HHS Public Access

Author manuscript

Epilepsia. Author manuscript; available in PMC 2024 August 10.

Published in final edited form as:

Epilepsia. 2024 August ; 65(8): 2341–2353. doi:10.1111/epi.18029.

Population-Based Study of Rare Epilepsy Incidence in a US Urban Population

Kristen Barbour, MD[1], **Niu Tian, MD, PhD**[2], **Elissa G. Yozawitz, MD**[3], **Steven Wolf, MD**[4,5], **Patricia E. McGoldrick, NP, MPA, MSN**[4,5], **Tristan T. Sands, MD, PhD**[6], **Aaron Nelson, MD**[7], **Natasha Basma, MPH**[8], **Zachary M. Grinspan, MD, MS**[8]

[1]University of California San Diego, San Diego, CA;

[2]Centers for Disease Control and Prevention, Atlanta, GA;

[3]Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, NY;

[4]Boston Children's Health Physicians, Hawthorne, NY;

[5]New York Medical College, Valhalla, NY;

[6]Columbia University Irving Medical Center, New York, NY;

[7]New York University Langone Medical Center, New York, NY;

[8]Weill Cornell Medicine, New York, NY

Abstract

Objective.—This study was undertaken to estimate incidence of rare epilepsies and compare with literature.

Methods.—We used electronic health record text search to identify children with 28 rare epilepsies in New York City (2010–2014). We estimated cumulative incidence and compared with literature.

Results.—Eight of 28 rare epilepsies had 5 or more prior estimates, and our measurements were within the published range for all. The most common were infantile spasms syndrome (1 in 2,920 live births), Lennox-Gastaut syndrome (1 in 9,690), and seizures associated with tuberous sclerosis complex (1 in 14,300). Sixteen of 28 had fewer than 5 prior estimates, and of these, we provided additional estimates for early infantile developmental and epileptic encephalopathy (1 in 32,700), epilepsy with myoclonic atonic seizures (1 in 34,100), Sturge-Weber syndrome plus seizures/epilepsy (1 in 40,900), epilepsy in infancy with migrating focal seizures (1 in 54,500), Aicardi syndrome plus seizures/epilepsy (1 in 71,600), hypothalamic hamartoma with seizures (1

Corresponding author: Zachary Grinspan, MD, MS, 402 East 67th Street Room LA 220, New York, NY 10065, zag9005@med.cornell.edu, Fax: 917-210-3261.

Author contributions. ZG conceptualized the idea and supervised the project. ZG collected data with assistance from EY, SW, PM, TS, and AN. Authors KB, NB, and ZG analyzed data. KB and ZG wrote the manuscript. All authors (KB, NT, EY, SW, PM, TS, AN, NB and ZG) provided critical review, commentary, and/or revision of writing.

Disclaimer. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention, of the US Department of Health and Human Services, or of the US Government.

Ethical Publication Statement. 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.

in 225,000), and Rasmussen syndrome (1 in 450,000). Five of 28 had no prior estimates, and of these, we provided a new estimate for developmental/epileptic encephalopathy with spike-and-wave activation in sleep and/or continuous spikes and waves during sleep (1 in 34,100). Data was limited for the remaining 12 rare epilepsies that were all genetic epilepsies, including PCDH19, CDKL5, Alpers disease, SCN8A, KCNQ2, SCN2A, GLUT1 deficiency, Phelan-McDermid syndrome, MERRF, dup15q syndrome, ring chromosome 14, and ring chromosome 20.

Significance.—We estimated the incidence of rare epilepsies using population-based EHR data and literature review. More research is needed to better estimate the incidence of genetic epilepsies with nonspecific clinical features. Electronic health records may be a valuable data source for studying rare epilepsies and other rare diseases, particularly as genetic testing becomes more widely adopted.

Keywords

early infantile developmental and epileptic encephalopathy; Sturge-Weber syndrome; epilepsy with myoclonic atonic seizures; Rasmussen syndrome; epilepsy in infancy with migrating focal seizures

INTRODUCTION

The economic, emotional, and physical burden of rare epilepsies is lifelong with profound morbidity and mortality.[1] There are reliable epidemiologic estimates for a minority of these diseases. However, for some rare epilepsies, published incidences are based on informal estimates and not direct measurements, for example for Sturge-Weber syndrome.[2, 3] And for others, such as ring chromosome 20, estimates are limited to counts of individual cases.

From a public health standpoint, the epidemiologic study of rare epilepsies potentially provides value in several areas. Epidemiology research can address critical surveillance gaps for rare disorders, including rare epilepsies. Improved population-based data helps to characterize the morbidity and mortality profile. Data allow for studying and addressing health care disparities among people with epilepsy from lower socioeconomic groups and among underrepresented minorities. Funding agencies can use research to leverage limited resources by prioritizing disorders with a significant burden of disease and to guide policy making. Industry uses data to understand the business case for development of pharmaceuticals and medical devices. Accurate incidence measures help clinicians prioritize testing when evaluating new patients.

Electronic health records (EHRs) represent a potentially valuable source of information about the epidemiology of rare epilepsies. While there are gaps in administrative codes (eg, International Classification of Diseases [ICD] codes) for epilepsy related conditions,[4] natural language processing can be an effective tool to identify children with rare epilepsies via text analysis of clinical notes.[5] The objectives of this study were to: (1) provide incidence estimates for 28 rare epilepsies in children aged 0–14 years using EHR data from 6 large health care systems in New York City (NYC) from 2010 to 2014; and (2) compare our incidences to prior estimates for each rare epilepsy by conducting a literature review.

METHODS

EHR-Based Epidemiologic Estimates

Disease population of interest.—We studied 28 rare epilepsies that were previously reported by investigators (Table S1).[4] Diagnoses were made by their treating clinicians, and we extracted diagnoses by reviewing clinical text in EHRs. Some individuals were counted in multiple rare epilepsy groups, eg, diagnosis of both ISS and tuberous sclerosis complex (TSC).

Most clinical text had diagnoses clearly documented. There were 2 exceptions. First, some patients were noted as having continuous spikes and waves during sleep (CSWS) without additional clinical information to rule in or rule out a diagnosis of developmental/epileptic encephalopathy with spike-and-wave activation in sleep (D/EE-SWAS). Therefore, we used a combined group that included D/EE-SWAS and/or CSWS. Second, we encountered vague clinical text when coding Lennox-Gastaut syndrome (LGS) and therefore made a diagnosis when individuals had (1) multiple seizure types that were characteristic of LGS, (2) developmental delay or intellectual disability, and (3) slow spike and waves ≤ 2.5 Hz on EEG reports. The ILAE classification of LGS requires the presence of tonic seizures.[6] However, we did not require tonic seizures, since this would exclude children who develop tonic seizures later in diagnosis[7] and those with tonic seizures not documented in clinical notes,[8] and to maintain consistency with prior epidemiologic estimates that did not require tonic seizures.[9–11]

Epidemiologic context.—The at risk population in 2010 was estimated to be 40,904 annual live births in Bronx/Manhattan (48.65% females), and this number was used for all birth years.

Ascertainment and confirmation of cases.—We ascertained cases using EHR data from 6 health care systems in NYC: Weill Cornell Medicine (WCM), Columbia University Medical Center (CUMC), Mount Sinai Health System (MSHS), Continuum Hospitals (now merged with MSHS), Montefiore Medical Center (MMC), and New York University Langone Medical Center (NYU). The study was approved by institutional review boards (IRB) at WCM, CUMC, MSHS, MMC, and NYU, facilitated by a central IRB (Biomedical Research Alliance of New York). Each medical center queried inpatient, outpatient, and electroencephalography (EEG) encounters for pediatric and adult patients with seizures/epilepsy (ICD-9 345.x) or convulsions (ICD-9 780.39) from 2010 to 2014 and stored data in the Rare Epilepsies in New York City (RENYC) database. Patients with diverse racial and ethnic backgrounds (15% Black, 8% Hispanic, 41% White, and 44% other) were included.[12]

EHR data was designed to approximate a population-based estimate for 2 boroughs in New York City (Bronx County and New York County/Manhattan) for the following reasons. We expected children with new onset seizures to be seen through at least 1 encounter within the 6 large healthcare systems in NYC, either during an outpatient visit, emergency room visit, inpatient admission, or EEG recording. Data would not have included pediatricians or clinicians outside the healthcare systems. However, in NYC, childhood onset rare epilepsies

were referred to pediatric neurology and nearly all pediatric neurologists (and all EEG facilities) were affiliated with these healthcare systems.

In more detail – nearly all Bronx-based pediatric neurologists were affiliated with the medical centers in the study, including physicians from MMC (which includes MMC, Children's Hospital at Montefiore, and Weiler Hospital) and MSHS (which includes MSHS and Lincoln Hospital). Two institutions providing outpatient pediatric neurology services (BronxCare Hospital and Jacobi Medical Center) were not affiliated with the medical centers in the study. However, BronxCare and Jacobi Medical Center physicians referred children to Children's Hospital at Montefiore for EEG, and our data captured these EEG encounters. Since video EEG is a key component of management for epilepsies, we expected to find these patients through MMC's medical record system. All Manhattan-based pediatric neurologists during the study period were affiliated with the medical centers in our consortium, including those who see patients at the public city hospitals (Harlem Hospital – CUMC, Bellevue Hospital – NYU, Metropolitan Hospital – MSHS).

Rare epilepsy cases were ascertained by searching text of clinical notes for terms associated with rare epilepsies and validated using manual chart review.[5] We recorded name, date of birth, and zip code. We combined records for individuals with the same name and date of birth (removed duplicates). We selected individuals from Bronx and Manhattan zip codes.

Estimating cumulative incidence.—We estimated cumulative incidence by calculating the average number of cases in Bronx/Manhattan per birth year divided by annual live births. Birth years corresponded to when we expected diagnosis and follow up (Table 1). For example, we included individuals aged 0–3 years with infantile spasms syndrome (ISS) using dates of birth during 2011–2013. Among the rare epilepsies, we included ages up to a maximum of 14 years because we expected diagnoses by this age and to remain consistent with prior rare epilepsy epidemiologic estimates.[9, 13, 14] We estimated 95% confidence intervals using standard error = 1/square root(numerator count).

Literature Review

Inclusion criteria.—We conducted a literature review of studies estimating the incidence of 28 rare epilepsies. We searched for articles in PubMed and Google using (1) "incidence" *and* disease name, (2) "prevalence" *and* disease name, and (3) "epidemiology" *and* disease name. We used synonyms of disease names when appropriate (Table S2). We supplemented this search by reviewing in-text citations. Articles that measured incidence and cumulative incidence were included. Cumulative incidence represents the accumulated risk by a certain age. Cumulative incidence is comparable to childhood prevalence if certain epidemiologic factors are present: similar age ranges are used for estimates, the diagnosis is expected within this time, the disease is not expected to resolve during this time, and there is low mortality during this time. For this reason, we included childhood prevalence data when measured within an appropriate age range in childhood. We included estimates of childhood prevalence data measured in children aged <3 years for early infantile developmental epileptic encephalopathy (EIDEE, previously called Ohtahara syndrome and early myoclonic encephalopathy), epilepsy in infancy with migrating focal

seizures (EIMFS), KCNQ2 plus seizures/epilepsy, and GLUT1 deficiency. We only included incidence data and not childhood prevalence for ISS because there were multiple prior incidence estimates (16 studies). We excluded prevalence estimates in adults ages >18 years. We excluded geographic disease clusters (regions with a higher disease incidence). We excluded articles that did not describe methods.

Prior literature estimates of incidence.—We reported prior literature incidences, adjusted prior literature incidences (disease plus seizures), and range of adjusted prior literature incidences. When 5 or more studies were available for a rare epilepsy, we noted if our EHR-based estimate of cumulative incidence was within the range of prior literature incidences.

Seizures are not a universal feature of all rare epilepsies. Therefore, we adjusted published estimates to reflect individuals with the rare epilepsy and presence of seizures/epilepsy. For example, if a study measured the incidence of TSC to be 1 in 6,000, we assumed 85% had seizures and used an adjusted incidence of 1 in 7,058 live births ([1/6,000] x 0.85). We assumed seizures were associated with 85% of individuals with TSC,[15–17] 70% with Rett syndrome,[18, 19] 85% with Angelman syndrome,[20] 85% with Sturge-Weber syndrome,[21, 22] 92% with Aicardi syndrome,[23] and 25% with Prader-Willi syndrome.[24] Two studies estimating disease incidence provided the occurrence of seizures in their cohort, and we used these numbers – 84% in an SCN2A cohort[25] and 95% for SCN8A.[26]

We re-calculated epidemiologic estimates using raw study data to help with labeling the numerators/denominators used in calculations, and to standardize terminology describing epidemiologic estimates.[27] We used the term “cumulative incidence” for studies that calculated the number of cases divided by number of study years (numerator) divided by annual live births (denominator). We used the term “prevalence” for studies that calculated the number of cases (numerator) divided by the total population in age group (denominator). We used the term “incidence” for studies that calculated the number of new cases divided by number of study years (numerator) divided by annual live births (denominator). “Annual live births” is equivalent to number of live births per birth year.

Methodological characteristic of selected studies.—We documented the number of cases, study years, country, data source, and age criteria. We noted data sources, including “clinical data” (eg, EHR data), physician or family “surveys,” “other” data sources (eg, genetic labs, family support groups, education/rehab facilities, prospective study, registry, claims database), “multiple data sources,” and “unknown/unspecified” data source. We noted if diagnostic criteria were “described” (in text), “referenced” (cited another study), “none” (eg, used clinician or family’s diagnosis), or “unknown/unspecified.” We reported if studies had a process for removing duplicates, and coded as “yes,” “unknown/unspecified,” or “single data source” (ie, data from 1 hospital and therefore less likely to have duplicates). We reported when studies corrected for under-ascertainment.

RESULTS

EHR-Based Epidemiologic Estimates

Ascertainment and confirmation of cases.—Data included clinical text from 77,924 individuals with administrative codes for seizures, epilepsy, and/or convulsions in the RENYC database, of which 2,068 (2.7%) had a rare epilepsy.[5] To estimate cumulative incidence in the childhood period, we included 167 individuals born within the specified date of birth ranges and living in the appropriate zip codes for the Bronx (94/167, 56%) and Manhattan (73/167, 44%).

Estimating cumulative incidence.—We identified cases for 20 of 28 rare epilepsies and estimated cumulative incidence (Table 1). The cumulative incidences were: ISS (1 in 2,920 live births), LGS (1 in 9,690), seizures/epilepsy associated with TSC (1 in 14,300), seizures/epilepsy associated with Rett syndrome (1 in 27,900 females), Dravet syndrome (1 in 31,800), EIDEE (1 in 32,700), D/EE-SWAS and/or CSWS (1 in 34,100), EMAS (1 in 34,100), seizures/epilepsy associated with Angelman syndrome (1 in 40,900), seizures/epilepsy associated with Sturge-Weber syndrome (1 in 40,900), neuronal ceroid lipofuscinosis (NCL, 1 in 47,700), EIMFS (1 in 54,500), seizures/epilepsy associated with Aicardi syndrome (1 in 71,600), seizures/epilepsy associated with Prader-Willi syndrome (1 in 71,600), hypothalamic hamartoma with seizures (1 in 225,000), and Rasmussen syndrome (1 in 450,000).

We underestimated the incidence of rare genetic epilepsies with nonspecific clinical features since genetic testing was not widely adopted during our study period (2010–2014). Therefore, our estimates of rare genetic epilepsies represent minimum estimates, including for seizures/epilepsy associated with KCNQ2 (1 in 81,800), GLUT1 deficiency (1 in 164,000), seizures/epilepsy associated with Phelan-McDermid syndrome (1 in 286,000), and dup15q syndrome (1 in 450,000). We identified no cases for PCDH19, CDKL5, Alpers disease, SCN8A, SCN2A, myoclonic epilepsy with ragged-red fibers, ring chromosome 14, and ring chromosome 20.

Literature Review

Prior literature incidence.—We identified 103 incidence estimates from 83 previous studies (Table 2; Figure 1). Eight of the 28 rare epilepsies had 5 or more studies available and our estimates were within prior literature ranges for all, including for ISS (prior literature range = 1 in 1,500–4,850 live births vs current study = 1 in 2,920 live births), LGS (3,570–50,100 vs 9,690), seizures/epilepsy associated with TSC (5,010–28,300 vs 14,300), seizures/epilepsy associated with Rett syndrome (6,800–65,000 females vs 27,900), Dravet syndrome (15,400–40,900 vs 31,800), seizures/epilepsy associated with Angelman syndrome (11,800–61,400 vs 40,900), NCL (25,600–179,000 vs 47,700), and seizures/epilepsy associated with Prader-Willi syndrome (40,000–122,000 vs 71,600).

Sixteen of 28 epilepsies had fewer than 5 prior estimates, of which, we provided new estimates for EIDEE, EMAS, seizures/epilepsy associated with Aicardi syndrome, Sturge-Weber syndrome, EIMFS, hypothalamic hamartoma with seizures, and Rasmussen

syndrome. Five of 28 epilepsies had no prior estimates, of which, we provided a new estimate for D/EE-SWAS and/or CSWS. More research is needed to provide incidence estimates for rare genetic epilepsies, including PCDH19, CDKL5, Alpers disease, SCN8A, KCNQ2, SCN2A, GLUT1 deficiency, Phelan-McDermid syndrome, MERRF, dup15q syndrome, ring chromosome 14, and ring chromosome 20. Two excluded studies were conducted in regions known to have a higher incidence than the general population (disease cluster).[28, 29]

Prior literature calculations.—Methodological characteristics of prior literature are described in Figure 2 and Table S2. Seventy-eight of 83 studies described their epidemiologic calculation (Table S2). Five different calculations were used across 78 studies, and we described these using standardized terminology (Table 3). For standardization purposes, we revised cumulative incidence estimates for 3 studies. Two of these used a nonstandard calculation – number of new cases divided by number of study years (numerator) divided by total population in age group (denominator).[30, 31] This calculation annualizes the numerator but not the denominator, which makes the estimate appear smaller than other prior studies. One study used Kaplan-Meier estimation to correct for possible under-ascertainment[32] and we reported their unadjusted cumulative incidences. Our unadjusted estimates were similar to their adjusted, with 1 exception, LGS was more common in their study (1 in 7,600) than our calculation (1 in 26,100).

DISCUSSION

Estimates of Cumulative Incidence

Summary of findings.—We used clinical data from 6 large health care systems in NYC and literature review to study the incidence of 28 rare epilepsies. Eight of 28 rare epilepsies had at least 5 previously published incidence estimates, and our results were within the range of prior estimates for all, strengthening confidence in our methods. We provided new estimates of cumulative incidence for 8 rare epilepsies that had limited prior data. More research is needed to estimate the incidence of rare genetic epilepsies.

Epilepsies with limited prior estimates.—There were only 1 or 2 prior estimates for 12 of 28 rare epilepsies. Of which we provided new estimates for four – Sturge-Weber syndrome, EIMFS, seizures/epilepsy associated with hypothalamic hamartoma, and Rasmussen syndrome. For Sturge-Weber syndrome, 1 study found an incidence of 1 in 23,600,[31] compared to 1 in 40,900 in current study. For EIMFS, 1 study found an incidence of 1 in 22,200,[33] and another found 1 in 247,000.[34] Our study estimated 1 in 54,500, closer to the higher estimate. For hypothalamic hamartoma, 1 study found an incidence of 1 in 52,200,[32] and another 1 in 200,000.[35] Our study estimated 1 in 225,000, closer to the lower estimate. For Rasmussen syndrome, 1 study estimated 1 in 652,000,[30] compared to 1 in 450,000 in current study.

There were only 3 or 4 prior estimates for 3 of 28 rare epilepsies and we provided new estimates for these (ie, EIDEE, EMAS, and seizures/epilepsy associated with Aicardi syndrome). Prior incidence estimates for EIDEE were inconsistent with some studies suggesting 1 in 9,970[32] and 1 in 27,800,[33] while another 2 found 1 in 100,000.[36, 37] Our

estimate (1 in 32,700 live births) was closer to the more common estimates. Incidence estimates for EMAS ranged from 1 in 7,450 to 50,000[32, 37, 38] and we estimated 1 in 34,100. Prior incidence estimates for seizures/epilepsy associated with Aicardi syndrome ranged from 1 in 54,300 to 1 in 172,000[39–42] and we estimated 1 in 71,600 – closer to the more common estimate.

Epilepsies with no prior estimates.—Five of 28 rare epilepsies had no prior estimates published, and within this group, we provided a new estimate of cumulative incidence for D/EE-SWAS and/or CSWS (1 in 34,100 live births).

Rare genetic epilepsies.—We observed the greatest need for data estimating the incidence of rare genetic epilepsies. Almost all the rare genetic epilepsies with nonspecific clinical features had only 1, or no, prior incidence estimates. The best data was a study by Symonds et al. who offered universal genetic testing for all children with early life epilepsy (age < 3 years).[38] As genetic testing becomes more widely used clinically, there are opportunities for future research to update epidemiologic estimates using EHR data.

Limitations

Limitations in EHR-Based Epidemiologic Estimates.—This study has several limitations. First, genetic testing was not widely adopted during our study period (2010–2014), and therefore, we underestimate the incidence of some genetic epilepsies. A second limitation is that we found no or few cases for several rare epilepsies, which could be attributed to the disease having an ultra-rare occurrence, under-ascertainment with our study methods for a specific disease (eg, insufficient keywords in text search), or clinical underdiagnosis in our study population (eg, genetic epilepsies). A third limitation is that our healthcare systems-based data may not have accurately estimated cases. There may have been an influx/efflux of individuals moving to or from a region after a rare epilepsy diagnosis (eg, to seek medical specialists or community services in the region). Or, individuals may have been referred to pediatric neurology and EEG but never established care, or received subspecialist care outside NYC, and therefore missing from our data. Lastly, some may have died prior to receiving a rare epilepsy diagnosis.

Limitations in prior rare epilepsy epidemiology literature.—Our review revealed limitations in prior literature that can be addressed in future research. One important limitation is that a sizable minority of rare epilepsy studies (41%) relied on 10 or fewer cases for their epidemiologic estimate, and some were from the 1970s. Only 31% of prior studies relied on multiple data sources, and many used clinical data alone (36%) or surveys alone (17%). Third, we were surprised to find that most studies (81%) did not specify if they removed duplicate cases, and duplicates could result in overestimating incidence. There is a need for new data sources to study rare epilepsies.

Lastly, we were prompted to review the underlying calculations of prior epidemiologic estimates after observing differences between studies. In doing so we found another limitation: in studies measuring cumulative incidence, nearly half called this “incidence” when it would have been better characterized as “cumulative incidence” since it captured the

risk of total cases in an age group, not only new cases. Further, we found that only two thirds of prior studies used our standardized terminology to describe calculations.

Public Health Significance

Although rare diseases collectively account for 26% of cases of severe disabilities in children,[43] their rare occurrence individually makes it difficult to create adequate data sources for research.[44] The majority of rare epilepsies had limited prior epidemiologic data, particularly for the genetic epilepsies. Our findings help fill surveillance gaps, provide references to identify the clinically important rare epilepsies, and help with the decision about genetic testing during the diagnosis process.

Furthermore, we demonstrated the utility of using text analysis of clinical notes to create new data sources for studying rare diseases. New or underutilized existing data sources can be used to conduct surveillance for other newly discovered rare epilepsies and can be used to study and address the racial and economic disparities observed in the diagnosis, management, and outcomes of people with epilepsy.[45, 46]

Conclusion.

We estimated the cumulative incidence of 28 rare epilepsies using EHR data and literature review, the most common being ISS, LGS, and seizures/epilepsy associated with TSC. Among these 28 epilepsies, 8 had sufficient prior literature, and our results were in line with prior research, providing validation for our results. We provided new estimates of cumulative incidence for 8 rare epilepsies with limited prior data. Additional research is needed to estimate the incidence of rare genetic epilepsies.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments.

This publication was supported by the Centers for Disease Control and Prevention of the US Department of Health and Human Services (CDC/HHS) as part of a financial assistance award totaling $899,766 with 100% percent funded by CDC/HHS. The authors acknowledge Dr. Dale Hesdorffer for guidance and support with this project.

Disclosure of Conflicts of Interest.

Patricia McGoldrick has served as a speaker for Eisai, Greenwich and Sunovion and on advisory boards to UCB, Neuropace and Supernus. Steven Wolf has served as speaker or consultant for Greenwich Pharma, Eisai Pharma, Neuropace, Lundbeck, UCB, Biomarin, Aquestive, and Zogenix, Neurilis. Tristan Sands has served as a consultant for Biomarin. Zachary Grinspan receives funding for his research from Weill Cornell Medicine, the Pediatric Epilepsy Research Foundation, Clara Inspired, and the Orphan Disease Center. He has performed consulting work for Alpha Insights and Bio-Pharm Solutions (South Korea). The remaining authors have no conflicts of interest.

REFERENCES

1. Ho NT, Kroner B, Grinspan Z, Fureman B, Farrell K, Zhang J, et al. Comorbidities of Rare Epilepsies: Results from the Rare Epilepsy Network J Pediatr. 2018 Dec;203:249–258 e245. [PubMed: 30195559]
2. Comi AM. Sturge-Weber syndrome Handb Clin Neurol. 2015;132:157–168. [PubMed: 26564078]
3. Singh AK, Keenaghan M. Sturge-Weber Syndrome. StatPearls. Treasure Island (FL)2022.

4. Grinspan ZM, Tian N, Yozawitz EG, McGoldrick PE, Wolf SM, McDonough TL, et al. Common terms for rare epilepsies: Synonyms, associated terms, and links to structured vocabularies Epilepsia Open. 2018 Mar;3:91–97. [PubMed: 29588993]
5. Barbour K, Tian N, Yozawitz EG, Wolf S, McGoldrick PE, Sands TT, et al. Creating rare epilepsy cohorts using keyword search in electronic health records Epilepsia. 2023 Oct;64:2738–2749. [PubMed: 37498137]
6. Zuberi SM, Wirrell E, Yozawitz E, Wilmshurst JM, Specchio N, Riney K, et al. ILAE classification and definition of epilepsy syndromes with onset in neonates and infants: Position statement by the ILAE Task Force on Nosology and Definitions Epilepsia. 2022 Jun;63:1349–1397. [PubMed: 35503712]
7. Arzimanoglou A, French J, Blume WT, Cross JH, Ernst JP, Feucht M, et al. Lennox-Gastaut syndrome: a consensus approach on diagnosis, assessment, management, and trial methodology Lancet Neurol. 2009 Jan;8:82–93. [PubMed: 19081517]
8. Nightscales R, Chen Z, Barnard S, Auvrez C, Tao G, Sivathamboo S, et al. Applying the ILAE diagnostic criteria for Lennox-Gastaut syndrome in the real-world setting: A multicenter retrospective cohort study Epilepsia Open. 2023 Dec 22.
9. Heiskala H Community-based study of Lennox-Gastaut syndrome Epilepsia. 1997 May;38:526–531. [PubMed: 9184597]
10. Rantala H, Putkonen T. Occurrence, outcome, and prognostic factors of infantile spasms and Lennox-Gastaut syndrome Epilepsia. 1999 Mar;40:286–289. [PubMed: 10080506]
11. Trevathan E, Murphy CC, Yeargin-Allsopp M. Prevalence and descriptive epidemiology of Lennox-Gastaut syndrome among Atlanta children Epilepsia. 1997 Dec;38:1283–1288. [PubMed: 9578523]
12. PCORI. New York City Clinical Data Research Network (NYC-CDRN). Available at: https://www.pcori.org/research-results/2015/new-york-city-clinical-data-research-network-nyc-cdrn.
13. Strzelczyk A, Schubert-Bast S, Simon A, Wyatt G, Holland R, Rosenow F. Epidemiology, healthcare resource use, and mortality in patients with probable Lennox-Gastaut syndrome: A population-based study on German health insurance data Epilepsy Behav. 2021 Feb;115:107647. [PubMed: 33358132]
14. Terai K, Munesue T, Hiratani M, Jiang ZY, Jibiki I, Yamaguchi N. The prevalence of Rett syndrome in Fukui prefecture Brain & development. 1995 Mar-Apr;17:153–154. [PubMed: 7625553]
15. Devlin LA, Shepherd CH, Crawford H, Morrison PJ. Tuberous sclerosis complex: clinical features, diagnosis, and prevalence within Northern Ireland Dev Med Child Neurol. 2006 Jun;48:495–499. [PubMed: 16700943]
16. Sparagana SP, Delgado MR, Batchelor LL, Roach ES. Seizure remission and antiepileptic drug discontinuation in children with tuberous sclerosis complex Arch Neurol. 2003 Sep;60:1286–1289. [PubMed: 12975296]
17. Webb DW, Fryer AE, Osborne JP. Morbidity associated with tuberous sclerosis: a population study Dev Med Child Neurol. 1996 Feb;38:146–155. [PubMed: 8603782]
18. Cooper RA, Kerr AM, Amos PM. Rett syndrome: critical examination of clinical features, serial EEG and video-monitoring in understanding and management Eur J Paediatr Neurol. 1998;2:127–135.
19. Glaze DG, Percy AK, Skinner S, Motil KJ, Neul JL, Barrish JO, et al. Epilepsy and the natural history of Rett syndrome Neurology. 2010 Mar 16;74:909–912. [PubMed: 20231667]
20. Clayton-Smith J Clinical research on Angelman syndrome in the United Kingdom: observations on 82 affected individuals Am J Med Genet. 1993 Apr 1;46:12–15. [PubMed: 7684188]
21. Powell S, Fosi T, Sloneem J, Hawkins C, Richardson H, Aylett S. Neurological presentations and cognitive outcome in Sturge-Weber syndrome Eur J Paediatr Neurol. 2021 Sep;34:21–32.
22. Sujansky E, Conradi S. Outcome of Sturge-Weber syndrome in 52 adults Am J Med Genet. 1995 May 22;57:35–45. [PubMed: 7645596]
23. Rosser TL, Acosta MT, Packer RJ. Aicardi syndrome: spectrum of disease and long-term prognosis in 77 females Pediatr Neurol. 2002 Nov;27:343–346. [PubMed: 12504201]

24. Vendrame M, Maski KP, Chatterjee M, Heshmati A, Krishnamoorthy K, Tan WH, et al. Epilepsy in Prader-Willi syndrome: clinical characteristics and correlation to genotype Epilepsy Behav. 2010 Nov;19:306–310. [PubMed: 20727826]
25. Wolff M, Johannesen KM, Hedrich UBS, Masnada S, Rubboli G, Gardella E, et al. Genetic and phenotypic heterogeneity suggest therapeutic implications in SCN2A-related disorders Brain. 2017 May 1;140:1316–1336. [PubMed: 28379373]
26. Johannesen KM, Liu Y, Koko M, Gjerulfsen CE, Sonnenberg L, Schubert J, et al. Genotype-phenotype correlations in SCN8A-related disorders reveal prognostic and therapeutic implications Brain. 2022 Sep 14;145:2991–3009. [PubMed: 34431999]
27. Guidelines for epidemiologic studies on epilepsy. Commission on Epidemiology and Prognosis, International League Against Epilepsy Epilepsia. 1993 Jul-Aug;34:592–596. [PubMed: 8330566]
28. Moore SJ, Buckley DJ, MacMillan A, Marshall HD, Steele L, Ray PN, et al. The clinical and genetic epidemiology of neuronal ceroid lipofuscinosis in Newfoundland Clin Genet. 2008 Sep;74:213–222. [PubMed: 18684116]
29. Santavuori P, Haltia M, Rapola J. Infantile type of so-called neuronal ceroid-lipofuscinosis Dev Med Child Neurol. 1974 Oct;16:644–653.
30. Bien CG, Tiemeier H, Sassen R, Kuczaty S, Urbach H, von Lehe M, et al. Rasmussen encephalitis: incidence and course under randomized therapy with tacrolimus or intravenous immunoglobulins Epilepsia. 2013 Mar;54:543–550. [PubMed: 23216622]
31. Rihani HT, Dalvin LA, Hodge DO, Pulido JS. Incidence of Sturge-Weber syndrome and associated ocular involvement in Olmsted County, Minnesota, United States Ophthalmic Genet. 2020 Apr;41:108–124. [PubMed: 32233696]
32. Poke G, Stanley J, Scheffer IE, Sadleir LG. Epidemiology of Developmental and Epileptic Encephalopathy and of Intellectual Disability and Epilepsy in Children Neurology. 2023 Mar 28;100:e1363–e1375. [PubMed: 36581463]
33. Howell KB, Freeman JL, Mackay MT, Fahey MC, Archer J, Berkovic SF, et al. The severe epilepsy syndromes of infancy: A population-based study Epilepsia. 2021 Feb;62:358–370. [PubMed: 33475165]
34. McTague A, Appleton R, Avula S, Cross JH, King MD, Jacques TS, et al. Migrating partial seizures of infancy: expansion of the electroclinical, radiological and pathological disease spectrum Brain. 2013 May;136:1578–1591. [PubMed: 23599387]
35. Brandberg G, Raininko R, Eeg-Olofsson O. Hypothalamic hamartoma with gelastic seizures in Swedish children and adolescents Eur J Paediatr Neurol. 2004;8:35–44. [PubMed: 15023373]
36. Hino-Fukuyo N, Haginoya K, Iinuma K, Uematsu M, Tsuchiya S. Neuroepidemiology of West syndrome and early infantile epileptic encephalopathy in Miyagi Prefecture, Japan Epilepsy Res. 2009 Dec;87:299–301. [PubMed: 19828294]
37. Hunter MB, Yoong M, Sumpter RE, Verity K, Shetty J, McLellan A, et al. Incidence of early-onset epilepsy: A prospective population-based study Seizure. 2020 Feb;75:49–54. [PubMed: 31874359]
38. Symonds JD, Elliott KS, Shetty J, Armstrong M, Brunklaus A, Cutcutache I, et al. Early childhood epilepsies: epidemiology, classification, aetiology, and socio-economic determinants Brain. 2021 Oct 22;144:2879–2891. [PubMed: 34687210]
39. Kroner BL, Preiss LR, Ardini MA, Gaillard WD. New incidence, prevalence, and survival of Aicardi syndrome from 408 cases J Child Neurol. 2008 May;23:531–535. [PubMed: 18182643]
40. Lund C, Bjornvold M, Tuft M, Kostov H, Rosby O, Selmer KK. Aicardi syndrome: an epidemiologic and clinical study in Norway Pediatr Neurol. 2015 Feb;52:182–186 e183. [PubMed: 25443581]
41. Palmer L, Zetterlund B, Hard AL, Steneryd K, Kyllerman M. Aicardi syndrome: presentation at onset in Swedish children born in 1975–2002 Neuropediatrics. 2006 Jun;37:154–158. [PubMed: 16967367]
42. Shirley K, O'Keefe M, McKee S, McLoone E. A clinical study of Aicardi syndrome in Northern Ireland: the spectrum of ophthalmic findings Eye (Lond). 2016 Jul;30:1011–1016. [PubMed: 27101753]
43. Guillem P, Cans C, Robert-Gnansia E, Ayme S, Jouk PS. Rare diseases in disabled children: an epidemiological survey Arch Dis Child. 2008 Feb;93:115–118. [PubMed: 17942587]

44. Institute of Medicine (US) Committee on the Public Health Dimensions of the Epilepsies. Epilepsy Across the Spectrum: Promoting Health and Understanding. England MJ, Liverman CT, Schultz AM, et al., editors. Washington, DC: National Academies Press; 2012 Accessed February 1, 2023.

45. Blank LJ. Socioeconomic disparities in epilepsy care Curr Opin Neurol. 2022 Apr 1;35:169–174. [PubMed: 35044956]

46. Halley MC, Halverson CME, Tabor HK, Goldenberg AJ. Rare Disease, Advocacy and Justice: Intersecting Disparities in Research and Clinical Care Am J Bioeth. 2023 May 19:1–10.

KEY POINTS

- We estimated the cumulative incidence of 28 rare epilepsies in New York City from 2010 to 2014 using electronic health records.
- The most common were infantile spasms syndrome (1 in 2,920), Lennox-Gastaut syndrome (1 in 9,690), and tuberous sclerosis (1 in 14,300).
- Our literature review showed a need for new data sources. Most rare epilepsies had limited, or no, prior epidemiologic data.
- We provide new incidence estimates for 8 rare epilepsies with limited prior epidemiologic data.
- Electronic health records may be a valuable data source for epidemiological study of rare epilepsies and other rare diseases.

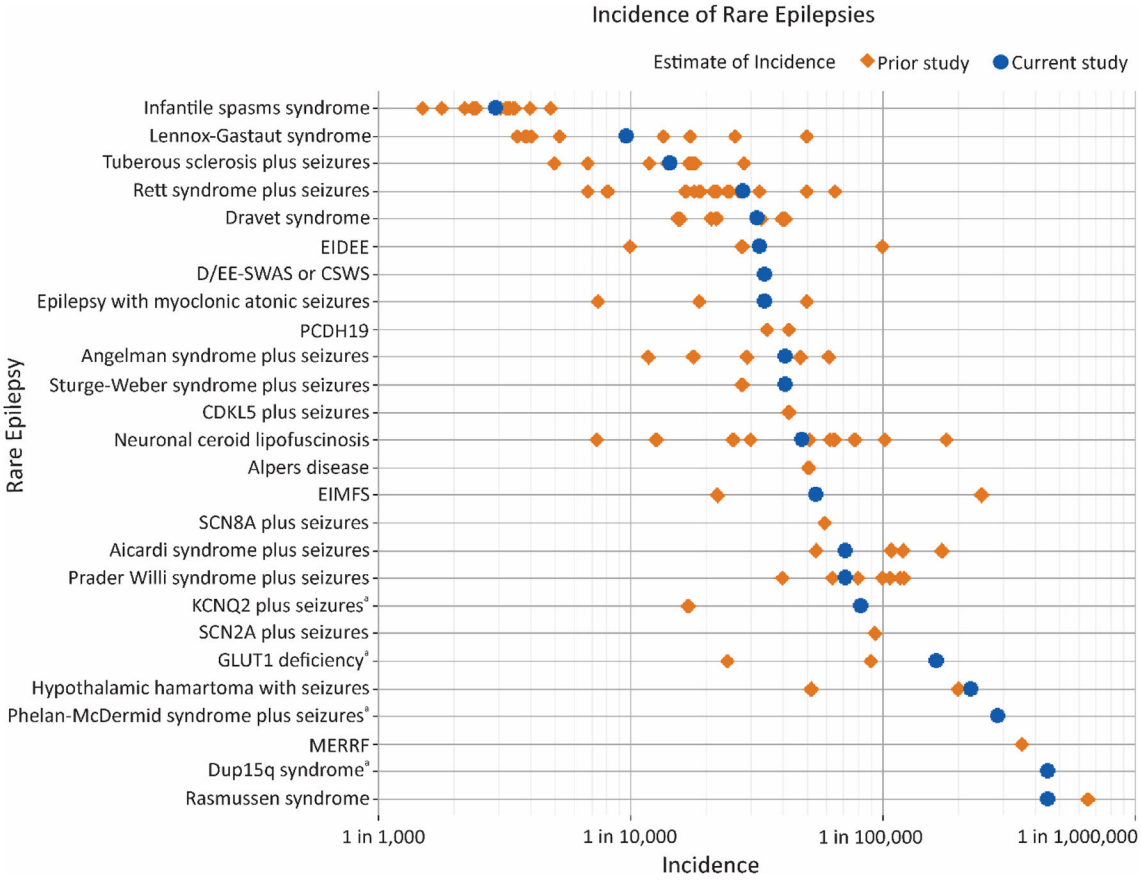

Figure 1.

Incidence of rare epilepsies in prior literature (orange diamonds) and current study (blue dots).

Note. [a]The current study underestimated the incidence of genetic epilepsies with nonspecific clinical features since genetic testing was less widely adopted during the study period (2010–2014). Abbreviations: EIDEE, early infantile developmental epileptic encephalopathy (Ohtahara syndrome and early myoclonic encephalopathy); D/EE-SWAS, developmental/epileptic encephalopathy with spike-and-wave activation in sleep; CSWS, continuous spikes and waves during sleep; EIMFS, epilepsy in infancy with migrating focal seizures; MERRF, myoclonic epilepsy with red ragged fibers.

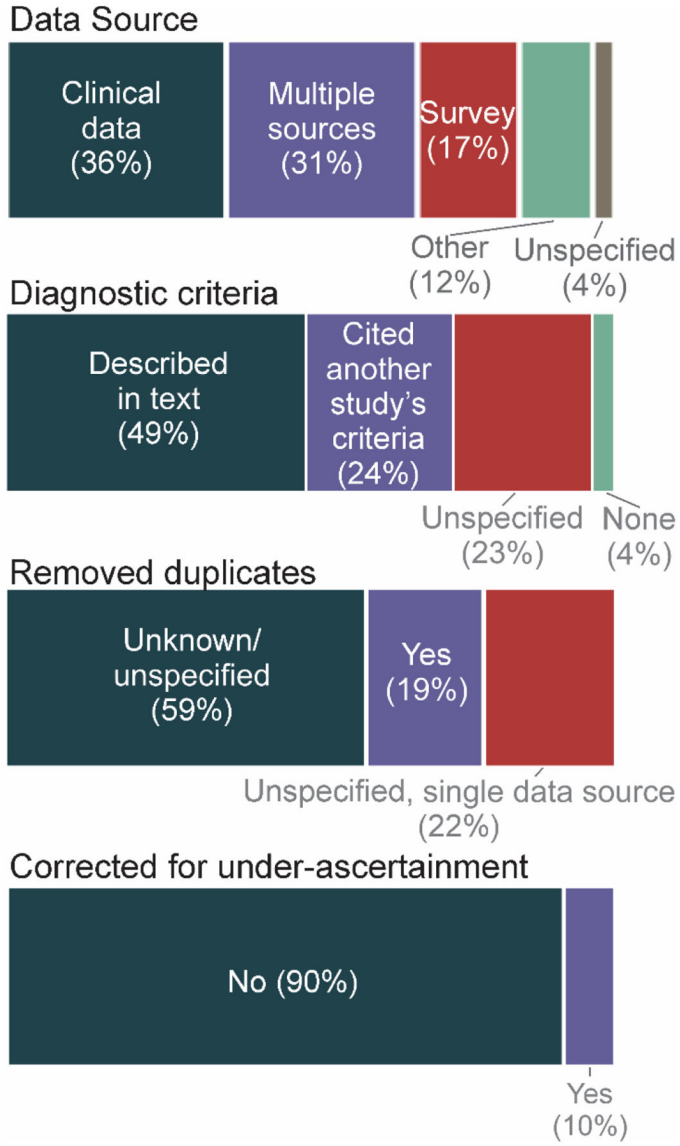

Figure 2.
Methods of 83 studies estimating the incidence of rare epilepsies.

Table 1.

Cumulative incidence of rare epilepsies in the Bronx and Manhattan, New York City (2010–2014)

Rare Epilepsy	Year of birth	Age during study period, y	Count (n)	Cumulative incidence and 95% CI (1 in x)
ISS	2011–2013	0 – 3	42	2,900 (2,140 – 3,920)
LGS	2000–2008	2 – 14	38	9,690 (7,050 – 13,300)
TSC plus seizures/epilepsy	2007–2013	0 – 7	20	14,300 (9,230 – 22,200)
Rett syndrome plus seizures/epilepsy	2006–2012	0 – 8	5	27,900 females (11,600 – 67,000)
Dravet syndrome	2006–2012	0 – 8	9	31,800 (16,500 – 61,100)
EIDEE	2010–2013	0 – 4	5	32,700 (13,600 – 78,600)
D/EE-SWAS and/or CSWS	2005–2009	1 – 9	6	34,100 (15,300 – 75,900)
EMAS	2006–2010	0 – 8	6	34,100 (15,300 – 75,900)
Angelman syndrome plus seizures/epilepsy	2007–2009	1 – 7	3	40,900 (13,200 – 127,000)
Sturge-Weber syndrome plus seizures/ epilepsy	2006–2012	0 – 8	7	40,900 (19,500 – 85,800)
NCL	2000–2006	4 – 14	6	47,700 (21,400 – 106,000)
EIMFS	2010–2013	0 – 4	3	54,500 (17,600 – 169,000)
Aicardi syndrome plus seizures/epilepsy	2006–2012	0 – 8	4	71,600 (26,900 – 191,000)
Prader-Willi syndrome plus seizures/ epilepsy	2006–2012	0 – 8	4	71,600 (26,900 – 191,000)
KCNQ2 plus seizures/epilepsy[a]	2010–2013	0 – 4	2	81,800 (20,500 – 327,000)
GLUT1 deficiency[a]	2006–2013	0 – 8	2	164,000 (41,000 – 656,000)
Hypothalamic hamartoma with seizures	2000–2010	0 – 14	2	225,000 (56,300 – 900,000)
Phelan-McDermid syndrome plus seizures/ epilepsy[a]	2006–2012	0 – 8	1	286,000 (40,300 – 2,030,000)
Dup15q syndrome[a]	2000–2010	0 – 8	1	450,000 (63,400 – 3,190,000)
Rasmussen syndrome	2000–2010	0 – 14	1	450,000 (63,400 – 3,190,000)

[a]Cumulative incidence represents minimum estimates of incidence since the current study underestimated the occurrence of genetic epilepsies with nonspecific clinical features. Abbreviations: CI, confidence interval; ISS, infantile spasms syndrome; LGS, Lennox-Gastaut syndrome; TSC, tuberous sclerosis complex; EIDEE, early infantile developmental epileptic encephalopathy (Ohtahara syndrome and early myoclonic encephalopathy); D/EE-SWAS, developmental/epileptic encephalopathy with spike-and-wave activation in sleep; CSWS, continuous spikes and waves during sleep; EMAS, epilepsy with myoclonic atonic seizures/Doose syndrome; NCL, neuronal ceroid lipofuscinosis; EIMFS, epilepsy in infancy with migrating focal seizures.

Table 2.

Incidence of rare epilepsies in prior literature, with select adjustments to estimate the incidence of those with disease plus seizures

Rare Disease	Prior literature Incidence (1 in x)	Adjusted for seizures Incidence (1 in x)
Infantile spasms syndrome		
Brna et al., Can J Neurol Sci, 2001	3,260	3,260
Hino-Fukuyo, Epilepsy Res, 2009	2,380	2,380
Howell, Epilepsia, 2021	3,060	3,060
Howitz, Arch Dis Child, 1978	3,000 to 4,000	3,500
Hunter et al., Seizure, 2020	1,500	1,500
Hwang, Brain Dev, 2001	4,000	4,000
Lee & Ong, Brain Dev, 2001	3,230	3,230
Luovigsson, Epilepsia, 1994	3,330	3,330
Matsuo et al., Brain Dev, 2001	3,230	3,230
Poke et al., Neurology, 2023[a]	1,800	1,800
Primec et al., Epilepsia, 2002	4,850	4,850
Rantala, Epilepsia, 1999	2,440	2,440
Riikonen, Dev Med Child Neurol, 1979	2,430	2,440
Sidenvall, Epilepsia, 1995	2,220	2,220
Symonds, Brain, 2021	3,260	3,260
Trevathan, Epilepsia, 1999	3,450	3,450
Lennox-Gastaut syndrome		
Chin et al., Seizure, 2021	17,300	17,300
Cowan et al., Epilepsia, 1989	5,260	5,260
Heiskala, Epilepsia, 1997	47,600 to 52,600	50,100
Poke et al., Neurology, 2023[a]	26,100	26,100
Rantala & Putkonen, Epilepsia, 1999	3,570	3,570
Sidenvall et al., Seizure, 1996	4,060	4,060
Strzelczyk et al., Epilepsy Behav, 2021	13,500	13,500
Trevathan et al., Epilepsia, 1997	3,850	3,850
Tuberous sclerosis complex		
Ching-Yuen Chu et al., Orphanet J Rare Dis, 2020	15,000	17,700
Ebrahimi-Fakhari, Orphanet J Rare Dis, 2018	10,100	11,900
Hong et al., Neuroepidemiology, 2009	14,600	17,200
Hunt & Lindenbaum, J Med Genet, 1984	15,400	18,100
Osborne et al., Ann N Y Acad Sci, 1991	5,800	6,820
Sampson et al., J Med Genet, 1989	12,000	14,100
Symonds, Brain, 2021[b]	28,300	28,300
Wiederholt, Neurology, 1985	4,260	5,010

Rare Disease	Prior literature Incidence (1 in x)	Adjusted for seizures Incidence (1 in x)
Rett syndrome		
Bienvenu, Pediatr Neurol, 2006	17,300 females	24,700 females
Burd et al., Am J Med Genet, 1991	19,800 females	28,300 females
Fehr, Pediatr Res, 2011	11,600 females	16,600 females
Hagberg, Brain Dev, 1985	15,384 females	22,000 females
Hunter et al., Seizure, 2020[b]	100,000 males and females	100,000 males and females
Kerr & Stephenson, Am J Med Genet Suppl, 1986	12,500 females	17,900 females
Kozinetz et al., Pediatrics, 1993	22,800 females	32,600 females
Laurvick, J Pediatr, 2006	18,900 females	27,000 females
Pini et al., Clin Genet, 1996	4,760 females	6,800 females
Sarajlija, Neuroepidemiology, 2015	16,900 females	24,200 females
Skjeldal et al., Brain Dev, 1997	5,700 females	8,140 females
Talvik et al., Acta Paediatr, 1995	15,000 females	21,400 females
Terai et al., Brain Dev, 1995	45,500 females	65,000 females
Wong & Li, J Child Neurol, 2007	13,200 females	18,900 females
Dravet syndrome		
Bayat, Epilepsia, 2015	22,000	22,000
Brunklaus et al., Brain, 2012	40,900	40,900
Hurst, Epilepsia, 1990	40,000	40,000
Poke et al., Neurology, 2023[a]	20,900	20,900
Rosander, Dev Med Child Neurol, 2015	33,000	33,000
Symonds, Brain, 2021	15,400	15,400
Wu, Pediatrics, 2015	15,700	15,700
Early infantile developmental and epileptic encephalopathy		
Hino-Fukuyo, Epilepsy Res, 2009	100,000	100,000
Howell, Epilepsia, 2021	27,777	27,800
Hunter et al., Seizure, 2020	100,000	100,000
Symonds, Brain, 2021	9,970	9,970
Epilepsy with myoclonic-atonic seizures		
Hunter et al., Seizure, 2020	50,000	50,000
Poke et al., Neurology, 2023[a]	7,450	7,450
Symonds, Brain, 2021	18,800	18,800
PCDH19 plus seizures/epilepsy		
Poke et al., Neurology, 2023[a]	34,800	34,800
Symonds, Brain, 2019[c]	42,400	42,400
Angelman syndrome		
Ehara et al., Brain Dev, 1995	15,100	17,800
Mertz, Am J Med Genet A, 2013	24,600	28,900

Rare Disease	Prior literature Incidence (1 in x)	Adjusted for seizures Incidence (1 in x)
Oiglane-Shlik et al., Am J Med Genet A, 2006	52,200	61,400
Petersen, Am J Med Genet, 1995	10,000	11,800
Thomson, Disabil Rehabil, 2006	40,000	47,100
Sturge-Weber syndrome		
Rihani, Ophthalmic Genet, 2020[a]	23,600	27,800
CDKL5 plus seizures/epilepsy		
Symonds, Brain, 2019	42,400	42,400
Neuronal ceroid lipofuscinosis		
Augestad, J Child Neurol, 2006	25,600	25,600
Cardona, Am J Med Genet, 1995	179,000	179,000
Claussen, Am J Med Genet, 1992	78,100	78,100
Crow, Neuropediatrics, 1997	62,100	62,100
Elleder, Eur J Paediatr Neurol, 1997	76,900	76,900
Moore, Clin Genet, 2008[d]	7,350	7,350
Santavuori et al., Dev Med Child Neurol, 1974[d]	12,700	12,700
Santorelli, Orphanet J Rare Dis, 2013	102,000	102,000
Taschner, Mol Genet Metab, 1999	51,300	51,300
Teixeira et al., J Neurol, 2003	64,516	64,516
Uvebrant, Neuropediatrics, 1997	10,200 to 50,000	30,100
Alpers disease		
Darin, Ann Neurol, 2001	51,000	51,000
Epilepsy in infancy with migrating focal seizures		
Howell, Epilepsia, 2021	22,222	22,200
McTague, Brain, 2013	246,913	247,000
SCN8A plus seizures/epilepsy		
Johannesen, Brain, 2022	56,200	59,200
Aicardi syndrome		
Kroner, J Child Neurol, 2008	93,000 to 105,000	108,000
Lund et al., Pediatr Neurol, 2015	158,000	172,000
Palmer, Neuropediatrics, 2006	50,000	54,300
Shirley et al., Eye (Lond), 2016	111,000	121,000
Prader Willi syndrome		
Lionti et al., Am J Med Genet A, 2015	15,800	63,200
Oiglane-Shlik et al., Am J Med Genet A, 2006	30,400	122,000
Smith, Arch Dis Child, 2003	25,000	100,000
Stromme, Dev Med Child Neurol, 2000	10,000	40,000
Thomson et al., J Intellect Disabil Res, 2006	29,500	118,000
Vogels, Eur J Hum Genet, 2004	26,676	107,000

Rare Disease	Prior literature Incidence (1 in x)	Adjusted for seizures Incidence (1 in x)
Whittington, J Med Genet, 2001	20,000	80,000
KCNQ2 related epilepsy		
Symonds, Brain, 2019	17,000	17,000
SCN2A plus seizures/epilepsy		
Wolff, Brain, 2017	78,600	93,600
Glut1 deficiency		
Coman, J Paediatr Child Health, 2006	90,000	90,000
Symonds, Brain, 2019	24,300	24,300
Hypothalamic hamartoma with seizures		
Brandberg et al., Eur J Paediatr Neurol, 2004	200,000	200,000
Poke et al., Neurology, 2023[a]	52,200	52,200
MERRF		
Darin, Ann Neurol, 2001	359,000	359,000
Rasmussen syndrome		
Bien et al., Epilepsia, 2012[a]	652,000	652,000

[a]Cumululative incidence recalculated using standard formula.

[b]Estimates not adjusted for presence of seizures since studies only included those with seizures.

[c]Cumulative incidence estimated to be 20,600 live born females.

[d]Studies excluded because they were performed in locations where a geographic cluster of cases had been identified.

Table 3.

Standardized terms used in the current study to describe epidemiologic calculations, compared to terminology used in prior literature

	Calculation		Terminology used in prior literature, n (%)						
Standard Term	**Numerator**	**Denominator**	**Birth incid**	**Birth prev**	**Incid**	**Cumul. incid**	**Prev**	**Incid/ Prev**	**Occur**
Cumul. incid	Number of cases divided by number of study years	Annual live births	2 (5)	3 (8)	18 (46)	7 (18)	6 (15)	1 (3)	2 (5)
Prev	Number of cases	Total population in age group	0	0	0	0	23 (100)	0	0
Incid	Number of new cases divided by number of study years	Annual live births	0	1 (8)	11 (85)	1 (8)	0	0	0
Nonstandard calculation	Number of new cases divided by number of study years	Total population in age group	0	0	1 (33)	1 (33)	1 (33)	0	0
Other non-standard	Number of cases	Total population in age group adjusted for “leading edge” and age of onset	0	0	0	1 (33)	0	0	0

Abbreviations: Standard = standardized, cumul = cumulative, incid = incidence, prev = prevalence, occur = occurrence.