# Health and economic benefits of advanced pneumatic compression devices in patients with phlebolymphedema

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## ABSTRACT

**Objective:** Phlebolymphedema (chronic venous insufficiency-related lymphedema) is a common and costly condition. Nevertheless, there is a dearth of evidence comparing phlebolymphedema therapeutic interventions. This study sought to examine the medical resource utilization and phlebolymphedema-related cost associated with Flexitouch (FLX; Tactile Medical, Minneapolis, Minn) advanced pneumatic compression devices (APCDs) relative to conservative therapy (CONS) alone, simple pneumatic compression devices (SPCDs), and other APCDs in a representative U.S. population of phlebolymphedema patients.

**Methods:** This was a longitudinal matched case-control analysis of deidentified private insurance claims. The study used administrative claims data from Blue Health Intelligence for the complete years 2012 through 2016. Patients were continuously enrolled for at least 18 months, diagnosed with phlebolymphedema, and received at least one claim for CONS either alone or in addition to pneumatic compression (SPCDs or APCDs). The main outcomes included direct phlebolymphedema- and sequelae-related medical resource utilization and costs.

**Results:** After case matching, the study included 86 patients on CONS (87 on FLX), 34 on SPCDs (23 on FLX), and 69 on other APCDs (67 on FLX). Compared with CONS, FLX was associated with 69% lower per patient per year total phlebolymphedema- and sequelae-related costs net of any pneumatic compression device-related costs ($3839 vs $12,253; $P = .001$). This was driven by 59% fewer mean annual hospitalizations (0.13 vs 0.32; $P < .001$) corresponding to 82% lower inpatient costs and 55% lower outpatient hospital costs. FLX was also associated with 52% lower outpatient physical therapy and occupational therapy costs and 56% lower other outpatient-related costs. Compared with SPCDs, FLX was associated with 85% lower total costs ($1153 vs $7449; $P = .008$) driven by 93% lower inpatient costs ($297 vs $4215; $P = .002$), 84% lower outpatient hospital costs ($368 vs $2347; $P = .020$), and 85% lower other outpatient-related costs ($353 vs $2313; $P = .023$). Compared with APCDs, FLX was associated with 53% lower total costs ($3973 vs $8436; $P = .032$) because of lower outpatient costs and lower rates of cellulitis (22.4% vs 44.9% of patients; $P = .02$).

**Conclusions:** This analysis indicates significant benefits attributable to FLX compared with alternative compression therapies that can help reduce the notable economic burden of phlebolymphedema. (J Vasc Surg 2018;■:1-10.)

**Keywords:** Phlebolymphedema; Venous ulcer; Cellulitis; Pneumatic compression device; Flexitouch; Medical resource utilization

Phlebolymphedema is a vascular condition that results in lower extremity edema from the combined effects of chronic venous insufficiency (CVI) and lymphedema.[1-3] In the United States, phlebolymphedema is a common and expensive condition. However, the prevalence and direct costs of phlebolymphedema are not well documented, and the condition is widely considered to be underdiagnosed.[1,4,5] CVI alone is considered a major public health problem in the United States, and between 3.0% and 11% of the population experience edema and negative skin changes due to CVI.[6]

Phlebolymphedema occurs in advanced forms of CVI as a pathophysiologic consequence of venous hypertension and related lymphatic overload. The condition can be aggravated by lymphatic damage from repeated episodes of cellulitis. There is a high incidence of venous leg ulcers (VLUs) among patients with phlebolymphedema driven by the severity of CVI in this population of

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patients and exacerbated by the edema. VLUs are open wounds that reflect the venous hypertension associated with reflux or obstruction in the venous system.[7] VLUs are estimated to affect >500,000 people annually in the United States, although incidence is not well documented and actual incidence of VLUs may be substantially higher.[8] Because approximately 50% of VLUs recur within 10 years,[9] this chronicity compounds their economic impact and need for repetitive care. In the United States, VLUs result in treatment costs between $2.5 and $3.5 billion and a loss of >2 million workdays annually.[10] A study of the economics of VLU treatment demonstrated an annual average yearly cost per patient of $15,732, which tripled if the VLU failed to heal.[11] In addition, VLUs cause severe debilitation and discomfort of patients, leading to greater rates of absenteeism,[8] with indirect costs that amplify the economic impact.

Patients with phlebolymphedema and patients with VLUs in particular are more difficult to manage than those with lymphedema in the absence of CVI.[2] As such, there is greater urgency for earlier diagnosis and treatment to reduce downstream sequelae of phlebolymphedema, including nonhealing and recurrent VLUs, which can be complicated by cellulitis and septic shock.[2,12,13] More aggressive and earlier treatment of CVI is needed to prevent such complications, to reduce hospitalizations, and ultimately to reduce the overall cost of care.[14]

The current recommended treatment of phlebolymphedema is compression therapy to reduce tissue edema[2] and, potentially, superficial surgery to treat VLUs.[15] The Effect of Surgery and Compression on Healing and Recurrence (ESCHAR) trial, a randomized controlled trial with >500 patients, showed that the 6-month healing rate for chronic venous ulceration is 65% in both the compression and superficial surgery groups. Treatment of the underlying lymphedema is usually conducted in two phases. The first (reduction) phase consists of "conservative therapy" (CONS), which includes professionally administered manual lymphatic drainage, multilayer bandaging, compression garments, decongestive exercises to reduce edema, preventive skin care, education in self-management, and, for the venous component, wound dressings for an open VLU. Adjunctive treatment during this phase may also include use of a pneumatic compression device (PCD). PCDs assume a major role in the second (maintenance) phase, in which patients optimize the attained edema reduction with home-based treatments. PCDs have been shown to significantly improve lymphatic circulatory function,[16,17] to reduce edema volume,[18-20] and to improve patient-reported symptoms and quality of life.[20,21] Compared with simple PCDs (SPCDs), advanced PCDs (APCDs) provide a greater degree of adjustability and programmability as well as greater degrees of edema reduction.[22]

Use of APCDs has been associated with significantly lower rates of cellulitis and outpatient care,[23] hastening of VLU healing,[24] and responsiveness in long-standing VLUs that resist healing with other methods.[25-27] However, systematic reviews have not addressed the therapeutic response to pneumatic compression therapy of phlebolymphedema within the context of an economic analysis.[28,29] Consequently, this study aimed to evaluate which specific phlebolymphedema compression strategy has the greatest potential to reduce both medical resource utilization (MRU) and direct medical costs within a representative privately insured U.S. population of phlebolymphedema patients with >1 year of treatment.

## ARTICLE HIGHLIGHTS

- **Type of Research:** Retrospective analysis of prospectively collected case-matched deidentified administrative claims data (Blue Health Intelligence)
- **Take Home Message:** Flexitouch (FLX) with conservative management of phlebolymphedema compared with management with conservative therapy, simple pneumatic compression devices, or advanced pneumatic compression devices was associated with 69%, 85%, and 53% lower per patient per year total costs ($P$ values < .001, .008, and .32, respectively), driven largely by lower inpatient and outpatient costs with FLX.
- **Recommendation:** The authors recommend FLX with conservative treatment to reduce costs in patients with phlebolymphedema compared with conservative therapy alone or simple or other advanced pneumatic compression devices.

## METHODS

**Setting and data source.** This study used deidentified Health Insurance Portability and Accountability Act-compliant commercial administrative claims data from the Blue Health Intelligence (BHI) research database for the complete years 2012 through 2016. The data set contained longitudinal information captured by commercial health insurance claims. The core BHI databases contain >165 million members of individual Blue Cross Blue Shield plans from across the United States. Study data were accessed by procedures compliant with the Health Insurance Portability and Accountability Act of 1996; therefore, informed consent or Institutional Review Board approval was not required.

**Study population.** Patients with a diagnosis of nonfilarial lymphedema were first identified on the basis of one inpatient or two outpatient primary or secondary lymphedema diagnosis codes (*International Classification of Diseases, Ninth Revision* [ICD-9] codes 457.0, 457.1, and 757.0 or *International Classification of Diseases, Tenth Revision* [ICD-10] codes I97.2, I89.0, and Q82.0). Patients were then required to be continuously enrolled

in the health plan with medical benefits for at least 12 months before and 6 months after the index date, defined as the earliest occurrence of phlebolymphedema treatment based on either the first occurrence of an inpatient claim or the second occurrence of an outpatient claim. Patients were then included only if they had a primary or secondary diagnosis of CVI within the 12-month period before the index date (ICD-9 codes 459.3x and 459.8x or ICD-10 code I87.2) and received at least one claim for CONS (active lymphedema treatment, including manual lymphatic drainage, lymphedema education, and lymphedema-related physical therapy [PT] or occupational therapy [OT]).

**Therapeutic interventions.** This study evaluated the impact of multiple compression modalities, including CONS, Flexitouch (FLX; Tactile Medical, Minneapolis, Minn; Healthcare Common Procedure Coding System [HCPCS] code E0652), SPCDs (HCPCS code E0651), and other APCDs (HCPCS code E0652), on phlebolymphedema- and sequelae-related MRU and costs. Those patients were then subdivided on the basis of the therapeutic intervention prescribed by the physician.

This study focuses on PCDs rather than on compression garments and compression bandaging, given the dearth of evidence around PCDs and that much research has already been conducted on garments, bandaging, and other modes of static compression. FLX was selected as the particular APCD of interest on the basis of its robust efficacy data[22,23] and the opportunity to evaluate its impact on MRU and costs in a high-risk phlebolymphedema cohort. In addition, the FLX manufacturer is the sole provider submitting the insurance claims, permitting a unique opportunity to crossmatch provider details (ie, National Provider Identifier number) with device code (ie, HCPCS code E0652).

**Patients' demographic and clinical characteristics.** The claims database included information on patients' demographic and socioeconomic characteristics, such as age, sex, commercial insurance type, and census region. In addition, baseline comorbid conditions were identified using the Elixhauser comorbidity index in the 12 months before treatment initiation index date.

**Medical resource use and cost.** A clinically relevant and broad set of medical resources and costs were defined and evaluated for each patient. The number of cellulitis infections was established by enumerating patients with a primary or a secondary diagnosis code for cellulitis. Additional medical resources included the absolute and mean number of per-patient hospitalizations, the absolute and mean number of per-patient outpatient hospital visits, and the absolute and mean number of patients receiving PT or OT. Costs were calculated per patient per year (PPPY), based on the setting in which they were incurred, including home health, emergency, inpatient, outpatient hospital, outpatient PT or OT, physician's office, laboratory, and other service locations. Prescription and medical equipment costs were not available in this data set. Only phlebolymphedema- and relevant sequelae-related medical resources and costs were considered. Resource use and cost data were designated phlebolymphedema or relevant sequelae related if the corresponding claim had a diagnosis code for primary or secondary lymphedema, cellulitis, ulcers, septic shock, erysipelas, lymphangitis, or other local skin infection.

**Statistical analysis.** Study groups were matched to control for differences in demographic and clinical characteristics using propensity scores derived from logistic regression. A stepwise model included the following covariates to control for and thus match on: Elixhauser comorbidity index components; age; sex; region of country; insurance type; and dummy indicators for breast cancer, melanoma, uterine cancer, ovarian cancer, prostate cancer, cervical cancer, vaginal cancer, vulvar cancer, lymphoma, soft tissue sarcoma, congestive heart failure, CVI, VLU, diabetes, iliac vein disorders, pulmonary hypertension, and postphlebitic syndrome.

All statistical tests were two sided with a significance level of $P < .05$. Baseline demographic and clinical characteristics were assessed using $\chi^2$ tests for categorical variables and *t*-tests for continuous variables. Costs were analyzed using a general linear model with gamma distribution and log link while controlling for age and sex. Distribution shape and transformation were assessed by modified Park test and Box-Cox test, respectively.[30] Dichotomous study outcomes (patients with or without an inpatient visit, outpatient visit, use of PT, and cellulitis disease) were assessed using a logistic model that controlled for varying length of follow-up time in which the log of follow-up time was used as an offset term in the model. In addition, to assess the number of inpatient visits, we fitted a Poisson model using the number of events and log transformed follow-up time as an offset variable to account for varying lengths of follow-up. The number of outpatient and PT visits was counted annually starting at the index date and assessed with a general linear model.

As study patients had differing lengths of follow-up times, study outcomes were annualized on a PPPY basis. All analyses were undertaken using SAS version 9.4 on a personal computer platform (SAS Institute, Cary, NC).

## RESULTS

**Study population.** The Fig presents the study sample. A total of 26,902 patients with lymphedema were identified as continuously enrolled with medical benefits for at least 12 months before and 6 months after the index date. Of those, 18,272 patients without a diagnosis for CVI were excluded, leaving 8630 patients with phlebolymphedema (CVI and lymphedema). Next,

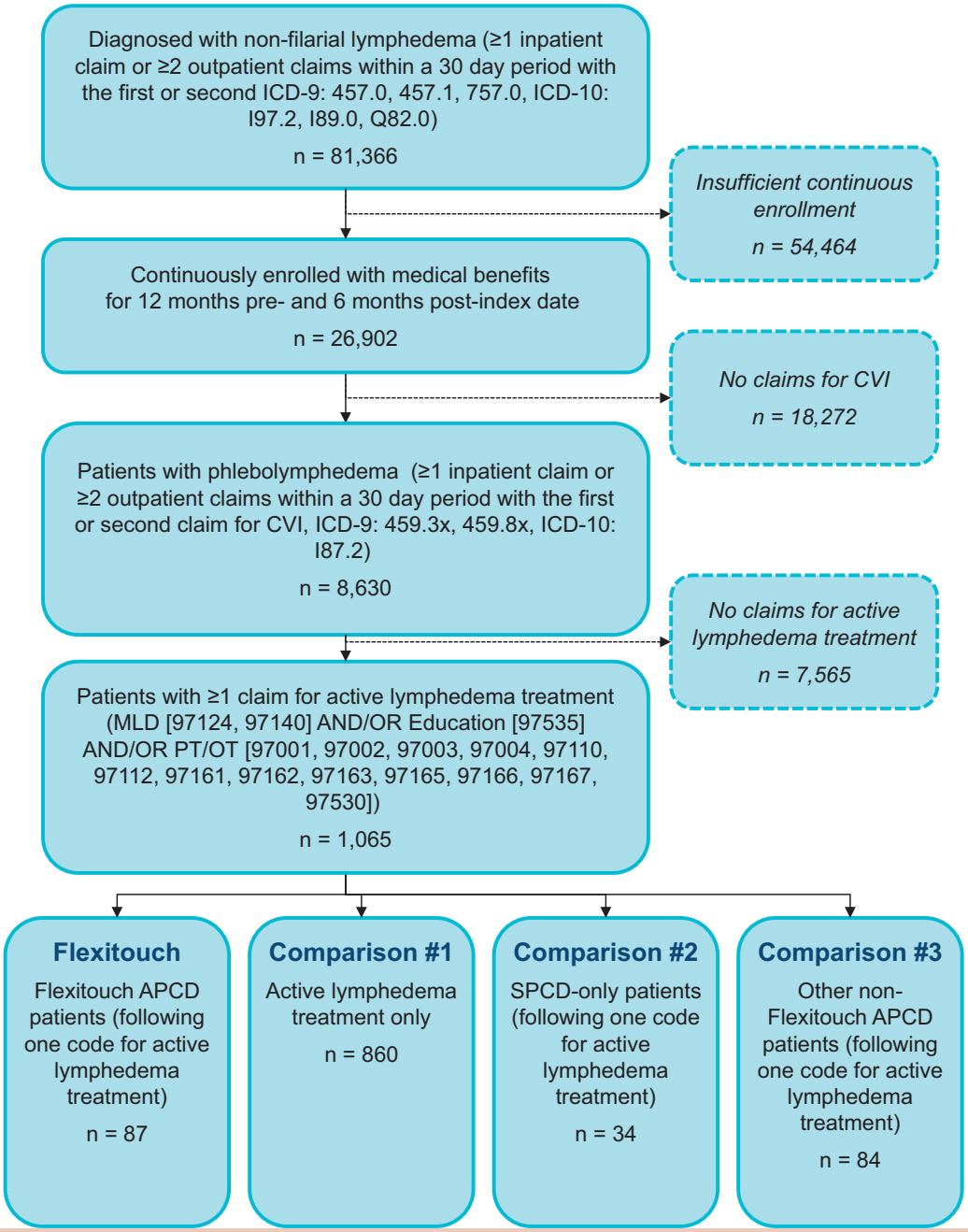


**Fig.** Study sample selection flow chart. *APCD,* Advanced pneumatic compression device; *CVI,* chronic venous insufficiency; *ICD-9, International Classification of Diseases, Ninth Revision*; *ICD-10, International Classification of Diseases, Tenth Revision*; *MLD,* manual lymphatic drainage; *OT,* occupational therapy; *PT,* physical therapy; *SPCD,* simple pneumatic compression device.

patients not receiving baseline CONS were excluded from analysis, leaving 1065 patients qualified for inclusion in the study.

Patients were then stratified on the basis of whether they received CONS alone, CONS + FLX, CONS + SPCDs, or CONS + APCDs. The majority of unmatched patients, 860 (80.8%), received CONS only, whereas 87 (8.2%) received CONS + FLX, 34 (3.2%) received CONS + SPCDs, and 84 (7.9%) received CONS + other APCDs.

Table I presents demographic and clinical characteristics of unmatched patients. Within this commercially insured population, most phlebolymphedema patients were between 45 and 64 years of age (mean ages: 55.6 years for CONS, 54.6 years for FLX, 57.3 years for SPCDs, and 54.3 years for other APCDs). There were no statistically significant differences in age distribution, sex, geography, or insurance type between unmatched study groups.

Among the clinical characteristics, VLUs were present in 89.6% of CONS patients, 92.0% of FLX patients, 94.1% of SPCD patients, and 94.0% of patients on other APCDs.

Table II presents demographic and clinical characteristics of the patients after application of propensity score matching. Study participants were well matched.

**Comparison group 1: FLX vs CONS.** Compared with CONS, FLX patients had 59% fewer mean annual phlebolymphedema- and sequelae-related hospitalizations (0.13 vs 0.32; $P < .001$; Table III). This corresponded to 82% lower inpatient hospital costs ($1560 vs $8715; $P = .003$; Table IV).

FLX patients also used PT or OT 38% less than their CONS counterparts (37.9% vs. 61.6% of patients; $P = .01$; Table III). This was associated with 52% lower outpatient PT or OT costs ($39 vs $81; $P = .015$). FLX patients also had 55% lower outpatient hospital costs ($1129 vs $2534; $P = .027$) and 56% lower other outpatient-related costs ($1090 vs $2453; $P = .029$; Table IV).

Overall, FLX was associated with 69% lower PPPY total phlebolymphedema- and sequelae-related costs compared with CONS ($3839 vs $12,253; $P = .001$; Table IV). The cost difference was driven by lower MRU and cost in both inpatient and outpatient settings.

**Comparison group 2: FLX vs SPCDs.** Compared with SPCDs, FLX was associated with 85% lower PPPY total phlebolymphedema- and sequelae-related costs ($1153 vs $7449; $P = .008$; Table IV). Similar to comparison group 1, lower costs were driven by lower inpatient costs ($297 vs $4215; $P = .002$), lower outpatient hospital costs ($368 vs $2347; $P = .020$), and lower other outpatient-related costs ($353 vs $2313; $P = .023$; Table IV).

**Comparison group 3: FLX vs other APCDs.** FLX patients had 53% lower PPPY total phlebolymphedema- and sequelae-related costs vs other APCDs ($3973 vs $8436; $P = .032$; Table IV). Total cost difference was driven by lower outpatient hospital costs ($1320 vs $3062; $P = .041$) and lower other outpatient-related costs ($1283 vs $3026; $P = .038$; Table IV).

Compared with other APCDs, FLX patients also had significantly lower rates of cellulitis (22.4% vs 44.9% of patients; $P = .02$). FLX patients were also more likely to access PT or OT compared with patients on other APCDs (38.8% vs 23.2% of patients; $P = .02$; Table III).

## DISCUSSION

This study demonstrates the significant opportunity that exists to have an impact on resource utilization and treatment cost of phlebolymphedema through the application of individual treatment strategies. Our data demonstrate a significant difference in phlebolymphedema- and sequelae-related MRU and costs for patients on FLX vs patients on CONS, SPCDs, and other APCDs, listed in order of magnitude of cost differences. Our results support the use of FLX specifically as an adjunct to CONS in this population of higher risk patients. Within the realm of intermittent pneumatic compression, it appears that individual devices can produce significantly different outcomes. To our knowledge, this is the first study to specifically evaluate the impact of alternative compression therapy modalities on MRU and costs, including inpatient, outpatient, and home health costs, in a phlebolymphedema population.

The majority of patients in this study had severe phlebolymphedema, reflected in the high rates of VLUs (89.6%-94.0% of phlebolymphedema patients). Patients with VLUs are generally considered more difficult to treat and are associated with a higher overall cost of treatment than of patients with other stages of CVI.[11] The PPPY phlebolymphedema- and sequelae-related costs associated with CONS, the most common treatment modality, averaged $12,253, which is approximate to the total costs for treating VLUs observed in the study of Ma et al[11] ($15,732 on average, or $10,563 among patients with healed, nonrecurrent VLUs).

Notably, the total disease-related costs for treating phlebolymphedema are substantially higher than the disease-related costs reported by Karaca-Mandic et al[23] within the broader lymphedema population ($2937). As opposed to the study of Karaca-Mandic et al, which does not control for clinical severity of lymphedema, this study looks at phlebolymphedema, the most severe form of CVI. Within this population of patients with more severe disease, the magnitude of our total cost differential compared with CONS (69% lower costs; $P = .001$), SPCDs (85% lower costs; $P = .008$), and other APCDs (53% lower costs; $P = .032$) is markedly greater than that observed by Karaca-Mandic et al[23] in the broader lymphedema population looking at FLX vs SPCDs. The higher cost associated with phlebolymphedema is often driven by the high cost of treatment for open ulcers, which FLX helps to heal, thereby reducing the economic burden associated with treatment of phlebolymphedema.[31]

In this study, cost differences across comparator arms (CONS, SPCDs, and other APCDs) are primarily driven by lower outpatient and inpatient costs. It is well established that diagnosis of phlebolymphedema is associated with greater risk of infections and development of VLUs,[32,33] which often lead to increased MRU and increased outpatient- and inpatient-related costs.[11] Effective treatment of phlebolymphedema is necessary to reduce the progression of phlebolymphedema and the serious and costly sequelae. This study demonstrates a significant economic benefit associated with FLX in the outpatient hospital setting, where FLX is associated with 55% lower costs vs CONS ($P = .027$), 84% lower costs vs SPCDs ($P = .020$), and 57% lower costs vs other APCDs ($P = .041$). FLX is further associated with 82% lower inpatient costs compared with CONS ($P = .003$) and 93% lower costs compared with SPCDs ($P = .002$). These lower outpatient and inpatient costs further highlight

**Table I.** Baseline characteristics of unmatched study sample

| | CONS (n = 860) | CONS + FLX (n = 87) | CONS + SPCDs (n = 34) | CONS + other APCDs (n = 84) | *P* value[a] | *P* value[b] | *P* value[c] |
|---|---|---|---|---|---|---|---|
| Follow-up, years, mean (SD) | 1.90 (0.83) | 1.62 (0.8) | 1.77 (1.03) | 1.76 (0.82) | .002 | .840 | .260 |
| Age, years | | | | | .399 | .514 | .514 |
| Mean (SD) | 55.63 (9.47) | 54.55 (10.00) | 57.26 (7.98) | 54.26 (9.46) | | | |
| 0-18 | 1 (0.1) | 0 (0.0) | 0 (0.0) | 1 (1.2) | | | |
| 19-44 | 92 (10.7) | 14 (16.1) | 3 (8.8) | 9 (10.7) | | | |
| 45-64 | 670 (77.9) | 66 (75.9) | 27 (79.4) | 65 (77.4) | | | |
| 65+ | 97 (11.3) | 7 (8.0) | 4 (11.8) | 9 (10.7) | | | |
| Sex | | | | | .401 | .023 | .625 |
| Female | 534 (62.1) | 58 (66.7) | 15 (44.1) | 53 (63.1) | | | |
| Male | 326 (37.9) | 29 (33.3) | 19 (55.9) | 31 (36.9) | | | |
| Insurance type | | | | | .394 | .906 | .350 |
| HMO | 59 (6.9) | 3 (3.4) | 2 (5.9) | 4 (4.8) | | | |
| PPO | 727 (84.5) | 78 (89.7) | 30 (88.2) | 74 (88.1) | | | |
| Point of service | 31 (3.6) | 4 (4.6) | 1 (2.9) | 1 (1.2) | | | |
| Indemnity | 22 (2.6) | 0 (0.0) | 0 (0.0) | 0 (0.0) | | | |
| Other | 21 (2.4) | 2 (2.3) | 1 (2.9) | 5 (6.0) | | | |
| Geographic region | | | | | .114 | .265 | .673 |
| Northeast | 238 (27.7) | 16 (18.4) | 12 (35.3) | 16 (19.0) | | | |
| South | 277 (32.2) | 38 (43.7) | 12 (35.3) | 42 (50.0) | | | |
| Midwest | 293 (34.1) | 29 (33.3) | 9 (26.5) | 21 (25.0) | | | |
| West | 52 (6.0) | 4 (4.6) | 1 (2.9) | 5 (6.0) | | | |
| Specific clinical characteristics | | | | | | | |
| Elixhauser comorbidity index | 5.36 (8.99) | 3.01 (7.04) | 1.82 (5.73) | 1.99 (6.71) | .005 | .185 | .656 |
| CVI | 869 (100.0) | 87 (100.0) | 34 (100) | 84 (100.0) | N/A | N/A | N/A |
| VLUs | 779 (89.6) | 80 (92.0) | 32 (94.1) | 79 (94.0) | .674 | .683 | .592 |
| Diabetes | 254 (29.2) | 23 (26.4) | 13 (38.2) | 30 (35.7) | .545 | .202 | .19 |
| Heart failure | 72 (8.3) | 7 (8.0) | 4 (11.8) | 5 (6.0) | .917 | .522 | .592 |
| Pulmonary hypertension | 21 (2.4) | 4 (4.6) | 1 (2.9) | 1 (1.2) | .232 | .487 | .186 |
| Iliac vein disorders (May-Thurner syndrome) | 26 (3.0) | 1 (1.1) | 0 (0.0) | 0 (0.0) | .317 | .530 | .324 |
| Postphlebitic syndrome | 6 (0.7) | 1 (1.1) | 1 (2.9) | 0 (0.0) | .639 | .487 | .324 |
| Breast cancer | 150 (17.3) | 16 (18.4) | 1 (2.9) | 6 (7.1) | .824 | .028 | .028 |
| Melanoma | 7 (0.8) | 1 (1.1) | 0 (0.0) | 1 (1.2) | .007 | .530 | .980 |
| Uterine cancer | 9 (1.0) | 1 (1.1) | 0 (0.0) | 2 (2.4) | .929 | .530 | .540 |
| Ovarian cancer | 7 (0.8) | 2 (2.3) | 0 (0.0) | 0 (0.0) | .174 | .373 | .162 |
| Prostate cancer | 7 (0.8) | 0 (0.0) | 1 (2.9) | 0 (0.0) | .398 | .108 | N/A |
| Cervical cancer | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (1.2) | N/A | N/A | 0.307 |
| Placental cancer | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | N/A | N/A | N/A |
| Vaginal cancer | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | N/A | N/A | N/A |
| Vulvar cancer | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | N/A | N/A | N/A |
| Lymphoma and leukemia | 10 (1.2) | 0 (0.0) | 1 (2.9) | 0 (0.0) | .312 | .108 | N/A |
| Soft tissue sarcoma | 4 (0.5) | 0 (0.0) | 0 (0.0) | 1 (1.2) | .524 | N/A | .307 |

*APCDs*, Advanced pneumatic compression devices; *CONS*, conservative therapy; *CVI*, chronic venous insufficiency; *FLX*, Flexitouch; *HMO*, health maintenance organization; *N/A*, not applicable; *PPO*, preferred provider organization; *SD*, standard deviation; *SPCDs*, simple pneumatic compression devices; *VLUs*, venous leg ulcers.
Values are reported as number (%) unless otherwise indicated.
[a]Comparison between FLX in conjunction with CONS vs CONS.
[b]Comparison of FLX vs single-chamber pneumatic compression devices, both in conjunction with CONS.
[c]Comparison of FLX vs other APCDs, both in conjunction with CONS.

**Table II.** Baseline characteristics of propensity score-matched study sample

| | Comparison group 1 | | | Comparison group 2 | | | Comparison group 3 | | |
|---|---|---|---|---|---|---|---|---|---|
| | CONS (n = 86) | CONS + FLX (n = 87) | *P* value[a] | CONS + FLX (n = 23) | CONS + SPCDs (n = 34) | *P* value[b] | CONS + FLX (n = 67) | CONS + other APCDs (n = 69) | *P* value[c] |
| Follow-up, years, mean (SD) | 1.87 (0.88) | 1.62 (0.80) | .077 | 1.69 (0.66) | 1.03 (1.36) | .922 | 1.56 (0.78) | 1.78 (0.81) | .092 |
| Age, years | | | .127 | | | .737 | | | .715 |
| Mean (SD) | 56.98 (9.20) | 54.55 (10.00) | | 58.78 (6.65) | 57.26 (7.98) | | 56.31 (9.28) | 54.41 (9.29) | |
| 0-18 | 0 (0.0) | 0 (0.0) | | 0 (0.0) | 0 (0.0) | | 0 (0.0) | 1 (1.4) | |
| 19-44 | 7 (8.1) | 14 (16.1) | | 1 (4.3) | 3 (8.8) | | 6 (9.0) | 8 (11.6) | |
| 45-64 | 66 (76.7) | 66 (75.9) | | 20 (87.0) | 27 (79.4) | | 54 (80.6) | 52 (75.4) | |
| 65+ | 13 (15.1) | 7 (8.0) | | 2 (8.7) | 4 (11.8) | | 7 (10.4) | 8 (11.6) | |
| Sex | | | .957 | | | .118 | | | .757 |
| Female | 57 (66.3) | 58 (66.7) | | 15 (65.2) | 15 (44.1) | | 41 (61.2) | 44 (63.8) | |
| Male | 29 (33.7) | 29 (16.8) | | 8 (34.8) | 19 (55.9) | | 26 (38.8) | 25 (36.2) | |
| Insurance type | | | 1.000 | | | .789 | | | .577 |
| HMO | 3 (3.5) | 3 (3.4) | | 1 (4.3) | 2 (5.9) | | 3 (4.5) | 3 (4.3) | |
| PPO | 77 (89.5) | 78 (89.7) | | 19 (82.6) | 30 (88.2) | | 58 (86.6) | 63 (91.3) | |
| Point of service | 4 (4.7) | 4 (4.6) | | 2 (8.7) | 1 (2.9) | | 4 (6.0) | 1 (1.4) | |
| Indemnity | 0 (0.0) | 0 (0.0) | | 0 (0.0) | 0 (0.0) | | 0 (0.0) | 0 (0.0) | |
| Other | 2 (2.3) | 2 (2.3) | | 1 (4.3) | 1 (2.9) | | 2 (3.0) | 2 (2.9) | |
| Geographic region | | | .999 | | | .340 | | | .553 |
| Northeast | 15 (17.4) | 16 (18.4) | | 8 (34.8) | 12 (35.3) | | 15 (22.4) | 9 (13.0) | |
| South | 38 (44.2) | 38 (43.7) | | 9 (39.1) | 12 (35.3) | | 31 (46.3) | 36 (52.2) | |
| Midwest | 29 (33.7) | 29 (33.3) | | 3 (13.0) | 9 (26.5) | | 18 (26.9) | 20 (29.0) | |
| West | 4 (4.7) | 4 (4.6) | | 3 (13.0) | 1 (2.9) | | 3 (4.5) | 4 (5.8) | |
| Specific clinical characteristics | | | | | | | | | |
| Elixhauser comorbidity index | 5.16 (8.45) | 3.01 (7.04) | .094 | 1.00 (5.58) | 1.82 (5.73) | .908 | 2.09 (6.50) | 2.21 (6.98) | .562 |
| CVI | 86 (100) | 87 (100) | N/A | 23 (100) | 34 (100) | N/A | 67 (100) | 69 (100) | N/A |
| VLUs | 80 (93.0) | 80 (92.0) | .790 | 20 (87.0) | 32 (94.1) | .348 | 62 (92.5) | 64 (92.8) | .961 |
| Diabetes | 28 (32.6) | 23 (26.4) | .377 | 7 (30.4) | 13 (38.2) | .545 | 23 (34.3) | 21 (30.4) | .628 |
| Heart failure | 6 (7.0) | 7 (8.0) | .790 | 0 (0.0) | 4 (7.0) | .088 | 4 (6.0) | 4 (5.8) | .966 |
| Pulmonary hypertension | 3 (3.5) | 4 (4.6) | .711 | 0 (0.0) | 1 (2.9) | .407 | 3 (4.5) | 1 (1.4) | .296 |
| Iliac vein disorders (May-Thurner syndrome) | 1 (1.2) | 1 (1.1) | .993 | 0 (0.0) | 0 (0.0) | N/A | 1 (1.5) | 0 (0.0) | .308 |
| Postphlebitic syndrome | 1 (1.2) | 1 (1.1) | .993 | 0 (0.0) | 1 (2.9) | .407 | 1 (1.5) | 0 (0.0) | .308 |
| Breast cancer | 15 (8.7) | 16 (18.4) | .871 | 2 (8.7) | 1 (2.9) | .340 | 8 (11.9) | 5 (3.7) | .352 |
| Melanoma | 1 (1.2) | 1 (1.1) | .993 | 0 (0.0) | 0 (0.0) | N/A | 1 (1.5) | 1 (1.4) | .983 |
| Uterine cancer | 0 (0.0) | 1 (1.1) | .319 | 0 (0.0) | 0 (0.0) | N/A | 1 (1.5) | 2 (2.9) | .577 |
| Ovarian cancer | 1 (1.2) | 2 (1.2) | .567 | 1 (4.3) | 0 (0.0) | .220 | 2 (3.0) | 0 (0.0) | .148 |
| Prostate cancer | 0 (0.0) | 0 (0.0) | N/A | 0 (0.0) | 1 (2.9) | .407 | 0 (0.0) | 0 (0.0) | N/A |
| Cervical cancer | 0 (0.0) | 0 (0.0) | N/A | 0 (0.0) | 0 (0.0) | N/A | 0 (0.0) | 1 (1.4) | .323 |
| Placental cancer | 0 (0.0) | 0 (0.0) | N/A | 0 (0.0) | 0 (0.0) | N/A | 0 (0.0) | 0 (0.0) | N/A |
| Vaginal cancer | 0 (0.0) | 0 (0.0) | N/A | 0 (0.0) | 0 (0.0) | N/A | 0 (0.0) | 0 (0.0) | N/A |
| Vulvar cancer | 0 (0.0) | 0 (0.0) | N/A | 0 (0.0) | 0 (0.0) | N/A | 0 (0.0) | 0 (0.0) | N/A |

(Continued on next page)

**Table II.** Continued.

| | Comparison group 1 | | | Comparison group 2 | | | Comparison group 3 | | |
|---|---|---|---|---|---|---|---|---|---|
| | CONS (n = 86) | CONS + FLX (n = 87) | *P* value[a] | CONS + FLX (n = 23) | CONS + SPCDs (n = 34) | *P* value[b] | CONS + FLX (n = 67) | CONS + other APCDs (n = 69) | *P* value[c] |
| Lymphoma and leukemia | 0 (0.0) | 0 (0.0) | N/A | 0 (0.0) | 1 (2.9) | .407 | 0 (0.0) | 0 (0.0) | N/A |
| Soft tissue sarcoma | 0 (0.0) | 0 (0.0) | N/A | 0 (0.0) | 0 (0.0) | N/A | 0 (0.0) | 1 (1.4) | .323 |

*APCDs,* Advanced pneumatic compression devices; *CONS,* conservative therapy; *CVI,* chronic venous insufficiency; *FLX,* Flexitouch; *HMO,* health maintenance organization; *N/A,* not applicable; *PPO,* preferred provider organization; *SD,* standard deviation; *SPCDs,* simple pneumatic compression devices; *VLUs,* venous leg ulcers.
Values are reported as number (%) unless otherwise indicated.
[a]Comparison of FLX in conjunction with CONS vs CONS.
[b]Comparison of FLX vs single-chamber pneumatic compression devices, both in conjunction with CONS.
[c]Comparison of FLX vs other APCDs, both in conjunction with CONS.

**Table III.** Phlebolymphedema-related medical resource utilization (MRU) across propensity score-matched groups

| | Comparison group 1 | | | Comparison group 2 | | | Comparison group 3 | | |
|---|---|---|---|---|---|---|---|---|---|
| | CONS (n = 86) | CONS + FLX (n = 87) | *P* value[a] | CONS + FLX (n = 23) | CONS + SPCDs (n = 34) | *P* value[b] | CONS + FLX (n = 67) | CONS + other APCDs (n = 69) | *P* value[c] |
| Patients with hospitalizations, % | 19.77 | 14.94 | .62 | 4.35 | 14.71 | .24 | 11.94 | 17.39 | .53 |
| Mean annual hospitalizations | 0.32 | 0.13 | <.001 | 0.02 | 0.10 | .29 | 0.12 | 0.19 | .89 |
| Patients with outpatient hospital visits, % | 90.70 | 100 | .95 | 100 | 97.06 | .96 | 100 | 100 | N/A |
| Mean annual outpatient hospital visits | 6.91 | 8.41 | .41 | 4.61 | 8.78 | .11 | 9.41 | 11.74 | .37 |
| Patients with cellulitis diagnoses, % | 37.21 | 24.14 | .14 | 38.24 | 21.74 | .18 | 22.39 | 44.93 | .02 |
| Mean courses of PT or OT | 1.01 | 0.76 | .38 | 0.39 | 0.20 | .24 | 0.73 | 0.42 | .17 |
| Patients using PT or OT, % | 61.63 | 37.93 | .01 | 34.78 | 20.59 | .23 | 38.81 | 23.19 | .02 |

*APCDs,* Advanced pneumatic compression devices; *CONS,* conservative therapy; *FLX,* Flexitouch; *OT,* occupational therapy; *PT,* physical therapy; *SPCDs,* simple pneumatic compression devices.
[a]Comparison of FLX in conjunction with CONS vs CONS.
[b]Comparison of FLX vs single-chamber pneumatic compression devices, both in conjunction with CONS.
[c]Comparison of FLX vs other APCDs, both in conjunction with CONS.

the effectiveness of FLX in management of phlebolymphedema and related sequelae.

In addition, receipt of FLX was associated with 50% lower rates of cellulitis compared with other APCDs, representing a major direct health benefit for FLX over the broader class of APCDs. Cellulitis is a major driver of MRU and both inpatient and outpatient costs in patients with VLUs. Among patients with VLUs, more than two-thirds of hospital admissions were due to cellulitis that was resistant to outpatient treatment and led to a tripling of costs for such patients.[11] Cellulitis also creates a vicious circle in which the episodes of cellulitis damage existing lymphatic vessels, further worsening the lymphedema.[24,34] Given the high clinical and cost burden of cellulitis and the vicious circle within phlebolymphedema, it is paramount for clinicians to curb cellulitis early. Within lymphedema, a previous claims-based study by Karaca-Mandic et al[23] demonstrated a 79% decline in episodes of cellulitis in cancer-associated lymphedema after FLX use as opposed to no significant decline in those using SPCDs. Across both studies, FLX is demonstrated to be an effective tool for reducing the rates of cellulitis.

A previous systematic review by Berliner et al[28] found mixed evidence for the use of PCDs for treatment of CVI and VLUs and concluded that the available data could not reliably inform optimal choice of compression therapy. However, Berliner et al did not differentiate between specific devices and PCD approaches, and the review was based on studies performed two decades earlier. Our study suggests that FLX, with previously documented, physiologically based therapeutic impact,[16,22,35,36] is more effective than other APCDs, presumably on the basis of a more directly targeted effect on lymphatic function than with other devices that lack this targeted impact.[16]

Our study further supports the need for better awareness and diagnosis of phlebolymphedema. Of the 26,902

**Table IV.** Phlebolymphedema-related mean costs across propensity score-matched groups[a,b]

| | Comparison group 1 | | | Comparison group 2 | | | Comparison group 3 | | |
|---|---|---|---|---|---|---|---|---|---|
| | CONS (n = 86) | CONS + FLX (n = 87) | *P* value | CONS + FLX (n = 23) | CONS + SPCDs (n = 34) | *P* value | CONS + FLX (n = 67) | CONS + other APCDs (n = 69) | *P* value |
| Total cost | $12,253 | $3839 | **.001** | $1153 | $7449 | **.008** | $3973 | $8436 | **.032** |
| Home health | $370 | $334 | .681 | $408 | $522 | .923 | $380 | $511 | .508 |
| Emergency | $11 | $33 | .514 | $6 | $7 | .523 | $36 | $45 | .504 |
| Inpatient | $8715 | $1560 | **.003** | $297 | $4215 | **.002** | $1468 | $4186 | .287 |
| Outpatient hospital | $2534 | $1129 | **.027** | $368 | $2347 | **.020** | $1320 | $3062 | **.041** |
| Outpatient PT or OT | $81 | $39 | **.015** | $16 | $34 | .328 | $36 | $37 | .677 |
| All other outpatient | $2453 | $1090 | **.029** | $353 | $2313 | **.023** | $1283 | $3026 | **.038** |
| Office | $583 | $652 | .736 | $74 | $355 | .052 | $600 | $620 | .332 |
| Laboratory | $1 | $5 | .074 | $0 | $2 | .201 | $6 | $3 | .463 |
| Other service location | $39 | $126 | .645 | $0 | $0 | 1.000 | $163 | $8 | .238 |

*APCDs,* Advanced pneumatic compression devices; *CONS,* conservative therapy; *FLX,* Flexitouch; *OT,* occupational therapy; *PT,* physical therapy; *SPCDs,* simple pneumatic compression devices.
*P* values ≤.05 are considered statistically significant.
[a]Costs reported as per patient per year phlebolymphedema- and sequelae-related costs, excluding all SPCDs and accessory costs.
[b]A gamma/log link general linear model was used for estimating all cost outcomes. Adjusted estimates hold sex and age constant.

patients continuously enrolled with lymphedema, only 8630 (32%) had a diagnosis of CVI. This is similar to the study of Muluk et al,[35] in which 27% of lymphedema patients were identified with concurrent CVI. It is well established that CVI and lymphedema are underdiagnosed, and thus it is likely that a number of potentially eligible patients were excluded from observation because they were not properly diagnosed. The small sample sizes in the study treatment arms therefore speak more generally to the widespread underdiagnosis and undertreatment of patients with phlebolymphedema resulting from the lack of awareness of lymphedema as a consequence of CVI.

Our study has several limitations. First, claims data sets do not capture or account for compliance with prescribed compression modalities. Thus, compliance of the patient with any of the modalities evaluated is not known, and its impact on the reported outcomes cannot be assessed.

Second, ulcer healing cannot be determined directly from this analysis and is a limitation of an administrative database analysis. The reduced health care costs of FLX, however, can be related to a greater proportion of healed ulcers in the FLX group, as demonstrated by a previous cost analysis.[11] Reduced MRU with a healed venous ulcer is thus associated with decreased cost.

Third, this paper focuses on medical benefit claims and does not include pharmaceutical costs. However, a previous study found that pharmaceutical costs related to lymphedema were negligible across groups of patients.[37]

Fourth, established codes do not indicate phlebolymphedema disease severity; thus, we could not control for severity of phlebolymphedema in the propensity score matching. However, the advanced stage of the venous component in this cohort is objectively reflected in the >85% of patients with diagnosed VLUs (Table II).

Fifth, claims data sets include only coded services and do not capture patients' burden and indirect resource utilization. Our paper likely substantially underestimates the overall burden of phlebolymphedema and the broader impact associated with appropriate treatment on nonmedical costs (eg, transportation costs), indirect costs (eg, productivity, absenteeism), and intangible costs (eg, quality of life, psychosocial burden). A broader look at the full burden of phlebolymphedema is warranted in prospective future research.

Finally, the BHI data set used for analysis includes only commercially insured patients. Thus, our results may not be generalizable to patients covered by Medicaid or Medicare.

## CONCLUSIONS

Phlebolymphedema constitutes a substantial proportion of lymphedema patients in the United States and a significant cost burden that is still likely understated. Optimizing treatment to reduce costly complications is therefore an important goal. This analysis demonstrates the benefits attributable to FLX, a specific APCD, in reducing MRU and total costs for these patients relative to CONS, SPCDs, and other APCDs.

## AUTHOR CONTRIBUTIONS

Conception and design: ML, JG, SH, JI, LG, PKM, TO, SR
Analysis and interpretation: ML, JG, SH, JI, TN, PKM

Data collection: TN
Writing the article: ML
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Statistical analysis: ML, JG, JI, LG, TN, PKM
Obtained funding: SH
Overall responsibility: SR

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