Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

HHS Public Access

Author manuscript

Epilepsy Res. Author manuscript; available in PMC 2021 October 01.

Published in final edited form as:

Epilepsy Res. 2020 October ; 166: 106406. doi:10.1016/j.eplepsyres.2020.106406.

Delays and Disparities in Diagnosis for Adults with Epilepsy: Findings from U.S. Medicaid Data

Wyatt P. Bensken, BS[a], **Suparna M. Navale, MS, MPH**[a], **Angeline S. Andrew, PhD**[b], **Barbara C. Jobst, MD, PHD**[b], **Martha Sajatovic, MD**[c], **Siran M. Koroukian, PhD**[a]

[a]Department of Population and Quantitative Health Sciences School of Medicine, Case Western Reserve University, Cleveland, OH

[b]Department of Neurology, Geisel School of Medicine, Dartmouth-Hitchcock Medical Center, Lebanon, NH

[c]Departments of Neurology and Psychiatry, University Hospitals Cleveland Medical Center, School of Medicine, Case Western Reserve University, Cleveland, OH

Abstract

Objective: To identify disparities in care pathways and time from first seizure to epilepsy diagnosis, we examined 2010–2014 Medicaid claims (including pharmacy) data from 16 States for individuals with incident epilepsy, leading up to epilepsy diagnosis.

Methods: We identified adults (18–64) with an incident epilepsy diagnosis from 1/2012 through 6/2014. These individuals were enrolled in Medicaid for the entire study period and had no history of anti-epileptic drug (AED) use before their first seizure claim. We identified care pathways and calculated the duration from initial seizure to epilepsy diagnosis. We tested associations between these pathways and race/ethnicity, as well as time differences between care pathways using a Chi-squared and Kruskal-Wallis tests.

Results: The 14,337 adults followed five different care pathways. Their overall median duration from first seizure code to epilepsy diagnosis code was 19.0 months (interquartile range: 4.6, 30.4), and 56.0% filled an AED prescription. Some minorities were more likely to follow pathways with increased durations and delay to diagnosis, and the duration to diagnosis varied significantly across the care pathways.

Significance: The many different care pathways seen in people with epilepsy show substantial and significant time delays between first seizure diagnosis and epilepsy diagnosis, including significant racial/ethnic disparities that warrant attention.

Corresponding Author: Wyatt Bensken, BS, 10900 Euclid Ave, WG-43, Cleveland, Ohio 4106, wpb27@case.edu, 216.368.1134.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Statistical Analysis conducted by Mr. Wyatt P. Bensken, Case Western Reserve University School of Medicine

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

1. Introduction

Proper diagnosis and treatment for people with epilepsy (PWE) is critical to reducing the burden of seizures, both for the healthcare system as well as the individual. Seizures account for roughly 1 million emergency department visits each year, and result in continued adverse social consequences for an individual, such as unemployment or driving restrictions, and the diagnostic uncertainty has an impact on the individual's overall well-being.[1–4] Between 40–50% of individuals who are untreated after a first unprovoked seizure will have a recurrent seizure within the next two years.[5] With the risk and consequences of recurrent seizures, it is critical that individuals who have, or are likely to have, epilepsy are properly diagnosed and promptly treated following a standard clinical care pathway to reduce the risk of future seizures and associated injuries. This need has gone as far as being recognized as a national priority for Healthy People 2020, a national health promotion agenda, which includes an objective aimed at increasing the proportion of adults with uncontrolled seizures who receive appropriate care.[6]

Previous studies have demonstrated treatment gaps, suggesting that up to one-third of patients remain untreated with an anti-epileptic drug (AED) three years after diagnosis, and 41% of patients have multiple events before their recorded index seizure date.[7–9] Importantly, studies that seek to understand the care and outcomes for PWE often assume, and rely on, a standard clinical pathway that progresses in the order of seizure episode which is followed by an epilepsy diagnosis and AED prescription.[10–13] The purpose of our study was to examine both clinical care pathways for PWE using real-world data and the time from first seizure to epilepsy diagnosis to identify the duration of delays to epilepsy diagnosis and care, especially with respect to potential racial/ethnic disparities. We further examined all-cause use of the emergency department in the time between the first seizure claim and the first epilepsy claim to assess resource utilization. Our overall intent in conducting this work is to inform clinical care, research and policy such that individuals with epilepsy get timely referral and appropriate treatment.

2. Materials and Methods

The Institutional Review Board at Case Western Reserve University (Protocol # 2018-0780) and the Privacy Board of the Centers for Medicare and Medicaid Services approved this study (CMS; Data Users Agreement # 52636).

2.1 Data Source

The data analyzed for this study come from the most recently available Medicaid claims data for the following 16 geographically and demographically diverse states for 2010 through 2014: California, Georgia, Iowa, Louisiana, Michigan, Minnesota, Missouri, Mississippi, New Jersey, Pennsylvania, South Dakota, Tennessee, Utah, Vermont, West Virginia, and Wyoming. These data included personal summary (PS), inpatient (IP), other therapy (OT), and pharmacy (RX) information. The PS file provided demographic and monthly enrollment information. The IP and the OT files include information on clinical encounters and diagnoses, while the OT files contain outpatient (institutional and non-institutional) claims. The RX file provided pharmacy data including prescriptions filled. Race and ethnicity

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

categories available included: White, Black, American Indian, Alaskan Native, Asian, Pacific Islander, Native Hawaiians and Other Pacific Islander, Hispanic, More than 1 Race, and Unknown. Groups were collapsed to account for small individual counts.

2.2 Inclusion Criteria

Individuals were included in the analyses if their first recorded epilepsy diagnosis (identified by ICD-9-CM 345.XX) occurred from January 2012 through June 2014, allowing for a minimum of 2-year look-back and 6-month follow-up (n = 88,812). To identify incident cases, the minimum lookback period of 2 years represents the absolute minimum amount of epilepsy-free time up to an individual's first epilepsy date, and most individuals had more than 2 years' epilepsy-free time in their lookback period. Epilepsy diagnosis was identified in either the IP or OT files (which includes outpatient hospital claims). From this, the first and each subsequent seizure claim, from the start of the study period to their epilepsy diagnosis date, was identified by ICD-9-CM 780.39. The use of anti-epileptic drugs (AEDs) was also identified, relying on the published list of AEDs from the American Epilepsy Society, matched to their National Drug Codes (NDCs).[14] The cohort was further restricted to those individuals who were between 18 and 65 years of age at the time of their first seizure (n = 67,175); enrolled in Medicaid for the entire study period of 60 months (n = 29,875), and had no AED record prior to their first seizure leaving our study population to 14,337 individuals. Further, this only included individuals who had both seizure and epilepsy diagnosis codes. Anyone with solely an epilepsy diagnosis code (and no previous seizure codes) was not included.

2.3 Identifying the Pathways

Clinical knowledge as well as previously published algorithms guided initial construction of the pathways, however we also followed a data-driven approach. Specifically, we knew we would identify individuals who were diagnosed with epilepsy after 1 or 2 seizure claims, which would roughly follow the practical definition of epilepsy.[15] However, during data analysis we discovered paths of individuals who had more than 2 claims as well as variation with when AEDs were initiated. While these pathways were partially pre-specified, we also hypothesized that the pathway with the most claims would be the shortest to diagnosis.

The time between the first recorded seizure and the first epilepsy diagnosis was calculated in days but reported here in months for ease of interpretation. The total number of emergency department visits between the first seizure and first epilepsy date was also recorded.

2.4 Statistical Analyses

In addition to descriptive analyses, a Chi-squared test was used to test the association between race/ethnicity and care path – to examine potential disparities in path. Further, we used the non-parametric Kruskal-Wallis rank sum test to assess differences in mean time from seizure to epilepsy diagnosis across paths. Similarly, a Kruskal-Wallis rank sum test was used to assess for differences in means of number of emergency department visits between paths. For both of these, a Dunn test with Bonferroni correction for multiple comparisons was used post-hoc to examine pairwise relationships. For all tests the level of significance was 0.05.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Data analysis was conducted using Version 9.4 of SAS as well as R version 3.6.1. In order to comply with the data protection requirements of the Data Users Agreement, cell sizes that are less than 11 must be masked. For this reason, certain values must also be masked to prevent calculation of those small sizes. This is denoted as less than, <, indicating that the true value is less than the listed value.

2.5 Data Availability

Access to these data are restricted to the study team under a Data Users Agreement from the Centers for Medicare and Medicaid Services.

3. Results

In total, 14,337 individuals (16% of the original source group) met the inclusion criteria for the analysis cohort. Just over half were White (54.4%), and female (51.4%), with an overall mean age of 44.1 (±13.3) years (Table 1). These individuals followed 5 care paths after their first seizure (Figure 2). Path 1 (29.9%) included those individuals who had one seizure claim, followed by an epilepsy claim, and 32.6% went on to fill an anti-epileptic drug (AED). Path 2 (9.3%) included individuals who had 1 seizure claim, and filled an AED prior to their epilepsy diagnosis. Path 3 (41.8%) was the most common path and included individuals who had 3 or more seizure claims before reaching an epilepsy diagnosis. In total 63.7% of Path 3 filled an AED, with 15.3% of those who filled medication filling this after their epilepsy diagnosis. Path 4 (16.2%) included individuals who had two seizure claims, followed by an epilepsy claim, and 46.7% went on to fill an AED. Finally, Path 5 (2.8%) was the least common, and included individuals who had two seizure claims and filled an AED prescription at some point prior to the diagnosis of epilepsy (Table 1 and Figure 2).

Overall, only 56.0% of individuals diagnosed with epilepsy filled an AED after their first seizure date. There were 1,979 individuals who received an AED after their first seizure and continued to have seizure claims, including 1,401 individuals in Path 3 and 578 individuals in Path 4. For those individuals in Path 3, the path with repeated seizure claims before epilepsy diagnosis, 84.7% of those who filled an AED filled it before their epilepsy diagnosis.

Care pathways differed by race/ethnicity (χ^2 (degrees of freedom: 16) = 28.71, $p = 0.03$). As is observed there were a high proportion of American Indian, Alaskan Native, Asian Pacific Islander, Native Hawaiians, and Other Pacific Islanders (AIAN/API/NHOPI) in Path 3 compared to the other race/ethnicities, while Path 1 included high proportions of White and Black individuals (Figure 4).

The average time from first seizure to epilepsy diagnosis was 19.2 (± 14.8) months, with a median of 19.0 (IQR: 4.6, 30.4) months (Table 1). Significant differences in time were observed between pathways (χ^2 (degrees of freedom: 4) = 2440.2, $p < 0.001$) with all pairwise comparisons significant except between Path 2 and Path 4, Path 2 and Path 5, and Path 4 and Path 5 ($p = 0.85$, $p = 1.00$, $p = 0.45$) (Figure 3). Examining potential racial disparities within paths, it became clear that White individuals were generally more likely to take the longest within a pathway, except in Path 2 (Table 2, Figure 5). The median time

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

from first seizure to second seizure claims ranged from 0.7 months (Path 5) to 4.7 months (Path 4). For path 3, there was a median of 1.4 months (IQR: 0.2 – 5.5) from 2nd to 3rd seizure claims.

There was an average of 2.2 (± 9.1) emergency department visits with a median of 0 (IQR: 0, 2), although this ranged from 2.9 for Path 3 to 1.1 for Path 1 (Table 1). These differences were significant (χ^2 (4) = 1078.8, $p < 0.001$), including all of the pairwise comparisons except between Paths 2 and 4 (p =0.83) Paths 2 and 5 (p = 0.10) and Paths 3 and 5 (p = 1.00).

4. Discussion

Our study found that, in a cohort of over 14,000 Medicaid enrollees with epilepsy, the median time from seizure to epilepsy diagnosis was 19.0 months, 44.0% of people diagnosed with epilepsy are not on an AED within 6-months post diagnosis, and that there are significant racial/ethnic disparities in obtaining appropriate diagnosis with American Indian, Alaskan Native, Asian, Pacific Islander, Native Hawaiians and Other Pacific Islander's (AIAN/API/NHOPI) taking the longest. Further, there appear to be multiple pathways from new-onset seizure to epilepsy diagnosis and care which contrast with the expectation that that individuals with new onset seizures will get timely diagnosis and early treatment.[15] Presently, most algorithms to identify people with epilepsy in large health care data are based around these clinical definitions translating directly to the patient care pathway. However, as this study identified, approximately half of individuals diagnosed with epilepsy are not on AED at least 6-months post-diagnosis, and for those that are prescribed AED, there is wide variation in when treatment is initiated. Notably, once given a diagnosis with an epilepsy code the median time to filling an AED was fairly consistent across paths, yet remained highly variable when filling an AED came before formal diagnosis (Table 1). This further underscores the nuance and complexity of care and pathways that exist between an initial visit for a seizure and eventual epilepsy diagnosis. The variable trajectories of care also suggest that previously published methods of identifying people with epilepsy, many of which required AED as inclusion criterion, may exclude meaningful cohorts of individuals with epilepsy. This exclusion bias may differentially and negatively impact some racial sub-groups.

When examining the time from initial seizure event to epilepsy diagnosis, it becomes immediately clear there are substantial and highly variable time delays (Figure 3). While the average median time was a staggering 20-months, nearly two years, the range between pathways was from just over 7 months to nearly 27 months (Table 2). These time delays coupled with the observed variation in care pathways underscore the complexities that exist in progression from incident seizure to proper epilepsy diagnosis. Qualitative work has demonstrated the importance of a prompt diagnosis for the patient, as it provides patients with relief in knowing there may be hope in managing their condition, and this study confirms that this is, generally, not happening.[16–18] In fact, these delays, which we observed to frequently reach multi-year levels, are likely negatively impacting patients and their wellbeing.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Even though most of the patients studied here had no emergency department visits over follow-up, the number of emergency department visits, a negative health event for people with epilepsy, varied directly with the clinical path and the duration between the initial seizure and the epilepsy diagnosis. Notably, Path 1, the path with the shortest mean time to diagnosis, also had the fewest number of emergency department visits between the first seizure and the first epilepsy diagnosis. Path 3, with the longest mean time to diagnosis had second highest number of visits. This may suggest that a shorter time to the appropriate diagnosis may help reduce the number of emergency department visits before that diagnosis. As there is no clear pattern of the relationship between the length of time from first seizure to treatment initiation and the number of emergency department visits, it is hard to definitively state the effect that utilization of the emergency department plays in the time to treatment initiation, leaving the opportunity for future work to examine patterns of utilization, including non-emergency department events (hospitalization, outpatient visits, etc.).

A critical piece of this study was not just to identify overall pathways between an initial seizure and the time to epilepsy diagnosis but also to examine racial/ethnic disparities in these pathways and timing occurred. A substantial strength of this study is its large sample size and racial/ethnic diversity. This enabled an examination of racial/ethnic subgroups and the identification of a significant relationship between race/ethnicity and pathway (Figure 4). Compared with other race/ethnicities, more AIAN/API/NHOPI were in Path 3 – the path that featured numerous encounters for seizure and the longest time-delays to epilepsy diagnosis (Figure 4).

Furthermore, racial-ethnic groups differed within and across pathways in the time between initial seizure to epilepsy diagnosis (Figure 5, Table 2). What is most interesting is that White patients generally take the longest time within a given pathway, although they were overall more likely to follow the pathway (#1) taking the shortest time (Figure 5, Table 2). However, one exception to this rule occurs among AIAN/API/NHOPI who take the longest time for Path 2 (Figure 5, Table 2). Though these racial/ethnic disparities are not in the anticipated direction, these disparities still reinforce the significant differences among the pathways and the racial-ethnic groups – underscoring the complexity and deviations from an ideal, “one case fits all”, care pathway. Because cultural barriers may influence and delay an individual’s care-seeking behavior, these barriers deserve consideration when examining and intervening to mitigate these results, and would motivate qualitative and mixed-methods work.[19–22] It is important to note, however, that in this study we collapsed a number of racial and ethnic groups due to small sample sizes, and therefore caution should be taken in assuming a homogenous effect across these groups. These cultural factors likely vary, and understanding the nuance between these groups is an important direction for future research.

Racial/ethnic disparities are known in epilepsy care, such as receiving surgery, in epilepsy costs, and possibly in epilepsy prevalence.[23–31] However, this is the first study we know of to clearly demonstrate racial/ethnic disparities in care pathways and the time to diagnosis. This meaningfully contributes to the epilepsy literature by heightening awareness of the need to understand the full-scope of disparities and providing details about the great variation and disparities that exist even in the most basic of situations, in this case care

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

pathways. Future research and policy efforts need to address health disparities with respect to care pathways and clinicians may need to be especially vigilant that individuals from minority groups identified in this analysis get timely and appropriate diagnostic evaluation and treatment.

This study also has limitations. The most important limitation is the variable and flexible diagnosis of epilepsy. While it is clear that an individual who has two or more unprovoked seizures should be diagnosed with epilepsy, we did not use two other criteria within current care guidelines that would permit an epilepsy diagnosis before a second seizure occurs. This flexibility means that our study diagnosis of epilepsy based on ICD-9-CM codes may be incomplete. Furthermore, claims data is limited in its depth of clinical knowledge and data available do not always match what may be the complete clinical picture. For example, because the medication data consist of prescriptions filled but not written, lack of a mention of an AED in the data may not mean that it was not prescribed but rather that the patient did not fill it. Similarly, each identified seizure was a claim or clinical encounter, but may represent a single seizure episode and seizures for which an individual did not seek care are unaccounted for in our analysis. Finally, an important consideration in claims data is the 'recipient indicator' category which indicates the availability of traditional fee-for-service or managed care programs and may serve as a proxy for completeness. However, when we examined differences by the different categories of recipient indicator, our results did not change in any meaningful way, and therefore we did not incorporate any inclusion/exclusion criteria relevant to this variable.

As this study was of Medicaid enrollees, and required individuals to be enrolled in Medicaid before their epilepsy diagnosis meaning there were other qualifying conditions, this study's findings may not be widely representative of the epilepsy population at large. Medicaid eligibility may also vary from state to state. However, this population is representative of the most vulnerable segment of PWE, given the low-income threshold required to enroll in Medicaid, and/or disability status, indicating high disease severity and high burden of multiple and co-occurring chronic physical and psychiatric conditions. As we also required full 60-months enrollment, we excluded individuals who had gaps in coverage, a particularly important population for disparities work. In addition, using a population of individuals who are enrolled on Medicaid will theoretically reduce the influence of the issue of access, at least to some extent, and provides an opportunity to evaluate these delays in individuals who should generally have reduced barriers to care. Other limitations include only having a 6-month follow-up period after epilepsy to capture AED use and only requiring one epilepsy claim. These specific limitations are likely biasing our estimates of AED use, such that we are capturing individuals who may not require medication. Future studies should closely examine how the paths identified, as well as the time delays and associated disparities, compare in other populations and how difference in pathways may reflect disease severity.

5. Conclusion

This study is the first we know of to identify and quantify previously unaccounted for nuances in the pathways to an epilepsy diagnosis as well as overall delays in diagnosis and treatment for people with epilepsy, with a substantial number of individuals taking close to

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

two years for diagnosis. Furthermore, it calls attention to clear racial/ethnic disparities in care pathway and this time to diagnosis. This not only motivates the need for better methodological approaches to study people with epilepsy, but calls attention to these often-lengthy delays that should stimulate reflection and adjustment in clinical practice to ensure that people with epilepsy are properly diagnosed and treated efficiently and appropriately. Reducing this time is critical to improving the quality of life and outcomes for people living with epilepsy, and doing so in an equitable way will work towards eliminating health disparities.

Acknowledgements

The authors would like to acknowledge the CDC for funding this study (Special Interest Project 3 U48 DP005030-05S1). Further, the authors thank the entire Epilepsy Referral Study Team at Case Western Reserve University, Dartmouth Hitchcock Medical Center (DHMC), and the Centers for Disease Control and Prevention (CDC) for their contributions to this project. This includes: Rosemarie Kobau and Matthew Zack from the CDC as well as Morgan Mazanec, Richard Luo, and Samantha Schmidt from DHMC.

Financial Disclosures:

Wyatt P. Bensken has none to report.

Angeline S. Andrew has none to report.

Suparna M. Navale has none to report.

Barbara C. Jobst has received research support from Neuropace, Inc., Eisai Inc., Sunovion Inc. as well as from the National Institutes of Health, the Center for Disease Control, the Diamond Foundation and the National Science Foundation.

Martha Sajatovic has received funding from Nuromate, Otsuka, Alkermes, Janssen, International Society for Bipolar Disorders, Reuter Foundation, Woodruff Foundation, Reinberger Foundation, National Institutes of Health (NIH), Centers for Disease Control and Prevention (CDC), Patient-Centered Outcomes Research Institute (PCORI), served as a consultant for Alkermes, Bracket, Otsuka, Janssen, Neurocrine, Health Analytics, Frontline Medical Communications, and received royalties from Springer Press, Johns Hopkins University Press, Oxford Press, UpToDate.

CME activities: American Physician's Institute, MCM Education, CMEology, Potomac Center for Medical Education, Global Medical Education, Creative Educational Concepts, Psychopharmacology Institute

Siran M. Koroukian is supported by grants from the National Cancer Institute, Case Comprehensive Cancer Center (P30 CA043703); American Cancer Society (RSGI CPHPS-132678); Ohio Medicaid Technical Assistance and Policy Program (MEDTAPP); National Institutes of Health (R15 NR017792, and UH3-DE025487); and by contracts from Cleveland Clinic Foundation, including a subcontract from Celgene Corporation.

Study funded by CDC (Special Interest Project 3 U48 DP005030-05S1)

References

1. Huff JS, Morris DL, Kothari RU, Gibbs MA. Emergency Department Management of Patients with Seizures: A Multicenter Study. Academic Emergency Medicine 2001;8:622–628. [PubMed: 11388937]
2. Hauser WA, Beghi E. First seizure definitions and worldwide incidence and mortality. Epilepsia 2008;49 Suppl 1:8–12.
3. Krumholz A, Wiebe S, Gronseth GS, et al. Evidence-based guideline: Management of an unprovoked first seizure in adults: Report of the Guideline Development Subcommittee of the American Academy of Neurology and the American Epilepsy Society. Neurology 2015;84:1705–1713. [PubMed: 25901057]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

4. Pallin DJ, Goldstein JN, Moussally JS, Pelletier AJ, Green AR, Camargo CA Jr. Seizure visits in US emergency departments: epidemiology and potential disparities in care. Int J Emerg Med 2008;1:97–105. [PubMed: 19384659]
5. Berg AT. Risk of recurrence after a first unprovoked seizure. Epilepsia 2008;49 Suppl 1:13–18.
6. Healthy People 2020: DH-6 Increase the proportion of people with epilepsy and uncontrolled seizures who receive appropriate medical care Revised. Washington, DC: U.S. Department of Health and Human Services, Office of Disease Prevention and Health Promotion.
7. Kalilani L, Faught E, Kim H, et al. Assessment and effect of a gap between new-onset epilepsy diagnosis and treatment in the US. Neurology 2019;92:e2197–e2208. [PubMed: 30971487]
8. Faught E, Helmers S, Thurman D, Kim H, Kalilani L. Patient characteristics and treatment patterns in patients with newly diagnosed epilepsy: A US database analysis. Epilepsy Behav 2018;85:37–44. [PubMed: 29906700]
9. Firkin AL, Marco DJ, Saya S, et al. Mind the gap: Multiple events and lengthy delays before presentation with a “first seizure”. Epilepsia 2015;56:1534–1541. [PubMed: 26332423]
10. Bakaki PM, Koroukian SM, Jackson LW, Albert JM, Kaiboriboon K. Defining incident cases of epilepsy in administrative data. Epilepsy Res 2013;106:273–279. [PubMed: 23791310]
11. Moura LM, Price M, Cole AJ, Hoch DB, Hsu J. Accuracy of claims-based algorithms for epilepsy research: Revealing the unseen performance of claims-based studies. Epilepsia 2017;58:683–691. [PubMed: 28199007]
12. Reid AY, St Germaine-Smith C, Liu M, et al. Development and validation of a case definition for epilepsy for use with administrative health data. Epilepsy Res 2012;102:173–179. [PubMed: 22727659]
13. Thurman DJ, Beghi E, Begley CE, et al. Standards for epidemiologic studies and surveillance of epilepsy. Epilepsia 2011;52:2–26. [PubMed: 21899536]
14. Vossler D, Weingarten M, Gidal B. Current Review in Clinical Science: Summary of Antiepileptic Drugs Available in the United States of America: American Epilepsy Society, 2018.
15. Fisher RS, Acevedo C, Arzimanoglou A, et al. ILAE official report: a practical clinical definition of epilepsy. Epilepsia 2014;55:475–482. [PubMed: 24730690]
16. Miller WR, Buelow JM, Bakas T. Older adults and new-onset epilepsy: experiences with diagnosis. J Neurosci Nurs 2014;46:2–10. [PubMed: 24399162]
17. Pembroke S, Higgins A, Pender N, Elliott N. Becoming comfortable with “my” epilepsy: Strategies that patients use in the journey from diagnosis to acceptance and disclosure. Epilepsy Behav 2017;70:217–223. [PubMed: 28437750]
18. Rawlings GH, Brown I, Stone B, Reuber M. Written accounts of living with epilepsy: A thematic analysis. Epilepsy Behav 2017;72:63–70. [PubMed: 28575769]
19. Musto AE, Rutherford A, Malek D. Addressing Cultural Barriers to Diagnosis and Treatment of Epilepsy in Hispanic Communities. JAMA Neurol 2019;76:137. [PubMed: 30534937]
20. Charyton C, Elliott JO, Lu B, Moore JL. The impact of social support on health related quality of life in persons with epilepsy. Epilepsy Behav 2009;16:640–645. [PubMed: 19854111]
21. Leaffer EB, Jacoby A, Benn E, et al. Associates of stigma in an incident epilepsy population from northern Manhattan, New York City. Epilepsy Behav 2011;21:60–64. [PubMed: 21482485]
22. Rani A, Thomas PT. Parental Knoweldge, Attitude, and Perception about Epilepsy and Sociocultural Barriers to Treatment. J Epilepsy Res 2019;9:65–75. [PubMed: 31482058]
23. Sanchez Fernandez I, Stephen C, Loddenkemper T. Disparities in epilepsy surgery in the United States of America. J Neurol 2017;264:1735–1745. [PubMed: 28702686]
24. Burneo JG, Black L, Knowlton RC, Faught E, Morawetz R, Kuzniecky RI. Racial disparities in the use of surgical treatment for intractable temporal lobe epilepsy. Neurology 2005;64:50–54. [PubMed: 15642903]
25. Kroner BL, Fahimi M, Kenyon A, Thurman DJ, Gaillard WD. Racial and socioeconomic disparities in epilepsy in the District of Columbia. Epilepsy Res 2013;103:279–287. [PubMed: 22858309]
26. Pisu M, Richman J, Szaflarski JP, et al. High health care costs in minority groups of older US Medicare beneficiaries with epilepsy. Epilepsia 2019;60:1462–1471. [PubMed: 31169918]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

27. Kobau R, Zahran H, Grant D, Thurman DJ, Price PH, Zack MM. Prevalence of active epilepsy and health-related quality of life among adults with self-reported epilepsy in California: California Health Interview Survey, 2003. Epilepsia 2007;48:1904–1913. [PubMed: 17565591]

28. Ottman R, Lipton RB, Ettinger AB, et al. Comorbidities of epilepsy: results from the Epilepsy Comorbidities and Health (EPIC) survey. Epilepsia 2011;52:308–315. [PubMed: 21269285]

29. Kobau R, Gilliam F, Thurman DJ. Prevalence of self-reported epilepsy or seizure disorder and its associations with self-reported depression and anxiety: results from the 2004 HealthStyles Survey. Epilepsia 2006;47:1915–1921. [PubMed: 17116032]

30. Kelvin EA, Hesdorffer DC, Bagiella E, et al. Prevalence of self-reported epilepsy in a multiracial and multiethnic community in New York City. Epilepsy Res 2007;77:141–150. [PubMed: 18023147]

31. Burneo JG, Jette N, Theodore W, et al. Disparities in epilepsy: report of a systematic review by the North American Commission of the International League Against Epilepsy. Epilepsia 2009;50:2285–2295. [PubMed: 19732134]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Highlights

- There are previously unaccounted for variations in care pathways for people with epilepsy
- There could be substantial amounts of time between seizure and epilepsy diagnosis
- These pathways and delays are not uniform between racial/ethnic groups, indicating potential disparities in diagnosis and treatment
- Methodologies to identify PWE in health care data may need to be adapted to better represent these real-world care patterns

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

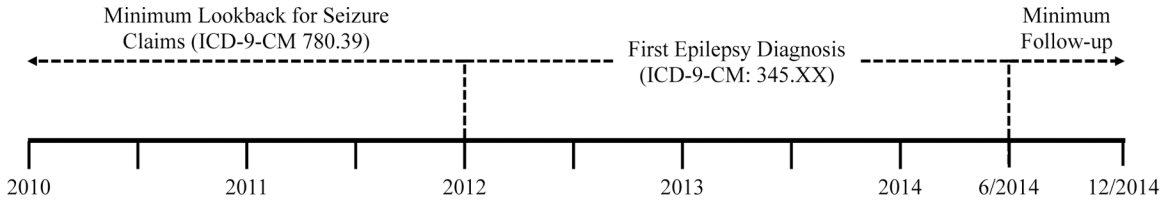

Figure 1.

Timeline showing the timeframe in which first epilepsy diagnosis was identified, as well as the minimum lookback and follow-up periods. The minimum lookback time for seizure demonstrates that at the minimum we would have 2-years of epilepsy-free claims leading up to the epilepsy diagnosis, for a person whose first epilepsy claim were to be on January 1, 2012. Most individuals had more than just the 2-year minimum. Seizure claims were identified at any time point up to their first epilepsy diagnosis date (not restricted to 2-years).

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

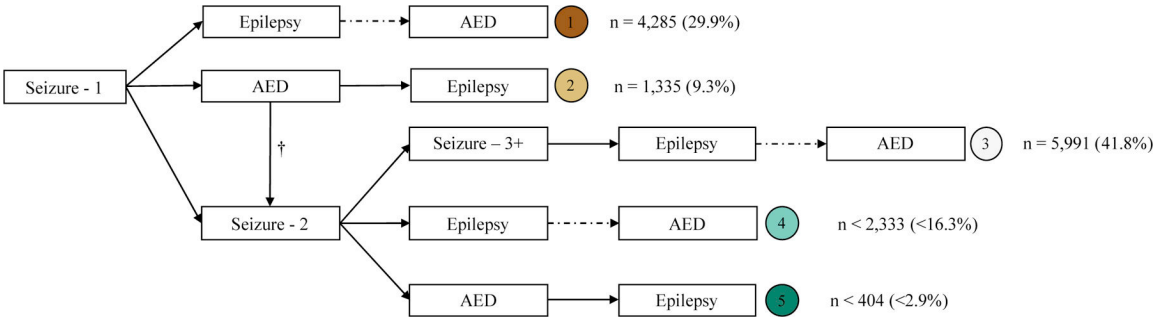

Figure 2.

The 5 care pathways that emerged in the analysis. The dashed lines represent that only a portion of individuals will go from epilepsy diagnosis to treatment (see Table 1). †There were 1,979 individuals who received an AED after their first seizure and continued to have seizure claims (1,401 individuals in Path 3 and 578 individuals in Path 4).

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

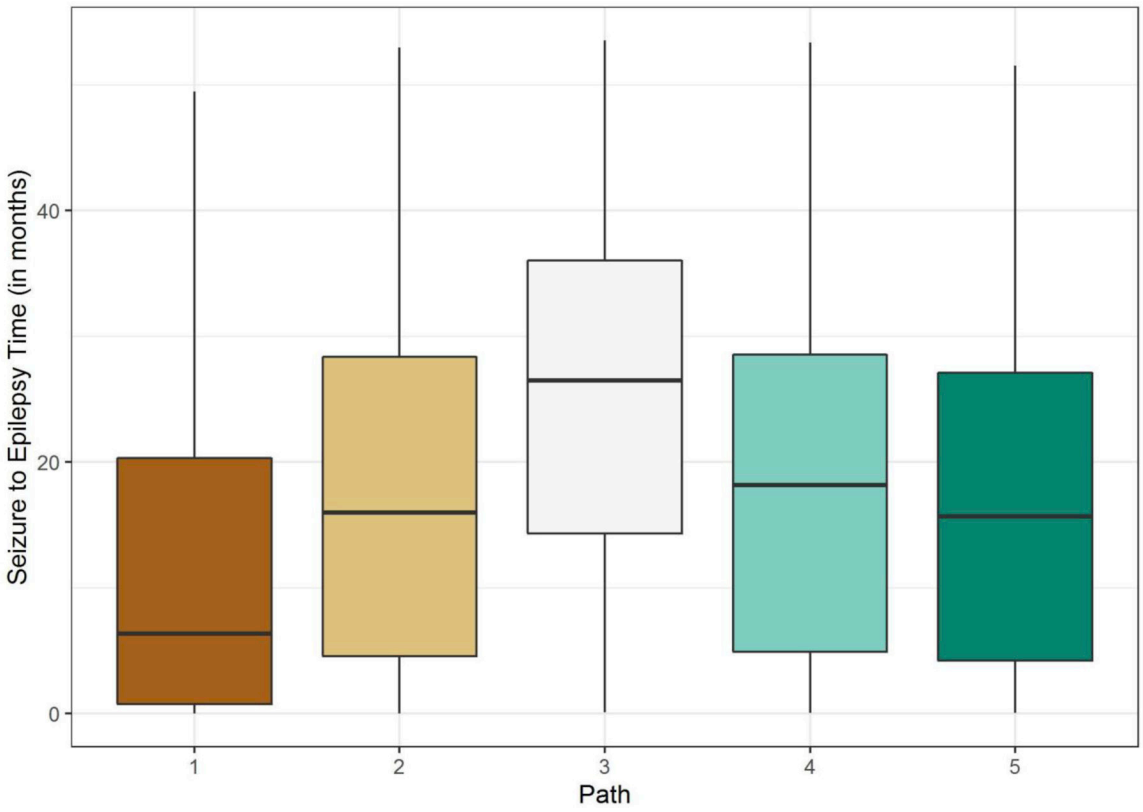

Figure 3.

Time (median, interquartile range, and range) from seizure to epilepsy diagnosis (in months) by pathway, as shown in Figure 1, demonstrating the substantial delays between seizure and epilepsy diagnosis as well as significant difference between pathways. There are significant differences both globally ($p < 0.001$), as well as between all pairwise comparisons except between Path 2 and Path 4, Path 2 and Path 5, and Path 4 and Path 5 ($p = 0.85$, $p = 1.00$, $p = 0.45$, respectively). Note: outliers have been visually removed in order to comply with data protection requirements under the Data Users Agreement.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

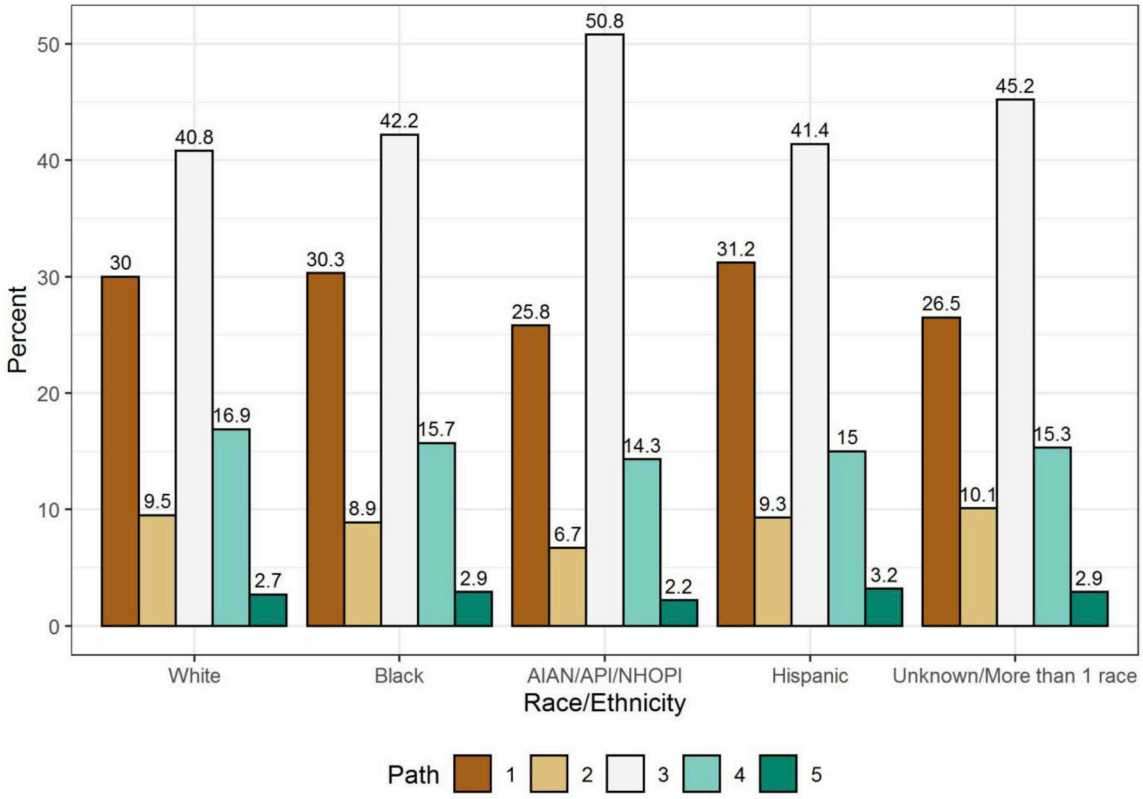

Figure 4.

Proportion of pathway within race/ethnicity groups, demonstrating the disproportionate number of American Indian, Alaskan Native, Asian, Pacific Islander, Native Hawaiians and Other Pacific Islander (AIAN/API/NHOPI) who fall into Path 3, the path with the longest time between seizure and epilepsy, compared to the other races.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

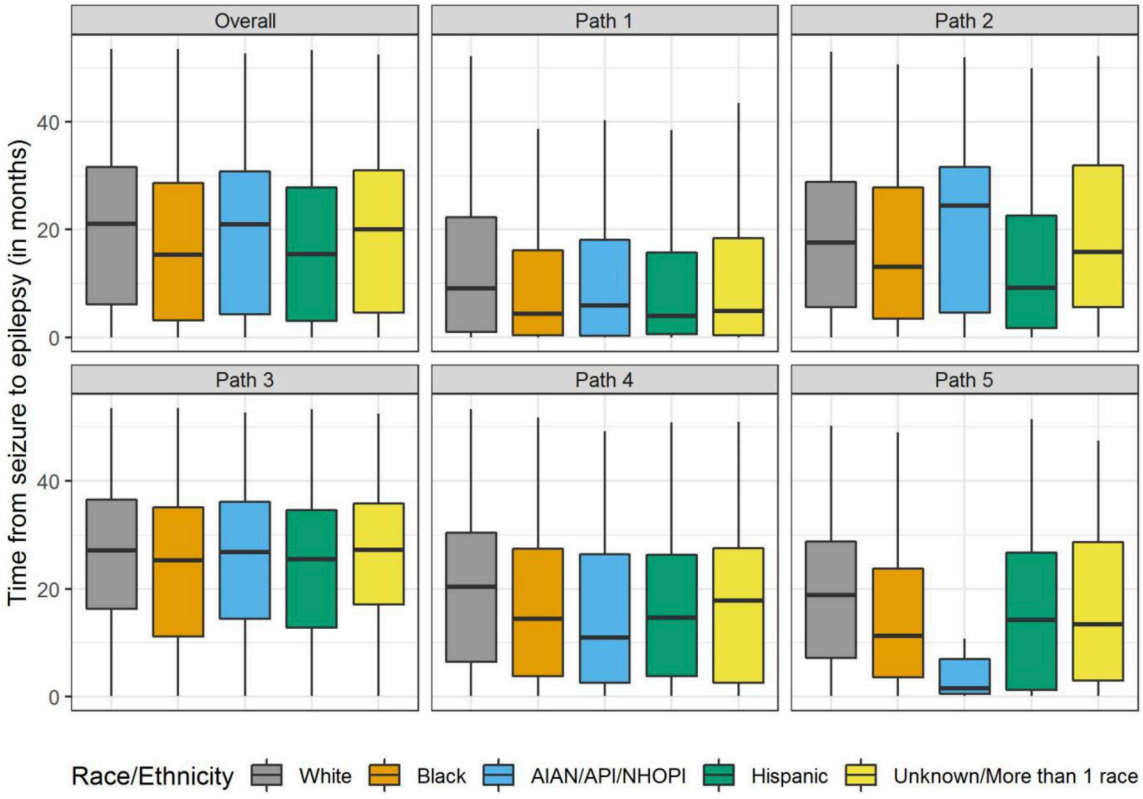

Figure 5.

Time (median, interquartile range, and range) from seizure to epilepsy (in months), by path and race/ethnicity. The upper left panel represents the overall values, and the others are stratified first by path and then by race/ethnicity. This figure demonstrates the highly variable time from seizure to epilepsy diagnosis across paths and race/ethnicity. Note: outliers have been visually removed in order to comply with data protection requirements under the Data Users Agreement.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Table 1.

Demographic data on the entire cohort (Total) as well as stratified by pathway.

	Total n = 14,337	**Path 1 n = 4,285 (29.9)**	**Path 2 n = 1,335 (9.3)**	**Path 3 n = 5,991 (41.8)**	**Path 4 n = 2,323 (16.2)**	**Path 5 n = 403 (2.8)**
Race/Ethnicity n (%)						
White	7,804 (54.4)	2,343 (54.7)	745 (55.8)	3,186 (53.2)	1,317 (56.7)	213 (52.9)
Black	3,968 (27.7)	1,203 (28.1)	354 (26.5)	1,676 (28.0)	621 (26.7)	114 (28.3)
AIAN/API/NHOPI	356 (2.5)	92 (2.1)	24 (1.8)	181 (3.0)	51 (2.2)	< 11 (< 2.7)
Hispanic	1,315 (9.2)	410 (9.6)	122 (9.1)	544 (9.1)	197 (8.5)	> 40 (> 9.9)
Unknown/More than 1 race	894 (6.2)	237 (5.5)	90 (6.7)	404 (6.7)	137 (5.9)	26 (6.5)
Sex n (%)						
Male	6,970 (48.6)	2,130 (49.7)	586 (43.9)	2,900 (48.4)	1,176 (50.6)	178 (44.2)
Age (at epilepsy)						
Mean (SD)	44.0 (13.3)	43.8 (13.3)	42.1 (13.5)	44.9 (13.1)	43.8 (13.2)	41.6 (14.2)
Time from 1st seizure to epilepsy						
Mean (SD)	19.2 (14.8)	11.5 (12.6)	17.8 (14.1)	25.4 (14.0)	18.7 (14.3)	17.1 (13.5)
Median [IQR]	19.0 [4.6 – 30.4]	6.4 [0.8 – 20.3]	16.0 [4.6 – 28.4]	26.5 [14.3 – 36.0]	18.2 [4.9 – 28.5]	15.7 [4.2 – 27.1]
Time from 1st seizure to 2nd seizure						
Mean (SD)	---	---	---	4.2 (6.3)	8.8 (10.2)	3.6 (5.8)
Median (IQR)	---	---	---	1.4 [0.2 – 5.8]	4.7 [0.6 – 13.3]	0.7 [0.03 – 5.2]
Time from 1st seizure to AED‡						
Mean (SD)	---	---	5.3 (7.7)	5.0 (7.8)	3.2 (5.7)	7.8 (8.6)
Median (IQR)	---	---	1.4 [0.1 – 7.6]	1.0 [0.1 – 6.8]	0.5 [0.0 – 3.3]	5.1 [0.4 – 13.0]
Time from epilepsy to AED‡						
Mean (SD)	---	4.8 (6.2)	---	4.7 (6.1)	4.5 (6.3)	---
Median (IQR)	---	1.8 [0.1 – 7.9]	---	2.0 [0.2 – 7.2]	1.4 [0.2 – 6.4]	---
Number of Emergency Department visits						
Mean (SD)	2.2 (9.1)	1.1 (11.2)	2.8 (10.1)	2.9 (7.7)	2.2 (7.7)	2.5 (5.5)
Median [IQR]	0 [0 – 2]	0 [0 – 0]	0 [0 – 2]	1 [0 – 3]	0 [0 – 2]	1 [0 – 2]
Anti-Epileptic Drug (AED); n (%)	8,033 (56.0)	1,395 (32.6)	1,335 (100)	3,815 (63.7)†	1,085 (46.7)†	403 (100)

Time is reported in months.

*The pathway required they be on an AED before epilepsy, therefore all individuals were on an AED.

†This value represents overall treatment. Path 3: 1,401 individuals received an AED between first and second seizures, 1,830 after their second seizure but before epilepsy diagnosis, and 584 after epilepsy diagnosis. Path 4: 578 of these individuals received an AED prior to their second seizure, 507 filled their first AED after their epilepsy diagnosis. AIAN/API/NHOPI: American Indian, Alaskan Native, Asian, Pacific Islander, Native Hawaiians and Other Pacific Islander. For Path 5, < the value is reported due to the need to mask small cell size.

[‡]The time to AED has been stratified for Paths 3 and 4, so the time from seizure to AED includes only those individuals who filled an AED before epilepsy diagnosis, and the time from epilepsy to AED includes only those individuals who filled an AED after epilepsy diagnosis.

Author Manuscript
Author Manuscript
Author Manuscript
Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 2.

Path- and race/ethnicity-stratified size, median, and interquartile range for time from seizure to epilepsy diagnosis.

		White	Black	AIAN/API/NHOPI	Hispanic	Unknown/More than 1 race
Path 1	n	2,343	1,203	92	410	237
	Median [IQR]	9.2 [1.0 – 22.3]	4.4 [0.4 – 16.1]	5.8 [0.3 – 18.2]	4.0 [0.6 – 15.8]	4.9 [0.4 – 18.5]
Path 2	n	745	354	24	122	90
	Median [IQR]	17.6 [5.6 – 28.9]	13.1 [3.5 – 27.8]	24.5 [4.6 – 31.6]	9.3 [1.8 – 22.6]	15.9 [5.6 – 31.9]
Path 3	n	3,186	1,676	181	544	404
	Median [IQR]	27.1 [16.3 – 36.6]	25.3 [11.2 – 35.1]	26.9 [14.5 – 36.1]	25.5 [12.8 – 34.6]	27.3 [17.1 – 35.8]
Path 4	n	1,317	621	51	197	137
	Median [IQR]	20.4 [6.5 – 30.4]	14.4 [3.8 – 27.4]	11.0 [2.5 – 26.4]	14.7 [3.8 – 26.4]	17.8 [2.5 – 27.5]
Path 5	n	213	114	< 11	> 40	26
	Median [IQR]	18.8 [7.2 – 28.8]	11.2 [3.6 – 23.7]	1.5 [0.5 – 7.0]	14.2 [1.2 – 26.7]	13.5 [3.0 – 28.6]

Note: AIAN/API/NHOPI: American Indian, Alaskan Native, Asian, Pacific Islander, Native Hawaiians and Other Pacific Islander