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Healthcare resource utilization and costs before and after lacosamide initiation as adjunctive therapy among patients with epilepsy in the United States

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ABSTRACT

Objective: The objective of this study was to evaluate all-cause and epilepsy-specific healthcare resource utilization and costs following lacosamide (LCM) initiation as adjunctive therapy for the treatment of epilepsy.
Methods: A noninterventional retrospective database analysis was conducted that examined patients diagnosed as having epilepsy who added LCM to existing antiepileptic drug (AED) therapy between 2009 and 2016 (the first LCM prescription was the index event). This study used a single-case design whereby patients served as their own controls. Patients were further required to have a minimum of 12 months of continuous eligibility before (preindex period) and after (postindex period) their index event. In the 12-month postindex period, the only allowed AED regimen change was the addition of LCM. Demographic and clinical characteristics were measured at index and during the preindex period, respectively. All-cause and epilepsy-specific healthcare resource utilization and costs were measured and compared in the pre- and postindex periods. Paired *t*- and McNemar's tests were conducted to assess the significant differences between pre- and postindex. Univariate analyses were used to analyze the impact of LCM on specific subpopulations.
Results: The study sample comprised of 2171 patients: mean (standard deviation [SD]) age: 38.9 (19.3) years; 52.6% female. Just over half (56%) of these patients were on monotherapy before adding LCM. Prior to adding LCM, 28.8% of patients had an epilepsy-specific inpatient (IP) admission, and 35.7% of patients had an all-cause IP admission, compared with 18.2% and 26.1% of patients in the post-LCM period, respectively (both $p < 0.0001$). Likewise, 35.6% of patients had an epilepsy-specific emergency room (ER) visit, and 50.0% had an all-cause ER visit prior to adding LCM, compared with 23.8% and 42.1% in post-LCM, respectively (both $p < 0.0001$). After adding LCM, one-year mean [SD] epilepsy-specific IP admission costs decreased by 42.9% ($13,647 [$52,290] to $7788 [$32,321]), and all-cause IP admission costs decreased by 38.6% ($20,654 [$72,716] to $12,688 [$46,120]) (both $p < 0.0001$). One-year epilepsy-specific mean [SD] ER costs decreased by 35.2% ($691 [$1756] to $448 [$1909]; $p < 0.0001$), and all-cause ER cost decreased by 17.8% ($1217 [$3014] to $1000 [$2970]; $p < 0.01$).
Conclusions: Epilepsy-related IP hospitalizations and ER visits (indicators of seizures) were significantly reduced in patients with epilepsy 12 months after adding LCM as an adjunctive therapy to existing AED treatment in a real-world setting, leading to reduced healthcare resource utilization and epilepsy costs.

1. Introduction

Epilepsy is a complex neurological disorder characterized by recurrent unprovoked seizures affecting people of all ages [1,2]. The International League Against Epilepsy (ILAE) have classified seizures into focal (partial) onset, generalized onset, and unknown (cryptogenic) onset [3]. There are an estimated 3.4 million people living with epilepsy in the US, and 1 in 26 will develop epilepsy in their lifetime [1,2,4].

Abbreviations: AED, antiepileptic drug; CNS, central nervous system; DCI, Deyo–Charlson Comorbidity index; EEG, electroencephalogram; ER, emergency room; ESCI, epilepsy-specific risk adjustment comorbidity index; GABA, gamma-aminobutyric acid; GERD, gastroesophageal reflux disease; HRU, healthcare resource utilization; ICD-9-CM, International Classification of Disease, 9th Revision, Clinical Modification; IP, inpatient; IRR, incidence rate ratio; LCM, lacosamide; NS, not significant; OP, outpatient; OR, odds ratio; SD, standard deviation; UTI, urinary tract infection.

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Epilepsy places a substantial economic burden on the US healthcare system but estimates of these costs vary. Evidence from published studies suggests that the annual cost (direct and indirect) of epilepsy in the US has increased from $12.5 billion in 1995 [5] to $36.8 billion in 2014 [6]. A systematic review of the published literature found that the total direct healthcare costs per patient with epilepsy (adjusted to 2013 dollars) ranged from $10,192 to $47,862, with epilepsy-specific costs per patient ranging from $1022 to $19,749 [7].

Monotherapy with antiepileptic drugs (AEDs) is the preferred treatment for epilepsy [8,9]. However, approximately one-third of patients with focal epilepsy are unresponsive to AED therapy, and they continue to experience poor seizure control [10]. Patients who fail to achieve adequate seizure control with two tolerated and appropriately administered AED treatment regimens (either monotherapy or polytherapy) are referred to as having treatment-refractory epilepsy [11,12]. Studies have shown that patients with refractory epilepsy incur higher healthcare resource utilization (HRU) and costs compared with those with nonrefractory epilepsy [11,13].

Several third-generation AEDs have been approved for the treatment of epilepsy, providing new treatment options, particularly for patients with treatment-refractory epilepsy [14]. Lacosamide (LCM) is a third-generation AED approved as both a monotherapy and as adjunctive therapy for focal epilepsy in those 4 years of age and older [15]. The mechanism of action of LCM enhances the slow inactivation of voltage-gated sodium channels [16]. The efficacy and safety of LCM have been established in randomized/nonrandomized clinical trials and observational studies [17–25]; however, there are limited data regarding HRU and cost burden associated with adjunctive treatment with LCM in real-world clinical practice [11,26]. The current study evaluates all-cause and epilepsy-specific HRU and costs among adult and patients with pediatric epilepsy before and after initiating LCM as an adjunctive therapy for treatment of focal, generalized, and other seizures.

2. Methods

2.1. Study design and data source

This retrospective claims-based analysis used administrative medical and pharmacy claims from the IBM MarketScan® Commercial Claims and Encounters (Commercial) and Medicare Supplemental and Coordinated Benefits (Medicare) databases between January 1, 2009 and July 1, 2016. These data sources contain anonymized health records of millions of individuals enrolled in primary employer-sponsored or Medicare supplemental insurance plans. Both databases are compliant with the Health Insurance Portability and Accountability Act of 1996; therefore, institutional review board approval was not necessary for this study.

Patients with epilepsy who initiated LCM (index date) as an adjunctive therapy were selected. Healthcare resource utilization and costs were compared between the 12 months before and 12 months after the index date. This study used a single-case design, with each patient acting as their own control. This design reduced heterogeneity and minimized confounding, as patients' pre-LCM AED regimens vary widely, making selection of one particular comparator infeasible. Patients receiving a polytherapy AED regimen before the addition of LCM also served as an internal control for the addition of any adjunctive therapy, eliminating the need for a reference group.

2.2. Patient selection

Patients were included in this study if they met at least one of the following criteria: a) two or more medical claims with a diagnosis code for epilepsy (International Classification of Diseases, Ninth/Tenth Edition, Clinical Modification [ICD-9-CM] 345.xx/ICD-10 code G40.xx) in any diagnosis position among separate medical encounters (≥30 days to ≤ 365 days apart); b) at least one claim with ICD-9-CM code 345.xx or ICD-10 code G40.xx, and one or more claims with ICD-9-CM code 780.3x, or ICD-10 code R56.9 in any diagnosis position among separate medical encounters (≥30 days to ≤365 days apart). Patients were required to have at least two pharmacy claims for LCM between January 1, 2009 and July 1, 2016, with the second claim within 6 months of the first claim. The first claim for LCM is defined as the index date. Patients were further required to have one or more claims for one or more non-LCM AED(s) in the 12-month preindex period and one or more claims for the same non-LCM AED(s) in the 12-month postindex period. No AED regimen changes were allowed between the preindex and postindex periods, with the exception of the addition of LCM. At a least one-day supply for each non-LCM AED was required to overlap with the index date. All patients were required to have continuous enrollment with medical and pharmacy coverage for the 12-month pre- and postindex periods.

2.3. Outcome measures

2.3.1. Healthcare resource utilization and cost

All-cause and epilepsy-specific direct HRU and costs in the 12-month pre- and postindex periods were measured overall and by service category (inpatient, outpatient [hospital observation stays, emergency room (ER) visits, nonneurology and neurology outpatient office visits, and other outpatient services], and pharmacy). Healthcare costs and HRU were considered epilepsy-specific for claims with ICD-9-CM 345.xx or ICD-10-CM G40.xx as a primary diagnosis or ICD-9-CM 780.39 or ICD-10-CM R56.9 in any position on the claim. Healthcare costs were based on paid amounts of adjudicated claims, including insurer and health plan payments, and patient cost-sharing in the form of copayment, deductibles, and coinsurance. All healthcare costs were expressed in 2016 constant US dollars, adjusted using the Medical Care component of the Consumer Price Index [27].

2.3.2. Key covariates

Demographic characteristics including age, gender, geographic region (northeast, north central, south, west, or unknown), insurance plan type (fee-for-service, managed care, other, unknown), and urban/rural residence were measured on the index date. Clinical characteristics including Deyo–Charlson Comorbidity index (DCI), epilepsy-specific risk adjustment comorbidity index (ESCI) [28], type of epilepsy diagnosis (focal, generalized, other), number of unique AED and non-AED medications, number of and specific central nervous system (CNS)-related comorbidities (aggression, anxiety, anoxic brain injury, autism, bipolar disorder, cerebrovascular disease [excluding stroke], CNS infections, delusional disorders, dementia, depression, disturbance of conduct disorder, encephalopathy, head/traumatic brain injury, headache [excluding migraine], manic disorder, meningioma, meningitis, migraine, other episodic mood disorders, personality disorder, psychoses, schizophrenia, stroke, tuberous sclerosis, suicidal ideation), number of and specific other comorbidities (alcohol dependence, anemia, aspiration pneumonia, asthma, cancer, cardiac arrhythmias, cardiovascular disease, chronic pulmonary disease, diabetes, drug abuse, dysphagia, fibromyalgia, fracture [pathological, traumatic], gastroesophageal reflux disease [GERD], hyperlipidemia, hypertension, metastatic cancer, moderate-to-severe liver disease, renal disease, peripheral vascular disease, paraplegia/hemiplegia, pulmonary circulation disorder, solid tumors without metastases, urinary tract infection [UTI]), epilepsy-specific procedures and treatments (epilepsy-related surgeries, vagus nerve stimulation, video electroencephalogram [EEG]), concomitant medications (antipsychotics, anxiolytics, sleep medications, opioids, muscle relaxants, gamma-aminobutyric acid [GABA] analogs [gabapentin/pregabalin]), and specific AED medication(s) used (brivaracetam, carbamazepine, divalproex, eslicarbazepine, fosphenytoin, lamotrigine, levetiracetam, oxcarbazepine, perampanel, phenobarbital, phenytoin, rufinamide, tiagabine, topiramate, valproate, vigabatrin, zonisamide) were assessed in the 12-month preindex period.

2.4. Statistical analyses

Dependent and independent variables were summarized descriptively. Categorical variables were reported as counts and percentages, and continuous variables were expressed as means and standard deviations (SDs). Pre- and postindex comparisons were performed using paired tests of significance (paired *t*-tests for comparison of means and McNemar's tests for comparison of proportions).

Univariate analyses were performed to measure the effects of selected patient characteristics on probability of an inpatient admission or ER visit (all-cause and epilepsy-specific) and on cost differences from pre- to postindex periods (total inpatient costs and total cost of medical services, both all-cause and epilepsy-specific). These patient characteristics included baseline therapy type (monotherapy or polytherapy), age, sex, location (urban or rural), type of epilepsy (focal epilepsy, generalized epilepsy, other epilepsies), ESCI (0, 1, 2, 3, or 4+), number of CNS conditions (0, 1, 2, or 3+), specific CNS conditions (anxiety/depression, cerebrovascular, encephalopathy, headache, migraine, stroke, head/traumatic brain injury), other comorbid conditions (cancer, cardiac arrhythmias, cardiovascular disease, hyperlipidemia, hypertension, UTI), and concomitant medications (GABA analogs, antipsychotics, opioids, muscle relaxants). The mean and percentage for both pre- and postindex periods, along with the difference (postindex minus preindex) and associated p-value (McNemar's test for utilization; paired *t*-test for cost), were reported.

3. Results

3.1. Study sample

Of 22,213 patients with epilepsy with claims for LCM identified between January 1, 2009 and July 1, 2016, 2171 patients met the final study eligibility criteria (Fig. 1).

3.2. Patient characteristics

On average, patients were 38.9 years of age (SD, 19.3) and slightly more likely to be female (52.6%).The majority (66.2%) of patients had a diagnosis for focal seizures/epilepsy. Patients had a mean (SD) ESCI score of 1.2 (2.2). More than half (56.6%) of the patients had a CNS-related comorbidity, with anxiety (15.4%), headache (14.0%), and depression (13.0%) being the most common. Before initiation of LCM, levetiracetam (54.4%), lamotrigine (24.9%), and topiramate (16.1%) were the most commonly used AEDs (Table 1).

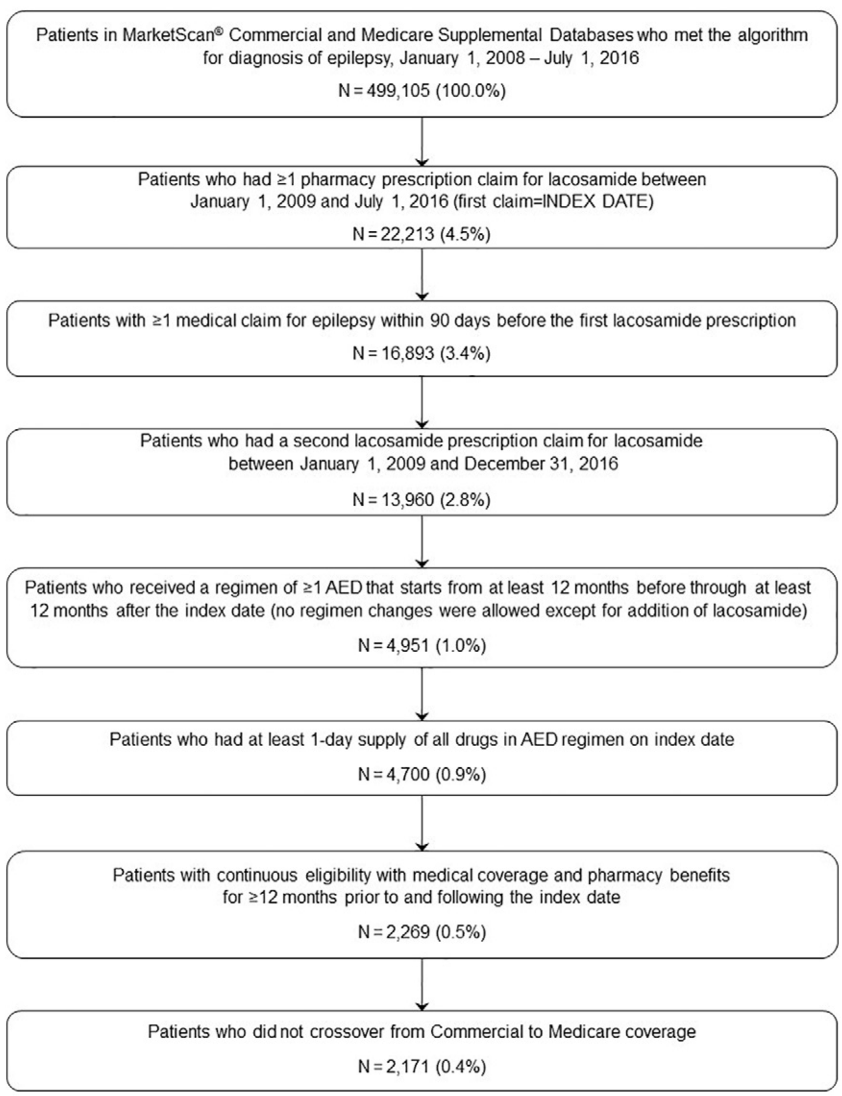


Fig. 1. Patient selection process. Among 22,213 patients with epilepsy with claims for LCM identified between January 1, 2009 and July 1, 2016, a total of 2171 patients met the final study eligibility criteria and were included in the analyses.

Table 1
Patient characteristics at index date.

Characteristics	All patients (N = 2171)
Mean (SD) age, years	38.9 (19.3)
Sex, N (%)	
Male	1028 (47.4%)
Female	1143 (52.6%)
Payer, N (%)	
Commercial	1957 (90.1%)
Medicare	214 (9.9%)
Type of seizures/epilepsy, N (%)[a]	
Focal	1438 (66.2%)
Generalized	814 (37.5%)
Other	1370 (63.1%)
Mean (SD) ESCI [28]	1.2 (2.2)
ESCI, N (%)	
0	1319 (60.8%)
1–2	459 (21.1%)
3–4	220 (10.1%)
5+	173 (8.0%)
Patients with any CNS comorbidity	1228 (56.6%)
Number of CNS conditions, N (%)	
0	1162 (53.5%)
1	491 (22.6%)
2	292 (13.5%)
3+	226 (10.4%)
Top 10 CNS-related comorbidities and procedures, N (%)	
Anxiety	334 (15.4%)
Headache (excluding migraine)	304 (14.0%)
Depression	283 (13.0%)
Cerebrovascular disease (excluding stroke)	265 (12.2%)
Encephalopathy	199 (9.2%)
Migraine	179 (8.2%)
Head injury/traumatic brain injury	161 (7.4%)
Brain tumor	158 (7.3%)
Stroke	149 (6.9%)
Meningitis	82 (3.8%)
Top 10 other comorbidities, N (%)	
Hypertension	503 (23.2%)
Hyperlipidemia	312 (14.4%)
Cardiovascular disease	304 (14.0%)
Cardiac arrhythmias	245 (11.3%)
Cancer	213 (9.8%)
UTI	209 (9.6%)
GERD	202 (9.3%)
Hypothyroidism	201 (9.3%)
Diabetes	186 (8.6%)
Anemia	183 (8.4%)
Concomitant medications noted in >10% of patients, N (%)	
Anxiolytics	985 (45.4%)
Opioids	720 (33.2%)
Muscle relaxants	223 (10.3%)
GABA analogs	251 (11.6%)
AED medication noted in >10% of patients, N (%)	
Levetiracetam	1181 (54.4%)
Lamotrigine	541 (24.9%)
Topiramate	349 (16.1%)
Oxcarbazepine	281 (12.9%)
Divalproex	252 (11.6%)
Carbamazepine	222 (10.2%)

[a] Categories are not mutually exclusive.

Table 2
Healthcare resource utilization before and after the addition of LCM, within the 12-month preindex and postindex periods, respectively.

	All patients (N = 2171)	
	Preindex period	Postindex period
All-cause healthcare utilization		
Patients with at least one inpatient admission, N (%)	775 (35.7%)	566 (26.1%)***
Patients with outpatient services, N (%)		
Hospital observation stays	199 (9.2%)	163 (7.5%)*
ER visit	1085 (50.0%)	915 (42.1%)***
Outpatient office visit	2150 (99.0%)	2141 (98.6%)[ns]
Epilepsy-specific healthcare utilization[a]		
Patients with at least one inpatient admission, N (%)	625 (28.8%)	396 (18.2%)***
Patients with outpatient service, N (%)		
Hospital observation stays	124 (5.7%)	93 (4.3%)*
ER visit	772 (35.6%)	517 (23.8%)***
Outpatient office visit	2025 (93.3%)	2052 (94.5%)[ns]

*** $p < 0.0001$.
* $p < 0.05$.
[ns] $p \geq 0.05$ for difference between pre- and postindex periods.
[a] Healthcare resource utilization for encounters with a primary diagnosis of ICD-9-CM 345.xx or ICD-10-CM G40.xx, or ICD-9-CM 780.39 or ICD-10-CM R56.9 in any position.

3.3. Healthcare resource utilization and costs

There were significant differences in most of the HRU measures examined before and after the addition of LCM. Specifically, the percentages of patients with all-cause inpatient admissions (35.7% vs. 26.1%; $p < 0.0001$), ER visits (50.0% vs. 42.1%; $p < 0.0001$), and hospital observation stays (9.2% vs. 7.5%; $p < 0.05$) declined after the addition of LCM (Table 2). Similarly, the percentage of patients with epilepsy-specific inpatient admissions (28.8% vs. 18.2%; $p < 0.0001$), ER visits (35.6% vs. 23.8%; $p < 0.0001$), and hospital observation stays (5.7% vs. 4.3%; $p < 0.05$) all declined upon the addition of LCM (Table 2).

In line with the trends observed for HRU, the addition of LCM to existing AED therapy resulted in reduced inpatient hospitalization, ER, and total medical costs (both all-cause and epilepsy-specific). After the addition of LCM, significant decreases were observed in all-cause healthcare costs for inpatient admissions ($20,654 vs. $12,688; $p < 0.0001$), ER visits ($1217 vs. $1000; $p < 0.01$), and total medical expenses ($34,917 vs. $28,717; $p < 0.01$). Total all-cause pharmacy costs increased ($8749 vs. $15,502; $p < 0.0001$). Total all-cause healthcare expenditure (medical plus pharmacy costs) was similar after LCM initiation ($43,666 vs. $44,219). As observed for all-cause costs, epilepsy-specific costs for inpatient admission decreased after LCM initiation from $13,647 to $7788 ($p < 0.0001$), while ER visit costs fell from $691 to $448 ($p < 0.0001$), and total medical expenditures declined from $18,066 to $13,313 ($p < 0.0001$). The epilepsy-specific pharmacy costs increased significantly from $4940 in the preindex period to $10,882 in the postindex period ($p < 0.0001$), but like all-cause expenses, there was no significant change in total epilepsy-specific healthcare expenditures ($23,006 vs. $24,195) (Fig. 2).

In univariate analysis, LCM was found to exert significant benefits across most subpopulations of patients with epilepsy analyzed (Figs. 3 and 4). The proportion of patients with an inpatient admission or ER visit (all-cause and epilepsy-specific) decreased significantly after the addition of LCM in almost all subpopulations of patients (Fig. 3a–d). However, several interesting exceptions were observed for all-cause and epilepsy-specific cost differences after the addition of LCM (Fig. 4a–d). While patients who were on a monotherapy regimen before the addition of LCM had a significant reduction in inpatient and total medical costs (both all-cause and epilepsy-specific), no significant cost reduction was observed in patients who received polytherapy before LCM addition. There was no significant change in any cost among patients without CNS comorbidities after the addition of LCM; however, the difference in costs increased with the number of CNS comorbid conditions observed. Finally, patients 55 years of age and older tended to have significant reductions in both all-cause and epilepsy-specific inpatient and medical costs, while there was no significant change in healthcare cost in patients <55 years of age after the addition of LCM.

4. Discussion

To our knowledge, this is the first retrospective analysis to provide insights into HRU and costs before and after initiation of LCM as

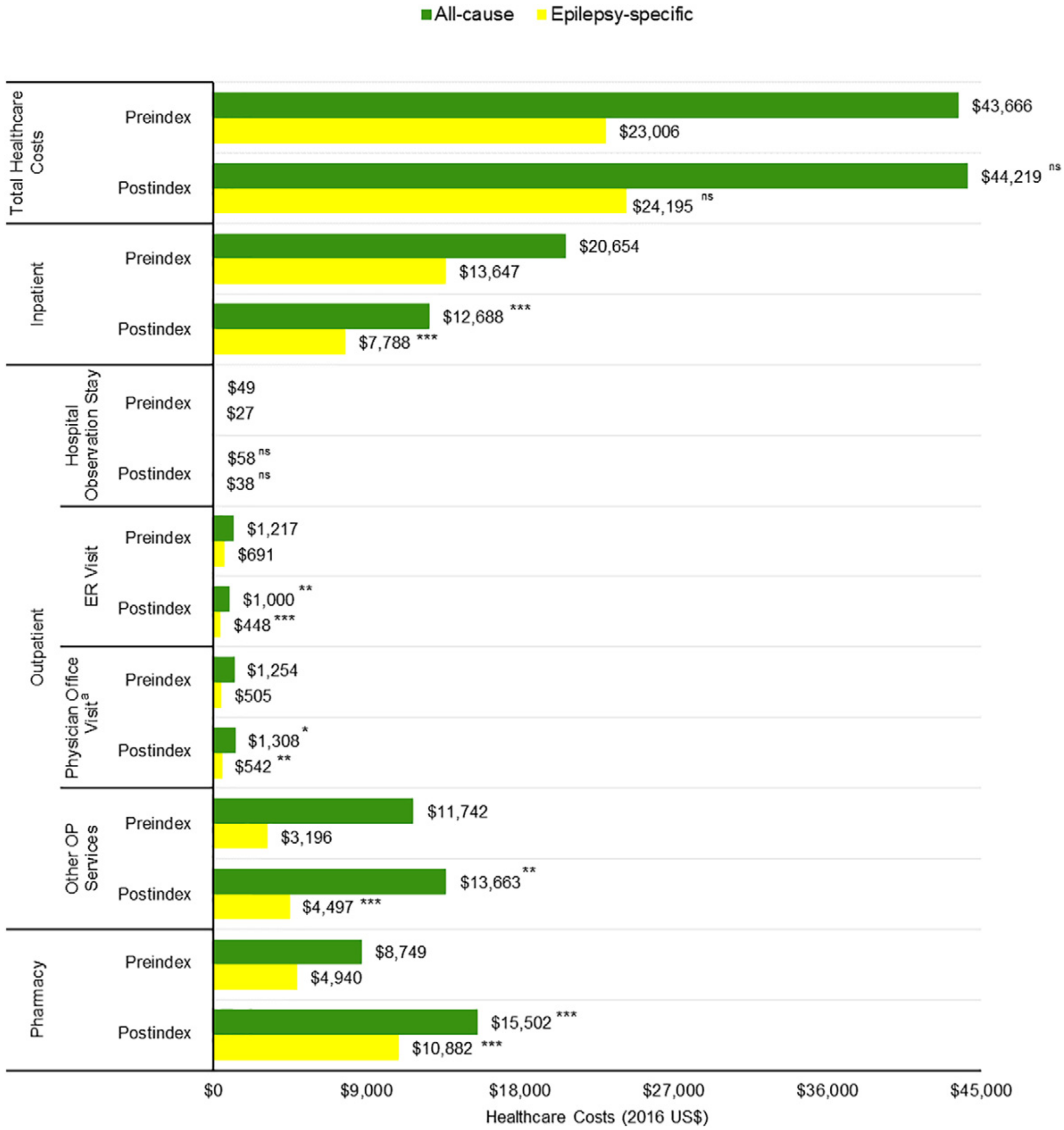


Fig. 2. Comparison of healthcare costs before and after the addition of LCM, within the 12-month preindex and postindex periods, respectively. As well as total healthcare costs, specific costs relating to inpatient and outpatient care and pharmacy costs were assessed. ER, emergency room; NS, not significant; OP, outpatient. ***$p < 0.0001$; **$p < 0.01$; *$p < 0.05$; ns $p \geq 0.05$ for cost comparisons of pre- vs. postindex periods. [a]Differences (preindex vs. postindex) in all-cause physician visit costs by specialty were $349 vs. $376 ($p = 0.0030$) for neurologist and $905 vs. $1208 ($p = 0.127$) for nonneurologist visits. Differences (preindex vs. postindex) in epilepsy-specific physician visit costs by specialty were $298 vs. $326 ($p < 0.0001$) for neurologist and $207 vs. $216 ($p = 0.172$) for nonneurologist visits.

adjunctive therapy among patients with epilepsy in a real-world setting. Results showed that the percentage of patients with all-cause and epilepsy-specific inpatient hospitalizations and ER visits fell significantly in the 12 months following the addition of LCM. Although pharmacy costs increased after LCM addition, this increase was offset by reduced all-cause and epilepsy-specific inpatient, ER, and total medical costs.

The magnitude of resource and economic burden posed by epilepsy is well-documented [5,7,11,29–33]. In a systematic review based on literature published between 1995 to 2013, overall epilepsy costs per person were estimated to range between $1022 and $19,749 [7]. The differences in costs and associated HRU burden are likely to be due in part to whether a patient's epilepsy is well-controlled or uncontrolled. A claims-based study by Manjunath et al. [32] assessed healthcare utilization and costs among patients with uncontrolled epilepsy and those with well-controlled epilepsy. As might be expected, the study found that patients with uncontrolled epilepsy had higher incidence rate ratio (IRR) for hospitalization (IRR: 5.4–6.7), ER visit (IRR: 3.7–5.0), or outpatient visits (IRR: 1.4–1.7) compared with the well-controlled cohort. Furthermore, the total direct costs were higher in patients with uncontrolled epilepsy (adjusted cost difference [95% confidence interval (CI)] Medicaid = $12,258 [$10,482–$14,083]; employer = $14,582 [$12,019–$17,097]) compared with those in the well-controlled cohort [32]. Another retrospective study reported higher odds for all-cause or epilepsy-specific hospitalization (odds ratio [OR]: 1.8, 2.2) and ER visit (OR: 1.6, 1.9, respectively), along with higher costs (all-cause: $23,238 vs. $13,839; epilepsy-specific: $12,399 vs. $5511; both $p < 0.001$) among patients with uncontrolled epilepsy versus patients who are stable [29]. Although we did not directly quantify the resource and economic burden of epilepsy, the pattern of HRU and cost data observed in this study largely endorses the previously reported findings on substantial healthcare burden exerted by epilepsy [5,7,11,29–33]. In addition, the study also suggests that the addition of

LCM to an AED regimen results in improved symptom control, which may alleviate some of the resource and cost burden associated with epilepsy.

There is very limited evidence on the real-world utilization and costs associated with adjunctive therapy in patients with epilepsy [11,26]. A retrospective study evaluated the effect of monotherapy/sequential

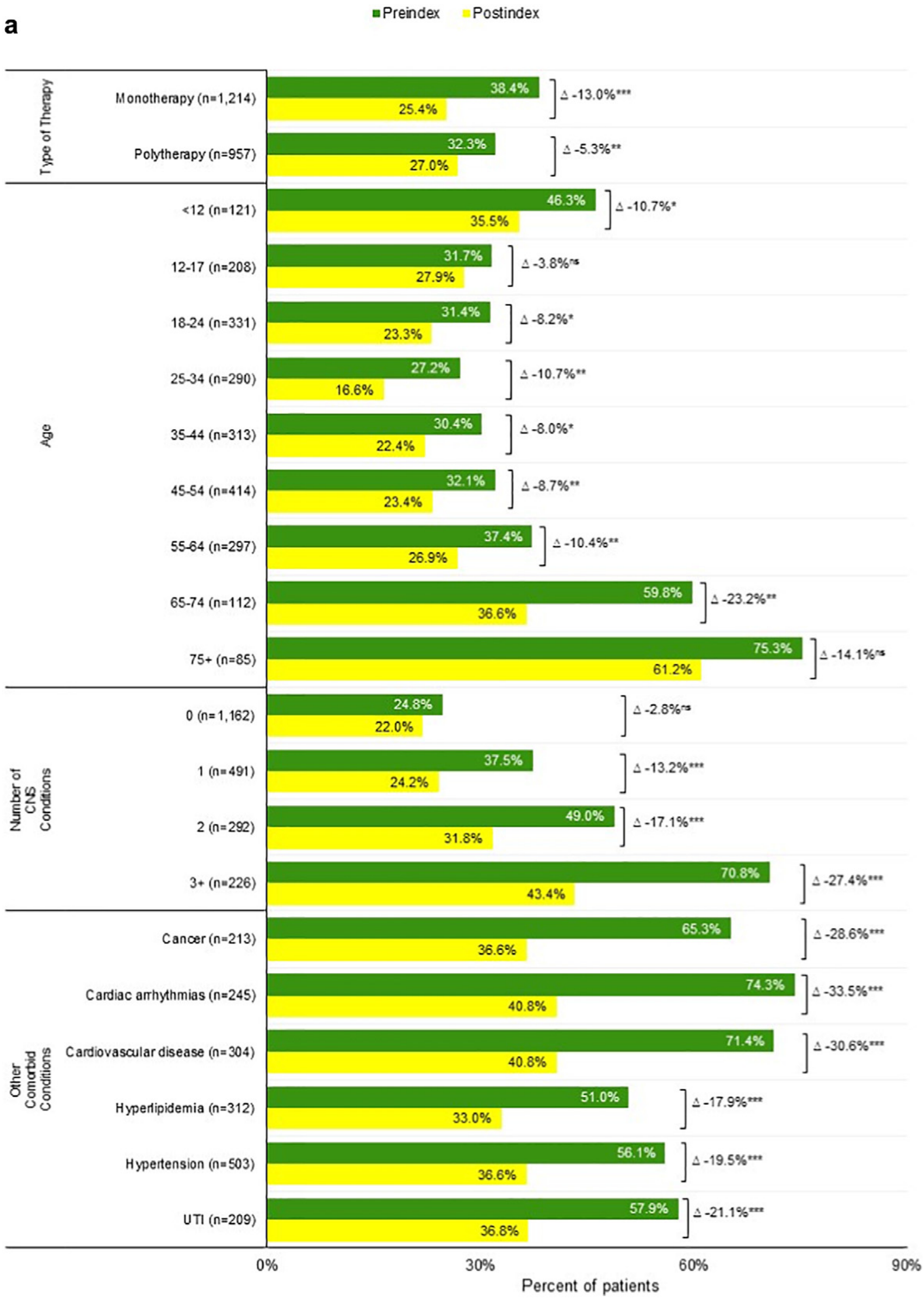


Fig. 3. Univariate analysis of all-cause inpatient admissions (a), all-cause ER visits (b), epilepsy-specific inpatient admissions (c), and epilepsy-specific ER visits (d) before and after the addition of LCM, within the 12-month preindex and postindex periods, respectively, according to selected patient characteristics at index date. CNS, central nervous system; ER, emergency room; NS, not significant; UTI, urinary tract infection. Δ represents the difference between pre- and postindex periods. ***p < 0.0001; **p < 0.01; *p < 0.05; ns p ≥ 0.05 for differences between pre- and postindex periods.

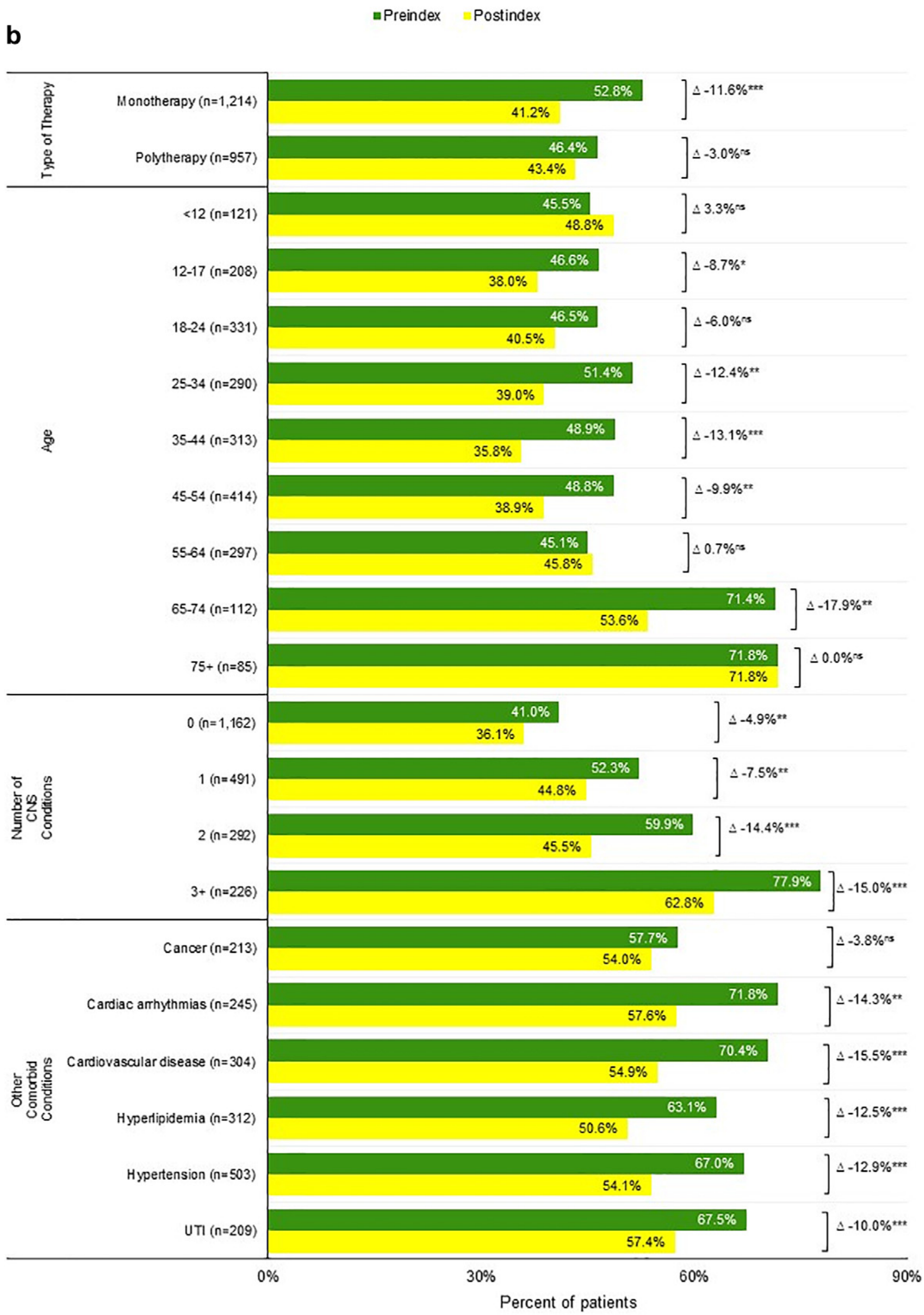
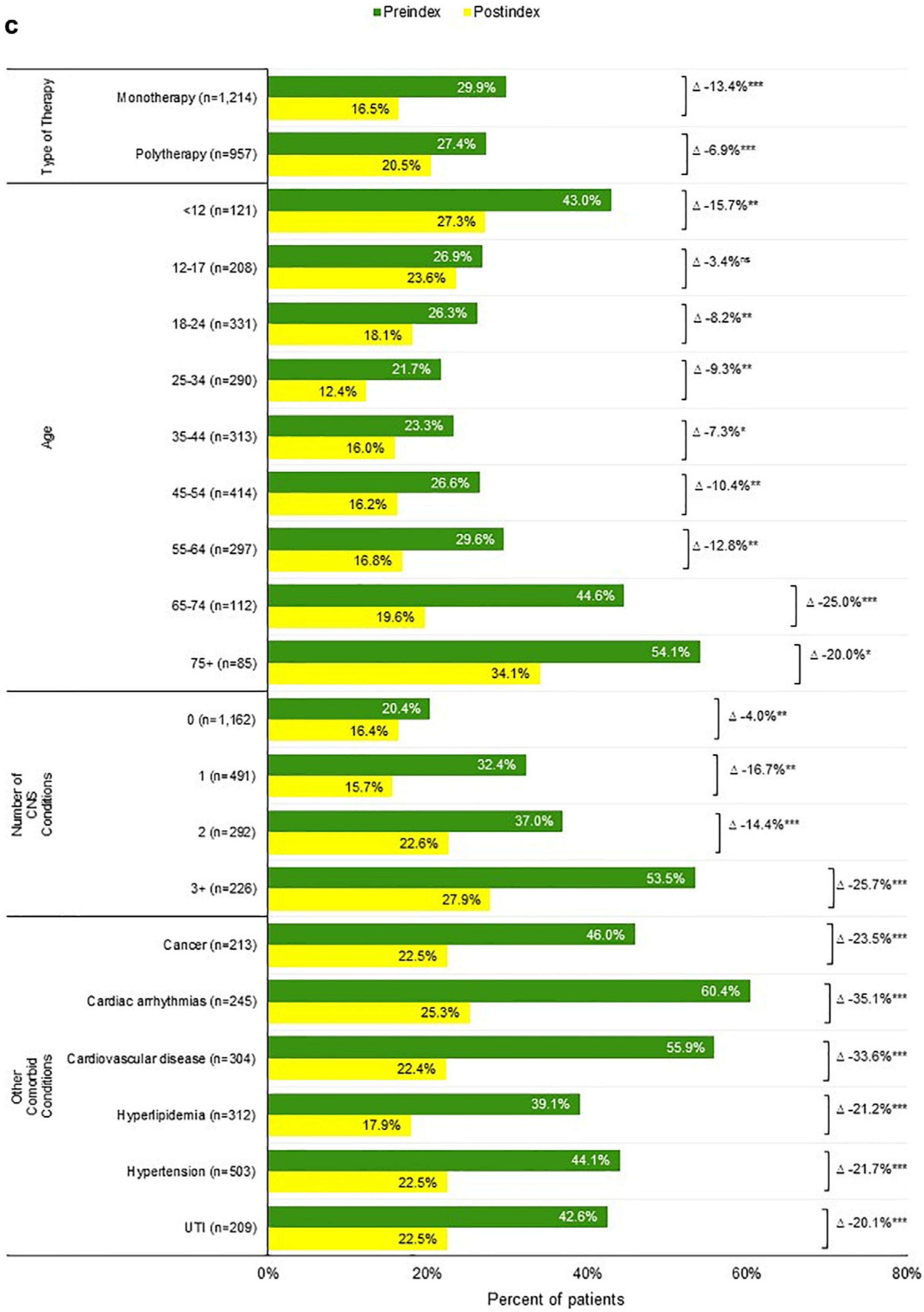


Fig. 3 (*continued*).

monotherapy versus adjunctive therapy on HRU and costs for patients with potentially drug-resistant focal epilepsy. The study reported that patients who transitioned from monotherapy to adjunctive therapy experienced a significant decrease in all-cause and epilepsy-specific hospitalizations. Furthermore, transition from monotherapy to adjunctive therapy was found to reduce adjusted all-cause cost by 30% (from 4205 to $2944/month) and epilepsy-specific cost by 43.2% (from $1601 to $909/month) [26]. Congruent with these findings [26],



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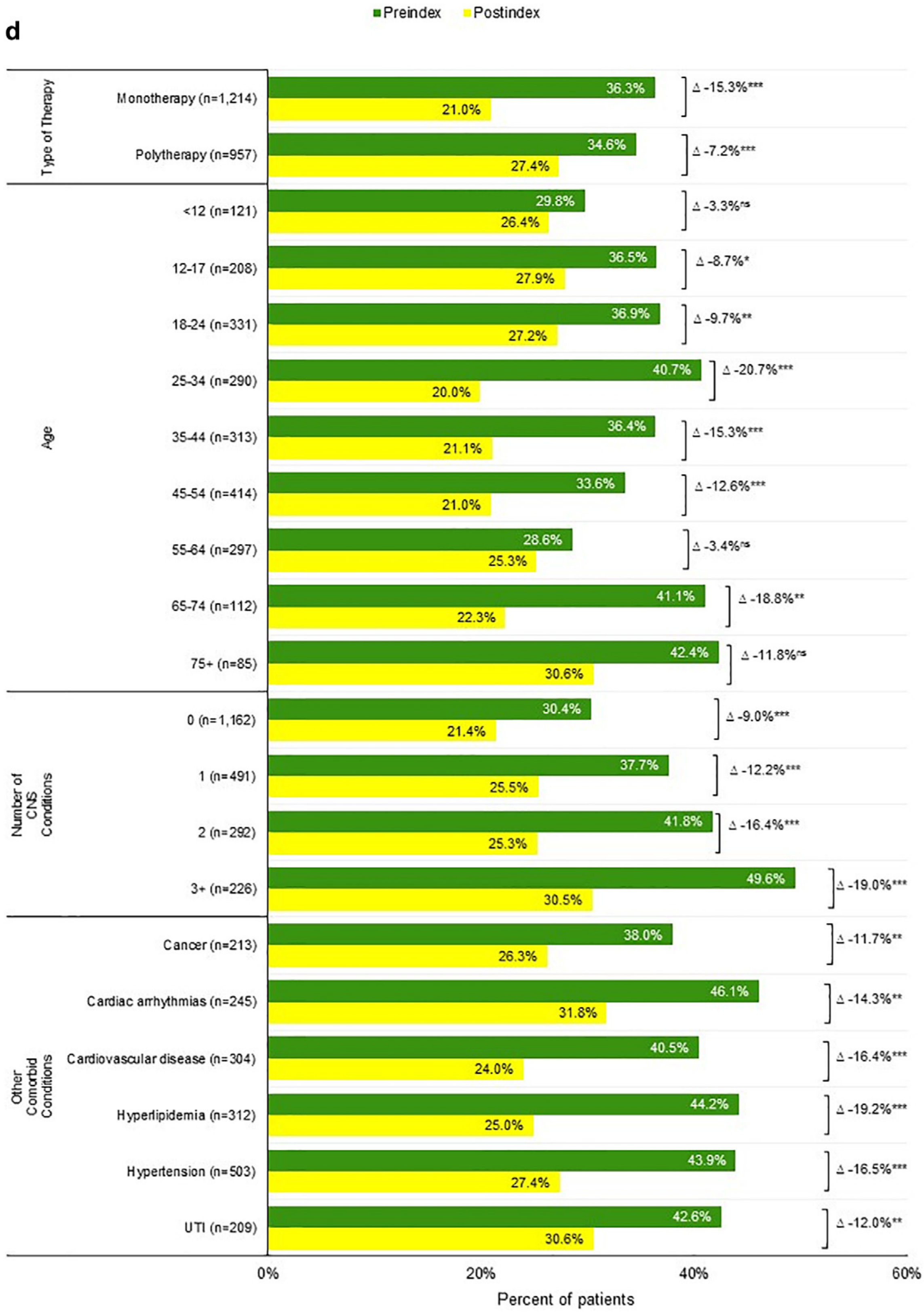
initiation of adjunctive LCM therapy among patients with epilepsy in the present analysis resulted in significant reduction in the percentage of patients with all-cause and epilepsy-specific inpatient admissions and ER visits over 12 months follow-up period [26]. Furthermore, unadjusted all-cause inpatient hospitalization costs decreased by 38.6% (Δ$7966; $p < 0.001$), and epilepsy-specific inpatient hospitalization costs decreased by 42.9% (Δ$5859; $p < 0.001$). The all-cause and epilepsy-specific costs for ER visits decreased by 17.8% (Δ$217; $p < 0.01$)



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and 35.2% (Δ\$243; $p < 0.01$), respectively. Additionally, the total medical costs during the 12-month postindex period decreased (all-cause: Δ\$6200; $p < 0.01$; epilepsy-specific: Δ\$4753; $p < 0.001$) despite higher pharmacy costs (all-cause: Δ\$6753; epilepsy-specific: Δ\$5942; both $p < 0.001$). Univariate analyses showed that adjunctive therapy with LCM resulted in significant reductions in all-cause or epilepsy-specific inpatient and ER admissions in nearly all patient subpopulations examined. However, reductions in costs were more prominent in patients on monotherapy before LCM addition versus those on polytherapy, patients with multiple CNS comorbidities versus those without a CNS comorbidity, and older patients compared with younger patients.

The results of this study are subject to several limitations including those that are inherent to any retrospective analysis. First, the study design, which included patients whose only change to their AED regimen

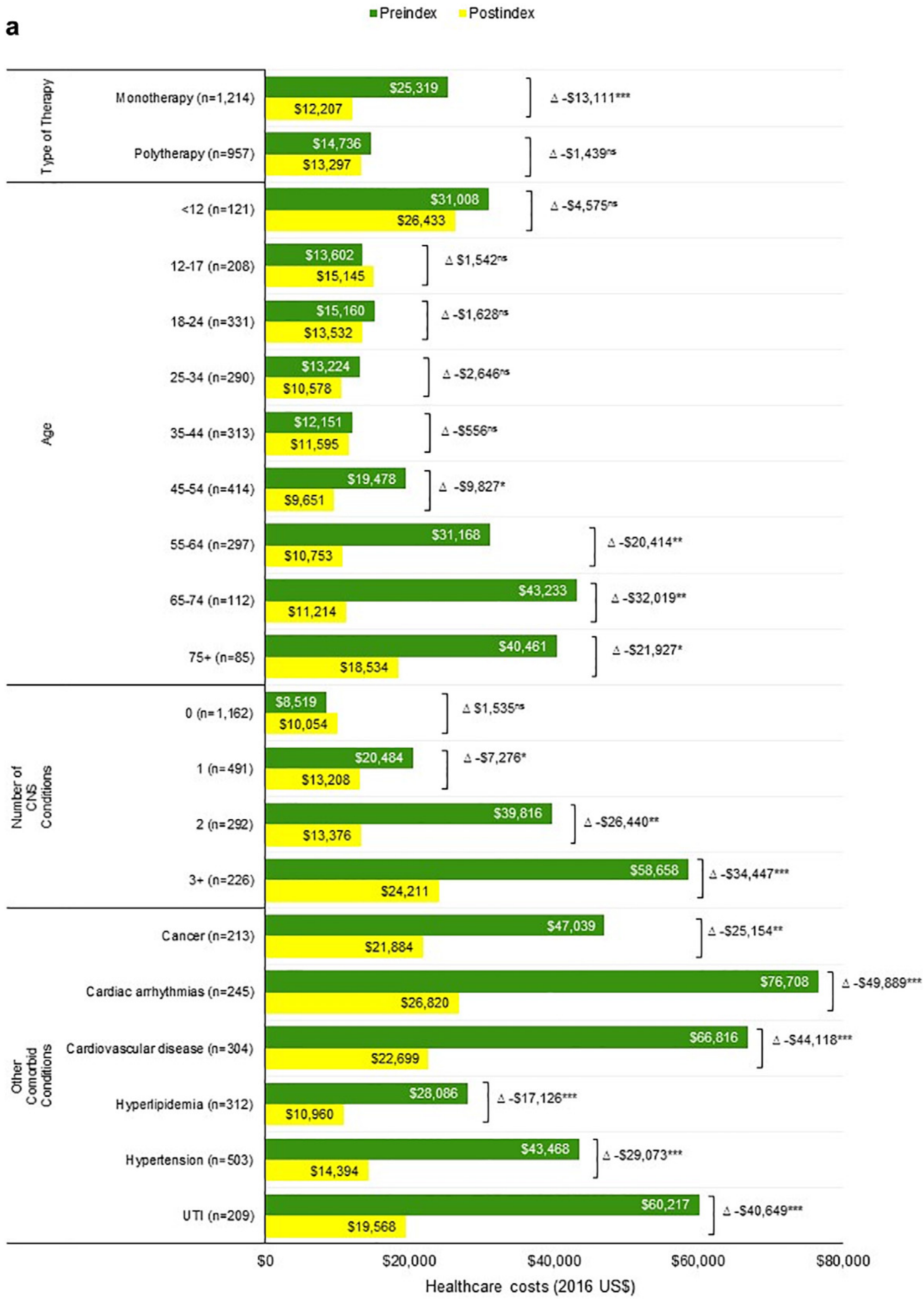
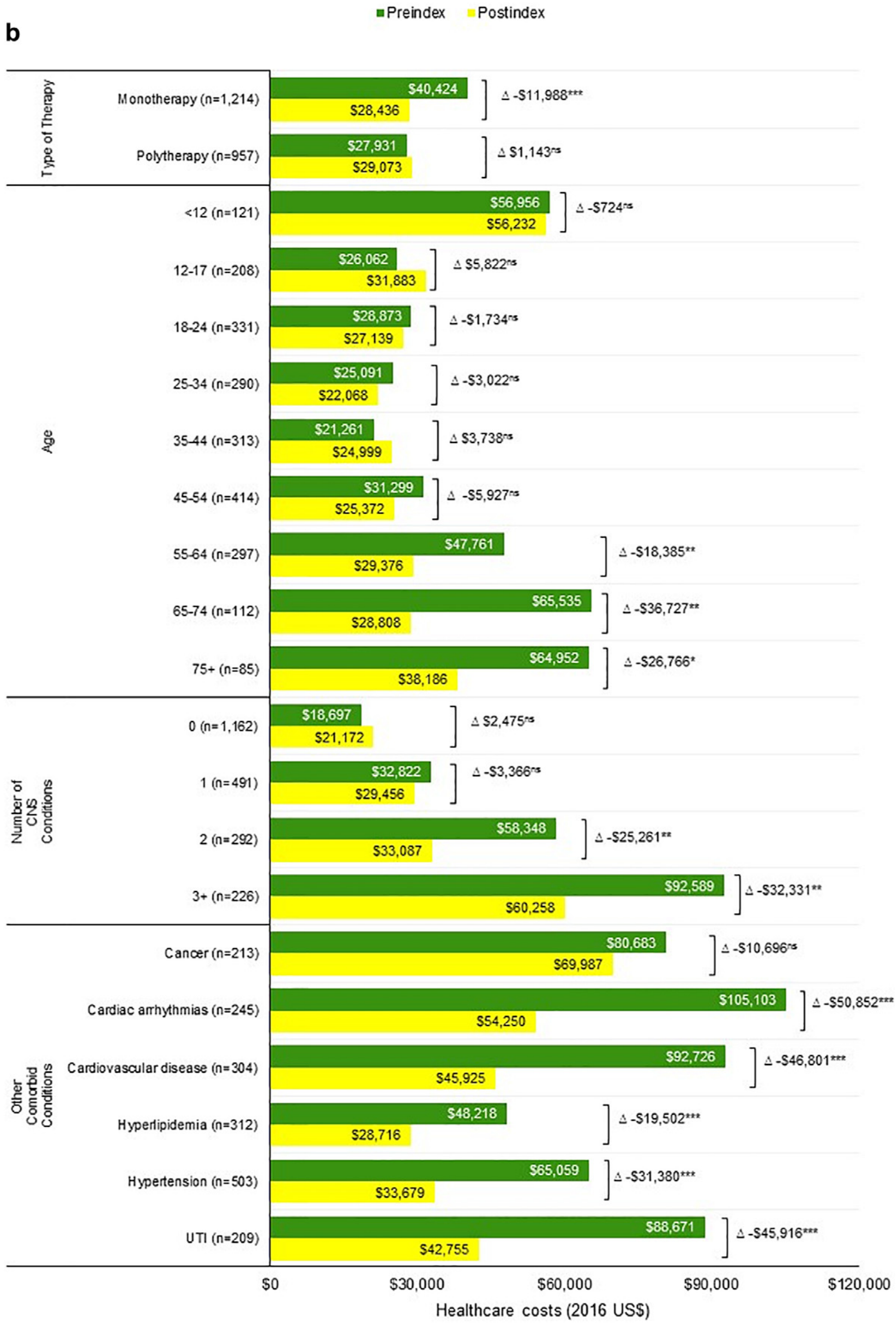


Fig. 4. Univariate analysis of all-cause inpatient costs (a), all-cause medical costs (b), epilepsy-specific inpatient costs (c), and epilepsy-specific medical costs (d) before and after the addition of LCM, within the 12-month preindex and postindex periods, respectively, according to selected patient characteristics at index date. CNS, central nervous system; NS, not significant; UTI, urinary tract infection. Δ represents the difference between pre- and postindex periods. *** $p < 0.0001$; ** $p < 0.01$; * $p < 0.05$; ns $p \geq 0.05$ for differences between pre- and postindex periods.



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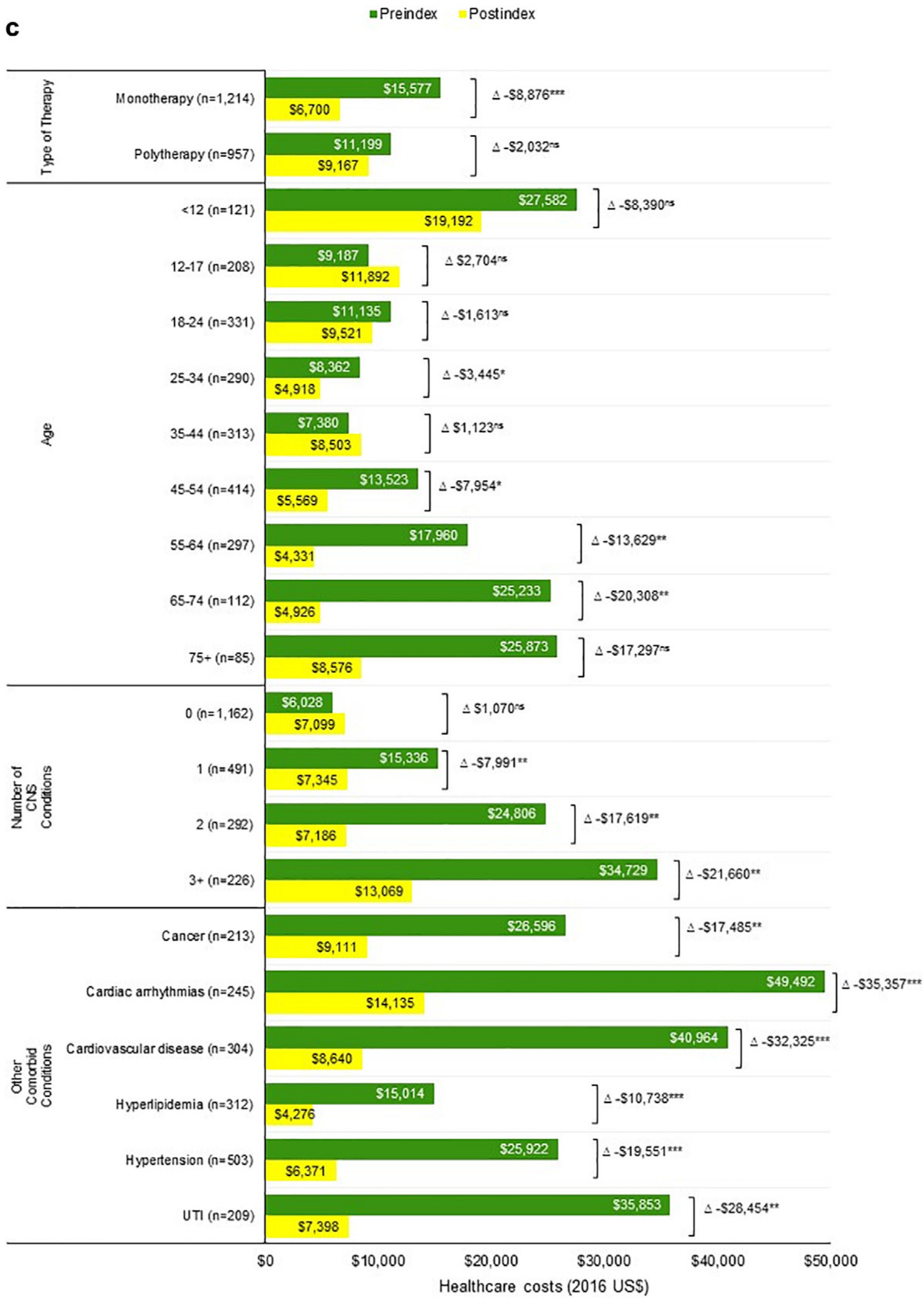

Fig. 4 (*continued*).

was the introduction of LCM, introduced bias towards patients who may have better course of disease than those who needed further modification of their AED regimen in the one-year observation period. Second, as this study was limited to only those individuals with commercial or private Medicare supplemental coverage, results may not be generalizable to patients with epilepsy with other insurance or without health insurance coverage. Third, administrative healthcare claims data are not collected for research purposes, and the coding on administrative claims is recorded to support reimbursement; therefore, there is a possibility of misclassification of epilepsy diagnosis, covariates, or study outcomes

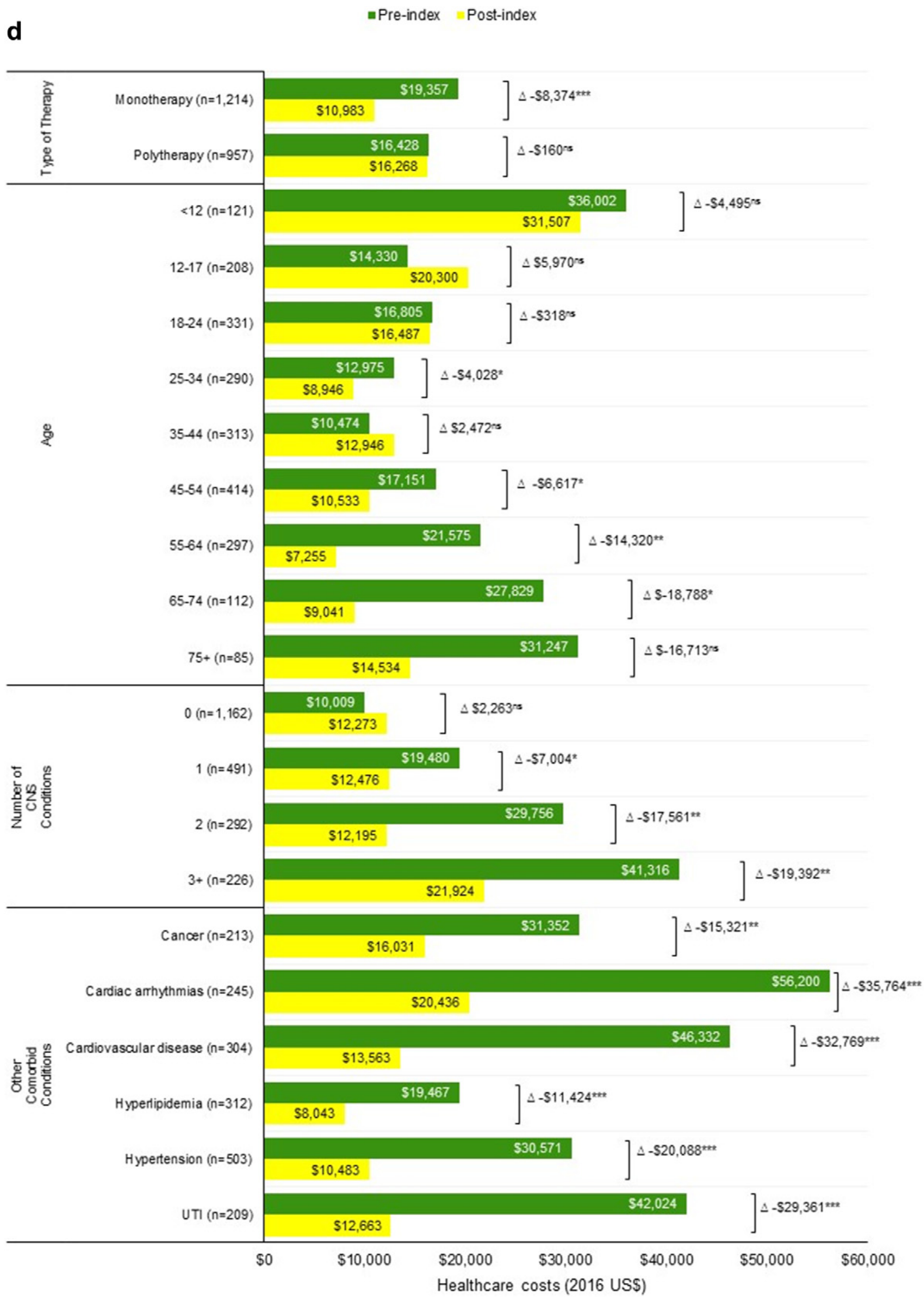

Fig. 4 (*continued*).

which are not verified through chart review. Finally, the current study employed a 24-month study period, and therefore, patients with intermittent insurance coverage were not included.

While we acknowledge the above limitations of this study, it does have strengths that add to the existing body of literature for epilepsy treatment. In contrast with the previous work that examined overall utilization, cost, and treatment patterns in patients with epilepsy, this study more specifically evaluated change in HRU and costs among patients with epilepsy after the initiation of LCM using a large nationally representative administrative claims database.

5. Conclusion

This study showed that initiation of adjunctive therapy with LCM was associated with fewer inpatient stays and ER visits, leading to reduced healthcare resource utilization and epilepsy costs. This study contributes to the literature that adjunctive therapy, particularly with LCM, may be successful in patients with treatment-refractory epilepsy. Future studies assessing long-term treatment with LCM as an adjunctive therapy are warranted to provide further information on the sustainability of the HRU and cost reductions in a real-world setting.

Declaration of Competing Interest

David M. Labiner is Head of the Department and Professor of Neurology at The University of Arizona College of Medicine and has received research grants from Aquestive, Biogen, and UCB Pharma. Carolyn R. Lew is an employee of IBM Watson Health, which received compensation from UCB Pharma for the overall conduct of the study and preparation of this manuscript. Barbara H. Johnson was an employee of IBM Watson Health at the time this analysis was conducted. Jesse Fishman was an employee of UCB Pharma at the time this analysis was conducted. Melinda Martin is an employee of UCB Pharma.

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Author contributions

All authors were involved in the study design, collection, analysis, and interpretation of the data, reviewed all drafts of the manuscript, and approved the content of the final version for submission.

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This work was supported by UCB Pharma. The study includes authors employed by UCB Pharma who played a role in the study design, data collection, analysis, and interpretation of the data, and the decision to submit the article for publication.

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