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## Excess prevalence of preexisting chronic conditions in older adults with incident epilepsy

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### Abstract

**Objective:** Prior studies have examined chronic conditions in older adults with prevalent epilepsy, but rarely among those with incident epilepsy. Identifying the chronic conditions with which older adults present at epilepsy incidence assists with the evaluation of disease burden in this patient population and informs coordinated care development. The aim of this study was to identify preexisting chronic conditions with excess prevalence in older adults with incident epilepsy compared to those without.

**Methods:** Using a random sample of 4 999 999 fee-for-service Medicare beneficiaries aged >65 years, we conducted a retrospective cohort study of epilepsy incidence in 2019. Non-Hispanic Black and Hispanic beneficiaries were oversampled. We identified preexisting chronic conditions from the 2016–2018 Medicare Beneficiary Summary Files and compared chronic condition

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#### AUTHOR CONTRIBUTIONS

Concept and design: Siran M. Koroukian, Nicholas K. Schiltz, and David F. Warner. Funding and acquisition of the data: Siran M. Koroukian, Nicholas K. Schiltz, and David F. Warner. Data analysis: Siran M. Koroukian, Hannah L. Fein, Long Vu, Wyatt P. Bensken, Nicholas K. Schiltz, and David F. Warner. Content expertise: Martha Sajatovic and Gena R. Ghearing. Interpretation of the findings: all authors. Manuscript revision and approval of the final version: all authors.

#### CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

#### SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

prevalence between Medicare beneficiaries with and without incident epilepsy in 2019. We characterized variations in preexisting excess chronic condition prevalence by age, sex, and race/ethnicity, adjusting for the racial/ethnic oversampling.

**Results:** We observed excess prevalence of most preexisting chronic conditions in beneficiaries with incident epilepsy ( $n = 20\,545$ , weighted  $n = 19\,631$ ). For stroke, for example, the adjusted prevalence rate ratio (APRR) was 4.82 (99% CI: 4.60, 5.04), meaning that, compared to those without epilepsy, beneficiaries with incident epilepsy in 2019 had 4.82 times the stroke prevalence. Similarly, beneficiaries with incident epilepsy had a higher prevalence rate for preexisting neurological conditions (APRR = 3.17, 99% CI = 3.08–3.27), substance use disorders (APRR = 3.00, 99% CI = 2.81–3.19), and psychiatric disorders (APRR = 1.98, 99% CI = 1.94–2.01). For most documented chronic conditions, excess prevalence among beneficiaries with incident epilepsy in 2019 was larger for younger age groups compared to older age groups, and for Hispanic beneficiaries compared to both non-Hispanic White and non-Hispanic Black beneficiaries.

**Significance:** Compared to epilepsy-free Medicare beneficiaries, those with incident epilepsy in 2019 had a higher prevalence of most preexisting chronic conditions. Our findings highlight the importance of health promotion and prevention, multidisciplinary care, and elucidating shared pathophysiology to identify opportunities for prevention.

## Keywords

excess prevalence of chronic conditions; incident epilepsy; Medicare beneficiaries

## 1 | INTRODUCTION

Epilepsy is the third most common neurological disorder in adults aged 65 years or older. Its incidence increases after age 50 years and peaks at age 75 years and older to reach an incidence of up to 247 per 100 000.<sup>1</sup> The projected increase in the population aged 65 years and older—from 56.1 million in 2020 to 80.0 million in 2040 and 94.7 in 2060<sup>2</sup>—implies that the number of older adults with epilepsy will also rise considerably in the next several decades. As epilepsy incidence increases with age so too does the prevalence of several chronic conditions,<sup>3–5</sup> which complicates both the management of epilepsy and that of the co-occurring chronic conditions. This is particularly the case in terms of stroke, which is the most common cause of epilepsy among older adults.<sup>6–8</sup>

Most prior studies that have examined comprehensive sets of comorbid chronic conditions in older adults with epilepsy have focused on those with *prevalent* epilepsy, but fewer have examined more than a few comorbidities among those with new onset or *incident* epilepsy. The overwhelming focus on prevalent epilepsy makes it difficult to understand which chronic conditions may be risk factors for epilepsy onset.

Extant prevalence-based studies show that older adults with epilepsy have higher prevalence of chronic conditions than their counterparts with no epilepsy. For example, in a cross-sectional analysis using data from the Canadian Longitudinal Study on Aging, Husein et al.<sup>9</sup> showed that, compared to their counterparts without epilepsy, older adults with

epilepsy have a greater burden of heart disease, peripheral vascular disease, hypertension, chronic pulmonary obstructive disease (COPD), and stroke. Several other studies have shown that persons living with epilepsy are more likely to have cardiovascular disease,<sup>10-12</sup> COPD,<sup>10,12</sup> and neurodevelopmental disorders,<sup>13</sup> as well as psychiatric conditions, including mood and anxiety disorders, attention-deficit/hyperactivity disorder, psychosis, and pain disorders,<sup>11,12,14-17</sup> although we note that not all of these studies were limited to older adults.

Similar associations have also been shown in the few studies of incident epilepsy among older adults, with incident epilepsy being higher among those presenting with hypertension,<sup>18,19</sup> stroke,<sup>7,18-20</sup> neurological conditions,<sup>21</sup> depression and other psychiatric disorders,<sup>21,22</sup> and substance use disorders.<sup>21,23</sup> In one of the largest studies to date, Pugh et al.<sup>24</sup> analyzed risk factors for incident epilepsy in >1 million veterans aged 66 years and older. The findings showed that cerebrovascular disease, with or without dementia, brain tumor, head injury, and other central nervous system disorders were strongly associated with incident epilepsy. On the other hand, the metabolic conditions of obesity and hypercholesterolemia were associated with a lower likelihood of incident epilepsy. Although focused on midlife adults (45–64 years of age), findings from the Atherosclerotic Risk in Communities study linked to Medicare fee-for-service (FFS) claims data<sup>19</sup> similarly showed that stroke, hypertension, and diabetes were associated with incident epilepsy.

Many of the above-referenced studies have been relatively small longitudinal panels, used data from nonrepresentative or specialized populations, and/or have focused on a limited number of chronic conditions. Given the relatively low rate of incident epilepsy, most of the more comprehensive studies using large data sources have thus focused on prevalent cases of epilepsy. We overcome these limitations in the present study. Using a representative sample of nearly 5 million older US Medicare beneficiaries, we evaluate the excess prevalence of 67 chronic diseases and other potentially disabling conditions among those diagnosed with incident epilepsy in 2019 compared to those without epilepsy.

## 2 | MATERIALS AND METHODS

This study examined excess prevalence of preexisting chronic conditions among older US Medicare beneficiaries with incident epilepsy in 2019. This study was approved by the institutional review boards of both the University of Alabama at Birmingham (IRB-300008132) and Case Western Reserve University (STUDY 20211334) and was subject to a data use agreement with Centers for Medicare and Medicaid Services (CMS; 2022–58035).

### 2.1 | Data source and study population

We randomly sampled 4 999 999 beneficiaries aged >65 years enrolled in the US Medicare FFS program in 2016–2019 to conduct a retrospective cohort study. Our decision to limit our study population to 4 999 999 individuals (rather than the entire Medicare FFS population) was driven by budgetary constraints. To identify cases at risk of incident epilepsy in 2019 (described below), our cohort was defined as beneficiaries who received their care exclusively through the FFS system in each of 2016, 2017, and 2018 and had no epilepsy-

related claims in those years. The 3-year lookback period has been validated in prior studies<sup>21,25</sup> as appropriate to ensure completeness of claims data necessary to distinguish prevalent and incident cases without being overly restrictive (and thus underestimating incidence). Managed care enrollees were excluded because the claims histories for these beneficiaries were not available. The cohort defined by these criteria was extracted by CMS. As this sample was retrieved as part of a larger project, non-Hispanic Black and Hispanic beneficiaries were oversampled at 1.5 and 1.75 times their representation in the population, respectively, to ensure adequate cases for the broader project aims. Three beneficiary records were subsequently excluded because they were younger than 67 years and thus had a lookback period that included ages of <65. The final sample contained 4 999 996 FFS beneficiaries aged 67 years and older.

We used the 2016–2019 Medicare Beneficiary Summary File (MBSF), including the Base Segment, the Chronic Disease Segment, and the Other Chronic or Potentially Disabling Conditions Segment. These MBSF segments include one record per individual per year with information on basic demographic variables and summary indicators for 30 chronic conditions and 37 potentially disabling conditions aggregated from the claims.

## 2.2 | Variables of interest

**2.2.1 | Incident epilepsy**—Incident epilepsy in 2019 was identified in the MBSF Other Chronic or Potentially Disabling Conditions segment, based on end of year assessment using an algorithm similar to prior studies<sup>7,21,26,27</sup>: at least one inpatient claim or two outpatient nondrug claims occurring at least 1 day apart (International Classification of Diseases, 10th Revision [ICD-10] G40.x) in a 2-year period.<sup>28</sup> This ICD-10 algorithm has been validated previously.<sup>29</sup> ICD-10 codes replaced the ICD-9 codes on October 1, 2015, and thus the entirety of our data lookback period used the same codes.

**2.2.2 | Chronic conditions**—We assessed preexisting chronic conditions based on the 30 conditions available in the 2018 Chronic Conditions Segment and the 37 conditions available in the 2018 Potentially Disabling Conditions Segment of MBSF, identified by the Chronic Conditions Data Warehouse (CCW). CCW classified beneficiaries as having a condition if they met the diagnostic criteria and had sufficient FFS coverage in that year.<sup>28</sup> Only conditions recorded in these MBSF segments were available. We used chronic conditions from 2018 to ensure their prevalent status in 2019.

For parsimony and ease of interpretation, we grouped these conditions into 14 clinically meaningful disorder categories and analyzed the data accordingly. Condition categories included cancers, cardiovascular, congenital, developmental, metabolic, musculoskeletal, neurological, organ failure, other chronic, psychiatric, respiratory, sensory impairment and eye-related, stroke, and substance use disorders. See Table S1 for details on the categorization of each of the 67 chronic and potentially disabling conditions. These classifications were reviewed by the clinicians on the research team.

**2.2.3 | Beneficiary demographics**—Demographic characteristics were taken from the administrative records. Age, at the end of 2019 (or at death), was grouped as 67–69, 70–74, 75–79, 80–84, 85–89, and 90+ years. Sex was coded as male or female. Beneficiary

race/ethnicity was coded as Hispanic (any race), non-Hispanic Black, non-Hispanic Other, and non-Hispanic White using the RTI Race Code, a validated variable that augments the traditional CMS race code by applying an algorithm to identify more beneficiaries of Hispanic or Asian origin based on first or last name.<sup>30</sup> Too few beneficiaries were identified as Asian/Pacific Islander, American Indian/Alaska Native to be analyzed separately, and thus they were combined into the “non-Hispanic Other” category.

**2.3 | Analytic approach**—We define prevalence rate as the number of individuals presenting with a certain comorbidity in 2018 divided by the total number of individuals separately in people with and without epilepsy in 2019.

In our analysis, we address the following research question: If one is diagnosed with incident epilepsy, what conditions did they already have? Accordingly, we estimated logistic regression models in which a given preexisting chronic condition was the outcome variable and epilepsy was a predictor variable. Models in which epilepsy was the outcome variable and a given preexisting chronic condition was the independent variable were equivalent to the models presented herein, as they yield the same coefficients. We used the predicted marginal effects from the logistic regression models to estimate the prevalence rate of each of the 14 clinically meaningful preexisting chronic condition categories by incident epilepsy status in 2019. We then calculated the unadjusted and age-, sex-, race/ethnicity-adjusted prevalence rate ratios (PRRs and APRRs, respectively) to compare those with incident epilepsy to those without to identify excess prevalence. Analyses were weighted to account for racial/ethnic oversampling. We used a 99% confidence threshold ( $\alpha = .01$ ) to balance the risk of type I and type II errors with the large sample size; however, we focused on the magnitude of differences rather than statistical significance alone when making comparisons. We used Stata MP version 17 to conduct these analyses.<sup>31</sup>

Our analysis proceeded in three steps. First, to document excess prevalence, for each chronic condition category we estimated an unadjusted model where incident epilepsy was the only predictor and an adjusted model where age group and sex were additional predictors. These results are presented in tabular form. Second, we conducted sensitivity analyses replicating the prior analyses using the prevalence of each chronic condition in 2016 and 2017 to determine whether our findings differed depending on time proximity to 2019 epilepsy incidence. These results are available in Table S2. Lastly, we estimated models that included interaction terms between incident epilepsy status and each of age group, sex, and race/ethnicity to examine whether there were disparities in the association between epilepsy incidence and preexisting chronic condition prevalence. We graphed these results using the ggplot2 package in R Studio (v3.3.6).

### 3 | RESULTS

Among the 4 999 996 beneficiaries in our sample, adjusted for the racial/ethnic oversampling, we identified 20 545 older adults with incident epilepsy (weighted  $n = 19\,631$ ). The mean age was 77.5 years (SE = .003) and the median age was 76 years (interquartile range = 10); 55.0% were female, and 77.4% were Non-Hispanic White. The

demographic characteristics of the sample closely adhere to the total population aged 65 years and older enrolled in the Medicare FFS program.<sup>32</sup>

Table 1 shows the weighted demographic characteristics of the total study population and by incident epilepsy status. Beneficiaries with incident epilepsy were older (mean = 78.8, SE = .054) than those without (mean = 77.49, SE = .003) and significantly so ( $p < .001$ ). We observed fewer younger beneficiaries among those with incident epilepsy compared to those without epilepsy (8.1% vs. 9.2% in the 67–69-year age group, and 27.1% vs. 34.2% in the 70–74-year age group) but more older beneficiaries among those with incident epilepsy than those without (18.2% vs. 15.6% in the 80–84-year age group, 14.0% vs. 9.9% in the 85–89-year age group, and 9.9% vs. 7.8% in the 90 years and older age group;  $p < .001$ ). The distribution by sex did not differ between individuals with and without incident epilepsy ( $p = .157$ ).

The distribution by incident epilepsy status differed markedly by race/ethnicity ( $p < .001$ ). Notably, we observed a higher percentage of non-Hispanic Black beneficiaries among those with incident epilepsy than those without (16.9% vs. 9.8%). Non-Hispanic White and other race beneficiaries were less represented among those with incident epilepsy than those without (71.5% vs. 77.4% and 4.5% vs. 5.9%, respectively). There was little difference in the percentage of Hispanic beneficiaries by incident epilepsy status (7.1% vs. 6.9%).

Table 2 shows the number of beneficiaries presenting with chronic conditions in each of 14 clinical meaningful categories in 2018 for the total sample and differentiating between those with incident epilepsy in 2019 and those without. In addition, the table shows the unadjusted PRR and age- and sex-adjusted PRR and 99% confidence interval (CI) for each chronic condition category, comparing beneficiaries with incident epilepsy and those without. In the total population, the three most prevalent conditions were metabolic disorders (e.g., hypertension, hyperlipidemia, and diabetes; 68.7%), musculoskeletal conditions (e.g., arthritis, chronic pain/fatigue, and mobility impairments; 42.2%), and cardiovascular disease (e.g., acute myocardial infarction, heart failure, and peripheral vascular disease; 36.1%).

Examination of the PRRs indicates that beneficiaries with epilepsy onset in 2019 exhibited excess prevalence in each of the chronic condition categories in 2018 compared to those without incident epilepsy. Adjusting for age and sex differences between those with and without incident epilepsy did little to account for this excess prevalence. Similarly, adjusting for age, sex, and race/ethnicity did not alter the findings substantively (not shown). The greatest excess prevalence in preexisting conditions was observed, not surprisingly, for stroke, with an APRR of 4.82 (99% CI = 4.60–5.04), meaning that the prevalence of stroke in 2018 was 4.82 times higher among those who subsequently experience epilepsy onset in 2019 compared to those who did not. In addition to stroke, the APRRs were substantially higher for preexisting developmental conditions (4.64, 99% CI = 4.09–5.19), neurological conditions (3.17, 99% CI = 3.08–3.27), substance use disorders (3.00, 99% CI = 2.81–3.19), and congenital conditions (2.47, 99% CI = 2.15–2.78). Beneficiaries with epilepsy onset in 2019 were also approximately twice as likely to have psychiatric disorders in 2018 (APRR = 1.98, 99% CI = 1.94–2.03) compared to those who did not have epilepsy onset. We note that,



although statistically significant, excess prevalence of sensory impairment and eye-related conditions, metabolic disorders, and cancers was relatively modest.

Next, we conducted sensitivity analysis examining preexisting chronic disease burden documented in the years 2016 and 2017 among beneficiaries with incident epilepsy in 2019. For most conditions, the estimated APRRs were slightly smaller when estimating excess prevalence from these earlier years (e.g., stroke APRR in 2016 = 3.18, 99% CI = 2.98–3.38; in 2017 = 3.56, 99% CI = 3.36–3.76), but the overall pattern of findings was substantively consistent, regardless of which year the preexisting conditions were measured (see Table S2).

Lastly, we examined whether there were age, sex, or racial/ethnic disparities in the association between epilepsy incidence and preexisting chronic condition prevalence. There were significant differences by age (13 of the 14 chronic condition categories had statistically significant omnibus tests; Figure 1). Differences by sex were small, largely nonsignificant (7 of the 14 categories had statistically significant omnibus tests) and inconsistent (Figure 2); therefore, these results are not discussed in the article. We found significant disparities by race/ethnicity (for 11 of the categories Figure 3).

Across chronic conditions categories (except for metabolic conditions), excess prevalence among beneficiaries with incident epilepsy, compared to those without, was generally more pronounced in younger age groups than in older age groups. The pattern of age disparities varied by chronic condition (Figure 1). Post hoc significance tests (not shown) indicated, however, that—except for cardiovascular, neurologic, and psychiatric conditions—after age 85–90 years there was no evidence of preexisting excess prevalence among beneficiaries experiencing epilepsy onset.

Racial/ethnic disparities in preexisting excess prevalence of chronic conditions were widespread among beneficiaries with incident epilepsy (Figure 3); only congenital, developmental, and substance use disorders did not differ. Excess prevalence among Hispanic beneficiaries with incident epilepsy, compared to those without, was higher than both non-Hispanic White and non-Hispanic Black beneficiaries for all 11 condition categories where there were racial/ethnic disparities. Non-Hispanic Black beneficiaries with incident epilepsy exhibited greater excess prevalence than non-Hispanic White beneficiaries for six chronic condition categories (cardiovascular, metabolic, musculoskeletal, neurological, organ failure, and psychiatric).

## 4 | DISCUSSION

In this study, we examined whether incident epilepsy was associated with the prevalence of preexisting chronic and potentially disabling conditions in Medicare beneficiaries. Our study population included nearly 5 million older adults enrolled in the traditional FFS program, with oversamples of non-Hispanic Black and Hispanic beneficiaries. Our findings showed that beneficiaries with incident epilepsy had a higher prevalence of all 14 preexisting chronic condition categories examined than their epilepsy-free counterparts, with especially

disproportionate excess prevalence of stroke, developmental, neurological, substance use disorders, congenital, and psychiatric conditions.

Excess prevalence was greater among younger beneficiaries than older beneficiaries in 13 of the 14 conditions examined. The reason of this age-patterning is unclear. It could reflect differential mortality or that chronic conditions become more common with age; in either case, differences between older age-group beneficiaries with incident epilepsy and those without would be lessened as we observe.

We documented pervasive racial/ethnic disparities. Excess prevalence was higher for Hispanic beneficiaries with incident epilepsy compared to both non-Hispanic White and non-Hispanic Black beneficiaries in 11 of the 14 chronic condition categories; non-Hispanic Black beneficiaries had higher excess prevalence than non-Hispanic White beneficiaries in approximately half of the condition categories. Although our study does not account for illness severity, the differences in excess prevalence of preexisting chronic conditions among beneficiaries by race/ethnicity are striking, as they may reflect differences in biological, neighborhood, psychosocial, socioeconomic, and behavioral factors<sup>33</sup>; health care-seeking behaviors, including delays in follow-up care<sup>34</sup> or lower participation in programs aimed at risk factor management (e.g., cardiac rehabilitation following the diagnosis of coronary heart disease)<sup>35</sup>; and the quality and comprehensiveness of reporting of symptoms and diagnoses during health care encounters, by both the patient and the provider,<sup>36</sup> which may vary greatly across patients and providers. In addition, these preexisting conditions may have potentially differential effects relative to the risk of developing epilepsy<sup>37</sup> within the context of known disparities in social determinants of health.<sup>38</sup> The excess burden of preexisting chronic conditions will likely further contribute to racial/ethnic disparities in epilepsy treatment.

The link between epilepsy onset and several of the preexisting conditions, including stroke and developmental, neurological, and psychiatric conditions, seems evident, given their association with brain pathology. The same is true of the excess prevalence of substance use disorders, which over time lead to neurological damage.<sup>39</sup> Although excess prevalence of other conditions—such as metabolic disorders, cardiovascular disease, and organ (kidney, liver) failure—is not obvious, it may be explained through shared pathophysiology and cascade effects observed in multiple chronic conditions. For example, hypertension and hyperlipidemia increase risk for cardiovascular and cerebrovascular disease, leading to stroke and/or vascular dementia, and eventually epilepsy.<sup>40</sup> Elucidating these associations by examining co-occurring preexisting multiple chronic conditions in older adults with epilepsy onset is a next step.

Our findings have important clinical implications given the high burden of preexisting, and potentially co-occurring, chronic conditions in older adults with incident epilepsy. This calls for a multidisciplinary approach to their care, including attending to their metabolic and cardiovascular health, both preventively and curatively.

Our study has multiple strengths. Although a number of studies document chronic disease burden in older adults with prevalent epilepsy,<sup>9,13,18-20</sup> our study is among the few and



the largest to do so among a nationally representative sample of those with incident epilepsy, using more recent data than previous studies. We also examined a large number of chronic conditions, whereas many prior studies have focused on a limited number of chronic conditions.<sup>14,16,18,20,22,41,42</sup> In addition, the oversampling of non-Hispanic Black and Hispanic beneficiaries allowed us to evaluate disparities in chronic disease burden across these racial/ethnic subgroups. This is especially important for Hispanic beneficiaries, as prior studies of epilepsy incidence have typically been limited to single states with high percentages of Hispanic residents<sup>43</sup> or have not examined Hispanic ethnicity.<sup>7</sup> Lastly, our use of predicted marginal effects permitted comparisons of excess prevalence of preexisting chronic conditions in Medicare beneficiaries with epilepsy across different race/ethnicity groups, rather than only comparing to the non-Hispanic White reference category.

Our findings should be interpreted while mindful of the following limitations. First, we examined preexisting chronic conditions individually; however, given the shared pathophysiology among the different conditions noted earlier, it is imperative to study chronic disease burden while accounting for the co-occurrence of these conditions. Second, we were unable to account for disease severity; however, examining co-occurring conditions could be useful in that respect. Third, we examined chronic disease burden in beneficiaries with incident epilepsy in 2019 accounting for preexisting conditions documented in 2018. Given the administrative nature of Medicare data, there may be concerns about the accuracy of the time ordering of incident epilepsy in 2019 with prevalent chronic conditions 2018. Our sensitivity analyses using chronic conditions prevalent in 2016 and 2017, however, increase confidence that such time order issues—should they exist—are of little consequence given that our substantive conclusions are robust to using prevalent conditions from earlier years. Lastly, we note that persons with incident epilepsy were identified based on the epilepsy summary measures in the Medicare Beneficiary Summary File, created by CCW.<sup>28</sup> The CCW bases its criteria on the presence of relevant diagnosis codes in at least one inpatient claim or two outpatient nondrug claims occurring at least 1 day apart (ICD-10 G40.x) in a 2-year period. In a 2012 Canadian study validating coding algorithms from claims data, Reid et al. reported that the most accurate algorithm to identify incident epilepsy cases was based on two physician claims, or one hospitalization in 2 years,<sup>44</sup> similar to the algorithm used by the CCW, which also includes claims from emergency department (ED) visits. The algorithm by Reid et al. yielded a sensitivity of 93.1%, specificity of 93.0%, positive predictive value (PPV) of 91.9%, and negative predictive value (NPV) of 94.0%. Adding ED claims resulted in improved sensitivity and NPV (99.3% for both), but lower specificity and PPV (84.2% and 84.3%, respectively). We note, however, that results from validation studies are snapshots unique to the institution or setting in which they are conducted, and that the findings may vary considerably across studies and across time. Nonetheless, we consider these metrics concerning the quality of administrative data to correctly identify persons with incident epilepsy to be reassuring. With regard to using antiseizure medications as an additional criterion to identify persons with epilepsy, as used in some previous studies,<sup>25,45</sup> we opted not to account for them in our study to ensure that persons with incident epilepsy are accounted for, regardless of whether they are (yet) under active treatment for the condition.

In conclusion, using data from nearly 5 million Medicare beneficiaries with incident epilepsy, we documented a high burden of preexisting chronic conditions, and substantial variations by age and race/ethnicity. Our findings have numerous implications. For health practitioners, the high burden of nonneurological conditions in the period preceding epilepsy calls for close surveillance, as well as the need for multidisciplinary care, especially given that comorbidities are associated with increased risk of mortality,<sup>46</sup> functional status, quality of life, and health care utilization.<sup>47</sup> Nearly 80% of medical costs are related to the management of comorbid conditions, rather than that of epilepsy.<sup>48</sup> For researchers, the findings call for the analysis of constellations of preexisting conditions to further elucidate shared pathophysiology and identify opportunities for prevention.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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## DATA AVAILABILITY STATEMENT

We are unable to share the data used in our current analyses. US Medicare research identifiable files are available for purchase from the Centers for Medicare and Medicaid Services after securing a data users agreement.

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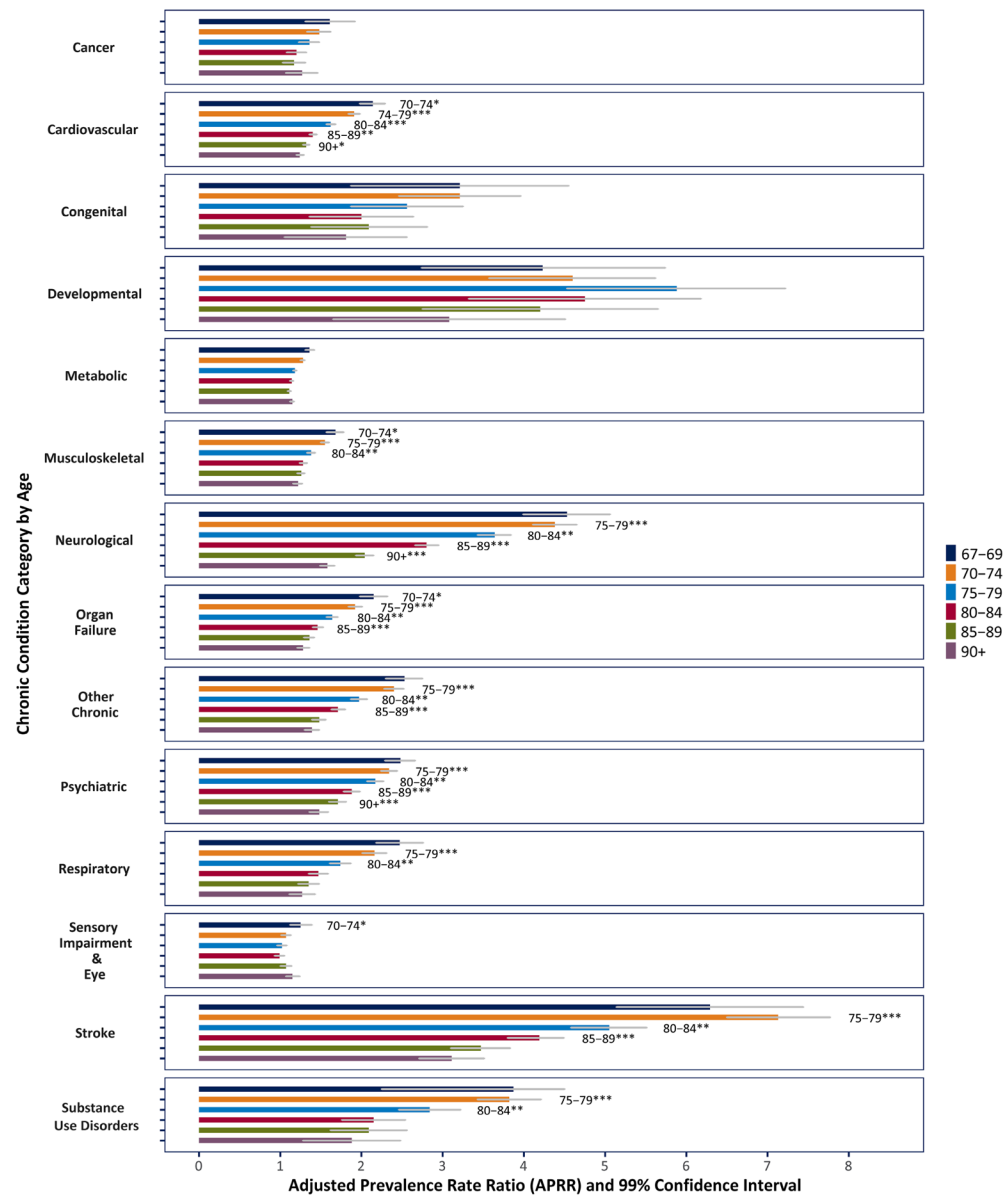
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**Key points**

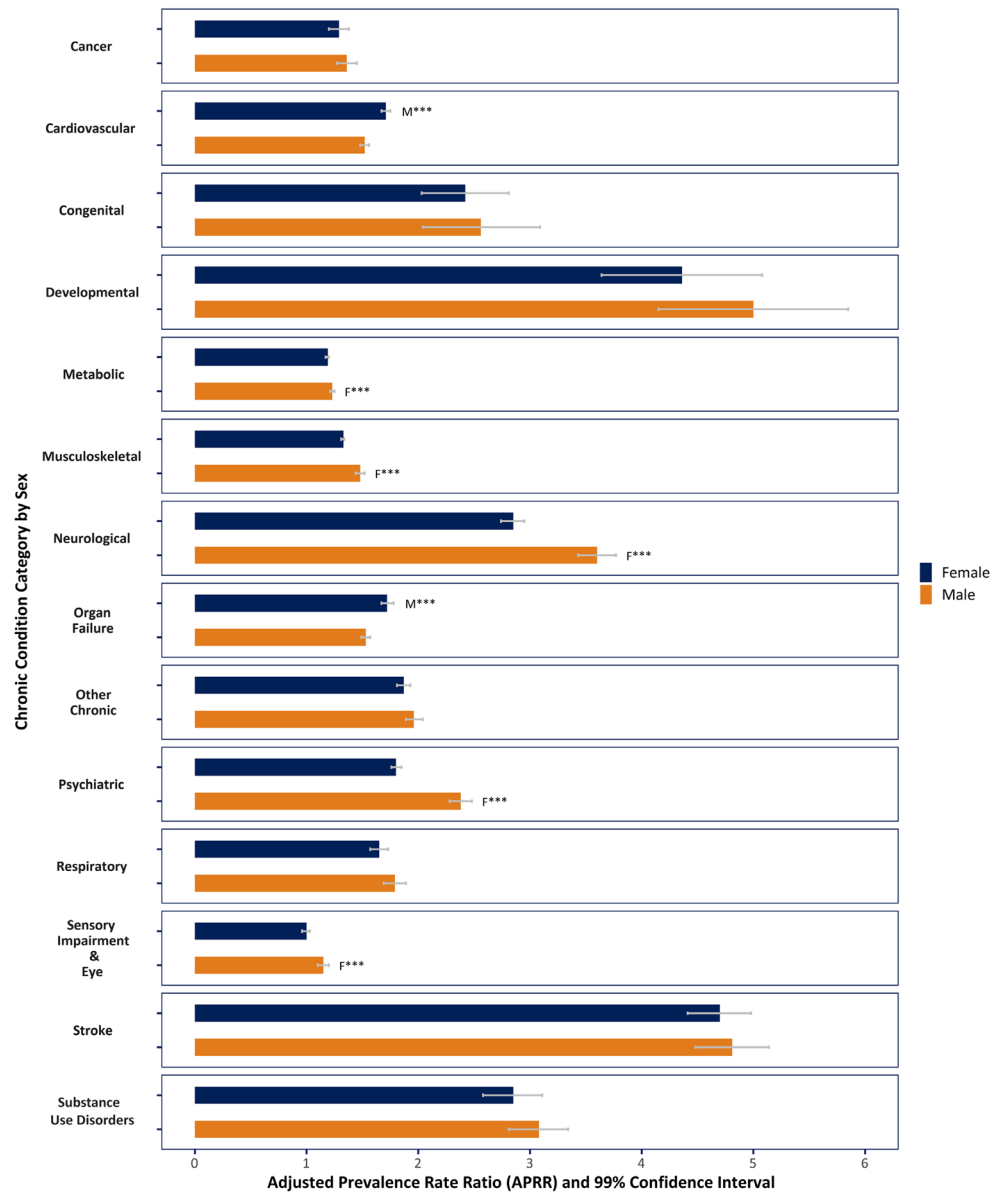
- We identified preexisting chronic conditions with excess prevalence in older adults with incident epilepsy compared to those without.
- We observed excess prevalence of most preexisting chronic conditions in older adults with incident epilepsy, especially for stroke.
- Excess prevalence was greater for younger than for older age groups.
- Excess prevalence was also greater in Hispanic beneficiaries with incident epilepsy than in their non-Hispanic White and non-Hispanic Black counterparts.
- Our findings highlight the importance of health promotion and prevention and of providing multidisciplinary care.



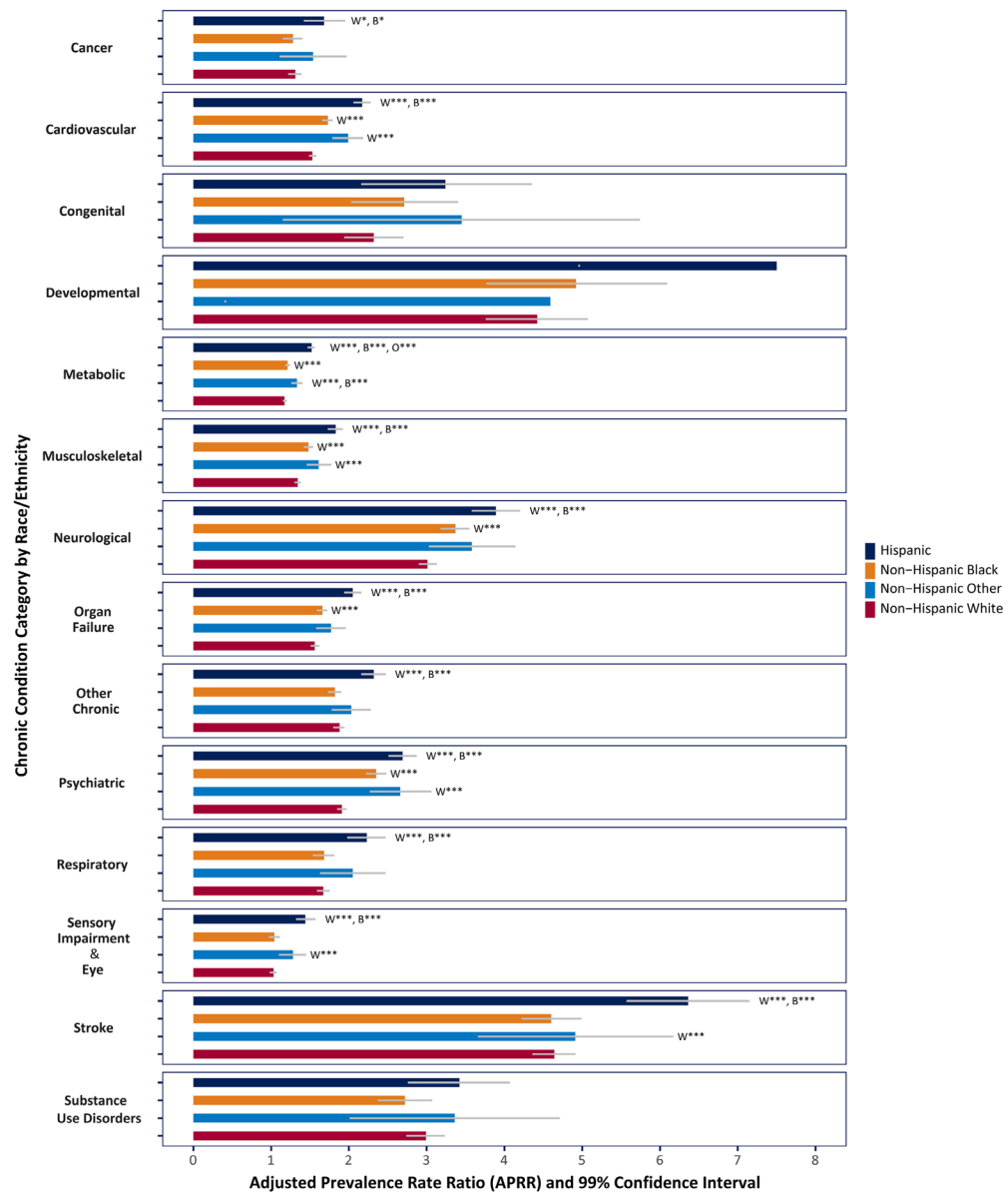


**FIGURE 1.**

Age-specific excess prevalence of each preexisting chronic condition among beneficiaries with incident epilepsy adjusting for sex and race/ethnicity. (i) Age group superscripts indicate APRR is significantly higher (\* $p < .01$ , \*\* $p < .001$ , \*\*\* $p < .0001$ ) in pairwise comparison than APRR for 67–69, 70–74, 75–79, 80–84, 85–89, and 90+ year age groups, respectively; (ii) the absence of superscripts indicates that the comparisons are not statistically significant; and (iii) significance tests adjusted for multiple comparisons within chronic conditions.

**FIGURE 2.**

Sex-specific excess prevalence of each preexisting chronic condition among beneficiaries with incident epilepsy, adjusting for age and race/ethnicity. (i) <sup>F/M</sup>Superscripts indicate APRR is significantly higher ( $*p < .01$ ,  $***p < .0001$ ) in pairwise comparison than APRR for females (F) and males (M), respectively; (ii) the absence of superscripts indicates that the comparisons are not statistically significant.

**FIGURE 3.**

Race/ethnicity-specific excess prevalence of each preexisting chronic condition among beneficiaries with incident epilepsy, adjusting for age and sex. <sup>B,O,W</sup>Superscripts indicate APRR is significantly higher ( $*p < .01$ ,  $***p < .0001$ ) in pairwise comparison than APRR for Hispanic (H), non-Hispanic Black (B), non-Hispanic Other (O), or non-Hispanic White (W) individuals, respectively; (ii) the absence of superscripts indicates that the comparisons are not statistically significant; and (iii) significance tests adjusted for multiple comparisons within chronic conditions.

**TABLE 1**  
Demographic characteristics of the study population of US Medicare fee-for-service beneficiaries, by incident epilepsy status.<sup>a</sup>

Total	All, N = 4 999 996	Incident epilepsy, n = 19631	No incident epilepsy, n = 4 980 365
Age group, years, n (%) <sup>b</sup>			
67–69	457 546 (9.2)	1584 (8.1)	455 962 (9.2)
70–74	1 707 106 (34.1)	5327 (27.1)	1 701 778 (34.2)
75–79	1 168 335 (23.4)	4449 (22.7)	1 163 886 (23.4)
80–84	780 085 (15.6)	3581 (18.2)	776 504 (15.6)
85–89	498 199 (10.0)	2741 (14.0)	495 458 (9.9)
90+	388 726 (7.8)	1950 (9.9)	386 776 (7.8)
Sex, n (%) <sup>b</sup>			
Female	2 751 238 (55.0)	10 703 (54.5)	2 740 536 (55.0)
Male	2 248 758 (45.0)	8929 (45.5)	2 239 829 (45.0)
Race/ethnicity, n (%) <sup>b</sup>			
Hispanic	345 999 (6.9)	1401 (7.1)	344 599 (6.9)
Non-Hispanic Black	489 000 (9.8)	3313 (16.9)	485 687 (9.8)
Non-Hispanic Other	295 500 (5.9)	882 (4.5)	294 618 (5.9)
Non-Hispanic White	3 869 497 (77.4)	14 036 (71.5)	3 855 461 (77.4)

<sup>a</sup> All values weighted to adjust for racial/ethnic oversampling.  
<sup>b</sup> Weighted *n* rounded to nearest whole person and thus may not add to the total within the row or the column.

Prevalence of chronic conditions grouped into 14 clinically meaningful categories among sample of US Medicare fee-for-service beneficiaries by incident epilepsy status.<sup>a</sup>

TABLE 2

Chronic condition category	All, N = 4999996, n (%) <sup>b</sup>	Incident epilepsy, n (%) <sup>c</sup>	No incident epilepsy, n = 4980365, n (%) <sup>c</sup>	Unadjusted <sup>d</sup>		Age- and sex-adjusted <sup>d</sup>	
				PRR	99% CI	APRR	99% CI
Cancer	510 231 (10.2)	2748 (14.0)	507 483 (10.2)	1.37	(1.31–1.44)	1.33	(1.27–1.39)
Cardiovascular	1 806 333 (36.1)	11 503 (58.6)	1 794 830 (36.0)	1.63	(1.60–1.65)	1.61	(1.58–1.64)
Congenital	41 666 (.8)	411 (2.1)	41 255 (.8)	2.53	(2.20–2.85)	2.47	(2.15–2.78)
Developmental	27 087 (.5)	478 (2.4)	26 609 (.5)	4.56	(4.02–5.10)	4.64	(4.09–5.19)
Metabolic	3 437 206 (68.7)	16 418 (83.6)	3 420 789 (68.7)	1.22	(1.21–1.23)	1.20	(1.19–1.21)
Musculoskeletal	2 111 755 (42.2)	11 558 (58.9)	2 100 196 (42.2)	1.40	(1.37–1.42)	1.39	(1.37–1.41)
Neurological	606 851 (12.1)	7085 (36.1)	599 766 (12.0)	3.00	(2.92–3.07)	3.17	(3.08–3.27)
Organ failure	1 440 876 (28.8)	9415 (48.0)	1 431 462 (28.7)	1.67	(1.64–1.70)	1.65	(1.62–1.69)
Other chronic <sup>e</sup>	1 012 968 (20.3)	7847 (40.0)	1 005 122 (20.2)	1.98	(1.94–2.03)	1.94	(1.90–1.99)
Psychiatric	1 084 007 (21.7)	8248 (42.0)	1 075 758 (21.6)	1.95	(1.90–1.99)	1.98	(1.94–2.03)
Respiratory	623 200 (12.5)	4250 (21.6)	618 952 (12.4)	1.74	(1.68–1.80)	1.70	(1.64–1.76)
Sensory impairment & eye-related	1 550 253 (31.0)	6536 (33.3)	1 543 717 (31.0)	1.07	(1.05–1.10)	1.05	(1.02–1.08)
Stroke	160 553 (3.2)	3123 (15.9)	157 430 (3.2)	5.03	(4.82–5.25)	4.82	(4.60–5.04)
Substance use disorders	137 593 (2.8)	1570 (8.0)	136 023 (2.7)	2.93	(2.74–3.11)	3.00	(2.81–3.19)

Abbreviations: APRR, adjusted prevalence rate ratio; CI, confidence interval; PRR, prevalence rate ratio.

<sup>a</sup> All values weighted to adjust for racial/ethnic oversampling.

<sup>b</sup> Weighted *n* rounded to nearest whole person; percentage with condition, not mutually exclusive.

<sup>c</sup> Weighted *n* rounded to nearest whole person and thus may not add to the value for all within row; column percentage with condition, not mutually exclusive.

<sup>d</sup> PRR, APRR, and CI based on predicted margins derived from survey-adjusted logistic regression model; see text for details.

<sup>e</sup> Other chronic conditions not elsewhere classified include anemia, human immunodeficiency virus/acquired immunodeficiency syndrome, and viral hepatitis (general).