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The Prevalence and Factors Associated with Antiepileptic Drug Use in US Nursing Home Residents

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Abstract

Background: Antiepileptic drugs (AEDs) are commonly used by nursing home residents, both on and off label. The landscape of AED use has changed over the past two decades. Despite this, contemporaneous research on AED use in US nursing home residents is scant.

Objective: To estimate the prevalence, describe prescribing patterns, identify factors associated with AED use, and assess whether these factors differ among AEDs with expanded indications in older adults (i.e., gabapentin, pregabalin, topiramate, and lamotrigine).

Methods: We conducted a cross- sectional study among 549,240 long stay older residents who enrolled in fee- for- service Medicare and lived in 15,111 US nursing homes on September 1, 2016. Demographics and conditions associated with AED indications, epilepsy comorbidities, and safety came from the Minimum Data (MDS 3.0). Part D claims identified AED use. Robust Poisson models and multinomial logistic models for clustered data estimated adjusted prevalence ratios (aPR), adjusted odds ratios (aOR) and 95% confidence intervals (CI).

Results: Overall, 24.0% used AEDs [gabapentin (13.3%), levetiracetam (4.7%) phenytoin (1.9%), pregabalin (1.8%), and lamotrigine (1.2%)]. AED use was associated with epilepsy (aPR = 3.73; 95% CI = 3.69–3.77), bipolar disorder (aPR = 1.20; 95% CI = 1.18–1.22), pain

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Ethical Approval: This study used routinely- collected administrative and claims dataset and was approved by the University of Massachusetts Medical School Institutional Review Board (protocal number H00011964).

Conflict of Interest: Danni Zhao, Divya Shridharmurthy, Matthew J. Alcusky, Yiyang Yuan, Anthony P. Nunes, Anne L. Hume, Jonggyu Baek, and Kate L. Lapane declare that they have no conflict of interest.

($aPR_{moderate/\ severe\ vs.\ no\ pain}$ =1.42; 95% CI = 1.40–1.44), diabetes (aPR = 1.27; 95% CI = 1.26–1.28), anxiety (aPR = 1.12; 95% CI = 1.11– 1.13), depression (aPR = 1.17; 95% CI = 1.15– 1.18), or stroke (aPR = 1.08; 95% CI = 1.06– 1.09). Residents with advancing age ($aPR_{85+\ vs.\ 65–74\ years}$ = 0.73; 95% CI= 0.73– 0.74), Alzheimer's disease/ dementia (aPR = 0.87; 95% CI = 0.86– 0.88), or cognitive impairment ($aPR_{severe\ vs.\ no\ impairment}$ = 0.62; 95% CI = 0.61– 0.63) had decreased AED use. Gabapentinoid use was highly associated with pain ($aOR_{moderate/severe\ vs.\ no\ pain}$ = 2.07; 95% CI = 2.01– 2.12) and diabetes (aOR = 1.79; 95% CI = 1.76– 1.82), but not with an epilepsy indication.

Conclusions: AED use was common in nursing homes, with gabapentin most commonly used (presumably for pain). That multiple comorbidities were associated with AED use underscores the need for future studies to investigate the safety and effectiveness of AED use in nursing homes residents.

1. INTRODUCTION

From 1993 to 2016, the US Food and Drug Administration (FDA) approved 18 antiepileptic drugs (AEDs) [1–2] and expanded labeled indications for some AEDs (e.g., gabapentin and pregabalin for postherpetic neuralgia, topiramate for migraines, and lamotrigine for bipolar disorder) [3–4]. In nursing homes, AED use has increased and prescribing patterns have likely changed. In the 1990s, the prevalence of AEDs was approximately 10% in US nursing homes [5–7], with phenytoin, a first- generation AED, most commonly prescribed [5]. By 2013, the prevalence of AEDs in nursing homes in two states increased to 14.3% with gabapentin most commonly prescribed [8]. In an Italian nursing home, 32% used AEDs [48].Recent nationwide data regarding AED use in nursing home residents are lacking.

Historic data showed that factors associated with increased AED use in older nursing home residents include younger age, epilepsy, bipolar disorder, peripheral vascular disease and geographic area with greater use noted in the Northeast [5,9]. Given the newer AEDs available in the US, the expansion of indications, and lack of clinical guidelines navigating AED therapy in the nursing home setting, these findings are unlikely relevant to contemporary clinical practice. Because AED use may carry risks such as falls and fractures, adverse cognitive effects, and drug- drug interactions [10–17], a contemporary understanding of how AEDs are being used in nursing homes is warranted.

Using a contemporary national database of all US long stay older nursing home residents enrolled in fee- for- service Medicare, this study sought to estimate the prevalence, describe prescribing patterns, identify factors associated with AED use, and assess whether these factors differ among AEDs with expanded indications in older adults (i.e., gabapentin, pregabalin, topiramate, and lamotrigine). To our knowledge, this is the first nationwide study to assess the pattern of AED in the US nursing home settings since 1999.

2. METHODS

2.1 Data Sources

We linked three data sources including Minimum Data Set 3.0 (MDS 3.0, 2016), Master Beneficiary Summary File, and Medicare Part D pharmacy claims by residents' unique

beneficiary IDs. The MDS 3.0 is a standardized clinical assessment tool used on all residents of US Medicare and/ or Medicaid- certified nursing homes (over 96% of all US nursing homes). Comprehensive assessments are performed within 7 days of nursing home admission, every year, and whenever there are significant changes in residents' health conditions [18]. An abbreviated assessment is administered quarterly [18]. During the assessment process, registered nurses conduct interviews with residents to collect information on residents' demography and health conditions including comorbidities, functional status, and mood [19–20]. The MDS 3.0 items are valid and reliable capturing information on residents' demographics and health conditions [19].

2.2 Study Design

We conducted a cross- sectional study among older adults who resided in US nursing homes on September 1, 2016 (the index date). Given the lack of seasonality in AED use [8], the point prevalence estimated on this date is intended to be representative of 2016 AED usage and patterns.

2.3 Study Sample

The inclusion criteria were: 1) residing in US nursing homes on the index date, i.e., September 1, 2016; 2) having an admission, annual, or quarterly MDS assessment between June 1, 2016 and September 1, 2016; 3) age ≥ 65 years. The exclusion criteria were: 1) in comatose state; 2) with skilled nursing facility stay; and 3) not continuously enrolled in Medicare Part D in June, July, August, and September, 2016. We excluded residents in a comatose state because the prescribing patterns for this population should be different from general nursing home residents. Medications are bundled into the per diem payment for skilled nursing facility stays. We excluded these residents because medication claims were not billed to Medicare Part D claims. If multiple assessments were identified within the 90-day time window, we used information in the assessment closest to the index date.

2.4 Measurements of Antiepileptic Drug Use

There were 27 AEDs available in the US market in September 2016, including 9 first-generation, 9 second- generation, and 9 third- generation AEDs (Supplemental Table 1 in Online Resource 1). Gabapentin, pregabalin, lamotrigine, and topiramate have expanded indications in older adults (Supplemental Table 1 in Online Resource 1). This classification of AEDs was based on guidelines developed by the American Academy of Neurology (AAN) [1–2], prior research [21], and year of initial US approval. AED use was determined based on Medicare Part D claims. Specifically, if residents had an AED claim on the index date, or if the prescription fill date plus day supply covered the index date, the resident was classified as an AED user. We created 27 binary variables to capture use of each AED on the index date. Next, four binary variables were created to indicate the use of first- generation, second-generation, third- generation, or any AEDs, respectively. A five- level categorical outcome variable was created to indicate the use of AEDs with expanded indications in older adults (gabapentinoids (i.e. gabapentin and pregabalin), topiramate, lamotrigine, other AEDs, or no AED use). The primary outcome variable was any AED use on the index date and the secondary one was use of AEDs with expanded indications.

2.5 Measurements of Covariates

Based on literature [5,9], we developed a list of covariates: demographic variables, conditions associated with AED indications, conditions associated with epilepsy comorbidities, and conditions associated with AED safety. The details of covariate assessments in MDS 3.0 were included in Supplemental Methods in Online Resource 1.

2.5.1 Demographic variables—*Age* was categorized into three groups, i.e., 65– 74, 75– 84, and ≥85 years. *Gender* was based on self- report and if needed, registered nurses assisted in correctly identifying gender of residents as men or women [18]. We collapsed some categories of race/ ethnicity in the MDS 3.0 assessments and created a four- category variable of *race/ ethnicity,* i.e., non- Hispanic white, non- Hispanic black, Hispanic, and others due to small number of respondents in some individual categories. Geographic area was determined based on locations of nursing home facilities, and categorized into West, Midwest, Northeast, and South according to US Census Divisions and Regions [22].

2.5.2 Conditions associated with AED indications/ contradictions—An active clinical diagnosis of e*pilepsy* and *bipolar* disorder was defined based on Section I of the MDS 3.0 [3–4]. *Pain* was considered as a potentially appropriate use for antiepileptic drugs. *Pain* was assessed by the Pain Assessment Interview in the MDS 3.0, with both self-assessed and staff- assessed pain [18], from which we derived a three- level *pain* variable (no pain, mild/ infrequent pain, and moderate/ severe pain) [23–26]. We did not include other expanded indications of AEDs (Supplemental Table 1 in Online Resource 1) because these variables were not included as part of the MDS 3.0.

Hepatic or renal insufficiency/ failure can be potential contraindications for AED use in older nursing home residents. Hepatic insufficiency/failure was not assessed in MDS 3.0. Renal insufficiency/ failure was assessed but had a large proportion of missing responses. As such, we did not include hepatic or renal insufficiency/ failure as potential contraindications for AED use.

2.5.3 Conditions associated with epilepsy comorbidities—The following conditions often co-occur with epilepsy [5,27]: *diabetes, anxiety*, *depression*, *stroke*, *Alzheimer's disease*/ *dementia*, *peripheral vascular disease (PVD)* and *arthritis*. All variables were binary, indicating the presence of the condition. *Cognitive impairment* was also included as a validated four- level categorical variable (i.e., no impairment/ intact, mild impairment, moderate impairment, and severe impairment) based on items in Brief Interview for Mental Status (BIMS) and Cognitive Performance Scale (CPS) [28].

2.5.4 Conditions associated with AED safety—The following conditions have been associated with AED safety [10–16]. *Fracture* was coded as a binary variable indicating the presence of any fractures. *Physical functioning* was determined from the validated MDS Activities of Daily Living (ADL) Self- Performance Hierarchy Scale, and categorized to no/ mild physical functioning impairment, moderate impairment, and severe impairment [29].

2.6 Statistical Analysis

We estimated the prevalence of AED use, overall, by generation and by individual agent. Then, we described the study sample by calculating proportions for categorical variables stratified by AED use. To examine AED prescribing patterns, we reported the five most commonly prescribed AEDs. Additional analyses were conducted to provide more detail on AED use including AEDs with expanded indications in older adults (i.e., gabapentin, pregabalin, topiramate, and lamotrigine), and proportions of residents with concurrent epilepsy who were treated with AEDs. To explore the factors associated with AED use, we first selected covariates whose prevalence differed among AED users and non- users by 5% or more (i.e., age, epilepsy, pain, diabetes, anxiety, depression, Alzheimer's disease/ dementia, and cognitive impairment). Next, we included all demographic variables (age, gender and race), FDA- approved indications for some AEDs (epilepsy and bipolar disorder), and stroke. Stroke was included because it most frequently causes new- onset seizure in older adults [30]. Before entering covariates in the models, we calculated Cramer's V coefficients and variance inflation factor (VIF) to assess pairwise correlation and overall multicollinearity of covariates, respectively. Cramer's V was chosen over χ^2 statistics in that we had a very large sample size, and χ^2 test is likely to return all statistically significant results considering its test sensitivity. Covariates were considered highly correlated if their Cramer's V coefficient equaled 0.5 or larger [31], but none met this threshold. VIFs for all covariates were less than 1.5, indicating multicollinearity was unlikely present. Lastly, we conducted two multivariable regression models including all covariates selected. To examine factors associated with any AED use, we conducted extensions of robust Poisson regression which estimated prevalence ratios (aPR) and 95% confidence intervals (CI) [32–33]. To identify factors associated with the use of AEDs with expanded indications in older adults, we performed multinomial logistic regression for clustered data which estimated odds ratios (aOR) and 95% confidence intervals (CI) [34]. The odds ratios (ORs) should approximate prevalence ratios (PRs) due to rare outcomes (Supplemental Table 2 in Online Resource 1). Both models accounted for the clustering of residents within nursing home facilities by using a generalized estimating equation (GEE) method and applied a sandwich variance estimator with an independent correlation structure. All statistical analyses were conducted in SAS, version 9.4 (SAS Institute, Inc., Cary, NC).

3. RESULTS

3.1 Prevalence and Prescribing Patterns of Antiepileptic Drugs

Our final study sample consisted of 549, 240 long stay residents who lived in 15,111 nursing homes (Figure 1). Overall, the prevalence of AED use was 24.0%, of which 81.6% were second- generation AED agents and 21.8% were first- generation AEDs. Gabapentin (13.3%), levetiracetam (4.7%), phenytoin (1.9%), pregabalin (1.8%), and lamotrigine (1.2%) were most commonly prescribed (Supplemental Table 2 in Online Resource 1). AEDs with expanded indications in older adults were used by 68.2% AED users. For gabapentin or pregabalin users, approximately half were in pain and one in ten had a diagnosis of epilepsy. About 38.3% of topiramate users had documented pain and 36.7% had epilepsy. Approximately 29.8% of lamotrigine users had bipolar disorder and 41.1% had a diagnosis

of epilepsy. About one- third of residents with epilepsy were not treated with any AEDs, and this finding was consistent across age groups.

3.2 Characteristics of the Sample by AED Use

The majority of residents were 75 years and older, women, and non- Hispanic white (Table 1). Overall, 9.6% of residents had diagnoses of epilepsy, 4.7% of residents had bipolar disorders, and 24.3% reported pain. Among AED users, 29.9% had epilepsy compared to 3.4% of non- users (Table 1). About 11.2% residents had stroke. Approximately 72.7% residents had cognitive impairment, and similar proportion of residents comorbid with Alzheimer's disease or dementia. Compared to 65.8% non- users with Alzheimer's disease or dementia, 51.7% AED users had the disease. Mood disorders were also prevalent, with 32.2% of residents having a diagnosis of anxiety, and 53.0% comorbid with depression Diabetes was prevalent among 41.7% AED users and 30.2% non- users (Table 1).

3.3 Factors Associated with Antiepileptic Drug Use

Table 2 and Table 3 shows the factors associated with the use of any AEDs and AEDs with expanded indications, respectively. The prevalence of AED use was less in those with advanced age. Compared to the prevalence of AED use in those aged 65– 74 years, the prevalence was 0.93 fold lower (95% CI = 0.92– 0.94) in residents aged 75– 84 years and 0.73 fold lower in those aged 85 years and older (95% CI= 0.73– 0.74).

For AED indications, residents who had a diagnosis of epilepsy had 3.73- fold prevalence of AED use compared to those without the disorder (95% CI = 3.69– 3.77), though in gabapentinoid users, the prevalence of AEDs did not differ much by epilepsy indications. Residents with comorbid bipolar disorders were associated with 0.2- fold increased likelihood of AED use (95% CI = 1.18– 1.22). Those who in pain had higher prevalence of AED use compared to those without pain ($aPR_{mild/\ infrequent\ vs.\ no\ pain}$ = 1.42; 95% CI = 1.41– 1.44; $aPR_{moderate/\ severe\ vs.\ no\ pain}$ = 1.42; 95% CI = 1.40– 1.44). Notably, pain was strongly associated with the use of gabapentinoids ($aOR_{mild/\ infrequent\ vs.\ no\ pain}$ = 2.07; 95% CI = 2.02– 2.11; $aOR_{moderate/\ severe\ vs.\ no\ pain}$ = 2.07; 95% CI = 2.01– 2.12) and topiramate ($aOR_{mild/\ infrequent\ vs.\ no\ pain}$ = 1.43; 95% CI= 1.22– 1.67; $aOR_{moderate/\ severe\ vs.\ no\ pain}$ = 1.45; 95% CI= 1.28– 1.64).

For epilepsy comorbidities, the prevalence of AED use was higher among residents with diabetes, anxiety, depression or stroke. Use of gabapentinoids was highly associated with diabetes (aOR = 1.79; 95% CI = 1.76– 1.82). Having Alzheimer's disease/ dementia or cognitive impairment was associated with decreased use of any AEDs.

4. DISCUSSION

We found that one in four long stay older nursing home residents enrolled in fee- for- service Medicare received AEDs. Second- generation AED agents were the most commonly used. Factors associated with increased AED use included having a diagnosis of epilepsy, bipolar disorder, pain, diabetes, anxiety, depression, or stroke. Residents with advancing age, Alzheimer's disease, dementia, or cognitive impairment were associated with decreased use

of AEDs. Use of gabapentinoids was strongly associated with having pain but not with epilepsy indication.

The prevalence of AED use has increased from approximately 10% in all US nursing homes in the 1990s to 24.0% in 2016 [5–7]. The reasons for this increase are likely multifactorial. One explanation is the rise in epilepsy prevalence, i.e., from 4.7%- 6.3% in 1990s [35] to 9.1% in the current study. Another explanation is the growing use of newer- generation AEDs, with increased tolerability and reduced side effects including less drug interactions relative to first- generation AEDs [36]. The most likely cause is their growing use beyond the treatment of epilepsy. Gabapentin was the most commonly used AED in our study, and its use has increased for multiple types of pain [37]. Nevertheless, whether or not the increased use of AEDs in nursing home residents is cause for alarm is unclear. Longitudinal studies of AED use and adverse health outcomes in nursing home residents are warranted.

We found that 15.1% nursing home residents used gabapentinoids (13.3% of gabapentin and 1.8% of pregabalin). Our analyses suggest that the use of gabapentinoids was highly associated with pain and diabetes, but not with an epilepsy indication. Though gabapentinoids have expanded indications for neuropathic pain, and are often used in patients with diabetes, the observed strong association between gabapentinoid use and pain in this study was unlikely solely due to on- label prescribing of gabapentinoids for neuropathic pain. Rather, we suspect that gabapentinoids might also be prescribed off- label for other types of pain. Prior research has reported up to 95% of gabapentin being extensively prescribed off- label in clinical practices [38–39]. Furthermore, gabapentin and pregabalin has been prescribed for almost any type of pain [37]. The increasing use of gabapentinoids for pain may reflect clinicians' desire to seek an alternative to opioids for pain management, partly in response to the opioid epidemic [40]. Nonetheless, the evidence regarding safety and effectiveness of off- label gabapentinoids prescribing is scant [37]. Gabapentinoids may cause sedation, dizziness, cognitive impairment when taken alone, and respiratory depression when taken with other central- nervous system depressants [37,41]. Research to understand the risks of gabapentin and pregabalin use in nursing homes settings is a pressing need.

Consistent with prior studies [5,7,9], decreased AED use was associated with advancing age, although the reason for this trend remains unclear. Greater AED use might be expected in older age groups in that the incidence of epilepsy increases with aging in community dwelling adults [42–43], i.e. from 4.7 per 1000 person- years among those aged 65– 69 years to 8.5 per 1000 person- years in those aged 85 and older [42]. Antiepileptic drug use was also found to decrease with conditions associated with decreased cognitive function. One hypothesis might be that physicians are less inclined to prescribe AEDs for those who already have impaired cognitive performance considering the adverse cognitive effects associated with AEDs [44]. Previous research has mixed findings on AED use and cognitive performance [5,45], perhaps due to differences in how interactions between cognitive function and other covariates were handled. Further research is required to investigate the extent to which reduced AED use with advancing age and cognitive decline in nursing home population represents cautious prescribing, or undertreatment of conditions for which AEDs may provide benefit.

As expected, the presence of epilepsy and bipolar disorder were strongly associated with greater AED use, in alignment with previous studies [5,9]. Having anxiety, depression or diabetes was associated with greater use, suggesting that they might be significant comorbidities among AED users. In support of this, a previous study found that nursing home residents with AED use had higher prevalence of depression compared to overall nursing home population [8]. Therefore, co- medications of antidepressants [43], antipsychotic medications [43], and antihyperglycemic drugs can be common among AED users. Considering that AEDs is susceptible to adverse drug- drug interactions in older adults [10], and that older nursing home residents with polypharmacy regimens have increased susceptibility to adverse drug events including fall -related injuries [46– 47], future work is needed to evaluate the safety of co- medications among AED users in nursing home residents.

This study has several strengths. First, using a comprehensive data source, it is the first national study on AED use in all Medicare/ Medicaid- certified US nursing homes since 1999, providing current data on cross- sectional AED use in this setting. Second, we focused on AEDs, a class of medications with safety concerns in older adults yet understudied in the vulnerable nursing home population. The study also has limitations inherent to administrative data sources. In community dwelling settings, concerns may be raised that drug records in administrative claims data do not always equate to drugs taken by patients because of issues with adherence. In the nursing home setting, this concern is unlikely because daily medication administration is conducted under supervision of nursing home staff. The prevalence of AEDs may be underestimated because we did not account for time spent in hospitals. We assumed no seasonal variations of AED use existed [8] among nursing home residents, therefore the point prevalence a single day in September, 2016 was assumed to be representative of the point prevalence throughout 2016. Information on drug indications were lacking. As such, we were not able to describe AED on/ off label use or assess the appropriateness of use.

5. CONCLUSIONS

One in four long stay older nursing home residents enrolled in fee- for- service Medicare used AEDs. Gabapentin was the most commonly prescribed agent, presumably for pain. Multiple comorbidities were associated with AED use. Nonetheless, little evidence exists to inform risk- benefit balance of AED regimens in this vulnerable population. Further study is required to investigate the safety and effectiveness of AED use in nursing homes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Key Points:

- This cross- sectional study of virtually all US long stay older nursing home residents enrolled in fee- for- service Medicare found that one in four residents used antiepileptic drugs (AED) in 2016.
- Gabapentin was the most commonly prescribed agent, presumably for pain. Multiple comorbidities were associated with AED use.
- Little evidence exists to inform risk- benefit balance of AED regimens in the nursing home population. Further study is required to investigate the safety and effectiveness of AED use in nursing homes.

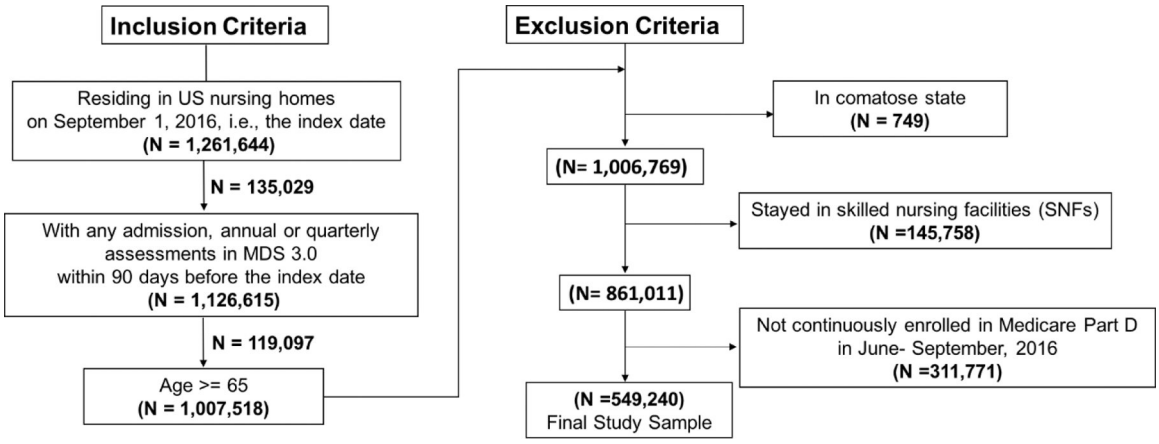

Figure 1.
Study Sample Selection

Table 1.

Characteristics of Residents in US Nursing Homes on September 1, 2016, Stratified by Antiepileptic Drug Use (n = 549,240)

Characteristics	Antiepileptic Drug User (n =128,228)	Non-User (n =421,012)
Age in years		
65– 74	31.5	16.6
75–84	34.2	29.8
≥ 85	34.3	53.6
Gender		
Women	69.9	72.4
Race/ ethnicity[a]		
Non- Hispanic white	80.8	82.8
Non- Hispanic black	14.5	12.1
Hispanic	1.9	2.0
Others	2.6	3.0
Geographic area		
West	10.8	11.1
Midwest	26.6	28.1
Northeast	20.5	23.4
South	37.4	42.2
Epilepsy[a]	29.9	3.4
Bipolar disorder[a]	7.1	4.0
Pain[a]		
No pain	63.9	78.4
Mild/ infrequent pain	22.8	13.5
Moderate/ severe pain	12.3	7.2
Diabetes[a]	41.7	30.2
Anxiety[a]	36.7	30.9
Depression[a]	59.9	50.9
Stroke[a]	14.6	10.2
Alzheimer’s disease/ dementia[a]	51.7	65.8
Peripheral vascular disease	14.3	11.0
Arthritis	32.4	31.1
Cognitive impairment[a]		
No impairment	39.7	24.5
Mild impairment	23.9	21.3
Moderate impairment	27.0	39.3
Severe impairment	8.5	13.8

Characteristics	Antiepileptic Drug User (n =128,228)	Non-User (n =421,012)
Fractures[a]	3.5	3.7
Physical functioning[a]		
No/ mild impairment	22.3	20.4
Moderate impairment	55.0	56.0
Severe impairment	22.6	23.6

Data are expressed as % unless otherwise specified.

[a]Missing data on race/ ethnicity ($n_{AED\ users}$ = 399, $n_{non\text{-}\ users}$ = 1,032), epilepsy ($n_{AED\ users}$ = 17, $n_{non\text{-}\ users}$ = 58), bipolar disorder ($n_{AED\ users}$ = 15, $n_{non\text{-}\ users}$ = 61), pain ($n_{AED\ users}$ = 1,254, $n_{non\text{-}\ users}$ = 3,765), diabetes ($n_{AED\ users}$ = 20, $n_{non\text{-}\ users}$ = 80), anxiety ($n_{AED\ users}$ = 37, $n_{non\text{-}\ users}$ = 106), depression ($n_{AED\ users}$ = 28, $n_{non\text{-}\ users}$ = 111), stroke ($n_{AED\ users}$ = 26, $n_{non\text{-}\ users}$ = 98), Alzheimer's disease / dementia ($n_{AED\ users}$ = 8, $n_{non\text{-}\ users}$ = 39), cognitive impairment ($n_{AED\ users}$ = 1,302, $n_{non\text{-}\ users}$ = 4,522), fractures ($n_{AED\ users}$ = 24, $n_{non\text{-}\ users}$ = 99), and physical functioning ($n_{AED\ users}$ = 95, $n_{non\text{-}\ users}$ = 250).

Table 2.

Factors Associated with Any Antiepileptic Drug Use[a]

Factor	Prevalence Ratios	
	Crude (95% Confidence Interval)	Adjusted[b] (95% Confidence Interval)
Age group		
≥ 85 years	0.59 (0.58– 0.60)	0.73 (0.73– 0.74)
75–84 years	1.15 (1.14– 1.17)	0.93 (0.92– 0.94)
65 – 74 years	1.00 (ref)	1.00 (ref)
Gender		
Women	1.04 (1.03– 1.06)	1.05 (1.04– 1.06)
Race/ ethnicity		
Non- Hispanic black	1.17 (1.16– 1.19)	1.04 (1.03– 1.06)
Hispanic	0.97 (0.93– 1.00)	1.06 (1.03– 1.10)
Others	0.89 (0.86– 0.93)	0.98 (0.95– 1.01)
Non- Hispanic white	1.00 (ref)	1.00 (ref)
Epilepsy	4.00 (3.97– 4.04)	3.73 (3.69– 3.77)
Bipolar disorder	1.61 (1.59– 1.64)	1.20 (1.18– 1.22)
Pain		
Moderate/ severe pain	1.50 (1.48– 1.52)	1.42 (1.40– 1.44)
Mild/ infrequent	1.56 (1.54– 1.58)	1.42 (1.41– 1.44)
No pain	1.00 (ref)	1.00 (ref)
Diabetes	1.45 (1.43– 1.46)	1.27 (1.26– 1.28)
Anxiety	1.22 (1.21– 1.24)	1.12 (1.11– 1.13)
Depression	1.31 (1.29– 1.32)	1.17 (1.15– 1.18)
Stroke	1.35 (1.33– 1.36)	1.08 (1.06– 1.09)
Alzheimer’s disease/ dementia	0.66 (0.65– 0.67)	0.87 (0.86– 0.88)
Cognitive impairment		
Severe	0.69 (0.68– 0.70)	0.62 (0.61– 0.63)
Moderate	0.66 (0.65– 0.66)	0.69 (0.68– 0.70)
Mild	1.10 (1.09– 1.11)	0.86 (0.85– 0.87)
No impairment	1.00 (ref)	1.00 (ref)

[a]Complete case analysis was performed (N = 537,149).

[b]The adjusted prevalence ratios were estimated from the extensions of robust Poisson regression model with all covariates selected, i.e., age, gender, race/ ethnicity, epilepsy, bipolar disorder, pain, diabetes, anxiety, depression, stroke, Alzheimer’s disease/ dementia, and cognitive impairment.

Table 3.

Factors Associated with the Use of Antiepileptic Drugs with Expanded Indications in Older Adults[a]

Factor	Adjusted[b] Odds Ratios (95% Confidence Interval)		
	Gabapentinoids[c]	Topiramate	Lamotrigine
Age group			
≥ 85 years	0.75 (0.73– 0.77)	0.24 (0.20– 0.27)	0.38 (0.34– 0.42)
75–84 years	1.08 (1.06– 1.11)	1.85 (1.65– 2.07)	1.38 (1.27– 1.49)
65 – 74 years	1.00 (ref)	1.00 (ref)	1.00 (ref)
Gender			
Women	1.18 (1.15– 1.20)	1.52 (1.35– 1.70)	1.15 (1.06– 1.24)
Race/ ethnicity			
Non- Hispanic black	1.06 (1.03– 1.10)	0.64 (0.54– 0.76)	0.58 (0.51– 0.65)
Hispanic	1.16 (1.08– 1.24)	0.92 (0.62– 1.39)	0.65 (0.48– 0.87)
Others	1.03 (0.97– 1.09)	0.92 (0.67– 1.26)	0.59 (0.46– 0.77)
Non- Hispanic white	1.00 (ref)	1.00 (ref)	1.00 (ref)
Epilepsy	1.09 (1.04– 1.14)	7.35 (6.50– 8.32)	11.13 (10.21– 12.13)
Bipolar disorder	1.01 (0.97– 1.06)	2.90 (2.53– 3.34)	7.70 (7.07– 8.38)
Pain			
Moderate/ severe pain	2.07 (2.01– 2.12)	1.45 (1.28– 1.64)	1.08 (0.99– 1.19)
Mild/ infrequent	2.07 (2.02– 2.11)	1.43 (1.22– 1.67)	0.99 (0.87– 1.12)
No pain	1.00 (ref)	1.00 (ref)	1.00 (ref)
Diabetes	1.79 (1.76– 1.82)	1.14 (1.02– 1.26)	1.01 (0.94– 1.09)
Anxiety	1.16 (1.14– 1.18)	1.33 (1.20– 1.48)	1.43 (1.33– 1.54)
Depression	1.39 (1.37– 1.42)	1.47 (1.32– 1.64)	1.28 (1.20– 1.38)
Stroke	1.14 (1.11– 1.17)	0.85 (0.73– 1.00)	0.87 (0.77– 0.97)
Alzheimer’s disease/ dementia	0.81 (0.79– 0.83)	0.88 (0.78– 0.98)	1.18 (1.08– 1.28)
Cognitive impairment			
Severe	0.27 (0.26– 0.28)	0.52 (0.43– 0.64)	0.66 (0.58– 0.75)
Moderate	0.45 (0.44– 0.47)	0.76 (0.66– 0.87)	0.73 (0.67– 0.80)
Mild	0.72 (0.71– 0.74)	1.02 (0.90– 1.16)	0.90 (0.82– 0.98)
No impairment	1.00 (ref)	1.00 (ref)	1.00 (ref)

[a] Complete case (CC) analysis was performed (N = 517,981) among residents who only received one type of AED (N = 529,564).

[b] The adjusted odds ratios were estimated from the multinomial regression model with clustered data including all covariates selected, i.e., age, gender, race/ ethnicity, epilepsy, bipolar disorder, pain, diabetes, anxiety, depression, stroke, Alzheimer’s disease/ dementia, and cognitive impairment. The reference group is ‘no AED use’.

[c] Includes: gabapentin and pregabalin.