Risk Factors of Epilepsy Outcomes Comorbidities in Population with Epilepsy

Final Report

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MUSC
MEDICAL UNIVERSITY OF SOUTH CAROLINA

Risk Factors of Epilepsy Outcomes

Comorbidities in Population with Epilepsy South Carolina

Final Report

THE MEDICAL UNIVERSITY OF SOUTH CAROLINA
In Partnership with

The SC Revenue and Fiscal Affairs
Health & Demographics Section

PRINCIPAL INVESTIGATOR
Anbesaw Selassie, Dr.PH

Co-Principal Investigator
Braxton Wannamaker, MD

Investigators
Gigi Smith, PhD, RN, CPNP
Janelle Wagner, PhD
Jonathan Edwards, MD
Gabriel Martz, MD
Chris Finney, MS
Karen St. Marie, BA

Epidemiologist & Research Manager
Dulaney Wilson, PhD

Research Associate
Angela Malek, PhD (Post-Doctoral)

CDC Technical Advisor
Rosemarie Kobau, MPH, MPP
David Thurman, MD, MPH

Project Office: (843) 876-1100

Executive Summary

The Medical University of South Carolina (MUSC) received funding from the CDC, National Center for Chronic Disease Prevention and Health Promotion (NCCDPHP) to investigate comorbidities in population with epilepsy in South Carolina (SC) and the risk associated in negative outcomes that include frequent hospitalization, long-term disability, and mortality. This funding was the natural extension of the well-developed epilepsy and seizure disorder surveillance system that was supported by the CDC to determine population-based incidence and prevalence of epilepsy. SC has been and continues to be a leader in public health surveillance of epilepsy because of population-based data sets maintained by the SC Revenue and Fiscal Affairs, Health and Demographics (H&D) Section with high data quality, completeness, and representativeness. With the support of SC Department of Health and Environmental Control (DHEC), Division of Chronic Disease Epidemiology, H&D, the SC Advocates for Epilepsy (SAFE), and MUSC, a strong partnership was established to fulfill the charge of the award and improve the lives of persons with epilepsy. The information presented in this report is the culminating point of four years of hard work to measure the burden of comorbidities and the risk associated with deleterious outcomes using state-of-the-art measurement and analytic techniques. However, due to the large size of the study cohort (N=120,129 persons with a diagnosis of seizure or epilepsy), detailed information from medical records was obtained from 2,604 representative sample of persons with seizure and/or epilepsy diagnoses to validate diagnosis of epilepsy and the comorbid conditions are valid and reliable. Key findings include:

Mortality

- The net increase in all-cause mortality among persons with epilepsy (PWE) is 80% higher than persons with lower extremity fracture (LEF) and 133% higher than persons with migraine, a neurological disease closely related to epilepsy.
- The population attributable risk of mortality due to comorbid conditions in PWE is influenced by number of comorbidities suggesting the need for a coordinated public health effort to reduce the risk of death.

Morbidity

- The association of epilepsy with neurodevelopmental comorbidities, particularly intellectual disability, cognitive dysfunction, and autism spectrum disorders is profoundly strong; similarly stroke cerebral palsy, depression, anxiety, substance abuse, and ADHD is very

strong accounting for the largest proportion of premature mortality in young children and adolescents.

- Of the 19 somatic comorbidities, blacks with epilepsy have significantly higher prevalence of diabetes, cardiovascular diseases, stroke, HIV/AIDS, vision loss; similarly, alcoholism and schizophrenia are more prevalent among blacks.
- Persons residing in rural communities have significantly higher burden of comorbidities than persons residing in urban communities.
- 50.6% of PWE have a median household income of less than $36,000.00 for a family of 4 and they have more than 2.5x higher risk of comorbidities than persons in higher income with a median household income of >$54,000 for a family of 4.
- Given the magnitude of comorbid diseases that are often more serious than the epilepsy itself, an innovative chronic disease management intervention involving community engaged research is critical to reduce irreversible deterioration in general health.

Incidence and Prevalence

- The period prevalence of epilepsy over the 15 years of ongoing surveillance activities (2000-2014) ranged from 13.4 to 25.9 per 1,000 population depending on the definition of epilepsy. Thus, the most conservative estimate of prevalence of epilepsy under rigid estimation is 13.4 per 1,000 populations (1.34%) while the most sensitive estimation indicates 25.9 per 1,000 populations (2.59%).
- The average cumulative incidence of epilepsy per 1,000 person-year is 0.91; estimation requires a multifaceted surveillance to capture incident encounters from all sources of care.
- PWE are 1.47 times more likely to have been blacks, 1.27 times more likely to have been Hispanics, and 1.18 times other races than whites after adjusting for other demographic characteristics, mortality status, and comorbid conditions.
- Nearly 78% of persons diagnosed with seizure unspecified, ICD-9-CM 789.39, have comparable burden of comorbidity especially when ancillary evidence from other clinical procedures indicated in epilepsy diagnosis such as vagal nerve stimulator implantation, epilepsy surgery, ketogenic diet in children and adolescents ≤18 years of age or video EEG performed and evidence of epileptiform activity recorded in the medical record are considered. Counting the uncounted and minimizing false negatives should be the primary aim of population-based epilepsy surveillance.
- With the advent of ICD-10-CM, the incidence and prevalence of epilepsy may be affected by unstable PPV of the diagnosis codes and timely evaluation is critical.

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Technical Report

Project Title: Risk Factors of Epilepsy Outcomes—Comorbidities in Population with Epilepsy in South Carolina (Grant No. DP003251)

Project Background: This epidemiological investigation of quantifying the magnitude and the implications of comorbidities among persons with epilepsy (PWE) evolved from the earlier CDC-NCCDPHP funded study entitled the South Carolina Epidemiological Study of Epilepsy and Seizure Disorders (SC-ESESD), Grant No. U36/CCU319276. The study found that the prevalence of active epilepsy in SC is 1.1% (95% CI=0.9−1.2) with 53.7% having at least one co-occurring diagnosis although not specific to preceding or following epilepsy. Yet this level of co-occurring diagnoses were too high when considered in the context of comorbid conditions, which have been found to the worsening of seizures, cognitive decline, poor general health, and higher mortality rate (Austin JK., 2007; Elliott JO et al., 2009). Further, studies have shown for many categories of comorbid conditions, the effects of the comorbidities were more problematic and have a greater influence on subjective health status than the seizures (Austin JK., 2007; Gillam et al., 2005). The most frequently cited comorbidities in this regard are depression and anxiety, which severely compromises patients' abilities to self-manage their epilepsies and predisposes them to substance abuse and suicide (Hermann BP, et al., 2000; Johnson EK, et al., 2004). Somatic comorbidities such as stroke, heart disease, arthritis, cancer, migraine, and asthma have been reported to be significantly higher among PWE than the general population (Strine TW, et al., 2005). Likewise, injuries subsequent to clinically established epilepsy are prevalent problems because of the unpredictability of seizure that predisposes them to traumatic events despite treatment with antiepileptic drugs (AED) and mental alertness (Neufield MY, et al. 2005; Tellez-Zenteno JF, et al. 2008). Of all causes, comorbid injury accounts for the highest standardized mortality rate among PWE (Kirby S, et al. 1995; Nilsson L. et al., 1997).

Furthermore, socioeconomic status (SES) has been linked with higher risk of comorbidities due to lifestyle and access to care issues disproportionately affecting PWE in low SES. Median household income in SC ranks in the lowest quintile distribution in the US and poverty is quite prevalent in the state increasing the need for further epidemiological investigation. Cognizant of the magnitude of the problem of comorbidity in PWE and the multifaceted data sources available in the state as proven from earlier studies, CDC awarded the Medical University of South Carolina to conduct population-based epidemiological investigation to investigate the influence of comorbidities on the outcome of epilepsy. To undertake this investigation, the following specific aims were developed.

Specific aims

Specific Aim 1: Compare the magnitude and distribution of common comorbid conditions among PWE (case group) relative to people with lower extremity fracture (LEF) and people with migraine (comparative groups).

HA1a: We predict that, compared to people with LEF or people with migraine, PWE will have significantly higher rate ratios (RR) of comorbid conditions.

This hypothesis is confirmed and the findings published in peer reviewed manuscripts (Selassie AW et al. 2014). The prevalence of the comorbidities was higher in PWE compared with people with migraine for all comorbidities listed except peptic ulcer and gastric reflux. Compared with LEF, PWE had significantly higher proportions of all the listed comorbidities in the current analyses except osteoporosis. Please see Tables 5 and 6 for summary of these finding (Selassie AW et al. 2014). Similar patterns were observed in neurodevelopmental and mental health comorbidities in children, adolescents and young adults with epilepsy compared with migrainers and those with LEF (Wagner JL et al. 2015; Wagner JL et al. 2016).

HA1b: We predict that among PWE, blacks will have significantly higher RR of comorbid conditions than whites.

This hypothesis has been affirmed and partial information published in Epilepsy Research and Epilepsia. A complete manuscript on racial disparity in epilepsy care and the impact thereof on mortality attributable to epilepsy is in preparation. Our data indicate PWE are 1.47 times more likely to have been blacks, 1.27 times Hispanics, and 1.18 times other races than whites after adjusting for other demographic characteristics, mortality status, and comorbid conditions (Table 10).

HA1c: We predict that among PWE, persons residing in rural and underserved counties will have significantly higher RR of comorbid conditions than those residing in urban counties.

This hypothesis has been affirmed in regard to the difference between rural and urban residents and manuscript is pending to identify the factors accounting for the differences in the distribution of comorbid conditions. In some instances, where diagnosis require advanced imaging, rural areas fare better than urban perhaps because of underdiagnoses rather than lower prevalence. Generally significant

differences exist in the prevalence of comorbid conditions in both directions. Our data indicate no difference between rural and urban residents with epilepsy regarding HIV/AIDS, Osteoporosis, Parkinson's disease, alcoholism, and abuse of illicit drugs while significant differences existed in the remaining 27 comorbid conditions of epilepsy. (Table 8)

H_A1d: We predict that there is inverse relationship between socioeconomic (SES) gradient and the number of comorbid conditions among PWE, i.e., the lower SES the higher the counts of comorbid conditions. We will determine SES by payer status and geocoded zip code data.

This specific aim is accomplished and manuscript to this effect is in preparation (Table 9). The process of estimating median household income is based on macro level analysis based on census tract data on median household income. While this is the standard approach to approximate household income due to the difficulty of individual household surveys, with the assumption that households with similar income cluster in the same area, this assumption is confounded by factors other than income, such as systemic racism, social isolation, and discriminatory neighborhood provisions deliberately designed to guard minority integration.

Specific Aim 2: Determine the implications of epilepsy comorbidity on mortality and seizure conditions.

H_A 2a: We predict that PWE with comorbid condition(s) are more likely to have higher mortality (all cause) rate than those without comorbidity.

This hypothesis is properly evaluated and affirmed. All-cause mortality rate of PWE for all ages is 80% higher than persons with LEF who have comparable mortality rate as the general population of the state. In comparison to persons with migraine, mortality rate in PWE is 126% higher than migrainers after adjusting for potential confounders (Table 10). Further assessment of mortality in children and adolescents age 18 and younger provided more detailed information about risk of death considered as epilepsy-related such as cerebral palsy, intellectual disability, sudden death, status epilepticus, and the direct effect of epileptic seizures (Selassie et al., 2015). The study showed the estimated five-year risk of death of was 6.32 times higher in children and adolescents with epilepsy than their counterparts with migraine. Conversely, the 5-year risk of death in children and adolescents with LEF

was similar with children and adolescents in the general population. Both of these findings are published as noted in the dissemination section of this report.

H_A 2b: We predict that PWE with comorbid condition(s) are more likely to have higher occurrences of sudden unexplained death (SUDEP) than those without comorbidity.

This aim is partially accomplished as noted in the aforementioned response. The main barrier we faced to accomplish this objective was the lack of interest or perhaps willingness of the coroners to collaborate. On several occasions our request was unheeded and communication with the Coroners' Association was with the President of the Association, who often gave us no response. Since SUDEP is a diagnosis of omission when all other causes are ruled out, the epidemiological evidence to establish a death in a PWE as SUDEP relies on underlying cause of death described as 'cardiorespiratory arrest' and the contributing cause mentions epilepsy. Currently we are working with Dr. Wannamaker on his private practice cohort of more than 3,000 PWE where more detailed information on those who died is available.

H_A 2c: We predict that PWE with more counts of comorbid conditions are more likely to have higher frequency of seizures.

This hypothesis is partially affirmed. While the risk of death is significantly higher with comorbid conditions, the severity of seizure was harder to quantify than we initially thought. The approximation of severity of seizure by the frequency of hospital admissions and outpatient encounters as a proxy marker of seizure severity has been criticized by the reviewers based on the review critique we received on this measurement approach. Most measures of severity of seizure rely on duration and frequency of seizure, response to AEDs, and EEG evidence of severity. However, these measures are difficult to determine in a large population-based epidemiological studies where the venues of patient care are uneven regarding the skillset and resources needed to establish these objective markers of severity. However, we still believe epilepsy-related mortality and seizure-related clinical encounters, including epilepsy surgery, could be used as a proxy measure of severity of seizure and we have continued collecting information on these proxy measures.

Specific Aim 3: Determine the association of comorbidities and individual characteristics, AEDs, recency of the onset of epilepsy, and type of seizure controlling for potential confounders.

H_A 3a: We predict that the risk of psychiatric comorbidities is socioeconomic dependent after adjusting for age, duration of epilepsy, race, gender, and other potential confounders.

This hypothesis has been affirmed among children and adolescents (Age<19 years) and young adults (Age 19-25). Our study found that mental health comorbidities are independently associated with low SES, when low SES is approximated by primary health insurance payer (Medicaid and medically indigent assistant programs). These findings are published (Wagner et al, 2015; Wagner et al., 2016). *Additional manuscripts on the influence of SES derived from geospatial economic indicators of household income on mental health comorbidities are in progress.*

H_A 3b: We predict that somatic comorbidities (including injuries), psychiatric, and cognitive comorbidities are more likely to occur among epilepsy patients treated with more than two AEDs and patients with generalized tonic clonic seizures.

This hypothesis has not been affirmed because of the challenges of collecting AED data from chart review. Although 2,604 medical records of PWE have been abstracted (Table 11), completeness of AED on medical records prior to 2011 is very low. Our effort to utilize the National Drug Code (NDC), while information is available in the administrative data, has multiple codes assigned for the same AED depending on dosage, manufacturer's proprietary names, and routes of administration. As an example, phenobarbitone alone has >103 NDCs in the US market making the task unwieldy.

H_A 3c: We predict that refractory cases of epilepsy that undergo/had epilepsy surgery have fewer epilepsy comorbidities compared to pre-surgery.

This hypothesis is not completed because of the very low number of epilepsy surgeries carried out in South Carolina and there is inadequate statistical power to test this hypothesis. Data may need to be pooled from multiple years to arrive at a reasonable sample size to conduct this test. However, qualitative data analysis on some of the patients who underwent epilepsy surgery is in consideration in collaboration with SAFE.

Specific Aim 4: Determine the population attributable risk of hospitalizations accounted by epilepsy comorbidities and the direct medical care cost.

H_A 4a: We predict that PWE with comorbid conditions will have higher rates of hospitalization as compared to the population of PWE without comorbidity as measured by population attributable risk in percent.

This hypothesis is affirmed. The population attributable risk (PAR) of hospital admission was estimated ([PAR = Pe (RRe-1) / [1 + Pe (RRe-1)], where Pe is the prevalence of the exposure (e.g., proportion with >1 comorbid condition) and RRe is the relative risk of hospitalization rate due to that exposure). Although the overall PAR estimate is 15-18% higher with comorbid condition, we are planning to analyze the data stratified by year and accounting for the correlation effect of multiple adjustment and assumption of no interaction between the risk factors. Wand et al., 2009 *have proposed a SAS code for calculating PAR as an extension of PROC PHREG. One of the manuscripts we are developing will utilize this approach.*

H_A 4b: We predict that direct medical care cost of PWE with comorbid conditions is significantly higher than those PWE without comorbid conditions.

This hypothesis is in progress and in track for completion. We have consulted with Dr. Chuck Begley, a health economist at UT in Houston serving as the project external advisor on the best approach to approximate direct medical care cost from medical care charge available in our dataset. While the data are already at hand, refining the approach is pending input from a health economist with experience in the Uniform Billing (UB) methods of direct medical care cost analyses.

Major Milestones

All of the major milestones outlined in the original application have been accomplished. Below is the brief summary of these activities.

1. External Advisory Committee Formation by the first quarter of Year 1. This objective is accomplished according to the timeline. Three nationally recognized experts in the field, Drs. Charles Begley, Dale Hesdorffer, and Karen Parko, have agreed to serve as external advisors. As proposed in the application, the committee met in Charleston during the 2nd year of funding and at the AES annual meetings in San Diego CA and Baltimore, MD. Members of the committee have been generous in their times including participation in a community rally organized by SAFE in Charleston to encourage community members to actively advocate for epilepsy.

2. Personnel development and mentoring was one of the areas targeted to effectively promote epilepsy research in SC. Cognizant of this important task, a key personnel with PhD in epidemiology and data management skill, Dr. Dulaney Wilson was hired to serve as the project manager and epidemiologist for all project activities. We also offered a post-doctoral fellowship position to Dr. Angela Malek who has PhD in epidemiology from the University of Pittsburg and nearly two years of post-doctoral fellowship in neuroepidemiology. Additionally, two AHIMA certified medical record abstractors were hired through subcontract with SC DHEC.

3. Initial IRB approval and subsequent annual renewals continued to hold important priority in the project. Although the initial Human Subject approval was expedited due to minimal risk to participants of the study and compliance with Federal Wide Assurance, multiple amendments were implemented to adapt with the evolving project activities. This also included competency and certification from the Miami Clinical Trials and Research Studies by all investigators and project personnel. Training of abstractors and other personnel in epilepsy clinical symptomatology and what information to look for in chart reviews were carried out by the clinical team of investigators.

4. Continued study protocol refinement and comparison group—we made significant changes during Year 1. The inclusion of SAFE as a community partner in response to the comment provided by the CDC external reviewers and replacing syncope with migraine as a comparison group were the salient changes. After investigation of frequent differential diagnosis in a sample of records from three of the hospitals in the Low Country and a discussion among the clinical investigators, migraine which has often been described in the literature as a borderland diagnosis with epilepsy (Kasteleijn-Nolst T. et al, 2012), was considered appropriate. This protocol was changed before chart abstraction was initiated and pilot data analysis affirmed the decision. The inclusion of SAFE as the community participant and Ms. Karen St. Marie as investigator was a watershed in elevated participant recruitment through community engagement. We also noted this partnership was mutually beneficial as noted from expanded chapters of SAFE in many administrative regions of the state

enabled by the financial support from subcontract funding from the project. Our progress would have not been the same without the participation of SAFE.

5. Developing and pilot testing the data abstraction tool was completed in the 3rd quarter of Year 1. This was a major milestone that anchored the study to a successful course. The abstraction tool along with other information is available at our webpage, http://academicdepartments.musc.edu/epilepsyresearch/projects.htm, for downloading through agreement with the project until the time restriction for resource sharing expires in October 2019. Chart review was implemented on a representative sample of medical records following the CDC technical guideline developed for neurological trauma. With changes in the filing of medical records from paper to electronic format, there were challenges in accessing the records in a timely manner in some of the hospitals with impact on our progress. However, this has been resolved over time and through the support of the medical record staff.

Project Methods

The pivotal point and the data core of the study is the statewide epilepsy and seizure disorder surveillance system (SC-ESDSS). This system has all the attributes of a good surveillance system (Fig. 1). It is established through the partnership of SC DHEC and Health and Demographics section of the Revenue and Fiscal Affairs Office and the CDC NCCDPHP Epilepsy Program Office. The state entities have statutory authority to

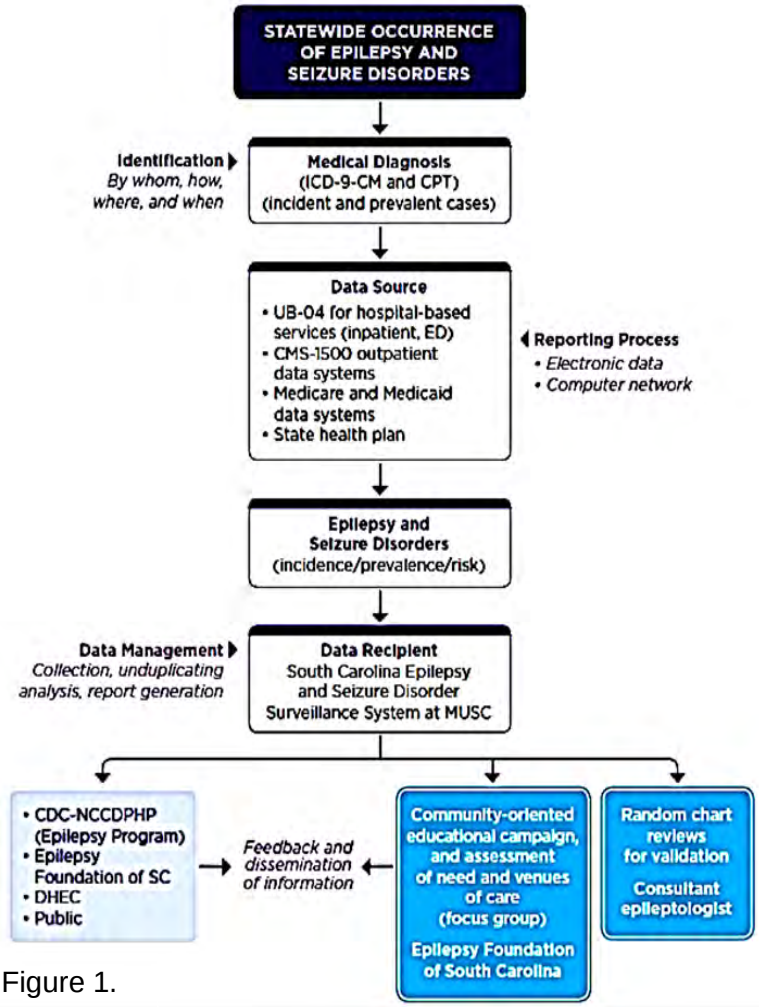

Figure 1.

The South Carolina Epilepsy and Seizure Disorders Surveillance System

receive data from hospital organizations and other health and human service agencies. The component of the system, as shown in the flow chart, incorporates processes for case ascertainment, unduplication of observations for the same event, data management, a feedback and dissemination activities. Perhaps the strength of the system is the multifaceted data sources that provide complementary information to increase data usefulness. SC-ESDSS has unique personal identifiers to link files across other data platforms such as medical record files, death files, and a follow back capability to track persons who consent to participate in special studies. Among the system attributes we periodically evaluated, the predictive value positive (PVP), representativeness, and usefulness are important attributes of the system that enabled us to monitor the temporal pattern of epilepsy and seizure disorders in the state and take appropriate interventions when needed. Information on discharge disposition enables evaluating short-term outcomes such as in-hospital death, discharge to rehab, and long-term care facilities including nursing home. The weak points of the system are missingness and/or nonspecific 5^{th} digit diagnoses codes coded with 9 (nnn.n9). We anticipate this is going to be more challenging with 6-digit alphanumeric codes in the newly implemented ICD-10-CM. The other weak point is timelines where there a lag time of 9 months before healthcare encounter data is processed from the date of patient encounter to accessing the data for surveillance activities making this system less useful for public health actions that require immediate intervention like communicable diseases. Taken together, this surveillance system is an important and useful system for epilepsy surveillance to determine, 1) the magnitude and distribution of comorbid conditions of epilepsy and the factors contributing for the high prevalence in population subgroups. The Uniform Billing (UB) data in SC has 1 primary and 14 secondary diagnosis codes to identify secondary billable clinical conditions identified in the patient allowing recognition of comorbidities; 2) the implications of epilepsy on acute care mortality; 3) the association of common comorbid conditions with types of epilepsy; and 4) the population attributable risk of hospitalizations and the direct medical care cost accounted by epilepsy comorbidities.

All eligible subjects were identified from healthcare encounter data from January 1, 2000 through December 31, 2014. Pertinent data on demographic characteristics, comorbidities and direct medical care cost data were obtained from the respective administrative data sources. Data were restricted to state residents for estimates of incidence and prevalence of epilepsy.

Sources of Complementary Data

1. Mortality data was obtained from the South Carolina Department of Health, Division of Public Health Statistics and Information System (SC PHSIS). It is gleaned from the standardized death certificate form and organized into multiple-causes of death data (MCDD) electronic file. MCDD has an underlying cause of death field—presumed to be the proximal clinical condition that resulted in death—and up to twenty contributing causes of death fields. Because the criteria of identifying underlying cause in MCDD differs from how epilepsy-related deaths are identified, we reviewed electronic abstract of the death certificate to identify potential clues to the causes of death for SUDEP and other sudden causes of death. MCDD continues to provide annual causes of death among persons with epilepsy since 2000.
2. Medical record abstraction was conducted using the same methods we have used since initial funding in 2000 for chart reviews. In this operational process, we partnered with the DHEC Bureau of Chronic Disease, Division of Chronic Disease Epidemiology to hire certified Accredited Health Information Management Analysts (AHIMA) to conduct the medical record reviews. The project abstraction coordinator was responsible for making the arrangements to review the records. Each abstractor was trained to enter the information needed on the data abstraction form in a laptop computer using Microsoft Access data entry screen. The laptop computers have the data dictionary that abstractors could check as needed. The design of the data entry screen precluded entry of illegal and out-of-range values by using abstraction guides incorporated into the abstraction tool. Abstractors were instructed never to second-guess any statement or coding values recorded in the chart and to flag the record if any discrepancy is noted.

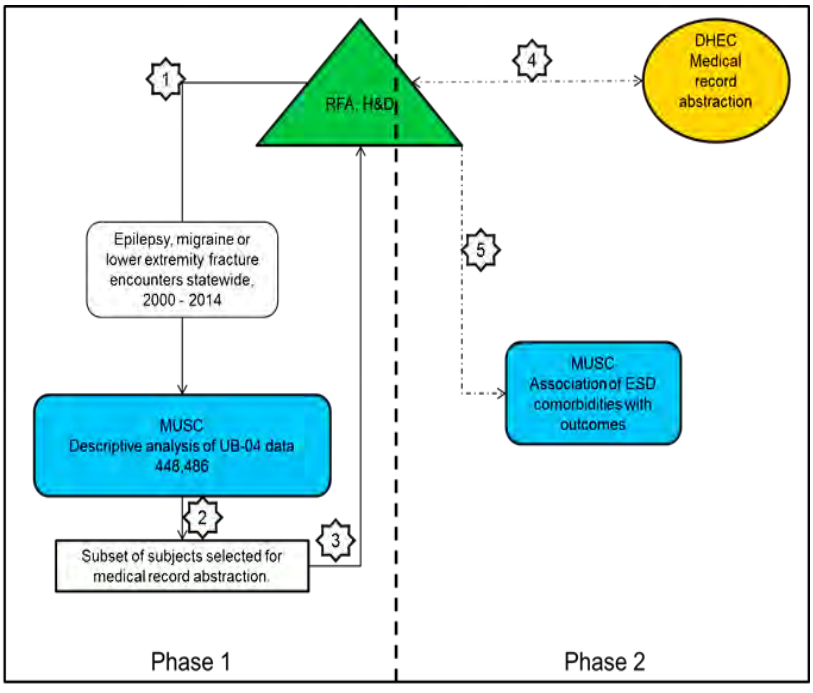

Figure 2. Study procedure

Study Procedure

This study was executed in two phases (Figure 2). Phase 1 was designed to provide data to inform the prevalence study, addressing objectives 1, 2 and 4. In Phase 1, data on all visits fitting the case ascertainment criteria were identified by the SC RFA H&D (Step 1). Anonymous data with uniquely assigned random number were forwarded to MUSC for descriptive analysis (Step 2). A sample of records was selected for medical record abstraction(Step3).

Phase 2 was designed to obtain additional data to address objective 3, the association of reported comorbid conditions with the degree and severity of epilepsy. In this phase, the sample of records were returned to H&D who provided identifying information to DHEC for medical record abstraction (Step 4). After abstraction, the data were returned to H&D and stripped of names before transfer to MUSC for further analysis (Step 5).

The study design incorporates two comparison groups: 1) individuals diagnosed with migraine (a chronic, episodic neurological condition similar to epilepsy with comparable use of medications) without an epilepsy diagnosis (PWM); 2) a representative sample of trauma patients with isolated fracture of the lower extremities (PWLF). The two groups were used for detailed risk analysis and understanding of the underlying risk factors that contribute for differential rates of comorbid conditions among the discriminated groups. First, migraine is a neurological condition with comparable treatments as those with epilepsy. It is essential to identify a control group that is likely to have comparability in patterns of comorbidity with PWE to washout the bias expected if we limit the comparison group to the general population (approximated by the 'healthier' LEF controls). This aspect of the study is seeking to answer the research question, "Do PWE with comorbid conditions have worse outcomes when compared with migraine patients that are likely to have comparable burden of comorbidity?" We feel this is important consideration since migraine patients also have higher levels of chronic somatic comorbidities, particularly cardiovascular, diabetes and upper GI problems, enabling us to tease out the extent to which risk of death or hospitalization is enhanced by epilepsy. Trauma controls with tibia, fibula or ankle fracture are highly comparable to the general population with regard to comorbidity patterns based on a comparison of selected comorbidities from the SC BRFSS. Sixty percent of the fracture cohort acquired the injury from traffic crashes, 30% from falls, 7% from interpersonal violence, and the rest from other causes. It is therefore

clear that these patients are similar to the general population with the exception of the fracture they sustained. Fractures are evenly distributed throughout the state and have similar urban-rural patterns. Thus, controls with fracture of the extremities are alternate sample for the general population with the benefit of having a complete clinical profile on their health status.

Case Ascertainment

PWE, PWM, and PWLF were ascertained using International Classification of Diseases, 9th revision, Clinical Modification (ICD-9-CM) diagnosis codes for epilepsy (ICD-9-CM codes 345.0, 345.1, 345.4-345.6, 345.8, or 345.9), seizure ("seizure, not otherwise specified" ICD-9-CM code 780.39), migraine (ICD-9-CM code 346.x), and fracture of the tibia, fibula, or ankle (ICD-9-CM codes 823.x and 824.x).

In the clinical setting, epilepsy is defined as two or more unprovoked seizures occurring at least 24 hours apart with multiple seizures within 24 hours counted as one seizure episode (ILAE, 1993). In this study, clinically established epilepsy was determined based on the aforementioned ICD-9-CM coded diagnoses of epilepsy. Until 2007 when CMS changed the reimbursement criteria for unspecified seizures (780.39), this code was assigned to protect PWE from the stigma associated with epilepsy diagnosis such as employment discriminations, loss of driving privileges, and insurance rate hikes if seizure is well controlled with medication or seizure is nocturnal. Our data validation indicates 78% of the diagnosis coded as 780.39 were

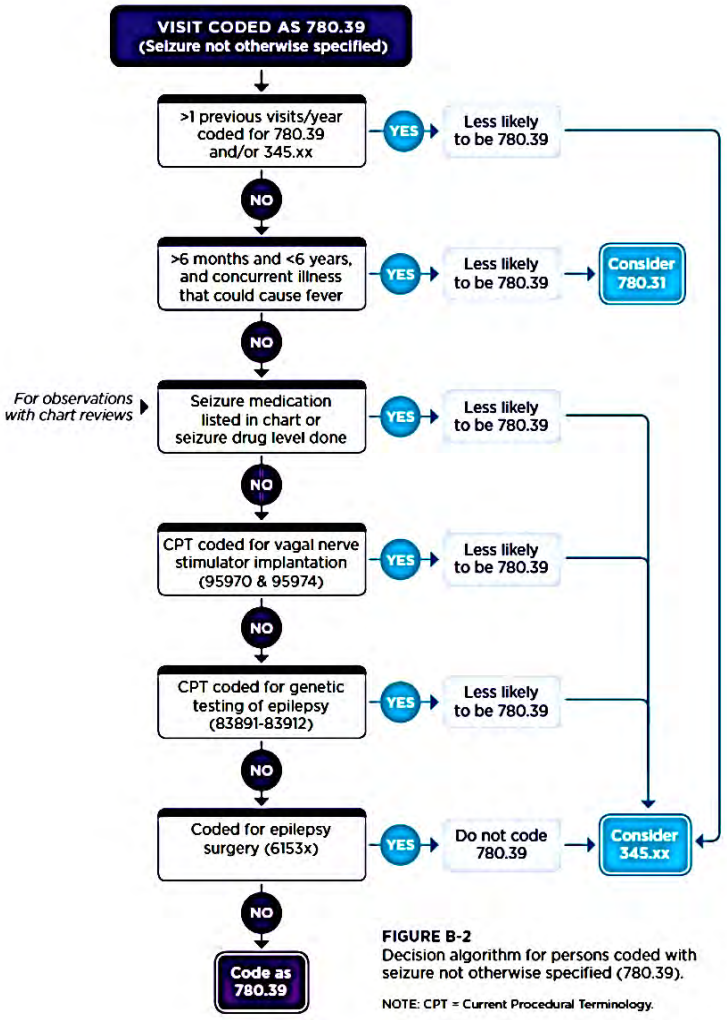

Figure 3. SCESDSS Decision Algorithm to Ascertain Epilepsy Among Persons Identified with Seizure NOS

indeed 345.x. Cognizant of this problem and affirmation from physician surveys, a decision algorithm was developed to identify probable cases of 780.39 that were most likely epilepsy (Figure 3). Using this algorithm, a SAS program was developed to recode 780.39 cases that qualified as 345.x. To operationalize the various possible combination of seizure diagnosis, we classified patients with seizure encounters into four groups depending on the degree of certainty: 1) "Definite" epilepsy: when two or more clinical encounters were coded for epilepsy OR one visit with epilepsy PLUS a previous visit within the same year coded for unspecified seizure (ICD-9-CM 780.39); 2) "Probable" epilepsy: when one visit coded for epilepsy with ADE prescription during the study period; 3) "Possible" epilepsy: two or more visits coded for unspecified seizure within one year OR a single visit coded for unspecified seizure WITH other clinical procedures indicated in epilepsy diagnosis invoked and current procedure terminology (CPT) codes for vagal nerve stimulator implantation, epilepsy surgery, ketogenic diet in children and adolescents ≤18 years of age or video EEG performed and evidence of epileptiform activity recorded in the medical record; and 4) "Undetermined" when a single visit is coded with 780.39.

In the course of earlier work, epilepsy diagnoses present in South Carolina data from 2001 through 2006 were validated with medical record review and measures of predictive value positive (PVP) was assessed. Accordingly, a diagnosis coded with 345.x has high PVP of 96.2% while unspecified seizure coded with 780.39 was largely a diagnosis of epilepsy in 71.8% of the cases as summarized in the Table 1.

Table 1. Measures of Validity, SC, 2001-2006

UB-04 Classification	Status through medical review		Total
	Epilepsy (345.x)	Seizures (780.3x)	
Epilepsy (345.x)	601	24	625
Seizures (780.3x)	1042	408	1450
Total	1643	432	2075

PVP of 345.x for epilepsy = (601/625) = 96.2%
PVP of 780.3x for seizure = (408/1450) = 28.1%
Misclassification rate of 780.3x as seizure=(1042/1450) = 71.8%

Changes in the billing reimbursement policy in 2006 resulted in a significant increase in the use of ICD-9-CM codes for epilepsy (with a corresponding decrease in codes for unspecified seizure) while at the same time the pattern of coding for migraine and LEF stayed constant across time (Figure 4). Although this pattern of coding changes was initially observed in our surveillance data, the explanation on what contributed to this change in the pattern of coding was reported by Cardenas et al, 2014. Anecdotal evidence

from neurology and epileptology colleagues shows that prior to the 2006 coding mandate, physicians were likely to assign a seizure diagnosis rather than an epilepsy diagnosis in order to avert negative consequences for the patient as described earlier. This coding shift is unlikely to reflect a change in incidence or prevalence but a move towards appropriate coding and thus, we expect that our decision algorithm will perform as well for later data. In fact the current pattern of coding of 780.39 closely corresponds to our PVP rate of 28% affirming that our algorithm is indeed reliable.

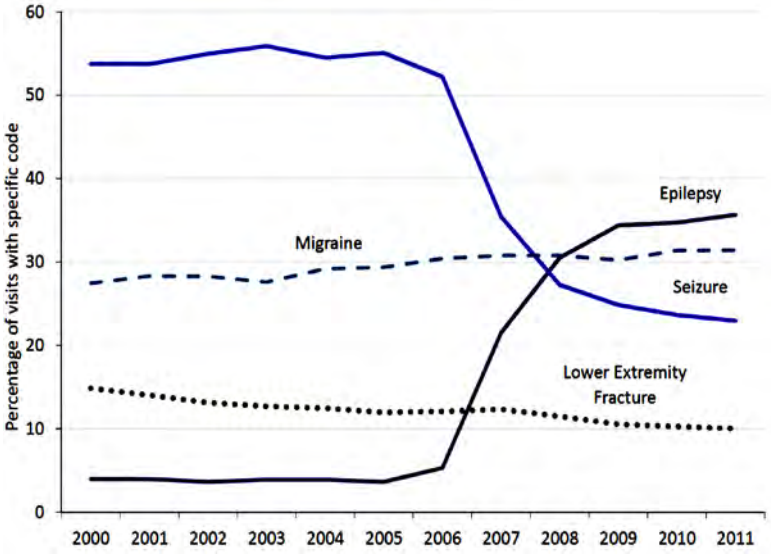

Figure 4. Pattern of coding between 780.39 and 345.x in SC, 2000-2011

Comorbidity Ascertainment and Variable Definitions

The primary focus of this study was the prevalence and effect of comorbid conditions on PWE. Thirty-six common comorbidities of epilepsy, defined as diagnosis of other clinical conditions that occur at higher frequency in PWE than what is expected in the general population (Thurman et al., 2011; Rai D et al., 2012). The ICD-9-CM codes used to define these comorbidities are listed in Appendix A. Since individuals can have many of these comorbid conditions due to accrual effect over 15 years of observation, count of the comorbid conditions was included in the analysis, categorized as none, 1-2, 3-5, ≥6.

Age at first diagnosis was categorized as ≤5, 6-12, 13-18, 19-34, 35-64, 65 and older. Rural/urban residence was defined using Rural Urban Commuting Area (RUCA) codes specific to zip codes, the smallest geographic area available in these data (USDA Economic Research Service, 2011; WWAMI Rural Health Research Center, 2015). RUCA codes range from 1 to 10 and incorporate measures of urbanization, population density and commuting time to urban areas. As individuals may have lived in multiple zip codes over the study period, we determined the RUCA designation for each individual based on the most frequent zip code reported for that individual. Individuals were further grouped on the basis of a dichotomous RUCA code aggregate—Urban=RUCA 1.0, 1.1, 2.0, 2.1, 2.2, 3.0, 4.1, 5.1, 7.1, 8.1, 10.1; Rural=all other RUCA (WWAMI Rural Health Research Center, 2015). Insurance status was grouped as uninsured (including self-pay), Medicare,

Medicaid (includes indigent care) and commercial. Income was assigned based on the median income of the most frequent zip code of residence. Using guidelines from the U.S. Department of Housing and Urban Development, income was categorized based on a percentage of the SC median household income: (1) under $36,000 (80%), (2) $36,000 to $54,000 (>80% to 120%), and (3) $54,000 and over (≥120%). (U.S. Department of Housing and Urban Development, 2012)

Data analysis

The associations of demographic and clinical characteristics were evaluated with chi square tests of homogeneity and independence. Stratum-specific 95% confidence intervals (CI) were constructed for the independent variables under the assumption of independence and normal approximation. Overlapping CIs within the same category likely suggest no significant difference in stratum-specific proportions while *P*-values <0.05 across groups suggest significant difference of two proportions. Distributional assumptions of continuous variables were explored with numerical and graphical methods. The association of the independent variables with the outcome of interest was evaluated with Cox Proportional Hazard (CPH) regression or logistic regression modeling. All analyses were conducted using SAS software, version 9.4 (SAS Institute, 2012).

Results

[1] Population-based demographic characteristics of the cohort in the study

From January 1, 2000 through December 31, 2014, there were 8,834,462 hospitalizations, ED or OPD visits (for 374,602 individuals) that included a diagnosis of epilepsy, seizure, migraine or isolated lower extremity fracture who met the aforementioned criteria. The distribution of demographic characteristics of the cohort included in the analyses are shown in Table 2. A special column is included to show isolated *status epilepticus*, predominantly *grand mal status* (ICD-9-CM =341), that did not meet the definition of epilepsy. We have recently published on the unique mortality risk associated with status in our cohort (Malek et al., 2016). To assist in visual display of the table, we shaded the columns that are particularly important to highlight. PWE that met our rigid definition of epilepsy have significantly higher proportion of blacks, rural residents, >5 comorbid conditions, low household income than either migraine or LEF (p<0.01). Conversely, significantly higher proportion of PWM were females or white. Similarly, significantly higher proportion of PWLF is also white. A striking feature of status epilepticus is the preponderance of the elderly,

Table 2. Demographic characteristics of the surveillance population by diagnosis category

pulation Characteristics	Definite Epilepsy n=62,121		Defnite +Probable n=87,327		Definite +Poss n=94,923		Def+Prob+Poss n=120,129		Migraine n=154,083		Lower Ext Fracture n=100,390		Status Epilepticus n=1,517	
Race														
White	37,612	(60.5)	54,732	(62.7)	56,876	(59.9)	73,996	(61.6)	**108,191**	**(70.2)**	**69,371**	**(69.1)**	833	(54.9)
Black	**23,376**	**(37.6)**	30,498	(34.9)	36,104	(38.0)	43,226	(36.0)	42,037	(27.3)	27,426	(27.3)	612	(40.3)
Other	676	(1.1)	1,256	(1.4)	1,174	(1.2)	1,754	(1.5)	2,266	(1.5)	2,218	(2.2)	46	(3.0)
Hispanic	457	(0.7)	841	(1.0)	769	(0.8)	1,153	(1.0)	1,589	(1.0)	1,375	(1.4)	26	(1.7)
Rural														
Urban	41,608	(67.0)	57,280	(65.6)	62,632	(66.0)	78,304	(65.2)	105,012	(68.2)	64,723	(64.5)	999	(65.9)
Rural	**19,355**	**(31.2)**	25,833	(29.6)	30,033	(31.6)	36,511	(30.4)	41,597	(27.0)	28,564	(28.5)	354	(23.3)
Missing	1,158	(1.9)	4,214	(4.8)	2,258	(2.4)	5,314	(4.4)	7,474	(4.9)	7,103	(7.1)	164	(10.8)
Age group first diagnosis														
0 to 5	3,590	(5.8)	4,853	(5.6)	7,710	(8.1)	8,973	(7.5)	175	(0.1)	4,476	(4.5)	237	(15.6)
6 to 12	2,549	(4.1)	3,526	(4.0)	4,797	(5.1)	5,774	(4.8)	2,581	(1.7)	7,612	(7.6)	55	(3.6)
13 to 18	3,399	(5.5)	4,515	(5.2)	5,943	(6.3)	7,059	(5.9)	9,390	(6.1)	10,599	(10.6)	26	(1.7)
19 to 34	12,440	(20.0)	17,471	(20.0)	17,032	(17.9)	22,063	(18.4)	56,236	(36.5)	18,898	(18.8)	132	(8.7)
35 to 64	28,716	(46.2)	39,526	(45.3)	40,079	(42.2)	50,889	(42.4)	75,834	(49.2)	42,123	(42.0)	543	(35.8)
65+	11,427	(18.4)	17,436	(20.0)	19,362	(20.4)	25,371	(21.1)	9,867	(6.4)	16,682	(16.6)	**524**	**(34.5)**
Sex														
Female	31,793	(51.2)	45,103	(51.6)	48,172	(50.7)	61,482	(51.2)	**122,789**	**(79.7)**	52,484	(52.3)	735	(48.5)
Male	30,328	(48.8)	42,224	(48.4)	46,751	(49.3)	58,647	(48.8)	31,294	(20.3)	47,906	(47.7)	782	(51.5)
payer														
Uninsured	5,865	(9.4)	9,305	(10.7)	9,348	(9.8)	12,788	(10.6)	24,843	(16.1)	17,486	(17.4)	172	(11.3)
Medicare	25,536	(41.1)	34,138	(39.1)	37,547	(39.6)	46,149	(38.4)	25,960	(16.8)	24,613	(24.5)	608	(40.1)
Medicaid	15,713	(25.3)	21,100	(24.2)	24,510	(25.8)	29,897	(24.9)	30,145	(19.6)	16,855	(16.8)	343	(22.6)
Commercial	15,007	(24.2)	22,784	(26.1)	23,518	(24.8)	31,295	(26.1)	73,135	(47.5)	41,436	(41.3)	394	(26.0)
No. of comorbid conditions														
No comorbidities	3,154	(5.1)	7,267	(8.3)	7,031	(7.4)	11,144	(9.3)	23,990	(15.6)	30,410	(30.3)	256	(16.9)
1 to 2	9,742	(15.7)	16,212	(18.6)	17,423	(18.4)	23,893	(19.9)	44,280	(28.7)	28,821	(28.7)	391	(25.8)
3 to 5	17,725	(28.5)	24,796	(28.4)	28,376	(29.9)	35,447	(29.5)	48,021	(31.2)	23,034	(22.9)	467	(30.8)
6 to 7	**11,517**	**(18.5)**	14,775	(16.9)	16,419	(17.3)	19,677	(16.4)	19,446	(12.6)	8,740	(8.7)	189	(12.5)
8 or more	**19,983**	**(32.2)**	24,277	(27.8)	25,674	(27.0)	29,968	(24.9)	18,346	(11.9)	9,385	(9.3)	214	(14.1)
income														
Low (<$36K)	**31,409**	**(50.6)**	42,535	(48.7)	48,813	(51.4)	59,939	(49.9)	63,408	(41.2)	40,211	(40.1)	674	(44.4)
Mod ($36K-$54K)	22,522	(36.3)	32,063	(36.7)	33,707	(35.5)	43,248	(36.0)	63,224	(41.0)	41,192	(41.0)	582	(38.4)
High (>$54K)	7,502	(12.1)	11,721	(13.4)	11,281	(11.9)	15,500	(12.9)	25,899	(16.8)	17,774	(17.7)	234	(15.4)
Missing	688	(1.1)	1,008	(1.2)	1,122	(1.2)	1,442	(1.2)	1,552	(1.0)	1,213	(1.2)	27	(1.8)

persons age 65 and older, with nearly double the proportion from the expected. This suggests that the onset of status is provoked by chronic underlying vascular problems that lead to onset of stroke or malignant neoplasms. Our published data (Malek et al., 2016) show that these conditions were underlying diagnosis in persons with status epilepticus. Similarly, we have demonstrated that stroke incidence was 2.5 times higher following adult-onset epilepsy suggesting occult cerebrovascular disease as potential etiology of epilepsy (Wannamaker et al., 2015).

[2] Period Prevalence of Epilepsy under various definitions 2000-2014

When the calculation of prevalence of epilepsy was centered on the SC census population of 2010 as the denominator (4.636 million individuals), the period prevalence of epilepsy over the 15 years ranged from 13.4 to 25.9 per 1,000 population depending on the definition of epilepsy (Table 3). Thus, the most conservative estimate of prevalence of epilepsy under rigid estimation is 13.4 per 1,000 populations (1.34%) while the most sensitive estimation indicates 25.9 per 1,000 populations (2.59%). Our estimate of prevalence of active and inactive epilepsy in SC based on BRFSS was 2% (Ferguson et al., 2008).

Table 3. Prevalence of epilepsy, 2000-2014 using the four groups

Epilepsy Group		Epilepsy Frequency	Rate/1,000
1	Definite Only	62,121	13.4
2	Definite and probable	87,327	18.8
3	Definite and possible	94,923	20.5
4	Definite, probable or possible	120,129	25.9

[3] Incidence of epilepsy from 2007 to 2012

Data used to calculate annual incidence were limited to individuals with a first diagnosis from 2007 to 2012. The use of 2007 as the beginning point allows the review of several years of data to ensure that the individual had no earlier diagnosis of epilepsy or seizure. Further, coding changes were implemented in 2006 that resulted in a significant switch from the use of seizure NOS diagnosis code (ICD-9-CM 780.39) to an epilepsy diagnosis code as described on page 16. Limiting the analysis to cases with first diagnosis of 2007 or later should avoid confusion based on coding practices. For epidemiological count of the incidence of epilepsy in a large population, the time needed to observe a seizure event is truly epilepsy requires a follow-up period in which a second seizure could be observed.

Thus, 2012 was chosen as the terminal point to accrue a minimum of 3-person years of observation. Table 4 shows the estimated annual incidence of epilepsy in SC.

Table 4. Annualized Incidence per 1,000 person-year of SC population at risk

Year	Definite Only	Definite+ Probable	Definite+ Possible	Definite+Probable+ Possible
2007	0.98	1.34	1.28	1.64
2008	1.00	1.55	1.29	1.84
2009	0.99	1.59	1.26	1.87
2010	0.95	1.57	1.20	1.82
2011	0.81	1.37	1.06	1.62
2012	0.70	1.24	0.95	1.50
Average	0.91	1.44	1.17	1.71

[4] Common Comorbidities of Epilepsy

The magnitude and distribution of common comorbid conditions were described for PWE, PWM and PWLF. Table 5 shows the prevalence of common comorbid conditions of epilepsy accrued over 15-years of data, which significantly reduced the proportion of individuals without comorbid conditions. In general, regardless of definition, the prevalence of the specific comorbidities examined were significantly higher in PWE than either PWM or PWLF. Although not shown in the table, statistical significance comparing the difference of the proportion of epilepsy with migraine, and epilepsy with LEF was the method we employed to declare the proportions are statistically significant and it was not based by the overlapping of the width of 95% confidence intervals (CI). Because of the large sample size under each cohort of the three conditions, there was adequate power, as could be seen from the narrow 95% CI, to observe significant differences even when changes are minor.

The prevalence of all 19 somatic comorbidities were much larger in PWE than in PWM. The magnitude was much larger in Alzheimer's disease, 11.20 times, and the smallest with gastric reflux (GERD) with 1.12 times larger than in PWE. Other comorbidities where the prevalence gap is wider include Parkinson's disease (6.67x), stroke (4.07x), vision loss (4.0x), and TBI (2.23x).

In regard to the prevalence of the 13 neurosomatic/psychiatric comorbidties, the magnitude of difference is much larger ranging the smallest in anxiety disorder (1.08x), to the largest with cognitive dysfunction (47.0x). Similar wide gap is observed with the prevalence of cerebral palsy (46x) intellectual disability (42x), and autism (17x) making these

comorbidties the signature comorbidties of epilepsy. Other comorbidities worth noting include schizophrenia (4.86x), alcoholism (3.46x), and personality disorders (2.2x)

In a polytomous logistic regression modeling (Table 6), the odds that epilepsy has stronger association with these comorbidities than migraine in reference to LEF after adjusting for demographic characteristics, and mortality was examined. The effect of each comorbid condition was evaluated on a three-level response in an ordinal scale using cumulative logit parameterization. The assumption of ordinality of the three-level response was tested and affirmed. This modeling technique has unique strength such as direct comparison of the confidence intervals between epilepsy and migraine for each comorbid conditions since the confidence intervals are constructed from pooled variance. Table 7 is the summary of the strength of association of comorbidities comparing epilepsy and migraine.

[5] Common Comorbidities of Epilepsy by Demographic Characteristics

A. Race and Ethnicity—significant differences exist among the race/ethnic groups in the 32 common comorbidities of epilepsy (Table 8). Of the 19 somatic comorbidities, blacks have significantly higher prevalence in 9 of the conditions: anemia, Alzheimer, CVD, diabetes, HIV/AIDS, nutritional deficiency, GI bleed, stroke, and vision loss (bolded font). Conversely, whites also have higher prevalence in 9 of the conditions: asthma/pulmonary diseases, GERD, hearing loss, intestinal problems, migraine, MS, osteoporosis, Parkinson's disease, and peptic ulcer (highlighted). Persons other than white or black have significantly lower prevalence of all somatic comorbidities excepting hearing loss, MS, and vision loss.

In regard to the 13 neurodevelopmental/psychiatric comorbidities, whites tend to have significantly higher prevalence in 7 of the conditions: anxiety, depression, drug abuse personality disorder, psychoses, suicidal ideation/attempt, and ADHD (highlighted). Conversely, blacks tend to have significantly higher comorbidities than whites in 5 of the conditions: alcoholism, schizophrenia, cerebral palsy, cognitive dysfunction, and ID. Significant differences existed in all neurodevelopmental comorbidities but autism spectrum disorders among the groups self-identified as other races/ethnicities. Overall, the prevalence of neurodevelopmental/psychiatric comorbidities are significantly lower in other races/ethnicities than white or blacks in all but cerebral palsy and cognitive dysfunction.

Table 5. Distribution of the common comorbidities of epilepsy by epilepsy diagnosis category and the comparison cohorts of migraine and lower extremity fracture, 2000-2014

Comorbidity Type	Epilepsy Diagnosis Category			Definite and probable	Definite and possible	Definite, probable, and possible	Comparison Cohorts	
	Definite (n=62,096)	Probable (n=25,166)	Possible (n=32,784)	(n=87,262)	(n=94,880)	(n=120,046)	Migraine (n=154,039)	Lower Extremity Fracture (n=100,360)
Somatic Disorders								
Anemia	35.2 (34.9-35.6)	22.6 (22.1-23.1)	27.5 (27.0-28.0)	31.6 (31.3-31.9)	32.6 (32.3-32.9)	30.5 (30.2-30.7)	19.5 (19.3-19.7)	15.1 (14.9-15.3)
Alzheimer Disease	5.6 (5.4-5.8)	4.4 (4.1- 4.7)	5.9 (5.7-6.2)	5.2 (5.1- 5.4)	5.7 (5.6-5.9)	5.4 (5.3-5.6)	0.5 (0.4-0.5)	1.9 (1.9-2.0)
Asthma/Pulmonary Dis.	41.8 (41.4-42.2)	29.7 (29.2-30.3)	35.7 (35.2-36.2)	38.3 (38.0-38.6)	39.7 (39.4-40.0)	37.6 (37.3-37.9)	32.8 (32.5-33.0)	23.8 (23.5-24.1)
Cardiovascular Disease	68.1 (67.7-68.4)	55.8 (55.2-56.4)	57.5 (57.0-58.0)	64.5 (64.2-64.9)	64.4 (64.1-64.7)	62.6 (62.3-62.9)	49.5 (49.2-49.7)	43.6 (43.3-43.9)
Diabetes	28.2 (27.8-28.6)	22.6 (22.0-23.1)	23.6 (23.1-24.0)	26.6 (26.3-26.9)	26.6 (26.3-26.9)	25.8 (25.5-26.0)	15.4 (15.2-15.6)	17.1 (16.8-17.3)
GI Bleed	13.2 (13.0-13.5)	7.6 (7.3- 7.9)	10.2 (9.8-10.5)	11.6 (11.4-11.8)	12.2 (12.0-12.4)	11.2 (11.0-11.4)	7.2 (7.1-7.3)	5.4 (5.3-5.5)
Hearing Loss	3.4 (3.2-3.5)	2.1 (2.0- 2.3)	2.1 (1.9-2.2)	3.0 (2.9- 3.1)	2.9 (2.8-3.0)	2.8 (2.7-2.9)	1.3 (1.3-1.4)	1.4 (1.3-1.5)
HIV/ AIDS	1.4 (1.3-1.5)	1.0 (0.9- 1.1)	1.6 (1.4-1.7)	1.3 (1.2- 1.4)	1.5 (1.4-1.6)	1.4 (1.3-1.4)	0.5 (0.5-0.5)	0.4 (0.4-0.5)
Intestinal Problems	45.4 (45.0-45.8)	31.2 (30.6-31.8)	32.9 (32.4-33.4)	41.3 (41.0-41.6)	41.1 (40.8-41.4)	39.0 (38.7-39.3)	37.6 (37.4-37.9)	27.2 (26.9-27.5)
Migraine	14.4 (14.1-14.6)	9.3 (8.9- 9.6)	7.3 (7.1-7.6)	12.9 (12.7-13.1)	11.9 (11.7-12.1)	11.4 (11.2-11.6)	100.0 ----	4.6 (4.5-4.8)
Multiple Sclerosis	1.2 (1.1-1.2)	0.8 (0.6- 0.9)	0.7 (0.6-0.7)	1.0 (1.0- 1.1)	1.0 (0.9-1.0)	0.9 (0.9-1.0)	0.8 (0.8-0.9)	0.4 (0.4-0.5)
Nutritional Deficiency	18.2 (17.9-18.6)	10.9 (10.5-11.3)	13.5 (13.2-13.9)	16.1 (15.9-16.4)	16.6 (16.4-16.9)	15.4 (15.2-15.6)	4.0 (3.9-4.1)	5.5 (5.4-5.6)
Osteoporosis	6.9 (6.7-7.1)	4.6 (4.4- 4.9)	4.6 (4.4-4.9)	6.3 (6.1- 6.4)	6.1 (6.0-6.3)	5.8 (5.7-5.9)	3.3 (3.2-3.4)	5.6 (5.4-5.7)
Parkinson's Disease	2.0 (1.9-2.1)	1.5 (1.4- 1.7)	2.0 (1.8-2.1)	1.9 (1.8- 2.0)	2.0 (1.9-2.1)	1.9 (1.8-2.0)	0.3 (0.3-0.3)	0.6 (0.5-0.6)
Peptic Ulcer	28.6 (28.3-29.0)	18.5 (18.1-19.0)	20.5 (20.1-21.0)	25.7 (25.4-26.0)	25.8 (25.5-26.1)	24.3 (24.1-24.5)	25.9 (25.7-26.1)	15.5 (15.3-15.7)
Gastric Reflux	41.7 (41.3-42.1)	29.0 (28.5-29.6)	26.3 (25.9-26.8)	38.1 (37.7-38.4)	36.4 (36.1-36.7)	34.9 (34.6-35.1)	37.3 (37.1-37.6)	24.5 (24.2-24.7)
Stroke	28.1 (27.7-28.4)	18.7 (18.2-19.2)	25.1 (24.6-25.6)	25.4 (25.1-25.7)	27.1 (26.8-27.3)	25.3 (25.1-25.6)	6.9 (6.7-7.0)	7.0 (6.9-7.2)
Traumatic Brain Injury	19.6 (19.3-19.9)	11.8 (11.4-12.2)	13.0 (12.6-13.3)	17.3 (17.1-17.6)	17.3 (17.1-17.5)	16.2 (15.9-16.4)	8.8 (8.7-9.0)	8.4 (8.2-8.6)
Vision Loss	4.0 (3.9-4.2)	1.9 (1.8- 2.1)	2.6 (2.4-2.7)	3.4 (3.3- 3.5)	3.5 (3.4-3.6)	3.2 (3.1-3.3)	1.0 (0.9-1.0)	1.1 (1.0-1.1)
Neurodevelopmental/Psychiatric Disorders								
Alcoholism	18.7 (18.4-19.1)	11.4 (11.0-11.8)	14.5 (14.1-14.9)	16.6 (16.4-16.9)	17.3 (17.0-17.5)	16.1 (15.8-16.3)	5.4 (5.3-5.5)	8.6 (8.5-8.8)
Anxiety	36.7 (36.3-37.1)	26.0 (25.5-26.5)	22.9 (22.4-23.3)	33.6 (33.3-33.9)	31.9 (31.6-32.2)	30.7 (30.4-30.9)	34.0 (33.8-34.2)	17.0 (16.7-17.2)
Depression	38.1 (37.7-38.5)	26.6 (26.0-27.1)	25.2 (24.7-25.7)	34.8 (34.5-35.1)	33.6 (33.3-33.9)	32.2 (31.9-32.4)	32.1 (31.9-32.3)	18.2 (18.0-18.4)
Drug Abuse	18.2 (17.9-18.5)	10.9 (10.5-11.3)	12.2 (11.8-12.5)	16.1 (15.9-16.3)	16.1 (15.9-16.4)	15.0 (14.8-15.2)	9.0 (8.8-9.1)	6.8 (6.7-7.0)
Personality Disorder	5.7 (5.5- 5.8)	3.0 (2.8- 3.2)	3.7 (3.5-3.9)	4.9 (4.7- 5.0)	5.0 (4.8-5.1)	4.6 (4.4-4.7)	2.6 (2.5-2.7)	1.2 (1.1-1.3)
Psychoses	24.4 (24.1-24.8)	15.8 (15.4-16.3)	16.3 (15.9-16.7)	21.9 (21.7-22.2)	21.6 (21.4-21.9)	20.4 (20.2-20.6)	12.3 (12.1-12.5)	7.0 (6.8-7.1)
Schizophrenia	6.8 (6.6- 7.0)	4.1 (3.8- 4.3)	4.2 (4.0-4.4)	6.0 (5.8- 6.1)	5.9 (5.7-6.0)	5.5 (5.4-5.6)	1.4 (1.3-1.4)	1.3 (1.3-1.4)
Suicidal Ideation/Attempt	11.6 (11.3-11.8)	6.8 (6.5- 7.1)	7.0 (67-7..3)	10.2 (10.0-10.4)	10.0 (9.8-10.2)	9.3 (9.2-9.5)	6.1 (6.0-6.2)	3.5 (3.4-3.6)
ADHD	4.4 (4.3- 4.6)	3.2 (3.0- 3.4)	4.6 (4.4-4.8)	4.1 (3.9- 4.2)	4.5 (4.3-4.6)	4.2 (4.1-4.3)	3.0 (2.9-3.1)	2.4 (2.3-2.5)
Autism Spectrum Disorder	1.7 (1.6- 1.8)	1.0 (0.9- 1.1)	0.9 (0.8-1.0)	1.5 (1.4- 1.6)	1.4 (1.3-1.5)	1.3 (1.3-1.4)	0.1 (0.0-0.1)	0.1 (0.1-0.1)
Cerebral Palsy	4.6 (4.5-4.8)	1.6 (1.5- 1.8)	1.9 (1.8-2.1)	3.8 (3.6- 3.9)	3.7 (3.6-3.8)	3.3 (3.2-3.4)	0.1 (0.1-0.1)	0.1 (0.1-0.2)
Cognitive Dysfunction	4.7 (4.5- 4.8)	1.3 (1.2- 1.5)	2.0 (1.9-2.2)	3.7 (3.6- 3.8)	3.8 (3.6-3.9)	3.3 (3.2-3.4)	0.1 (0.1-0.2)	0.2 (0.1-0.2)
Intellectual Disability	8.4 (8.2- 8.6)	3.1 (2.9- 3.3)	3.7 (3.5-4.0)	6.9 (6.7- 7.1)	6.8 (6.7-7.0)	6.0 (5.9-6.2)	0.2 (0.2-0.2)	0.5 (0.4-0.5)

Table 6. Association of common comorbidities in persons with epilepsy and migraine compared to lower extremity fracture controls

Comorbid Condition	Epilepsy		Migraine	
	Adjusted†		Adjusted†	
	OR	(95% CI)	OR	(95% CI)
Somatic Comorbidities				
Cardiovascular Disease	1.97	(1.92–2.03)	1.45	(1.42–1.49)
Intestinal Problems	1.54	(1.50–1.58)	1.59	(1.56–1.63)
Asthma/Pulmonary	1.61	(1.57–1.65)	1.53	(1.50–1.56)
Gastric Esophageal Reflux (GERD)	1.59	(1.55–1.63)	1.78	(1.74–1.81)
Anemia	1.91	(1.86–1.96)	1.18	(1.15–1.21)
Stroke	4.20	(4.06–4.34)	1.65	(1.59–1.71)
Diabetes	1.29	(1.26–1.33)	0.89	(0.86–0.91)
Peptic Ulcer	1.57	(1.52–1.61)	1.78	(1.73–1.82)
Traumatic Brain Injury	1.59	(1.54–1.67)	0.81	(0.78–0.83)
Nutritional Deficiency	2.27	(2.18–2.37)	0.83	(0.79–0.88)
GI Bleed	1.80	(1.72–1.87)	1.42	(1.36–1.48)
Osteoporosis	0.87	(0.83–0.91)	0.65	(0.62–0.69)
Vision Loss	2.47	(2.28–2.68)	1.33	(1.22–1.45)
Hearing Loss	1.79	(1.67–1.93)	1.42	(1.31–1.53)
Parkinson’s Disease	2.45	(2.20–2.73)	1.01	(0.88–1.16)
HIV/ AIDS	2.17	(1.91–2.45)	1.13	(0.98–1.29)
Multiple Sclerosis	2.25	(1.98–2.54)	1.68	(1.50–1.89)
Migraine	3.37	(3.23–3.52)		--
Psychiatric & Neurodevelopmental				
Depression	2.12	(2.06–2.17)	1.62	(1.59–1.66)
Anxiety	2.29	(2.23–2.35)	1.87	(1.82–1.91)
Psychoses	3.17	(3.06–3.28)	1.51	(1.46–1.56)
Schizophrenia	3.15	(2.94–3.37)	0.85	(0.78–0.92)
Personality Disorder	3.61	(3.34–3.89)	1.67	(1.55–1.80)
Alcoholism	1.77	(1.71–1.82)	0.60	(0.58–0.62)
Drug Abuse	2.37	(2.29–2.45)	1.19	(1.15–1.23)
Suicidal Ideation/Attempt	2.95	(2.81–3.10)	1.44	(1.38–1.52)
Alzheimer’s Dementia	2.19	(2.05–2.33)	0.61	(0.56–0.68)
Intellectual Disability	12.88	(11.59–14.30)	0.48	(0.41–0.57)
Cognitive Dysfunction	28.09	(23.33–33.82)	1.77	(1.38–2.26)
Cerebral Palsy	2.46	(2.32−2.59)	0.78	(0.74-0.82)
ADHD	2.31	(2.16–2.47)	1.56	(1.46–1.67)
Autism Spectrum Disorder	22.15	(16.77–29.26)	1.21	(0.81–1.80)

†Adjusted for Age, Race, Gender, Insurance Status, and Mortality Status and number of comorbid conditions.

Table 7. Summary of Associations of Epilepsy and Migraine with Specific Comorbid Conditions compared to Controls* by their the Strengths of Association

	Adjustment	Profoundly Strong OR ≥10	Very Strong 2.0 ≤ OR < 10.0	Strong 1.5 ≤ OR < 2.0	Weak 1.0 < OR < 1.5	Neutral or Inverse OR ≤ 1.0
Epilepsy	Age, Race, Gender, Insurance Status, Mortality Status	Intellectual Disability, Cognitive Dysfunction, ASD	Stroke, Nutritional Deficiency, Vision loss, Parkinson's disease, HIV/AIDS, MS, Migraine, Depression, Anxiety, Psychoses, Schizophrenia, Personality Disorder, Drug Abuse, Suicidal Ideation, Alzheimer's , ADHD, Cerebral Palsy	Cardiovascular, Intestinal, Asthma, Gastric reflux, Anemia, Peptic ulcer, TBI, GI bleed, Hearing loss, Alcoholism	Diabetes	Osteoporosis
Migraine	Age, Race, Gender, Insurance Status, Mortality Status			Intestinal, Asthma, Gastric reflux, Stroke, Peptic Ulcer, MS, Depression, Anxiety, Personality disorder Psychoses, Cognitive dysfunction, ADHD	Cardiovascular, Anemia, Vision loss, Hearing loss, GI bleed, Drug abuse, Suicidal ideation, ASD	Diabetes, TBI, Nutritional Deficiency, Osteoporosis, Parkinson's, HIV/AIDS, Schizophrenia, Alcoholism, Alzheimer's, Intellectual Disability, Cerebral Palsy

*Control group = Persons with Lower extremity Fractures (Tibia, Fibula, and Ankle) with minimal injury to other body regions

Table 8. Distribution of Comorbidities by race, ethnicity and major diagnostic categories of epilepsy diagnosis

	Definite Epilepsy						Definite and Probable Epilepsy					
	White	Black		Other			White	Black		Other		
Somatic Disorders												
Anemia	11,500 (30.6%)	**10,175 (43.5%)**	W	138 (19.2%)	W	B	14,782 (27.0%)	12,505 (41.0%)	W	297 (14.2%)	W	B
Alzheimers Disease	2,063 (5.5%)	**1,387 (5.9%)**	W	15 (2.3%)	W	B	2,850 (5.2%)	1,705 (5.6%)		23 (1.7%)	W	B
Asthma/Pulmonary Disease	16,248 (43.2%)	9,389 (40.2%)	W	200 (27.4%)	W	B	21,349 (39.0%)	11,656 (38.2%)		288 (21.0%)	W	B
Cardiovascular Disease	24,830 (66.0%)	**16,982 (72.6%)**	W	309 (42.5%)	W	B	34,131 (62.4%)	21,508 (70.5%)	W	489 (35.1%)	W	B
Diabetes	9,134 (24.3%)	**8,186 (35.0%)**	W	127 (17.9%)	W	B	12,483 (22.8%)	10,415 (34.1%)	W	204 (15.3%)	W	B
Gastric Reflux (GERD)	16,605 (44.1%)	8,992 (38.4%)	W	188 (28.5%)	W	B	21,789 (39.8%)	11,022 (36.1%)	W	253 (20.4%)	W	B
GI Bleed	4,896 (13.0%)	**3,243 (13.9%)**	W	50 (6.6%)		B	6,167 (11.3%)	3,877 (12.7%)	W	58 (4.2%)	W	B
Hearing Loss	1,440 (3.8%)	613 (2.6%)	W	21 (2.9%)			1,878 (3.4%)	706 (2.3%)	W	27 (2.1%)	W	
HIV/ AIDS	211 (0.6%)	**666 (2.8%)**	W	5 (1.2%)	W	B	282 (0.5%)	840 (2.8%)	W	8 (1.0%)	W	B
Intestinal Problems	17,393 (46.2%)	10,503 (44.9%)	W	187 (27.0%)	W	B	22,785 (41.6%)	12,858 (42.2%)		277 (20.8%)	W	B
Migraine	6,542 (17.4%)	2,275 (9.7%)	W	58 (9.5%)	W		8,331 (15.2%)	2,788 (9.1%)	W	74 (6.9%)	W	B
Multiple Sclerosis (MS)	490 (1.3%)	222 (0.9%)	W	6 (0.8%)			635 (1.2%)	263 (0.9%)	W	11 (0.7%)		
Nutritional Deficiency	6,181 (16.4%)	**5,039 (21.6%)**	W	78 (10.7%)	W	B	7,847 (14.3%)	6,098 (20.0%)	W	103 (7.2%)	W	B
Osteoporosis	3,443 (9.2%)	823 (3.5%)	W	26 (2.6%)	W		4,429 (8.1%)	991 (3.2%)	W	35 (2.0%)	W	B
Parkinson's Disease	905 (2.4%)	347 (1.5%)	W	9 (1.0%)	W		1,199 (2.2%)	433 (1.4%)	W	13 (0.7%)	W	B
Peptic Ulcer	10,942 (29.1%)	6,660 (28.5%)		113 (16.2%)	W	B	14,113 (25.8%)	8,106 (26.6%)	W	147 (11.5%)	W	B
Stroke	9,525 (25.3%)	**7,747 (33.1%)**	W	125 (16.5%)	W	B	12,492 (22.8%)	9,433 (30.9%)	W	172 (12.0%)	W	B
Traumatic Brain Injury	8,152 (21.7%)	3,876 (16.6%)	W	76 (12.3%)	W	B	10,349 (18.9%)	4,604 (15.1%)	W	110 (9.0%)		B
Vision Loss	1,336 (3.6%)	**1,117 (4.8%)**	W	27 (4.3%)			1,626 (3.0%)	1,308 (4.3%)	W	35 (2.8%)		
Neurodevelopmental/Psychiatric Disorders												
Alcoholism	6,358 (16.9%)	**5,192 (22.2%)**	W	59 (8.5%)	W	B	8,211 (15.0%)	6,172 (20.2%)	W	88 (6.9%)	W	B
Anxiety	16,689 (44.4%)	5,848 (25.0%)	W	145 (22.1%)	W		21,879 (40.0%)	7,110 (23.3%)	W	207 (16.7%)	W	B
Depression	17,095 (45.5%)	6,333 (27.1%)	W	138 (21.4%)	W	B	22,302 (40.7%)	7,711 (25.3%)	W	204 (16.9%)	W	B
Drug Abuse	7,193 (19.1%)	4,013 (17.2%)	W	63 (8.4%)	W	B	9,138 (16.7%)	4,785 (15.7%)	W	82 (6.2%)	W	B
Personality Disorder	2,665 (7.1%)	815 (3.5%)	W	17 (2.6%)	W		3,277 (6.0%)	950 (3.1%)	W	23 (2.0%)	W	B
Psychoses	10,435 (27.7%)	4,579 (19.6%)	W	99 (14.3%)	W	B	13,422 (24.5%)	5,515 (18.1%)	W	136 (10.8%)	W	B
Schizophrenia	2,115 (5.6%)	**2,045 (8.7%)**	W	23 (3.4%)	W	B	2,653 (4.8%)	2,518 (8.3%)	W	35 (2.9%)	W	B
Suicidal Ideation/Attempt	5,203 (13.8%)	1,921 (8.2%)	W	39 (5.8%)	W	B	6,508 (11.9%)	2,308 (7.6%)	W	51 (4.3%)	W	B
ADHD	2,000 (5.3%)	708 (3.0%)	W	25 (3.0%)	W		2,627 (4.8%)	867 (2.8%)	W	34 (2.3%)	W	
Autism Spectrum Disorder	646 (1.7%)	372 (1.6%)		9 (1.8%)			808 (1.5%)	453 (1.5%)		14 (1.4%)		
Cerebral Palsy	1,652 (4.4%)	**1,132 (4.8%)**	W	51 (7.9%)	W	B	1,922 (3.5%)	1,254 (4.1%)	W	63 (5.3%)	W	B
Cognitive Dysfunction	1,544 (4.1%)	**1,243 (5.3%)**	W	53 (10.6%)	W	B	1,738 (3.2%)	1,365 (4.5%)	W	63 (6.8%)	W	B
Intellectual Disability (ID)	2,775 (7.4%)	**2,383 (10.2%)**	W	33 (6.7%)		B	3,218 (5.9%)	2,693 (8.8%)	W	51 (5.0%)		B

B = statistically significant difference than Black W =statistically significant difference than White

B. Urban-Rural Differences—Among PWE, significantly more blacks than whites live in underserved rural South Carolina. In 11 of the 19 (58%) somatic comorbidities (bold font), persons residing in rural parts of the state have significantly higher prevalence of these conditions (Table 9). In 4 of the 19 comorbid conditions (21%) that are highlighted, PWE residing in urban areas have higher prevalence of these comorbidities. No difference existed in the prevalence of 4 of the comorbidities (HIV/AIDS, osteoporosis, Parkinson's disease, vision loss) between urban and rural residence. Conversely, only in 2 of the 13 neurodevelopmental/psychiatric comorbidities (cerebral palsy and ID), the prevalence is significantly higher among rural residents while in 69% of these comorbidities, urban residents have higher prevalence. Taken together, the preponderance of comorbidities that require routine clinical maintenance are significantly higher among PWE in rural areas while neuro developmental comorbidities that require psychiatric care tend to be higher among urban residents. Whether or not this distribution emanated from self-selection or resulted from random occurrence has yet to be determined.

C. Socioeconomic Differences—we approximated socioeconomic status (SES) with median household income based on zip code of the place of residence with the longest duration of stay. A three-level strata of SES was derived as described in the method section of this report (pp 14-15). The frequency of occurrence of comorbidities were cross classified by the SES strata (Table 10). Among persons with definite epilepsy, 50.6% were low SES with household income of less than $36,000 for a family of 4. This is 150% of the federal poverty line (FPL) while the median household income of SC in 2012 was $44,500. Therefore the upper limit of the low income strata in our cohort of PWE is 19% below the state median household income and 30% below US median household income. This suggests that half of the PWE in SC are in poverty.

PWE in low income strata have higher burden of 4 of the 19 somatic comorbidities—anemia, asthma/pulmonary diseases, HIV/AIDS, and vision loss—than either of the upper two strata of SES. A pronounced burden in 9 of the 13 neurodevelopmental/psychiatric comorbidities are found in the low SES group that include—alcoholism, drug abuse, schizophrenia, suicidal ideation, ADHD, autism, cerebral palsy, cognitive dysfunction, and intellectual disability. Since an overwhelming proportion of PWE in low SES are under Medicaid insurance, the low count in somatic comorbidities is mostly attributable to limited investigation of clinical conditions other than the presenting illness, a pattern we observed

Table 9. Distribution of epilepsy by urban-rural place of residence and diagnosis category

	Definite Epilepsy			Definite and Probable Epilepsy		
	Urban	Rural	*P*-value	Urban	Rural	*P*-value*
Somatic Disorders						
Anemia	14,137 (34.0%)	**7,546 (39.0%)**	<.0001	17,732 (31.0%)	9,459 (36.6%)	<.0001
Alzheimer's Disease	2,213 (5.3%)	**1,234 (6.4%)**	<.0001	2,944 (5.1%)	1,580 (6.1%)	<.0001
Asthma/Pulmonary Disease	17,206 (41.4%)	**8,409 (43.4%)**	<.0001	22,081 (38.5%)	10,668 (41.3%)	<.0001
Cardiovascular Disease	27,881 (67.0%)	**13,798 (71.3%)**	<.0001	36,714 (64.1%)	17,982 (69.6%)	<.0001
Diabetes	11,198 (26.9%)	**6,085 (31.4%)**	<.0001	14,737 (25.7%)	7,906 (30.6%)	<.0001
Gastric Reflux	17,255 (41.5%)	**8,407 (43.4%)**	<.0001	22,006 (38.4%)	10,726 (41.5%)	<.0001
GI Bleed	5,376 (12.9%)	**2,769 (14.3%)**	<.0001	6,637 (11.6%)	3,393 (13.1%)	<.0001
Hearing Loss	1,469 (3.5%)	603 (3.1%)	0.0085	1,832 (3.2%)	769 (3.0%)	0.0896
HIV/ AIDS	584 (1.4%)	299 (1.5%)	0.1742	749 (1.3%)	375 (1.5%)	0.0962
Intestinal Problems	18,759 (45.1%)	**9,184 (47.5%)**	<.0001	24,024 (41.9%)	11,612 (45.0%)	<.0001
Migraine	6,283 (15.1%)	2,539 (13.1%)	<.0001	7,882 (13.8%)	3,198 (12.4%)	<.0001
Multiple Sclerosis	513 (1.2%)	199 (1.0%)	0.0285	636 (1.1%)	251 (1.0%)	0.0717
Nutritional Deficiency	7,309 (17.6%)	**3,914 (20.2%)**	<.0001	9,074 (15.8%)	4,814 (18.6%)	<.0001
Osteoporosis	2,910 (7.0%)	1,328 (6.9%)	0.5491	3,680 (6.4%)	1,678 (6.5%)	0.6997
Parkinson's Disease	829 (2.0%)	418 (2.2%)	0.1745	1,080 (1.9%)	538 (2.1%)	0.0569
Peptic Ulcer	11,183 (26.9%)	**6,448 (33.3%)**	<.0001	14,143 (24.7%)	8,068 (31.2%)	<.0001
Stroke	11,183 (26.9%)	**6,072 (31.4%)**	<.0001	14,103 (24.6%)	7,633 (29.5%)	<.0001
Traumatic Brain Injury	8,456 (20.3%)	3,589 (18.5%)	<.0001	10,470 (18.3%)	4,400 (17.0%)	<.0001
Vision Loss	1,657 (4.0%)	823 (4.3%)	0.1166	1,965 (3.4%)	978 (3.8%)	0.0103
Neurodevelopmental/Psychiatric Disorders						
Alcoholism	7,821 (18.8%)	3,687 (19.0%)	0.4584	9,715 (17.0%)	4,511 (17.5%)	0.0756
Anxiety	15,756 (37.9%)	6,744 (34.8%)	<.0001	20,201 (35.3%)	8,577 (33.2%)	<.0001
Depression	16,489 (39.6%)	6,915 (35.7%)	<.0001	21,079 (36.8%)	8,746 (33.9%)	<.0001
Drug Abuse	7,685 (18.5%)	3,476 (18.0%)	0.129	9,548 (16.7%)	4,231 (16.4%)	0.2969
Personality Disorder	2,574 (6.2%)	907 (4.7%)	<.0001	3,124 (5.5%)	1,095 (4.2%)	<.0001
Psychoses	10,732 (25.8%)	4,288 (22.2%)	<.0001	13,440 (23.5%)	5,380 (20.8%)	<.0001
Schizophrenia	2,911 (7.0%)	1,250 (6.5%)	0.0142	3,606 (6.3%)	1,551 (6.0%)	0.107
Suicidal Ideation/Attempt	5,159 (12.4%)	1,980 (10.2%)	<.0001	6,383 (11.1%)	2,424 (9.4%)	<.0001
ADHD	2,045 (4.9%)	671 (3.5%)	<.0001	2,640 (4.6%)	852 (3.3%)	<.0001
Autism Spectrum Disorder	781 (1.9%)	252 (1.3%)	<.0001	945 (1.6%)	311 (1.2%)	<.0001
Cerebral Palsy	1,875 (4.5%)	**976 (5.0%)**	0.0035	2,123 (3.7%)	1,083 (4.2%)	0.0008
Cognitive Dysfunction	2,156 (5.2%)	734 (3.8%)	<.0001	2,386 (4.2%)	821 (3.2%)	<.0001
Intellectual Disability	3,251 (7.8%)	**1,961 (10.1%)**	<.0001	3,722 (6.5%)	2,246 (8.7%)	<.0001

in other clinical conditions such as TBI and TSCI. Conversely, higher counts of neurodevelopmental/psychiatric comorbidities are recognized because these conditions invoke service eligibility such as special education, Medicare, psychiatric care, substance abuse treatment.

13.1% of PWE are in the highest SES. They have the lowest proportion of comorbidities excepting hearing loss, multiple sclerosis, and TBI where no significant difference existed among the three groups. However there were still five neurodevelopmental/psychiatric comorbidities in which PWE in middle income have fewer counts than those in the highest household income — ADHD, autism, cerebral palsy, cognitive dysfunction, and intellectual disability. These comorbid conditions are primarily the result of inheritable disorders to which SES may have little influence. However, the higher prevalence in low SES may suggest some type of interaction between epilepsy and poverty, perhaps suggesting some of these comorbidities may have been potentiated by economic deprivation. Overall, the preponderance of comorbid conditions among PWE in low SES may suggest further investigation to identify what could be eliminated through public health intervention.

[5] Association of demographic and risk characteristics with epilepsy and migraine

Among the research questions the project investigated to establish the association of risk with epilepsy is age, gender, race/ethnicity, health insurance, categories of comorbidity, and mortality (Table 11). We used PWM and PWLF as comparators, the latter as a proxy for the general population. The analysis was conducted with polytomous logistic regression that allows PWLF serve as the control group for both epilepsy and migraine such that the parameters can be internally compared because the variances are pooled.

PWE were 1.80 times more likely to have been deceased than PWLF while PWM were about less than half likely to have been deceased compared to PWLF. The absolute net risk increase of mortality from all causes is 133% higher in PWE than PWM after adjusting for the variables in the model including the effect of comorbid conditions. In particular, risk of death in PWE is influenced by the number of comorbid diseases they have with demonstrable dose response (Table 12). These findings indicate that epilepsy is not only a disease that affects quality of health but also increases the risk of death.

Table 10. Distribution of Comorbidities by Median Household Income among persons with Definite and Definite with Probable Epilepsy

	Definite Epilepsy (n=62,121)			Definite and Probable Epilepsy		
	Low Income (<$36K)	Middle Income ($36K-$54K)	High Income (>$54K)	Low Income (<$36K)	Middle Income ($36K-$54K)	High Income (>$54K)
Somatic Disorders	N=(31,409)	N=(22,522)	N=(8,190)			
Anemia	**11,302 (36.0%)**	7,999 (35.5%)	2,306 (30.7%) L M	13,992 (32.9%)	10,202 (31.8%) L	3,032 (25.9%) L M
Alzheimers Disease	1,396 (4.4%)	1,571 (7.0%) L	442 (5.9%) L M	1,784 (4.2%)	2,107 (6.6%) L	613 (5.2%) L M
Asthma/Pulmonary Disease	**13,709 (43.6%)**	9,473 (42.1%) L	2,465 (32.9%) L M	17,434 (41.0%)	12,313 (38.4%) L	3,315 (28.3%) L M
Cardiovascular Disease	20,626 (65.7%)	16,229 (72.1%) L	4,933 (65.8%) M	26,672 (62.7%)	21,990 (68.6%) L	7,028 (60.0%) L M
Diabetes	8,793 (28.0%)	6,729 (29.9%) L	1,791 (23.9%) L M	11,427 (26.9%)	8,966 (28.0%) L	2,526 (21.6%) L M
Gastric Reflux	12,841 (40.9%)	9,819 (43.6%) L	2,970 (39.6%) M	16,148 (38.0%)	12,758 (39.8%) L	3,958 (33.8%) L M
GI Bleed	4,187 (13.3%)	3,071 (13.6%)	868 (11.6%) L M	5,087 (12.0%)	3,833 (12.0%)	1,101 (9.4%) L M
Hearing Loss	993 (3.2%)	784 (3.5%) L	276 (3.7%)	1,231 (2.9%)	1,002 (3.1%)	355 (3.0%)
HIV/ AIDS	**595 (1.9%)**	219 (1.0%) L	66 (0.9%) L	761 (1.8%)	280 (0.9%) L	90 (0.8%) L
Intestinal Problems	13,811 (44.0%)	10,731 (47.6%) L	3,321 (44.3%) M	17,270 (40.6%)	13,915 (43.4%) L	4,466 (38.1%) L M
Migraine	4,300 (13.7%)	3,548 (15.8%) L	992 (13.2%) M	5,380 (12.6%)	4,509 (14.1%) L	1,271 (10.8%) L M
Multiple Sclerosis	325 (1.0%)	304 (1.3%) L	84 (1.1%)	398 (0.9%)	390 (1.2%) L	111 (0.9%)
Nutritional Deficiency	5,798 (18.5%)	4,296 (19.1%)	1,094 (14.6%) L M	7,092 (16.7%)	5,369 (16.7%)	1,440 (12.3%) L M
Osteoporosis	1,632 (5.2%)	1,920 (8.5%) L	676 (9.0%) L	2,034 (4.8%)	2,474 (7.7%) L	875 (7.5%) L
Parkinson's Disease	496 (1.6%)	585 (2.6%) L	163 (2.2%) L	627 (1.5%)	769 (2.4%) L	226 (1.9%) L M
Peptic Ulcer	9,121 (29.0%)	6,683 (29.7%)	1,776 (23.7%) L M	11,318 (26.6%)	8,548 (26.7%)	2,338 (19.9%) L M
Stroke	8,262 (26.3%)	6,926 (30.8%) L	2,056 (27.4%) M	10,288 (24.2%)	8,868 (27.7%) L	2,746 (23.4%) M
Traumatic Brain Injury	6,123 (19.5%)	4,449 (19.8%)	1,447 (19.3%)	7,497 (17.6%)	5,555 (17.3%)	1,898 (16.2%) L M
Vision Loss	**1,413 (4.5%)**	784 (3.5%) L	276 (3.7%) L	1,677 (3.9%)	951 (3.0%) L	331 (2.8%) L
Neurodevelopmental/Psychiatric Disorders						
Alcoholism	**6,676 (21.3%)**	3,856 (17.1%) L	1,022 (13.6%) L M	8,172 (19.2%)	4,832 (15.1%) L	1,399 (11.9%) L M
Anxiety	11,114 (35.4%)	8,987 (39.9%) L	2,469 (32.9%) L M	14,047 (33.0%)	11,625 (36.3%) L	3,386 (28.9%) L M
Depression	11,306 (36.0%)	9,364 (41.6%) L	2,762 (36.8%) M	14,254 (33.5%)	12,113 (37.8%) L	3,703 (31.6%) L M
Drug Abuse	**6,425 (20.5%)**	3,806 (16.9%) L	989 (13.2%) L M	7,913 (18.6%)	4,732 (14.8%) L	1,299 (11.1%) L M
Personality Disorder	1,903 (6.1%)	1,215 (5.4%) L	361 (4.8%) L	2,304 (5.4%)	1,470 (4.6%) L	456 (3.9%) L M
Psychoses	7,737 (24.6%)	5,634 (25.0%)	1,650 (22.0%) L M	9,663 (22.7%)	7,110 (22.2%)	2,203 (18.8%) L M
Schizophrenia	**2,497 (7.9%)**	1,337 (5.9%) L	309 (4.1%) L M	3,108 (7.3%)	1,643 (5.1%) L	405 (3.5%) L M
Suicidal Ideation/Attempt	3,951 (12.6%)	2,477 (11.0%) L	696 (9.3%) L M	4,851 (11.4%)	3,075 (9.6%) L	897 (7.7%) L M
ADHD	1,663 (5.3%)	718 (3.2%) L	345 (4.6%) L M	2,097 (4.9%)	944 (2.9%) L	481 (4.1%) L M
Autism Spectrum Disorder	698 (2.2%)	203 (0.9%) L	128 (1.7%) L M	855 (2.0%)	263 (0.8%) L	163 (1.4%) L M
Cerebral Palsy	1,944 (6.2%)	637 (2.8%) L	253 (3.4%) L M	2,179 (5.1%)	754 (2.4%) L	313 (2.7%) L
Cognitive Dysfunction	2,038 (6.5%)	542 (2.4%) L	303 (4.0%) L M	2,269 (5.3%)	613 (1.9%) L	339 (2.9%) L M
Intellectual Disability	3,321 (10.6%)	1,337 (5.9%) L	468 (6.2%) L	3,808 (9.0%)	1,548 (4.8%) M	541 (4.6%) L

Table 11. Odds of selected risk characteristics in persons with epilepsy, migraine, compared to lower extremity fracture controls.

Characteristics	Epilepsy (n=62,188)	Migraine (n=154,039)
	OR† (95% CI)	OR† (95% CI)
Mortality Status		
Deceased	1.80 (1.74–1.86)	0.54 (0.51–0.56)
Alive	1.00	1.00
Somatic or Psychiatric/Neurodevelopmental Comorbidity		
Both	5.44 (5.25–5.63)	2.49 (2.42–2.55)
Psych/Neurodev. Only	3.70 (3.51–3.90)	1.51 (1.44–1.58)
Somatic Only	2.11 (2.04–2.18)	1.89 (1.84–1.94)
None	1.00	1.00
Age Group		
Mean Age (s.d.)*	41.6 (±22.5)	35.9 (±22.7)
0–5	2.38 (2.25–2.52)	0.87 (0.81–0.93)
6−12	1.17 (1.10–1.24)	2.27 (2.15–2.40)
13−18	1.45 (1.37–1.53)	4.20 (3.98–4.42)
19−34	1.70 (1.62–1.77)	5.84 (5.58–6.12)
35-64	1.32 (1.27–1.38)	2.92 (2.80–3.04)
65 & Older	1.00	1.00
Race/Ethnicity		
Black	1.47 (1.43–1.51)	0.90 (0.88–0.92)
Hispanic	1.27 (1.14–1.42)	0.92 (0.86–0.99)
Other	1.18 (1.08–1.29)	0.80 (0.74–0.88)
White	1.00	1.00
Gender		
Male	1.13 (1.11–1.15)	0.28 (0.28–0.29)
Female	1.00	1.00
Payer		
Uninsured	0.76 (0.73–0.78)	0.77 (0.75–0.79)
Medicare	1.79 (1.74–1.85)	0.67 (0.65–0.69)
Medicaid	1.76 (1.71–1.81)	0.94 (0.92–0.96)
Commercial	1.00	1.00

†Adjusted for all covariables in the model
* P<0.01 significantly different

Table 12. Hazard Ratio of mortality by number of comorbid condition and the definition of epilepsy

Counts of Comorbidities	Definite n=62,121	DefProb n=87,262	DefPoss n=94,880	DefProbPoss n=120,046
	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
No comorbidities	Referent	Referent	Referent	Referent
1 to 2	2.01 (1.56- 2.59)	2.16 (1.77- 2.63)	2.14 (1.86- 2.46)	2.29 (2.02- 2.61)
3 to 5	3.79 (2.96- 4.86)	3.87 (3.20- 4.69)	2.91 (2.54- 3.34)	3.30 (2.91- 3.74)
6 to 7	4.48 (3.49- 5.74)	4.51 (3.73- 5.46)	2.77 (2.41- 3.18)	3.23 (2.85- 3.67)
8 or more	4.50 (3.52- 5.77)	4.40 (3.64- 5.33)	2.41 (2.10- 2.77)	2.84 (2.50- 3.22)
At least one comorbidity	3.69 (2.89- 4.72)	3.69 (3.06- 4.46)	2.56 (2.23- 2.93)	2.29 (2.02- 2.61)

Despite the similarities of epilepsy and migraine in clinical symptomatology and paroxysms of attack, there are also discordant associations with comorbidities. PWE have 45% and 12% absolute net increase to have been with psychiatric/neurodevelomental comorbidities and somatic comorbidities, respectively, after adjusting for the covariables in the model. Thus epilepsy has a far-reaching consequence in health status even when compared with a closely related chronic disease like migraine. It is also important to note that, in SC PWE are 1.47 times more likely to be black than white. However, the underlying reasons why this higher odds occur among blacks than among whites has yet to be investigated.

Dissemination

During the tenure of the CDC awards on Epilepsy Surveillance including quantifying the burden of comorbidities, 17 manuscripts were published, 8 manuscripts are in progress and on track to be published by the end of summer 2017. Topical areas of published articles and presentations are as follows:

- Comorbidities of epilepsy
- Mortality in children and adolescents with epilepsy (2 manuscripts)
- Mortality in people with epilepsy
- Mortality following status epilepticus in individuals with and without epilepsy
- Risk of venous thromboembolism in people with epilepsy
- Risk of myocardial infarction in people with epilepsy
- Risk of stroke in people with adult-onset epilepsy

- Risk of severe and repetitive traumatic brain injury (TBI) in persons with epilepsy
- Risk of epilepsy after TBI
- Self-reported prevalence of epilepsy in SC
- Neurodevelopmental/mental health comorbidities of epilepsy <18 years of age
- Behavioral health in young adults with epilepsy and implications for transition of care
- Determining patients' needs through partnership with SAFE

Peer Reviewed Publications

1. Wagner J, Wilson D, Kellermann T; Smith G; Malek A; Wannamaker B; Selassie A. Behavioral Health in Young Adults with Epilepsy: Implications for Transition of Care. *Epilepsy Behav.* 2016 Dec. 65:7-12. PMID: 27829187
2. Malek AM, Wilson DA, Martz GU, Wannamaker BB, Wagner JL, Smith G, Edwards JC, Selassie AW. Mortality following status epilepticus in persons with and without epilepsy. *Seizure*. 2016 Sep 3;42:7-13. PMID: 27636327.
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Letter to the editor, Commentary, and Collaborative Publications**:**

1. Wannamaker BB, Wilson DA, Malek AM, Selassie AW. Response to "Vascular Precursor Epilepsy - Old wine in new skins?". *Epilepsy Behav.* 2015 Jul;48:105. doi: 10.1016/j.yebeh.2015.03.034. Epub 2015 May 9. PMID: 25972131.
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3. Thurman DJ, Beghi E, Begley CE, Berg A, ...,Selassie AW,...,Tomson T, Wiebe S. Standards for Epidemiologic Studies and Surveillance of Epilepsy. ILAE Epidemiology Commission Report. *Epilepsia.* 52(Suppl. 7):1, 2011

Abstracted Poster Presentations at National and International Conferences

1. Wilson DA, Selassie AW. Mortality disparity in people with epilepsy by race, South Carolina, 2000-2013. American Epilepsy Society, Philadelphia, PA. December 7, 2015.
2. Wilson DA, Wannamaker BB, Malek AM, Selassie AW. Myocardial infarction after adult-onset epilepsy: a population-based retrospective cohort study. American College of Epidemiology. Atlanta, GA. September 28, 2015.
3. Wilson DA, Selassie AW. Trends in healthcare charges and length of hospital stay for people with epilepsy, 2000-2013. Presented at the American Epilepsy Society Annual Conference in Seattle, Dec 7, 2014. AES 2014 Annual Meeting Abstracts. Epilepsy Currents: January/February 2015, Vol. 15, No. s1, pp. 1-578.
4. Malek A, Wilson D, Wannamaker B., Newman R, Vena J, Selassie A. Patterns of comorbidity in pregnant women with epilepsy. Presented at the American Epilepsy Society Annual Conference in Seattle, Dec 7, 2014. AES 2014 Annual Meeting Abstracts. Epilepsy Currents: January/February 2015, Vol. 15, No. s1, pp. 1-578.
5. Malek AM, Wilson DA, Wannamaker BB, Martz GU, Smith GG, Selassie AW. Status Epilepticus and Subsequent Epilepsy. Annals of Epidemiology 2014;24(9):699-7005.
6. Malek AM, Wilson DA, Wannamaker BB, Lackland DT, Selassie AW. The Hazard of Subsequent Stroke in Adult-Onset Epilepsy. American Epilepsy Society, Sun Dec 8 2013, Washington, D.C.
7. Wilson DA, Selassie AW. Risk of severe and repetitive traumatic brain injury in persons with epilepsy: A population-based case-control study. American Epilepsy Society, Sun Dec 8 2013, Washington, D.C.

8. Martz GU, Wilson DA, Malek AM, Selassie AW. Risk of venous thromboembolism among people with epilepsy: a population-based retrospective cohort study. American Epilepsy Society, Sun Dec 8 2013, Washington, D.C.
9. Wagner JL, Wilson DA, Smith GG, Selassie0020AW. Psychiatric Disorders in Youth with Epilepsy: A Comparison to Healthy Controls. American Epilepsy Society, Sun Dec 8 2013, Washington, D.C.
10. Sun W, Selassie A, Pritchard P. Ambulatory Health Care Visits for Epilepsy in the United States in 2006-2008, poster presentation at the American Academy of Neurology 65th Annual Meeting, San Diego, CA, March 16 – 23, 2013.
11. Wilson DA, Smith GM, Wannamaker BB, Selassie AW. Prevalence of Epilepsy and Socioeconomic Factors, South Carolina, 2006-2010. American Epilepsy Society; San Diego, CA. December 2, 2012
12. Selassie AW. Risk of Epilepsy after TBI: Prognosis and Prevention. Southeastern Epilepsy and EEG Annual Meeting. Charleston, SC June 6, 2011
13. Smith G, Ferguson PL, Wagner J, Wannamaker BB, Selassie AW. Stigma and self-efficacy in persons with epilepsy. Abstract presented to the American Epilepsy Society Annual Meeting, December 2007, Philadelphia, PA.

Medical Record Abstraction

Medical record abstraction is one of the most important activities in public health surveillance systems not only to extract additional information but also to validate the data values included in the electronic Uniform Billing (UB-04) reporting system. We have been conducting abstraction on the current project activity since 2012 and did the same for earlier projects on epilepsy. The abstraction process is systematically organized in collaboration with DHEC Division of Chronic Disease Epidemiology subcontracted for this activity. The data abstraction tool is well designed and piloted before embarking on full scale abstraction (Appendix B). It was developed by the epidemiologists and clinicians in the project in consultation with experienced abstractors in DHEC. During the piloting phase, changes and adjustments were made such that some variables with low yield were removed. In addition, as needed, the tool was modified to collect information from hospital-based outpatient (OPD) and ED charts where limited variables are available.

Training workshops for data abstractors were held. The sessions presented information on epilepsy diagnosis, properties of data quality, and went through the data abstraction tool. It included group practice with practice charts, and real-time chart abstractions in a group setting, allowing for questions and discussion on the abstraction tool. Feedback collected was then incorporated into the abstraction tool. Most of the training emphasized on the protocol for assigning diagnosis codes based on the discharge narratives in the charts whenever ICD-9-CM codes were missing or numbers' position switched. A protocol, based on International League Against Epilepsy (ILAE) guidelines, was developed for use

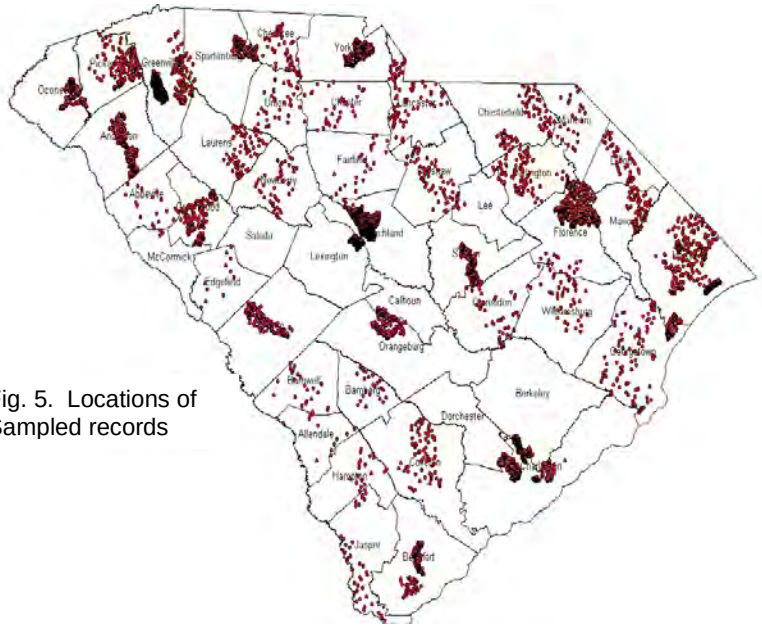

Fig. 5. Locations of Sampled records

in assigning ICD-9-CM codes for epilepsy and/or seizure diagnoses to missing or misaligned codes. The protocol was created with initial input from the then CDC technical advisor, Dr. David Thurman, and the clinical investigators in the team (Br. Braxton Wannamaker, Dr. Gigi Smith). As work progressed, the protocol was added to or changed as needed. Abstraction was clustered around major healthcare facilities with scattered distribution in smaller hospitals based on hospital ID plot (Figure 5).

Table 13. Characteristics by abstraction status

	All Individuals	Sampled	Abstracted	Validated
	448,848	3,016 (0.7%)	2,604 (0.6%)	2,414 (0.5%)
	n (%)	n (%)	n (%)	n (%)
Case/control status				
Definite Epilepsy	62,121 (13.8)	1,712 (56.8)	1,493 (57.3)	1,388 (57.5)
Probable Epilepsy	25,206 (5.6)	624 (20.7)	524 (20.1)	493 (20.4)
Possible Epilepsy	32,802 (7.3)	336 (11.1)	292 (11.2)	263 (10.9)
Undetermined Epilepsy	74,246 (16.5)	41 (1.4)	37 (1.4)	34 (1.4)
Migraine	154,083 (34.3)	204 (6.8)	173 (6.6)	157 (6.5)
Lower Extr. Fracture	100,390 (22.4)	99 (3.3)	85 (3.3)	79 (3.3)
Rural				
Urban	295,249 (65.8)	1,842 (61.1)	1,593 (61.2)	1,477 (61.2)
Rural	126,384 (28.2)	1,024 (34.0)	895 (34.4)	827 (34.3)
Missing	27,215 (6.1)	150 (5.0)	116 (4.5)	110 (4.6)
Age group at first diagnosis				
0 to 5	17,940 (4.0)	183 (6.1)	167 (6.4)	160 (6.6)
6 to 12	18,569 (4.1)	132 (4.4)	117 (4.5)	106 (4.4)
13 to 18	29,834 (6.6)	162 (5.4)	136 (5.2)	120 (5.0)
19 to 34	11,125 (2.5)	619 (20.5)	529 (20.3)	490 (20.3)
35 to 64	200,761 (44.7)	1,340 (44.4)	1,164 (44.7)	1,086 (45.0)
65+	70,519 (15.7)	580 (19.2)	491 (18.9)	452 (18.7)
Race				
White	300,665 (67.0)	1,845 (61.2)	1,584 (60.8)	1,485 (61.5)
Black	135,446 (30.2)	1,096 (36.3)	952 (36.6)	868 (36.0)
Other	7,792 (1.7)	41 (1.4)	37 (1.4)	32 (1.3)
Hispanic	4,945 (1.1)	34 (1.1)	31 (1.2)	29 (1.2)
Sex				
Female	272,055 (60.6)	1,570 (52.1)	1,355 (52.0)	1,261 (52.2)
Male	176,793 (39.4)	1,446 (47.9)	1,249 (48.0)	1,153 (47.8)
Payer				
Uninsured	66,676 (14.9)	367 (12.2)	316 (12.1)	290 (12.0)
Medicare	123,278 (27.5)	1,113 (36.9)	962 (36.9)	892 (37.0)
Medicaid	90,399 (20.1)	674 (22.3)	587 (22.5)	553 (22.9)
Commercial	168,495 (37.5)	862 (28.6)	739 (28.4)	679 (28.1)
Number of comorbidities				
No comorbidities	78,006 (17.4)	321 (10.6)	267 (10.3)	252 (10.4)
1 to 2	116,846 (26.0)	542 (18.0)	475 (18.2)	435 (18.0)
3 to 5	128,166 (28.6)	863 (28.6)	745 (28.6)	690 (28.6)
6 to 7	57,308 (12.8)	551 (18.3)	489 (18.8)	454 (18.8)
8 or more	68,522 (15.3)	739 (24.5)	628 (24.1)	583 (24.2)
Median income level of zip code of residence				
Low (<$36K)	195,239 (43.5)	1,496 (49.6)	1,301 (50.0)	1,198 (49.6)
Mod ($36K-$54K)	176,960 (39.4)	1,086 (36.0)	940 (36.1)	863 (35.7)
High (>$54K)	71,378 (15.9)	405 (13.4)	336 (12.9)	327 (13.5)
Missing	5,271 (1.2)	29 (1.0)	27 (1.0)	26 (1.1)

The sampling procedure and plan is included as Appendix C. Of a total sample of 3,016 cases, abstraction was completed on 2,604 records with 86.3% success rate. The records validated were 2,414 with 80.0% effective validation rate. Of those, 2,144 were diagnosis of epilepsy. Characteristics of the sampled records by abstraction and validation status are found in Table 13. As noted in the data abstraction tool, large amount of information is collected through medical record review. Although basic information has been validated and the result supports that the quality of the data is very good, the project ran out of time before extensive analysis was completed on all abstracted variables. However, we will recruit PhD students to work on the data and participate in manuscript development to make the best of the data collected.

Although we conducted PPV analyses on epilepsy surveillance on previous surveillance activities, this is the first time we assessed PPV in contrast to migraine considered a proximal diagnosis that could be misclassified as a variant of seizure. Taken together, both data completeness and PPV are high (Table 14). Perhaps a pitfall in these evaluations is the use of clinical narrative as the 'gold standard' to validate the UB-04 designation of the codes, which itself is the source of the coding information creating circular in argument about data validity. Other validation techniques such as EEG and/or other clinical markers are time consuming and expensive to carry out.

Table 14. Measures of Predictive Positive Value

UB-04 Classification (Administrative Data)	Status Through Medical Record Review		Total
	Epilepsy (345.x)	Migraine (346.x)	
Epilepsy (345.x)	2144	165	2309
Migraine (346.x)	16	157	173
Total	2160	322	2482
PPV of 345.x to affirm epilepsy		2144/2309	92.8%
PPV of 346.x to affirm migraine		157/173	90.8%

Unanswered questions worth pondering

While the current grant on the epidemiology of comorbidities of epilepsy enabled to quantify the burden of comorbid conditions and the risk factors in population subgroups with higher preponderance of occurrence than what is observable in the general population, i.e. the

background risk, the big question remains what the public health response needs to be. In particular somatic comorbidities that require frequent maintenance (type II diabetes, hypertension, stroke, etc.) that are aggravated by lifestyle factors—smoking, alcohol consumption, diet and exercise—are amenable for control through innovative community-engaged research (CEnR) and enhancing self-efficacy to self-management skills.

The CEnR approach will create and sustain a research partnership between academic researchers and a community-based team of individuals who either have epilepsy, are caregivers of someone with epilepsy, or provide services to people with epilepsy. If such research partnership is established, the academic researchers will contribute the framework of an evidence-based health promotion intervention and methods for rigorous scientific testing. The community partners will define the context for adapting, implementing, and interpreting the outcomes of this intervention to address the unique health needs of people with epilepsy. This will be accomplished within the context of a CEnR partnership that engages community-based organizations, local health care providers, and academic researchers in all aspects of the research, including development of the research questions, design of the study and interventions, and analysis, interpretation and dissemination of the results. Individuals from the community with skill and knowledge to manage basic health and medical care need will serve as Community Health Workers (CHWs). We strongly believe this is a viable plan and a natural extension of the surveillance information accumulated over a decade of CDC funding in South Carolina.

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APPENDIX A

ICD-9-CM codes for case and control group and comorbid condition definitions

Case: Epilepsy	345, 345.0, 345.1, 345.4 - 345.6, 345.8, 345.9
Seizure NOS	780.39 (Presumptive diagnosis of epilepsy with other clinical data)
Control 1: Migraine	346
Control 2: tibia, fibula or ankle fracture	823, 824
1. ADHD	314.0
2. Alcoholism	291.1, 291.2, 291.5, 291.8, 291.9, 303.90, 303.93, 305.00, 305.03, V11.3
3. Alzheimer's Dementia	331.0
4. Anemia	280.1–281.9, 285.9
5. Anxiety	300.0, 300.7
6. Asthma/ Pulmonary	490–496
7. Autism Spectrum	299.0
8. Cardiovascular Disease	401–405, 410–417, 420–429
9. Celiac Disease	579.0
10. Cerebral Palsy	343
11. Cognitive Dysfunction	315, V40.0
12. Cysticercosis	*123.1*
13. Depression	300.4, 309.0, 309.1, 311
14. Diabetes	250.00–250.33, 250.40–250.73, 250.90–250.93
15. Drug Abuse	292.0, 292.82–292.89, 292.9, 304.00–304.93, 305.20–305.93
16. Gastric Reflux	530.81
17. GI Bleed	578
18. Hearing Loss	389
19. HIV / AIDS	042, 044
20. Intestinal problems	560–569
21. Intellectual Disability	317–319
22. Migraine	346
23. Multiple Sclerosis	340
24. Nutritional Deficiencies	260–269
25. Onchocerciasis/Toxocariasis	*125.3, 128.0*
26. Osteoporosis	733.0, V82.81
27. Parkinson's Disease	332
28. Peptic Ulcer	531–535
29. Personality Disorder	301
30. Psychoses	293.8, 297–298.9, 299.10, 299.11
31. Schizophrenia	295
32. Somatoform Disorder	300.8
33. Stroke	430–438
34. Suicidal Ideation	300.9, V62.84
35. Traumatic Brain Injury	800, 801, 803, 804, 850–854,959.01
36. Vision Loss	369

APPENDIX B

Risk Factors of Epilepsy Outcomes:
Comorbidities in Population with Epilepsy
Data Abstraction Manual

SECTION 1: RANDOM SAMPLE INFORMATION (Verbatim from Random Sample)

1a. Date of Abstraction (DATEABS)
Description: Date on which record was abstracted.
Field Length: 8
Values: Date record actually abstracted -- mm/dd/ccyy

1b. Abstracter Initials (INITIALS)
Description: Initials of data abstracter.
Field Length: 2
Values: First and last name initials

1c. Hospital ID Number (HID) Random Sample Information
Description: Number identifying the hospital in which the individual was treated.
Field Length: 3
Values: A combination of numbers, which make up the hospital ID number
Note: May not be applicable if individual not seen in a hospital. Enter '999' if NA.

1d. Medical Record ID Number (MEDRECID) Random Sample Information
Description: A required, unique identification code.
Field length: 20
Values: The actual number found on the abstraction list

Note: Please enter medical record number from the random sample list we send you. Include dashes, letters, etc., and type exactly as the number appears on the abstraction list. This is only the number to link the data you send to the original file.

1e. Type of medical visit (TYPEVIS) Random Sample Information
Description: Type of medical visit.
Field length: 1
Values: 1 = hospital inpatient
2 = emergency department
3 = outpatient, primary care provider (GP, family practice, internist, pediatrician)
4 = outpatient, neurologist
5 = outpatient, epileptologist
6 = outpatient, other
9 = not STATED on abstraction list

1f. Admittance or Outpatient Visit Date (ADMIT) Random Sample Information

Description: Date when individual was admitted to the hospital, ED, or seen in clinic/office.
Field length: 8
Values: Date -- mm/dd/ccyy

Note: Enter 11/11/1111 if not found on the abstraction list. If admittance date differs on the medical record, make a note of the different date in the comments section.

1g. Discharge Date (DISD) Random Sample Information

Description: Date when individual was discharged from the hospital, if applicable.
Field length: 8
Values: Date in -- mm/dd/ccyy

Note: Enter 11/11/1111 if not found on the abstraction list. If discharge date differs on the medical record, make a note of the different date in the comments section.

1h. Case ID Number (CASEID) Random Sample Information

Description: A required, unique identification code.
Field length: 8
Values: The actual number found on the abstraction list.

Note: Please enter the Case ID Number from the random sample list we send you. Please type exactly as provided.

1i. Is Medical Record Available (RECAVAIL)

Description: Determines whether the chart was available to be abstracted.
Field length: 1
Values: 1= Yes
2 = No, clerk states (verbal or written) that record is being microfilmed/ microfiched or off-site storage
3 = No, clerk states (verbal or written) unable to locate but no reason given
4 = No, clerk states (verbal or written) other reason
5 = No identifiable reason

Note: If answers 2 through 5, program skips to Missing Record Comments at end of program. If Yes, program continues to next question.

SECTION 2: PERSONAL INFORMATION (From Here Forward from Medical Chart)

2a. Individual's Last Name (LNAME)
Description: The last name of the individual.
Field length: 40
Values: Any valid name
Note: Enter 999 in first column if not STATED in medical record.
Note: If the name on the medical record is different than the name on the random sample, enter the name from the medical record, including incorrect spelling. Document in the comment section and flag the record.

2b. Individual's First Name (FNAME)
Description: The first name of the individual.
Field length: 20
Values: Any valid name
Note: Enter 999 in first column if not STATED in medical record.

2c. Date of Birth (DOB)
Description: Individual's date of birth.
Field Length: 8
Values: mm/dd/ccyy
Note: Enter 11/11/1111 if not found in medical record.

2d. Age (AGE)
Description: Individual's age
Field Length: 3
Values: Age in years (acceptable range 0 to 120)
Note: Enter 999 if no age or DOB in medical record.

2e. Sex (SEX)
Description: The gender of the individual.
Field Length: 1
Values: M= Male
F= Female
U= Unknown/Not STATED in medical record

2f. Ethnicity (ETHNICITY)

Description: The ethnicity of the individual.
Field Length: 1
Values: 1 = Hispanic, Latino or Spanish origin
2 = Not of Hispanic, Latino or Spanish origin
9 = Unknown/Not STATED in medical record

2g. Race (RACE)

Description: The race of the individual.
Field Length: 1
Values: 1 = White
2 = Black, African-American
3 = Oriental / Asian
4 = American Indian
6 = Native Hawaiian or other Pacific Islander
8 = Other
9 = Unknown/Not STATED in medical record

2h. Height (HEIGHT)

Description: the individual's height in inches
Field length: 4
Values: from the H&P in medical record
Note: Enter 9999 if not STATED in medical record.

2i. Weight (WEIGHT)

Description: the individual's weight in pounds
Field length: 4
Values: from the H&P in medical record
Note: Enter 9999 if not STATED in medical record.

2j. Marital Status (MARISTAT)

Description: Current marital status of the individual.
Field length: 1
Values: 1 = Married (includes separated, stated common law marriages)
2 = Widowed
3 = Single (includes divorced)
5 = Minor child (<18, unless stated as married)
9 = Unknown/Not STATED in medical record

2k. Individual's Street Address (INDADDR)

Description: The street address of residence of the individual.
Field length: 40
Values: Any street address
Note: Be sure to get apartment and route numbers if applicable.
Note: Enter 999 in first column if not STATED in medical record.

2l. Individual's City (INDCITY)

Description: The city of residence of the individual.
Field length: 20
Values: Any city name
Note: Enter 999 in first column if not STATED in medical record.

2m. Individual's State (INDSTATE)

Description: The state of residence of the individual.
Field length: 2
Values: SC = South Carolina
NC = North Carolina
GA = Georgia
OT = Other
UK = Unknown/Not STATED in medical record

2n. Individual's Zip Code (INDZIP)

Description: The zip code of residence of the individual.
Field length: 5
Values: Five-digit number
Note: Enter 999 in first column if not STATED in medical record.

2o. Telephone Number (PHONE)

Description: Telephone number of the individual.
Field length: 13
Values: A telephone number with area code as stated in the medical record.
Note: Enter (000) 000-0000 if the number is not STATED in medical record. If the area is missing, enter (000) for area code and then the 7-digit number.

2p. Employment Status (EMPSTAT)

Description: Employment status of the individual.
Field length: 1
Values: 1 = Student
2 = Employed (full time or part time)
3 = Employed & attending school
4 = Retired
5 = Disabled
6 = Unemployed
7 = Minor Child under age 5
8 = None of the above
9 = Not STATED in medical record

2q. Driving Status (DRIVE)

Description: Are there driving restrictions?
Field Length: 1
Values: 1 = Yes
2 = No
3 = Not STATED in medical record.

2r. Family Structure (FAMSTRU)

Description: Family structure of individual
Field length: 2
Values: 1 = Lives alone
2 = Lives with spouse/significant other
3 = Lives with parent(s)
4 = Lives with relative other than parent
5 = Lives with foster parent
6 = Lives with hired caregiver
7 = Lives in rehabilitation facility
8 = Lives in nursing home
10 = Lives in state residential facility
11 = Lives in group home
12 = Lives in detention or corrections facility
13 = Other
9 = Not STATED in medical record

2s. Insurance Status (INSSTA)

Description: Insurance of individual
Field length: 1
Values: 1 = no medical insurance/self-pay
2 = Medicaid (Includes Select Health, Absolute Total Care, BlueChoice HealthPlan Medicaid, Carolina Medical Homes, First Choice by Select Health of SC, Palmetto Physician Connections, South Carolina Solutions, United Health Care Community Plan)
3 = Medicare
4 = HMO
5 = Other private insurance
6 = Champus, TRI Care, or VA
9 = not STATED in medical record

SECTION 3: SECTION 3: DIAGNOSIS & SEIZURE SPECIFICS

Enter '999' in text fields if no information in medical record.

3a. Chief Complaint (PREDIAG)

Description: Chief complaint
Field length: 40
Values: Medical reason for the visit or diagnosis

3b. Discharge Diagnosis (POSTDIAG)

Description: Discharge diagnosis
Field length: 40
Values: Health care providers' discharge diagnosis

3c. Primary Diagnosis Code/ICD-9 Code (DIAG1)

Description: An ICD-9 CM code and rubric assigned to the diagnosis.
Field Length: 5
Values: Code that the hospital, clinic, or office listed first.
Note: Decimal points are not entered. Enter 5 nine's (99999) if no code is found.
Note: Do not Add Zeros to any three digit N-Code found in the record.

3d-l. Secondary ICD-9 Codes (DIAG2-DIAG10)

Description: An ICD-9 CM code and rubric assigned to the diagnoses.
Field Length: 5 for each, for up to 9 codes
Values: Any code listed in the medical record.
Note: Decimal points are not entered. Enter 5 nine's (99999) if no code is found.
Note: Do not Add Zeros to any three digit N-Code found in the record.

3m. AED medication prescribed at discharge (MEDRX1)

Description: Maintenance anti-epileptic medications prescribed this visit at discharge.
Field Length: Checklist of anti-epileptic medications
Values: Check off medication if listed in medical record as discharge medication.

3n. AED medication prescribed at discharge (MEDRX2)

Description: Maintenance anti-epileptic medication prescribed this visit at discharge.
Field Length: Checklist of anti-epileptic medications
Values: Check off medication if listed in medical record as discharge medication.

3o. AED medication prescribed at discharge (MEDRX3)

Description: Maintenance anti-epileptic medication prescribed this visit at discharge.
Field Length: Checklist of anti-epileptic medications
Values: Check off medication if listed in medical record as discharge medication.

3p. Other AED medication(s) at discharge (MEDRX4)

Description: Other maintenance anti-epileptic medication prescribed this visit at discharge.
Field Length: 40
Values: List other medications not in previous three questions

3q. Other medication(s) at discharge (MEDRX5)

Description: Other medications listed including over the counter and supplements.
Field Length: 40
Values: List any other medications, prescription and over-the-counter and supplements.

3r. Seizure treatments prescribed other than medication (OTHTRT)

Description: Other non-drug treatments prescribed to individual.

Field Length: 1

Values: 1 = Vagus nerve stimulator

2 = Neurosurgery (e.g. epilepsy surgery: lobectomy, hemispherectomy, corpus callosotomy, etc.)

3 = Ketogenic diet or other epilepsy diet (e.g. Modified Atkins for Epilepsy, Sugar Busters, Low Glycemic)

4 = other (e.g. Neuropace RNS, etc.)

9 = not STATED in medical record

3s. Seizure visit (SZVISIT)

Description: Is this visit in reference to a current (day of visit or occurring since last visit) seizure, possible seizure, seizure-like episode, or epilepsy?

Field Length: 1

Values: 1 = Purpose of visit related to a current seizure

2 = Initial visit not related to seizure, but seizure occurred during visit

3 = No current seizure, but visit related to seizure treatment, assessment, etc.

(If 1, 2, or 3, rest of sections 3, 4, & 5 refer to this seizure or seizure-like episode)

4 = None of the above, visit not related to seizures (skip to 6a)

The following questions in this section and next 2 sections refer to the CURRENT seizure or seizure-like episode.

3t. Date of current seizure or seizure-like episode (SZDATE)

Description: Date of recent seizure or seizure-like episode (may be date of visit or date of most recent episode since last visit)

Field Length: 8

Values: Any month, day, and year – mm/dd/ccyy

Note: may be estimated if not explicitly stated in record. If not STATED at all in record, put 11/11/1111

3u-w. Narrative of current seizure or seizure-like episode (NTSEIZ)

Description: Description of the current seizure and/or seizure-like episode (what happened to patient before, during, and after this episode, or during typical episode)

Field Length: 40 for each of three lines

Values: Any description of the seizure episode(s). Please be as descriptive as possible.

3x. Seizure Type (SZTYPE1)

Description: Clinical determination by health care provider of current seizure type(s), seizure disorder, seizure-like episode, &/or epilepsy syndrome

Field Length: Checklist of seizure types

Values: Check off seizure type if listed in medical record describing this episode, or typical episode.

3y. Seizure Type (SZTYPE2)

Description: Clinical determination by health care provider of current seizure type(s), seizure disorder, seizure-like episode, &/or epilepsy syndrome

Field Length: Checklist of seizure types

Values: Check off seizure type if listed in medical record describing this episode, or typical episode.

3z. Seizure Type (SZTYPE3)

Description: Clinical determination by health care provider of current seizure type(s), seizure disorder, seizure-like episode, &/or epilepsy syndrome

Field Length: Checklist of seizure types

Values: Check off seizure type if listed in medical record describing this episode, or typical episode.

3aa. Other seizure type(s) (SZTYPE4)

Description: Other clinical determination by health care provider of current seizure type or seizure-like episode.

Field Length: 40

Values: Any additional seizure type(s) or epilepsy not included on above lists *(refer to list provided in class)*

3bb. Number of seizures or seizure-like episodes (NUMSZ)

Description: How many seizures or seizure-like episodes did the individual experience during this visit / admission / date of service?

Field Length: 1

Values: 1 = One seizure
2 = Two seizures
3 = More than two seizures
9 = Not STATED in medical record

3cc. Time of seizure or seizure-like episode onset (SZTIME)

Description: Time of onset of seizure or seizure-like episode (if cluster of seizures or seizure-like episodes, use time of onset of cluster).

Field Length: 1

Values: 1 = Morning (7 am to 11:59 am)
2 = Afternoon (noon to 5:59 pm)
3 = Evening (6 pm to 9:59 pm)
4 = Nighttime (10 pm to 6:59 am)
9 = Not STATED in medical record

Note: May be estimated if approximate time mentioned in medical record.

3dd. Length of seizure (LENGTH)

Description: How long did the seizure or seizure-like episode last?

Field Length: 1

Values: 1 = 30 seconds or less
2 = >30 secs & up to 2 minutes
3 = > 2 minutes & up to 5 minutes
4 = More than 5 minutes
9 = Not STATED in medical record

3ee. Seizure or seizure-like episode witness (SZOBS)

Description: Who gave the details of the seizure or seizure-like episode?

Field Length: 1

Values: 1 = A health-care professional who directly witnessed the seizure or episode
2 = A non-health care professional who directly witnessed the seizure or episode
3 = Someone who spoke with an individual who directly witnessed the seizure or episode
4 = Self-reported
9 = Not STATED in medical record

3ff. Number of seizures or seizure-like episodes in the 3 months preceding this visit (SZFREQ)

Description: How many reported in last three months?

Field Length: 1

Values: 1 = none
2 = one to three
3 = four or more
4 = Not STATED in medical record

3gg. 3gg-ii. Emergent medication(s) given (MEDTRT1-3)

Description: Medications given pre-hospital, or by ED, if applicable.

Field Length: Checklist of anti-epileptic medications

Values: Check off medication if listed in medical record as given for seizure or seizure-like episode.

SECTION 4: CAUSE OF SEIZURE

Enter '999' in text fields if no information in medical record.

4a-c. Narrative of Cause of Seizure or seizure-like episode (CAUSE)

Description: Brief description of current circumstances that might have contributed to this seizure or seizure-like episode (what provoked this seizure?).

Field Length: 40 characters for each of three lines

Values: Any narrative that describes a possible current cause of seizure or seizure-like episode.

Note: Be as specific as possible.

4d. Injury (INJURY)

Description: Is there report that the individual's seizure or seizure-like episode occurred due to current injury?

Field Length: 1

Values: 1 = Yes, head injury

2 = Yes, injury other than to head

3 = Yes, injury to both head and elsewhere

4 = No (skip to 5f)

9 = Not STATED in medical record (skip to 5f)

4e. Injury Incident Location Type (INJLOC)

Description: Describes the type of place of occurrence of the current injury.
Field Length: 2
Values: 1 = Home
2 = Residential Institution
3 = School, other Institution and Public Administrative Area
4 = Sports or Recreation area
5 = Street or Highway
6 = Trade or Service Area
7 = Industrial or Construction Area
8 = Other Specified Place
9 = Unspecified Place or not STATED in medical record
10 = Farm

4f. Illness prior to current seizure or seizure-like episode (ILLNESS)

Description: Is there report that the individual is or has recently been ill?
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

4g. Fever prior to seizure or seizure-like episode (FEVER)

Description: Is there report that the individual has had an elevated temperature?
Field Length: 1
Values: 1 = Yes, stated in record but no temperature recorded
2 = Yes, 99.6 to 101.5 F degrees (37.6 to 38.6 C)
3 = Yes, greater than 101.5 F degrees (> 38.6 C)
4 = No
9 = Not STATED in medical record

4h. Sleep deprivation (SLEEP)

Description: Is there report that the individual has experienced sleep deprivation recently?
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

4i. Pregnancy (PREG)

Description: Is the individual pregnant?
Field Length: 1
Values: 1 = Yes, record states female is pregnant
2 = Teen or adult female is not pregnant (skip to 5m)
9 = Not STATED in medical record (skip to 5m)

4j. Eclampsia (ECLAMP)

Description: Does the individual have eclampsia (or pre-eclampsia, pregnancy-induced hypertension, PIH, toxemia)?
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

4k. Recent alcohol use

Description: Is there report of use of alcohol in the past 24 hours?
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

4l. Recent illicit drug use

Description: Is there report of use of illicit drugs in the past 24 hours?
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

4m. New Onset (NEWONSET)

Description: Is this visit in regard to the patient's first seizure or seizure-like episode?
Field Length: 1
Values: 1 = Yes *(skip to 6aa)*
2 = No (previous seizures noted, or history of seizures in medical record)
9 = Not STATED in medical record

4n. Medication change (MEDCHNG)

Description: Is there report that the individual has recently changed anti-epileptic medications?

Field Length: 1

Values: 1 = Yes
2 = No
9 = Not STATED in medical record

4o. Weight gain in children (WTGAIN)

Description: Is there report that the child has gained weight recently?

Field Length: 1

Values: 1 = Yes, pt aged 1-18 years has gained weight recently
2 = No, pt aged 1-18 years had not gained weight recently
8 = Not applicable (individual 18 years or older)
9 = Aged 1-18 years, but weight change not STATED in medical record

4p. Use of personal protective equipment (EQUIP)

Description: Is there report that the individual was using a prescribed helmet when seizure occurred (this would be different from the usual bicycle helmet, etc.)?

Field Length: 1

Values: 1 = Yes, individual was using prescribed helmet
2 = No, individual was not using prescribed helmet
9 = Not STATED in medical record

4q. Nonadherence with medication (NONCOMP)

Description: Is there report that the individual has recently not been adherent to his/her seizure medication regimen?

Field Length: 1

Values: 1 = Yes
2 = No
9 = Not STATED in medical record

SECTION 5: MEDICAL HISTORY

Note: Enter "YES" if the record *states* previous history for the following.
Enter "NO" if the record *states* NO previous history for the following.
Enter "999" if no previous history information is documented in the medical record.

5a. Previous seizure disorder or epilepsy diagnosis (PREVSEIZ)

Description: Is there an earlier diagnosis or some evidence of, seizure disorder or epilepsy in the past?
Field Length: 1
Values: 1 = Yes (some evidence of previous seizures in chart)
2 = No (no mention of any previous seizures) (skip to 6aa)
9 = Not STATED in medical record (skip to 6aa)

5b. Previous seizure type (PREVTYP1)

Description: Previous clinical determination of type of seizure(s), seizure disorder(s), or epilepsy?
Field Length: Checklist of seizure types
Values: Check off seizure type if previous determination of seizure, seizure disorder, or epilepsy

5c. Previous seizure type (PREVTYP2)

Description: Previous clinical determination of type of seizure(s), seizure disorder(s), or epilepsy?
Field Length: Checklist of seizure types
Values: Check off seizure type if previous determination of seizure, seizure disorder, or epilepsy

5d. Previous seizure type (PREVTYP3)

Description: Previous clinical determination of type of seizure(s), seizure disorder(s), or epilepsy?
Field Length: Checklist of seizure types
Values: Check off seizure type if previous determination of seizure, seizure disorder, or epilepsy

5e. Other previous seizure type(s) (PREVTYP4)

Description: Other previous clinical determination of type of seizure(s), seizure disorder(s), or epilepsy?
Field Length: 40
Values: Any previous seizure type(s) not included on above lists *(refer to list provided in class)*

5f-h. Narrative of past seizure(s) (PREVNAR)

Description: Description of past seizure(s) – what happens to patient before, during, & after.
Field Length: 40 for each of 3 lines
Values: Any description of previous seizure(s). Please be as descriptive as possible.

5i. Onset of seizure disorder/epilepsy (SZONSET)

Description: Date of original onset of seizure disorder or epilepsy.
Field Length: 8
Values: mm/dd/ccyy
Note: enter 11/11/1111 if not found in medical record. Can estimate date if an approximate date is mentioned in medical record.

5j. Date of Seizure (PREVDATE)

Description: Date when individual had most recent seizure other than current seizure or seizure-like episode.
Field Length: 8
Values: Any month, day, and year -- mm/dd/ccyy
Note: Put 11/11/1111, if not STATED in medical record. May be estimated if approximate date mentioned in medical record.

5k. Multiple seizure types (MULTTYPE)

Description: How many types of seizures has the individual experienced?
Field Length: 1
Values: 1 = One
2 = Two
3 = More than two
9 = Not STATED in medical record.

5l. Frequency of seizures (FREQSEIZ)

Description: How frequently does individual experience any seizure activity?
Field Length: 1
Values: 1 = Less than once a year
2 = More than once a year
3 = More than once a month
4 = More than once a week
5 = More than once a day
9 = Not STATED in medical record

The next questions refer to the time PRIOR to this visit/admission/date of service.

5m. Previous EEG (PREVEEG)

Description: Has individual previously had an EEG?
Field Length: 1
Values: 1= Yes, but no comment as to results in chart
2 = Yes, normal
3 = Yes, abnormal
9 = Not STATED in chart

5n. Previous video EEG (PREVVEEG)

Description: Has individual previously had a video EEG?
Field Length: 1
Values: 1= Yes, but no comment as to results in chart
2 = Yes, normal
3 = Yes, abnormal
9 = Not STATED in chart

5o. Previous CT scan of the head (PREVCT)

Description: Has individual previously had a CT scan of the head?
Field Length: 1
Values: 1= Yes, but no comment as to results in chart
2 = Yes, normal
3 = Yes, abnormal
9 = Not STATED in chart

5p. Previous MRI of the head (PREVMRI)

Description: Has individual previously had a MRI of the head?
Field Length: 1
Values: 1= Yes, but no comment as to results in chart
2 = Yes, normal
3 = Yes, abnormal
9 = Not STATED in chart

5q. Previous MEG of the head (PREVMEG)

Description: Has individual previously had a MEG of the head?
Field Length: 1
Values: 1 = Yes, but no comment as to results in chart
2 = Yes, normal
3 = Yes, abnormal
9 = Not STATED in chart

5r. Previous SPECT of the head (PREVSPECT)

Description: Has individual previously had a SPECT of the head?
Field Length: 1
Values: 1 = Yes, but no comment as to results in chart
2 = Yes, normal
3 = Yes, abnormal
9 = Not STATED in chart

5s. Previous PET of the head (PREVPET)

Description: Has individual previously had a PET of the head?
Field Length: 1
Values: 1 = Yes, but no comment as to results in chart
2 = Yes, normal
3 = Yes, abnormal
9 = Not STATED in chart

5t. Previous seizure treatments - medication (PREVMED)

Description: Has individual been on anti-epileptic medication in past?
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

5u. Previous seizure treatments – neurosurgery (PREVSURG)

Description: Has individual had neurosurgery for epilepsy (lobectomy, resection, hemispherectomy, corpus callosotomy, subpial transection) in the past?
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

5v. Previous seizure treatments – vagus nerve stimulator (PREVVNS)

Description: Has individual had a vagus nerve stimulator implanted for epilepsy in the past?
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

5w. Previous seizure treatments – ketogenic diet (PREVKETO)

Description: Has individual been on an epilepsy diet, e.g. ketogenic diet, modified Atkin's diet for epilepsy, sugar buster's, low glycemic diet, etc. in the past for epilepsy?
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

5x. Previous seizure treatments – other (PREVOTH)

Description: Has individual received some other treatment for epilepsy other than medication, ketogenic diet, vagus nerve stimulator, or neurosurgery?
Field Length: 40
Values: Description of other treatments, including alternative therapies.

5y. Present medication (PRESMED1)

Description: All present anti-epileptic medication.
Field Length: Checklist of anti-epileptic medications.
Values: Check off medication patient taking at onset of visit.

5z. Present medication (PRESMED2)

Description: All present anti-epileptic medication.
Field Length: Checklist of anti-epileptic medications.
Values: Check off medication patient taking at onset of visit

5aa. Present medication (PRESMED3)

Description: All present anti-epileptic medication.
Field Length: Checklist of anti-epileptic medications.
Values: Check off medication patient taking at onset of visit

5bb. Other present medication(s) (PRESMED4)

Description: Any other present anti-epileptic medications.
Field Length: 40
Values: List any medications not given in previous 3 fields, including prescription and over-the counter medications and supplements.

5cc. Previous medication nonadherence (PREVNONC)

Description: Prior to this episode, does the individual have a history of epilepsy medication nonadherence?
Field Length: 1
Values: 1 = Yes, skipping doses
2 = Yes, stopping medication
3 = Yes, but not specified
4 = No
9 = Not STATED in medical record
Note: If '1' and '2', choose '2'.

5dd. Previous TBI (PREVTBI)

Description: Does the patient's medical history include a previous TBI?
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

5ee. Regular use of alcohol (REGALC)

Description: Is there report of regular use of alcohol?
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

5ff. Recently stopped alcohol use (STOPALC)

Description: Has the individual recently stopped alcohol use?
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

5gg. Regular use of illicit drugs (REGDRUG)

Description: Is there report of regular use of illicit drugs?
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

5hh. Recently stopped illicit drug use (STOPDRUG)

Description: Has the individual recently stopped illicit drug use?
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

5ii. Smoking history (SMOKE)

Description: Individual's smoking status
Field Length: 1
Values: 1 = current smoker
2 = quit
3 = never smoked
9 = Not STATED in medical record

5jj. Tobacco use (TOBACCO)

Description: Use of other tobacco products such as chewing tobacco, dipping tobacco or smoking a pipe.
Field Length: 1
Values: 1 = current user
2 = quit
3 = never used
9 = Not STATED in medical record

5kk. Previous illness or injury (ETIOLOGY)

Description: Any past illness, condition, or injury in the patient's history that initially caused the seizure disorder/epilepsy.
Field Length: 40
Values: Previous illness, condition, or injury that initially caused seizures/epilepsy.

5ll. Family history of seizures (FAMHX)

Description: Family history of seizures, seizure disorders, or epilepsy.
Field Length: 1
Values: 1 = Yes
2 = No (skip to section 7)
9 = Not STATED in medical record (skip to section 7)

5mm. Specifics of seizure family history (SPECFMHX)

Description: What type of seizure, etc., is mentioned in family history?
Field Length: 40
Values: Write whether family history of seizures, seizure disorder, or epilepsy, and what type, as well as family member(s) with disorder.

SECTION 6: COMORBID CONDITIONS

Is there report of the following comorbidities in the individual's record?

6a. Psychotic and manic disorders – including bipolar disorder

Description:
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

6b. Anxiety Disorders – including PTSD

Description:
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

6c. Suicidality and ideation

Description:
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

6d. Suicide Attempts

Description:
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

6e. Unipolar Depression

Description:
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

6f. Cardiovascular diseases
Description:
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

6g. Stroke
Description:
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

6h. Diabetes mellitus
Description:
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

6i. Asthma and chronic bronchitis
Description:
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

6j. Celiac disease
Description:
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

6k. Peptic ulcer and gastritis
Description:
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

6l. Mild Cognitive limitations (does not include intellectual disability or MR)
Description:
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

6m. Intellectual Disability (may also be listed as Mental Retardation)
Description:
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

6n. Learning disabilities
Description:
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

6o. Nutritional deficiencies
Description:
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

6p. Anemia
Description:
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

6q. HIV and AIDS
Description:
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

6r. Cysticercosis
Description:
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

6s. Multiple sclerosis
Description:
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

6t. Traumatic Brain Injury
Description:
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

6u. Fractures
Description:
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

6v. Paralysis
Description:
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

6w. Anemia
Description:
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

6x. Other co-morbidities (COMORBID)

Description: Any other current medical &/or psychological conditions noted in record.
Field Length: 40 for each of 4 lines
Values: List all other current medical conditions.

SECTION 7: DIAGNOSTIC TESTS

A physician's interpretation, such as in the H&P or notes, is preferable to determining results from departmental print-out.

7a. ti-epileptic drug level 1 (AED1)

Description: Blood drug level of an anti-epileptic drug and results
Field Length: 1
Values: 1 = Test ordered, no results/interpretation in chart
2 = Test done, and within therapeutic range
3 = Test done, and below therapeutic range
4 = Test done, and above therapeutic range
9 = Not STATED in medical record

7b. Anti-epileptic drug level 2 (AED2)

Description: Blood drug level of an anti-epileptic drug and results
Field Length: 1
Values: 1 = Test ordered, no results/interpretation in chart
2 = Test done, and within therapeutic range
3 = Test done, and below therapeutic range
4 = Test done, and above therapeutic range
9 = Not STATED in medical record

7c. Blood Alcohol Level (BAL)

Description: BAL and Results?
Field Length: 1
Values: 1 = Test ordered, no results/interpretation in chart
2 = BAL was done and value is 0-10 BAC in mg/dl (Negative)
3 = BAL was done and value is > 10 BAC in mg/dl
9 = Not STATED in medical record

7d. Toxicology Screen (TOX)

Description: Toxicology screen and Results?
Field Length: 1
Values: 1 = Test ordered, no results/interpretation in chart
2 = Toxicology screen was done and Negative
3 = Toxicology was done and At least one positive result
9 = Not STATED in medical record

7e. CT Information (CT)

Description: CT of the head and Results?
Field length: 1
Values: 1 = Test ordered, no results/interpretation in chart
2 = CT was taken and Normal
3 = CT was taken and Abnormal
9 = Not STATED in medical record

7f. MRI Information (MRI)

Description: MRI of the head and Results?
Field length: 1
Values: 1 = Test ordered, no results/interpretation in chart
2 = MRI was taken and Normal
3 = MRI was taken and Abnormal
9 = Not STATED in medical record

7g. EEG Information (EEG)

Description: EEG and Results?
Field length: 1
Values: 1 = Test ordered, no results/interpretation in chart
2 = EEG was taken and Normal
3 = EEG was taken and Abnormal
9 = Not STATED in medical record

7h. Video EEG Information (VEEG)

Description: Video EEG and Results?
Field length: 1
Values: 1 = Test ordered, no results/interpretation in chart
2 = EEG was taken and Normal
3 = EEG was taken and Abnormal
9 = Not STATED in medical record

7i. EKG Information (EKG)

Description: EKG and results?
Field length: 1
Values: 1 = Test ordered, no results/interpretation in chart
2 = EKG was taken and Normal
3 = EKG was taken and Abnormal
9 = Not STATED in medical record

7j. Neuropsychological Testing

Description: cognitive or neuropsychological testing
Field Length: 1
Values: 1 = referral made, testing not yet completed
2=results in chart; impairment noted
3= results in chart; no impairment

7k. MEG of the head

Description: MEG of the head
Field Length: 1
Values: 1 = Yes, but no comment as to results in chart
2 = Yes, normal
3 = Yes, abnormal
9 = Not STATED in chart

7l. SPECT of the head

Description: Has individual previously had a SPECT of the head?
Field Length: 1
Values: 1 = Yes, but no comment as to results in chart
2 = Yes, normal
3 = Yes, abnormal
9 = Not STATED in chart

7m. PET of the head

Description: PET of the head?
Field Length: 1
Values: 1 = Yes, but no comment as to results in chart
2 = Yes, normal
3 = Yes, abnormal
9 = Not STATED in chart

7n. Genetic Testing (to help establish true epilepsy)

Description: Was any genetic test ordered or listed?
Field Length: 1
Values: 1 = Yes, but no comment as to results in chart
2 = Yes, normal
3 = Yes, abnormal
9 = Not STATED in chart

7o. Other tests

Description: other test and results?
Field length: 40
Values: List any other tests reported and whether normal or abnormal.

7p. Neurology consultation (NEUROCON)

Description: Was the patient seen by a neurologist?
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record.

7q. Other consultation (OTHERCON)

Description: Was the patient seen by some other specialist regarding their seizure or seizure-like episode?
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

7r. Other consultation specifics (CONSPEC)

Description: By what other type of specialist was the patient seen?
Field Length: 40
Values: Specify what other specialist (list only specialties - if only name available, leave empty).

7s. Psychiatric evaluation (PSYCHIATRY)

Description: Was the individual evaluated by a psychiatrist?
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

7t. Psychological evaluation (PSYCHOLOGY)

Description: Was the individual evaluated by a psychologist or therapist?
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

SECTION 8: DISCHARGE DISPOSITION

8a. Patient discharged to (DISCHTO)

Description: Determines the type of facility the patient was discharged to.

Field length: 1

Values:
0 = Transferred to another acute care hospital
1 = Returned home, self-care
2 = Returned home, requiring non-skilled assistance (family member, etc.)
3 = Returned home, requiring home health services and/or outpatient rehabilitation
4 = Transferred to a residential facility without skilled nursing services or with an unknown level of nursing care
5 = Transferred to a residential facility with skilled nursing services
6 = Transferred to an inpatient rehabilitation facility
7 = Died
10 = Left against medical advice (AMA)
11 = Correctional facility - includes prison, jail and detention centers
8 = Other
9 = Unknown/Not STATED in medical record

SECTION 9: REFERRALS

9a. Primary Care Physician or pediatrician (PHCP)

Description: Is a primary care physician listed (may include PCP, pediatrician, internist, family health clinic, family practice physician, etc)?

Field Length: 1

Values:
1 = Yes
2 = No
9 = Not STATED in medical record

9b. Primary care physician or pediatrician referral (REFHCP)

Description: Did the individual receive a referral to a primary care physician (see above)?

Field Length: 1

Values:
1 = Yes
2 = No
9 = Not STATED in medical record

9c. Neurologist (NEURO)

Description: Is a neurologist listed?
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

9d. Neurologist referral (REFNEURO)

Description: Did the individual receive a referral to a neurologist?
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

9e. Epileptologist (EPIL)

Description: Is the individual currently under the care of an epileptologist/epilepsy specialist?
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

9f. Epileptologist referral (REFEPIL)

Description: Did the individual receive a referral to an epileptologist/epilepsy specialist?
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

9g. Neurosurgical referral (REFNS)

Description: Did the individual receive a referral to a neurosurgeon?
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

9h. Referral for EEG or VEEG tests (REFEEG)

Description: Did the individual receive a referral for an EEG or VEEG?
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

9i. Referral for an MRI (REFMRI)

Description: Did the individual receive a referral for an MRI?
Field Length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

9j. Referral to an Epilepsy Center (REFEC)

Description: Did the individual receive a referral to an epilepsy center?
Field length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

9k. Referral to behavioral medicine/mental health specialist

Description: Did the individual receive a referral to a psychiatrist/ psychologist/social worker?
Field length: 1
Values: 1 = Yes: Specify psychiatrist, psychologist, or social worker
2 = No
9 = Not STATED in medical record

9l. Did the individual attend visits to the behavioral medicine/mental health specialist?

Description: Did the individual visit the psychiatrist/ psychologist/social worker?
Field length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

9m. Did the individual receive psychological therapy/intervention?

Description: Did the individual receive psychological therapy/intervention?
Field length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

9n. If 9m =1, what type of therapy did the individual receive?

Description: Specific type of therapy
Field length: 1
Values: 1 = CBT
2= Motivational Interviewing
3=Family therapy
9 = Not STATED in medical record

9o. If 9m=1, was it individual or group therapy.

Description: Individual vs. Group Therapy?
Field length: 1
Values: 1 = Individual
2 = Group
9 = Not STATED in medical record

9p. Was medication prescribed for mental health/behavioral medicine diagnoses?

Description: Was medication prescribed for mental health/behavioral medicine diagnosis?
Field length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

9q. Referral to an Epilepsy support group such as Epilepsy Foundation of America, South Carolina Advocates for Epilepsy

Description: Did the individual receive a referral to an epilepsy support group?
Field length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

9r. Referral and/or resources provided to patient (e.g. educational handouts, other supportive organizations, etc.)

Description: Did the individual receive any educational handouts or a referral to any other supportive organizations?
Field length: 1
Values: 1 = Yes
2 = No
9 = Not STATED in medical record

SECTION 10: CLOSING

10a. 10a. Abstractor Comments (COMMENTS)

Description: Does the abstractor have any comments about this record?
Field length: 1
Values: 1 = Yes
2 = No (skip to 10g)

10b. 10b-c. Abstracter Administrative Comments (COMMENT1-2)

Description: Informative remarks made by the data abstracter to add additional insight to this particular patient record.
Field Length: 40 for each of 2 lines
Values: Any narrative (administrative problems – random sample info different from chart, chart difficult to read, etc.)

10d. 10d-f. Abstractor Clinical Comments (COMMENT3-5)

Description: Informative remarks made by the data abstracter to add additional insight to this particular patient record.
Field Length: 40 for each of 3 lines
Values: Any narrative (clinically-related problems – need to add something extra for which there was no entry place, note that question mark written in text was copied from chart, note that question mark written in text due to illegible chart, etc.)

10g. Flagged for Special Review (FLAG)

Description: Does this record need to be flagged for special review?
Field length: 1
Values: 1 = Yes
2 = No

Note: A record would need to be reviewed by another abstractor if there is contradictory information in the chart (ex. a pregnant male), information in medical record not matching random sample or other problems.

Note: Reason(s) for flag should be recorded in Abstractor Comments.

Appendix C

Sampling

A sample of 3,016 (~5% of the total cohort) records was drawn for abstraction during Phase 2. We used a two-stage sampling design to select the records for abstraction (Fig. 6). The sampling frame is all eligible cases and controls. The primary sampling unit (PSU) was stratified by case and control status. The majority (90%) of the records were from people with epilepsy with a small percentage of people with migraine (7%) and people with lower extremity fracture (3%) in order to compare the prevalence of comorbidities across the control groups. The resulting sample included 2,713 records of people with epilepsy, 204 records of people with migraine and 99 records of people with lower extremity fracture. The secondary sampling unit (SSU) was based on the hospital bed size. We expected to get more detailed and more records from larger hospitals so we were interested in abstracting most (75%) of the sample from those hospitals. However, we were also interested in determining if hospital size affects billing and discharge diagnoses so we have selected to abstract 25% of the sample from smaller hospitals. The PSU serves as the sample frame to select the SSU using the stratified random sampling approach. The stratification variable for the secondary sample is the hospital size. A sampling proportion of 0.25 small hospitals (100 beds or less) and 0.75 larger hospitals (more than 100 beds) are randomly selected from the strata. The resulting study sample was comprised of approximately one quarter small hospital records and three quarters large hospital records. The figure illustrates the sampling distribution.

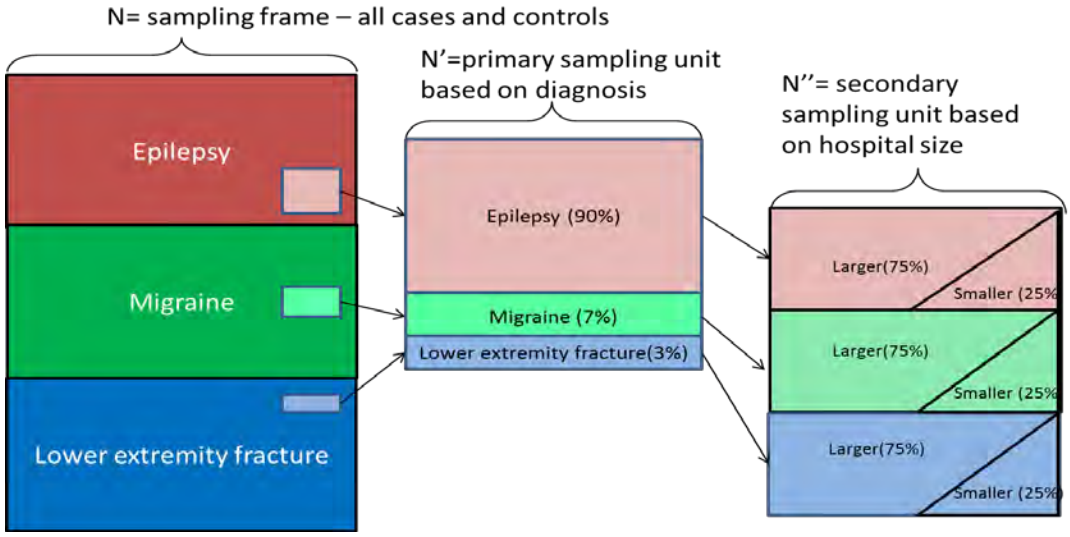
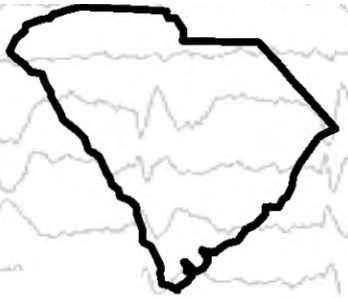


Figure 6. Sampling scheme

Risk Factors of Epilepsy Outcomes Comorbidities in Population with Epilepsy
South Carolina



Medical University of South Carolina
Department of Public Health Sciences
135 Canon Street, Suite 303
Charleston, SC 29425