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Psychosocial Impact of Postmastectomy Lymphedema Syndrome: Insights From a National Claims Database Analysis of Antidepressant Prescription Fills

Daniel Najafali, BS*†
Jennifer K. Shah, BA, BS†
Thomas M. Johnstone, BS‡
Justin M. Camacho, MBA§
Priscila C. Cevallos, BS, MS¶
Kometh Thawanyarat, BA‖
Yelissa Navarro, BS‖
Rahim S. Nazerali, MD†
Clifford C. Sheckter, MD, MS†

Background: Postmastectomy lymphedema syndrome (PMLS) has been associated with lower quality of life due to symptoms and financial consequences. This study assessed the impact of PMLS on psychosocial well-being using antidepressant fill patterns. We hypothesized that PMLS increased the odds and duration of antidepressant fills.

Methods: Mastectomy encounters in the Merative MarketScan Research Databases, 2007–2022, were extracted using Current Procedural Terminology codes. Among these, patients who developed PMLS and filled antidepressant prescriptions were identified using the *International Classification of Diseases, Ninth and Tenth Revision*, codes and generic drug names. Univariate and multivariate logistic regression tests were performed for statistical analyses.

Results: Of 300,075 patients meeting criteria (median [interquartile range] age, 52 [45–59] y), 24,753 (8.2%) experienced PMLS. In a multivariate regression, younger age, less recent surgical year, and higher Elixhauser Comorbidity Index scores were associated with heightened odds of PMLS ($P < 0.001$). In a multivariate regression, PMLS diagnoses increased odds of filling antidepressant prescriptions (26.8% versus 16.5%; odds ratio 1.55; $P < 0.001$). Time to last postmastectomy antidepressant fill was greater for patients with PMLS ($P < 0.001$). In a propensity score–matched model of patients with PMLS with and without lymphedema interventions, such interventions did not impact time to last postmastectomy antidepressant fill ($P = 0.963$).

Conclusions: Patients with PMLS were associated with increased antidepressant fills compared with those without lymphedema. Lymphedema surgery did not impact duration of postmastectomy antidepressant fills. Future studies should evaluate the longitudinal abilities of surgical interventions to ameliorate depression in patients with PMLS. *(Plast Reconstr Surg Glob Open 2025;13:e7012; doi: 10.1097/GOX.0000000000007012; Published online 5 August 2025.)*

*From the *Carle Illinois College of Medicine, University of Illinois Urbana-Champaign, Urbana, IL; †Division of Plastic and Reconstructive Surgery, Stanford University School of Medicine, Stanford, CA; ‡Stanford University School of Medicine, Stanford, CA; §Drexel University College of Medicine, Philadelphia, PA; ¶Geisel School of Medicine, Dartmouth University, Hanover, NH; and ‖Medical College of Georgia at Augusta University, AU/UGA Medical Partnership, Athens, GA.*

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Daniel Najafali and Jennifer K. Shah contributed equally and are considered co-first authors.

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INTRODUCTION

Postmastectomy lymphedema syndrome (PMLS) complicates the lives of breast cancer survivors in 5%–20% of patients.[1] Survivors with PMLS have severe psychosocial ramifications, which encompass diminished self-esteem, depression, social anxiety, sexual dysfunction, and relationship difficulties.[2–5]

Breast cancer is a challenging disease that is reported to affect nearly 2.3 million individuals worldwide every year.[6,7] It is the most common cancer in women and the second leading cause of cancer-related fatalities among women. The increased prevalence of breast cancer diagnoses

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around the world is largely attributed to advancements in medical technology that have ultimately enhanced survival time.[8] This increase in survival also increases the number of women living with complications from breast cancer treatment.

Strong evidence highlights the negative implications PMLS has on quality of life (QoL). In 2021, approximately 61% of adults in the United States with a major depressive episode received treatment, and among patients with severe impairment, this number increased to 74.8%.[9] Moreover, women have been observed to use antidepressants more than men across all age groups, with almost one-fourth of women 60 years and older taking antidepressants.[10] This study examined and quantified antidepressant usage among survivors with and without PMLS as a surrogate for patients' psychosocial well-being. It was hypothesized that breast cancer survivors with PMLS have higher psychiatric burden, as evidenced by greater odds of and duration of postmastectomy antidepressant fills compared with patients without PMLS. Determining if PMLS is predictive of taking antidepressants and the time point that patients stop filling their antidepressants after diagnosis and surgery will better characterize the true impact of PMLS.

Takeaways

Question: What is the impact of postmastectomy lymphedema syndrome (PMLS) on psychosocial well-being using antidepressant fill patterns?

Findings: Patients with PMLS had higher antidepressant fills than those without lymphedema. Lymphedema surgery did not impact duration of postmastectomy antidepressant fills.

Meaning: Surgical treatment of PMLS was not associated with decreased odds of antidepressant fills, suggesting that it does not improve depressive symptoms. Capturing the benefits of lymphedema surgery may be better suited for a patient-reported outcome measure to determine how factors such as volumetric decrease and fitting into clothing easier contribute to overall quality of life.

METHODS

Data Source and Study Cohort

We conducted a retrospective analysis of the Merative MarketScan Research Databases, a large multipayer database, to evaluate demographic characteristics of adult female patients who developed PMLS with or without a subsequent lymphedema intervention and characterize postmastectomy antidepressant fills as a proxy for well-being in this population between January 1, 2007, and December 31, 2022.[11] The Merative MarketScan Research Databases contain inpatient and outpatient claims involving 152,654,207 unique patients as well as prescription data. Those who underwent an index mastectomy, experienced PMLS (as defined by International Classification of Disease codes), or underwent any subsequent lymphedema interventions, including direct excision, liposuction, lymphovenous bypass, and vascularized lymph node transplant, were identified using the Current Procedural Terminology codes and the *International Classification of Diseases, Ninth*(*ICD-9*) and *Tenth* (*ICD-10*) *Revision*, codes. (**See table, Supplemental Digital Content 1**, which displays the Current Procedural Terminology codes used to identify patients in the Merative MarketScan Research Databases who underwent mastectomy and lymphedema interventions, **https://links.lww.com/PRSGO/E228**.) (**See table, Supplemental Digital Content 2**, which displays the ICD-9 and ICD-10 codes used to identify patients in the Merative MarketScan Research Databases with diagnoses of PMLS. Comorbidities, assessed by the Elixhauser Index, were evaluated by the Elixhauser module in Stata, version 16.1 [Stagg, 2015; StataCorp LLC, College Station, TX], **https://links.lww.com/PRSGO/E229**.)

Diagnosis and Prescription Claims

Insurance claims data were used to identify the year in which the index mastectomy was performed, patient age at the time of surgery, comorbidities, PMLS diagnoses, and surgical lymphedema interventions between 2007 and 2022. Comorbidities were assessed and reported with the Elixhauser Comorbidity Index using *ICD-9* and *ICD-10* codes. In this assessment, *ICD-9* codes were included unless patients had an existing *ICD-10* diagnosis, in which case only *ICD-10* diagnoses were evaluated.

Pharmaceutical claims data were used to identify prescriptions of antidepressants filled after the index mastectomy. Antidepressant categories included selective serotonin reuptake inhibitors (SSRIs), serotonin–norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants, monoamine oxidase inhibitors, atypical antidepressants, and other antidepressants. (**See table, Supplemental Digital Content 3**, which displays the generic drug names used to categorize antidepressants filled by patients in the Merative MarketScan Research Databases after the index mastectomy procedure, **https://links.lww.com/PRSGO/E230**.) Patients were excluded if they filled an antidepressant prescription before the index mastectomy. Postmastectomy antidepressant fill dates were recorded.

Outcomes

The following outcomes were analyzed within the study population: (1) developing PMLS, (2) filling 1 or more antidepressant prescriptions after the index mastectomy, and (3) time (in days) from the index mastectomy to the last postmastectomy antidepressant fill.

Statistical Analysis, Time-to-Event Analysis, and Propensity Score Matching

Wilcoxon–Mann-Whitney and Pearson χ^2 tests were used to assess variations in demographic, operative, and antidepressant fill characteristics between patients who developed PMLS and those who did not. We used multivariate logistic regression to calculate adjusted odds ratios for experiencing PMLS after the index mastectomy. The following covariates were included: age (18–44, 45–54,

55 y or older), year of the index mastectomy (2007–2010, 2011–2014, 2015–2018, 2019–2022), and comorbidities, as measured and reported with the Elixhauser Comorbidity Index (0, 1 or 2, 3 or more). Multivariate logistic regression additionally calculated adjusted odds ratio for filling at least 1 antidepressant prescription after the index mastectomy. The following covariates were included: age (18–44, 45–54, 55 y or older); year of the index mastectomy (2007–2010, 2011–2014, 2015–2018, 2019–2022); comorbidities, as measured and reported with the Elixhauser Comorbidity Index (0, 1 or 2, 3 or more); and presence or absence of a PMLS diagnosis.

Kaplan–Meier curves were generated to demonstrate time from the index mastectomy to the last postmastectomy antidepressant fill. This approach was used to allow for inclusion of patients with varying amounts of follow-up time and demonstrate cumulative incidence patterns. Log-rank tests compared the Kaplan–Meier curves (1) among those who did and did not develop PMLS and (2) among those who, within the PMLS subgroup, did and did not undergo a lymphedema intervention. Among patients with PMLS who underwent surgical interventions for lymphedema, an additional Kaplan–Meier curve was generated to demonstrate time from the lymphedema intervention to the last postmastectomy antidepressant fill.

Propensity score matching was used to determine the impact of lymphedema interventions on time from mastectomy to last antidepressant fill among patients who developed PMLS and filled at least 1 postmastectomy antidepressant prescription. Individual propensity scores were calculated through logistic regression modeling on the following covariates: age (18–44, 45–54, 55 y or older), year of the index mastectomy (2007–2010, 2011–2014, 2015–2018, 2019–2022), and comorbidities, as measured and reported with the Elixhauser Comorbidity Index (0, 1 or 2, 3 or more). Patients who did not undergo a lymphedema treatment and those who did undergo a lymphedema treatment were then matched 1:1 via exact matching using the generated propensity scores. Matching patients on surgery year enabled comparison of patients with comparable follow-up time. After 1:1 propensity score matching, linear regression was used to calculate the average difference in time (in days) to the last postmastectomy antidepressant fill attributable to undergoing a lymphedema intervention.

Shapiro–Wilk testing was used to determine whether continuous variables were normally distributed. Pearson χ^2, Wilcoxon–Mann-Whitney, log-rank, and multivariate regression tests were used for statistical analysis. *P* values less than 0.05 were considered statistically significant. All analyses were completed using Stata, version 17 (StataCorp LLC).

RESULTS

Patient Characteristics

Among the 300,075 patients who met inclusion criteria, 24,753 (8.2%) experienced PMLS after the index mastectomy (Fig. 1). Of those, 494 (2.0% of patients with PMLS) underwent a surgical intervention for lymphedema. Median (interquartile range [IQR]) age of patients who developed PMLS was less (51 [45–57] y) than that of patients who did not develop PMLS (52 [45–59] y) ($P < 0.001$) and more often underwent the index mastectomy less recently ($P < 0.001$). Compared with patients who did not develop PMLS, those with PMLS more often underwent the index mastectomy in the South US region (44.1% versus 39.6%) and less often in the Northeast US region (17.1% versus 21.6%) ($P < 0.001$). Patients with PMLS had higher levels of comorbidities than those who did not develop PMLS; 39.0% of patients with PMLS had Elixhauser Index scores of 3 or more compared with only 27.5% of those who did not develop PMLS ($P < 0.001$). A greater proportion of patients with PMLS than those without PMLS filled at least 1 postmastectomy antidepressant at any point during the study period (26.8% versus 16.5%; $P < 0.001$). Before their PMLS diagnosis, 10.9% of patients with PMLS filled at least 1 antidepressant. After their PMLS diagnosis, 23.3% of patients with PMLS filled at least 1 antidepressant. Patients with PMLS more often filled SSRIs (12.6% versus 8.2%; $P < 0.001$), SNRIs (14.0% versus 7.3%; $P < 0.001$), tricyclic antidepressants (3.5% versus 1.9%; $P < 0.001$), atypical antidepressants (4.8% versus 2.7%; $P < 0.001$), and other antidepressants (2.6% versus 1.8%; $P < 0.001$). Median (IQR) time from mastectomy to last antidepressant fill was greater for patients who experienced PMLS (917 [434–1747] d) than that of patients who did not experience PMLS (791 [340–1591]) ($P < 0.001$). Among patients with PMLS, median (IQR) time from mastectomy to PMLS diagnosis was 162 (56–353) days. Among patients with PMLS who underwent a lymphedema intervention, median (IQR) time from mastectomy to the lymphedema intervention was 407 (168–805) days (Table 1).

Predictors of PMLS

Table 2 describes independent associations between patient characteristics and developing PMLS in a multivariate logistic regression analysis. Older age (55 y or older, relative to 18–44 y) and undergoing the index mastectomy after 2010 were protective against developing PMLS ($P < 0.001$), whereas Elixhauser Index scores more than 0 increased odds of developing PMLS ($P < 0.001$).

Predictors of Postmastectomy Antidepressant Fills

Table 3 reports patient characteristics associated with filling at least 1 postmastectomy antidepressant prescription in a multivariate logistic regression. Older age (45 y or older, relative to 18–44 y) and undergoing the index mastectomy after 2010 were protective against filling 1 or more antidepressant prescription ($P < 0.001$). Conversely, Elixhauser Index scores more than 0 ($P < 0.001$) and experiencing PMLS ($P < 0.001$) elevated odds of filling postmastectomy antidepressants.

Impact of PMLS and Interventions on Time to Last Postmastectomy Antidepressant Fill

Figure 2 depicts Kaplan–Meier estimates of time to last postmastectomy antidepressant fill between those who did

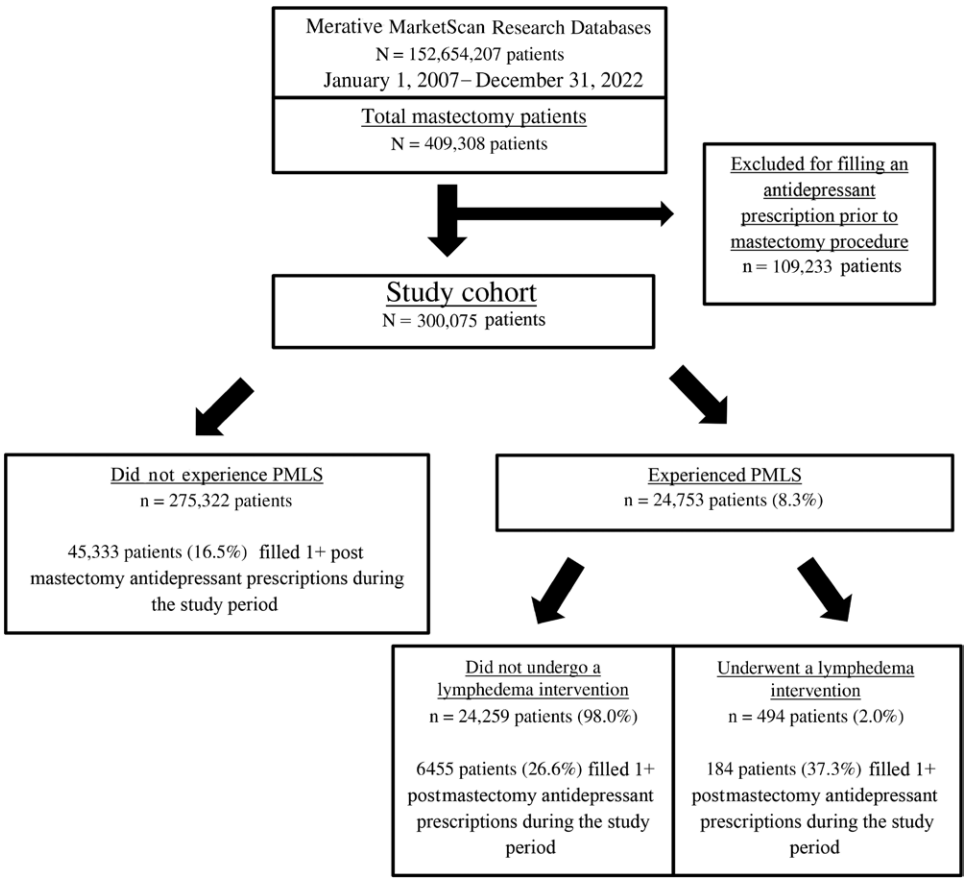

Fig. 1. Flow diagram of patients undergoing mastectomy with or without subsequent development of PMLS and lymphedema interventions in the Merative MarketScan Research Databases. Patients were identified through Current Procedural Terminology, *ICD-9*, and *ICD-10* codes (**Supplemental Digital Content 1, https://links.lww.com/PRSGO/E228**) (**Supplemental Digital Content 2, https://links.lww.com/PRSGO/E229**).

not develop PMLS and those who did develop PMLS. The median time to last fill was 791 days for patients who did not develop PMLS and 917 days for those who did develop PMLS ($P < 0.001$).

Figure 3 demonstrates Kaplan–Meier estimates of time to last postmastectomy antidepressant fill within those who developed PMLS among those who did not undergo a lymphedema intervention and those who did undergo a lymphedema intervention. The median time to last fill was 905 days for patients who did not undergo a lymphedema intervention and 1355 days for those who did undergo a lymphedema intervention ($P < 0.001$).

Propensity score matching of the cohort was used due to the possibility of confounding and small sample sizes. Table 4 compares the covariate characteristics before and after propensity score matching and demonstrates acquired balance in these characteristics after matching. Patients with PMLS filling at least 1 postmastectomy antidepressant prescription and undergoing a lymphedema intervention were matched 1:1 with those with PMLS filling at least 1 postmastectomy antidepressant prescription who did not undergo a lymphedema intervention (n = 6455) on age, surgery year, and Elixhauser Comorbidity Index categories through exact matching. Given effective matching, linear regression was used to calculate the average difference in time from the index mastectomy to the last antidepressant fill attributable to surgical lymphedema interventions for PMLS within this matched cohort (Table 5). In this model, surgical interventions for PMLS did not significantly impact postmastectomy time to last antidepressant fill ($P = 0.963$).

Figure 4 depicts a Kaplan–Meier estimation of time to last antidepressant fill after postmastectomy initiation of antidepressants, a PMLS diagnosis, and a lymphedema intervention (n = 169). The median time to last fill from the surgical intervention for PMLS was 1186 days.

DISCUSSION

This study investigated the psychosocial impact of PMLS using antidepressant fills as a proxy for patients' QoL. The study's findings highlighted that patients with PMLS have significantly higher odds of filling antidepressants and remain on antidepressants longer than those without PMLS. Additionally, the study demonstrated that the profile of a PMLS patient is a younger woman with more comorbidities. A small portion (~2%) of patients with PMLS undergo an intervention for

Table 1. Characteristics of the Study Cohort (N = 300,075) Among Those Who Did Not Experience PMLS (n = 275,322) and Those Who Did Experience PMLS (n = 24,753)

Characteristic	Did Not Experience PMLS (n = 275,322), n (%)	Experienced PMLS (n = 24,753), n (%)	*P*
Age, y			<0.001
18–44	62,572 (22.7)	5709 (23.1)	
45–54	98,699 (35.9)	9899 (40.0)	
55+	114,051 (41.4)	9145 (36.9)	
Age, y			<0.001
Median (IQR)	52 (45–59)	51 (45–57)	
Surgery year			<0.001
2007–2010	115,854 (42.1)	11,309 (45.7)	
2011–2014	70,124 (25.5)	6315 (25.5)	
2015–2018	51,895 (18.8)	4676 (18.9)	
2019–2022	37,449 (13.6)	2453 (9.9)	
Region			<0.001
Northeast	59,413 (21.6)	4221 (17.1)	
North Central	55,816 (20.3)	5103 (20.6)	
South	108,932 (39.6)	10,928 (44.1)	
West	45,845 (16.6)	4065 (16.4)	
Unknown	5316 (1.9)	436 (1.8)	
No. comorbidities (Elixhauser Index)			<0.001
0	150,578 (54.7)	11,937 (48.2)	
1 or 2	48,930 (17.8)	3159 (12.8)	
3+	75,814 (27.5)	9657 (39.0)	
Underwent a surgical intervention for PMLS			—
No	—	24,259 (98.0)	
Yes	—	494 (2.0)	
Filled 1+ antidepressant Rx*			
Anytime during the study period	45,333 (16.5)	6639 (26.8)	<0.001
Before PMLS diagnosis	—	2698 (10.9)	—
After PMLS diagnosis	—	5778 (23.3)	—
Antidepressant type filled*			
SSRI	22,691 (8.2)	3122 (12.6)	<0.001
SNRI	20,034 (7.3)	3455 (14.0)	<0.001
TCA	5163 (1.9)	860 (3.5)	<0.001
MAOI	14 (0.01)	N < 11	—
Atypical antidepressant	7404 (2.7)	1180 (4.8)	<0.001
Other	4998 (1.8)	654 (2.6)	<0.001
Time (d) from mastectomy to median (IQR)			
Last antidepressant fill (n = 51,972)	791 (340–1591)	917 (434–1747)	<0.001
PMLS diagnosis (n = 24,753)	—	162 (56, 353)	—
Lymphedema intervention (n = 494)	—	407 (168, 805)	—

Entries are frequency (percentage) unless otherwise specified. Statistical analyses conducted included χ^2 tests and independent *t* tests.
*Entries may not sum to 100% as patients may meet the criteria for multiple categories. Generic drug names used to categorize antidepressants can be found in **Supplemental Digital Content 3** (https://links.lww.com/PRSGO/E230).
MAOI, monoamine oxidase inhibitor; TCA, tricyclic antidepressant.

lymphedema. In a 1:1 propensity matched model, PMLS interventions did not significantly impact time to last antidepressant fill.

Factors Influencing Time to Intervention and Surgery for Patients with PMLS

The median (IQR) time from mastectomy to PMLS diagnosis was 162 (56–363) days and the median (IQR) time to intervention was 407 (168–805) days. It is reported that the incidence of lymphedema increases with time, at least up to 2 years after cancer diagnosis or surgery.[12] Patients with lymphedema are encouraged to pursue conservative measures such as compression sleeves, lymphatic massage, and physical therapy, among other strategies before pursuing surgery. With respect to insurance coverage for lymphedema surgery, patients may need to have undergone failed physical therapy. In our cohort, we found that older age and undergoing mastectomy after 2010 were protective for PMLS and filling antidepressants, whereas higher comorbidities were associated with increased odds of developing PMLS and filling antidepressants. This can be explained, in part, that lymphedema remains an underrecognized condition depending on severity and the increased incidence that occurs since diagnosis or surgery.[8] Before performing matching, it was found that patients with PMLS who did not have a lymphedema intervention had their last fill significantly earlier than those who did undergo an intervention. Patients experiencing more psychosocial distress

Table 2. Patient Factors Associated With Experiencing PMLS After the Index Mastectomy Procedure in the Study Cohort (N = 300,075) in a Multivariate Logistic Regression

Characteristic	Average OR of PMLS (95% CI)	*P*
Age, y		
18–44	1	—
45–54	1.01 (0.98–1.05)	0.563
55+	**0.84 (0.81–0.87)**	<0.001
Surgery year		
2007–2010	1	—
2011–2014	**0.80 (0.78–0.83)**	<0.001
2015–2018	**0.52 (0.50–0.55)**	<0.001
2019–2022	**0.37 (0.35–0.39)**	<0.001
Elixhauser Index		
0	1	—
1 or 2	**1.17 (1.12–1.23)**	<0.001
3+	**2.57 (2.48–2.67)**	<0.001

24,753 patients experienced PMLS.
Bold values indicate statistical significance ($P < 0.05$).
CI, confidence interval; OR, odds ratio.

Table 3. Patient Factors Associated With Filling At Least 1 Antidepressant Prescription After the Index Mastectomy Procedure in the Study Cohort (N = 300,075) in a Multivariate Logistic Regression

Characteristic	Average OR of 1+ Antidepressant Prescription (95% CI)	*P*
Age, y		
18–44	1	—
45–54	**0.92 (0.89–0.94)**	<0.001
55+	**0.62 (0.61–0.64)**	<0.001
Surgery year		
2007–2010	1	—
2011–2014	**0.55 (0.54–0.57)**	<0.001
2015–2018	**0.32 (0.31–0.33)**	<0.001
2019–2022	**0.21 (0.20–0.22)**	<0.001
Elixhauser Index		
0	1	—
1 or 2	**2.42 (2.35–2.50)**	<0.001
3+	**5.02 (4.88–5.17)**	<0.001
Experienced PMLS		
No	1	—
Yes	**1.55 (1.50–1.60)**	<0.001

Patients who filled antidepressant prescriptions preceding the index mastectomy procedure were excluded from our study; 51,972 patients filled at least 1 antidepressant prescription throughout the study period.
Bold values indicate statistical significance ($P < 0.05$).
CI, confidence interval; OR, odds ratio.

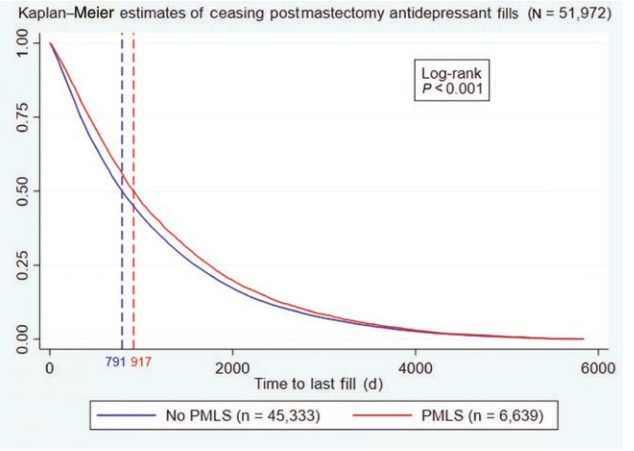

Fig. 2. Kaplan–Meier curves for time to last antidepressant fill after postmastectomy initiation of antidepressants (N = 51,972), among those who did not develop PMLS (n = 45,333) and those who did develop PMLS (n = 6639).

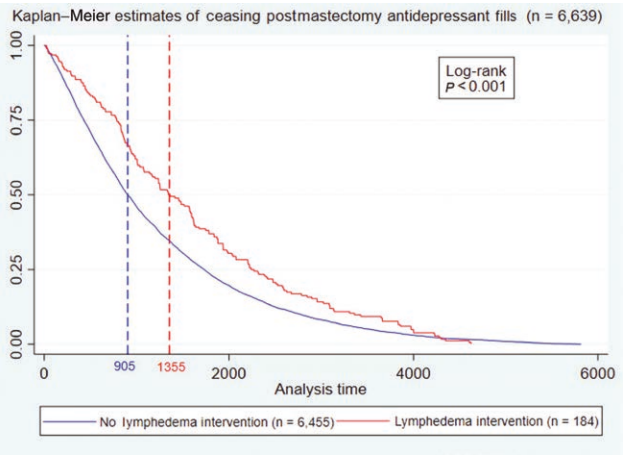

Fig. 3. Kaplan–Meier curves for time to last antidepressant fill after postmastectomy initiation of antidepressants and a PMLS diagnosis (N = 6639), among those who did not undergo a PMLS intervention (n = 6455) and those who did undergo a lymphedema intervention (n = 184).

may be more likely to undergo interventions and are more likely to fill antidepressant prescriptions longer. In addition, patients with PMLS undergoing surgery may be experiencing greater distress based on the severity of their lymphedema (eg, greater volume and increased disability) and may face increased stress for requiring an additional surgical procedure that may have been unanticipated.

Antidepressant Treatment Modalities and the Psychosocial Influences of PMLS

With respect to treatment modalities and regimens for patients, the antidepressant medications were categorized based on their classification. As other studies have indicated for depression and anxiety, the standard of care predominates with the majority of patients taking SSRIs or SNRIs. The potential psychosocial impact of PMLS is captured in this study, and the findings emphasize that the PMLS cohort outpaces the non-PMLS cohort when it comes to filling antidepressants. Studies have linked the psychological influences of PMLS to extend beyond anxiety and depression to include a negative impact on sexual function, body image, and daily relationships.[2,3,8,13,14] It has been reported that individuals' body image and physical limitations may require them to make substantial changes to their everyday lives, such as making modifications to their intimate experiences with their partner or changing professions to accommodate their symptoms. In addition, survivors with lymphedema have reported losing control of

Table 4. Comparison of Patient Characteristics Among Those Who Experienced PMLS and Filled At Least 1 Postmastectomy Antidepressant, Sorted by Those Who Did and Did Not Undergo a Lymphedema Intervention, Before and After Propensity Score Matching for Assessment

	Before Propensity Score Matching			After Propensity Score Matching		
Characteristic	No Lymphedema Intervention (n = 6455), n (%)	Lymphedema Intervention (n = 184) No. (%)	*P*	No Lymphedema Intervention (n = 184), n (%)	Lymphedema Intervention (n = 184) No. (%)	*P*
Age, y			**<0.001**			>0.999
18–44	1749 (27.1)	72 (39.1)		72 (39.1)	72 (39.1)	
45–54	2801 (43.4)	87 (47.3)		87 (47.3)	87 (47.3)	
55+	1905 (29.5)	25 (13.6)		25 (13.6)	25 (13.6)	
Surgery year			0.151			>0.999
2007–2010	3018 (46.7)	98 (53.3)		98 (53.3)	98 (53.3)	
2011–2014	1604 (24.9)	37 (20.1)		37 (20.1)	37 (20.1)	
2015–2018	1289 (20.0)	—		—	—	
2019–2022	544 (8.4)	n < 11 (<6.0%)		n < 11 (<6.0%)	n < 11 (<6.0%)	
No. comorbidities (Elixhauser Index)			0.114			>0.999
				54 (29.3)	54 (29.3)	
0	2370 (36.7)	54 (29.3)		27 (14.7)	27 (14.7)	
1 or 2	796 (12.3)	27 (14.7)		103 (56.0)	103 (56.0)	
3+	3289 (51.0)	103 (56.0)				

Bold values indicate statistical significance ($P < 0.05$).

Table 5. The Impact of Surgical Lymphedema Interventions on Time From the Index Mastectomy Procedure to the Last Antidepressant Fill Among Matched Patients Delineated in Table 4 (n = 368) in a Linear Regression

Characteristic	Average Difference in Time (d) From Mastectomy to Last Antidepressant Fill (95% CI)	*P*
Underwent a surgical intervention for PMLS		
No	0	—
Yes	–6.130 (–267.576 to 255.315)	0.963

CI, confidence interval.

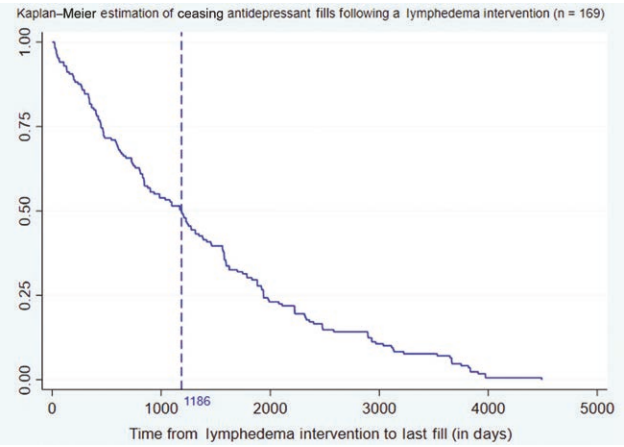

Fig. 4. Kaplan–Meier curves for time to last antidepressant fill after postmastectomy initiation of antidepressants, a PMLS diagnosis, and a lymphedema intervention (n = 169). Time (in days) from the lymphedema intervention is represented on the *x*-axis.

their bodies and appearance.[15–17] Having such feelings has been noted to result in not finding themselves physically attractive and having lower self-confidence.[18–21] Certainly, all the aforementioned consequences of PMLS can be factors that may indicate prescribing a patient psychological medications for PMLS. Studies such as a recent systematic review and meta-analysis have emphasized the negative impact that lymphedema has on QoL.[22] Additionally, predictors for psychological distress have been reported.[2]

PMLS and QoL

Interventions for PMLS aim to improve function of the affected extremity, but the ultimate goal is to impact on a patient's QoL. However, studies do not always emphasize or frame the impact of the intervention from the viewpoint of QoL. Inherently, the gold standard of assessing treatment efficacy focuses on the quantity and quality of lymphedema by measuring the circumference of the affected extremity—which places the focus on volume rather than the impacts of treatment on QoL. Other measures include handgrip strength and mobility of the extremity or shoulder, which are proxies for function of the extremity. Asking more directly regarding a patient's ability to perform tasks of daily living or duties related to their job may more accurately capture if PMLS is a hindrance. The results of noninvasive measures on QoL have been conflicting. In a systematic review and meta-analysis focusing on randomized trials, it was determined that manual lymphatic drainage did not significantly reduce or prevent lymphedema.[23] However, there are studies such as that of Williams et al[24] that report significant benefits with manual lymphatic drainage regarding improved QoL measures. Other interventions such as

low-level laser therapy was found to reduce limb volume and increase shoulder mobility and grip strength compared with placebo.[25] Without reporting beyond the physical findings of treatment, it remains unclear how these changes truly impact a patient's QoL. It has been determined that patients with lymphedema can have a negative body image. Interviews revealed that patients will remove their therapies (eg, elastic bandages and lymphatic pump) at times of intimacy to appear more attractive to their partners, and in the workplace, some people cannot carry out their normal duties, so they will opt to change professions or jobs.[4,26] Such studies place into context the degree to which PMLS can impact patients. Ahmed et al[27] found that breast cancer survivors without a diagnosis of lymphedema had low knowledge levels regarding lymphedema and its treatments and that patients with arm symptoms had lower health-related QoL scores compared with those who did not have those symptoms. Perhaps more efforts toward educating patients and providers can improve this finding. Moreover, outcomes from PMLS studies should not solely focus on physical appearance and comment on QoL measures and encompass patients' mental well-being.

Tools such as the LYMPH-Q aim to use a validated survey instrument to assess "the impact of arm lymphedema on how patients feel" by asking how often they have felt "hopeless, depressed, fed-up, unattractive, frustrated, etc."[28,29] Having objective measures for lymphedema is particularly important as insurance companies justify denying patients secondary to a lack of objective findings. Although informative, the LYMPH-Q initially consisted of 15 patients who were mostly White, and their complications and lived experiences may have heavily influenced their reported results.[30] Other tools such as the Lymphedema Life Impact Scale and the Lymphedema Quality of Life questionnaire have also been used.[31] Measuring prescription fills and dependency on them after diagnosis and surgery may overcome these limitations, as taking psychiatric medication is multifactorial. Halting psychiatric medications has been reported by patients to be due to alleviation of symptoms but can also be due to other reasons beyond relief of depression.[32] Additionally, cessation of antidepressant medications does not necessarily imply resolution of depressive symptoms or that patients will not experience a subsequent relapse of their depression.[33] It is important to emphasize that QoL is critical and factors such as volumetric decrease and fitting into clothing easier certainly can contribute to QoL, but if these interventions are not improving QoL, there may be minimal benefit to patients. Perhaps using measures of QoL, such as the gold standard Patient-Reported Outcomes Measurement Information System instrument, can provide more insight into treatment efficacy.[34–36]

Limitations

Despite the strengths in size and scope conferred by our database design, a national claims study has inherent limitations. For example, we did not have the staging or severity of the patient's lymphedema from established *ICD* coding systems, nor did we have relevant qualitative data, such as QoL instruments or surveys. We similarly lacked the ability to gauge breast cancer disease severity and specific treatment approaches undertaken as a result, which may impact incidence and severity of PMLS. Moreover, we did not have information regarding other psychiatric interventions such as therapy or psychiatric appointments or physician and patient perspectives for antidepressant decision-making, which is multifactorial. Despite these shortcomings of national claims databases, our study raises and examines an important question regarding the extent to which PMLS may affect a patient's psychosocial well-being and how targeted interventions may affect their prescription patterns. Future studies with greater capacity for more granular analysis and inclusion of additional patient-specific variables will help further elucidate the relationships posed in this analysis.

CONCLUSIONS

Patients with PMLS were associated with increased antidepressant prescription fills compared with mastectomy patients without lymphedema. Additionally, among patients who initiated antidepressants after mastectomy, time to last antidepressant fill from the index mastectomy was greater in patients with PMLS than in counterparts without PMLS. Surgical treatment of PMLS was not associated with decreased odds of antidepressant fills, suggesting that lymphedema interventions may not ameliorate depressive symptoms. Additional studies on this topic should consider evaluation of other benefits of lymphedema procedures, which may not be captured with antidepressant filling.

Clifford C. Sheckter, MD, MS
Division of Plastic and Reconstructive Surgery
Stanford University School of Medicine
291 Campus Drive
Stanford, CA 94305; and
Regional Burn Center
Santa Clara Valley Medical Center
770 Welch Road #400
Palo Alto, CA 94304
E-mail: sheckter@stanford.edu

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