

# Comparing Surgical Site Occurrences in 1 versus 2-stage Breast Reconstruction via Federated EMR Network

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**Background:** TriNetX (TriNetX Inc., Cambridge, Mass.) is a federated electronic medical record network. The TriNetX system conducts customized search queries of over 36 million electronic medical records, and returns results in just minutes. To our group's knowledge, TriNetX has not been previously used in plastic surgery research. This study aimed to utilize a continuously updated federated network of 36,000,000 electronic medical records (TriNetX) for comparing 90-day postoperative outcomes between prosthetic breast reconstruction techniques.

**Methods:** Using TriNetX, we analyzed the records of approximately 36 million patients in 31 health care organizations. The de-identified records of 18,744,519 women (age 18–9) were retrospectively screened. A cohort of 4747 patients with a diagnosis of malignant neoplasm of the breast, any stage, having undergone mastectomy, and breast reconstruction with tissue expander was compared with a second cohort of 870 patients diagnosed with malignant neoplasm of the breast, any stage, mastectomy, and immediate insertion of breast implant following mastectomy. Surgical site occurrences occurring within 90 days postoperatively were compared using propensity score matching.

**Results:** Propensity score matching resulted in 870 patients in both well-balanced cohorts. There were no statistically significant differences between the balanced cohorts with respect to 90-day surgical site occurrences.

**Conclusions:** TriNetX enables data-driven clinical research such as retrospective cohort comparison. During the 90-day postoperative period, there were fewer complications noted in the single-stage cohort for all outcomes studied; although this comparison was not statistically significant, we believe it demonstrates a clinically significant finding that single-stage direct-to-implant is at least as safe as the more complicated 2-stage approach. (*Plast Reconstr Surg Glob Open* 2021;9:e3385; doi: 10.1097/GOX.0000000000003385; Published online 22 January 2021.)

## INTRODUCTION

With an annual incidence exceeding 250,000 and a 10-year survival rate of 83% according to the American Cancer Society, the impetus to serve the breast cancer patient population with optimal reconstructive treatment planning remains at an all-time high.<sup>1</sup> The merits of the 2 most common techniques for surgical breast reconstruction following mastectomy—single-stage

Direct-To-Implant (DTI) and 2-stage reconstruction using tissue expanders—have been well documented.<sup>2–4</sup> Yet, the choice between these 2 reconstructive options can be challenging for both the surgeon and patient depending on individual goals of care.

TriNetX (Cambridge, Mass.) is a federated electronic medical record (EMR) network.<sup>5,6</sup> In essence, TriNetX serves as an umbrella organization under which the EMRs of participating healthcare organizations, research firms, pharmaceutical companies, and many others are aggregated into an accessible and searchable database for all members of the network, in real time. The TriNetX system enables the user to conduct customized search queries of

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over 36 million EMRs (and counting), and returns the results in just minutes.

Given the opportunity provided by such a powerful clinical database, our team endeavored to pose what we believe to be the first-ever plastic-surgery–related research query to the TriNetX system. Specifically, we sought to investigate how the incidence of surgical site outcomes (SSOs) by postoperative day (POD) 90 compares between patients undergoing single-stage DTI breast reconstruction versus 2-stage reconstruction using tissue expanders. Through this case study using TriNetX to compare SSOs between breast reconstruction techniques, we aimed to demonstrate the potential utility of a federated EMR network to help guide clinical research questions in the field of plastic surgery.

### METHODS

At the time of our search in January 2020, the analytics subset contained EMRs from approximately 36 million patients in 31 health care organizations predominantly in the United States. The de-identified records of 18,744,519 women (age 18–99) were retrospectively screened using the TriNetX platform (TriNetX Inc.) (Fig. 1).

To ensure accuracy, CPT and ICD-10 codes were used to identify surgical procedures, medical diagnoses, and SSOs. Inclusion criteria consisted of the EMRs of female patients who had been diagnosed with malignant neoplasm of the breast, any stage (ICD-10 C50) and had undergone mastectomy (CPT 19303) with breast reconstruction with either immediate insertion of tissue expander (CPT 19357) or immediate insertion of breast implant following mastectomy (CPT 19340). Any EMRs belonging to patients who were not of female gender, were not an adult over the age of 18, were pregnant, were incarcerated, experienced an SSO outside the POD 90 window, or not meeting all the aforementioned criteria by CPT and ICD-10 codes were excluded. Following application of inclusion and exclusion criteria, a cohort of 4747

patients with malignant neoplasm of the breast, any stage, who underwent mastectomy and breast reconstruction with tissue expander were compared with a second cohort of 870 patients with malignant neoplasm of the breast, any stage, who underwent mastectomy and immediate insertion of breast implant following mastectomy.

Following creation of these 2 breast reconstruction cohorts, the TriNetX system was able to apply propensity score matching with ICD-10 codes for factors including age, race, elevated BMI status (E66), smoking (Z87.891), irradiation (Z92.3), and diabetes (E08-E13). As such, our 870 DTI patients were paired with the 870 Expander patients that were their closest co-morbid and demographic matches before comparison.

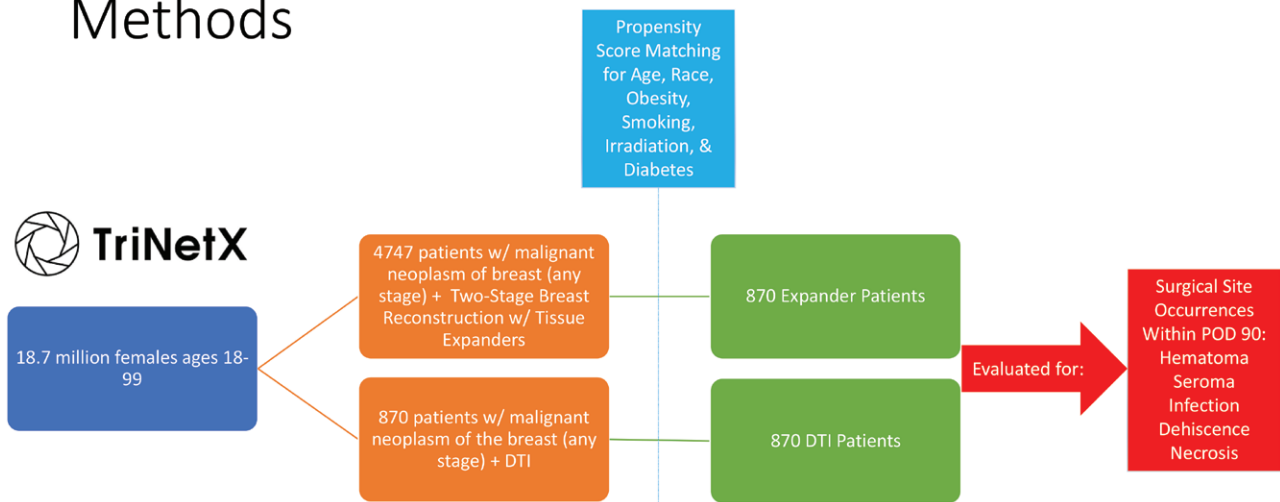
After optimization of the 2 cohorts for direct comparison, SSOs were identified and counted with ICD-10 codes including hematoma (N64.89), seroma (N64.89), infection (T81.4), dehiscence (T81.3), and necrosis (I96) occurring within 90 days after the index event in the patients’ records. Outcomes were assessed with and without propensity score matching for confounding factors.

### RESULTS

Propensity score matching for age, race, overweight and obesity, smoking, irradiation, and diabetes resulted in 870 patients in both cohorts. Before propensity score matching, several between-groups factors were found to be significantly different ( $P < 0.05$ ) and therefore potential confounders including age ( $P = 0.0021$ ), race ( $P < 0.001$ ), and personal history of irradiation ( $P = 0.0027$ ).

Following propensity score matching by the TriNetX system, there were no observed significant differences ( $P > 0.05$ ) between the 2 cohorts. Specifically, following propensity score matching and before comparison of SSOs within POD90, the expander versus DTI cohort demographics included mean age 51.8 versus 51.9, White race 87.7% versus 88%, elevated BMI status 19% versus 19.9%, smoking 16.4% versus 16.7%, irradiation 8.84%

## Methods



**Fig. 1.** TriNetX search strategy that allowed the authors to narrow down the EMRs of an initial 18.7 million female patients into 2 propensity score matched 870-patient cohorts (870 expander patients and 870 DTI patients) for direct comparison of SSOs within POD 90.

versus 8.9%, and diabetes 7.1% versus 8.1%, respectively (Fig. 2).

There were no statistically significant differences but there was a clear trend in favor of DTI between the balanced cohorts with respect to SSOs within POD 90 ( $P > 0.05$ ). The specific incidence of each SSO by cohort was as follows: Hematoma: DTI risk 11.219%, expander risk 13.966%, risk ratio 0.80 (95%CI: 0.61–1.057,  $P = 0.11$ ); Infection DTI risk 4.662%, expander risk 6.272%, risk ratio 0.74 (95%CI: 0.499–1.106,  $P = 0.1422$ ); Seroma DTI risk 11.219%, expander risk 13.966%, risk ratio 0.803 (95%CI: 0.611–1.057,  $P = 0.1163$ ); Dehiscence DTI risk 2.543%, expander risk 4.152%, risk ratio 0.613 (95%CI: 0.363–1.032,  $P = 0.0628$ ); Necrosis DTI risk 2.665%, expander risk 3.797%, risk ratio 0.702 (95%CI 0.416–1.185,  $P = 0.1828$ ) (Fig. 3).

### DISCUSSION

This study is the first application of a federated EMR network to the field of plastic surgery. The database most closely resembling a federated EMR network that is currently in use for plastic surgery research is the Tracking Outcomes in plastic surgery database facilitated by the American Society of Plastic Surgeons.<sup>7</sup> In comparison with TriNetX, Tracking Outcomes in Plastic Surgery consists entirely of surgeon self-reported outcomes and procedural data rather than of patient EMRs.

A comparison between the Tissue Expander and DTI cohorts before and after propensity score matching demonstrates one of the primary advantages of the TriNetX system. Before propensity score matching, our cohorts differed significantly ( $P < 0.05$ ) for characteristics including age, race, and personal history of irradiation. Each of these factors has been demonstrated in previous studies to influence healing and potential SSOs and therefore having even one be significantly different between our cohorts would potentially serve to confound our findings.<sup>8–11</sup>

Following application of propensity score matching, there were no longer any significant differences between our Tissue Expander and DTI cohorts before posing our SSO research question (Fig. 2). The ability to create matched cohorts with such closely related comorbidities and demography increases internal validity by avoiding the influence of confounding variables before comparison. The fact that this propensity score matching was drawn from a pool of nearly 4800 tissue expander patients to find the 870 closest DTI matches, and was performed in a matter of seconds, suggests an increase in productivity several orders of magnitude above the capacity of a small team of human researchers. An additional advantage of the efficiency and scale of TriNetX is the elimination of the vast difference in the techniques and technologies that would presumably have otherwise developed during the time a team of human researchers would have needed to generate a dataset of comparable size.

In terms of our comparison of DTI versus 2-stage expansion, we found no statistically significant differences between the 2 groups in terms of SSOs within POD 90, although fewer complications were noted in the single-stage cohort for all SSOs studied (Fig. 3). Therefore, we consider the lack of statistical significance to be of particular clinical significance, in that it suggests that DTI is potentially at least as safe as 2-stage expansion.

Before conducting our study, the premier investigation of DTI versus 2-stage expansion was the BRIOs Randomized Control Trial from 2016, which found a statistically significant 29% incidence of SSOs associated with DTI when compared with a 5% SSO incidence following 2-stage expansion.<sup>12</sup> This study made use of a cohort of 142 patients and, despite the difference in SSOs, found no significant difference between the 2 groups in terms of overall patient satisfaction. The lack of significant difference between the 2 techniques in overall patient satisfaction potentially suggests that revision surgeries following DTI to achieve an optimal outcome do not seem to negatively

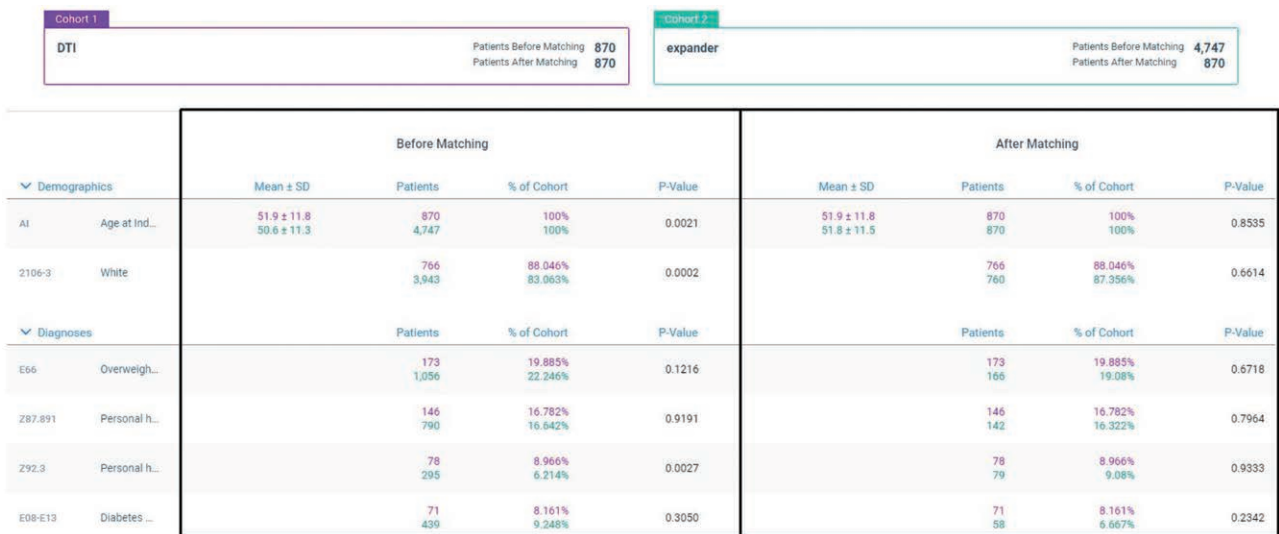


Fig. 2. After balancing, the expander vs DTI demographics mean age was 51.8 vs 51.9, White 87.7% vs 88.0%, obesity 19.0% vs 19.9%, smoking 16.4% vs 16.7%, irradiation 8.84% vs 8.90%, and diabetes 7.1% vs 8.1%, respectively (all  $P$  values not significant,  $P > 0.05$ ).

SSO	DTI Risk	Expander Risk	Risk Ratio
Hematoma	11.219%	13.966%	0.80 (95%CI: 0.61-1.057, p=0.11)
Infection	4.662%	6.272%	0.74 (95%CI: 0.499-1.106, p=0.1422)
Seroma	11.219%	13.966%	0.803 (95%CI: 0.611-1.057, p=0.1163)
Dehiscence	2.543%	4.152%	0.613 (95%CI: 0.363-1.032, p=0.0628)
Necrosis	2.665%	3.797%	0.702 (95%CI 0.416-1.185, p=0.1828)

**Fig. 3.** No statistically significant ( $P > 0.05$ ) differences between the balanced cohorts (DTI vs Expander) for SSOs within POD 90.

impact patient sentiment. One possible explanation for the lack of difference in patient satisfaction is that the discomfort that multiple expansion events and delay of expansion period that the Tissue Expanders group experienced may be similar to the discomfort of undergoing immediate revision surgery following DTI. Subsequent to the BRIOS RCT, Negenborn's group performed a regression analysis, which further stratified the DTI patients who experienced SSOs during the BRIOS trial as tending to have larger breasts, be younger in age, and having undergone adjuvant chemotherapy.<sup>13</sup> By identifying specific characteristics that place DTI patients at a higher risk for SSOs, Negenborn's group underscores the need for careful patient selection when considering DTI, a premise that our authorship group feels should be universally agreeable. Furthermore, the findings of Negenborn's group may imply that patient selection for the BRIOS RCT's head-to-head comparison between DTI versus 2-stage tissue expansion was not fully optimized. Given that patients selected for 2-stage reconstruction typically have more comorbidities and challenges to begin with, such as smoking, radiation, or thinner mastectomy flaps, the importance of patient selection to compare cohorts cannot be overstated.

Although medical factors including the incidence of SSOs and individual patient characteristics are essential considerations in deciding between DTI and 2-stage expansion, the socioeconomic and psychological impacts of any treatment plan also merit contemplation. Using cost-utility analysis, Krishnan et al demonstrated a significant monetary savings of over \$550 for patients who underwent DTI. Krishnan's work also showed an increase in quality-adjusted life years of 0.89, in favor of DTI, thereby suggesting not only a financial but also psychosocial advantage over 2-stage tissue expansion.<sup>14</sup>

The results of our study suggest that DTI is at least as safe as 2-stage expansion in terms of SSOs within POD 90. Although this assertion appears to be at odds with the finding of the BRIOS trial, there are a few key differences worth noting. Firstly, this study is a retrospective cohort

study and thus, despite our best efforts, associations we have identified may have been susceptible to confounding. Our study has the benefits of a large cohort size and a closely matched patient population; however, reliance on a national database also introduces limitations that must be acknowledged. Possibly our study's greatest limitation is the lack of availability of anatomical and technical details of interest. Specifically, although our study includes more than 10 times the number of patients than the BRIOS RCT by leveraging the power of TriNetX, our analysis was unable to control for factors including prepectoral or subpectoral device positioning and use of acellular dermal matrix. Lastly, our search's reliance on individual HCO's accuracy of CPT and ICD-10 coding was another potential source of confounding, as the accuracy of these factors are inherent to the EMRs comprising the database.

We believe that federated EMR networks, such as TriNetX, have vast potential to challenge and verify scientific findings using sample sizes and turnaround times not easily replicated by individual centers. Accordingly, we recognize the need to design an additional prospective cohort study that is able to control for not only factors such as device positioning and use of acellular dermal matrix, but also for the patient selection criteria advocated for by Negenborn, including breast size, patient age, and presence of adjuvant chemotherapy.

## CONCLUSIONS

TriNetX enables data-driven clinical research such as retrospective cohort comparison. The platform uses continuously updated patient data points harmonized from many EMR sources. The research network is growing and now extends to over 30 health care organizations and covers tens of millions of patients, mostly within the United States. This study represents, to the authors' knowledge, the first description using TriNetX in plastic surgery. During the 90-day postoperative period, there were fewer complications noted in the single-stage cohort for all outcomes



studied; although this comparison was not statistically significant, we believe it demonstrates a clinically significant finding that single-stage direct-to-implant is at least as safe as the more complicated 2-stage approach. Therefore, these findings should be validated in future prospective randomized controlled clinical trials that compare surgical outcomes between prosthetic breast reconstruction techniques. For research questions for which there is a paucity of historical data, the use of a federated EMR network to survey thousands of patient charts in a very short period of time may circumvent the need for meta-analysis before planning future prospective RCTs.

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