation was a mastectomy or post-mastectomy breast reconstruction operation. Patients undergoing lumpectomy in coordination with BSO had similar rates of all measured postoperative complications. Similarly, Tevis et al have previously reported that among patients undergoing coordinated breast, plastic, and gynecologic operations, mastectomy was associated with higher odds (OR 1.90) of developing a postoperative complication<sup>14</sup>. Our results suggest that performing mastectomy or post-mastectomy breast reconstruction separately from BSO may be a safer approach. However, lumpectomy or post-lumpectomy breast reconstruction performed in coordination with BSO may be a reasonable alternative to staged procedures in appropriately selected patients.

The present study also incorporated a cost analysis to provide additional metrics for consideration, and we found that staging breast surgery and BSO did not increase healthcare costs. To date, this is the largest study evaluating the cost-effectiveness of coordinating versus staging breast and gynecologic operations. A previously published review of cases from a single institution in Ireland suggested that coordinating BSO and breast surgery was more cost effective than staging the procedures<sup>21</sup>. Factors thought to influence this higher cost in staged operations included multiple admissions, repeat anesthetic administrations, longer operative times, and multiple recovery periods and medications<sup>21,22</sup>. Notably, Chapman et. al. reported staged breast and gynecologic surgeries resulted in longer cumulative operating time (8 vs. 6 hours) and in-hospital length of stay (4 vs. 3 days) compared to coordinated procedures<sup>20</sup>. However, there are costs that may be associated with surgery beyond those accrued in the index hospitalization. A strength of our cost analysis is that is also captures charges indirectly related to surgery such as outpatient visits, imaging, pharmaceutical claims, and rehabilitation costs, which may more holistically evaluate the impact of coordinating breast and gynecologic surgery. Higher rates of

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postoperative complications in those undergoing coordinated operations may be associated with an increase in hospital readmissions, outpatient visits, and medication expenses<sup>23,24</sup>, which could offset the potential cost-savings of fewer operations, shorter operative time, and shorter index hospitalization length of stay.

This study has several limitations that are worth considering when interpreting the results. First, this was a retrospective study, and thus outcomes may have been influenced by selection bias within the cohort. Because of limitations in what data could be retrieved from MarketScan<sup>®</sup>, we were unable to reliably identify and control for unilateral vs. bilateral breast operations, which may influence the outcomes of interest. Moreover, this Marketscan<sup>®</sup> cohort contained substantially more patients being treated for breast cancer than those who were undergoing risk-reducing mastectomy as a preventative measure against new breast cancers. Thus, these results may not be generalizable to the pathogenic mutation carriers undergoing risk-reducing mastectomy in addition to risk-reducing BSO. Furthermore, Marketscan<sup>®</sup> contains fewer individual patient records in the later years of the dataset, potentially leading to a lower capture rate of patients in 2014 and 2015, where greater availability and use of genetic testing may have uncovered more BRCA mutations. The lower capture rate for this period may have also introduced selection bias. Furthermore, the staged group had a longer follow up period for post-operative complications (up to 180 days to account for both operations vs. 90 days in the coordinated group). However, despite a longer measurement period, postoperative complication rates remained lower for the staged group. Finally, the cost analysis included all inpatient and outpatient healthcare charges within a 2-year period from the first surgical billing code, meaning charges that may not have been attributable to surgery could have been included and potential charges related to the surgery that occurred before the initial procedure date could be missing from the analysis.

To build on the findings of this study, further work should identify the impact of coordinated breast and gynecologic operations on outcomes such as length of stay, operative time, and time to adjuvant therapy in patients with cancer as these factors may also influence surgical decision making regarding timing of each operation. Furthermore, additional data are needed to identify which patient characteristics portend better outcomes for breast and gynecologic operations performed simultaneously. Prospective studies would be useful in evaluating the safety, efficacy, and cost-effectiveness of coordinated versus staged operations and may reduce the effect of selection bias in retrospective analyses.

#### Conclusions

In this retrospective review of a large national claims database, patients who underwent a coordinated breast operation and BSO had higher rates of post-operative complications when compared to patients who underwent the staged operations, an effect predominantly seen in those who underwent mastectomy rather than lumpectomy. We also determined that staged and coordinated procedures are similar in cost. While these results suggest that staging mastectomy and BSO may be safer for patients with invasive breast cancer or high-risk mutations for breast and ovarian cancer, they also suggest coordinated lumpectomy and BSO may be a viable option in appropriately-selected candidates. Further work will identify

which patient characteristics are associated with superior outcomes after coordinated breast and gynecologic operations.

## **Supplementary Material**

Refer to Web version on PubMed Central for supplementary material.

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#### References

- Daly MB, Pal T, Berry MP, et al. Genetic/familial high-risk assessment: breast, ovarian, and pancreatic, version 2.2021, NCCN clinical practice guidelines in oncology. Journal of the National Comprehensive Cancer Network. 2021;19(1):77–102. [PubMed: 33406487]
- Ludwig KK, Neuner J, Butler A, Geurts JL, Kong AL. Risk reduction and survival benefit of prophylactic surgery in BRCA mutation carriers, a systematic review. The American Journal of Surgery. 2016/10/01/2016;212(4):660–669. doi:10.1016/j.amjsurg.2016.06.010 [PubMed: 27649974]
- AlHilli MM, Al-Hilli Z. Perioperative Management of Women Undergoing Risk-reducing Surgery for Hereditary Breast and Ovarian Cancer. Journal of Minimally Invasive Gynecology. 2019/02/01/ 2019;26(2):253–265. doi:10.1016/j.jmig.2018.09.767 [PubMed: 30240898]
- Schrag D, Kuntz KM, Garber JE, Weeks JC. Life expectancy gains from cancer prevention strategies for women with breast cancer and BRCA1 or BRCA2 mutations. Jama. Feb 2 2000;283(5):617–24. doi:10.1001/jama.283.5.617 [PubMed: 10665701]
- Kauff ND, Domchek SM, Friebel TM, et al. Risk-reducing salpingo-oophorectomy for the prevention of BRCA1- and BRCA2-associated breast and gynecologic cancer: a multicenter, prospective study. J Clin Oncol. Mar 10 2008;26(8):1331–7. doi:10.1200/jco.2007.13.9626 [PubMed: 18268356]
- Agnantis NJ, Paraskevaidis E, Roukos D. Preventing Breast, Ovarian Cancer in BRCA Carriers: Rational of Prophylactic Surgery and Promises of Surveillance. Annals of Surgical Oncology. 2004/12/01 2004;11(12):1030–1034. doi:10.1245/ASO.2004.09.910 [PubMed: 15545500]
- 7. Bayraktar S, Arun B. BRCA mutation genetic testing implications in the United States. Breast. Feb 2017;31:224–232. doi:10.1016/j.breast.2016.11.021 [PubMed: 27931006]
- Domchek SM, Friebel TM, Singer CF, et al. Association of risk-reducing surgery in BRCA1 or BRCA2 mutation carriers with cancer risk and mortality. Jama. Sep 1 2010;304(9):967–75. doi:10.1001/jama.2010.1237 [PubMed: 20810374]
- Verheijen RHM, Hermsen B. The clinical implications of genetics. BRCA1- and BRCA2-positive: how do I proceed? Implications for ovarian cancer prevention. Annals of Oncology. 2008/07/01/ 2008;19:v84–v86. doi:10.1093/annonc/mdn317 [PubMed: 18611907]
- Metcalfe K, Lynch HT, Foulkes WD, et al. Effect of Oophorectomy on Survival After Breast Cancer in BRCA1 and BRCA2 Mutation Carriers. JAMA Oncology. 2015;1(3):306–313. doi:10.1001/jamaoncol.2015.0658 [PubMed: 26181175]
- Pierce LJ, Levin AM, Rebbeck TR, et al. Ten-Year Multi-Institutional Results of Breast-Conserving Surgery and Radiotherapy in BRCA1/2-Associated Stage I/II Breast Cancer. Journal of Clinical Oncology. 2006/06/01 2006;24(16):2437–2443. doi:10.1200/JCO.2005.02.7888 [PubMed: 16636335]
- Valachis A, Nearchou AD, Lind P. Surgical management of breast cancer in BRCA-mutation carriers: a systematic review and meta-analysis. Breast Cancer Res Treat. Apr 2014;144(3):443– 55. doi:10.1007/s10549-014-2890-1 [PubMed: 24567198]

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- Batista LI, Lu KH, Beahm EK, Arun BK, Bodurka DC, Meric-Bernstam F. Coordinated prophylactic surgical management for women with hereditary breast-ovarian cancer syndrome. BMC Cancer. 2008/04/14 2008;8(1):101. doi:10.1186/1471-2407-8-101 [PubMed: 18410690]
- Tevis SE, Steiman JG, Neuman HB, Greenberg CC, Wilke LG. Postoperative complications in combined gynecologic, plastic, and breast surgery: An analysis from National Surgical Quality Improvement Program. Breast J. Nov 2019;25(6):1111–1116. doi:10.1111/tbj.13429 [PubMed: 31280491]
- Jayaraman AP, Boyd T, Hampton SN, Haddock NT, Teotia SS. The Impact of Combined Risk-Reducing Gynecological Surgeries on Outcomes in DIEP Flap and Tissue-Expander Breast Reconstruction. Plast Surg (Oakv). May 2020;28(2):112–116. doi:10.1177/2292550320925905 [PubMed: 32596186]
- 16. Del Corral GA, Wes AM, Fischer JP, Serletti JM, Wu LC. Outcomes and Cost Analysis in High-Risk Patients Undergoing Simultaneous Free Flap Breast Reconstruction and Gynecologic Procedures. Ann Plast Surg. Nov 2015;75(5):534–8. doi:10.1097/sap.000000000000156 [PubMed: 24691318]
- Elmi M, Azin A, Elnahas A, McCready DR, Cil TD. Concurrent risk-reduction surgery in patients with increased lifetime risk for breast and ovarian cancer: an analysis of the National Surgical Quality Improvement Program (NSQIP) database. Breast Cancer Res Treat. Aug 2018;171(1):217–223. doi:10.1007/s10549-018-4818-7 [PubMed: 29761322]
- Sroka CJ, Nagaraja HN. Odds ratios from logistic, geometric, Poisson, and negative binomial regression models. BMC Medical Research Methodology. 2018/10/20 2018;18(1):112. doi:10.1186/s12874-018-0568-9 [PubMed: 30342488]
- Ma IT, Gray RJ, Wasif N, et al. Outcomes of Concurrent Breast and Gynecologic Risk Reduction Surgery. Ann Surg Oncol. Jan 2017;24(1):77–83. doi:10.1245/s10434-016-5479-6 [PubMed: 27581610]
- Chapman JS, Roddy E, Panighetti A, et al. Comparing coordinated versus sequential salpingooophorectomy for BRCA1 and BRCA2 mutation carriers with breast cancer. Clinical breast cancer. 2016;16(6):494–499. [PubMed: 27495996]
- 21. Khadim MF, Eastwood P, Price J, Morrison P, Khan K. Multidisciplinary one-stage risk-reducing gynaecological and breast surgery with immediate reconstruction in BRCA-gene carrier women. Eur J Surg Oncol. Dec 2013;39(12):1346–50. doi:10.1016/j.ejso.2013.09.018
- 22. Holzmer S, Davila A, Martin MC. Cost Utility Analysis of Staged Versus Single-Stage Cleft Lip and Palate Repair. Ann Plast Surg. May 2020;84(5S Suppl 4):S300–s306. doi:10.1097/ sap.00000000002255 [PubMed: 32049761]
- Lawson EH, Hall BL, Louie R, et al. Association Between Occurrence of a Postoperative Complication and Readmission: Implications for Quality Improvement and Cost Savings. Annals of Surgery. 2013;258(1)
- 24. Encinosa WE, Hellinger FJ. Advances in Patient Safety What Happens After a Patient Safety Event? Medical Expenditures and Outcomes in Medicare. In: Henriksen K, Battles JB, Marks ES, Lewin DI, eds. Advances in Patient Safety: From Research to Implementation (Volume 1: Research Findings). Agency for Healthcare Research and Quality (US); 2005.

## Synopsis

In this review of 4228 patients who underwent both breast surgery and bilateral salpingooophorectomy, staged operations were associated with similar healthcare costs but lower rates of postoperative complications compared to coordinated operations, an effect most evident among those whose breast operation was a mastectomy.

## Table 1.

Clinical and demographic characteristics of patients undergoing staged versus coordinated surgeries

	Breast Surg		
Characteristics	Coordinated (N=412) n (%)	Staged (N=3816) n (%)	P-value
Age category			0.55
18 - 45	180 (43.7%)	1565 (41.0%)	
46 - 55	169 (41.0%)	1619 (42.4%)	
>55	63 (15.3%)	632 (16.6%)	
Breast Cancer			0.02
Yes	400 (97.1%)	3766 (98.7%)	
No	12 (2.9%)	50 (1.3%)	
Region			0.1
Northeast	76 (18.5%)	877 (23.0%)	
North-central	103 (25.0%)	847 (22.2%)	
South	152 (36.9%)	1469 (38.5%)	
West	72 (17.5%)	562 (14.7%)	
Unknown	9 (2.2%)	61 (1.6%)	
Elixhauser Comorbidity Index			0.06
0 – 3	298 (72.3%)	2924 (76.6%)	
> 3	114 (27.7%)	892 (23.4%)	
Year			<0.01
2010	81 (19.7%)	873 (22.9%)	
2011	81 (19.7%)	901 (23.6%)	
2012	89 (21.6%)	761 (19.9%)	
2013	74 (18.0%)	670 (17.6%)	
2014	50 (12.2%)	472 (12.4%)	
2015	37 (9.0%)	139 (3.6%)	
Breast Surgery			<0.01
Lumpectomy	85 (20.6%)	1328 (34.8%)	
Mastectomy	327 (79.4%)	2488 (65.2%)	
Reconstruction			<0.01
None	133 (32.3%)	2028 (53.1%)	
Post-Lumpectomy Breast Reconstruction	23 (5.6%)	165 (4.3%)	
Immediate Implant Placement	32 (7.8%)	230 (6.0%)	
Delayed Implant Placement	189 (45.9%)	1172 (30.7%)	
Autologous Tissue-Based	26 (6.3%)	173 (4.5%)	
Unspecified Reconstruction	9 (2.2%)	48 (1.3%)	
BSO Surgical Approach			0.90
Laparoscopic	329 (79.9%)	3030 (79.4%)	
Open	83 (20.2%)	786 (20.6%)	

	Breast Surgery and BSO			
Characteristics	Coordinated (N=412) n (%)	Staged (N=3816) n (%)	P-value	
Concurrent Hysterectomy			<0.01	
Yes	140 (34.0%)	2100 (55.0%)		
No	272 (66.0%)	1716 (45.0%)		
Axillary Lymph Node Dissection			0.74	
Yes	141 (34.2%)	1272 (33.3%)		
No	271 (65.8%)	2544 (66.7%)		
Neoadjuvant Chemotherapy			<0.01	
Yes	109 (26.5%)	596 (15.6%)		
No	303 (73.5%)	3220 (84.4%)		
Adjuvant Chemotherapy			0.91	
Yes	143 (34.7%)	1337 (35.0%)		
No	269 (65.2%)	2479 (65.0%)		
Adjuvant Endocrine Therapy			0.23	
Yes	48 (11.7%)	529 (13.9%)		
No	364 (88.4%)	3287 (86.1%)		

## Table 2.

Clinical and demographic characteristics of patients included in the cost analysis

	Breast Surg		
Characteristics	Coordinated (N=321) n (%)	Staged (N=2542) n (%)	P-value
Age category			0.46
18 - 45	143 (44.6%)	1049 (41.3%)	
46 - 55	130 (40.5%)	1060 (41.7%)	
>55	48 (15.0%)	433 (17.0%)	
Breast Cancer			0.03
Yes	312 (97.2%)	2514 (98.9%)	
No	9 (2.8%)	28 (1.1%)	
Region			0.30
Northeast	59 (18.4%)	592 (23.3%)	
North-central	85 (26.5%)	583 (22.9%)	
South	116 (36.1%)	918 (36.1%)	
West	53 (16.5%)	395 (15.5%)	
Unknown	8 (2.5%)	54 (2.1%)	
Elixhauser Comorbidity Index			0.24
0 – 3	235 (73.2%)	1939 (76.3%)	
> 3	86 (26.8%)	603 (23.7%)	
Year			0.62
2010	79 (24.6%)	622 (24.5%)	
2011	80 (24.9%)	676 (26.6%)	
2012	89 (27.7%)	624 (24.6%)	
2013	73 (22.7%)	620 (24.4%)	
Breast Surgery			<0.01
Lumpectomy	62 (19.3%)	861 (33.9%)	
Mastectomy	259 (80.7%)	1681 (66.1%)	
Reconstruction			<0.01
None	106 (33.0%)	1162 (45.7%)	
Post-Lumpectomy Breast Reconstruction	15 (4.7%)	125 (4.9%)	
Immediate Implant Placement	24 (7.5%)	170 (6.7%)	
Delayed Implant Placement	153 (47.7%)	914 (36.0%)	
Autologous Tissue-Based	19 (5.9%)	144 (5.7%)	
Unspecified Reconstruction	4 (1.3%)	27 (1.1%)	
BSO Surgical Approach			1.00
Laparoscopic	255 (79.4%)	2019 (79.4%)	
Open	66 (20.6%)	523 (20.6%)	
Concurrent Hysterectomy			<0.01
Yes	105 (32.7%)	1334 (52.5%)	

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	Breast Surgery and BSO				
Characteristics	Coordinated (N=321) n (%)	Staged (N=2542) n (%)	P-value		
No	216 (67.3%)	1208 (47.5%)			
Axillary Lymph Node Dissection			0.53		
Yes	115 (35.8%)	863 (34.0%)			
No	206 (64.2%)	1679 (66.1%)			
Neoadjuvant Chemotherapy			<0.01		
Yes	85 (26.5%)	383 (15.1%)			
No	236 (73.5%)	2159 (84.9%)			
Adjuvant Chemotherapy			1.00		
Yes	116 (36.1%)	917 (36.1%)			
No	205 (63.9%)	1625 (63.9%)			
Adjuvant Endocrine Therapy			0.30		
Yes	38 (11.8%)	357 (14.0%)			
No	283 (88.2%)	2185 (86.0%)			

#### Table 3.

Comparison of postoperative complications in staged versus coordinated procedures

	Breast Surge		
Postoperative complication	Coordinated (N=412) n (%)	Staged (N=3816) n (%)	P-value
Surgical Site Infection	45 (10.9%)	249 (6.5%)	<0.01
Seroma	33 (8.0%)	211 (5.5%)	0.045
Implant Removal	13 (3.2%)	65 (1.7%)	0.051
Hematoma	16 (3.9%)	91 (2.4%)	0.07
Blood transfusion	0 (0%)	1 (<0.1%)	1.0
Wound dehiscence	20 (4.9%)	226 (5.9%)	0.44
Ileus	5 (1.2%)	36 (0.9%)	0.59
Cardiac	1 (0.2%)	6 (0.2%)	0.51
Respiratory	1 (0.2%)	4 (0.1%)	0.40
DVT/PE	10 (2.4%)	39 (1.0%)	0.02
Any complication	99 (24.0%)	664 (17.7%)	<0.01

#### Table 4.

Subgroup comparison of postoperative complications in staged versus coordinated procedures stratified by mastectomy vs. lumpectomy

	Lumpectomy/Post-lumpectomy Reconstruction and BSO			Mastectomy/Post-	mastectomy Reco and BSO	onstruction
Postoperative complication	Coordinated (N=85) n (%)	Staged (N=1328) n (%)	P-value	Coordinated (N=327) n (%)	Staged (N=2487) n (%)	P-value
Surgical Site Infection	3 (3.5%)	51 (3.8%)	1.0	42 (12.8%)	198 (8.0%)	<0.01
Seroma	6 (7.1%)	61 (4.6%)	0.29	27 (8.3%)	150 (6.0%)	0.14
Implant Removal	***	***	***	12 (3.7%)	60 (2.4%)	0.19
Hematoma	1 (1.2%)	17 (1.2%)	1.0	15 (4.6%)	74 (3.0%)	0.13
Blood transfusion	0 (0%)	0 (0%)	1.0	0 (0%)	1 (<0.1%)	1.0
Wound dehiscence	2 (2.4%)	30 (2.3%)	1.0	18 (5.5%)	196 (7.9%)	0.15
Ileus	2 (2.4%)	16 (1.2%)	0.30	3 (0.9%)	20 (0.8%)	0.74
Cardiac	0 (0%)	1 (0.1%)	1.0	1 (0.3%)	5 (0.2%)	0.52
Respiratory	0 (0%)	0 (0%)	1.0	1 (0.3%)	4 (0.2%)	0.46
DVT/PE	0 (0%)	10 (0.8%)	1.0	10 (3.1%)	29 (1.2%)	0.01
Any complication	11 (12.9%)	155 (11.7%)	0.73	88 (26.9%)	519 (20.9%)	0.01

#### Table 5.

Comparison of two-year healthcare charges in staged versus coordinated breast surgery and BSO

	Breast Surgery and BSO		
	Coordinated (n=321)	Staged (n=2542)	P-value
Total charges, median (IQR)	\$106,500 (\$59,738-\$166,289)	\$101,555 (\$65,950-\$162,980)	0.96
Total charges, mean (SD)	\$135,377 (\$125,148)	\$130,057 (\$107,829)	