Description of Non-arbo-related Encephalitis Associated Hospitalizations in Louisiana, 1999-2007

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Abstract

Analysis of the Louisiana Hospital Inpatient Hospital Discharge Database (LAHIDD) for the years from 1999 to 2007 provided information for describing characteristics, frequencies, cost, and length of hospital stay for non-arbo-related encephalitis associated hospitalizations. The data from the LAHIDD database was separated from the main database creating a new database with only non-arbo-related encephalitis cases. There were 1905 cases of encephalitis discharged from the hospital in 1542 patients, the total cost of treatment was over 70 million dollars and contributed to more than 20,000 days in the hospital. Unknown causes of encephalitis was the most common etiology diagnosed, while herpetic encephalitis was the most common diagnosis when there was a known etiology. The gender distribution was significantly different when looking at the total number of patients, with females being more likely to have encephalitis. However, when looking at individual categories of encephalitis only Lupus and demyelinating diseases of the central nervous system, which are known as common mimickers of encephalitis or encephalitis results as complications of the disease, had significantly more women. The AIDS-defining diseases such as meningoencephalitis due to toxoplasmosis and Progressive multifocal leukoencephalopathy (PMLE) seen in immuno-compromised patients, occurred more commonly in men. The ages for the all encephalitis patients ranged from birth with most newborns having herpetic encephalitis to 98 years old. There were 5 patients diagnosed with 8 cases of Subacute sclerosing panencephalitis (SSPE), a very rare chronic infection seen mostly in developing nations in children between 10 and 14; all patients in Louisiana were over 30 years old with the oldest patient being 96 years old. Since the database does not contain information on diagnostic tests performed on patients, it is difficult to understand how the patients may have been diagnosed with this disease. If the patients did in fact have SSPE, they would make up the largest cohort of patients over 21 to have ever been diagnosed with SSPE. The average cost of treatment while in the hospital for all cases was $38,477 and the average length of stay was about 11 days. However, these numbers may be a underestimate of the burden encephalitis has not only on the health care industry as well as the individual affect by the disease, only a small percentage of patients will be discharged with no further medical needs, while the vast majority will need further rehabilitation and treatment for recovery increasing the burden of encephalitis.

Background and Rationale

Encephalitis is an inflammation of the brain parenchyma causing a severe neurological syndrome, with multiple clinical manifestations including fever, headache, and altered levels of consciousness (Glaser, et al., 2003) (Roos, 1999). Over 100 different pathogens have been identified as a cause of encephalitis, not limited to viral infections including herpes viruses and arboviruses, but also bacterial infections, fungi, parasites, and several toxins (Glaser, et al., 2003) (Khetsuriani, Holman, & Anderson, 2002). Noninfectious diseases have also been linked to illnesses many times indistinguishable from infectious encephalitis, including some autoimmune diseases (systemic lupus erythematosus), and other autoimmune diseases with demyelination characteristics (DeMarcaida & Reik, 1999) (Whitley & Gnann, 2002).

While there has been much advancement in identifying the etiologic agent of some patients' encephalitis, many unanswered questions still exist leaving many cases of unknown etiology. Reports have noted that the cause of many cases of encephalitis (32%-75%), remain unknown (Glaser, et al., 2003) (Khetsuriani, Holman, & Anderson, 2002) (Siversten & Christensen, 1996). Three states (New York, Tennessee, and California) have programs implemented by the Emerging Infections Program run by the CDC to conduct an enhanced encephalitis surveillance program with the purpose of reducing the number of unknown etiologically related cases (Khetsuriani, Holman, & Anderson, 2002). California and Tennessee's annual reports show that even with enhanced testing, many etiologies still remain unknown (Tennessee Department of Health Communicable and Environmental Disease Services, 2006) (Acute Communicable Disease Control, California, 2007). While this program aims to identify the unknown causes of encephalitis, it excludes many potential cases, including those who are immune-compromised, and children under 6 months (Glaser, et al., 2003).

Along with the above noted difficulties in identifying the cause of a person's encephalitis, many clinical conditions exist that may mimic typical encephalitis symptoms (Granerod & Crowcroft, 2007). A lack of specific definition contributes to the difficulty in distinguishing encephalitis from other conditions. Furthermore, it is difficult to generalize the epidemiology of encephalitis, because only a few studies on arbo-related encephalitis exist, and many cases are never reported to health authorities (Granerod & Crowcroft, 2007) (Khetsuriani, Holman, & Anderson, 2002). Many of the current studies are not population-based, focus on specific pathogens, or their studies focus on specific subsets of the population (Rantala & Uhari, 1989), (Khetsuriani, Holman, & Anderson, 2002). One paper which looked at the burden of encephalitis-associated hospitalizations in the United States between 1988 and 1997 used the National Hospital Discharge Survey (NHDS), a nationwide sample of all hospital discharge data (Khetsuriani, Holman, & Anderson, 2002) to provide the first national estimate of the impact encephalitis has in the United States. It also highlighted many of the difficulties associated with research on encephalitis as a generalized category (Khetsuriani, Holman, & Anderson, 2002).

Arboviruses causing encephalitis have been well documented, and characterized by incidence, etiology, and public health impact (Division of Vector-Borne Infectious Diseases, 2005) (Louisiana Office of Public Health, Infectious Disease Epidemiology Section, 2006) (Louisiana State Center for Health Statisitics, 2006). The CDC has focused much attention to arboviral related encephalitis surveillance, and vector surveillance. The data has been well documented over the past 5 to 10 years (Division of Vector-Borne Infectious Diseases, 2005). Currently in Louisiana, the Louisiana ArboVirus Surveillance program monitors all reported cases of encephalitis related to arboviral infections (Louisiana Office of Public Health, Infectious Disease Epidemiology Section, 2006). St. Louis encephalitis and West Nile virus related encephalitis are the two most reported arbo-viral infections found in the state. Between 2001 and 2004, there were more than 550 identified human cases resulting in 39 deaths (Smith & Xu, 2004). In the Louisiana Hospital Inpatient Discharge Database (LAHIDD),

210 cases of encephalitis were related to arboviruses. The Louisiana Health Report published yearly only mentions encephalitis as it related to arboviruses (Louisiana State Center for Health Statisitics, 2006). These cases were excluded from the current study in order to describe non-arboviral encephalitis.

Herpes Simplex virus (HSV-1) related encephalitis is also well documented, it is now recognized as the most common non-arbo-related encephalitis in developed countries, with an estimated incidence between 1in 250,000 and 1 in 100,000 persons per year (Cinque, Cleator, Weber, Moneyne, Sindic, & vonLoon, 1996). In recent research, HSV-1 and varicella zoster virus (VZV) related encephalitis has been the two most commonly identified causes of encephalitis (Khetsuriani, Holman, & Anderson, 2002) (Whitley & Gnann, 2002). Both of these are fairly common diseases that have the rare fatal outcomes of encephalitis (Whitley & Gnann, 2002). Herpetic encephalitis is a major public health concern due to the high mortality associated with it (McGrath, Anderson, Croxson, & Powell, 1997). It is estimated, that without intervention using an effective treatment, Acyclovir, only 2.5% of those experiencing herpetic encephalitis will return to a normal lifestyle (Whitley & Gnann, 2002) (McGrath, Anderson, Croxson, & Powell, 1997). Even after treatment, the mortality rate for those with HSV-1 related encephalitis is 28% at 18 months (McGrath, Anderson, Croxson, & Powell, 1997).

Recently, HIV related encephalitis has increased the burden of encephalitis-associated hospitalizations (Khetsuriani, Holman, & Anderson, 2002). Many types of encephalitis are more common in immuno-compromised patients, rates of encephalitis due to toxoplasmosis, HSV-1, cytomegalovirus, encephalopathy (HIV-related), and Progressive multifocal leukoencephalopathy (PMLE) are increasing as HIV infected patients move into the later stages of AIDS and at risk for opportunistic infections (Center for Disease Control, 2004). This population has had an impact on the gender and age distribution of encephalitis cases, and when HIV cases are removed, no observed gender differences exist, with HIV cases included, males seem to be predominately affected (Bossi, et al., 1996) (Khetsuriani, Holman, & Anderson, 2002).

A recent review paper on the epidemiology of acute encephalitis from Granerod and Crowcroft suggests that when taking into account all encephalitis that is non-arboviral related, there may not be a clear seasonal pattern due to the number and types of infections associated with encephalitis. They also suggested that there does not appear to be a temporal trend in incidence, meaning that incidences over extended periods of times have been comparable. However, they note, while temporal trend, has not been observed, the causes of encephalitis, and what is known about the etiology of various factors has changed (Granerod & Crowcroft, 2007) (Khetsuriani, Holman, & Anderson, 2002) (Davison, Crowcroft, Ramsay, Brown, & Andrews, 2003) (Lewis & Glaser, 2005). Typically in the United States, and most other developed nations, non-arbo-related encephalitis is correlated with sporadic infections, and rare complications (of outcomes including measles, mumps, rubella, vaccine associated, and VZV) as opposed to endemic conditions experienced in many developing nations (Granerod & Crowcroft, 2007) (Booss & Esiri, 2003). Overall, the significance of this study using the Louisiana Hospital Inpatient Discharge Database is to look at trends in non-arbo related encephalitis in Louisiana since this topic has not been examined in depth to provide information on trends, and to describe characteristics associated with encephalitis that is not arboviral related.

Research Question

What are the characteristics associated with non-arbo-related encephalitis diagnoses in the Louisiana Hospital Inpatient Discharge Database (LAHIDD) from 1999 to 2007? The objective of this study is to evaluate the burden and describe non-arboviral related encephalitis-associated hospitalizations in Louisiana between 1999 and 2007. The data to be analyzed is derived from the Louisiana Impatient Hospital Discharge Database, which includes all hospitalizations in the state of Louisiana during the years listed above.

Population and Methods

Data Sources: A database was created compiling all reported encephalitis cases in Louisiana using the Louisiana Hospital Inpatient Discharge Database (LAHIDD) for the years 1999 through 2007. Once this database was created, representing all reported cases of encephalitis in Louisiana, cases that were previously classified in the West Nile database were removed, as well as all other cases of arbo-related viral encephalitis. The original database had 2143 cases, and once all arbo-related encephalitis cases were removed, the total number left was 1905 cases in 1542 patients with any non-arbo-related encephalitis diagnosis. The hospital discharge data is a cumulative record submitted quarterly or yearly of all patients admitted to all hospitals in Louisiana, regardless of length of stay, and outcome (The Louisiana State Center for Health Statistics, 2004). The diagnoses were coded using the *International Classification of Diseases, 9th Revision (ICD9-Updated)* (US Public Health Service adn Health care Financing Administration, 1998). All data on patients was retained in the database, and those with multiple admittances over the eight year time period were included and noted as repeated visits.

Limitations of the research: The LAHIDD database is a collection of all hospital discharge records for the state of Louisiana obtained yearly, however, the purpose of these records is typically not for research purposes, but to provide information on the patients discharged. For this reason, the data does not provide behavioral characteristics which could have led to the disease; the database also does not provide tests and results that were used to diagnose patients as they were. There are nine discharge diagnosis codes to list the patients' diagnosis; however, there is not a set order or definition given to how the patients were given their diagnosis. The description below identifies how patients were classified into a category of encephalitis with the data available in the Hospital Inpatient Discharge Database.

Table 1. Codes and Disease diagnosis for encephalitis from the *International Classification of Diseases, 9th revision*

ICD-9 Code	Disease Diagnosis	ICD-9 Code	Disease Diagnosis
Included in analysis		**Excluded from analysis**	
Known causes:		**Arbo-related encephalitis:**	
Viral		062	Mosquito-borne viral encephalitis
0462	Subacute sclerosing panencephalitis (SSPE)	0620	Japanese encephalitis
0463	Progressive multifocal leukoencephalopathy (PMLE)	0621	Western equine encephalitis
0468	Other specified slow virus infection of Central Nervous System	0622	Eastern equine encephalitis
0498	Other specified non-arthropod borne encephalitis	0623	St. Louis encephalitis
0520	Post-varicella encephalitis	0624	Australian encephalitis
0543	Herpetic meningoencephalitis	0625	California encephalitis
0550	Post-measles encephalitis	0628	Other specified mosquito-borne encephalitis
071	Rabies	0629	Mosquito-borne viral encephalitis, unspecified
0722	Mumps encephalitis	063	Tick-borne viral encephalitis
3230	Encephalitis in viral disease classified elsewhere	0630	Russian Spring summer (Taiga) encephalitis
Other infectious causes		0632	Central European encephalitis
0136-01366	Tuberculosis encephalitis	0638	Other specified tick-borne viral encephalitis
0361	Meningococcal encephalitis	0639	Tick-borne encephalitis, unspecified
09041	Congenital syphilitic encephalitis	064	Viral encephalitis transmitted by other and unspecified arthropods
09481	Syphilitic encephalitis	1390	Late effects of viral encephalitis
1300	Meningoencephalitis due to Toxoplasmosis	3231	Encephalitis in rickettsial diseases classified elsewhere
3222	Encephalitis in protozoal disease classified elsewhere	V050	Need for prophylactic vaccination against arthropod-borne viral encephalitis
3236	Post infectious encephalitis		
3234	Other encephalitis due to infection classified elsewhere		
Other Causes			
3235	Encephalitis following immunization procedures		
3237	Toxic encephalitis		
3237	Other causes of encephalitis		
Unknown causes:			
0469	Unspecified slow virus infection of Central Nervous System		
0499	Viral encephalitis not otherwise specified		
323	Encephalitis, myelitis, and encephalomyelitis		
3239	Unspecified cause of encephalitis		

Classifications: All patients in the LAHIDD database who had at least one ICD-9Updated code (Table 1) for encephalitis listed in one of the nine discharged diagnosis code was classified as having encephalitis. These cases were further coded for more specific causes of non-arbo-related encephalitis. The main etiologic categories of encephalitis found in the discharge databases were classified as shown in Table 2.

Table 2. Number of Encephalitis cases by category

Encephalitis Classification	Total number of cases (%)	Number of patients (%)
Other (bacterial, fungal, measles, unspecified meningitis, post infectious, syphilis, toxic, varicella, viral, and other)	391 (20.5)	331 (21.5)
Unspecified (encephalopathic, and unspecified)	613 (32.2)	512 (33.2)
Herpetic	276 (14.5)	237 (18.7)
PMLE	149 (7.8)	109 (7.1)
HIV associated*+	63 (3.3)*	56 (3.6)*
Toxoplasmosis	63 (3.3)	51 (3.3)
Meningococcal	33 (1.7)	30 (1.9)
SSPE	8 (0.4)	5 (0.3)
Systemic Lupus Erythematosus+	234 (12.3)	159 (10.3)
Demyelination+	75 (3.9)	52 (3.4)
TOTAL	**1905**	**1542**

*Note: HIV associated excludes all HIV+ patients who are classified elsewhere, in total there was 310 cases of encephalitis in 252 HIV+ patients.

+Classified on basis of having "Unknown" or "Other" of encephalitis as well as listed diagnosis

Further, three additional categories were created, included and used in the analysis based on having at least one code for encephalitis, either "unknown cause of encephalitis", or "other cause of encephalitis." These categories were: "HIV associated encephalitis, not otherwise specified", "demyelinating disease," and "systemic lupus erythematosus." The category "demyelinating diseases" was comprised of three groups: those with a diagnosis of "multiple sclerosis," "SICCA Syndrome," or "demyelinating disease of the Central Nervous System."

Hospitalizations for patients with HIV may fall under multiple classifications of encephalitis besides HIV associated encephalitis not otherwise specified (HIV, NOS). Cases with HIV which had a known etiology included PMLE, herpetic meningoencephalitis, and meningoencephalitis due to toxoplasmosis most commonly; further data can be found in table 3. There were 310 cases of encephalitis in people with HIV (both symptomatic, and asymptomatic). Once duplicate cases were noted, 252 patients had HIV in the database.

Table 3. Number of HIV+ patients and cases when HIV was the primary diagnosis compared to secondary diagnosis

Diagnosis	Number (%), Total visits	Number (%), 1st visit
HIV as Primary Diagnosis		
HIV	64 (20.6)	56 (22.2)
HIV as Secondary Diagnosis		
PMLE	131 (42.3)	97 (38.5)
Toxoplasmosis	61 (19.70)	48 (19.1)
Herpetic	27 (8.70)	24 (9.5)
Meningococcal	8 (2.60)	8 (3.2)
Bacterial unspecified	5 (1.60)	5 (2.0)
Varicella	3 (1.00)	3 (1.2)
Viral unspecified	3 (1.00)	3 (1.2)
Fungal Meningitis	2 (0.70)	2 (0.8)
Toxic	2 (0.70)	1 (0.4)
Bacterial Meningitis	1 (0.30)	1 (0.4)
Lupus	1 (0.30)	1 (0.4)
Meningitis unspecified	1 (0.30)	2 (0.8)
SSPE	1 (0.30)	1 (0.4)
Total	**310 (16.3% of total cases)**	**252 (16.3% of patients)**

Data Analysis: For the purpose of the analysis, results will be presented using cases (1905) and the number of patients (1542). This will allow us to look at the results not only accounting for the total number of outcomes, but also have better estimations of the true burden of each etiology for encephalitis without overestimating for disease which may be more prone to having patients admitted to the hospital multiple times with the same etiology. The year and month of hospital admission reflect the total number of cases, regardless of if the patient was admitted previously for encephalitis, in order to determine if there are any yearly trends or seasonality trends in encephalitis cases.

The average length of stay, total number of days contributed, mean cost of stay, and total cost for all treatments for each of the 10 main diagnosis categories chosen for this paper also represents the total number of hospital-associated encephalitis cases. The standard deviations for the average length of stay and the hospital associated charges are also presented, as well as a categorization of hospital charges for the 10 most common types of encephalitis diagnosis. The mean cost, total cost, average length of stay, and total length of stay for all cases of HIV-associated encephalitis were also calculated from data in the LAHIDD database.

Analysis was done on gender, age distribution, discharge type, admit type and source, and location based on parish, using statistical packages including SAS v.9.1 and EpiInfo. Race was not analyzed because of the significant number of missing cases (over 22.0%).

Results

Encephalitis represents a mixed bag of etiologic agents, and symptoms, and has a wide population and varied distribution, therefore a global and overarching description of encephalitis as a single category neglects many of the important features of each etiologic category. Overall, in Louisiana between 1999 and 2007, there were 1,905 cases of encephalitis diagnosed in 1,542 patients who ranged in age from newborn to 98 years old with a median age of 44.2 years (S.D. 22.5). The LAHIDD database over those years had a total of 4,837,991 cases entered; the rate for all encephalitis related cases was 39.4 per 100,000 cases in the hospital setting in Louisiana.

When looking at all encephalitis cases, there is no distinct temporal yearly trend in Louisiana between 1999 and 2007 as presented in figure 1. In 2003 and 2007, a decrease in the number of encephalitis cases was observed. There does not appear to be any clear patterns of seasonality for encephalitis as a general category. The months February, August, and October had the highest number of total cases, however, no specific etiology can be attributed to those specific increases. It appears that unspecified causes of encephalitis and other causes of encephalitis may have complementary patters of seasonal distribution, as previously described in research by Khetsuriani, et al., and shown in figure 2 presenting the data from the LAHIDD database on month admitted for all cases (Khetsuriani, Holman, & Anderson, 2002).

In the LAHIDD data, 23 different types of encephalitis were diagnosed over the eight year time period. Many of these diagnoses had a limited number of cases, so they were further grouped together in order to define 10 main diagnoses of encephalitis identified in table 2. Each classification was analyzed individually for gender distribution, age distribution, discharge type, admit type, admit source, and yearly trends, seasonality.

Herpetic Encephalitis: Herpetic encephalitis was the most common known diagnosis for encephalitis cases, 276 cases of hospital associated herpetic encephalitis was diagnosed in 237 patients. The gender distribution was similar, 48.5% females and 51.5% males, with no significant difference observed (p-value=0.650). The average age for patients with a main diagnosis was 48.6 years old (S.D.=25.9), those over 40 years old were more likely to have a diagnosis of herpetic encephalitis, however, herpetic encephalitis accounted for 19 of the 34 cases in children less than 1 year old, and was present in 24 patients with HIV.

Most patients diagnosed with herpetic encephalitis were admitted through the emergency room as an emergency case (135 of 237 patients), and another 60 patients were admitted as an urgent case. These findings are consistent with previous studies, noting that herpetic encephalitis is one of the most common causes of encephalitis with known origin (McGrath, Anderson, Croxson, & Powell, 1997), representing 15.4% of all patients diagnosed with encephalitis, and 23.0% of patients diagnosed with an identified cause of encephalitis in Louisiana between 1999 and 2007. When looking at all cases of herpetic encephalitis, 43.1% had a routine discharge, while 10.9% had a fatal outcome, 38.4% were moved to another facility (including short term care, long term care, and home health care), and 19 people were identified as “reserved for national assignment.”

A temporal yearly trend was not observed for cases of herpetic encephalitis, between 25 and 35 cases were diagnosed per year. There also does not appear to be any seasonal trend in herpetic encephalitis cases, only slight peaks in numbers for February and March over the 8 years (29 and 35 cases), and a slight decrease in September over the 8 years (11 cases).

Meningococcal Encephalitis: Meningococcal encephalitis results from an infection of Neisseria meningitidis a gram negative bacteria causing an acute infection of the brain (Adams, Victor, & Roper, 1977). Meningococcal encephalitis accounted for only 1.9% of the total patients with any form of encephalitis there were 33 cases diagnosed in 30 patients, 8 of whom were also HIV positive. The

gender distribution was similar, 46.7% females and 53.3% males, with no significant difference observed (p-value=0.715). The average age for patients with a diagnosis of meningococcal encephalitis was 40.2 years old (S.D.=20.5), with most cases falling between the age group of 20 to 44.

Most patients diagnosed with meningococcal encephalitis were admitted through the emergency room as an emergency case (22 of 30 patients). When looking at all cases of meningococcal encephalitis, over 50% were discharged routinely, 12.1% had a fatal outcome, and 27.3% were moved to another facility (including short term care, long term care, and home health care).

A temporal yearly trend may be observed for cases of meningococcal encephalitis, in 1999, no cases of meningococcal encephalitis were diagnosed, while in 2007, seven cases were diagnosed, and for the years 2000 to 2006, there were between two and five diagnosed cases per year. There does not appear to be any seasonal trend in the number of cases diagnosed with meningococcal encephalitis.

HIV-associated, not otherwise specified (HIV, NOS): HIV-associated encephalitis NOS is made up of all patients who were HIV+ and did not have another encephalitis diagnosis such as meningoencephalitis due to toxoplasmosis, herpetic encephalitis, or PMLE. There were 56 patients contributing 64 cases of encephalitis associated hospitalizations, making up 3.6% of patients seen between 1999 and 2007. However, there were 252 patients who were HIV+ contributing 310 cases of encephalitis when looking at all diagnoses of encephalitis in those with HIV. There was a significant difference in the gender distribution, 67.9% of the HIV, NOS cases were males, while the other 32.1% were females (p-value=0.008). When looking at all patients with HIV regardless of classification, males were 3.03 (95% C.I = 2.24, 4.10) more likely than females to be HIV+ in the encephalitis database. The average age was 42.5 years old (S.D.=10.5), with most falling in the 20 to 44 age group, and no cases were reported in those under 20 years old. One patient classified as being discharged with lupus, also had HIV and was 11 years old, making this the youngest patient in the database with HIV.

Most patients diagnosed with HIV associated encephalitis NOS were admitted through the emergency room as emergency cases (38 of 56 cases). Others were either admitted from a physician referral or a clinic referral. When looking at cases of HIV encephalitis NOS, 57.1% were routinely discharged, while 22.3% had a fatal outcome. Two of four patients diagnosed in this category (HIV, NOS) “left the hospital against medical advice”, and the other two were “reserved for national assignment.”

There is not a yearly temporal trend in the number of HIV associated encephalitis NOS cases from 2000 to 20007, in 1999 the fewest number of cases were discharged, while 2002 had the highest number of cases discharged (nine cases). A slight decrease in the number of cases with HIV associated encephalitis NOS for 2005 through 2007 is observed. There also does not appear to be a temporal trend in seasonality, when looking at all cases discharged between 1999 and 2007 combined, the highest month, May had 10 cases total, and the lowest month, January had two cases over the eight year time period.

Meningoencephalitis due to Toxoplasmosis: Toxoplasmosis was diagnosed in 51 patients, contributing to 63 cases (3.3%) of the encephalitis cases between 1999 and 2007. Of those 51 patients, 48 were HIV+ cases. The gender distribution was significantly different between males and females (p-value<0.001), with over 78% of the patients being HIV+ males. The average age for patients with a diagnosis of meningoencephalitis due to toxoplasmosis was 38.1 years old (S.D.=8.7), there were no cases in those younger than 20 or older than 65, with most cases falling in the 20 to 44 age range.

Most patients diagnosed with meningoencephalitis toxoplasmosis were admitted through the emergency room as an emergency case (35 of 51 patients), and 11 additional patients were admitted as an urgent case. Most patients (42.3%), had a routine discharge, while 11.8% had a fatal outcome. The

rest of patients were either moved to another short term facility, long term facility, or received home health care.

A temporal yearly trend may be observed for cases of meningoencephalitis due to toxoplasmosis, in 2000, 14 cases were diagnosed, and during 2001 10 cases were diagnosed, in the years leading up to 2006, the numbers of cases significantly decreased to between 3 and 5 cases, with another increase in 2006 (p-value=0.006). There does not appear to be any seasonal trend in the number of cases diagnosed with meningoencephalitis due to toxoplasmosis. When looking at seasonality, there is an increase in cases for the months of July, August and December. The other moths appear to stay fairly constant when combining the data for all eight years.

Progressive multifocal leukoencephalitis (PMLE): PMLE accounted for 149 cases in 109 patients in the LAHIDD database, and 38.5% (97 of 252 HIV+ patients) of cases in HIV+ patients. This was the most common type of encephalitis in HIV+ patients. A significant difference was observed in the gender distribution, 67.0% were males (p-value<0.001). The average age for patients was 42.9 years old (S.D.=12.3). Most patients were between the 20 to 44 age group, one case was diagnosed in a person in the 1 to 4 age group, and one case in the 15 to 19 age group.

Most patients diagnosed with PMLE were admitted through the emergency room as an emergency case (76 patients of 109 diagnosed with PMLE). Other forms of referral were through a physician, a clinic, or transfer from another hospital. When looking at all cases of PMLE, during a patient's first visit with a diagnosis of PMLE, 53 of 109 had a routine discharge, while 18 had a fatal outcome. Overall, 25 cases of 149 had a fatal outcome, and 30.8% were transferred to another facility, including long and short term care and home care. When looking at the fatal outcomes, 22 of the 25 cases were in patients who were HIV+.

There does not appear to be a temporal trend related to the number of PMLE cases diagnosed per year, between 11 (in 2003) and 24 (in 2005) cases were diagnosed per year. There also is not a seasonal trend associated with PMLE, however, the least amount of cases were diagnosed in April, while November and December had the highest number when combining data from all years with 19 cases total in each of those months.

Subacute sclerosing panencephalitis (SSPE): SSPE is now one of the rarest encephalititides diagnosed in developed countries, while its incidence has remained high in areas of the Middle East and India (Office of Communications and Public Liason, 2007). However, during the 8 year time period of the LAHIDD database, there were 8 cases in 5 patients diagnosed throughout the state. Gender was not significantly different, 60% (3 of 5 patients) were males (p-value=0.655). The average age for those diagnosed with SSPE is 46.6 years old (S.D. 27.8). The oldest person diagnosed with SSPE was 96 years old, while the youngest was 31 years old. In previous literature the oldest diagnosed person was 36 years old, and the mean age for an SSPE diagnosis is between 11 and 13 years old, in children who were previously diagnosed with a measles infection in developing countries (Office of Communications and Public Liason, 2007). One patient diagnosed with SSPE, was also HIV+, and had a routine discharge.

Of the 5 patients, 3 were admitted as emergency cases, and one was classified as an elective admit type. Two of the patients were discharged routinely, and one patient had a fatal outcome (admitted as an elective case). The remaining 3 patients were transferred to a long term facility or discharged to a home health care unit. The 96 year old patient was discharged to home health care.

Cases were diagnosed between 2000 and 2005, with no cases before or after those dates. The cases may have some seasonality, most of the cases (7 out of 8) were diagnosed between October and February, and the last case was admitted in May. One patient was admitted three times: during 2000, 2001 and 2005. The other patient was admitted at the beginning of 2000 and during their second admission in December of 2000, had a fatal outcome.

Other causes of Encephalitis: This category of encephalitis diagnoses represents a wide variety of infections including bacterial, viral, fungal infections, post-infectious encephalitis, toxin associated encephalitis, other unspecified meningitis related illnesses, herpes zoster virus, measles associated encephalitis, as well as other causes of encephalitis specified elsewhere. These categories were combined due to the limited number of infections in each subgroup. This category is comprised of 391 cases from 331 patients, contributing 21.5% of the patients admitted to the hospital for all encephalitis between 1999 and 2007. Gender distribution was not significantly different (p-value=0.128), males contributed slightly more cases representing 54.1% of the patients admitted with other causes of encephalitis. The average age was 39.9 years old (S.D.=25.1), with most cases occurring in patients older than 20 years old. There were 34 patients who were between 0 and 4 years old, most diagnosed with herpes zoster virus.

Most patients diagnosed with other types of encephalitis were either admitted through the emergency room (N=162) or through a physician referral (N=114). When looking at children at birth diagnosed with encephalitis, four of seven falls in this category, with the other three diagnosed with herpetic encephalitis. Over 58% of patients in this group had a routine discharge, while 22 (6.6%) had a fatal outcome, and 32 (9.7%) were "reserved for national assignment."

A yearly temporal trend or seasonality would be difficult to determine in this group due to the mixed nature of the encephalitis diagnoses classifications. 2004 and 2005 had the highest number of cases, with 54 in each year, and 2007 had the fewest number of cases (N=17). When looking at trends using a statistical package, this data is statistically significant, meaning the number of other cases varied significantly by year (p-value>0.05). When looking at the data for all cases, there were between 23 and 40 cases of other encephalitis diagnosed in each month when all data was combined. January had the highest number of total cases, and July had the fewest number of cases.

Unspecified cause of Encephalitis: Unspecified encephalitis was the most common diagnosis for all encephalitis cases; over 33.2% of the patients received this diagnosis. There were 613 cases from 512 patients, with no significant difference in the gender distribution, 47.1% of the cases were males, while 52.9% of the cases were females (p-value=0.185). The average age for patients with unknown causes of encephalitis was 45.7 years old (S.D.=225). All age groups were represented in this category, with unknown encephalitis contributing the most cases in all of the age groups except in those under 4. There were 54 cases in 48 patients that had an unknown cause of encephalitis that were also HIV+. These patients were classified as having HIV, NOS. There were also 30 cases of Lupus and 46 cases of demyelinating of the central nervous system associated encephalitis that were reclassified from an unknown cause to their respective category.

For those admitted with an unknown cause of encephalitis, 261 patients were admitted through the emergency room as an emergency, while the majority of the remaining patients were either admitted through a physician referral (N=182), or transferred from another hospital (N=47). One patient was admitted due to court or law enforcement reasons. Most patients were discharged routinely (269 of 512 patients), 33.6% were transferred to another facility or home health care, 8.8% were "reserved for national assignment", and only 24 had a fatal outcome (4.7%).

Trends for the unspecified cases, either yearly or seasonally are difficult to determine due to the lack of information on the etiology of the type of encephalitis a patient may actually have. When looking at yearly data, there were between 45 (in 2000) and 92 (in 2004) cases of unknown encephalitis diagnosed per year in Louisiana. When looking at the cases by diagnosis month when all years were combined, October had the fewest number of cases (N=42), while August had the highest number of cases (N=71).

Systemic Lupus Erythematosus: This category was comprised of cases that had either an "unknown cause of encephalitis" or an "other cause of encephalitis", who also had a diagnosis of "Systemic Lupus Erythematosus", due to the nature of the disease, and its ability to cause inflammation in multiple systems, including the central nervous system (Marcaida & Reik, 1999). As stated above 30 cases were previously classified as "unknown cause of encephalitis", as well as 204 cases classified as "other cause of encephalitis" which were all reclassified as "Lupus." The 243 cases (12.3% of total cases) were present in 159 individual patients (10.3% of patients).

Lupus had the highest number of patients discharged from hospitals multiple times with the same diagnosis of either "other encephalitis" or "unknown encephalitis" as well as "Lupus." SLE is a chronic, remitting, and relapsing disease that may lead patients to enter the hospital on numerous occasions (Marcaida & Reik, 1999). One patient was discharged from the hospital 8 times during the nine year time period data is presented on. A significant difference in the gender distribution was observed, 91.2% of the patients were females, while only 8.8% of the patients were males (p-value=0.001). The average age of patients was 42.4 years old (S.D.=15.4), with most patients falling in the age groups between 20 to 64 years old. Two patients were in the 10 to 14 years age group, one 11 years old and the other 12 years old.

For those admitted with Lupus as one of the diagnosis codes, 90 patients were admitted through the emergency room as an emergency, while the majority of the remaining patients were either admitted through a physician referral (N=51), or transferred from another hospital (N=12). Most patients were discharged routinely (105 of 243 patients), while 5 had a fatal outcome (3.1%).

When looking at the yearly data for all cases of Lupus discharged from Louisiana hospitals between 1999 and 2007, there appears to a steady number of cases from 1999 to 2006 with between 21 and 37 cases per year, however, in 2007 only 9 cases of lupus were diagnosed in the hospital discharge data. This decrease in the number of cases is true for almost all encephalitis diagnosis categories, except those diagnosed with herpetic encephalitis, meningococcal encephalitis, PMLE, and toxoplasmosis (all categories highly related to HIV). Seasonality does not appear to have an effect on the number of cases related to lupus, there were between 11 (August) and 26 (February) cases per month when data from all years was combined.

Demyelinating diseases associated encephalitis: The category "demyelinating diseases" was comprised of three groups: those with a diagnosis of "multiple sclerosis," "SICCA Syndrome," or "demyelinating disease of the Central Nervous System," who also had a diagnosis of "other encephalitis" (29 cases) or "unknown cause of encephalitis" (46 cases). Overall 75 cases of "demyelinating diseases" were diagnosed in 52 patients in the Encephalitis database (3.4%). There was a significant difference in the gender distribution, 69.2% of the patients were females while 30.8% of the patients were males (p-value=0.006). The average age for patients was 54.1 years old (S.D.=19.0). This group had the highest average age for all categories of encephalitis-associated hospitalizations, with most patients being at least 20 years old.

For those admitted with a demyelinating disease as one of the diagnosis codes, 19 patients were admitted through the emergency room as an emergency, while the majority of the remaining patients were either admitted through a physician referral (N=27), as an elective admit type. Most patients were discharged routinely, while 2 had a fatal outcome. 11 other patients were moved to either another short term facility or received home health care.

When looking at the yearly data for all cases of those diagnosed with a demyelinating disease with encephalitis from 1999 to 2007, the highest number of cases were seen in 2005 and 2006 (N=12 and 14 respectively), while 1999 had the lowest number of cases (N=2). Seasonality does not appear to

have an effect on the number of cases related to demyelinating diseases, there were between 3 (January and August) and 14 (October) cases per month when data from all years was combined.

Length of Stay and Cost of Encephalitis-associated hospitalization: Encephalitis-associated hospitalizations accounted for more than $70 million dollars in total hospital charges in Louisiana alone from 1999 to 2007 and contributed an estimated 20,000 days spent Louisiana hospitals, or about 2,592 days per year. Over 32% of encephalitis cases required a hospital stay between two to five days, with the longest hospital stay totaling 100 days for an HIV+ patient diagnosed with meningoencephalitis due to toxoplasmosis. 104 cases required a hospital stay between 0 days (meaning admit and discharge occurred on the same day), and one day. The average hospital stay for cases regardless of classification was about 11 days per case.

Encephalitis associated hospitalizations due to a known cause had a significantly longer hospital stay (12.1; S.D=11.3) than those with an unknown cause of encephalitis (10.4days; S.D=9.9; p-value=0.004). The average hospital stay for HIV+ patients was also significant longer (12.6 days; S.D.=11.5) than for those who were HIV negative (10.4 days; S.D.=10.3; p-value=0.0045). Table 4 presents the mean cost of treatment per case, the total cost of treatment for all cases associated with a specific encephalitis classification, the mean length of stay per case, and the total length of stay for all cases associated with a specific encephalitis classification.

Herpetic Encephalitis had the highest average cost of treatment per person costing on average $58,504 per case, while SSPE had the lowest cost of treatment per person costing on average $8,666 per case, as well as having the lowest contribution to the total cost of treatment for all cases. Of the 1905 cases discharged from hospitals, 78 did not have data on the hospital charges associated with their hospital stay. Unspecified encephalitis and herpetic encephalitis contributed the highest amounts of total cost of treatment. When looking at all those with HIV, regardless of encephalitis classification, the mean cost of treatment was $36,627, and the total cost contributed was significantly higher when all HIV cases were combined, and totaled over $10 million dollars in hospital treatment during the 8 year time period from 1999 to 2007.

Table 4. Top 10 Encephalitis category mean cost of hospital charges, total cost for all cases, mean length of hospital stay, and total days contributed for all cases in each category

Diagnosis	Average cost (S.D.)/case*	Total Cost*	Average length of stay (days)/case	Total length of stay (days)	Total Cases
Unspecified	$34,166 (46,910)	$20,158,152	9.66 (9.99)	919	613
Herpetic	$58,504 (63,677)	$15,620,765	14.35 (12.63)	622	276
Other	$37,291 (68,918)	$13,947,122	10.04 (10.63)	3,925	391
Lupus	$34,560 (34,773)	$7,706,908	10.69 (11.04)	2,501	234
PMLE	$32,741 (56,556)	$4,682,104	10.44 (8.91)	1,556	149
Toxoplasmosis	$41,335 (50,624)	$2,521,483	16.51 (14.58)	1,040	63
Demylination	$28,620 (35,103)	$2,032,089	9.48 (8.95)	711	75
Meningococcal	$56,047 (69,173)	$1,793,506	13.85 (15.81)	457	33
HIV, NOS**	$30,469 (27,845)	$1,767,206	9.87 (7.40)	3,961	63
SSPE	$8,666 (3,360)	$69,490	5.50 (3.42)	44	8
Total	$38,477 (54,664)	$70,298,825	10.89 (10.92)	20,736	1905

***Missing 78 cases**
****HIV (all cases): mean cost (S.D)=$36,627(41,517), Total cost=$10,841,752, mean stay(days)=12.15(10.97), Total days=3767, Total cases=310**

Discussion and Conclusion

Encephalitis associated hospitalizations in Louisiana contributed more than $70 million dollars in hospital costs, and 20,736 days spent in hospitals in 1,905 cases of encephalitis in 1,542 patients. On average, there were 19 deaths per year attributed to herpetic encephalitis, while unknown encephalitis contributed the most number of cases overall. While a figure associated with the hospital costs is presented, this number significantly underestimates the total burden of this disease, 19.2% of the cases were discharged to long-term care and home health care. Many of the etiologies related to encephalitis require a long term rehabilitation plan which will further contribute to the overall burden of encephalitis. Khetsuriana, et al., noted that their population based sample only accounted for the initial hospitalization, and not the later costs that would be associated with rehabilitation required for many of the patients admitted with encephalitis (Khetsuriani, Holman, & Anderson, 2002). Due to the nature of many of the etiologies of encephalitis, including herpetic encephalitis and meningococcal encephalitis, and the negative neurological outcomes related to the diseases it can be assumed that the costs associated with treatment after hospital discharge are sizeable (Whitley R. J., 1990) (Adams, Victor, & Roper, 1977).

Compared to previous studies using samples of the total population affected by encephalitis, the LAHIDD database includes all cases that are discharged from hospitals, including demographic and identification information for most patients. Based upon this information the number of patients and replicate cases were determined. Using all cases compared to just the initial visit by a patient did not bias the numbers significantly, except for etiologies which had multiple patients discharged from the hospital with the same encephalitis etiology. If only the total number of cases were used, herpetic encephalitis may have been underestimated, making up only 14.5% of the cases, while when looking at the number of patients, it made up 18.7% of the patients in the LAHIDD database. Lupus was overestimated when using the number of cases, representing 12.3% of the total cases, while only making up 10.3% of the total number of patients. This overestimation would be due to the fact that patients with a diagnosis of Lupus (SLE) had the highest number of repeat visits for patients diagnosed with encephalitis.

SLE is an autoimmune chronic and relapsing disease which could lead to patients being admitted to the hospital multiple times. Along with the potential for SLE to mimic encephalitis, it may also be caused by a complication in steroid treated patients (Granerod & Crowcroft, 2007), (Marcaida & Reik, 1999). There are a number of other diseases and clinical presentations which may also mimic encephalitis such as serum sickness, some meningitis diagnoses, as well as other demyelinating diseases (Marcaida & Reik, 1999). SLE and demyelinating diseases represented 13.7% of the patients discharged from the hospital with at least one diagnosis of encephalitis, either because of other causes of encephalitis or unknown causes of encephalitis. Due to the nature of the diseases, it is possible these classifications led to an overestimation on the burden of encephalitis in a hospital setting. Multiple sclerosis, SICCA syndrome, and other demyelinating causes of the central nervous system have all also been noted to be potential mimickers of encephalitis due to their role as inflammatory-mediated demyelinating diseases which could cause inflammation in the central nervous system (Trapp & Klaus-Armin, 2008). The LAHIDD database does not include information on the diagnostic procedures used to classify a person with encephalitis which is a potential limitation to the database.

Unknown cause of encephalitis was the most common encephalitis diagnosis in the LAHIDD database, it accounted for 32.2% of all cases, after those with HIV, Lupus, and demyelinating diseases were reclassified into their specified category. Before moving those cases, unknown causes of encephalitis accounted for 39% of all cases. This percentage is less than most reported studies where

unknown causes of encephalitis account for between 48% and 85% of all cases (Khetsuriani, Holman, & Anderson, 2002) (Nicolosi, Hauser, Beghi, & Kurland, 1986) (Ishikawa, Asano, Morishima, & al., 1993). Even in the Emerging Infectious Disease (EID) programs set up in California and Tennessee, extensive testing was done on a number of encephalitis cases that met the encephalitis patient case definition, and yet a high percentage of all cases remained unknown in cause (Acute Communicable Disease Control, California, 2007) (Glaser, et al., 2003), (Tennessee Department of Health Communicable and Environmental Disease Services, 2006). While results in the current study show that unknown causes of encephalitis only account for 32.2% of all cases, these cases still made up the largest category of encephalitis cases in the LAHIDD database. Khetsuriani, et al., describes multiple possibilities which may help account for the high number of unknown encephalitis cases. Depending on hospital and laboratory technology available certain techniques may not be available for testing samples which may make encephalitis etiology identification difficult. Further, many diagnoses require state-of-the art, and costly techniques that may not be available to all persons in the hospital limiting the diagnosis they may be able to get (Khetsuriani, Holman, & Anderson, 2002).

In previous studies, varicella-zoster virus encephalitis cases made up a decent percentage of the known encephalitis cases. In a Finnish study on childhood encephalitis, they found varicella to be the most common etiology, making up 25% of all cases, while another paper found that the number of varicella cases associated with encephalitis was 3 times higher than then number of encephalitis cases due to HSV-1 (Koskiniemi & Vaheri, 1989), (Rantala & Uhari, 1989). Recently, a decrease in the number of varicella cases due to the increased vaccination rates has led to a decrease in the number of post-infectious encephalitis cases world-wide (Seward, Watson, Peterson, & al., 2002). In the results from the current study there were only 25 cases of varicella-zoster virus associated encephalitis accounting for 1.3% of all cases. In a recent paper, varicella-zoster virus accounted for 2.5% of all hospital cases (known and unknown), however the study results were unreliable due to the low numbers of cases (Khetsuriani, Holman, & Anderson, 2002). Vaccination of other childhood diseases has also significantly reduced the number of post-infectious diseases, such as measles and mump (Rantala & Uhari, 1989). In the LAHIDD database there was only one cases of post-measles encephalitis in a 58 year old man who was admitted as an emergency case, but later discharged routinely, and there were no cases related to mumps. Over 50 other patients were diagnosed with post-infectious encephalitis, but did not have a specific etiology associated with them.

Between 1999 and 2005 there were, however, eight cases in five patients of SSPE, a chronic infection with progressive neurological disorder caused by an altered form of the measles virus. It typically affects children 2 to 10 years after the original illness has occurred (Office of Communications and Public Liason, 2007). In developed nations the incidence has decreased significantly due to the availability and use of the measles vaccine, making it a very rare encephalitis in the United States (Campbell, Andrews, Brown, & Miller, 2007) (Office of Communications and Public Liason, 2007). In developing countries, especially the Middle East, India, and Africa, SSPE is a more common illness in children with an average age at onset of 6 to 13 years old (Campbell, Andrews, Brown, & Miller, 2007) (Office of Communications and Public Liason, 2007). In one review paper it was noted the oldest onset for a case was 56 years old in the Middle East, but for the United States the oldest reported case was 32 years old (Campbell, Andrews, Brown, & Miller, 2007). Most of the papers that were reviewed for incident rates, and number of cases are from before the measles vaccination was available (Campbell, Andrews, Brown, & Miller, 2007). In a recent paper by Bellini, et al., the mean age at onset was 7.7 years old for SSPE cases in the United States (range: 1.8-13 years) (Bellini, Rota, Lowe, & et al., 2005). In the LAHIDD database the average age at onset was 46.6 years old (range=31-96), which is almost 36

years older than the collective average noted in the review paper of 9.9 years old (Campbell, Andrews, Brown, & Miller, 2007).

Some possible explanations for this huge age gap may be due to doctor misclassification; however, the patients were not diagnosed in the same parishes or hospitals. Another possibility is that they had been previously diagnosed with SSPE when they were younger, and the doctor felt this may have contributed or caused their current case of encephalitis. Most patients diagnosed with SSPE typically have a fatal outcome within 5 years of diagnosis, so this explanation is not a likely cause for the diagnosis of eight SSPE cases in patients. Finally, in the review by Campbell, et al., they mention the possibility for longer latency periods of the encephalitis in those who have received the measles vaccination, however, the delay in illness would not account for the 38 year increase in average age (Campbell, Andrews, Brown, & Miller, 2007). Further diagnostic and testing information would have been useful in determining how these cases were diagnosed as SSPE as opposed to other post-infectious encephalitis diagnoses that may be more common in older patients.

There were 252 HIV+ with encephalitis in the LAHIDD database from 1999 to 2007, representing 16.3% of the patients, 196 of the HIV+ patients were diagnosed with a defined type encephalitis, while 52 patients were diagnosed with either other causes of encephalitis or unknown cause of encephalitis. Meningoencephalitis due to toxoplasmosis and PMLE (a demyelinating disease caused by JC virus) were the most common etiologies associated with patients who were HIV+. Multiple papers have noted that with increased HAART treatment use, mortality due to these AIDS defining conditions. However, other studies note that many patients with PMLE may be either unresponsive to HAART treatment or a side effect after treatment has started (Wyen, Lehmann, Fatkenheur, & Hoffman, 2005). Toxoplasmosis was identified in 51 patients, 48 of them were HIV+, and PMLE was identified in 109 patients, 97 of them were HIV+. HIV is having a major impact on the types of encephalitis that are becoming more common.

There are multiple limitations to this study. Much of the results presented are in the form of basic frequencies used to describe the characteristics associated with encephalitis that are non-arbo-related using the LAHIDD database. Since no behavior data or diagnostic data was present or available to use, no risk assessment or further characteristics describing the data could be discussed further than the patients gender, age group, admit data, admit type, admit source, discharge type, and location. There is also the potential for differential diagnoses and diagnostic criteria used throughout the state, depending on the technologies available for testing to determine further characteristics of the patients' encephalitis. Other limitations are the ability to differentiate between certain subgroups of encephalitis, such as for herpetic encephalitis, there is only one ICD-9 diagnosis code (0534), while there are two main forms (HSV-1, more common and HSV-2). While some data was presented on individual categories, many of the diagnosis groups that had less than 10 to 15 cases were typically grouped in the "other cause of encephalitis" category, thus many of the subgroups were not adequately analyzed.

These limitations may have some effect on potential biases within the paper such as certain diagnosis errors or misclassifications of encephalitis diagnoses which may have led to an over-estimation of the burden of encephalitis on Louisiana between 1999 and 2007. However, many cases of encephalitis go undiagnosed and unreported, and would not be reported on the hospital discharge database. Previous studies used population based samples to obtain estimates of encephalitis burden; the data available for this study represents every diagnosed cases of non-arbo-related encephalitis in Louisiana that was discharged from a hospital. The data set represents an entire population sample for the state of Louisiana during 1999 to 2007 for diagnosis of encephalitis.

This data can be viewed in multiple ways that include the whole spectrum of public health concerns and can be further expanded on to provide a more in-depth picture of the burden encephalitis-

associated hospitalizations may be having in the health care industry. The data available in the discharge database gives a general picture of the financial burden associated with this disease, however, as noted above, many patients with encephalitis will not return to a normal lifestyle, and will require further treatment and services which all cost money and contribute to the overall burden associated with encephalitis. Additionally, there are many social and behavioral aspects that may be related to certain encephalitis classifications and the outcomes associated with those diagnoses. There is no data provided in the LAHIDD database that would help determine if there are predictors, confounders or effect modifiers which could have an impact not only on having encephalitis, but also the outcome associated with that encephalitis. One category of encephalitis that was briefly mentioned, but categorized as "Other encephalitis" is the diagnosis of "toxic encephalitis," this may be caused by certain environmental aspects that are not included in the data available in the LAHIDD database. All fields of public health have a stake in future descriptions of encephalitis and the outside factors that may influence, reduces, or change the course of encephalitis-associated hospitalizations.

In the past two decades, encephalitis cases due to once rare diseases have increased, in part due to immune-compromised patients, including those who are HIV positive. However, the cases are not limited to HIV+ patients, many encephalitis categories are directly related to post-infections of many childhood diseases including the varicella-zoster virus (chicken pox) and measles, herpes simplex virus (HSV-1 and 2), as well as many newly emerging diseases that could have a likely impact on the number of encephalitis cases seen in the future. Much work has gone into describing and characterizing arbo-related types of encephalitis including West Nile encephalitis, St. Louis encephalitis, and more recently Nipah Valley encephalitis. Due to the nature of data available through the LAHIDD database, and the uncertainty in many of causes of encephalitis (over 32% diagnosed with an unknown cause of encephalitis), there is the possibility that many of these cases may be related to emerging causes and past infections, and environmental factors that we have not yet identified as risk factors.

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Appendix: Tables and Graphs

Table 5. Gender distribution for the 10 main classifications of encephalitis

	Patient Gender		
Diagnosis	Female N (%)	Male N (%)	p-value
Demyelination	36 (69.2)	16 (30.8)	0.006*
HIV	18 (32.1)	38 (67.9)	0.008*
Herpetic	115 (48.5)	122 (51.5)	0.650
Lupus	145 (91.2)	14 (8.8)	<0.001*
Meningococcal	14 (46.7)	16 (53.3)	0.715
Other	152 (45.9)	179 (54.1)	0.128
PMLE	36 (33.0)	73 (67.0)	<0.001*
SSPE	2 (40.0)	3 (60.0)	0.6547
Toxoplasmosis	11 (21.6)	40 (78.4)	<0.001*
Unspecified	271 (52.9)	241 (47.1)	0.185
Total	800 (51.9)	742 (48.1)	

*Significant difference in gender (p-value <0.05)

Table 6. Patient age groups and average age for 10 main classifications of encephalitis

	Patient Age Group (years)								
Diagnosis	0 to 1	1 to 4	5 to 9	10 to 14	15 to 19	20 to 44	45 to 64	65+	**Mean (SD)**
Demylination	0	1	0	1	0	15	16	19	54.1 (19.0)
HIV	0	0	0	0	0	35	19	2	42.5 (10.5)
Herpetic	19	5	2	5	6	65	51	84	48.6 (25.9)
Lupus	0	0	0	2	7	83	48	19	42.4 (15.4)
Meningococcal	1	0	0	2	1	13	8	4	40.2 (20.5)
Other	8	26	21	17	12	94	87	66	39.9 (25.1)
PMLE	0	1	0	0	1	72	28	8	42.9 (12.3)
SSPE	0	0	0	0	0	4	0	1	46.6 (27.8)
Toxoplasmosis	0	0	0	0	0	37	14	0	38.1 (8.7)
Unspecified	6	18	23	23	23	138	151	130	45.7 (24.0)
Total	**34**	**51**	**46**	**50**	**50**	**556**	**422**	**333**	**44.2 (22.5)**

Table 7. Gender distribution for all patients based on HIV status

	Patients HIV Status	
Gender	Positive	Negative
Male	177	565
Female	75	725

chisq=59.03, p<0.0001
OR= 3.03 (2.24, 4.10)

Table 8. Patient admit source for 10 classifications of Encephalitis

	Patient Admit Source									
Diagnosis	Physician referral	Emergency room	Transfer from Hospital	Clinic referral	HMO referral	Transfer from another heath care facility	Transfer from skilled nursing home	Child delivery	Court/Law enforcement	Information not available
Demylination	27	19	0	1	0	0	0	0	0	5
HIV	13	38	1	1	0	1	0	0	0	0
Herpetic	60	135	20	4	0	2	1	3	0	0
Lupus	51	90	10	0	0	1	1	0	0	5
Meningococcal	7	21	2	1	0	1	0	0	0	0
Other	114	162	22	8	1	2	1	4	0	5
PMLE	23	76	5	4	0	0	0	0	0	1
SSPE	1	3	0	0	0	0	0	0	0	0
Toxoplasmosis	12	35	2	0	0	0	0	0	0	0
Unspecified	182	261	47	8	1	3	0	0	1	3
Total	**490**	**840**	**109**	**27**	**2**	**5**	**3**	**7**	**1**	**18**

Table 9. All cases admit type for 10 main classifications of encephalitis

	All cases Admit Type				
Diagnosis	Elective	Emergency	Urgent	Newborn	Missing
Demylination	32	29	14	0	0
HIV	8	41	14	0	0
Herpetic	51	146	75	3	1
Lupus	70	127	37	0	0
Meningococcal	8	22	3	0	0
Other	97	182	104	4	4
PMLE	19	99	31	0	0
SSPE	1	4	3	0	0
Toxoplasmosis	7	42	14	0	0
Unspecified	156	298	152	2	5
Total	**449**	**990**	**447**	**9**	**10**

Table 10. Patients admit type for 10 main classifications of encephalitis

	Patients Admit Type				
Diagnosis	Elective	Emergency	Urgent	Newborn	Missing
Demylination	24	19	9	0	0
HIV	6	38	12	0	0
Herpetic	36	135	62	3	1
Lupus	45	90	24	0	0
Meningococcal	7	21	2	0	0
Other	78	162	83	4	4
PMLE	11	76	22	0	0
SSPE	0	3	2	0	0
Toxoplasmosis	5	35	11	0	0
Unspecified	119	261	126	1	5
Total	**331**	**840**	**353**	**8**	**10**

Table 11. All cases discharge type for 10 main classifications of encephalitis

	Discharge Type								
Diagnosis	Routine	Expired*	Another short-term facility	Home health care	Left against medical advice	Long-term care and other facilities	Missing	Other	Reserved for National Assignment
Demylination	40	2	5	11	0	9	0	0	8
HIV	32	13	8	2	2	4	0	0	2
Herpetic	119	30	38	35	1	33	0	0	20
Lupus	154	6	20	36	1	12	0	0	5
Meningococcal	16	4	3	4	1	2	0	0	3
Other	224	23	48	33	0	30	0	1	32
PMLE	73	25	19	10	0	17	1	0	3
SSPE	2	1	0	1	0	4	0	0	0
Toxoplasmosis	34	7	4	3	0	9	0	1	5
Unspecified	316	30	94	65	1	46	0	1	60
Total	**1010**	**142**	**239**	**200**	**6**	**166**	**1**	**3**	**138**

*Expired cases included: All expired cases and those discharged to Hospice due to the nature of hospice care

Table 12. Patients discharge type for 10 main classifications of encephalitis

	Discharge Type *Rank=1								
Diagnosis	Routine	Expired*	Another short-term facility	Home health care	Left against medical advice	Long-term care and other facilities	Missing	Other	Reserved for National Assignment
Demylination	31	2	5	6	0	5	0	0	3
HIV	28	12	8	1	2	3	0	0	2
Herpetic	102	26	32	27	1	30	0	0	19
Lupus	105	5	16	21	0	8	0	0	4
Meningococcal	15	4	3	4	0	2	0	0	2
Other	193	22	42	25	0	23	0	0	26
PMLE	53	18	16	8	0	11	1	0	2
SSPE	2	0	0	1	0	2	0	0	0
Toxoplasmosis	30	6	4	2	0	7	0	0	2
Unspecified	269	24	81	53	1	38	0	1	45
Total	**828**	**119**	**207**	**148**	**4**	**129**	**1**	**1**	**105**

*Expired cases included: All expired cases and those discharged to Hospice due to the nature of hospice care

Table 13.Month admit of all cases for 10 main classifications of encephalitis

	Month Admit for all cases diagnosed with Encephalitis											
Diagnosis	Jan	Feb	March	April	May	June	July	Aug	Sept	Oct	Nov	Dec
Demylination	3	6	5	9	4	8	4	3	7	14	7	5
HIV	2	8	2	8	10	6	4	6	7	4	3	3
Herpetic	24	29	35	22	29	23	19	20	11	24	18	22
Lupus	23	26	17	19	20	20	25	11	21	18	16	18
Meningococcal	4	3	1	2	3	4	2	4	3	3	1	3
Other	40	29	37	37	30	27	23	37	29	34	38	30
PMLE	12	9	10	4	11	11	10	11	16	17	19	19
SSPE	1	2	0	0	1	0	0	0	0	1	2	1
Toxoplasmosis	6	2	3	3	4	5	11	8	4	6	3	8
Unspecified	50	56	50	49	47	48	49	71	56	44	42	51
Total	**165**	**170**	**160**	**153**	**159**	**152**	**147**	**171**	**154**	**165**	**149**	**160**

Table 14. Year admit of all cases for 10 main classifications of encephalitis

	Year Admit for all cases of encephalitis								
Diagnosis	1999	2000	2001	2002	2003	2004	2005	2006	2007
Demylination	2	7	5	9	9	9	12	14	8
HIV	4	9	7	9	8	8	6	6	6
Herpetic	33	34	31	34	25	27	35	28	29
Lupus	21	28	28	37	33	30	27	21	9
Meningococcal	0	2	3	5	3	5	4	4	7
Other	45	40	48	56	29	54	54	48	17
PMLE	18	12	15	19	11	20	24	12	18
SSPE	0	2	2	1	0	2	1	0	0
Toxoplasmosis	9	14	10	5	3	3	3	9	7
Unspecified	63	45	65	65	71	92	74	89	49
Total	**195**	**193**	**214**	**240**	**192**	**250**	**240**	**231**	**150**

Table 15. Cases of encephalitis grouped by charges and main encephalitis diagnosis

	Cases charges grouped by diagnosis											
Diagnosis	$0 - 5,000	$5,001 - 10,000	$10,001 - 15,000	$15,001 - 20,000	$20,001 - 25,000	$25,001 - 30,000	$30,001 - 40,000	$40,001 - 50,000	$50,001 - 70,000	$70,001 - 100,000	$100,001 - 200,000	$200,001 +
Demylination	5	12	13	13	6	5	6	1	5	1	4	0
HIV	4	7	8	9	7	4	4	5	4	4	2	0
Herpetic	6	22	20	19	29	17	34	20	29	25	34	9
Lupus	20	28	32	33	7	12	20	22	19	15	14	1
Meningococcal	1	2	5	1	3	3	3	2	5	2	3	2
Other	36	54	41	44	31	22	46	22	34	18	23	3
PMLE	7	27	20	16	12	9	16	12	12	9	2	1
SSPE	2	2	4	0	0	0	0	0	0	0	0	0
Toxoplasmosis	3	10	5	8	4	5	3	6	7	7	1	2
Unspecified	66	105	66	68	45	41	55	40	37	32	22	13
Total	**150**	**269**	**214**	**211**	**144**	**118**	**187**	**130**	**152**	**116**	**105**	**31**

Table 16. Cases of encephalitis grouped by length of stay and main encephalitis diagnosis

	Length of Stay Groups (days)							
Diagnosis	0 to 1	2 to 5	6 to 10	11 to 20	21 to 30	31 to 40	41 to 50	51 +
Demylination	4	31	14	19	4	0	3	0
HIV	4	12	24	20	1	1	1	0
Herpetic	3	59	63	90	41	9	6	5
Lupus	13	85	54	47	24	6	1	4
Meningococcal	1	9	11	8	1	0	1	2
Other	21	141	110	79	24	3	4	9
PMLE	4	45	51	31	13	2	2	1
SSPE	0	5	2	1	0	0	0	0
Toxoplasmosis	2	10	13	17	15	5	0	1
Unspecified	52	213	152	136	36	13	5	6
Total	**104**	**610**	**494**	**448**	**159**	**39**	**23**	**28**

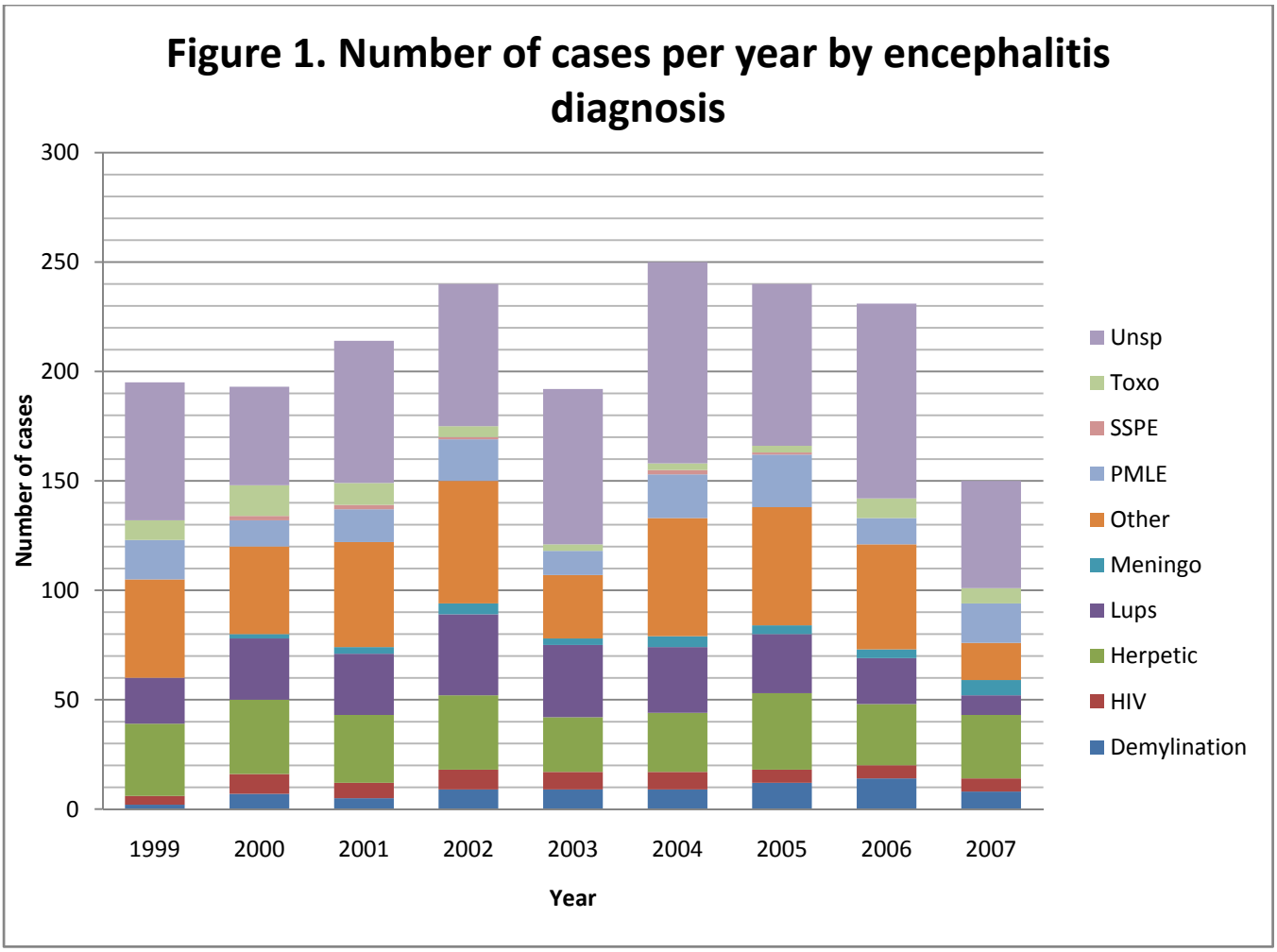
Figure 1. Number of cases per year by encephalitis diagnosis
Number of cases
300
250
200
150
100
50
0
1999
2000
2001
2002
2003
2004
2005
2006
2007
Year
Unsp
Toxo
SSPE
PMLE
Other
Meningo
Lups
Herpetic
HIV
Demylination
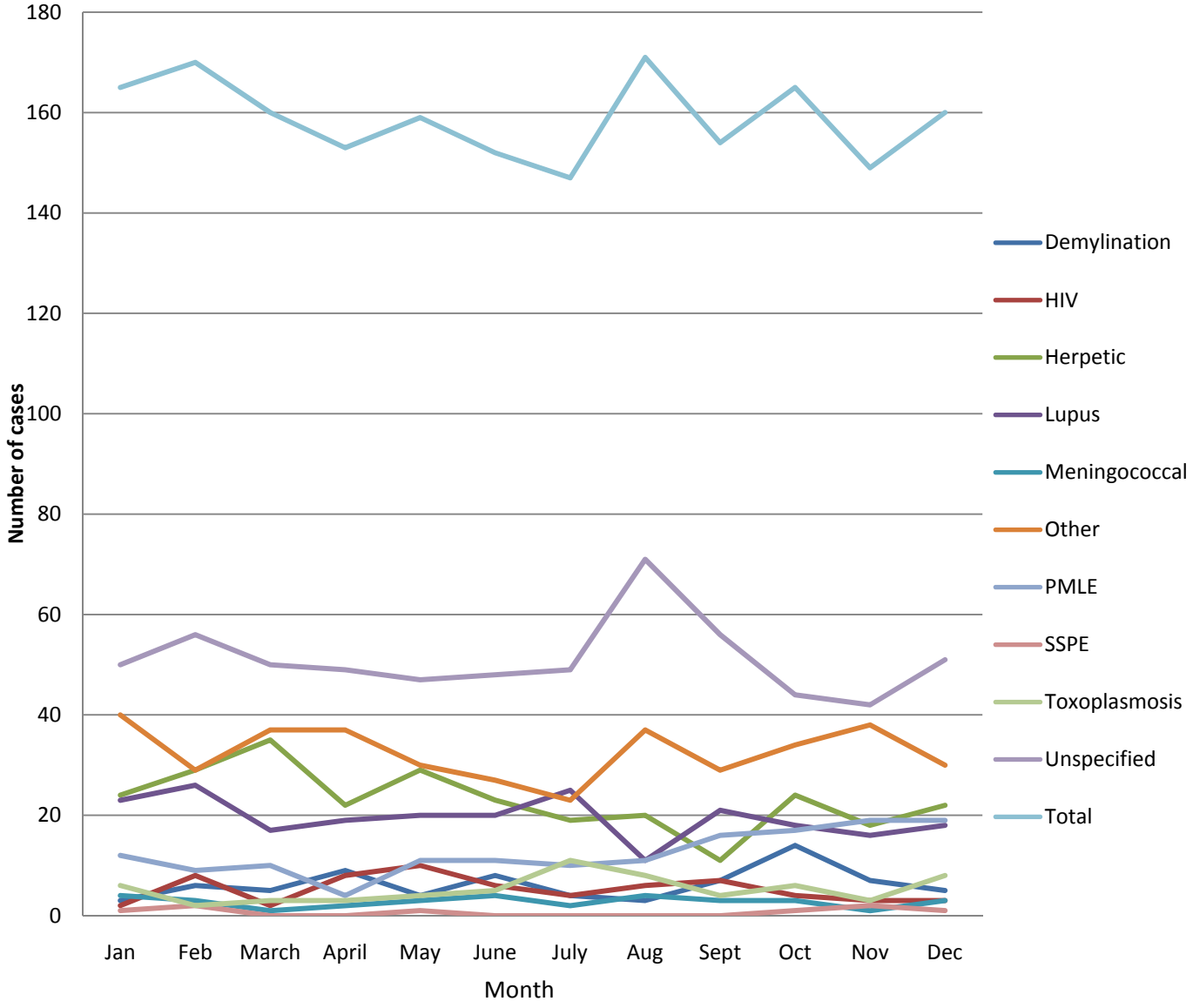
Figure 2. Total number of cases diagnosed per month for the main categories of encephalitis