Identification of Patients with Painful Diabetic Peripheral Neuropathy Who Have a Favorable Cost Profile with Pregabalin Treatment

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Abstract

Objective: To characterize patient populations with favorable costs after the initiation of pregabalin for the treatment of painful diabetic peripheral neuropathy (pDPN) relative to duloxetine, gabapentin, and amitriptyline.

Methods: Patients were identified from MarketScan having ≥ 1 claim for pDPN (ICD-9-CM codes 250.6 or 357.2) within 60 days of first prescription (index) for pregabalin, duloxetine, gabapentin, or amitriptyline in 2008 and continuous enrollment 12 months pre- and postindex. Pregabalin patients were propensity-score-matched to each comparator. Using cutoff values ≥ 80% proportion of days covered (PDC) and ≥ 65 years for age, pre- to postindex changes in healthcare costs were estimated for pregabalin vs. comparators.

Results: Of 987 patients initiated on pregabalin, 349 matched to duloxetine; 987 to gabapentin; 276 to amitriptyline. The pre- to postindex changes in total healthcare costs were similar between cohorts: $3272 with pregabalin vs. $2290 with duloxetine ($P = 0.5280); $3687 with pregabalin vs. $5498 with amitriptyline ($P = 0.5863); $3869 with pregabalin vs. $4106 with gabapentin ($P = 0.8303). For the high-age/high-PDC population, the pre- to postindex differences in mean total costs were significantly lower with pregabalin (P < 0.001) relative to comparators ($3573 vs. $8288 for duloxetine; $1423 vs. $3167 for gabapentin; -$2285 vs. $6160 for amitriptyline).

Conclusions: The association of lower total costs among older individuals with pDPN who maintain high adherence to pregabalin therapy relative to key comparators suggests a pharmacoeconomic advantage of pregabalin in this population combined with a need for strategies promoting adherence.

Key Words: diabetic neuropathy, painful, healthcare costs, adherence

INTRODUCTION

Painful diabetic peripheral neuropathy (pDPN) is a sequela of diabetes that has an estimated prevalence of 15% in the diabetic population. While almost 26 million individuals in the United States are currently affected by diabetes, the increasing prevalence of type 2 diabetes resulting from an epidemic of obesity and earlier diabetes onset, including in children and adolescents, suggests that the number of patients with pDPN will also increase.

Painful diabetic peripheral neuropathy is characterized by a substantial patient burden related to the reductions in patient function, quality of life, and productivity. Additionally, greater healthcare resource utilization and associated costs relative to the general population and to diabetic patients without
pDPN contribute to the high economic burden that is associated with pDPN. These burdens have also been reported to be greater at increasing levels of pDPN and pain severity. These burdens have also been reported to be greater at increasing levels of pDPN and pain severity.6,7,13,14

Published guidelines for the treatment of pDPN recommend tricyclic antidepressants, the serotonin-norepinephrine reuptake inhibitor duloxetine, and the anticonvulsants pregabalin and gabapentin as first-line treatment.15–17 However, only pregabalin and duloxetine have been specifically approved for pDPN; pregabalin is recommended if clinically appropriate based on Level A evidence, and duloxetine is recommended based on Level B evidence.17

Despite these recommendations, treatment of pDPN remains challenging due to the presence of comorbidities, contraindications, and the use of concomitant medications with potential interactions.18,19 Furthermore, suboptimal adherence to therapy has been reported in the clinical setting;20–24 for patients initiated on pregabalin, the proportion of days covered (PDC) during the subsequent 12-month period has been reported to range from 0.42 to 0.63,23,24 with poorer adherence suggested to result at least in part from subtherapeutic dosing.23

The challenge of appropriate pDPN treatment may be further exacerbated by the concern of cost containment among managed care organizations. Thus, the availability of gabapentin and TCAs as low-cost generic medications, which combined with an evidence base for their efficacy for pDPN, has sometimes resulted in prior authorization, or step edits that mandate use of these drugs prior to prescribing approved medications, even though restricting access to pregabalin has not been shown to result in lower overall health costs.25,26

As a consequence of the need to balance appropriate care with cost containment, identification of patient populations that may be characterized by lower healthcare costs after initiating a particular therapy relative to other treatments can help optimize disease management from both the economic and patient perspectives. Such identification may also serve as a surrogate for patient benefits, as by implication, lower healthcare costs generally result from a reduction in healthcare utilization. The objective of the current study is to characterize healthcare costs of patients newly prescribed pregabalin for pDPN who were considered likely to have a favorable cost profile, based on adherence and age, relative to patients prescribed duloxetine, gabapentin, and amitriptyline. Adherence was used as a variable because it has been considered a factor contributing to effectiveness, and previous studies in pDPN have suggested that higher adherence to therapy may be associated with lower healthcare costs.20,21 Similarly, age was evaluated because it may have a potential impact on costs for several reasons. Age may not only affect a drug’s efficacy and side effect profile, but increasing age is associated with the presence of comorbid conditions and a greater likelihood for the use of medications that may be considered inappropriate, both of which result in higher healthcare resource utilization and costs.27 Additionally, an association between older age and greater adherence has also been suggested in patients with pDPN.20,21

METHODS

Data Source

This was a retrospective study that utilized the MarketScan® Commercial Claims and Encounters Database (Truven Health Analytics Inc., Ann Arbor, MI, USA), which includes complete longitudinal records of inpatient services, outpatient services, long-term care, and prescription drug claims covered under a variety of fee-for-service and capitated health plans. Covered health plans include exclusive provider organizations (EPOs), preferred provider organizations (PPOs), point of service (POS) plans, indemnity plans, and health maintenance organizations (HMOs). The data are nationally representative, quality-controlled, and Health Insurance Portability and Accountability Act of 1996 (HIPAA) compliant.

Information available from the database includes member age, gender, census region, health insurance eligibility dates, facility claims, provider claims, pharmacy claims, and reimbursed and charged amounts for all claims. All claims for any given patient can be linked using unique encrypted identifiers.

Study Sample Selection

Subjects ≥ 18 years of age were identified from the database having ≥ 1 claims with an associated International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) code of 250.6 or 357.2 within 60 days prior to the first prescription (index event) for pregabalin, duloxetine, gabapentin, or amitriptyline between January 2008 and June 2009, inclusive; these codes have previously been used to identify patients with pDPN.11,12,28 All subjects were required to have continuous enrollment 12 months
pre- and postindex and were excluded if they had missing data for age or gender; a prescription for their index drug during the 12-month period prior to the index date; a prescription for more than 1 study drug on the index date; any claims with an ICD-9-CM diagnosis code for epilepsy (345.XX, 780.39), postherpetic neuralgia (053.1X), or fibromyalgia (729.1x) during the study period, were residents of any type of long-term care facility, were pregnant, had a cancer diagnosis or an organ transplant.

**Propensity Score Matching**

In the absence of a randomization protocol, propensity score matching\(^{29,30}\) was used to minimize selection bias between the pregabalin population and comparators with regard to demographic and clinical characteristics. Propensity scores were generated using all available baseline demographic and patient characteristics using a logistic regression model to predict the probability of treatment that included age at index, gender, Charlson Comorbidity Index (CCI) score,\(^{31}\) pre-index hypertension, pre-index mental disorders (including depression, bipolar disorder, anxiety, generalized anxiety disorder, panic disorder, or posttraumatic stress disorder), the number of pre-index opioid analgesic prescriptions, and pre-index total healthcare costs. The variables were selected by reviewing a list of available variables in claims data and those used in previous studies as key predictors of healthcare costs.\(^{24}\) Groups were matched pairwise using 1:1 matching of an observation in the smaller treatment group with the observation from the larger group with the nearest predictive probability.

**Cost Analysis**

Total costs and key cost driver variables were assessed by comparing the pre- to postindex differences in mean annual costs for pregabalin with duloxetine, gabapentin, and amitriptyline for patients categorized stratified in each cohort into 4 populations according to age and treatment adherence determined by the PDC. These populations were low age/low PDC; high age/low PDC; low age/high PDC; and high age/high PDC. Thresholds for high age and high PDC were ≥ 65 years and PDC ≥ 80%, respectively. These thresholds were chosen based on values that have been generally accepted in the literature for stratifying patients with respect to age and adherence. The relevance of these variables has also been suggested in studies of pregabalin.\(^{23,32}\)

Healthcare resource utilization cost categories included prescription costs; costs associated with outpatient visits; costs associated with inpatient visits; and total costs consisting of the sum of the individual cost categories. The claims-based costs used in the analysis were for all-cause resource utilization for the patients in the matched cohorts.

Post- minus pre-index total cost differences > $50,000 (or less than −$50,000) were set equal to $50,000 (−$50,000) in order to avoid results being driven by a few extreme outliers. To determine robustness of the results, a sensitivity analysis was performed using a threshold of ≥ 50% for adherence.

**Statistical Methods**

Age and CCI were compared between cohorts using 2-sample \(t\)-tests. Categorical demographic variables and proportions of patients with PDC ≥ 0.8 were compared between cohorts using chi-square tests. Wilcoxon 2-sample rank-sum tests were used to compare costs between cohorts. \(P\)-values < 0.05 were considered to be statistically significant. All analyses were performed using SAS version 9.2 (SAS Institute Inc., Cary, NC, U.S.A.) or R software version 2.13.2.\(^{33}\)

**RESULTS**

A total of 987 patients initiated on pregabalin and meeting the inclusion criteria were identified from the database, and of these, 349 were matched to patients initiated on duloxetine; all 987 were matched to patients initiated on gabapentin (of 1696 gabapentin patients); and 276 were matched to patients initiated on amitriptyline. The demographics of the matched populations were generally similar with respect to age, gender, and CCI (Table 1). However, significant differences were observed across the matched cohorts for geographic region and for plan type between pregabalin and the gabapentin and amitriptyline cohorts (Table 1).

Among the matched cohorts, the mean (± standard deviation) daily doses of medications (Table 2) were 165.3 ± 86.7 mg for pregabalin and 54.8 ± 21.7 mg for duloxetine; 155.3 ± 72.4 mg for pregabalin and 32.5 ± 24.7 mg for amitriptyline; and 158.5 ± 81.9 mg for pregabalin and 698.8 ± 537.7 mg for gabapentin. Adherence to therapy (Table 2) was significantly higher with duloxetine relative to pregabalin as indicated by the mean PDC (0.53 vs. 0.40; \(P < 0.0001\)) and the proportion of patients with PDC ≥ 0.8 (35.0% vs.
19.8%; \( P < 0.0001 \)). Similarly, adherence was significantly higher with gabapentin relative to pregabalin, both for mean PDC (0.44 vs. 0.40; \( P = 0.0025 \)) and PDC > 0.8 (24.1% vs. 19.9%; \( P = 0.0225 \)). In contrast, both adherence parameters were similar between pregabalin and amitriptyline, 0.36 vs. 0.37, respectively, for mean PDC (\( P = 0.8207 \)), and 17.8% vs. 18.5%, respectively, for PDC > 0.8 (\( P = 0.8251 \)). Across treatments, the average daily dose was generally higher among the patients with PDC ≥ 0.8 relative to those with PDC < 0.8 (Table 3).

Evaluating the pre- to postindex changes in healthcare costs for each of the age/adherence strata (Table 4) showed that only for the high age/high PDC group were the pre- to postindex differences in mean total costs consistently and significantly lower with pregabalin (\( P \leq 0.001 \)) relative to all comparators ($3373 vs. $8288 for duloxetine; $1423 vs. $3167 for gabapentin; $2285 vs. $6160 for amitriptyline). These total cost profiles among the patients with high age/high PDC resulted from pre- to postindex differences in inpatient and outpatient costs that were consistently and significantly lower (\( P \leq 0.001 \)) for pregabalin relative to comparators (Table 4).

While the change in prescription costs for the high-age-high-PDC subpopulation indicated significantly lower costs with pregabalin relative to duloxetine ($2199 vs. $2686; \( P \leq 0.001 \)), prescription costs were higher with pregabalin relative to gabapentin and amitriptyline, although the differences between comparators were not significant.

Total pre- to postindex changes in costs were significantly lower with pregabalin for the low-PDC/high-age population relative to both duloxetine ($1326 vs. $1703;
and amitriptyline ($2678 vs. $4476; P \leq 0.001)$. The changes in inpatient and prescription costs associated with pregabalin were both significantly lower than for duloxetine ($P \leq 0.05$), and the changes in inpatient costs associated with pregabalin were significantly lower than for amitriptyline ($P \leq 0.001$).

The sensitivity analysis (Table 5), which used a threshold of 50% for PDC, showed results that were consistent with the main analysis; only for the high-age/high-PDC subpopulation did pregabalin demonstrate significantly lower pre- to postindex differences in total costs relative to all comparators ($3378 vs. $6981$ for duloxetine; $3199 vs. $5005$ for gabapentin; $–1875$ vs. $3496$ for amitriptyline; $P \leq 0.001$ for all comparisons). As in the main analysis, this cost profile was a consequence of the cost differences for inpatient and outpatient costs, which were lower with pregabalin.

### DISCUSSION

Optimizing disease management is a desirable goal that can be expected to result in greater benefits to patients and reduce healthcare costs. Toward this goal, the results of this study consistently suggest that older age and greater adherence to therapy are variables that should be considered for optimizing pDPN management with pregabalin relative to other recommended first-line medications, that is, duloxetine, gabapentin, and amitriptyline. While the age factor identifies a specific population that may be targeted, greater adherence suggests the need for understanding the factors contributing to adherence and initiating strategies to promote adherence.

Although in the total cohorts, pre- to postindex differences in total costs were similar between pregabalin and each of the comparators, using specific cutoff values, the combination of older age and greater adherence consistently resulted in lower total healthcare resource utilization costs with pregabalin relative to all 3 comparators. These results were consistent in both the

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**Table 3. Average Daily Dose in Patients with High and Low Adherence Based on Proportion of Days Covered (PDC)**

<table>
<thead>
<tr>
<th>Paired treatment cohorts</th>
<th>Average daily dose, mg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>High adherence, PDC ≥ 0.8</td>
</tr>
<tr>
<td>Amitriptyline</td>
<td>39.0</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>155.3</td>
</tr>
<tr>
<td>Duloxetine</td>
<td>54.8</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>185.9</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>726.2</td>
</tr>
<tr>
<td>Pregabalin</td>
<td>171.2</td>
</tr>
</tbody>
</table>

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**Table 4. Pre- to Postindex Changes in Healthcare Costs for Pregabalin Vs. Comparators Using Cutoff Values ≥ 65 Years for High Age and ≥ 80% for High Proportion of Days Covered (PDC)**

<table>
<thead>
<tr>
<th>Cost Category</th>
<th>Low PDC/Low Age</th>
<th>Low PDC/High Age</th>
<th>High PDC/Low Age</th>
<th>High PDC/High Age</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pregabalin</td>
<td>Duloxetine</td>
<td>Pregabalin</td>
<td>Duloxetine</td>
</tr>
<tr>
<td>Outpatient</td>
<td>(n = 204)</td>
<td>(n = 167)</td>
<td>(n = 76)</td>
<td>(n = 60)</td>
</tr>
<tr>
<td></td>
<td>1267 (1248)</td>
<td>3080 (1814)</td>
<td>1420 (1283)</td>
<td>764 (1704)</td>
</tr>
<tr>
<td>Inpatient</td>
<td>1007 (1318)</td>
<td>2678 (792)</td>
<td>1313 (735)†</td>
<td>755 (2683)</td>
</tr>
<tr>
<td>Prescription</td>
<td>1087 (198)</td>
<td>732 (96)</td>
<td>3341 (819)</td>
<td>2199 (310)</td>
</tr>
<tr>
<td>Total</td>
<td>4231 (1557)</td>
<td>1326 (1934)*</td>
<td>1903 (2573)</td>
<td>3573 (3847)*</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Cost Category</th>
<th>Low PDC/Low Age</th>
<th>Low PDC/High Age</th>
<th>High PDC/Low Age</th>
<th>High PDC/High Age</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pregabalin</td>
<td>Gabapentin</td>
<td>Pregabalin</td>
<td>Gabapentin</td>
</tr>
<tr>
<td>Outpatient</td>
<td>(n = 480)</td>
<td>(n = 478)</td>
<td>(n = 311)</td>
<td>(n = 271)</td>
</tr>
<tr>
<td></td>
<td>2494 (582)</td>
<td>3028 (756)</td>
<td>1422 (868)†</td>
<td>1757 (1025)</td>
</tr>
<tr>
<td>Inpatient</td>
<td>898 (743)*</td>
<td>2155 (980)</td>
<td>320 (1343)*</td>
<td>-1219 (1465)*</td>
</tr>
<tr>
<td>Prescription</td>
<td>1164 (122)</td>
<td>369 (131)</td>
<td>3304 (379)</td>
<td>2136 (215)</td>
</tr>
<tr>
<td>Total</td>
<td>3912 (904)</td>
<td>4601 (1224)</td>
<td>3911 (1706)*</td>
<td>4484 (2007)</td>
</tr>
</tbody>
</table>

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*P ≤ 0.001; †P ≤ 0.05.*

*Cost difference calculated as postindex costs minus pre-index costs.*
main analysis and the sensitivity analysis. The more favorable cost profiles of pregabalin were obtained despite the significantly higher prescription costs relative to gabapentin and amitriptyline, and resulted from significantly lower inpatient and outpatient costs. In particular, for the comparison with amitriptyline, both inpatient and outpatients costs with pregabalin were characterized by the reductions in the postindex period relative to the pre-index period, whereas amitriptyline was characterized by cost increases. Although the reasons for the inpatient and outpatient costs with amitriptyline could not be ascertained, it should be noted that according to the modified Beers criteria, amitriptyline is considered inappropriate for use in older patients;4 the use of amitriptyline may be associated with a greater risk of adverse events or drug interactions.19,35

The potentially inappropriate use of amitriptyline in older individuals may also account for the more favorable total cost profile of pregabalin in the high-age/low-PDC population. Although duloxetine is not considered inappropriate for use in older individuals, it can be speculated that the more favorable cost profile of pregabalin for the high-age/low-PDC population could potentially be ascribed to the greater risk of duloxetine drug interactions relative to pregabalin.36,37

In contrast, the comparison between pregabalin and duloxetine showed that for the identified population, all cost categories were lower with pregabalin, including prescription costs. While other database studies, using different methodologies, compared the costs between duloxetine and pregabalin in patients with pDPN,22,38–40 the current analysis is the first to specifically characterize patients who may benefit from a specific therapy and to identify a modifiable characteristic that may impact costs, that is, patient adherence.

It should also be noted that significantly lower differences in total costs favoring pregabalin were observed for several other population strata vs. the comparators, including low PDC/high age relative to duloxetine and amitriptyline and high PDC/low age relative to gabapentin. In all cases, the more favorable cost profile of pregabalin was in part due to significantly lower pre- to postindex changes in inpatient costs relative to the comparator.

There are many factors that contribute to adherence, and a recent study of patients with neuropathic pain, including a population with pDPN, suggested that prescribing and maintenance of therapeutic doses results in greater adherence, and lower costs, than at subtherapeutic doses.23 In this regard, the mean dose of pregabalin, which ranged from 155.3 to 165.3 mg

### Table 5. Sensitivity Analysis of the Pre- to Postindex Changes in Healthcare Costs for Pregabalin Vs. Comparators Using Cutoff Values ≥ 65 Years for High Age and ≥ 50% for High Proportion of Days Covered (PDC)

<table>
<thead>
<tr>
<th>Cost Category</th>
<th>Low PDC/Low Age</th>
<th>Low PDC/High Age</th>
<th>High PDC/Low Age</th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pregabalin</td>
<td>Gabapentin</td>
<td>Pregabalin</td>
<td>Gabapentin</td>
</tr>
<tr>
<td></td>
<td>(n = 167)</td>
<td>(n = 131)</td>
<td>(n = 55)</td>
<td>(n = 43)</td>
</tr>
<tr>
<td>Outpatient</td>
<td>3270 (1099)</td>
<td>883 (1211)</td>
<td>958 (1591)</td>
<td>3637 (2320)</td>
</tr>
<tr>
<td>Inpatient</td>
<td>599 (1494)</td>
<td>–1056 (1619)</td>
<td>–1764 (1957)</td>
<td>–3366 (1745)</td>
</tr>
<tr>
<td>Prescription</td>
<td>917 (212)</td>
<td>515 (331)</td>
<td>510 (239)</td>
<td>582 (315)</td>
</tr>
<tr>
<td>Total</td>
<td>3891 (1767)</td>
<td>–216 (1983)</td>
<td>642 (2455)</td>
<td>741 (3186)</td>
</tr>
</tbody>
</table>

|               | Pregabalin      | Gabapentin      | Pregabalin      | Gabapentin        |
|               | (n = 384)       | (n = 376)       | (n = 241)       | (n = 204)         |
| Outpatient    | 2817 (609)      | 2943 (588)      | 2186 (660)      | 2157 (865)        |
| Inpatient     | 622 (858)†      | 1284 (902)      | 1530 (870)      | 1439 (1153)       |
| Prescription  | 861 (121)       | 970 (160)       | 366 (160)       | 196 (156)         |
| Total         | 3635 (1050)     | 3789 (1053)     | 4201 (1114)     | 3396 (1427)       |

|               | Pregabalin      | Gabapentin      | Pregabalin      | Gabapentin        |
|               | (n = 124)       | (n = 129)       | (n = 61)        | (n = 59)          |
| Outpatient    | 3950 (1123)†    | 4233 (1216)     | 1911 (1467)†    | 3486 (1352)       |
| Inpatient     | 2224 (1517)     | 2449 (1582)     | 1141 (1486)*    | 1796 (1061)       |
| Prescription  | 1096 (230)      | 553 (386)       | 639 (263)       | 462 (222)         |
| Total         | 5905 (1859)*    | 7423 (1855)     | 3793 (2038)*    | 5475 (1765)       |

$\text{Cost difference,}^†\text{ Mean (Standard Error), }\$\text{.}^\text{*}$

$\text{P} < 0.001; \text{P} < 0.05.$

‡Cost difference calculated as postindex costs minus pre-index costs.
across the cohorts, is lower than the therapeutic dose of 300 mg and thus may have contributed to the low rates of adherence, especially relative to duloxetine for which the mean dose, 54.8 mg, approximates the therapeutic dose of 60 mg. Furthermore, the mean doses of gabapentin (698.8 mg) and amitriptyline (32.5 mg) were also substantially lower than the average effective doses, although high doses of the latter drug are also associated with anticholinergic adverse effects. While reports of the relationship between dose and adherence have also been published for duloxetine in pDPN, it is worth identifying factors other than dose level that can be leveraged for improving patient adherence to therapy. However, in the current study, higher average doses were consistently observed among the patients with higher adherence, although some of the differences in doses between high and low adherence were small.

The sensitivity analysis demonstrated robustness of the results with regard to the importance of higher PDC in maintaining a favorable cost profile. However, the sensitivity analysis also highlighted several limitations of the study. In particular, the magnitude of the cost differences is dependent on the cutoff values used to stratify the populations. Thus, while older age and higher PDC were demonstrated to be patient characteristics likely to result in a more favorable cost profile with pregabalin relative to the comparators, differences in costs were observed when PDC ≥ 80% and PDC ≥ 50% were used. Although PDC was varied in the sensitivity analysis, age was not, potentially representing another limitation. However, in contrast to age, PDC is a variable that can be targeted for modification in a patient population, and it should also be noted that our choice of the cutoff values for the main analysis, 80% for PDC and 65 years for age, was based on clinical relevance; a PDC ≥ 80% is generally accepted as an indicator of a high rate of adherence in the clinical setting, and 65 years of age distinguishes between Medicare and commercial populations and thus is of interest to payors.

It should also be noted that although patients with epilepsy, postherpetic neuralgia, and fibromyalgia were excluded from the study, all 3 drugs are prescribed for a variety of conditions and are frequently used off-label. Because the specific reasons for the use of these drugs cannot be ascertained, it is possible that they were prescribed for conditions other than pDPN. Another limitation is that while we used healthcare resource utilization costs as a surrogate for patient benefits, outcomes are not captured in databases such as the 1 used here, and thus, it is not possible to know what specific benefits, if any, were obtained among the patients prescribed the evaluated medications.

CONCLUSIONS

Older age and high adherence to therapy were consistently shown to be associated with lower healthcare costs with pregabalin relative to duloxetine, gabapentin, and amitriptyline. This association suggests the pharmacoeconomic advantage of pregabalin relative to key comparators among older individuals with pDPN, combined with the need for strategies promoting adherence to therapy.

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