

Abstract

Utz, John Todd. An economic and social analysis of La Crosse encephalitis in North Carolina. (Under the direction of Charles S. Apperson)

La Crosse encephalitis (LACE), a viral illness vectored by mosquitoes, is endemic in western North Carolina. Clinical manifestations of La Crosse (LAC) virus infection range from mild fever to aseptic meningitis or frank encephalitis. Due to non-specific or sub-clinical symptoms and the absence of an accurate, timely diagnostic tool, the true incidence of LAC virus infection is unknown for the endemic foci of the illness. To estimate the socioeconomic burden of LACE in North Carolina, interviews of serologically confirmed LACE patients or the parent(s)/guardian(s) of the case patients were conducted. The estimated burden of LACE was divided into three categories: direct medical costs; indirect medical costs; and social costs. Direct medical cost is the dollar value associated with medical treatment and rehabilitation for LACE. Indirect medical costs refer to any lost income and/or expense required that is not involved in treatment or rehabilitation of a person with LACE. Social costs were measured with Disability Adjusted Life Years (DALYs) and the Impact of La Crosse Encephalitis Scale (ILCES). DALYs are a non-monetary estimate of productive life years lost due to an illness or health event, while ILCES scores measure the affect of LACE on the overall emotional and social well being of the case patient and family. Participants exhibited three severities of LACE: frank encephalitis with no sequelae (n = 4); frank encephalitis with limited sequelae (n = 16); and frank encephalitis with lifetime sequelae (n = 5). The total cumulative time of study, date of onset of LACE to date of interview, for all case patients within the three disease severity classes was 100.59 life years.

The total direct and indirect medical costs associated with LACE for 100.59 life years of the 25 patients with frank encephalitis was \$794,303, ranging from \$7,521 - 175,586 for individual case patients. On average, the direct and indirect medical costs of a single case of LACE were \$32,974 (\pm SD = 34,793, n = 25). The projected cost of a case of LACE with lifetime neurological sequelae ranged from \$48,775 to \$3,224,831 (n = 5), depending on severity of sequelae. Quantitative and qualitative measures of the socioeconomic burden of LACE are included in the analyses to create an estimate addressing both the economic and social impacts of LACE on the family. For the 25 LACE patients, 55.19 of 100.59 life years (54.83%) were impaired to some degree. Along with impaired life years, approximately 13.00 DALYs were accumulated for the 25 patients over 100.59 life years of study. ILCES scores demonstrate the majority of the social burden is borne by patients with lifetime, neurological sequelae (n = 5). Projected DALY estimates for individual patients with lifetime neurological sequelae ranged from 12.90 – 72.37 DALYs, depending on DALY type and estimated life expectancy used. The socioeconomic burden resulting from LACE is substantial, which highlights the importance of the illness in western North Carolina, as well as the need for active surveillance and prevention programs for the vector/virus complex.

**AN ECONOMIC AND SOCIAL ANALYSIS OF LA CROSSE ENCEPHALITIS IN
NORTH CAROLINA**

by

JOHN TODD UTZ

A thesis submitted to the Graduate Faculty of North Carolina State University in
partial fulfillment of the requirements for the Degree of Master of Science

ENTOMOLOGY

RALEIGH

2002

APPROVED BY:

J. Newt MacCormack

V. Kerry Smith

D. Wes Watson

**Charles S. Apperson
(Chair of Advisory Committee)**

DEDICATION

This work is dedicated to the people of the village of Lutsangani, Kenya. In particular, my “brother and sister” Nyamawi “Pera” and Rahema Mwamboa. Ninawashukuru sana watu wa Chonyi, maisha salama watu wangu.

BIOGRAPHY

John Todd Utz was born in St. Louis, Missouri on January 5, 1972 to John Howard and Mary Jo Utz. In 1990, he graduated from Granite City High School in Granite City, Illinois and attended Eastern Illinois University where he earned a B. S. in Zoology and Botany along with high school teaching certification in biology in May 1994. After college, he entered the United States Peace Corps and served as a volunteer secondary school science teacher in the village of Lutsangani in the tribal lands of Chonyi, Kenya from October 1994 to December 1996. Following his Peace Corps experience, Todd served as a volunteer teacher on the Eastern Navajo Reservation in Thoreau, New Mexico as a high school Science teacher at St. Bonaventure High School, in conjunction with the Americorps Volunteer Service for two years. After completion of service in New Mexico, Todd and Marnie Gail Gamble were married on July 17, 1999. Soon after marriage, both Marnie and Todd moved to western Turkey and taught at a national school for one year. In the fall of 2000, Todd entered the department of Entomology at North Carolina State University.

ACKNOWLEDGEMENTS

I would not have been able to complete this task without academic and personal support. I am thankful to Dr. Charles Apperson for providing me the opportunity to further my education and work towards a better understanding of La Crosse encephalitis in North Carolina. Along with Dr. Charles Apperson, my graduate committee, composed of Drs. Newt MacCormack, Kerry Smith and Wes Watson have provided guidance and support throughout the course of this study. I must also thank all the families that have participated in this investigation of La Crosse encephalitis. Due to their cooperation and candor, the public health and research communities will have a better understanding of the impact of La Crosse encephalitis on the individual, family and community. I am also grateful to the Cherokee Tribal Counsel for their cooperation and assistance over the course of this investigation. During the course of the investigation, Barbara Dietz at Mission Memorial Hospital, Eddie Welch at Indian Health Services, Dr. Martha Salyers at Buncombe County Health Center and Dr. William Huffstutter have been very helpful in providing information and guidance throughout the study.

I am also grateful to the Dearstyne research community, graduate students, faculty and staff of the Department of Entomology at North Carolina State University. As students, we are often under great stress and pressure during the pursuit of our various endeavors. Having a knowledgeable and supportive network of teachers, staff, graduate students and friends around me has made my graduate experience at NCSU more productive and enjoyable. Personally, I have been fortunate to have the support of my family and friends during all of my professional and personal

pursuits. Many thanks to my family and friends in ports and points around the globe. Lastly, I thank my friend, companion and wife, Marnie. She supports me and is a primary source of light and inspiration in my life.

TABLE OF CONTENTS

	Page
LIST OF TABLES	<i>ix</i>
LIST OF FIGURES	<i>x</i>
LIST OF APPENDICES	<i>xii</i>
CHAPTER 1: INTRODUCTION AND LITERATURE REVIEW	1
Background.....	2
Epidemiology of La Crosse Encephalitis.....	3
Geographic Distribution.....	3
Incidence of La Crosse Encephalitis.....	4
Seasonal Distribution, Age and Gender of LACE Cases.....	5
Clinical Manifestations and Sequelae of LACE.....	6
Symptoms of LACE.....	6
Sequelae Resulting from LACE.....	7
Biology of La Crosse Virus.....	9
Dynamics and Efficiency of Horizontal Transmission.....	10
Dynamics and Efficiency of Vertical Transmission.....	12
Need for Study.....	13
Assessing the Economic and Social Burden of Disease.....	15
Disability Adjusted Life Years.....	15
Impact of La Crosse Encephalitis Scale.....	18
Past Case Studies and Methods of Quantifying Burden.....	19
Plan of Research.....	26

References Cited.....	28
CHAPTER 2: AN ECONOMIC AND SOCIAL ANALYSIS OF LA	
CROSSE ENCEPHALITIS IN NORTH CAROLINA.....	36
Introduction.....	37
Materials and Methods.....	40
Study Population.....	40
Management of Interviews.....	40
Questionnaire.....	41
Direct Medical Costs.....	43
Indirect Medical Costs.....	45
Social Costs.....	46
Disability Adjusted Life Years.....	47
Dollar Costs: Estimates and Projections.....	50
Disease Severity and Age Classification.....	52
Data Analysis.....	53
Results and Discussion.....	55
Epidemiology of La Crosse Encephalitis.....	55
Reported Symptoms.....	56
Reported Sequelae.....	58
Direct Medical Measures.....	60
Indirect Medical Measures.....	64
Total Direct and Indirect Medical Costs.....	67
Social Costs/Impact.....	69

Impaired Life Years.....	69
Current Disability Adjusted Life Years.....	69
Projected Disability Adjusted Life Years.....	70
Impact of La Crosse Encephalitis Scale.....	71
Stressors.....	73
References Cited.....	81

LIST OF TABLES

		Page
Table 2.1	Epidemiological information for participants in La Crosse encephalitis study.....	86
Table 2.2	Chronic sequelae reported for La Crosse encephalitis case patients.....	87
Table 2.3	Direct medical costs in 2001 dollars for 24 case patients by age and sequelae class due to La Crosse encephalitis.....	88
Table 2.4	Projected lifetime direct medical costs in 2001 dollars for four lifetime (LS) sequelae class La Crosse encephalitis case patients with similar severity of sequelae from date of onset of illness.....	89
Table 2.5	Projected lifetime direct and indirect medical costs for La Crosse encephalitis case patient #025.....	90
Table 2.6	Direct medical days incurred as a result of La Crosse encephalitis for 25 case patients by age and sequelae class.....	91
Table 2.7	Procedures and services reported for La Crosse encephalitis case patients.....	92
Table 2.8	Indirect medical days lost due to La Crosse encephalitis by 25 case patients by age and sequelae class.....	93
Table 2.9	Indirect medical costs in 2001 dollars due to La Crosse encephalitis incurred by 25 case patients.....	94
Table 2.10	Total costs in 2001 dollars due to La Crosse encephalitis by age and sequelae class.....	95
Table 2.11	Lifetime Disability Adjusted Life Year (DALY) estimates for study participants experiencing lifetime sequelae from La Crosse encephalitis from date of onset of illness.....	96
Table 2.12	Projected Disability Adjusted Life Years for four La Crosse encephalitis case patients experiencing similar lifetime sequelae.....	97
Table 2.13	Participant identified stressors due to La Crosse encephalitis.....	98

LIST OF FIGURES

		Page
Figure 2.1	Reported number of La Crosse encephalitis cases in North Carolina between 1989 and 2001 compared to the number of La Crosse encephalitis cases included in this analysis.....	99
Figure 2.2	Age distribution of La Crosse encephalitis case patients included in study.....	101
Figure 2.3	La Crosse encephalitis (LACE) cases (n = 25) included in study by month of onset.....	103
Figure 2.4	Annual reported income (2000) of 25 families of La Crosse encephalitis case patients.....	105
Figure 2.5	Parent/adult patient reported symptoms of La Crosse encephalitis before hospitalization for 25 case patients..	107
Figure 2.6	Parent/adult patient reported sequelae following release from hospital for 25 LACE case patients.....	109
Figure 2.7	Age and La Crosse encephalitis sequelae class of study participants.....	111
Figure 2.8	Mean direct medical costs by La Crosse encephalitis (LACE) sequelae class for 24 case patients	113
Figure 2.9	Mean percent time impaired for 25 La Crosse encephalitis case patients by sequelae class.....	115
Figure 2.10	Mean percent burden calculated for two types of Disability Adjusted Life Years (DALYs) for 25 La Crosse encephalitis case patients assigned to sequelae classes for 100.59 Cumulative Life Years (CLY) of study.....	117
Figure 2.11	Projected Disability Adjusted Life Years (USDALY = United States DALY, SDALY = Standard DALY) for five La Crosse encephalitis case patients projected to have lifetime neurological sequelae.....	119
Figure 2.12	Scores for 24 La Crosse encephalitis (LACE) case patients on the Impact of La Crosse Encephalitis Scale (ILCES) by time elapsed from onset of illness.....	121

Figure 2.13	Total mean Impact of La Crosse Encephalitis Scale (ILCES) scores and overall percent burden resulting from La Crosse encephalitis for 24 case patients that were assigned to sequelae classes.....	123
Figure 2.14	Mean scores for Impact of La Crosse Encephalitis Scale (ILCES) by quality of life category and La Crosse encephalitis sequelae class for 24 case patients.....	125
Figure 2.15	Mean quality of life ratings (QOL) for 24 La Crosse encephalitis (LACE) case patients assigned to sequelae classes.....	127

LIST OF APPENDICES

		Page
Appendix 1	Contact of participants and conformation of interviews.....	129
Appendix 2	Formulas for calculating Disability Adjusted Life Years.....	130
Appendix 3	Survey Questionnaire.....	132
Appendix 4	Data obtained from interviews of families of 25 La Crosse encephalitis case patients from North Carolina between 1989 and 2001.....	144
	Key to Abbreviations.....	145
Appendix 4.1	Background Information.....	149
Appendix 4.2	Direct Medical Days.....	150
Appendix 4.3	Direct Medical Dollars.....	152
Appendix 4.4	Indirect Medical Days.....	154
Appendix 4.5	Indirect Medical Dollars.....	155
Appendix 4.6	Total Dollar Costs.....	157
Appendix 4.7	Reported Symptoms.....	158
Appendix 4.8	Reported Sequelae.....	160
Appendix 4.9	Hospital Disability Adjusted Life Years.....	162
Appendix 4.10	Recovery Disability Adjusted Life Years.....	164
Appendix 4.11	Impact of La Crosse Encephalitis Scale Scores.....	166
Appendix 4.12	Awareness of Illness and Required Procedures.....	168

Chapter 1

INTRODUCTION AND LITERATURE REVIEW

Background.

La Crosse (LAC) virus is a mosquito-transmitted bunyavirus of the California (CAL) serogroup that causes encephalitis in people, predominantly adolescents (Thompson and Gundersen 1983). LAC virus was first isolated in 1964 from the brain tissue of a four-year-old girl who died from complications of severe encephalitis in La Crosse, Wisconsin in 1960 (Grimstad 1988). The 30 to 180 annual human cases of La Crosse encephalitis (LACE) reported in the United States represent 8% to 30% of all mosquito-related encephalitis cases, making LACE the most common mosquito-borne disease in the United States (Rust *et al.* 1999). The primary vector for LAC virus is *Ochlerotatus triseriatus* (Say) the eastern treehole mosquito, which uses flooded tree holes and discarded, man-made containers as mosquito production sites (Thompson 1983). LAC virus has also been isolated from *Aedes albopictus* (Skuse), the Asian tiger mosquito, adjacent to the residences of LACE case patients in North Carolina and Tennessee (Gerhardt *et al.* 2001). The importance of *Aedes albopictus* as a vector of LAC virus has not been clearly established. However, in a recent epidemiological investigation in eastern Tennessee, three significant differences were identified between people infected with LAC virus and those not infected with LAC virus: time spent outdoors during the day; residing within 100 meters of one or more tree holes; and abundance of *Aedes albopictus* at residence (Erwin *et al.* 2002).

Epidemiology of La Crosse Encephalitis.

Geographic Distribution. Cases of LACE have been reported throughout the Midwestern US, ranging from Minnesota to Texas and east to New York and Georgia. Though isolations of the virus have been made in only 13 states, clinical cases of LACE have been reported in 24 states (Grimstad 1988). On average, the Centers For Disease Control and Prevention (CDC) reports 73 cases of LACE annually, with a range of 29 - 139 cases (Jones *et al.* 1999). Between 1996 and 1997, 252 cases of LACE were reported nationally (CDC 1998). Because LACE is misdiagnosed as “flu” or “summer cold”, the true number of mild or sub clinical cases is presently unknown, but estimated to be as great as 300,000 virus infections per year in the United States (Rust *et al.* 1999). Currently, a vaccine for LAC virus does not exist. Virus transmission must be prevented through mosquito control measures (reduction/eradication of mosquito production sites) and protection of susceptible humans through the use of repellants or avoidance of endemic areas. Historically, most cases of LACE have been reported for the Midwestern states of the United States (Kappus *et al.* 1983). However, LACE is endemic in North Carolina and is increasingly recognized in Tennessee, Virginia and West Virginia (CDC 1998). During 1996 - 1997, West Virginia reported 139 cases of LACE, which accounted for 55% of all cases reported nationally during the same time period (CDC 1998). Between 1996 and 1997, North Carolina ranked 8th in the nation for LACE cases, accounting for 2.8% of the 252 cases reported over the two-year period. During the same time period, LACE was the most frequently reported arthropod borne

encephalitis in the United States (CDC 1998). All reported LACE cases in North Carolina were contracted in the Blue Ridge Mountain area of western North Carolina, and most of these cases originated in or around the Cherokee Indian Reservation area of Jackson and Swain counties (Szumlas *et al.* 1996a).

Incidence of La Crosse Encephalitis. LACE is often misdiagnosed as “flu” or “summer cold”; therefore, the true incidence of mild or sub clinical infections is presently unknown, but estimated to be as great as 300,000 infections per year in the United States (Rust *et al.* 1999). The approximate annual incidence of reported LACE cases in the endemic foci is 20 - 30/100,000 (McJunkin *et al.* 1998). Exposure to mosquitoes is the primary risk factor for LACE (Erwin *et al.* 2002). Retrospective serologic surveys indicate that the ratio of inapparent-to-apparent LAC virus infections in children range from 26:1 to 1,571:1. Antibody prevalence increases with age, reaching 35% by adulthood in endemic areas (Kappus *et al.* 1983; Jones *et al.* 1999).

In a serosurvey conducted in counties adjacent to the Smoky Mountains in NC, it was reported that overall LAC virus antibody prevalence in 1,016 human blood serum samples was 9.6% (Szumlas *et al.* 1996a). On the Cherokee Indian Reservation, antibody prevalence was reported as 20.6%, and off the Reservation seroprevalence of LAC virus antibody was 4.5%. Off the Reservation, antibody positive samples ranged from 1.8% for the youngest age (< 15 years) group to 16.7% for the oldest group surveyed (75 – 100 years). On the Reservation, percentages dramatically increased from 16.7% (< 15 years) for the younger age groups to 53.9% (75 – 100) for the oldest age group (Szumlas

et al. 1996a). The increase in antibody prevalence with age indicates virus transmission is endemic in the Blue Ridge Mountain area of western NC.

More recently, in eastern Tennessee a marked increase in the number of LACE cases has been reported due to active surveillance for virus transmission. From 1964 to 1997, there were only 9 reported cases of LACE in Tennessee. In contrast, between 15 July and 15 October 1997, 10 cases of LACE were confirmed (Jones *et al.* 1999).

Seasonal Distribution, Age and Gender of LACE Cases. Cases of LACE generally occur throughout the summer months. In North Carolina, the majority of reported cases (94% of 54 cases) between 1964 and 1996 occurred from July to September (Szumlas *et al.* 1996a). Within the southeastern endemic foci of LACE, September is the month of highest incidence for the illness (Jones *et al.* 1999; McJunkin *et al.* 2001). Though LACE is commonly a pediatric illness, cases have been reported for people of all ages (Clark *et al.* 1980). However, the majority of LACE cases occur in children (Thompson and Gundersen 1983). Between 1996 and 1997, 98% (of 252 cases) of all LACE cases in the United States occurred in individuals aged < 18 years (CDC 1998). In West Virginia, all cases (127) occurring between 1987 and 1996 were found in children < 16 years, with a majority (71%) of these patients < 11 years. The mean age of LACE case patient was 7.8 (standard deviation \pm 3.5 years) and the highest incidence (33% of 127 cases) occurred in patients aged 6 – 8 years (McJunkin *et al.* 2001). In 1997, 10 cases of LACE were reported in eastern Tennessee. All 10 cases were in children < 14 years, with a mean age of 6.9 years (Jones *et al.* 1999).

Examining LACE cases in North Carolina, all but one of 54 cases have occurred in children < 15 years, with the greatest incidence (45.2%) occurring in patients aged 5 – 9 years (Szumlas *et al.* 1996a). Historically, males are believed to be at greater risk for LACE than females. During 1996 – 1997, males accounted for 61% (153 cases) of all cases reported nationally (CDC 1998). In the Southeastern endemic foci of LACE, males accounted for 70 – 90% of cases in 1999 and 2001 respectively (Jones *et al.* 1999; McJunkin *et al.* 2001).

Clinical Manifestations and Sequelae of LACE.

Symptoms of LACE. La Crosse encephalitis is easily misdiagnosed; therefore, the number of LACE cases annually is underestimated (Chun 1983). Clinical manifestations range from a mild fever to aseptic meningitis or frank encephalitis. LAC virus infection generally affects males < 16 years of age. The incubation period of the infection ranges from 7 to 15 days (Rust *et al.* 1999). In a typical case, a child will initially experience 2 - 3 days of cyclic fever, abdominal pain, headache, vomiting, stiff neck and lethargy. Similar symptoms were reported in a study of 127 LACE patients treated at a hospital in Charleston, West Virginia from 1987 through 1996 (McJunkin *et al.* 2001). The following symptoms were observed at onset of LACE: headache (83%); fever (86%); vomiting (70%); disorientation (42%); and seizures (46%). Coma, nuchal rigidity and focal neurological signs were reported as conditions upon admission to the hospital. A mean of 3.0 (\pm SD = 1.6) days in a pediatric intensive care unit and an average hospital stay of 6 days were also reported (McJunkin *et al.* 2001). Several other studies report similar primary symptoms of LACE (Cramblett *et al.*

1966; Hilty *et al.* 1972; Balfour *et al.* 1973; Deering 1983; Jones *et al.* 1999). In the acute phase of the LACE, 40 - 60 percent of patients have seizures (Chun 1983; Gundersen and Brown 1983). Most patients recover completely after 7 - 14 days, while a few experience long-term residual effects that may include chronic epilepsy, emotional lability, possible learning disabilities and lowered IQ (Chun 1983).

Sequelae Resulting from LACE. Currently, reports of frequency, duration and type of residual effects resulting from LACE range from no sequelae to severe, life-altering sequelae. Mathews and coworkers (1968) followed 33 serologically confirmed LACE case patients ranging in age from 2 - 15 years for one to six years after their illness. Case patients were subjected to a battery of tests ranging from intellectual ability, motor-sensory function, academic achievement and social adjustment. Although two LACE patients (6%) did score below average intelligence, there were no significant differences between the scores of the LACE group and a control group. Rie *et al.* (1973) reported similar results in a study of 29 children two years after release from the hospital for LACE. Visual-motor coordination and intellectual functioning were measured and compared to a control group. No differences were reported for the two groups. Furthermore, there was no difference in intellectual test scores when severity of illness (duration of hospitalization) was considered. Pre-illness intellectual scores were available for nine participants in the LACE group. When pre-illness scores were compared to post-illness scores, there was no difference. However, when participants were grouped by elapsed time since LACE, there was an

apparent loss in IQ for participants with a more recent illness (average of 8.5 months since illness) compared to participants with a longer time since illness, (average of 30.6 months since illness).

Alternatively, some studies have reported significant sequelae resulting from LACE. Balkhy and Schreiber (2000) examined five patients diagnosed with LACE one year after infection. Three of the five patients followed were still suffering from neurological sequelae, while a fourth experienced seizures for 6 months after initial infection. When follow-up data for 33 LACE patients from one to six years after illness were studied, 15% of the patients reported sequelae ranging from personality/behavioral problems (emotional lability and irritability), difficulties in school and partial paralysis. Eight follow-up EEGs were also performed; six were reported as abnormal (Balfour *et al.* 1973).

More recently, 28 patients were given cognitive tests 10 to 18 months following hospitalization for LACE. The mean IQ score was 87.8, which was significantly below the population mean score of 100. Ten (36%) of the 28 children earned scores considered to represent borderline intelligence (7 with scores between 70 and 79) or mentally retarded (3 with scores < 70). Fifteen (60%) of the 25 children evaluated were also diagnosed with attention-deficit-hyperactivity disorder (McJunkin *et al.* 2001).

Although the manifestations of the residual effects of LACE vary in intensity, the resulting sequelae can be severe, and in some cases life altering and life threatening. Since LACE is most prevalent in children, effects of sequelae are of greater importance on the future of the patient and ultimately the

community, making LACE an important public health issue, especially in the endemic foci.

Biology of La Crosse Virus.

Ochlerotatus triseriatus is the primary vector and over wintering host of LAC virus and an abundant mosquito in western NC (Thompson and Gundersen 1983; Szumlas *et al.* 1996b; Szumlas *et al.* 1996c). The cycle of LAC virus transmission involves vertebrate hosts (horizontal transmission) and *Oc. triseriatus* (vertical transmission and horizontal transmission). While transovarially infected mosquitoes are capable of transmitting virus (orally, venereally, and transovarially) upon emergence, orally and venereally infected mosquitoes must go through an extrinsic incubation period for 7 - 21 days before becoming infective (Rust *et al.* 1999). *Oc. triseriatus* is a container-inhabiting mosquito that uses naturally occurring basal tree-holes, preferably oak, and discarded, flooded containers (pots, buckets, rubbish, and discarded tires) as oviposition and larval production sites (DeFoliart 1983). Northern strains of *Oc. triseriatus* are capable of larval diapause in southern climates, but embryonic diapause is the primary overwintering state of development (Holzapfel and Bradshaw 1980). Humans are infected with the virus by the bite of an infective female (DeFoliart 1983).

Some studies have suggested that LAC virus infection can affect feeding, reproduction and oviposition in female *Oc. triseriatus*, but LAC virus most likely has no major negative effects on the adult mosquito (Rust *et al.* 1999). La Crosse virus does appear to detrimentally affect the survival of overwintering

eggs. McGraw *et al.* (1998) reported 16.7% mortality in LAC virus-positive eggs compared to 7.3% mortality for virus-negative eggs. Prevalence of LAC virus in overwintering eggs of *Oc. triseriatus* has been reported between 0.29% and 0.59% in a historically endemic LAC virus area of southwestern Wisconsin (Lisitzka *et al.* 1977). In La Crosse, Wisconsin, 0.2-0.8% of *Oc. triseriatus* larvae were reported positive for LAC virus (Rust *et al.* 1999).

Dynamics and Efficiency of Horizontal Transmission. Virus transmission occurs via two general routes, horizontally and vertically. Horizontal transmission occurs venereally and via feeding on a virus-infected vertebrate. Virus-positive males venereally infect female mosquitoes with LAC virus. Venereal virus transmission efficiency is greater if the female mates after feeding (49% of 39 individuals) than when mating occurs before feeding (4% of 554 individuals)(Thompson 1979). Alternatively, Patrican and DeFoliart (1987) report similar venereal transmission rates between females feeding just before mating (46% infected) and females feeding several days after mating (45% infected).

Horizontal transmission also occurs. When taking a blood meal, females can transmit LAC virus to susceptible hosts as well as be infected by virus amplifying hosts. Efficiency of oral transmission of LAC virus for *Oc. triseriatus* is reported at 70 - 77% (Watts *et al.* 1973). There appears to be an inverse relationship between body size and oral transmission infection rates. When larvae were reared at different nutritional levels (deprived, moderately deprived and non-deprived) in the laboratory, transmission rates of resulting adults differed

inversely according to size: 82% for small mosquitoes; 54% for medium/normal mosquitoes; and 52% for large mosquitoes (Grimstad and Haramis 1984).

Virus infection rates are also affected by mosquito size. After feeding on a viremic host, 90% of “small” adults developed a disseminating infection, while “normal” and “large” sized mosquito developed disseminating infections at similar rates, 75% and 73% of adults, respectively (Grimstad and Haramis 1984). A weakening of midgut barrier cells due to nutritional deprivation is a probable reason for the higher rate of disseminating infections in smaller mosquitoes than larger mosquitoes (Paulson and Hawley 1991).

The zoonotic cycle of horizontal transmission involves the gray squirrel (*Sciurus carolinensis*) and eastern chipmunk (*Tamias striatus*) as primary amplifying hosts for LAC virus, while the red fox (*Vulpes fulva*) and gray fox (*Procyon lotor*) are regarded to be secondary virus-amplifying hosts. Virus titers within an amplifying host must reach a certain threshold before mosquitoes can be infected after feeding. In chipmunks, viremia titers above $3.2 \log_{10}\text{SMICLD}_{50}/0.025 \text{ ml}$ are necessary for 50% or more of *Oc. triseriatus* to become infected after feeding, while viral titers of $3.4 \log_{10}\text{SMICLD}_{50}/0.025 \text{ ml}$ or greater produced 100% infection (Patrican *et al.* 1985). Infective viremias in the eastern chipmunk are transient, lasting for only 2 - 3 days (DeFoliart 1983). Similar results were reported for gray squirrels with viremia lasting between 2 - 4 days with a range of $1.5 - 4.5 \log_{10}\text{SMICLD}_{50}/0.025 \text{ ml}$ (Pantuwatana *et al.* 1972). Neither the eastern chipmunk nor the gray squirrel displayed clinical signs of virus infection (Pantuwatana *et al.* 1972). Viremias in the red and gray

fox occurred for 1 - 2 days (Amundson *et al.* 1985). The red and gray fox can also be infected with LAC virus after ingesting LAC virus-infected chipmunks or gray squirrels (Yuill 1983). Larger vertebrates like deer and dogs may be infected with the virus, but do not serve as amplifying hosts (DeFoliart 1983; Amundson *et al.* 1985). Due to the diurnal feeding habits of *Oc. triseriatus*, nocturnal mammals like deer mice, raccoons, opossums and flying squirrels are rarely infected (Rust *et al.* 1999).

Dynamics and Efficiency of Vertical Transmission. Vertical transmission of LAC virus occurs transovarially. Eggs of infected female mosquitoes are infected with LAC virus, producing a new generation of virus-positive male and female mosquitoes. A filial infection rate of 71% and a transovarial transmission rate of 98% were reported for *Oc. triseriatus* over 8 generations (Miller *et al.* 1977). Because transovarial transmission is not 100% efficient, horizontal transmission through oral and venereal routes is essential for long-term maintenance of the virus in *Oc. triseriatus* populations (Thompson and Beaty 1977).

Upon emergence, transovarially infected females are capable of transmitting LAC virus orally or transovarially. Ovarian infection of orally infected females by LAC virus is detectable at 8 - 14 days (Chandler *et al.* 1998). Orally infected females are not capable of transovarial transmission until the second gonotrophic cycle. In a study of the dynamics of transovarial transmission, Miller *et al.* (1979) reported transovarial infection rates of orally infected females were 0, 43 and 58% for the first, second and third gonotrophic cycle larvae,

respectively. Accordingly, orally infected females can only contribute virus-positive eggs to overwintering populations in gonotrophic cycles following oral infection. Since most *Oc. triseriatus* females are uniparous, transovarially and venereally infected females are primarily responsible for maintaining and amplifying LAC virus within a season and contributing LAC virus positive overwintering eggs. Both vertically and horizontally infected females can transmit LAC virus, but venereal and transovarial transmission play a primary role in the maintenance of LAC virus in endemic areas (Landry and DeFoliart 1987).

Need for Study.

La Crosse encephalitis is an under recognized disease and is of greater public health concern in western North Carolina than is presently acknowledged. The relatively high seroprevalence of LAC virus antibodies coupled with *Oc. triseriatus* being an abundant mosquito species in the LACE endemic area of western North Carolina suggests that transmission of LAC virus is prevalent (Szumlas *et al.* 1996a; Szumlas *et al.* 1996b; Szumlas *et al.* 1996c). Due to passive surveillance and non-specific symptomology, some LACE cases are not likely to be diagnosed by physicians, resulting in a deceptively low number of LACE cases being reported annually in western North Carolina.

Little information on the economic impacts of the morbidity and mortality of LAC encephalitis is presently available. In Illinois, between 1976 and 1980, the average hospitalization costs for a case of LAC encephalitis was estimated to be \$3,967 - \$5,750 with an average of 8.3 days of hospitalization per case. In a

typical year, Illinois reports an average of 12 cases of LAC encephalitis, producing an estimated annual hospitalization cost of \$47,604 - \$69,000 (Clark *et al.* 1983). Information in the Illinois study documents the economic cost of hospitalization due to LAC encephalitis, but no information concerning the follow up medical costs, indirect medical costs, or social costs was included. No such documentation of the economic and social burden of LACE is presently available for North Carolina.

The economic and social burden resulting from LACE could be reduced with increased awareness and community action. Because there is no immunization available for LAC virus infection, prevention of the disease is dependent on vector control and other prevention techniques. Elimination of man-made production sites is an effective strategy for decreasing mosquito production. With a decrease in mosquito populations, the probability of being infected with LAC virus also decreases. Community education programs about the biology of mosquitoes and virus transmission cycle can be effective tools for modifying human behavior with the ultimate goal of disease prevention.

In Yucatan, Mexico, a community education program based on vector biology and control or elimination of mosquito larval production sites (oviposition sites) of *Aedes aegypti*, a vector of dengue fever virus, was implemented to reduce disease morbidity (Lloyd *et al.* 1992). Members of the community who participated in the education program had fewer oviposition sites around their homes than those who did not participate in the education program. Community education programs, in concert with community participation in controlling and

eliminating oviposition sites, resulted in decreases in vector presence and ultimately the incidence of dengue fever in the area.

Active disease surveillance, community education and participation in the control or eradication of man-made mosquito production sites were components of a dengue virus prevention program in villages of Thailand (Eamchan *et al.* 1989). The program resulted in a decrease in the prevalence of homes with mosquito larvae presence from 67% to 20%; a decline in the percent of larvae presence in containers in one village from 30% to 5%; and a decrease in the number of containers with larvae per 100 households from 221 to 33.

Assessing the Economic and Social Burden of Disease.

I will apply methods used in previous economic analyses of diseases to create an economic and social analysis of LACE. Many different approaches and quantitative methods are used to gather information on the economic and social cost of disease. Before examining some past economic and social analyses of disease, a discussion of Disability Adjusted Life Years is warranted due to their use in past disease analysis.

Disability Adjusted Life Years (DALYs). DALYs, a form of Health Adjusted Life Years, are non-monetary indices reflecting lost time and productivity due to a disease that are unbiased relative to the economic and cultural background of a person with an illness (Murray and Lopez 1994). DALYs are designed to be unbiased regarding economic and educational levels of parents as well. Furthermore, DALYs also consider the age at onset of illness, the duration of illness, and the severity of each case (Murray and Lopez 1994). These variables

are important for assessing the actual burden of a case of LACE, which can manifest itself with varying degrees of severity and duration.

Currently, there is debate over the use of standard life expectancies, age weighting and discount rates in the calculation of DALYs (Anand and Hanson 1997). A standard life expectancy of 80 years for males and 82.5 years for females is used in the calculation of a standard DALY (Murray and Lopez 1994). A discount rate of 3% for future years of life lived and an age weighting function are recommended in the calculation of a standard DALY (Murray and Lopez 1994).

DALYs have been used to quantify the burden of human maladies for very large populations. As a result, the use of discount rates and age weighting functions can result in large differences in final DALY results. In an example illustrated by Fox-Rushby and Hanson (2001), DALY estimates for a single case can range from 13.8 years to 27.4 years depending on the use of age weights and discount rates. The difference of 13.6 DALYs between the two estimates represents a substantial amount of lost time and productivity in the context of one life span.

Standard life expectancies of 80 years for males and 82.5 years for females are used in the calculation of a standard DALY (Murray and Lopez 1994). Standard life expectancies are used in an attempt to standardize calculations across diseases and countries, resulting in comparable DALY estimates. Though the use of standard life expectancy does allow for more direct comparison of DALYs from different geographic regions, the practice does

sacrifice accuracy in the measurement of DALYs for a given country or region (Anand and Hanson 1997). Using the recommended standard life expectancies in countries or regions with life expectancies that are different (much higher or lower) would result in DALY estimates that were misleading or inaccurate for that region. Therefore, the use of standard life expectancies or regional life expectancies is dependent on the motivation for calculating DALYs.

Age is another point of contention in the calculation of DALYs because of the practice of age weighting for time lived at different ages. Age weights are used to account for differences of productivity at different years of life. In DALYs, age weights put greater value of time spent as a young and middle aged adult than time spent as a small child or elderly adult (Murray 1996). Anand and Hanson (1997) argue that assigning greater value to certain age groups is “ethically hard to defend” and “thoroughly unacceptable.” Murray and Acharya (1997) counter by arguing that certain age groups are critical for society to flourish, such as young and middle aged adults. Therefore, their health status may be of greater concern to society. In the end, the use of age weights depends greatly on the use of the final DALY estimate. An effective practice for addressing both views (age weighters vs. non age weighters) is to calculate DALYs with a standard age weighting function as well as no age weighting function, producing DALY results appreciable to either view (Fox-Rushby and Hanson 2001).

A discount rate of 3% for future years of life is recommended for the calculation of a standard DALY by Murray and Lopez (1994). By discounting

future life years, a greater value is placed on life lived presently than life in the future. Murray mentions that individuals can exhibit negative discount rates due to the prospect of a more valuable future life, such as expected income growth. The effect of age weighting coupled with discounting future life years can result in unrealistic conclusions. For example, if age weights and future life discounting were used, then the life of a 20 year old is more valuable than that of an infant. As a result, more resources should be applied to supporting the health of the 20 year old than the infant. In contrast, current societal attitudes and medical care trends do not support such a case (Anand and Hanson 1997). DALYs reported in global studies of disease are calculated with a 3% discount rate and without a discount rate due to the issues surrounding discounting (Murray 1996).

Because of the aforementioned controversy surrounding the constituent values used in DALY calculations, four types of DALYs will be calculated for the analyses of LACE. One set of DALYs will be calculated using the recommended (or standard) life expectancies, with and without age weights and future life discounts. Another set of DALYs will be calculated using US life expectancies from CDC life tables with and without age weights and future life discounts. Reporting the different types of DALYs associated with LACE in North Carolina should allow for comparison of DALYs for LACE to other DALY estimates for other illnesses, no matter which methods are used to assess impacts.

Impact of La Crosse Encephalitis Scale (ILCES). Measuring or estimating the impact of an illness on the everyday life of a patient is not straightforward because of the lack of consensus on a standard methodology. Furthermore, the

impact of an illness over time can change as the effects of an illness subside or the patient adjusts and is able to overcome the burden caused by the impairment. The ILCES was developed from the Impact of Pediatric Epilepsy Scale (IPES) described by Camfield *et al.* (2001). The IPES was originally developed to measure the general impact of pediatric epilepsy on the life of the patient and family. The format and content of the IPES was slightly modified to better address the impact of LACE. The ILCES is included in the survey to measure the social impact of LACE. It will also be used to gauge if there is a change in social impact of LACE over time. Though each case of LACE is unique, the ILCES will provide a broad view of the social impact of the illness. The IPES is used as a model for the ILCES because it is a tool used to measure the impact of pediatric epilepsy on families. Since seizures are often identified as a common sequela in severe cases of LACE, a modified IPES survey instrument should produce valid estimates of the social impact of LACE.

Past case Studies and Methods of Quantifying Burden.

Dengue Fever. In two recent studies conducted in Puerto Rico, the economic and social impacts of dengue fever were estimated. Meltzer *et al.* (1998) measured the economics of dengue fever between the years of 1984 - 1994. This decade was chosen because of two epidemics in 1986 and 1994. Confirmed and suspected cases of dengue fever were used as the basis for estimating the number of people affected by the disease. The annual DALYs lost per million people due to dengue fever ranged from 145 in 1984 to 1,492 in 1994. The annual average over 11 years was 658 DALYs lost per million people. The

information for the study was gathered using databases maintained at the San Juan Laboratories, Centers for Disease Control and Prevention.

In another study about the impact of a 1990 outbreak of dengue fever in a rural community in Puerto Rico, social costs were estimated using a “medical anthropological” approach (Torres 1997). The cost was reported in terms of lost paid and unpaid workdays, school days, or reduced activity days. Unsalaries work included the duties of housewives, work done for goods, and childcare. Loss of workdays by housewives had the greatest social impact on the community. The restriction of activities of a housewife ill with dengue fever or having a family member with dengue fever greatly disrupted the lives of all members of a household. Conversely, it was rare for a male to miss workdays due to a family member having dengue fever.

From an understanding of the culture of the area, Torres employed the use of “...ethnographic open-ended and structured interviews with the adult female caretaker of randomly selected households...” to obtain the information needed for the analysis. Loss of workdays (both salaried and non-salaried) was reported as well as psychological well-being. The average loss per household amounted to 31 days at \$305. To demonstrate the social burden of dengue fever, excerpts of interviews and the number of lost non-salaried workdays were used to gain a better understanding of the impact of the disease.

Torres categorized psychological costs into “stressors.” A stressor is a situation or effect that adds to the psychological burden of a disease. Four stressors were identified for the study of dengue fever: lack of information;

logistical problems; emotional distress; and economic burden. The stressors were measured in percent of psychological cost. The percent value of each stressor in the overall psychological cost, along with excerpts from interviews with families affected by dengue fever were effective in documenting the psychological costs of dengue fever in the communities surveyed.

Malaria. There are many analyses related to the cost of malaria (Sauerborn *et al.* 1991; Picard and Mills 1992; Ettlign *et al.* 1994; Konradsen *et al.* 1997). Because of the extensive geographic distribution of malaria and the large number of people affected each year, many different methods have been used in estimating the economic impact of the disease. With such a prominent and geographically diverse disease, workers had to account for a great number of variables, such as the diversity of the culture of people and economy (agricultural or industrial). Most investigations were assisted by local and/or national health care systems that are involved in active surveillance of the disease. In malaria studies, the emphasis was on lost workdays of factory employees and agricultural workers. Lost workdays for agricultural workers were generally weighted by season (growing season, harvest season and off-seasons).

In a study of households in Sri Lanka (Konradsen *et al.* 1997), community residents were surveyed to determine their age, gender and job. Residents not working due to age (too young or old) or disability were recorded. Next, tasks or job types within the community were defined and a recording format developed. Investigators visited every house in the community every other day and recorded

household activities of each member of the family. Daily activities were recorded as half or full day of work. A case of malaria was recorded only if it was confirmed by a blood test at a government or private medical facility. During a one-year period, 223 cases of malaria were reported in 134 individuals. The cost was reported as workdays lost, as well as US dollar cost and percent workdays lost per age group and gender. Since this study included only diagnosed cases, the predicted numbers would be much higher if non-diagnosed cases were included in the study, especially in rural communities where self-treatment or traditional means are used to treat the disease.

Sauerborn *et al.* (1991) performed a malaria study using household surveys (n = 626) in a rural district of Burkina Faso. Malaria occurrence and severity were rated by patient self-diagnoses (severe or mild case) and costs were divided into direct and indirect costs. Direct costs were reported as costs incurred by the patients and hospitals. Indirect costs were reported as loss of production due to illness (1 day for a mild case and 5 days for a severe case) and loss of time due to a family member's illness (1/3 day in a mild cases and 3/5 day in a severe cases).

In the analysis, US dollars were reported for the direct and indirect costs as well as total costs of malaria in the district surveyed. Number of lost days and corresponding dollar values were reported as well as a dollar value for premature death. The dollar values for premature death were calculated by multiplying the annual average total product of labor per person by the numbers of years lost and discounted at a rate of 8%, presumably to account for a loss in productivity

with age. Years lost were calculated by subtracting the age at death from the life expectancy of a person from that geographic area. Dollar values for lost workdays were calculated by dividing the annual production by the known number of workers giving the average annual product per person. Next, the average annual product per person was divided by the number of workdays in the season of the commodity (61 days for cotton, 245 days for food) giving lost production per lost day. Finally, the number of days lost was multiplied by the monetary value of the lost commodity to derive estimates of the total monetary loss due to lost workdays.

Ettling *et al.* (1994) conducted a nation wide, cluster sample survey in Malawi with the assistance of the Community Health Sciences Unit of the Ministry of Health. Information was gathered to calculate the direct medical costs (medical bills, medicine), prevention costs (mosquito coils, nets etc.) and indirect medical costs of malaria. The indirect medical costs were determined as lost workdays due to an adult illness or workdays lost caring for a sick child. A total cost was given per household, illustrating the substantial cost of malaria for low-income areas in Malawi.

Picard and Mills (1992) measured the effect of malaria on work time in two districts of Nepal. Patients with confirmed diagnoses of malaria were recruited from local medical centers with the assistance of the National Malaria Eradication Organization, a group that monitors malaria incidence. The standard of measure for the impact of malaria used was half days and whole days lost due to medically confirmed malaria. Short interviews were conducted examining the

amount of “work” (time which generated income and/or household duties) lost due to illness. In the end, results were presented in workdays lost due to malaria as well as measures demonstrating the loss of work productivity and efficiency due to malaria.

Hepatitis E. The socioeconomic impact of hepatitis E in Nepal was estimated by Clark *et al.* (1999). Monetary expenditures were surveyed by using self-reported open format questions. The information included direct costs as well as indirect costs. Direct medical costs included faith healers, traditional healers, medical bills and medicines. Indirect costs included lost wages, payment for replacement workers and health care providers. Finally, non-economic costs were measured by the ability of a person to perform daily tasks. This was measured via the World Health Organization’s Table of Disability Index. The direct and indirect costs were reported as component costs. For example, direct costs were divided into the following categories: outpatient; alternative healer; hospital; medicine; travel; and dietary. Indirect costs were broken into days unable to work, days worked below normal production level, and the days a substitute worker was needed. In addition, an overall dollar estimate of direct and indirect medical costs was reported.

Eastern Equine Encephalitis. In the United States in eastern Massachusetts, Villari and coworkers (1995) determined the economic impacts of eastern equine encephalitis (EEE). In the study, three costs were identified and estimated: direct medical cost; direct non-medical cost; and indirect costs. A questionnaire was used to obtain and divide the data needed into four parts.

First, general information was gathered on family structure, employment, and income. Medical histories were also obtained to help pinpoint time of onset of viral infection, natural history of the disease, and sequelae. Next, direct medical costs were examined (medical costs of diagnosis, treatment, rehabilitation and continuing care). Participants were asked to describe their use of hospital and non-hospital services. The third section focused on non-medical costs. Participants were asked to quantify all costs not included in the direct medical costs, but associated with the disease (home modifications, special clothing, special diets, transportation to and from medical providers, any domestic support, special education required and any other special resources consumed due to the illness). Finally, the questionnaire included a section on family income before, during and after the occurrence of illness. Any differences in income during this time were assumed to be due to the disease. Other information such as lost job opportunities was noted in this section. In the analysis, two categories of disease were used: "cases with transient effects" and "cases with residual effects." A final cost, or lifetime estimate per case, was reported.

In estimating costs associated with EEE, Villari *et al.* (1995) included projections as part of the overall cost estimates. The life expectancy of an EEE victim was assumed to be the same as a person without EEE. Medical costs associated with EEE were estimated as the average of costs from the fourth through the ninth year after infection. The average from the fourth through the sixth year was used in one case. Educational services claimed during interviews were given a dollar value through cooperation of local school district offices.

These costs were estimated up to the age of 21 years, at which time they would no longer apply. After the age of 21 years, institutional care costs were applied to each case. Care costs were estimated by dividing the annual Massachusetts expenditure for institutional care by the mean number of daily residents institutionalized. Finally, estimates of future earning losses were applied to each case. An average income of \$31,899 based on the mean income of males and females aged 14 and older in the United States was used. This estimate of annual income was applied to a work expectancy of 47 years (18 to 65 years) and discounted at 5% per year. All final estimates were expressed in 1990 dollars. The mean cost for cases experiencing “transient effects” (n = 3) was \$21,000. The economic burden of cases experiencing residual effects (n = 3) was estimated to reach \$3 million per case. It is noted that mosquito control measures for preventing outbreaks of EEE range between \$0.7 and 1.4 million, less than half the estimated cost of one case of EEE (Villari *et al.* 1995).

Plan of Research.

The economic and social burden imposed by LACE in North Carolina is presently unknown. In assessing the direct, indirect and social costs of LACE, I will use the following measures: (1) a dollar figure quantifying direct and some indirect costs; (2) lost work and/or school days; and (3) measures of social and emotional impact (DALYs, ILCES, stressors and reduced/compromised activity days). By using these indices, I will be able to estimate the true direct, indirect and social burden resulting from LACE.

Through investigator-administered interviews with case patients and/or the families of case patients, I will gather the information necessary to calculate an estimate of the economic and social impact of LACE on case patients, their families and communities. An estimate of the economic costs associated with LACE will highlight the importance of the illness. The investigation of the social impacts of LACE and resulting sequelae will highlight the severity and duration of residual sequelae associated with frank LACE. Furthermore, a socioeconomic analysis of LACE can serve as a catalyst for the development of a proactive approach to disease surveillance and prevention, an educational tool for the health care community and general population of North Carolina, as well as a useful disease case study to raise awareness of the total cost (medical and non-medical) of the disease.

REFERENCES CITED

- Amundson, T. E., T. M. Yuill, and G. R. DeFolliart. 1985.** Experimental La Crosse virus infection of red fox (*Vulpes fulva*), raccoon (*Procyon lotor*), opossum (*Didelphus virginiana*), and woodchuck (*Marmota monax*). *Am. J. Trop. Med. Hyg.* 34:586 – 595.
- Anand, S. and K. Hanson. 1997.** Disability-adjusted life years: a critical review. *J. Health Econ.* 16:685 – 702.
- Balfour H. H., R. A. Siem, H. Bauer, and P. G. Quie. 1973.** California arbovirus (La Crosse) infections: clinical and laboratory finding in 66 children with meningoencephalitis. *Pediatrics.* 52:680 – 691.
- Balkhy H. H. and J. R. Schreiber. 2000.** Severe La Crosse encephalitis with significant neurological sequelae. *Pediatr. Infect. Dis. J.* 19:77 – 80.
- Chandler, L. J., C. D. Blair, and B. J. Beaty. 1998.** La Crosse virus infection of *Aedes triseriatus* (Diptera: Culicidae) ovaries before dissemination of virus from the midgut. *J. Med. Entomol.* 35:566 – 572.
- Camfield, C., L. Breau, and P. Camfield. 2001.** Impact of pediatric epilepsy on the family: a new scale for clinical and research use. *Epilepsia.* 42:104 – 112.
- Chun, R. W. M. 1983.** Clinical aspects of La Crosse encephalitis: neurological and psychological sequelae. Pp. 193 – 201. *In: Calisher, C. H. and W. H. Thompson (eds.). 1983. California Serogroup Viruses.* Alan R. Liss, Inc. New York. 399 pp.
- Clark, G. G., R. J. Martin, H. L. Pretula, C. W. Langkop, and H. H. Rohrer. 1980.** California Group Virus infections in Illinois. *IMJ.* 157:91 – 96.

Clark, G. G., H. L. Pretula, C. W. Langkop, R.J.Maritn, and C. H. Calisher. 1983.

Occurrence of La Crosse (California serogroup) encephalitis viral infections in Illinois. *Am. J. Trop. Med. Hyg.* 32:838 – 843.

Clark, K. L., R. M. Howell, R. M. Scott, D. W. Vaughn. M. R. Shrestha, C. F.

Longer, and B. L. Innis. 1999. The socioeconomic impact of Hepatitis E in Nepal. *Am. J. Trop. Med. Hyg.* 61:505 – 510.

Center for Disease Control and Prevention. 1998. Arboviral infections of the central nervous system, United States, 1996 – 1997. *Morb. Mortal. Wkly. Rep.* 47:517 – 540.

Cramblett, H. G., H. Stegmiller, and C. Spencer. 1966. California encephalitis infections in children: clinical and laboratory studies. *JAMA.* 198:128 – 132.

Deering, W. M. 1983. Neurological aspects and treatment of La Crosse encephalitis. pp.187 – 191. *In:* C. H. Calisher and W. H. Thompson (eds.). 1983. *California Serogroup Viruses.* A. R. Liss, Inc. New York. 399 pp.

DeFoliart, G. R. 1983. *Aedes triseriatus:* Vector biology in relationship to the persistence of La Crosse virus in endemic foci. pp. 89 – 104. *In:* C. H. Calisher and W. H. Thompson (eds.). 1983. *California Serogroup Viruses.* A. R. Liss, Inc. New York. 399 pp.

Eamchan, P., A. Nisalak, H.M. Foy, and O. Chareonsook. 1989. Epidemiology and control of dengue virus infections in Thai villages in 1987. *Am. J. Trop. Med. Hyg.* 41:95 – 101.

Ettling, M., D. A. McFarland, L. F. Schultz, and L. Chitsulo. 1994. Economic impact of malaria in Malawian households. *Trop. Med. Parasitol.* 45:74 – 79.

- Fox-Rushby, J.A. and K. Hanson. 2001.** Calculating and presenting disability adjusted life years (DALYs) in cost effectiveness analysis. *Health Policy Plan.* 16:326 – 331.
- Gerhardt, R. R., D. L. Gottfried, C. S. Apperson, B. S. Davis, P. C. Erwin, A. B. Smith, N. A. Panella, E. E. Powell, and R. S. Nasci. 2001.** First isolation of La Crosse virus from naturally infected *Aedes albopictus*. *Emerg. Infect. Dis.* 7:807 – 903.
- Grimstad, P.R. 1988.** California group virus disease. Chapt. 19. pp. 99 – 136. *In:* T. P. Monath (ed.). *The Arboviruses: Epidemiology and Ecology, Vol. II.* CRC Press, Inc. Boca Raton, FL.
- Grimstead, P. R., and L. D. Haramis. 1984.** *Aedes triseriatus* (Diptera: Culicidae) and La Crosse virus III. Enhanced oral transmission by nutrition-deprived mosquitoes. *J. Med. Entomol.* 21:249 – 256.
- Gundersen, C. B. and K. L. Brown. 1983.** Clinical aspects of La Crosse encephalitis: preliminary report. pp. 169 – 177. *In:* C. H., Calisher and W. H. Thompson (eds.). 1983. *California Serogroup Viruses.* Alan R. Liss, Inc. New York. 399 pp.
- Hilty, M. D., R. E. Haynes, P. H. Azimi, and H. G. Cramblett. 1972.** California encephalitis in children. *Amer. J. Dis. Child.* 124:530 – 533.
- Holzappel, C. M., and W. E. Bradshaw. 1980.** Geography of larval dormancy in the tree-hole mosquito, *Aedes triseriatus* (Say). *Can. J. Zool.* 59:1014 – 1021.

Jones, T. R., A. S. Craig, R. S. Nasci, L. E. R. Patterson, P. C. Erwin, R. R.

Gerhardt, X. T. Ussery, and W. Schaffner. 1999. Newly recognized focus of La Crosse encephalitis in Tennessee. *Clin. Infect. Dis.* 28:93 – 97.

Kappus, K. D., T. P. Monath, R. M. Kaminski, and C. H. Calisher. 1983.

Reported encephalitis associated with California serogroup virus infections in the United States, 1963 – 1981. pp. 31 – 41. *In: C. H., Calisher and W. H. Thompson (eds.). 1983. California Serogroup Viruses.* Alan R. Liss, Inc. New York. 399 pp.

Konradsen, F., S. V. D. Hoek, P. H. Amerasinghe, and F. P. Amerasinghe. 1997.

Measuring the economic cost of malaria to households in Sri Lanka. *Am. J. Trop. Med. Hyg.* 56:656 – 660.

Landry, S. V., and G. R. DeFoliart. 1987. Parity rates of *Aedes triseriatus*

(Diptera: Culicidae) collected in a female-retaining ovitrap. *J. Med. Entomol.* 24:282 – 285.

Lisitza, M. A., G. R. DeFoliart, T. M. Yuill, and M. G. Karandinos. 1977.

Prevalence rates of La Crosse virus (California encephalitis group) in larvae from overwintering eggs of *Aedes triseriatus*. *Mosq. News.* 37:745 – 750.

Lloyd, L.S., P. Winch, J. Ortega-Canto, and C. Kendall. 1992. Results of a

community-based *Aedes aegypti* control program in Merida, Yucatan, Mexico. *Am. J. Trop. Med. Hyg.* 46:635 – 642.

Mathews, C. G., R. W. M. Chun, J. D. Grabow, and W. H. Thompson. 1968.

Psychological sequelae in children following California arbovirus encephalitis. *Neurology.* 18:1023 – 1030.

- McGraw, M. M., L. J. Chandler, L. P. Wasieloski, C. D. Blair, and B. J. Beaty. 1998.** Effect of La Crosse virus infection on overwintering of *Aedes triseriatus*. *Am. J. Trop. Med. Hyg.* 58:168 – 175.
- McJunkin, J. E., E. C. De Los Reyes, J. E. Irazuzta, M. J. Caceres, R. R. Khan, L. L. Minnich, K. D. Fu, G. D. Lovett, T. Tsai, and N. Thompson. 2001.** La Crosse encephalitis in children. *N. Engl. J. Med.* 344:801 – 807.
- McJunkin, J. E., R. R. Kahn, and T. F. Tsai. 1998.** California-La Crosse encephalitis. *Infect. Dis. Clin. North Am.* 12:83 – 93.
- Meltzer, M. I., J. G. Rigau-Perez, G. G. Clark, P. Reiter, and D. J. Gubler. 1998.** Using disability-adjusted life years to assess the economic impact of dengue in Puerto Rico: 1984-1994. *Am. J. Trop. Med. Hyg.* 59:265 – 271.
- Miller, B. R., G. R. DeFoliart, and T. M. Yuill. 1977.** Vertical transmission of La Crosse virus (California encephalitis group): transovarial and filial infection rates in *Aedes triseriatus* (Diptera: Culicidae). *J. Med. Entomol.* 14:437 – 440.
- Miller, B. R., G. R. DeFoliart, and T. M. Yuill. 1979.** *Aedes triseriatus* and La Crosse virus: lack of infection in eggs of the first ovarian cycle following oral infection of females. *Am. J. Trop. Med. Hyg.* 28:897 – 901.
- Murray, C.J.L. 1996.** Rethinking DALYs. Chapt. 1 pp. 1-98. *In: C.J.L. Murray and A.D. Lopez (ed.). The Global Burden of Disease: A Comprehensive Assessment of Mortality and Disability from Disease, Injuries, and Risk Factors in 1990 and Projected to 2020, (Global Burden of Disease and Injury series vol. I).* Harvard School of Public Health University Press. Boston, MA. 990 pp.

- Murray, C.J.L. and A.K. Acharya. 1997.** Understanding DALYs. *J. Health Econ.* 16:703 – 730.
- Murray, C. J .L. and A. D. Lopez. 1994.** Global comparative assessments in health sector: Disease burden, expenditures, and intervention packages. *Bull. W.H.O.* Geneva, Switzerland. 196pp.
- Patrican, L. A. and G. R. DeFoliart. 1987.** *Aedes triseriatus* and La Crosse virus: similar venereal infection rates in females given the first bloodmeal immediately before mating or several days after mating. *Am. J. Trop. Med. Hyg.* 36:684 – 652.
- Patrican, L. A., G. R. DeFoliart, and T. M. Yuill. 1985.** Oral infection and transmission of La Crosse virus by an exzootic strain of *Aedes triseriatus* feeding on chipmunks with a range of viremia levels. *Am. J. Trop. Med. Hyg.* 34:992 – 998.
- Paulson, S. L., and W. A. Hawley. 1991.** Effect of body size on the vector competence of field an laboratory populations of *Aedes triseriatus* for La Crosse virus. *J. Am. Mosq. Control Assoc.* 7:170 – 175.
- Picard, J., and A. Mills. 1992.** The effect of malaria on work time: analysis of data from two Nepali districts. *J. Trop. Med. Hyg.* 95:382 – 389.
- Pantuwatana, S., W. H. Thompson, D. M. Watts, and R. P. Hanson. 1972.** Experimental infection of chipmunks and squirrels with La Crosse and trivittatus viruses and biological transmission of La Crosse virus by *Ae. triseriatus*. *Am. J. Trop. Med. Hyg.* 21:476 – 481.

- Rie, H. E., M. D. Hilty, and H. G. Cramblett. 1973.** Intelligence and coordination following California encephalitis. *Am J. Dis. Child.* 125:827 – 282.
- Rust, R. S., W. H. Thompson, C. G. Mathews, B.F. Beaty, and R. W. M. Chun. 1999.** La Crosse and other forms of California encephalitis. *J. Child Neurol.* 14:1 – 14.
- Sauerborn, R., D. S. Shepard, M. B. Ettlign, U. Brinkmann, A. Nougara, and H. J. Diesfeld. 1991.** Estimating the direct and indirect economic cost of malaria in a rural district of Burkina Faso. *Trop. Med. Parasitol.* 42:219 – 223.
- Szumlas, D. E., C. S. Apperson, P. C. Hartig, D. B. Francy, and N. Karabatsos. 1996a.** Seroepidemiology of La Crosse virus infection in humans in western North Carolina. *Am. J. Trop. Med. Hyg.* 54:332 – 337.
- Szumlas, D. E., C. S. Apperson, E. E. Powell, P. C. Hartig, D.B. Francy, and N. Karabatsos. 1996b.** Relative abundance and species composition of mosquito populations (Diptera: Culicidae) in a La Crosse virus-endemic area in western North Carolina. *J. Med. Entomol.* 33:598 – 607.
- Szumlas, D. E., C. S. Apperson, and E. E. Powell. 1996c.** Seasonal occurrence and abundance of *Aedes triseriatus* and other mosquitoes in a La Crosse virus-endemic area in western North Carolina. *J. Am. Mosq. Control Assoc.* 12:184 – 193.
- Thompson, W. H. 1979.** Higher venereal infection and transmission rates with La Crosse virus in *Aedes triseriatus* engorged before mating. *Am. J. Trop. Med. Hyg.* 28:890 – 896.

- Thompson, W. H. 1983.** Vector-virus relationships. pp. 57 – 66. *In:* C. H. Calisher and W. H. Thompson (eds.). 1983. *California serogroup viruses*. A. R. Liss, Inc. New York. 399 pp.
- Thompson, W. H., and B. J. Beaty. 1977.** Venereal transmission of La Crosse (California encephalitis) arbovirus in *Aedes triseriatus* mosquitoes. *Science*. 196:530 – 531.
- Thompson, W. H., and C. B. Gundersen. 1983.** La Crosse encephalitis: Occurrence of disease and control in a suburban area. pp. 225 – 236. *In:* C. H. Calisher and W. H. Thompson (eds.). 1983. *California serogroup viruses*. A. R. Liss, Inc. New York. 399 pp.
- Torres, M. I. 1997.** Impact of an outbreak of dengue fever: a case study from rural Puerto Rico. *Human Organization* 56:19 – 27.
- Villari, P., A. Spielman, N. Kamar, M. McDowell, and R. J. Timperi. 1995.** The Economic burden imposed by a residual case of eastern Encephalitis. *Am. J. Trop. Med. Hyg.* 52:8 – 13.
- Watts, D. M., P. R. Grimstead, G. R. DeFoliart, T. M. Yuill, and R. P. Hanson. 1973.** Laboratory transmission of La Crosse encephalitis virus by several species of mosquitoes. *J. Med. Entomol.* 10:583 – 586.
- Yuill, T. M. 1983.** The role of mammals in the maintenance and dissemination of La Crosse virus. pp. 77 – 87. *In:* C. H. Calisher and W. H. Thompson (eds.). 1983. *California serogroup viruses*. A. R. Liss, Inc. New York. 399 pp.

CHAPTER 2

AN ECONOMIC AND SOCIAL ANALYSIS OF LA CROSSE ENCEPHALITIS IN NORTH CAROLINA

INTRODUCTION

La Crosse encephalitis (LACE) is a pediatric illness caused by La Crosse (LAC) virus, a mosquito-transmitted bunyavirus of the California (CAL) serogroup viruses (Thompson and Gundersen 1983). Historically, most cases of LACE have been reported for the Midwestern states (Kappus *et al.* 1983). However, LACE is endemic in North Carolina and increasingly recognized in Tennessee, Virginia and West Virginia (CDC 1998). From 1996 - 1997, West Virginia reported 139 cases of LACE, which accounted for 55% of all cases reported nationally during the same time period (CDC 1998). The primary vector for LAC virus is *Ochlerotatus triseriatus* (Say), the eastern tree hole mosquito (Thompson 1983). *Ochlerotatus triseriatus* is the most abundant mosquito in the LACE endemic area of western North Carolina and favors naturally occurring tree holes and discarded, water-filled containers and tires as oviposition sites (Szumlas *et al.* 1996a,b). La Crosse virus has also been isolated recently from *Aedes albopictus*, the Asian tiger mosquito, in North Carolina and Tennessee (Gerhardt *et al.* 2001). Although it has not been clearly established that *Aedes albopictus* (Skuse) is a LAC virus vector, the occurrence and abundance of this mosquito at the residences of LACE case patients was identified as a significant risk factor for the illness in eastern Tennessee (Erwin *et al.* 2002). Time spent outdoors during the day and residing within 100 meters of one or more tree holes were also identified as important risk factors of LACE encephalitis (Erwin *et al.* 2002).

Cases of La Crosse encephalitis have been reported in 24 states, ranging from Minnesota to Texas and east to New York and Georgia. An average of 73

cases is reported annually in the United States by the Centers for Disease Control and Prevention (Jones *et al.* 1999). Between 1996 and 1997, North Carolina ranked 8th in the nation for LACE cases, accounting for 2.8% of the 252 cases reported over the two-year period. During the same time period, LACE was the most frequently reported arthropod-borne encephalitis in the United States (CDC 1998). The first death reported in North Carolina from LACE occurred in the summer of 2000 (personal communication, J. N. MacCormack, Department of Health and Human Services, Division of Epidemiology). The fatality rate of LACE is low, ca. 0.5% of cases (Rust *et al.* 1999).

La Crosse encephalitis is often misdiagnosed as “flu” or “summer cold”; therefore, the true incidence of mild or sub clinical infections is presently unknown, but estimated to be as great as 300,000 infections per year in the United States (Rust *et al.* 1999). Retrospective serologic surveys indicate that the ratio of inapparent-to-apparent LAC virus infections in children range from 26:1 to 1,571:1. Antibody prevalence increases with age, reaching 35% by adulthood in some endemic areas (Jones *et al.* 1999).

In North Carolina, populations living off the Cherokee reservation had a LAC virus antibody prevalence range from 1.8% for the youngest age group, <15 years, to 16.7% for the oldest group, 75 – 100 years, surveyed. On the Reservation for the same age groups, seroprevalence dramatically increased from 16.7% to 53.9% (Szumlas *et al.* 1996c). All reported cases of LACE in North Carolina were contracted in the Blue Ridge Mountain area of western

North Carolina, with the majority of cases occurring in or around the Cherokee Indian Reservation area of Jackson and Swain counties (Szumlas *et al.* 1996c).

Transmission of LAC virus appears to be widespread in the southern Appalachian region, including western North Carolina. While the clinical manifestations of LAC virus infection have been adequately characterized (Jones *et al.* 1999; McJunkin *et al.* 1998), the economic and social impacts of LACE have not been clearly defined. In Illinois, the average cost of hospitalization per case of LACE in the early 1980s varied between \$3,967-5,750 with an average of 12 cases per year (Clark *et al.* 1983). Other costs associated with LACE, such as follow-up medical costs, indirect medical costs and social costs, were not included in this study. Furthermore, no attempt was made to project future economic or social burdens resulting from sequelae. For some case patients, residual effects have imposed life-long impairments. Reported residual effects of the illness include recurrent seizures, difficulties in school, behavioral problems, attention deficit disorder and mild mental retardation (Balfour *et al.* 1973; McJunkin *et al.* 2001).

Currently, no information is available concerning the economic and social burden of LACE in North Carolina. Accordingly, the objectives of this study were to measure the impact of LACE on individuals, families and communities by: (1) estimating the costs of medical treatment; (2) estimating non-medical expenses; (3) calculating an estimate of Disability Adjusted Life Years; and (4) measuring social and psychological burden of LACE on the case patients and families.

MATERIALS and METHODS

Study Population.

We identified La Crosse encephalitis patients from case records provided by the North Carolina Department of Health and Human Services, Division of Epidemiology and/or positive serology reports of LAC virus infection from the North Carolina State Laboratory of Public Health. Case patients for years 1989 to 2001 were contacted by mail and asked to participate in a study of the socio-economic impacts of LACE. A protocol for the study was reviewed and approved by the Institutional Review Board at North Carolina State University (Human Use Protocol IRB# 01XM).

Case patients or the parent(s)/guardian(s) of case patients who did not return reply forms were contacted by telephone and asked to return a completed reply form. Individuals not responding were considered non-repliers. Some LACE case patients could not be contacted because mailing addresses obtained from case records or serology reports were invalid or insufficient (see Appendix 1).

Interviews were conducted with 25 (86%) of 29 respondents. Four interviews were not conducted because participants either declined to be interviewed the day before the scheduled date or failed to show up for pre-scheduled meetings. Attempts to reschedule these interviews failed. These four case patients were all female: 7, 9, 14 and 20 years of age at the time of onset of LACE.

Management of Interviews.

Interviews were conducted with informed consent and lasted approximately two hours. Interviews were conducted with adult case patients (n = 2) or the

parent(s)/guardian(s) of case patients who were under 18 years of age. All interviews were conducted between June 2001 and April 2002.

Questionnaire.

Information on the socio-economic impacts of LACE was collected using a standardized questionnaire (see Appendix 3).

Background information. A family history was recorded to obtain background information on the composition of the family unit and responsibilities and activities of family members. A questionnaire was administered to assess annual household income the year before LACE. A travel history two weeks before recognition of any symptoms and a description of the events and disease symptoms leading up to and including hospitalization for LACE were recorded. Participants were asked to provide information on any family/parentally observed or medically diagnosed residual sequelae. Questions concerning sequelae were readdressed in each section of the interview to ensure that the descriptions of sequelae were consistently reported.

For this study, family members are defined as people who lived in the household as a primary residence and were considered to be a family member by the head(s) of household. Head(s) of household were considered to be the parent(s)/guardian(s) of the case patient or were the adult case patients. Dialogue concerning travel history and course of illness were recorded using audiocassettes and transcribed after the interview. The audiocassettes were erased shortly after transcription.

Categories of Cost. In the interview, questions were posed to assess three major categories of cost.

1. **Direct medical cost:** Costs of resources used directly in the treatment process (Neymark 1998). Direct medical costs included emergency professional transport of the patient; hospitalization; medication; follow-up medical care and procedures; all therapy and medical equipment; and educational costs.

2. **Indirect medical cost:** The value of lost production or productivity due to morbidity or mortality resulting from the disease (Neymark 1998). Indirect medical costs due to LACE included lost workdays and lost wages; lost school days; and private transportation costs associated with the medical care of the patient during hospitalization and recovery from LACE.

3. **Social cost:** Costs to the patient, family and community due to the patient's impairment.

Social costs were documented using several different methods. First, days of impairment due to LACE were recorded. Next, Disability Adjusted Life Years (DALYs) were calculated to quantify the burden imposed on the individual and community. Finally, parents rated the impact of LACE on the case patient's self esteem and, familial and peer relationships, using a novel rating scheme, the Impact of La Crosse Encephalitis Scale (ILCES), that is described below. Interview excerpts were used to illustrate the anxiety or stress and resulting emotional burden borne by the family (primarily parents) due to a case of LACE.

Direct Medical costs.

Hospital Costs. Direct medical costs were calculated using billing statements. In the event participants could not provide complete billing information, hospitals and other health care providers identified by the patient were contacted and the billing records were requested. At Cherokee Indian Hospital, patients on Medicare, Medicaid and/or Tribal obligation were charged a flat rate per day of service. To estimate the true direct medical costs for patients receiving care at Cherokee Indian Hospital, patient encounter record sheets were retrieved and retrospectively coded by a quality/risk manager at the hospital. Each code was then matched to a fee for that service.

Follow-up Direct Medical Costs. Costs of office visits and therapy were obtained from billing information. In the event all bills were not available for all office or therapy visits, an estimate based on the minimum fee for an office visit for case patients from the same geographic area was applied as the costs of those visits. Billing information for seizure medication was available only for one participant. To estimate the cost of medication for all case patients, a neurologist provided an estimate of the average weekly cost of seizure medication. This rate was applied to the number of weeks of seizure medication use reported during interviews.

Estimates of the annual direct costs for treatment of patients with projected lifetime neurological sequelae were obtained from their attending neurologists. For three of these five case patients, an annual office visit and seizure medication was noted as the minimum level of medical care required. Projected costs of long-term physical therapy were needed only for the two youngest patients with severe

sequelae. One patient was projected to require rehabilitative therapy until age 18 years and then need lifetime services similar to those described for the other 3 patients. The other patient is projected to need lifetime rehabilitative therapy.

Direct Medical Transport Costs. Emergency transport costs were calculated from records provided by the participants or ambulance companies. In the event the participants did not have copies of bills and could not recall which ambulance company provided service to them, costs were estimated by using geographically appropriate fee schedules provided by ambulance companies. Service rates were applied according to the geographic point of initiation of service. For ambulance cost estimates, a base emergency/critical care ambulance service rate and per mile fee were applied for each trip claimed by participants. Mileage estimates to medical facilities visited were obtained during the interview and confirmed by the investigators. The cost of air ambulance service was obtained from bills provided by participants or service providers. If air ambulance service was provided, but billing information was lacking (n = 1), an estimate of the service was calculated from the cost of similar services for other participants in the geographic area of service initiation.

Educational Costs. Rehabilitative services (speech, physical and occupational therapy) required by one participant were provided by the NC State Department of Education and the NC Developmental Evaluation Center. The costs of these services were obtained from these agencies. Other educational services provided for LACE patients (n= 3) during recovery included tutors, home schooling and specialist services. A standard hourly tutor rate (\$35/hour) was obtained from a

faculty team leader in Wake County, NC school district and applied to private tutor costs. Other services, such as in-school reading specialists and other specialized education services were estimated by calculating the hourly wage of a first year educational professional responsible for each particular service. Hourly wages were calculated using entry-level salary (without local supplements) and benefits package information provided by the North Carolina Wake County Department of Education (Wake County Schools 2002).

Direct Medical Days. Information concerning days hospitalized and days in coma were taken from interview transcripts. Days hospitalized were verified from billing statements as well as room type (Pediatric Intensive Care Unit [PICU] or private room). The reported number of days in coma was consistent with days in PICU or ICU. Days hospitalized and reported days in a coma state were used as indicators of the severity of the illness.

Indirect Medical Costs.

Lost Wages, Work Days and School Days. Indirect medical costs included all monetary expenditures related to the disease, but not associated with the direct medical costs. Estimates of days lost because of the disease included days of school and/or work missed during hospitalization as well as recovery and follow up care for the patient and/or family members. Dollar estimates for lost workdays were calculated by multiplying the number of days missed by a reported daily wage. The daily wage was calculated by dividing the weekly hours worked by 5 (five work days per week) and then multiplying the reported hourly wage by the average number of hours worked per day. In the case of variances in a normal work schedule ($n = 1$), a

daily work wage estimate was recorded and multiplied by the number of days of work missed due to LACE. Lost school days were documented if the illness occurred during the local school year. Days ill with LACE or in recovery from LACE over vacations and/or weekends were not included as lost school days.

Indirect Transport Costs. Indirect medical transport costs were calculated using reported number of round trips and round trip mileage from the case patient's residence to the care facility. Costs were calculated by multiplying reported mileage by the 2001 North Carolina state allowance for mileage, \$0.345/mile (NC Office of Budget 2002). Private transport costs included trips made during hospitalization, rehospitalization, follow up care visits and medical therapy.

Social Costs.

Total days of impairment due to LACE were calculated from information obtained from hospital records and interviews. Disability Adjusted Life Years and the ILCES, described below, were used to measure the social impact of LACE. Along with DALYs and the ILCES, the last section of the interview addressed the social/emotional costs of LACE. Participants were asked to describe their experiences during and after hospitalization for LACE as well as the quality of health care during hospitalization.

Impact of La Crosse Encephalitis Scale (ILCES). The ILCES was developed from the Impact of Pediatric Epilepsy Scale (IPES) (Camfield *et al.* 2001). The IPES was originally designed as a quick and easy-to-use measurement tool of the impact of pediatric epilepsy on the patient and family. The ILCES was included in the survey to measure the social impact of LACE by sequelae severity and over time.

Adult case patients or parent(s)/guardian(s) of adolescent case patients were asked to score for how quality of life attributes changed or were affected by LACE. As a component of the ILCES, an overall, general quality of life rating of the case patient's life was made. A score of 1 is the lowest rating while a score of 6 is the highest rating of quality of life (see Appendix 3). Though each case of LACE is unique, ILCES scores effectively measured and indicated the areas of greatest impact of LACE on the family and case patient. The ILCES responses were made from assessments of the quality of life of the case patient at the time of the interview, not at the onset of LACE.

Identification of Stressors. Participants were also given an opportunity to identify specific factors contributing to the emotional and psychological stress of dealing with the illness that were not otherwise addressed in the interview or ILCES. Responses to this section were audio taped and transcribed within two weeks after the interview. Since case patients often reported having poor memory of the event, patient accounts of the illness were only used for adult case patients (n = 2), because no other versions were available. After the completion of an interview, audio recorded sections were transcribed and commonly reported "stressors" were identified. A stressor is defined as an incident or condition that causes or adds to the social/psychological stress of an event (Torres 1997). A response was recorded for each parent/guardian interviewed, even if both parents of a case patient were interviewed and their responses were similar.

Disability Adjusted Life Years (DALYs). DALYs are non-monetary assessments of lost time and productivity due to a disease that are unbiased relative

to the economic and cultural background of a person with an illness (Murray and Lopez 1994; Murray 1996). DALYs are unbiased to the economic and educational levels of parents. Furthermore, DALYs also consider the age at onset of illness, the duration of illness and the severity of each case (Murray and Lopez 1994; Murray 1996). These variables are important for assessing the actual burden of a case of LACE, which can be manifested with varying degrees of severity and duration.

Currently, use of standard life expectancies, age weighting and discount rates in the calculation of DALYs is controversial (Anand and Hanson 1997). A standard life expectancy of 80 years for males and 82.5 years for females is commonly used in the calculation of a standard DALY (Murray and Lopez 1994; Murray 1996). A discount rate ($r = 0.03$) for future years of life lived is recommended as well as an age weighting function ($\beta = 0.04$) in the calculation of a standard DALY (Murray 1996; Murray and Lopez 1994).

DALYs reported in this study were calculated using different combinations of the age weighting function (β), discount rate (r) life expectancy and the age-weighting modulation factor (K). These parameters (r , K and β) were set at standard DALY values or 0, while two different life expectancy coefficients were used to calculate projected DALYs for patients experiencing lifetime sequelae from LACE. The two different life expectancies were the standard DALY (SDALY) life expectancy (80 years for males and 82.5 years for females) and a United States DALY (USDALY) based on life expectancies reported in United States Life Tables from National Vital Statistics Reports (Anderson and DeTurk 2002). The resulting

combinations produced the following four DALY [r, K, β] measures for cases projected to experience lifelong sequelae:

1. Standard DALY = SDALY [0.03,1,0.04];
2. Standard “0” DALY = SDALY [0,0,0];
3. United States DALY = USDALY [0.03,1,0.04]; and
4. United States “0” DALY = USDALY [0,0,0].

A DALY was calculated using the following equation:

$$D\{KCe^{-ra}/(r+\beta)^2\}[e^{-(r+\beta)(L+a)}[-(r+\beta)(L+a)-1]-e^{-(r+\beta)a}[-(r+\beta)a-1]]+(1-K/r)(1-e^{-rL}),$$

where K = age weighting modulation factor (1 or 0);
 D = disability weight (1 of 6 possible severities ranging from, 0 1 with 1 = death);
 C = age weighting constant (0.16243 or 0);
 r = discount rate (0.03 or 0);
 β = age weight function (0.04 or 0);
 L = duration of disability (in years);
 a = age of onset (in years); and
 $e = 2.72$ (approx.)(Fox-Rushby and Hanson 2001).

If the r equals zero and uniform age weighting is used, the equation simplifies to:

DALYs [0,0,0] = DL (Murray 1996).

DALYs calculated for the time period between the onset of illness and the date of the interview are not dependant on life expectancies. Therefore, only two sets of DALYs are reported for the patients during the study period, DALY [0,0,0] and DALY [0.03,1,0.04]. On the other hand, projected lifetime DALYs for patients with projected lifetime sequelae are dependant on life expectancies. Therefore, all four of the aforementioned DALY types have been reported. Since disability weight tables created for calculating DALYs resulting from LACE are currently unavailable,

base disability weights presented by Murray and Lopez (1994) were used for the calculation of all DALY types reported in this study (Table 1).

Table 1. Disability weights (*D*) used in calculating DALYs (Murray and Lopez 1994).

Class	Disability Description	Weight (<i>D</i>)
1	Limited ability to perform at least one activity in one of the following areas: recreation; education; procreation or occupation.	0.096
2	Limited ability to perform most activities in one of the following areas: recreation; education; procreation or occupation.	0.220
3	Limited ability to perform activities in two or more of the following areas: recreation; education; procreation or occupation.	0.400
4	Limited ability to perform most activities in all of the following areas: recreation; education; procreation or occupation.	0.600
5	Needs assistance with instrumental activities of daily living, such as meal preparation, shopping or housework.	0.810
6	Needs assistance with activities of daily living, such as eating, personal hygiene or toilet use.	0.920

Disability weights reported during the interview for patients with lifetime sequelae were approved by current attending neurologists and have been applied for projected severity of sequelae over time. Application of different types of DALYs will allow results of the present study to be compared to other economic studies of mosquito-borne diseases (Anand and Hanson 1997; Murray and Acharya 1997; Fox-Rushby and Hanson 2001).

Dollar costs: Estimates and Projections.

All costs encumbered between the age at onset of LACE and the date of interview are reported in 2001 dollars. Conversions of dollar costs were made using the consumer price index, “all urban consumers” population group for the appropriate category of costs (“medical care services” for medical costs and “all items” for loss of earning calculations) (US Dept. of Labor 2002). As “strongly recommended” by the Bureau of Labor Statistics, escalation calculations were made using annual percent changes that were not seasonally adjusted. Projected direct

and indirect medical costs for patients exhibiting lifetime sequelae were calculated using a 5% discount rate over time (Villari *et al.* 1995).

Estimated annual direct medical costs for patients with lifetime sequelae were obtained from their current-attending physicians. Estimated indirect medical costs associated with LACE were made for the two youngest participants in the study by their current attending health care providers. The direct medical costs included projected therapy and medical treatment up to age 18 years for the youngest participant and for life for the other participant. Due to the severity of neurological sequelae, the patient requiring lifetime therapy will require services provided by a state residential care facility after age 21 years, much like patients suffering from residual cases of Eastern equine encephalitis (Villari *et al.* 1995). Four state owned and operated residential medical care facilities servicing people with severe to profound mental retardation were contacted and asked to provide an estimate of the annual cost to reside and be cared for at the facility. The resulting average cost (\$124,030) was applied as the annual cost of care for the lifetime of the patient after 21 years of age. Commensurate with Villari *et al.* (1995), a 5% discount rate was applied to the estimate. As a result of the level of physical and mental impairment resulting from the severe sequelae experienced by the patient, employment is not likely to be obtained in the patient's lifetime. Lost earnings by a patient is part of the total estimated economic loss due to an illness (Villari *et al.* 1995). To estimate the loss of income, the annual average income reported for North Carolina was applied for an average working life of 47 years (18 - 65) with a 5% annual discount rate (NC

Dept. of Commerce 2002). Estimates of lost earnings did not include the value of benefit packages or other employee incentives.

In the event the cost of a service for a case patient was lacking due to missing records, the base cost estimate of the service was used. For example, all bills associated with office visits were not available; as a result, estimates were used in some cases. In estimating office visits, an estimate of the average base cost of an office visit (cost of office visit without any services) was applied for the geographic area of the participant. In the end, the reported direct and indirect medical costs associated with LACE are lower bound estimates of the economic burden associated with LACE. In one case, case # 012, direct medical costs were not available from the hospital service. As a result, this participant was not included in the direct medical cost portion of the analysis.

Disease Severity and Age Classification.

Each case patient who participated in the study was categorized by severity of illness using a classification scheme modified from Gundersen and Brown (1983). Case patients were categorized to characterize the variance in disease manifestations common to LACE case patients in our study. The three categories of severity used for LACE are as follows.

1. **Frank encephalitis with no sequelae (NS):** LACE with no observable residual sequelae.
2. **Frank encephalitis with intermediate or long-term sequelae (IS):** LACE with non-neurological residual sequelae resolving in 1 - 5 years.

- 3. Frank encephalitis with lifetime sequelae (LS):** LACE with neurological residual sequelae projected to be life-long by attending physician (primarily lifetime treatment for seizure activity with medication).

An initial disease severity classification of each case patient was made from information gathered during interviews. Attending physicians confirmed the classification of patients who were placed into the most severe (LS) category. All patients who were reported by their parent(s)/guardian(s) to exhibit educational/social sequelae that were not diagnosed medically were placed in the intermediate (IS) sequelae category. Patients were also divided into groups based on age at onset of LACE. Age groups were created so that a similar number of juvenile case patients would be represented in each age group. The age groups created were: <6 years; 6 – 10 years; 11 – 17 years; and > 17 years.

Data Analysis.

Descriptive statistics were calculated for the dataset (Microsoft Excel 2000, Microsoft Corp., Seattle, WA). Simple linear regression was used to test for any response of total ILCES scores over time (years since onset of LACE) for case patients (PROC REG, SAS Institute 1999 – 2001, Cary, NC). Analysis of variance was performed on the ranked responses for selected cost variables across sequelae and age classes using the nonparametric Kruskal-Wallis test (PROC NPAR1WAY, SAS Institute 1999 – 2001, Cary, NC). To separate statistically significant means, pairwise comparisons of means were performed using a one sided Wilcoxon rank sum test. The Bonferroni method was used to control for experimentalwise error ($\alpha = 0.05/k$) for pairwise comparisons between means within age groups ($k = 4$) and

sequelae classes ($k = 3$). The concordance of selected cost variables and case patients' real ages (ages at onset of LACE) was tested using a one-sided Kendall tau-beta rank correlation procedure at a significance level of $\alpha = 0.05$.

RESULTS AND DISCUSSION

Epidemiology of La Crosse Encephalitis.

Twenty-five serologically confirmed and/or reported LACE case patients with onset of illness between 1989 and 2001 participated in our study (Fig. 2.1). Forty percent (19 of 47) of all LACE cases reported to the NC Department of Health and Human Services, Division of Epidemiology during the same time period were included in this study. The age distribution of study participants was skewed towards adolescent age groups (Fig. 2.2). The overall mean age of all LACE patients was 12.65 (\pm SD = 17.0, n = 25) years, and the mean age for study participants < 16 years of age was 7.97 (\pm 4.41) years (Table 2.1). Adult case patients were 56.01 and 76.97 years of age. The large majority of study participants were male (80%). Males may experience increased contact with LAC virus because of greater exposure to mosquitoes as a result of more time spent out of doors (Rust *et al.* 1999). Most cases occurred during September, followed by August and then July (Fig. 2.3). The seasonal occurrence of cases for case patients in our study is similar to that reported in other studies of LACE in the Appalachian area (Szumlas *et al.* 1996c; Jones *et al.* 1999; McJunkin *et al.* 2001). Twenty-one (84%) of 25 case patients resided in the mountains of North Carolina. Travel histories of all LACE case patients but one correspond to LAC virus infection in the mountains of North Carolina. The travel history of one case patient is consistent with his claim of having been infected in Forsyth County, North Carolina.

Prior to illness, the great majority (80%) of participants and/or family members were not familiar with LACE. Those who were aware of the illness reported that they

had heard about a mosquito-borne disease in the Appalachian area, but were not aware of the name of the illness or virus, biology of the virus, vector or means of disease prevention. Ninety six percent (24 of 25) of the families of case patients did not participate in any type of support group during or after the patient's hospitalization. A majority (87.5%) of 24 respondents felt that their family would have generally benefited from such a group.

Participants reported a wide range of annual incomes, indicating that the occurrence of LACE was not affected by income level (Fig. 2.4). Twenty-three (92%) of 25 participants had some form of medical insurance, with 10 (43.5%) of the 23 participants' insurance provider being medicare or medicade.

Reported Symptoms.

Headache (92%) and seizure (88%) were the most frequently reported symptoms before admission to hospital, followed by fever (76%) and fatigue (72%). Grand mal seizures, described as violent, shaking seizures, were the most frequently reported type of seizure (64%) followed by petit mal seizures (48%), characterized as lacking violent, shaking movements (Fig 2.5). Confusion (36%) and personality change (19%) were symptoms that were reported over the period of several hours to six days. Patients experiencing confusion were also reported to experience mild aphasia and progress to profound aphasia in the span of several hours characterized by the inability to name parents and other family member, pets or even their present address or city of residence. Personality changes were varied. Some patients became markedly depressed and emotional throughout the day while others would become belligerent and at times violent (cursing and kicking at parents

and medical personnel). The change in behavior was distinctly different compared to “typical” behavior for the patient. In other studies, fever was the most frequently reported primary symptom of LACE (Crambett *et al.* 1966; Hilty *et al.* 1972; Balfour *et al.* 1973; Clark *et al.* 1980; Deering 1983; Gundersen and Brown 1983; McJunkin *et al.* 2001). During interviews, parents and/or caregivers reported fever only if they recalled measuring the patient’s temperature with a thermometer. Therefore, it is likely all patients experienced fever, but it was not measured and therefore not reported. Although the previously described symptoms were reported by family members or adult case patients, their descriptions of the illness is similar to previous reports of the clinical presentation of LACE (Crambette *et al.* 1966; Hilty *et al.* 1972; Balfour *et al.* 1973; Clark *et al.* 1980; Deering 1983; Gundersen and Brown 1983; McJunkin *et al.* 2001).

The general sequence of symptoms reported began with headache, fever and other flu-like signs of illness, then progressed to fatigue and irritability. Finally, case patients were transported to emergency care facilities after experiencing a seizure, or exhibiting profound behavioral changes, such as slurred speech or confusion/disorientation. On average, patients (n = 25) were ill 2.6 (\pm 1.8) days before hospitalization. Duration of illness before hospitalization is congruent with previous reports (Jones *et al.* 1999; McJunkin *et al.* 2001). Most patients (76%) were admitted to hospital upon first arrival to the emergency room. However, 24% of participants were taken to the emergency room and sent home after treatment for “summer flu” or non-specific viral infection. These patients (n = 6) returned to the emergency room after an average of 1.5 (\pm 1.2) days and were admitted to hospital.

Reported Sequelae.

After interviews were completed, case patients were grouped into three classes of sequelae: patients with no sequelae (“NS”, n = 4); patients with non-neurologic intermediate/long-term sequelae (“IS”, n = 16); and patients diagnosed with projected life-long neurologic sequelae with or without other non-neural sequelae (“LS”, n = 5). In our study population, 21 (84%) of 25 case patients experienced sequelae after release from the hospital for LACE (Fig 2.6). All participants placed in the most severe sequelae (LS) class were 11 years of age or younger at onset of LACE (Fig. 2.7).

Of patients (n = 4) in the NS category, the average duration of recovery was 8.6 weeks (\pm 9.0) with a range of 1.1 to 27.4 weeks. Currently, 20% of patients in our study experience recurrent seizures (Figure 2.6). This figure supports rates reported in other studies (Rust *et al.* 1999; Balkhy and Schreiber 2000).

Educational difficulties (80%) were the most frequently reported form of sequelae for all severity classes (Figure 2.6). More specifically, difficulties in math (36%) and English class (45%) were identified for school-aged patients. Thirteen (52%) of 25 participants were experiencing educational sequelae of some form at the time of the interview (Table 2.2). In some cases, parents reported behavioral problems, such as inability to concentrate or focus for long periods of time and hyperactivity, as the cause of the educational difficulties.

In general, lower grades, especially in math and English classes, were stated to illustrate educational difficulties experienced by patients. Patients still

experiencing educational sequelae are presently in remedial classes (n = 1), require “individual educational plans” (n = 2), attend tutoring programs (n = 8), or are currently under services provided by the NC Department of Education, but too young to attend classes (n = 1). One patient receives services from the NC Developmental Evaluation Center. Many of the educational services received by patients were a result of parents and teachers being proactive, thus bypassing the need for official placements in special education classes or reporting of “official” educational expenditures. As a result, participant-reported educational sequelae are unsupported by diagnoses or records of special services.

Other reported sequelae included emotional changes (68%) and difficulties in communicating (52%)(Figure 2.6). Emotional changes were characterized by the patients becoming withdrawn from playing with friends and becoming very “needy” of physical contact and attention from parents, especially mothers. Difficulties in communicating ranged from profound speech impairment (requiring therapy) to mild aphasia.

The family-reported educational sequelae in our study are generally more profound than clinically reported educational sequelae in some other studies (Mathews *et al.* 1968; Rie *et al.* 1972). Although this discrepancy does bring into question the validity of sequelae reported by non-medical professionals, the general symptoms and sequelae reported by parents and patients in our study are similar in type and severity to medically diagnosed sequelae reported in other studies (Crambette *et al.* 1966; Hilty *et al.* 1972; Rie *et al.* 1972; Balfour *et al.* 1973; Deering 1983; Gundersen and Brown 1983; Balkhy and Schreiber 2000; McJunkin *et al.*

2001). The greater frequency and duration of behavioral and educational sequelae reported by parents may be accounted for by the fact that parents have a more intimate knowledge of the patient's behavior and educational abilities/performance before and after onset of LACE.

Direct Medical Measures.

Direct Medical Costs (DMC). The direct medical costs covering 89.60 cumulative life years for 24 patients was \$631,872, for an average of \$26,328 (\pm \$27,291) per case (Table 2.3). Total medical costs increased with the severity of sequelae from mean estimates of \$16,462, \$21,176, and \$48,736 for the NS, IS and LS classes, respectively, but the differences in cost estimates were not statistically significant ($df = 2$; $X^2_{kw} = 1.725$ $P = 0.4221$)(Figure 2.8). Generally, mean hospital and therapy costs increased as the severity of sequelae increased. The LS class ($n = 5$) accounted for the majority of the estimated costs for therapy (mean total = \$4,449 \pm \$6,286). The LS class averaged greater mean costs for office visits (Wilcoxon rank sum test; $df = 1$; $t_w = 89.0$; $P = 0.0014$) and medication ($df = 1$; $t_w = 66.0$; $P < 0.001$) than the IS class, but not the NS class (office visit: $df = 1$; $t_w = 6.0$; $P = 0.0179$; medication: $df = 1$; $t_w = 3.0$; $P = 0.0667$) (Table 2.3).

There were no differences in direct medical costs between age classes of case patients ($df = 3$; $X^2_{kw} = 2.4013$; $P = 0.4934$)(Table 2.3). However, when the individual types of therapy costs were examined, occupational therapy costs and real age were concordant ($t_b = 0.36789$; $P = 0.01625$; pairs = 24). The two youngest patients required re-hospitalization due to sequelae, which cost \$9,815 or an average of \$4,908 per patient. When hospitalization costs for LACE reported by

Clark *et al.* (1983) are transformed to 2001 values, the per case direct medical costs range from \$13,967 to \$19,320, which is comparable to the overall mean hospitalization costs ($\$21,107 \pm 18,689$) in our study, (Table 2.3).

Parent-reported (n = 24) educational expenses totaled \$8,727, with an average of \$364 (± 959) per patient (Table 2.3). There was a positive association between education expenditures and real age ($t_b = 0.299$; $P = 0.0384$; pairs = 24). The cost of all services claimed by participants for case patients with educational sequelae could not be estimated. During interviews, participants explained that teachers gave special attention (one-on-one assistance) and consideration (modified assignments and quizzes) to patients with educational sequelae. The time spent for these activities by the teacher is a relevant indirect cost, but an estimate of the average time spent in assisting students with educational sequelae could not be made nor could a cost estimate for time be calculated. As stated earlier, 2 of 5 LS patients are not yet old enough to attend public school. Current and projected severity of sequelae experienced by these patients make it likely that they will be placed in special education and special service programs when they attend school. These program costs will further increase the overall educational costs resulting from LACE for these patients. Due to the inability to predict specific future educational sequelae and interventions, we were not able to make a dollar estimate for projected educational services.

Equipment Costs. Two participants in the study listed the cost of equipment associated with medical care and support of patients as an expense. One participant required short-term rental of a hospital bed; wheel chair, bedside toilet

and walker for home use with a total cost of \$310. Direct medical equipment costs for the other patient are ongoing and will occur over the patient's lifetime, but currently total \$6,920. Equipment required by the participant included therapeutic equipment such as a Rifton gait trainer, arm prompt set, hip positioner, chest prompt set and a thigh prompt set.

Projected Direct Medical Costs. For 4 of 5 LS case patients with similar projected sequelae, the total estimated lifetime direct medical cost is \$289,404 based on US life tables, with an average of \$72,351 ($\pm 29,511$) per case patient (Table 2.4). Direct medical expenses include seizure medication and an annual neurological exam for the expected lifetime of each patient. For the most severe case, the estimated lifetime direct medical cost ranges between \$2,511,029 - 2,567,953 (Table 2.5). The difference in costs between the more severe LS case and the four similar LS cases is due a projected need of more extensive medical care over the course of the patient's life.

Direct Medical Days. The length of hospitalization for all participants averaged 10.9 (± 11.1) nights (Table 2.6), which supports estimates reported in other studies (Clark *et al.* 1980; Clark *et al.* 1983; McJunkin *et al.* 2001). The total nights hospitalized, number of follow up office visits, weeks on medication, and weeks of therapy (except speech therapy) appeared to increase directly in relation to the severity of sequelae (Table 2.6). The LS class averaged more office visits than the NS class ($df = 1$; $t_w = 10.0$; $P = 0.0079$) and the IS class ($df = 1$; $t_w = 84.5$; $P = 0.0058$). The LS class also averaged more weeks on seizure medication than the IS class ($df = 1$; $t_w = 66.0$; $P < 0.001$). Speech therapy ($df = 2$; $X^2_{kw} = 1.6579$; $P =$

0.4365), occupational therapy weeks (df = 2; $\chi^2_{kw} = 5.9517$; $P = 0.0510$), physical therapy weeks (df = 2; $\chi^2_{kw} = 3.4634$; $P = 0.1770$) and total nights hospitalized (df = 2; $\chi^2_{kw} = 0.7847$; $P = 0.6755$) were not significantly different by sequelae class.

There were no significant differences between age groups and nights hospitalized (df = 3; $\chi^2_{kw} = 1.0203$; $P = 0.7963$), number of follow up office visits (df = 3; $\chi^2_{kw} = 2.4546$; $P = 0.4836$), weeks on medication (df = 2; $\chi^2_{kw} = 0.8201$; $P = 0.6636$; data not available for > 18 age group), speech therapy weeks (df = 3; $\chi^2_{kw} = 2.6227$; $P = 0.4535$), occupational therapy weeks (df = 3; $\chi^2_{kw} = 2.8270$; $P = 0.4191$) and physical therapy weeks (df = 3; $\chi^2_{kw} = 1.1745$; $P = 0.7591$) (Table 2.6). The real age of case patients and the number of speech therapy sessions during recovery were concordant ($t_b = 0.3128$, $P = 0.03035$, pairs = 25), suggesting speech impairment is more evident or more easily diagnosed with an increase in age.

Eighteen (82%) of 22 participants spent at least one night in an ICU with a mean stay of 2.0 (± 1.9) nights per case patient (Table 2.6). While in the hospital, family members reported an average of 2.8 (± 2.3) days of coma for LACE patients, which is consistent with the average number of nights spent in ICU (Table 2.6). The types of services and procedures required by patients illustrate the severity of the acute phase of LACE (Table 2.7). Twenty-nine percent (7) of 24 patients required a breathing tube at some point during emergency transport or hospitalization, while 20.8% (5) of 24 patients required a feeding tube during hospitalization. The percent of patients in our study that required a breathing tube is congruent with a previous report of 25% (of 127) of LACE patients requiring mechanical ventilation (McJunkin

et al. 2001). Thirteen (52%) of all patients in this study required some form of medical therapy following release from hospital (Table 2.7).

The two youngest patients in our study were re-hospitalized for a mean of 2.5 (± 0.71) nights (Tables 2.6 and 2.7). Both of these case patients were diagnosed with lifetime sequelae. No other patients in this study were re-hospitalized due to LACE.

Indirect Medical Measures.

Lost Workdays, Dollars and Mileage Costs. For all 25 case patients, a total of 1,150 family workdays were missed as a result of LACE, accounting for an estimated loss of \$125,733 of income (Tables 2.8 and 2.9). On average, 47.9 (± 78.6) workdays were lost per family, which is equivalent to an estimated average loss of \$5,030 ($\pm \$6,692$) per family (Tables 2.8 and 2.9). Generally, workdays were lost due to follow up medical appointments and staying home with the patient immediately following release from the hospital. In two cases, lost workdays were a result of mothers terminating employment to become full-time caretakers for case patients. In one such case, one year of work was missed, accounting for a loss in family income of \$16,935. In the other case, the patient did not suffer severe sequelae, but due to the severity of the acute phase of the illness, the mother did not work for fear the child would get a fever and relapse. She stayed out of work one month until she found a job that allowed her to bring her son to work with her. Since the mother was the sole income earner, the family lost \$2,927 of income that year.

In three cases, people other than parents lost workdays. In one case, the patient, a single male living alone, lost 120 work days, which accounted for \$20,871

in lost income. For another case patient, a sibling lost 10 workdays. In a third case, a single mother and patient were living with the mother's parents and lost a combined total of 83 days of work, or \$7,858 of income.

Along with lost workdays and wages, a total of 42,909 miles were traveled using private vehicles during the study period for all LACE patients, which is equivalent to \$14,804 (Table 2.9). There was an increase in mean mileage costs with increasing severity in sequelae class (Table 2.9). These differences can be explained in part by the need for continued follow up medical care for the LS sequelae class. The mean miles traveled for office visits by the LS ($n = 5$) class was 1,287.8 ($\pm 1,652.5$), which was greater than that of the IS class (218.9 ± 150.4 , $n = 16$) ($df = 1$, $t_w = 84.0$; $P = 0.0073$) and the NS class (23.5 ± 13.7 , $n = 4$) ($df = 1$; $t_w = 10.0$; $P = 0.0079$). The difference in mean miles traveled can be explained by the fact that the LS group also had a greater mean number of office visits than the IS and NS class. Mean miles traveled were also significantly greater for the IS class than the NS class ($df = 1$; $t_w = 14.0$; $P = 0.0019$). There was also a significant negative association between miles for office visits and real age of case patient (Kendall $t_b = -0.28670$, $P = 0.0233$, pairs = 25). On the other hand, distance from the case patients' home to follow up care facilities is also important to consider and could account for some of the differences in mileage between severity classes and age groups.

Lost School Days. Although the peak incidence of onset of LACE in our study occurred during September, patients could have become ill and recovered when school was not in session (Fig. 2.3). Even so, for all school aged participants ill

while school was in session ($n = 20$), a total of 686.3 school days were lost with an average of $34.3 (\pm 38.0)$ days per patient (Table 2.8). In one case, a patient's sibling was so affected by the severity of illness of her sister, the sibling missed 90 days of school (one semester). On average, the 6 - 10 year old age group lost the greatest number of days of school (42.0 ± 46.3 days) followed by age group 11 - 18 (31.9 ± 34.6 days) and finally the under 6 age group (17.4 ± 18.3 days)(Table 2.8). The oldest age group(> 17) was not included in the analysis of lost school days. The differences in mean days of school lost between age groups were not significant ($df = 2$; $X^2_{kw} = 4.3088$; $P = 0.1160$). There also appeared to be an increase in the number of lost school days in relation to the classes of sequelae severity, but these differences were not significant ($df = 2$; $X^2_{kw} = 2.2097$; $P = 0.3313$)(Table 2.8). In our study population, the two patients with the most severe sequelae due to LACE are not yet of school age, but are projected to need special care and most likely will miss school on a regular basis. Currently, the most severely affected case patient is of preschool age, but will not enter preschool because of extensive neurological sequelae.

Non-medical Equipment Cost. The family of the most severely affected case patient has spent \$21,896 for materials needed for non-medical care (Table 2.3). These materials include a van purchased specifically for transporting the patient to and from therapy and other medical appointments. Other items include specialized furniture and materials that assist the parents in feeding the patient and help the patient perform minimal activities of daily living, such as sitting up and rolling over. No other case patients made expenditures for non-medical equipment.

Projected Indirect Medical Costs and Days. The indirect medical costs for 4 of the 5 patients with projected lifetime sequelae could not be estimated. As noted in interviews, patients and families have been able to rearrange work schedules to meet required medical appointments, minimizing lost work or school days. Mileage costs would be incurred for mileage traveled for medical appointments by case patients and case patients' families, but cannot be predicted due to the possibility of case patients moving their residence, or medical services being established nearer to case patients.

The neurological sequelae experienced by the most severe case of LACE will prevent the case patient from obtaining employment in the future. As explained by Villari *et al.* (1995), the resulting loss of income is a cost of the illness. Though other indirect medical costs will occur over the lifetime of the patient, the frequency or duration of costs such as mileage and parental lost workdays cannot be predicted. Therefore, the sole indirect medical cost included for this case is the loss of future income for 47 working years, which is estimated to be \$622,5345 (Table 2.5).

Total Direct and Indirect Medical Costs.

The total direct and indirect medical cost associated with LACE for 24 of the 25 case patients is \$794,303 for 89.60 life years of study, with an average of \$32,974 (\pm 34,793,) per case (Table 2.10). As stated before, the LS patients in this study are projected to experience lifetime neurological sequelae. Using US life tables, a case of LACE resulting in lifetime neurological sequelae is estimated to cost between \$48,775 - 3,224,831 (Tables 2.4 and 2.5). Cases in the NS and IS categories are similar in severity to those in the transient category of EEE cases

described in Villari *et al.* (1995). The mean cost per case in NS and IS classes were \$17,353 and \$28,117, respectively (Table 2.10), which are lower than the estimated mean cost of \$35,415 of a transient case of EEE (Villari *et al.* 1995). Cost differences may be explained by the higher cost of living in Massachusetts as compared to North Carolina.

Within the LS category, lifetime direct medical cost estimates for the 4 similar cases based on U. S. life tables ranged from \$48,775 - 110,329 (Table 2.4). Since these estimates only include direct medical costs, we cannot compare our estimates to those of a residual case of EEE. Furthermore, the sequelae experienced in the 4 similar LS cases of LACE are less severe than the residual cases of EEE described by Villari *et al.* (1995). On the other hand, the most severe case of LACE within our study is similar in severity, but lower in lifetime cost at \$3,167,907 - 3,224,831 (Table 2.5) compared to \$4,973,061 for the lifetime costs of a residual case of EEE. Since the level of lifetime impairment are similar for the most severe case of LACE and the residual cases of EEE, similar lifetime services will be required for the LACE patient. The lower lifetime cost estimate for LACE can be accounted for by a lower estimated annual salary and regional differences in costs of health care services.

To compare estimated costs of LACE to those of a residual case of EEE (Villari *et al.* 1995), we used the consumer price index (CPI), medical care descriptor to transform in-patient and out-patient costs at \$908,061 (\$529,790 in 1990 dollars)(US dept of Labor 2002). For all other indirect costs, we used the All Items Descriptor to estimate costs, which totaled \$4,065,000 (\$2,416,332 in 1990 dollars)

producing a total cost for a residual case of EEE at \$4,973,061 (\$2,950,000 in 1990 dollars).

Social Costs/Impact.

Impaired Life Years. To quantify the individual burden imposed by LACE, the numbers of days impaired due to the illness were examined. Of 100.59 cumulative life years for 25 study participants, 55.15 were impaired years. This means, as a whole, 54.83% of the life years of the participants in this study were impaired to some degree due to LACE. When examining impairment time by sequelae class, the LS (df = 1; $t_w = 10.0$; $P = 0.0079$) and IS classes (df = 1; $t_w = 14.0$; $P = 0.0025$) had a greater mean percent time impaired than the NS class (Fig 2.9).

Current Disability Adjusted Life Years (DALYs). For 25 LACE patients, there were a total of 13.78 DALYs [0,0,0] or 12.66 DALYs [0.03,1,0.04] accumulated over 100.59 cumulative life years, representing 13.70% to 12.59% loss in productive life years, respectively. When the percent burden is based on DALY estimates, the LS class (n = 5) (DALYs [0,0,0]: df = 1; $t_w = 10.0$; $P = 0.0079$; DALYs [0.03,1,0.04]: df = 1; $t_w = 10.0$; $P = 0.0079$), and IS class (n = 16) (DALYs [0,0,0]: df = 1; $t_w = 12.0$; $P = 0.0025$, DALYs [0.03,1,0.04]: df = 1; $t_w = 13.0$; $P = 0.0014$), experienced a greater mean percent burden than the NS class (n = 4) (Fig. 2.10). The LS group experienced a greater mean burden than the IS group as well (DALYs [0,0,0]: df = 1; $t_w = 91.0$; $P < 0.001$; DALYs [0.03,1,0.04]: df = 1; $t_w = 84.0$; $P = 0.0074$). Examining DALYs [0.03,1,0.04] by age class, the 6 – 10 age group experienced a higher mean percent burden than the < 6 age group (df = 1; $t_w = 88.0$; $P < 0.001$). There was no correlation between percent burden by DALY type and real age

(DALYs [0,0,0]: $t_b = -0.23333$; $P = 0.05105$; pairs = 25; DALYs [0.03,1,0.04]: $t_b = 0.01333$; $P = 0.4628$; pairs = 25).

For our study population of LACE case patients, covering 100.59 cumulative life years from 1989 - 2001, an annual average of 0.137 DALYs [0,0,0] or 0.126 DALYs [0.03,1,0.04] per case was lost. From 1997 - 2001, there was an average of approximately 8 (7.4) cases of LACE per year reported in North Carolina (J. Newt MacCormack, NC Department of Health and Human Services, Division of Epidemiology). Using this average as an annual incidence for North Carolina, the annual mean DALYs due to LACE would be 1.10 DALYs [0,0,0] or 1.01 DALYs [0.03,1,0.04].

Projected Disability Adjusted Life Years (DALYs). Five participants in the study are projected to have life long neurological sequelae. Using DALY estimates as an indicator of disability, 4 of the 5 LS participants share a similar level of lifelong recurrent seizure activity, while the 5th participant's sequelae is much more profound. Depending on DALY type, an LS case of LACE can account for 12.90 – 72.37 DALYs per case patient, representing a burden of 17.46 – 92.00% of a case patient's remaining life years (Table 2.11).

In our study population, 5 (20%) of the 25 cases were placed in the LS category. As noted earlier, this frequency of lifetime neurological sequelae among LACE case patients supports the frequency of occurrence reported in other studies (Rust *et al.* 1999; Balkhy and Schreiber 2000). If this frequency of severe sequelae were applied to the 47 officially reported cases of LACE in North Carolina between 1989-2001 for discussion purposes, there would be approximately 10 persons

suffering from lifetime residual sequelae resulting from LACE. Using the 4 similar residual cases of LACE as a model for the projected 10 lifetime cases, the average lifetime direct medical costs and DALYs resulting from LACE for cases with lifetime sequelae between 1989 and 2001 would range from \$723,510 – \$726,090 and accumulate between 141.4 (USDALY [0.03,1,0.04]) and 299.6 (SDALY [0,0,0]) (Tables 2.4 and 2.12). If the frequency of occurrence of the most severe case of LACE in the present study is applied to the projected 10 LS cases of LACE, then 2 of these 10 LS cases would experience severe neurological sequelae. The lifetime costs would then be amplified to \$7,028,470 and DALYs would increase to between 174.3 (USDALY [0.03,1,0.04]) and 384.4 (SDALY [0,0,0]) for the same 12-year period.

Impact of La Crosse Encephalitis Scale (ILCES). In the study population, the ILCES scores for all case patients (n = 24) do not reflect a pattern of decreasing familial and individual social burden from LACE over time, suggesting that the familial and social burden of LACE does not necessarily decrease over time ($R^2 = 0.0153$; $P = 0.5647$) (Fig. 2.12). The mean total ILCES score was $-3.33 (\pm 8.29)$; range = $-21 - 10$) for 24 case patients, representing a slightly overall negative impact of LACE on the case patients and families of case patients as a result of LACE. The mean total ILCES scores by sequelae class decreased in relationship to increasing severity of sequelae, indicating that there is an increase in the overall burden associated with a case of LACE with lifetime neurological sequelae (Fig 2.13). The LS group was significantly different from the IS ($df = 1$; $t_w = 21.0$; $P = 0.0015$) and NS ($df = 1$; $t_w = 30.0$; $P = 0.0079$) groups. The NS class of case patients had a

positive ILCES score, indicating their quality of familial life had not been detrimentally affected by LACE. The lack of an effect was due primarily to the increased number of positive interactions among family members resulting from what was perceived to be a life threatening illness. In LACE cases with sequelae, the negative effects of the illness on the life of the patient overshadowed any positive effects of the illness on family relationships as a whole.

When ILCES scores are examined by major categories, mean scores for the LS class were lower than the NS class for social life ($df=1$; $t_w = 30.0$; $P = 0.0079$) and self esteem ($df = 1$; $t_w = 26.0$; $P = 0.0143$). The LS class case patients also had a lower mean score than IS class case patients for social life ($df = 1$; $t_w = 22.5$; $P = 0.0020$), school ($df = 1$; $t_w = 22.5$; $P = 0.0043$) and self esteem ($df = 1$; $t_w = 14.5$; $P = 0.0054$). Lower ILCES category means indicate a negative effect of LACE on the patient and family is more profound with increasing sequelae severity category (Fig. 2.14).

As a component of the ILCES, participants rated the current overall “Quality of Life” (QOL) of the case patient. The mean QOL rating for participants ($n = 24$) was $5.13 (\pm 1.26)$. Notably, the LS class QOL score (3.6 ± 1.67) was significantly lower than that of the IS class (5.4 ± 0.83) ($df = 1$; $t_w = 24.5$; $P = 0.0059$) and the NS class (6.0 ± 0) ($df = 1$; $t_w = 30.0$; $P = 0.0079$) (Fig. 2.15). The IS class was not significantly different from the NS class for QOL rating ($df = 1$; $t_w = 54.0$; $P = 0.1227$). When the mean percent burden by DALY type was examined, an increase in burden (or decrease in overall QOL) from LACE was evident, at least temporarily, for the IS class and greatly for the LS class (Figure 2.10). Likewise, the percent impaired life

years during the study were greater for the LS and IS classes than the NS class (Figure 2.9). Currently, 52% (13 of 25) of case patients are reported to experience sequelae of some form (Table 2.2). Of these case patients, 62% (8 of 13) are in the IS class. Because of the discrepancy between the above measures and the QOL ratings, we believe that parents of case patients without clinically diagnosed lifetime sequelae (recurrent seizures) viewed the QOL rating as a measure of the effectiveness of their parenting and care giving more so than a measure of the effect of LACE on the quality of life of the case patient.

Stressors. To further measure the impact of LACE, participants were asked to identify principal factors contributing to the frustration and emotional distress related to or resulting from the illness. Stressors have been used to analyze the impact of dengue fever in rural Puerto Rico (Torres 1997). When asked about the most frustrating aspects of LACE during and after hospitalization, an overwhelming majority of participants' answers (75.86%, n = 58) revolved around information issues (Table 2.13). Interestingly, lack of information was also the most frequently identified stressor in a study of dengue fever in Puerto Rico (Torres 1997). Lack of a diagnosis was frustrating to participants. Participants were not informed of serological confirmation of LACE for several days after admission to the hospital. And in a few cases, diagnosis was not confirmed until weeks or even months after release from the hospital. Participants felt that the lack of a timely diagnosis during hospitalization made the event confusing and stressful. After diagnosis, the lack of information regarding the course of recovery and possible long-term effects of the

illness compounded the emotional burden. The lack of information available to the public in an easily accessible, appropriate format was a primary complaint.

The following statements transcribed from interviews illustrate how the lack of information stressor affected LACE case patients and their families (Table 2.13).

Lack of Information

Case # 017

“[The most frustrating aspect during hospitalization was]...the time it took to pinpoint what was actually wrong.”

“Living with the illness after hospitalization is almost worse because you don’t know what the outcome is going to be.”

Case # 004

(Father) “ Not knowing what to expect or what he had, thinking he would be retarded for the rest of his life.”

(Mother) “ Thinking my child would die.”

Case # 007

“Lack of information about the disease and not having a diagnosis.”

Other notable concerns revolved around lack of awareness and/or lack of response demonstrated by local civic leaders and the community concerning LACE. The lack of local community education programs focusing on LACE was a primary complaint. Passing legislation to control litter and enforcing existing ordinances concerned with property maintenance were identified as positive steps local leaders could take to address the problem of LACE in their community. Other participants suggested that the LACE issue was being ignored by civic leaders for fear of possible negative impacts on the local economy resulting from avoidance of the area by tourists fearful of having a child infected with the disease. The following

comments have been extracted from interviews to illustrate how the lack of community awareness and worry about the future health of case patients has affected participants.

Lack of Community Awareness

Case # 022

“At Cherokee Hospital, they have posters that will tell you smoking is bad for you or teen pregnancy is out of control. We already know these things, but they have no posters about La Crosse encephalitis.”

Case # 015

“People don’t realize the effects the bite from one mosquito can cause. Before, she [the patient] had no problems. Now, she has learning disabilities in math and reading. She is clumsy, she is on seizure medication and complains of headaches.”

Case # 016

“The community is beginning to be informed, but there is not enough information out there. Information needs to be bombarded in the community weeks prior to the mosquito season so people can take preventative measures.”

Case # 017

“I think this tribe [Eastern Band of Cherokee] needs to have mandatory ordinances adopted to force people to clean up around their houses. They should have people available to help those who cannot do it themselves. They just need to clean up the junk.”

Case # 009

“People around here [Black Mountain, NC] do not know it [La Crosse encephalitis] is prevalent and they don’t know what it can actually do. People need to be educated by the paper and the news. Every time there is a new case people need to know about it.”

Worry about Patient’s Future Health

Case # 021

(Father) “I am probably overprotective and over-worried about illnesses now when it comes to her [case patient].”

(Mother) “It’s always in your subconscious; if she [case patient] gets a headache, we treat things a lot differently.”

Case # 011

“[I am] ...always worried about my child [case patient] getting the illness again.”

Case # 023

“Any time he [case patient] sneezes now, I jump and do not ignore any sign or symptom of any sickness because I’ll never know what it’ll be.”

Parents and adult patients were given the opportunity to comment on how LACE has impacted them and their family emotionally. Though we have addressed the social and emotional impact of the illness through the use of DALYs, the ILCES and stressors, the following quotes further illustrate the emotional impact of the illness. Some notable events that affected patients socially and/or emotionally, which are not addressed in the quotes below, are one patient had to attend summer school every summer while in high school, yet still graduated a semester late due to educational difficulties associated with LACE. Another patient with long-term neurological sequelae was not able to obtain a driver’s license until age 20 due to recurrent seizures and has been delayed in the progress towards a college degree.

Case # 025

“My daughter has backed away from me because I have to spend so much time with [the patient]. She understands why, but I can see she wants me to pay more attention to her.”

“I am always stressed. I work full time, that can be stressful and then I come home and I have all this work to do with [the patient], which is also stressful at times. I am the one who is pushing the patient to get better and improve, the rest of the family [husband and grand parents] just accept the patient as he is. I love the patient, but I think he can improve and get better, so that is why I push him and work with him so much when I get home from work.”

Case # 024

“During the recovery, we were exhausted and decided to cut back on a lot of activities. The patient didn’t do anything, but her siblings did not do a lot of extracurricular activities either due to our [the parents] being busy” (recovery was about 6 weeks).

“I started going to our family’s church again. I had stopped for reasons that seem very unimportant now. My daughter said, ‘Daddy, will you go to church with us?’ and I saw the importance of doing that. So, the effect of the illness goes beyond health delivery systems, disability, days off and economic measures.”

Case # 014

“There is no telling how far reaching the effects of her illness are. Everyone who has dealt with this must develop a great amount of patience with the learning disabilities. It was very frustrating to see her work so hard at school and bomb on tests; it is heartbreaking.”

Case # 012

“It was totally and emphatically emotionally draining, physically unbearable, your eyes don’t cry enough. We need support groups or at least a representative to visit the parent in the hospital. I was so unsure about the continuity of care for my child that I had to quit my job. We all suffered immeasurably during this time. It is horrible emotionally and financially.”

Case # 023

“He is very clingy and scares easily, he slept with me [mother] for 4 months after the illness and still sleeps with me about half the time. He is really unwilling or apprehensive to do things. He was really outgoing before, but now he has to really be encouraged and warm up to a situation.”

Case # 003

“I am scared to death to go outside in the summer time when the mosquitoes are out. I just refrain from it. I love to go fishing, but I just can’t go fishing in the areas where mosquitoes are because I am scared to death of getting bit again and I won’t make it to the hospital. It’s just terrible.”

Case # 021

“During the illness you fought the good fight, just tried to stay on top of things. I can’t begin to guess how this has affected our family emotionally.”

After identifying the most frustrating aspect of LACE during and after hospitalization and discussing the emotional impact of the illness, participants explained that a number of other stressors contributed to the overall anxiety from LACE. Logistical issues, such as taking care of other children and trying to maintain a sense of normalcy in their lives, were a continual concern of parents during the course of hospitalization and recovery for the patient.

Reported impaired life years, DALYs, ILCES scores and stressors demonstrate that LACE is a life-altering event for both patients and families of patients. Collectively, the economic, social and emotional impact of LACE in an endemic area such as western North Carolina warrants a more attentive approach to LACE by all public health and medical providers in the endemic foci. An active approach to prevention, surveillance, diagnosis and reporting of LACE cases needs to be developed and implemented by local and state public health offices and supported by the medical community of North Carolina.

Although 21 (84%) of 25 case patients resided in the mountains of North Carolina, 80% (20 of 25) of families in this study had not heard of LACE before a family member became ill, demonstrating a need for public education concerning LACE, LAC virus, prevention and vector biology. Currently, there is no vaccine available for LACE. The primary vector for LACE, *Ochlerotatus triseriatus*, is a container inhabiting species. Consequently, insecticide spraying is an ineffective strategy for vector control. As a result, prevention education and breeding site reduction are the principal methods available for lowering the incidence of LAC virus infections and LACE as well as decreasing the vector population in the endemic

area. Container reduction and community education campaigns have been effective in lowering the incidence of arboviral infection in other communities (Eamchan *et al.* 1989; Lloyd *et al.* 1992). Since *Oc. triseriatus* and LAC virus transmission have a predictable seasonal pattern, strategically timed public health campaigns can be effective tools for educating at risk populations about LACE.

Community education programs should be implemented to raise awareness about LACE and promote a proactive community response to mosquito control by mosquito bite prevention and breeding site reduction. The use of local media (television, radio and newspapers) and education centers (schools, libraries and community centers) to educate and disseminate educational materials to the public is one active step towards public health education concerning LAC virus transmission and LACE.

Along with prevention education, breeding site reduction programs are needed for the endemic area. *Ochlerotatus triseriatus* uses discarded, water filled containers and naturally occurring tree holes as oviposition sites. A decrease in the number of mosquito production sites would result in a decrease in the population of *Oc. triseriatus* and ultimately the risk of human LAC virus infection. Mosquito production site reduction programs could benefit from the inclusion of local schools and civic organizations involved with community “beautification” or “clean-up” programs as well as serve as another opportunity for community education about the LAC virus transmission cycle and LACE.

Through public education and the reduction of mosquito production sites, the annual incidence of LAC virus infection and LACE could be reduced. Active case

surveillance and reporting will provide more accurate data concerning the risk and rates of LAC virus infection in endemic areas than passive surveillance, as well as assist public health personnel in focusing disease prevention programs to high-risk areas.

Physicians should be encouraged to use the North Carolina State Public Health Laboratory for serologic testing to confirm their diagnoses of the disease and to test patients from disease endemic areas who exhibit symptoms related to LAC virus infection, especially during peak LAC virus transmission periods. Use of the current system of reporting or a more efficient system of reporting and information sharing among physicians and medical facilities, public health agencies and the research community needs to be implemented. Active case surveillance and reporting would be beneficial for tracking LACE in North Carolina; measuring the effectiveness or impact of any prevention programs; as well as provide valuable data for the possible identification and future investigation of questions concerning the transmission cycle of LAC virus.

REFERNCES CITED

- Anand, S. and K. Hanson. 1997.** Disability-adjusted life years: a critical review. *J. Health Econ.* 16:685 – 702.
- Anderson, R. N. and P. B. DeTurk. 2002.** United States Life Tables, 1999. National Vital Statistics Reports, National Center for Health Statistics. 50:1 – 38.
- Balfour H. H., R. A. Siem, H. Bauer, and P. G. Quie. 1973.** California arbovirus (La Crosse) infections: clinical and laboratory finding in 66 children with meningoencephalitis. *Pediatrics.* 52:680 – 691.
- Balkhy H. H. and J. R. Schreiber. 2000.** Severe La Crosse encephalitis with significant neurological sequelae. *Pediatr. Infect. Dis. J.* 19:77 – 80.
- Camfield, C., L. Breau, and P. Camfield. 2001.** Impact of pediatric epilepsy on the family: a new scale for clinical and research use. *Epilepsia.* 42:104 – 112.
- Center for Disease Control and Prevention. 1998.** Arboviral infections of the central nervous system, United States, 1996 – 1997. *Morb. Mortal. Wkly. Rep.* 47:517 – 540.
- Clark, G. G., R. J. Martin, H. L. Pretula, C. W. Langkop, and H. H. Rohrer. 1980.** California Group Virus infections in Illinois. *IMJ.* 157:91 – 96.
- Clark, G. G., H. L. Pretula, C. W. Langkop, R.J.Maritn, and C. H. Calisher. 1983.** Occurrence of La Crosse (California serogroup) encephalitis viral infections in Illinois. *Am. J. Trop. Med. Hyg.* 32:838 – 843.
- Cramblett, H. G., H. Stegmiller, and C. Spencer. 1966.** California encephalitis infections in children: clinical and laboratory studies. *JAMA.* 198:128 – 132.

- Deering, W. M. 1983.** Neurological aspects and treatment of La Crosse encephalitis. pp.187 – 191. *In:* C. H. Calisher and W. H. Thompson (eds. 1983. *California Serogroup Viruses*. A. R. Liss, Inc. New York. 399 pp.
- Eamchan, P., A. Nisalak, H.M. Foy, and O. Chareonsook. 1989.** Epidemiology and control of dengue virus infections in Thai villages in 1987. *Am. J. Trop. Med. Hyg.* 41:95 – 101.
- Erwin, P.C., T. F. Jones, R. R. Gerhardt, S. K. Halford, A. B. Smith, L. E. R. Patterson, K. L. Gottfried, K. L. Burkhalter, R. S. Nasci, and W. Schaffner. 2002.** La Crosse encephalitis in eastern Tennessee: clinical, environmental, and entomological characteristics from a blinded cohort study. *Am. J. Epidemiol.* 155:1060 – 1065.
- Fox-Rushby, J.A. and K. Hanson. 2001.** Calculating and presenting disability adjusted life years (DALYs) in cost effectiveness analysis. *Health Policy Plan.* 16:326 – 331.
- Gerhardt, R. R., D. L. Gottfried, C. S. Apperson, B. S. Davis, P. C. Erwin, A. B. Smith, N. A. Panella, E. E. Powell, and R. S. Nasci. 2001.** First isolation of La Crosse virus from naturally infected *Aedes albopictus*. *Emerg. Infect. Dis.* 7:807 – 903.
- Gundersen, C. B. and K. L. Brown. 1983.** Clinical aspects of La Crosse encephalitis: preliminary report. pp. 169 – 177. *In:* C. H., Calisher and W. H. Thompson (eds.). 1983. *California Serogroup Viruses*. Alan R. Liss, Inc. New York. 399 pp.

- Hilty M. D., R. E. Haynes, P. H. Azimi, and H. G. Cramblett. 1972.** California encephalitis in children. *Amer. J. Dis. Child.* 124:530 – 533.
- Jones, T. R., A. S. Craig, R. S. Nasci, L. E. R. Patterson, P. C. Erwin, R. R. Gerhardt, X. T. Ussery, and W. Schaffner. 1999.** Newly recognized focus of La Crosse encephalitis in Tennessee. *Clin. Infect. Dis.* 28:93 – 97.
- Kappus, K. D., T. P. Monath, R. M. Kaminski, and C. H. Calisher. 1983.** Reported encephalitis associated with California serogroup virus infections in the United States, 1963 – 1981. pp. 31 - 41. *In: C. H., Calisher and W. H. Thompson (eds.). 1983. California Serogroup Viruses. Alan R. Liss, Inc. New York. 399 pp.*
- Lloyd, L.S., P. Winch, J. Ortega-Canto, and C. Kendall. 1992.** Results of a community-based *Aedes aegypti* control program in Merida, Yucatan, Mexico. *Am. J. Trop. Med. Hyg.* 46:635 – 642.
- Mathews, C. G., R. W. M. Chun, J. D. Grabow, and W. H. Thompson. 1968.** Psychological sequelae in children following California arbovirus encephalitis. *Neurology.* 18:1023 – 1030.
- McJunkin, J. E., E. C. De Los Reyes, J. E. Irazuzta, M. J. Caceres, R. R. Khan, L. L. Minnich, K. D. Fu, G. D. Lovett, T. Tsai, and N. Thompson. 2001.** La Crosse encephalitis in children. *N. Engl. J. Med.* 344:801 – 807.
- McJunkin, J. E., R. R. Kahn, and T. F. Tsai. 1998.** California-La Crosse encephalitis. *Infect. Dis. Clin. North Am.* 12:83 – 93.
- Murray, C.J.L. 1996.** Rethinking DALYs. Chapt. 1 pp. 1-98. *In: C.J.L. Murray and A.D. Lopez (ed.). The Global Burden of Disease: A Comprehensive*

Assessment of Mortality and Disability from Disease, Injuries, and Risk Factors in 1990 and Projected to 2020. Harvard School of Public Health University Press. Boston, MA. 990 pp.

Murray, C.J.L. and A.K. Acharya. 1997. Understanding DALYs. *J. Health Econ.* 16:703 – 730.

Murray, C. J .L. and A. D. Lopez. 1994. Global comparative assessments in health sector: Disease burden, expenditures, and intervention packages. *Bull. W.H.O.* Geneva, Switzerland. 196pp.

Neymark, N. 1998. *Assessing the Economic Value of Anticancer Therapies.* Springer-Verlag, Berlin. 285pp.

North Carolina Department of Commerce, Economic Information Systems.

2002. <http://cmedis.commerce.state.nc.us>

North Carolina Office of State Budget and Management. 2002.

<http://www.osbm.state.nc.us>

Rie, H. E., M. D. Hilty, and H. G. Cramblett. 1973. Intelligence and coordination following California encephalitis. *Am J. Dis. Child.* 125:827 – 282.

Rust, R. S., W. H. Thompson, C. G. Mathews, B.F. Beaty, and R. W. M. Chun.

1999. La Crosse and other forms of California encephalitis. *J. Child Neurol.* 14:1 – 14.

Szumlas, D. E., C. S. Apperson, and E. E. Powell. 1996a. Seasonal occurrence and abundance of *Aedes triseriatus* and other mosquitoes in a La Crosse virus-endemic area in western North Carolina. *J. Am. Mosq. Control Assoc.* 12:184 – 193.

- Szumlas, D. E., C. S. Apperson, E. E. Powell, P. C. Hartig, D.B. Francy, and N. Karabatsos. 1996b.** Relative abundance and species composition of mosquito populations (Diptera: Culicidae) in a La Crosse virus-endemic area in western North Carolina. *J. Med. Entomol.* 33:598 – 607.
- Szumlas, D. E., C. S. Apperson, P. C. Hartig, D. B. Francy, and N. Karabatsos. 1996c.** Seroepidemiology of La Crosse virus infection in humans in western North Carolina. *Am. J. Trop. Med. Hyg.* 54:332 – 337.
- Thompson, W. H. 1983.** Vector-virus relationships. pp. 57 - 66. *In:* C. H. Calisher and W. H. Thompson (eds.). 1983. *California serogroup viruses*. A. R. Liss, Inc. New York. 399 pp.
- Thompson, W. H., and C. B. Gundersen. 1983.** La Crosse encephalitis: Occurrence of disease and control in a suburban area. pp. 225 - 236. *In:* C. H. Calisher and W. H. Thompson (eds.). 1983. *California serogroup viruses*. A. R. Liss, Inc. New York. 399 pp.
- Torres, M. I. 1997.** Impact of an outbreak of dengue fever: a case study from rural Puerto Rico. *Human Organization* 56:19 - 27.
- United States Department of Labor, Bureau of Labor Statistics. 2002.**
<http://www.bls.gov>
- Wake County Public School System. 2002.** <http://www.wcpss.net>
- Villari, P., A. Spielman, N. Komar, M. McDowell, and R. J. Timperi. 1995.** The economic burden imposed by a residual case of Eastern encephalitis. *Am. J. Trop. Med. Hyg.* 52:8 – 13.

Table 2.1. Epidemiological information for participants in La Crosse encephalitis study.

Category	n (%)	Age (years)		
		Mean (± SD)	Median	Range
All Participants	25 (100)	12.65 (17.01)	9.40	0.25 – 79.97
Participants ≤ 16 years	23 (92)	7.97 (4.41)	8.17	0.25 – 15.39
Race				
African American	1 (4)	7.00 (-)		
Caucasian	15 (64)	14.95 (20.96)	7.79	1.35 - 76.97
Hispanic	1 (4)	5.00 (-)		
Native American	7 (28)	9.12 (4.27)	9.78	0.25 - 13.45
Gender				
Female	5 (20)	13.68 (18.94)	8.81	0.25 - 76.97
Male	20 (80)	8.54 (2.37)	9.40	4.89 - 11.01

Table 2.2. Chronic sequelae (NS = no sequelae, IS = intermediate sequelae, LS = lifelong sequelae) reported for La Crosse encephalitis case patients.

Case number	Severity Class	Elapsed Time (years) from onset of illness to interview	Chronic Sequelae ^a
OO1	IS	1.75	E
OO2	LS	1.72	E, N
OO3	IS	2.80	- ^b
OO4	IS	2.89	-
OO5	NS	1.77	-
OO6	NS	9.92	-
OO7	IS	6.84	-
OO8	IS	1.84	E
OO9	IS	3.89	-
O10	IS	6.83	-
O11	NS	0.95	-
O12	NS	11.00	-
O13	LS	1.87	E, N
O14	LS	9.86	E, N
O15	LS	1.87	E, N
O16	IS	11.89	E
O17	IS	2.87	E
O18	IS	3.00	E
O19	IS	2.97	-
O20	IS	1.93	-
O21	IS	5.01	E
O22	IS	2.23	-
O23	IS	2.77	E
O24	IS	0.43	E
O25	LS	1.65	E, N

^aE = educational, N = neural. All neurological sequelae were confirmed by current attending neurologists and all educational sequelae were parent-reported.

^bNo long-term sequelae reported.

Table 2.3. Direct medical costs in 2001 dollars for 24 case patients by age and sequelae class due to La Crosse encephalitis.

Variable	Age or Sequelae Class	Number of case patients	Mean (±SD)	Median	Total	Range	Age or Sequelae Class	Number of case patients	Mean (±SD)	Median	Total Costs	Range	Age or Sequelae Class	Number of case patients	Mean (±SD)	Median	Total	Range	Age or Sequelae Class	Number of case patients	Mean (±SD)	Median	Total Costs	Range
Ground Transport Costs	<6	9	598 (700)	563	53,80	0-2,228	6-	7	1,484 (2,069)	1,034	10,384	0-6,084	11-	6	962 (398)	958	5,772	549-1,641	>17	2	267 (380)	267	537	0-539
	NS	3	340 (306)	430	1,020	0-591	IS	16	976 (1,430)	584	15,615	0-6,081	LS	5	1,088 (790)	1,083	5,438	0-2,228	T	24	920 (1,226)	588	2,207	0-6,081
Hospitalization and air lift costs	<6	9	22,121 (26,206)	14,965	199,082	5,751-91,019	6-	7	18,121 (15,815)	13,793	126,846	5,642-52,619	11-	6	20,712 (7,204)	19,196	124,270	12,863-30,833	>17	2	16,062 (2,419)	16,062	32,123	14,352-17,772
	NS	3	15,121 (3,304)	14,352	45,336	12,225-18,730	IS	16	18,039 (11,433)	15,180	288,611	5,642-52,619	LS	5	29,675 (34,552)	17,956	148,374	8,392-91,019	T	24	20,097 (17,888)	15,180	482,320	5,642-91,019
Total Hospitalization Costs	<6	9	22,718 (26,834)	15,528	204,461	5,751-93,246	6-	7	19,605 (17,814)	14,387	137,231	6,094-58,699	11-	6	21,674 (7,415)	20,029	130,041	13,849-31,762	>17	2	16,330 (2,798)	16,330	36,660	14,352-18,308
	NS	3	15,452 (3,452)	14,452	46,356	12,685-19,321	IS	16	19,015 (12,704)	15,979	304,226	5,751-58,699	LS	5	30,763 (35,203)	18,743	153,811	9,474-93,246	T	24	21,017 (18,689)	15,797	93,246	5,751-93,246
Office Costs ^b	<6	9	2,371 (5,315)	631	21,333	315-16,519	6-	7	1,529 (1,532)	1,162	10,700	373-4,777	11-	6	967 (1,019)	547	5,799	315-2,960	>17	2	750 (534)	750	1,500	373-1,127
	NS	3	355 (34)	315	1,003	315-373	IS	16	826 (697)	618	13,202	315-2,960	LS	5	5,026 (6,602)	1,426	25,126	1,162-16,519	T	24	1,639 (3,328)	647	39,330	315-16,519
Medication Costs ^c	<6	9	1,165 (2,231)	150	10,481	25-6,756	6-	6	2,825 (5,000)	750	16,950	50-12,850	11-	5	265 (245)	150	1,325	25-650	>17	0	-	-	-	-
	NS	2	175 (177)	175	350	50-300	IS	14	279 (342)	150	3,900	25-1,300	LS	4	6,127 (4,921)	4,603	24,506	2,450-12,850	T	20	1,438 (3,113)	175	28,756	25-12,850
Total Therapy Costs	<6	9	2,758 (4,940)	0	24,816	0-13,311	6-	7	286 (515)	0	2,000	0-1,280	11-	6	856 (2,096)	0	5,133	0-5,133	>17	2	0	0	0	0
	NS	3	559 (968)	0	1,676	0-1,676	IS	16	607 (1,397)	0	9,706	0-5,133	LS	5	4,449 (6,286)	0	22,243	0-13,311	T	24	1,401 (3,283)	0	33,624	0-13,311
Education Costs	<6	9	0	0	0	0	6-	7	180 (477)	0	1,260	0-1,260	11-	6	1,245 (1,666)	375	7,467	0-3,493	>17	2	0	0	0	0
	NS	3	0	0	0	0	IS	16	467 (1,146)	0	7,467	0-3,493	LS	5	252 (564)	0	1,260	0-1,260	T	24	364 (959)	0	8,727	0-3,493
Rehospitalization ground transport costs	<6	9	66 (197)	0	590	0-590	6-	7	0	0	0	0	11-	6	0	0	0	0	>17	2	0	0	0	0
	NS	3	0	0	0	0	IS	16	0	0	0	0	LS	5	118 (264)	0	590	0-590	T	24	25 (121)	0	590	0-590
Rehospitalization costs	<6	9	1,025 (2,035)	0	9,225	0-4,734	6-	7	0	0	0	0	11-	6	0	0	0	0	>17	2	0	0	0	0
	NS	3	0	0	0	0	IS	16	0	0	0	0	LS	5	1,845 (2,528)	0	9,225	0-4,734	T	24	385 (1,303)	0	9,225	0-4,734
Total Rehospitalization Costs	<6	9	1,091 (2,174)	0	9,815	0-5,324	6-	7	0	0	0	0	11-	6	0	0	0	0	>17	2	0	0	0	0
	NS	3	0	0	0	0	IS	16	0	0	0	0	LS	5	1,963 (2,704)	0	9,815	0-5,324	T	24	409 (1,391)	0	9,815	0-5,324
Total Direct Medical Costs	<6	9	30,870 (42,291)	18,479	277,824	6,216-141,242	6-	7	24,020 (18,959)	15,762	168,140	7,766-60,768	11-	6	25,013 (7,563)	23,904	150,074	15,228-34,055	>17	2	17,918 (2,147)	17,918	35,835	16,400-19,435
	NS	3	16,462 (3,194)	16,340	49,384	13,230-19,685	IS	16	21,176 (13,137)	18,696	388,809	6,216-60,768	LS	5	48,736 (53,135)	36,891	243,679	13,350-141,242	T	24	26,328 (27,291)	18,696	631,872	6,216-141,242

^a < 6 = all participants under the age of 6 years, 6 – 10 = all participants between the ages of 6 and 10 years, 11 – 17 = all patients between the age of 11 and 17 years, > 17 = all patients greater than 17 years of age; NS = all participants in the “No Sequelae” class, IS = all participants in the “Intermediate Sequelae” class, LS = all participants in the “Lifetime Sequelae” class, T = total for all case patients.

^b LS class > IS class (df = 1; $t_w = 89.0$; $P = 0.0014$). ^c LS class > IS class (df = 1; $t_w = 66.0$; $P < 0.001$).

Table 2.4. Projected lifetime direct medical costs in 2001 dollars for four lifetime (LS) sequelae class La Crosse encephalitis case patients with similar severity of sequelae from date of onset of illness.

Case Number	US Life Years remaining	Current Costs	Projected Cost	Total US Projected Cost	Standard Life Years remaining	Current Costs	Projected Costs	Total Standard Projected Cost
002	67.3	14,016	34,759	48,775	72.1	14,016	35,024	49,040
013 ^a	71.9	38,460	71,869	110,329	77.9	38,460	72,125	110,585
014	58.8	47,031	34,101	81,132	63.2	47,031	34,476	81,507
015	68.4	14,343	34,826	49,168	70.8	14,343	34,959	49,301
Total	266.4	113,850	175,553	289,404	284.0	113,850	176,582	290,433
Mean		28,463	43,889	72,351		28,463	44,146	72,609
(± SD)	-	(16,861)	(18,657)	(29,511)	-	(16,861)	(18,654)	(29,553)
Median	-	26,402	34,792	65,150	-	26,402	34,991	65,404

^aIncludes therapy costs up to age 18 based on currently projected early intervention services.

Table 2.5. Projected lifetime direct and indirect medical costs for La Crosse encephalitis case patient #025.

Cost Category	Projected Cost (US life years remaining = 72.5)	Projected Costs (S life years remaining = 77.0)
Best Case Scenario		
CDMC ^a	141,242	141,242
CIMC ^b	34,344	34,344
PDMC ^c	2,369,787	2,402,547
PIMC ^d	622,534	622,534
Total	3,167,907	3,200,667
Worst Case Scenario		
CDMC	141,242	141,242
CIMC	34,344	34,344
PDMC	2,426,711	2,459,471
PIMC	622,534	622,534
Total	3,224,831	3,257,591

^aCDMC = current direct medical costs.

^bCIMC = current indirect medical costs.

^cPDMC = projected direct medical costs.

^dPIMC = projected indirect medical costs.

Table 2.6. Direct medical days incurred as a result of La Crosse encephalitis for 25 case patients by age and sequelae class.

Variable	Age or Sequelae Class ^a	Number of case patients	Mean (±SD)	Median	Total	Range	Age or Sequelae Class	Number of case patients	Mean (±SD)	Median	Total Costs	Range	Age or Sequelae Class	Number of case patients	Mean (±SD)	Median	Total	Range	Age or Sequelae Class	Number of case patients	Mean (±SD)	Median	Total Costs	Range
Nights hospitalized	<6	9	12.0 (14.3)	7.0	108.0	6.0-50.0	6-10	7	11.29 (13.0)	7.0	79.0	4.0-40.0	11-17	6	8.0 (4.8)	8.0	59.0	6.0-19.0	>17	2	7.5 (3.5)	7.5	15.0	5.0-10.0
	NS	3	8.3 (1.5)	8.0	25.0	7.0-10.0	IS	16	10.0 (8.71)	7.0	159.0	4.0-40.0	LS	5	15.4 (19.6)	8.0	77.0	4.0-50.0	T	24	10.9 (11.1)	7.0	261.0	4.0-50.0
Nights in ICU	<6	9	2.9 (2.8)	2.0	25.0	0-8.0	6-10	7	1.3 (1.0)	2.0	9.0	0-2.0	11-17	6	2.3 (0.8)	2.5	14.0	1.0-3.0	>17	2	0.5 (0.7)	0.5	1.0	0-1.0
	NS	3	2.0 (3.5)	0	6.0	0-6.0	IS	16	1.9 (1.2)	2.0	30.0	0-4.0	LS	5	2.6 (3.1)	2.0	13.0	0.0-8.0	T	24	2.0 (1.9)	2.0	49.0	0-8.0
Nights in private room	<6	9	9.2 (12.4)	6.0	83.0	2.0-42.0	6-10	7	10 (12.5)	5.0	70.0	3.0-38.0	11-17	6	7.5 (5.4)	5.5	45.0	4.0-18.0	>17	2	7.0 (4.2)	7.0(4.2)	14.0	4.0-10.0
	NS	3	6.3 (4.0)	7.0	19.0	2.0-10.0	IS	16	8.1 (8.7)	5.5	129.0	3.0-38.0	LS	5	12.5 (16.5)	6.0	64.0	3.0-42.0	T	24	8.8 (10.1)	6.0	212.0	2.0-42.0
Days in coma	<6	8	2.8 (2.5)	2.5	22.0	0-7.0	6-10	6	3.2 (2.8)	3.0	19.0	0-8.0	11-17	7	2.7 (2.1)	3.0	7.0	0-6.0	>17	2	2.5 (2.1)	2.5	5.0	1.0-4.0
	NS	4	1.5 (1.7)	1.0	6.0	0-4.0	IS	15	3.4 (2.4)	3.0	51.0	0-8.0	LS	4	2.0 (1.8)	2.0	8.0	0-4.0	T	23	2.8 (2.3)	3.0	65.0	0-8.0
Number of Office visits ^b	<6	9	10.1 (16.8)	6.0	91.0	1.0-54.0	6-10	7	9.3 (11.6)	6.0	65.0	2.0-35.0	11-17	7	4.6 (4.8)	2.0	7.0	1.0-14.0	>17	2	8.5 (9.2)	8.5	17.0	2.0-15.0
	NS	4	1.5 (0.6)	1.5	6.0	1.0-2.0	IS	16	5.4 (4.4)	3.5	86.0	1.0-15.0	LS	5	22.6 (21.1)	8.0	113.0	8.0-54.0	T	25	8.2 (11.9)	4.0	205.0	1.0-54.0
Weeks of medication ^c	<6	9	26.1 (37.8)	6.0	235.0	1.0-54.0	6-10	6	113.0 (200.0)	30.0	678.0	2.0-514.0	11-17	7	10.6 (9.8)	5.0	53.0	1.0-26.0	>17	2	0	0	0	0
	NS	2	7.0 (7.1)	7.0	14.0	2.0-12.0	IS	14	11.1 (13.7)	6.0	156.0	1.0-52.0	LS	4	199.0 (210.1)	98.0	796.0	86.0-514.0	T	20	48.3 (114.4)	7	966.0	1.0-514.0
Weeks of occupational therapy	<6	9	18.7 (37.7)	0	168.0	0-98.0	6-10	7	0.0	0	0	0	11-17	7	0.9 (2.3)	0	6.0	0-6.0	>17	2	1.0 (1.4)	1.0	2.0	0-2.0
	NS	3	0.0	0	0	0	IS	16	0.4 (1.5)	0	6.0	0-6.0	LS	5	33.6 (47.1)	0	168.0	0-98.0	T	24	7.3 (24.0)	0	174.0	0-98.0
Weeks of physical therapy	<6	9	18.8 (37.6)	0	169.0	0-98.0	6-10	7	0.9 (2.3)	0	6.0	0-6.0	11-17	7	3.4 (9.1)	0	24.0	0-24.0	>17	2	2.0 (2.8)	2.0	4.0	0-4.0
	NS	3	0	0	0	0	IS	16	1.9 (6.1)	0	31.0	0-24.0	LS	5	33.6 (47.1)	0	168.0	0-98.0	T	24	8.3 (24.2)	0	199.0	0-98.0
Weeks of speech therapy	<6	8	0	0	0	0	6-10	7	1.4 (2.5)	0	10.0	0-6.0	11-17	7	0.9 (2.3)	0	6.0	0-6.0	>17	2	0.5 (0.7)	0.5	1.0	0-1.0
	NS	3	0	0	0	0	IS	15	1.1 (2.3)	0	16.0	0-6.0	LS	5	0	0	0	0	T	23	0.7 (1.9)	0	16.0	0-6.0

^a< 6 = all participants under the age of 6 years, 6 - 10 = all participants between the ages of 6 and 10 years, 11 – 17 = all patients between the age of 11 and 17 years, > 17 = all patients greater than 17 years of age; NS = all participants in the “No Sequelae” class, IS = all participants in the “Intermediate Sequelae” class, LS = all participants in the “Lifetime Sequelae” class, T = total for all case patients.

^bLS class > NS class (df = 1; t_w = 10.0; P = 0.0079) and LS class > IS class (df = 1; t_w = 84.5; P = 0.0058).

^cLS class > IS class (df = 1; t_w = 66.0; P < 0.001).

Table 2.7. Procedures and services reported for La Crosse encephalitis case patients.

Service or Intervention	n	No. (%)
Air lifted to hospital	25	5 (25.0)
Breathing Tube	24	7 (29.2)
Feeding Tube	24	5 (20.8)
Seizure medication	24	19 (79.2)
Therapy (any type)	25	13 (52.0)
Speech Therapy	25	7 (28.0)
Occupational Therapy	25	4 (16.0)
Physical Therapy	25	5 (20.0)
Home Nurse	25	4 (20.0)
Rehospitalization ^a	25	2 (8.0)

^aRehospitalization was required for the two youngest participants in the study.

Table 2.8. Indirect medical days lost due to La Crosse encephalitis by 25 case patients by age and sequelae class.

Variable	Age of Patients or Sequelae Class ^a	Number of case patients	Mean (±SD)	Median	Total	Range	Age or Sequelae Class	Number of case patients	Mean (±SD)	Median	Total	Range	Age of Patients or Sequelae Class	Number of case patients	Mean (±SD)	Median	Total	Range	Age of Patients or Sequelae Class	Number of case patients	Mean (±SD)	Median	Total	Range	
Mother Lost Work Days	<6	8	26.5 (24.3)	15.0	212.0	10.0-74.0	6-10	6	73.7 (143.1)	18.0	442.0	4.0-365.0	11-17	6	27.7 (22.4)	20.0	166.0	8.0-61.0	>17	0	0	0	0	0	0
	NS	3	17.3 (11.0)	12.0	52.0	10.0-30.0	IS	12	52.8 (100.3)	16.5	633.0	4.0-365.0	Ls	5	27.0 (27.3)	18.0	135.0	7.0-74.0	T	20	41.0 (78.9)	15.0	820.0	4.0-365.0	
Father Lost Work Days	<6	7	6.4 (4.4)	5.0	45.0	1.0-14.0	6-10	4	3.8 (4.8)	2.5	15.0	0.0-10.0	11-17	5	11.4 (11.0)	10.0	57.0	2.0-30.0	>17	0	0	0	0	0	0
	NS	2	5.5 (6.4)	5.5	11.0	1.0-10.0	IS	13	7.1 (7.7)	5.0	92.0	0.0-30.0	Ls	1	14.0	-	14.0	-	T	16	7.3 (7.3)	5.0	117.0	0.0-30.0	
Grand Total family Lost Work Days	<6	9	37.9 (44.7)	18.0	340.0	7.0-138.0	6-10	7	66.7 (136.3)	15.0	467.0	4.0-375.0	11-17	7	31.9 (27.0)	20.0	223.0	5.0-77.0	>17	1	120.0	-	120.0	-	-
	NS	3	21.0 (8.5)	20.0	63.0	13.0-30.0	IS	16	58.6 (93.8)	20.0	938.0	4.0-375.0	Ls	5	29.8 (33.4)	18.0	149.0	7.0-88.0	T	24	47.9 (78.6)	20.0	1150.0	4.0-375.0	
Patient Lost School Days	<6	7	17.4 (18.3)	15.0	122.0	0.0-51.0	6-10	7	42.0 (46.3)	30.0	294.0	0.0-125.0	11-17	6	31.9 (34.6)	20.0	191.3	1.0-90.0	>17	0	0	0	0	0	0
	NS	2	7.5 (10.6)	7.5	15.0	0.0-15.0	IS	15	33.3 (33.8)	20.0	499.3	0.0-90.0	Ls	3	57.3 (64.7)	36	172.0	6.0-130.0	T	20	34.3 (38.0)	19.5	686.3	0.0-130.0	

^a < 6 = all participants under the age of 6 years, 6 – 10 = all participants between the ages of 6 and 10 years, 11 – 17 = all patients between the age of 11 and 17 years, > 17 = all patients greater than 17 years of age; NS = all participants in the “No Sequelae” class, IS = all participants in the “Intermediate Sequelae” class, LS = all participants in the “Lifetime Sequelae” class, T = total for all case patients.

Table 2.9. Indirect medical costs in 2001 dollars due to La Crosse encephalitis incurred by 25 case patients.

Variable	Age or Sequelae Class ^a	Number of case patients	Mean (±SD)	Median	Total	Range	Age or Sequelae Class	Number of case patients	Mean (±SD)	Median	Total	Range	Age or Sequelae Class	Number of case patients	Mean (±SD)	Median	Total	Range	Age or Sequelae Class	Number of case patients	Mean (±SD)	Median	Total	Range
Total mileage ^b	<6	9	1,509 (1,719)	942	13,576	190-5,725	6-10	7	1,880 (2,034)	840	13,155	260-5,080	11-17	7	2,224 (3,402)	700	15,566	68-9,670	>17	2	306 (235)	306	612	140-472
	NS	4	262 (173)	253	1,045	68-472	IS	16	1,836 (2,429)	921	29,374	140-9,670	LS	5	2,498 (2,450)	1,220	12,490	260-5,725	T	25	1,717 (2,276)	840	42,909	68-670
Total mileage costs	<6	9	521 (593)	325	4,684	66-1,976	6-10	7	649 (702)	290	4,539	90-1,753	11-17	7	768 (1,174)	242	5,371	24-3,337	>17	2	106 (81)	106	212	49-163
	NS	4	91 (60)	88	361	24-163	IS	16	634 (838)	318 (838)	10,135	493,337	LS	5	862 (846)	421	4,310	90-1,976	T	25	593 (786)	290	14,804	24-3,337
Mother - lost wages	<6	9	2,103 (2,645)	883	18,924	0-8,142	6-10	7	3,028 (6,200)	447	21,191	0-16,935	11-17	7	1,762 (2,520)	870	12,334	0-7,004	>17	0	0	0	0	0
	NS	3	1,460 (1,273)	790	4,380	663-2,927	IS	15	2,508 (4,457)	897	37,609	0-16,935	LS	5	2,092 (3,408)	723	10,460	0-8,142	T	23	2,281 (3,876)	790	52,447	0-16,935
Father - lost wages	<6	7	915 (765)	884	6,403	0-2,332	6-10	5	1,849 (2,837)	751	9,245	0-6,760	11-17	5	5,783 (9,402)	1,740	28,911	286-22,500	>17	0	0	0	0	0
	NS	2	442 (625)	442	884	0-884	IS	13	2,661 (6,024)	993	34,583	0-22,500	LS	2	4,546 (3,132)	4,546	9,092	2,332-6,760	T	17	2,622 (5,377)	993	44,558	0-22,500
Total family - lost wages	<6	9	3,688 (4,490)	1,547	33,184	790-12,535	6-10	7	4,348 (6,717)	946	30,435	221-18,670	11-17	7	5,893 (7,547)	2,927	41,245	1,428-22,500	>17	2	10,436 (14,758)	0	20,871	0-20,871
	NS	4	1,316 (1,246)	1,169	5,264	0-2,927	IS	16	6,308 (7,752)	2,307	100,919	221-22,500	LS	5	3,911 (4,500)	1,149	19,551	447-10,474	T	25	5,030 (6,692)	2,131	125,733	0-22,500
Total indirect medical costs	<6	9	6,641 (11,097)	1,664	59,763	899-34,344	6-10	7	4,997 (7,345)	1,436	34,973	315-20,422	11-17	7	6,660 (7,622)	2,951	46,615	1,670-22,621	>17	2	10,541 (14,677)	10,541	21,082	163-20,919
	NS	4	1,406 (1,188)	1,256	5,624	163-2,951	IS	16	6,941 (7,923)	2,810	111,053	315-22,621	LS	5	9,151 (14,437)	1,569	45,755	537-34,344	T	25	6,498 (8,948)	2,304	162,432	163-34,344

^a < 6 = all participants under the age of 6 years, 6 – 10 = all participants between the ages of 6 and 10 years, 11 – 17 = all patients between the age of 11 and 17 years, > 17 = all patients greater than 17 years of age; NS = all participants in the “No Sequelae” class, IS = all participants in the “Intermediate Sequelae” class, LS = all participants in the “Lifetime Sequelae” class, T = total for all case patients. ^b LS class > IS class (df = 1, $t_w = 84.0$; $P = 0.0073$). ^c LS class > NS class (df = 1; $t_w = 10.0$; $P = 0.0079$). ^d IS class > NS class (df = 1; $t_w = 14.0$; $P = 0.0019$).

Table 2.10. Total costs in 2001 dollars due to La Crosse encephalitis by age and sequelae class.

Variable	Age or Sequelae Class ^a	Number of case patients	Mean (±SD)	Median	Total	Range	Age or Sequelae Class	Number of case patients	Mean (±SD)	Median	Total	Range	Age or Sequelae Class	Number of case patients	Mean (±SD)	Median	Total	Range	Age or Sequelae Class	Number of case patients	Mean (±SD)	Median	Total	Range
Total	<6	9	30,870	18,479	277,824	6,216-	6-	7	24,020	15,762	168,140	7,766-	11-	6	25,013	23,904	150,074	15,228-	>17	2	17,918	17,918	35,835	16,400-
Direct			(42,291)		141,242		10	(18,959)			60,768		17	(7,563)			34,055				(2,147)			19,435
Medical Costs	NS	3	16,462	16,400	49,384	13,300-	IS	16	21,176	18,696	338,809	6,216-	LS	5	48,736	36,891	243,679	13,350-	T	24	26,328	18,696	631,872	6,216-
			(3,194)		19,685			(13,137)			60,768			(53,135)			141,242				(27,291)			141,242
Total	<6	9	6,641	1,664	59,763	899-	6-	7	4,997	1,436	34,974	315-	11-	7	6,660	2,951	46,615	1,700-	>17	2	10,541	10,541	21,082	163-
Indirect			(11,097)		34,344		10	(7,345)			20,422		17	(7,622)			22,621				(14,677)			20,919
Medical Costs	NS	4	1,406	1,256	5,624	163-	IS	16	6,941	2,810	111,053	315-	LS	5	9,151	1,569	45,755	537-	T	25	6,498	2,304	162,432	163-
			(1,188)		2,951			(7,923)			22,621			(14,437)			34,344				(8,948)			34,344
Total	<6	9	37,510	21,298	337,587	7,521-	6-	7	29,0167	18,722	203,113	8,080-	11-	6	32,290	30,616	193,738	17,531-	>17	2	28,459	28,459	56,917	16,563-
Medical Costs	NS	3	17,353	16,563	52,058	14,198-	IS	16	28,117	22,012	449,862	7,521-	LS	5	57,887	38,460	289,434	14,016-	T	24	32,974	21,349	794,303	7,521-
			(3,616)		21,298			(19,034)			81,190			(67,397)			175,586				(34,793)			175,586

^a < 6 = all participants under the age of 6 years, 6 – 10 = all participants between the ages of 6 and 10 years, 11 – 17 = all patients between the age of 11 and 17 years, > 17 = all patients greater than 17 years of age; NS = all participants in the “No Sequelae” class, IS = all participants in the “Intermediate Sequelae” class, LS = all participants in the “Lifetime Sequelae” class, T = total for all case patients.

Table 2.11. Lifetime Disability Adjusted Life Year (DALY) estimates for study participants experiencing lifetime sequelae from La Crosse encephalitis from date of onset of illness.

Case Number	US Life Years remaining	USDALY [0,0,0]	% Disability	USDALY [0.03,1,0.04]	% Disability	S life Years remaining	SDALY [0,0,0]	% Disability	SDALY [0.03,1,0.04]	% Disability
002 ^a	69.07	27.64	40.02	14.32	20.74	73.87	29.56	40.02	14.45	19.56
013 ^a	73.90	29.58	40.03	12.90	17.46	79.75	31.92	40.03	13.03	16.34
014 ^a	68.70	27.51	40.05	14.65	21.33	73.10	29.27	40.052	14.76	20.20
015 ^a	70.32	28.14	40.02	14.69	20.89	72.72	29.10	40.02	14.75	20.30
025	74.10	68.17	92.00	30.61	41.31	78.66	72.37	92.00	30.85	39.21
Totals (n = 5)	356.09	181.05	50.84	87.17	24.48	378.10	192.22	50.84	87.84	23.23
Totals ^b (n = 4)	281.99	112.88	40.03	56.56	20.06	299.44	119.86	40.03	56.99	19.03

^aCases of LACE with similar projected lifetime sequelae

^bDoes not include case 025.

Table 2.12. Projected Disability Adjusted Life Years for four La Crosse encephalitis case patients experiencing similar lifetime sequelae.

Case Number	US-DALY [0,0,0]	US-DALY [0.03,1,0.04]	S-DALY [0,0,0]	S-DALY [0.03,1,0.04]
002	27.64	14.32	29.56	14.45
013	29.58	12.90	31.92	13.03
014	27.51	14.65	29.27	14.76
015	28.14	14.69	29.10	14.75
Total	112.88	56.56	119.86	56.99
Mean	28.22	14.14	29.96	14.25
Standard Deviation	0.95	0.84	1.32	0.82
Median	27.89	14.49	29.42	14.60
Range	27.51-29.58	12.90-14.69	29.10-31.92	13.03-14.76

Table 2.13. Participant identified stressors due to La Crosse encephalitis.

Stressor	During illness	After illness
	(n = 34) (% of total)	(n = 34) (% of total)
Lack of information ^a	26 (76)	19 (56)
Hospital restrictions on visitation	1 (3)	- ^b
Lack of social support from extended family	1 (3)	-
Logistical difficulties	1 (3)	2 (6)
Inability to help patient ^c	3 (9)	-
Lack of professionalism of medical staff	1 (3)	-
Lack of child improvement over time	1 (3)	-
Lack of community action/response to LACE	-	4 (12)
Lack of medical and mental health follow up	-	5 (15)
Watching patient struggle due to sequelae	-	3 (9)
Economic	-	1 (3%)
Total	34 (100)	34 (100)

^aIncludes lack of diagnosis, prognosis, and information on duration/severity of possible sequelae.

^bNo responses given for category of stressor.

^cInability to protect the patient from the illness and improve the patients condition.

Figure 2.1. Reported number of La Crosse encephalitis cases in North Carolina between 1989 and 2001 compared to the number of La Crosse encephalitis cases included in this analysis.

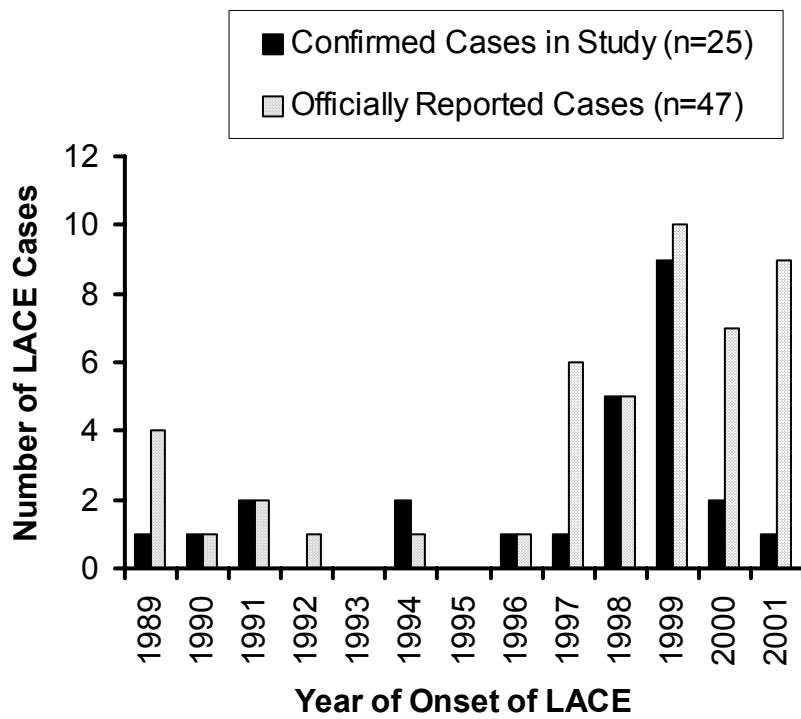


Figure 2.2. Age distribution of La Crosse encephalitis case patients included in study.

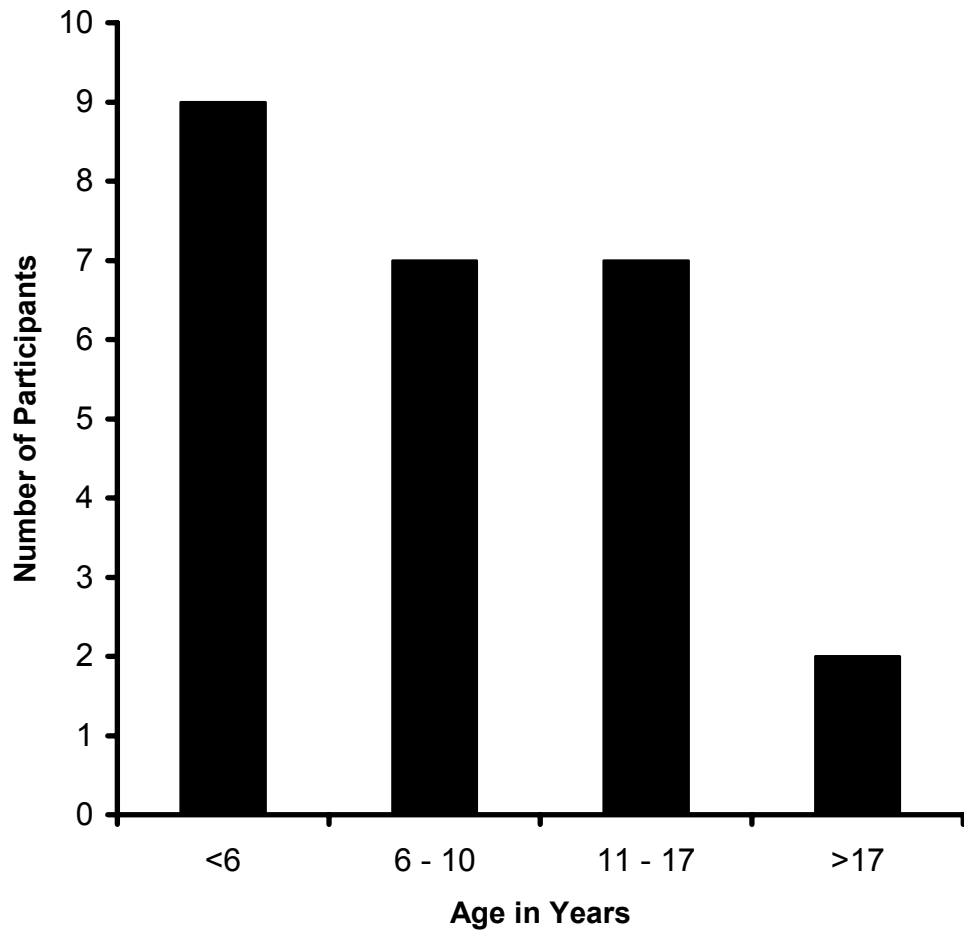


Figure 2.3. La Crosse encephalitis (LACE) cases (n = 25) included in study by month of onset.

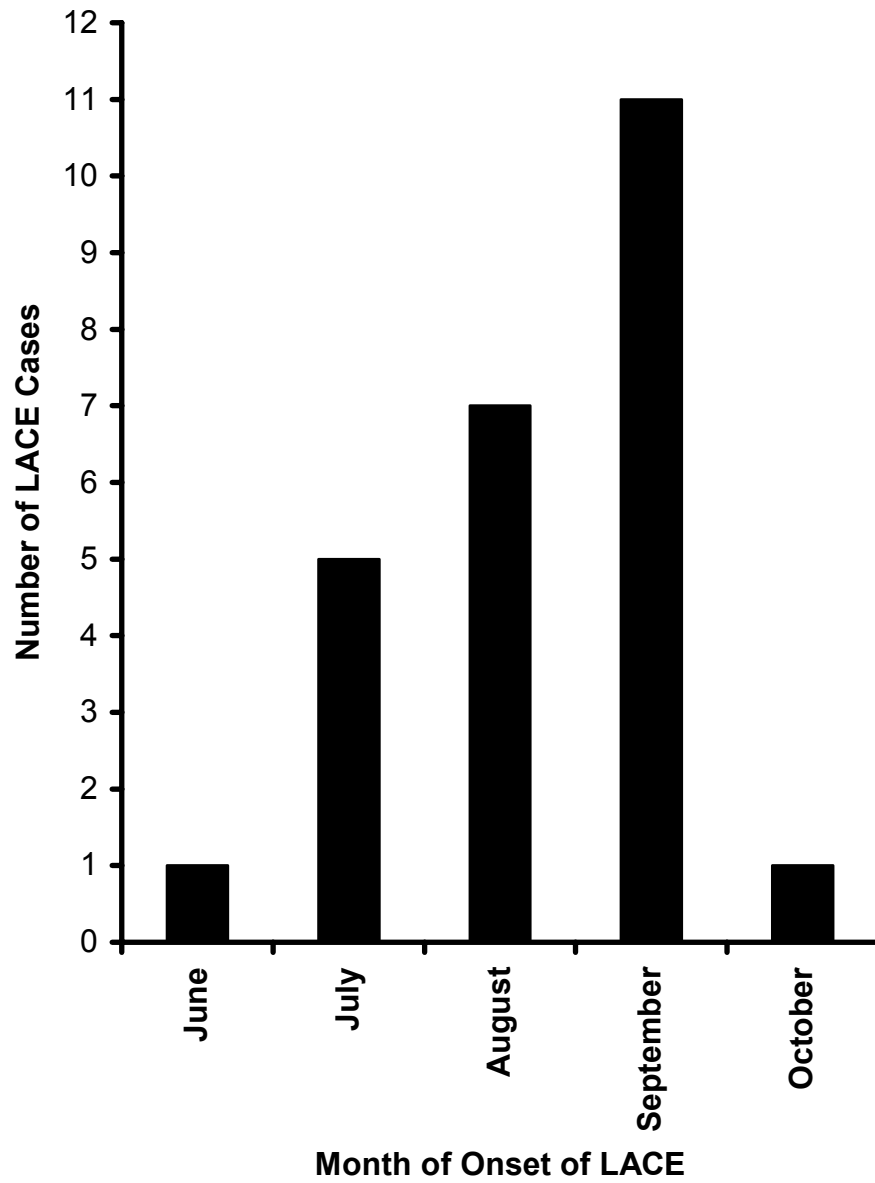


Figure 2.4. Annual reported income (2000) of 25 families of La Crosse encephalitis case patients.

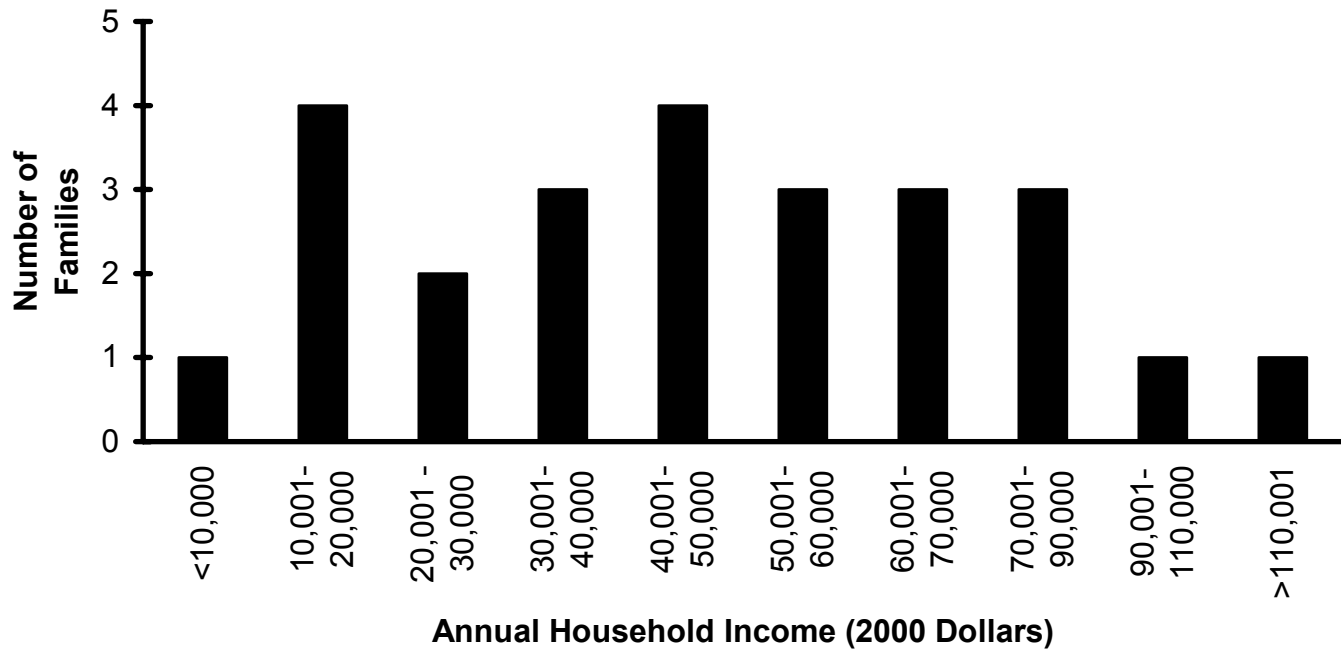


Figure 2.5. Parent/adult patient reported symptoms of La Crosse encephalitis before hospitalization for 25 case patients.

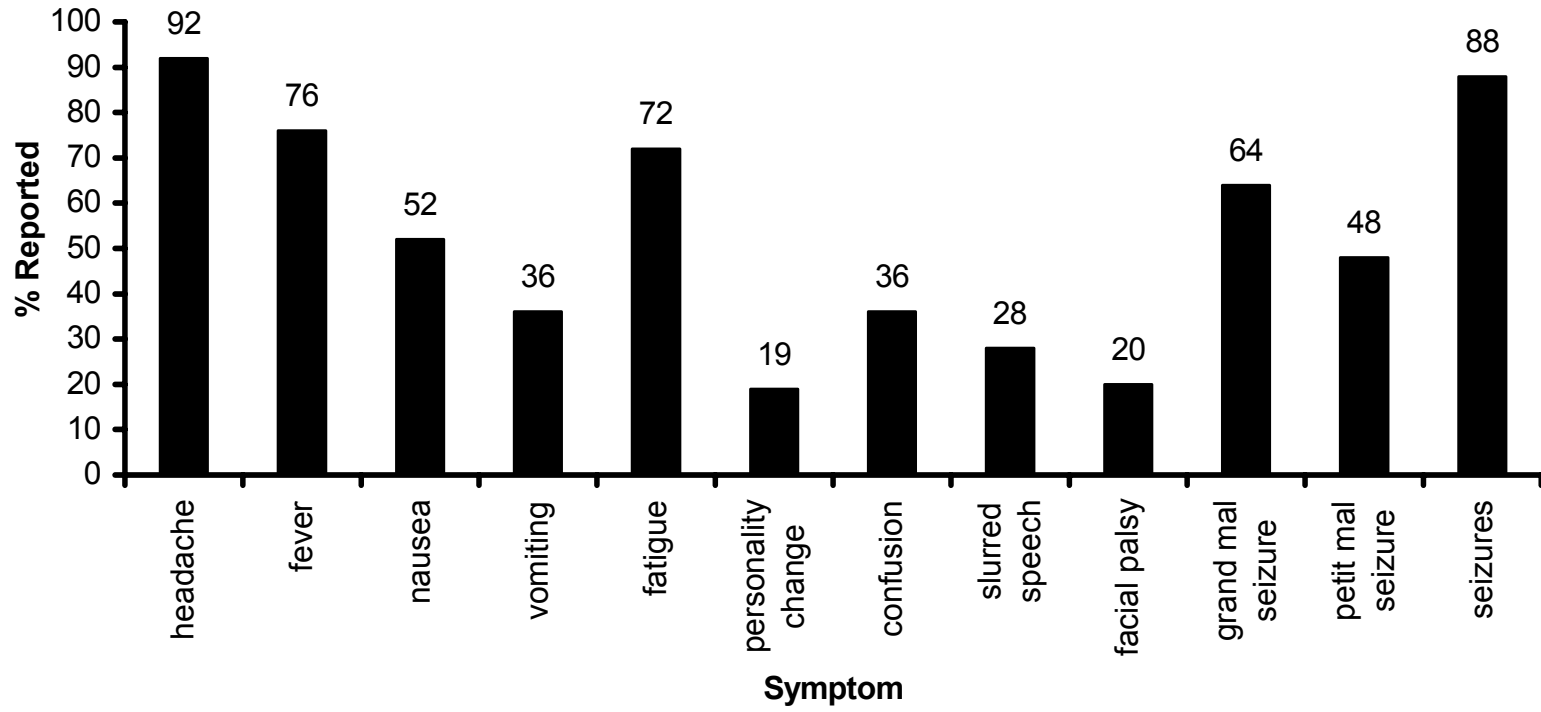


Figure 2.6. Parent/adult patient reported sequelae following release from hospital for 25 LACE case patients.

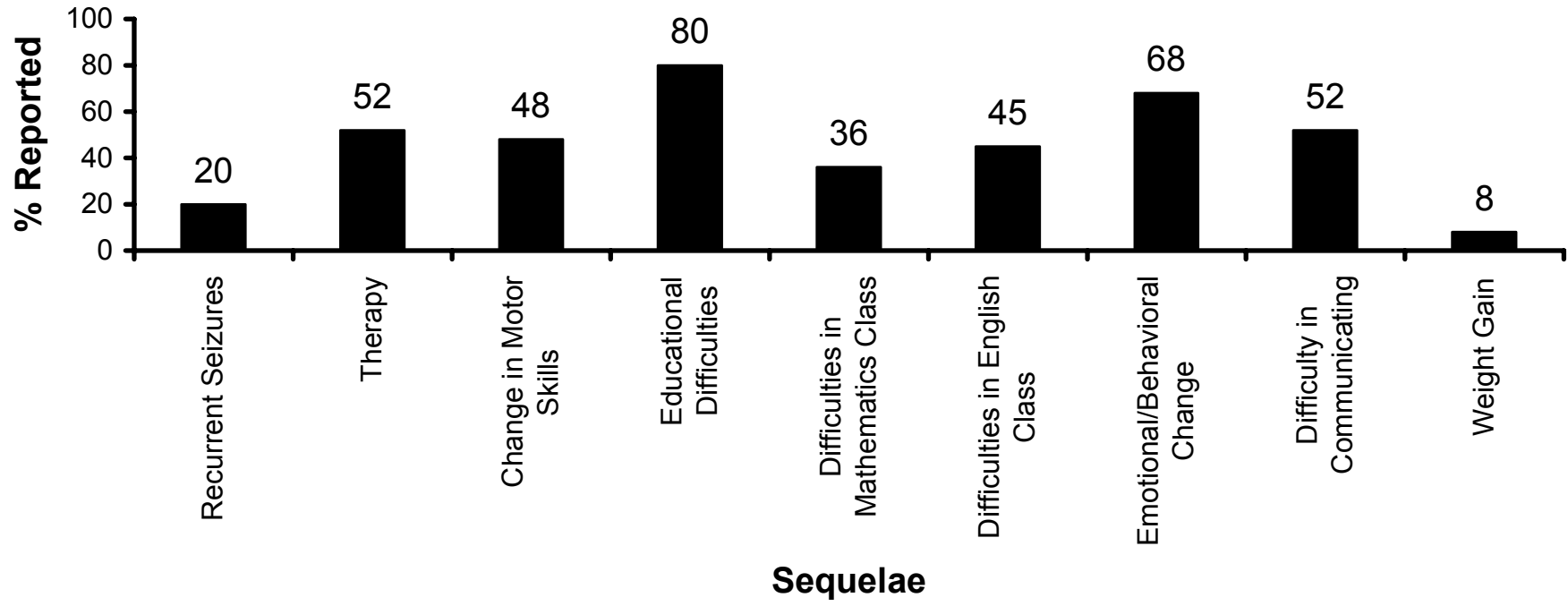


Figure 2.7. Age and La Crosse encephalitis sequelae class (NS = no sequelae, IS = intermediate sequelae, LS = lifetime sequelae) of study participants.

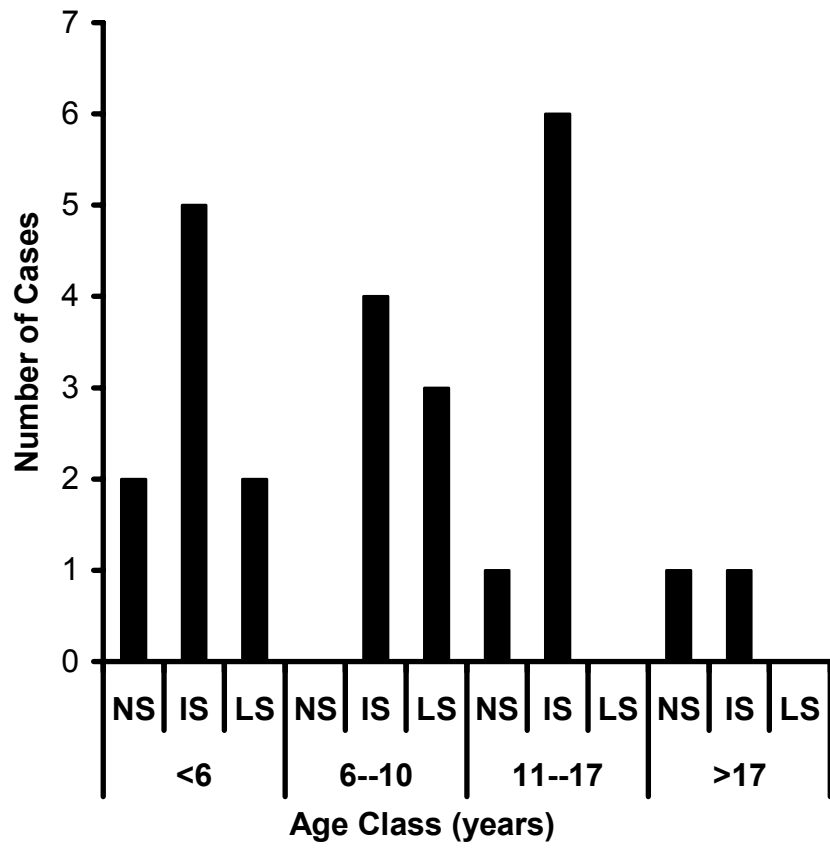


Figure 2.8. Mean direct medical costs by La Crosse encephalitis (LACE) sequelae class for 24 case patients (NS = no sequelae, IS = intermediate sequelae, LS = lifetime sequelae). Different letters represent significantly different values at $\alpha < 0.05$).

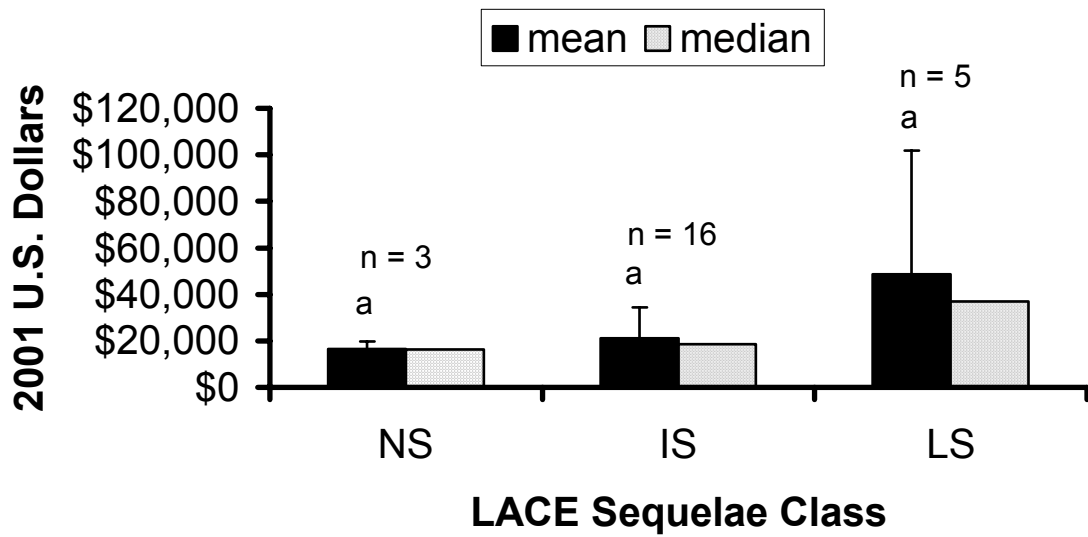


Figure 2.9. Mean percent time impaired for 25 La Crosse encephalitis case patients by sequelae class (NS = no sequelae, IS = Intermediate sequelae, LS = lifetime sequelae). Means for percent time impaired followed by a different letter are significantly different at $\alpha < 0.05$ by a Wilcoxon signed rank test.

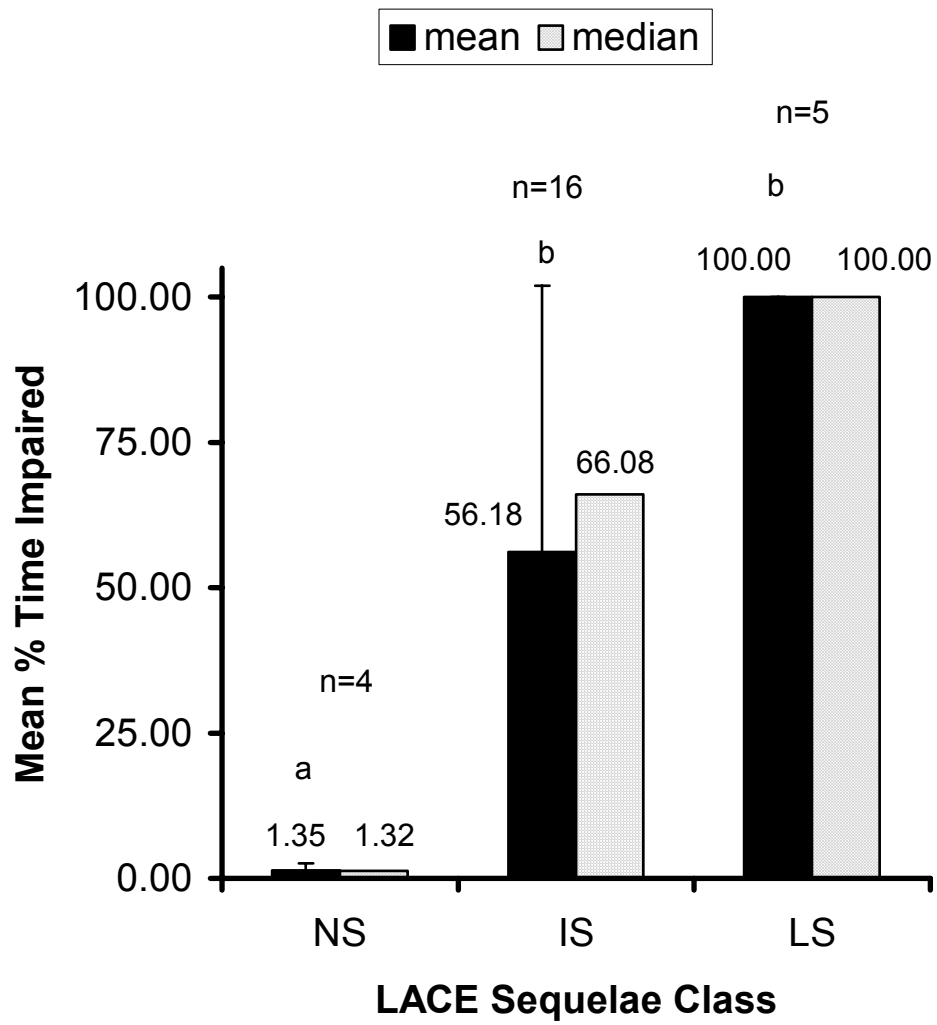


Figure 2.10. Mean percent burden calculated for two types of Disability Adjusted Life Years (DALYs) for 25 La Crosse encephalitis case patients assigned to sequelae classes (NS = no sequelae, IS = intermediate sequelae, LS = lifetime sequelae) for 100.59 Cumulative Life Years (CLY) of study. Mean percent burden followed by different letters are significantly different at $\alpha < 0.05$ by a Wilcoxon rank sum test.

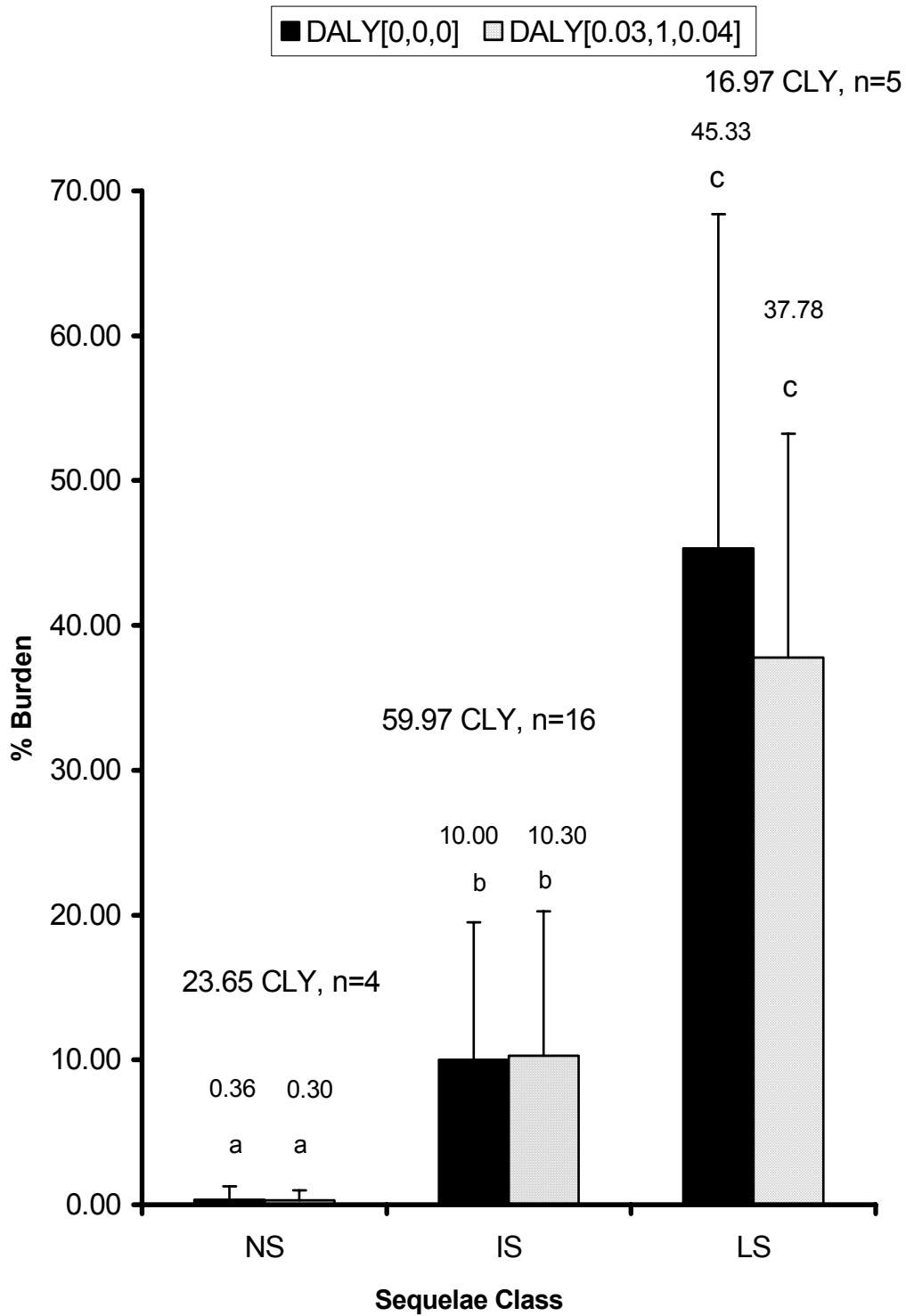


Figure 2.11. Projected Disability Adjusted Life Years (USDALY = United States DALY, SDALY = Standard DALY) for five La Crosse encephalitis case patients projected to have lifetime neurological sequelae.

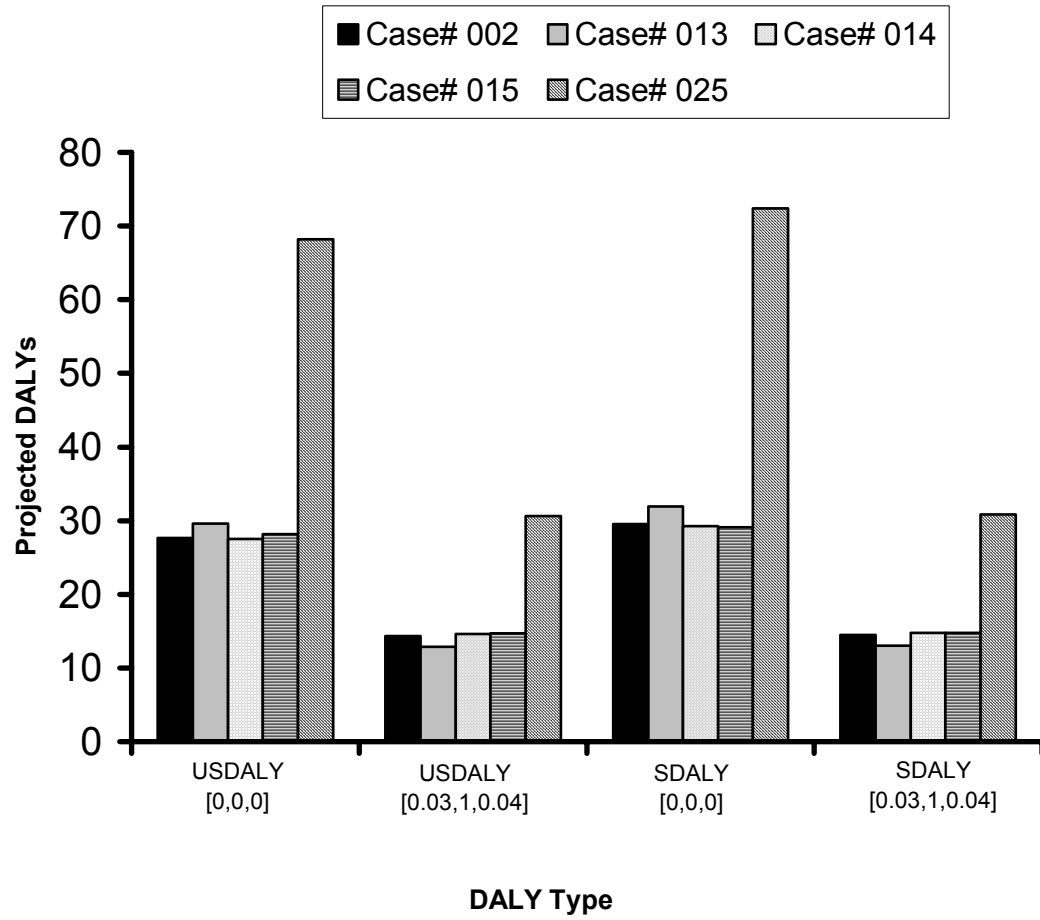


Figure 2.12. Scores for 24 La Crosse encephalitis (LACE) case patients on the Impact of La Crosse Encephalitis Scale (ILCES) by time elapsed from onset of illness.

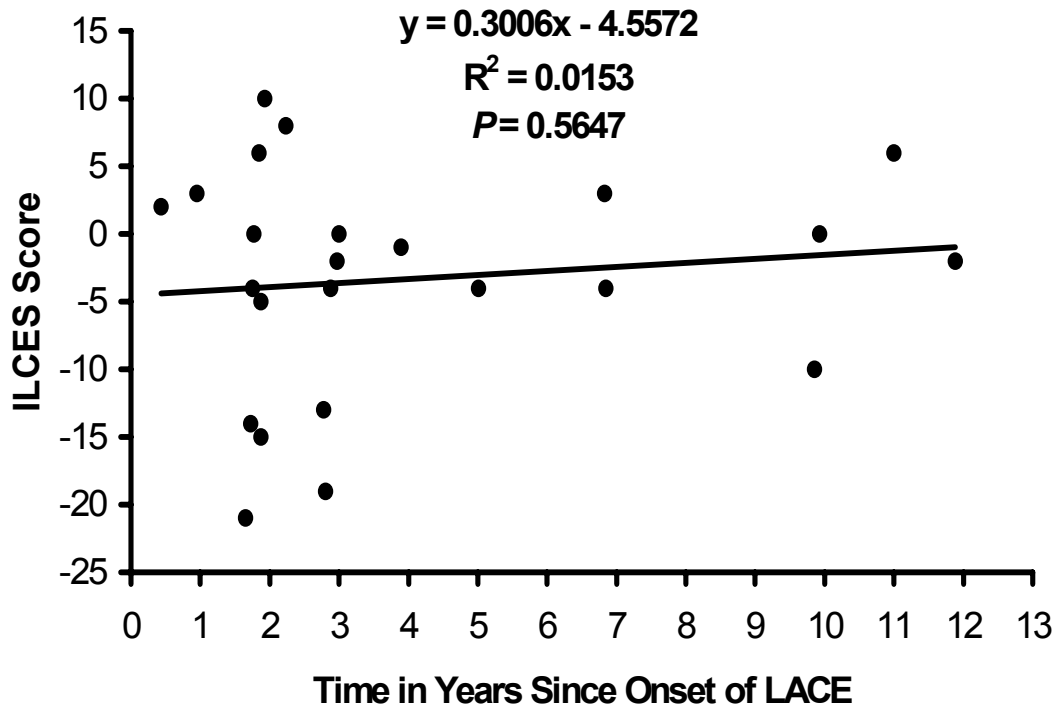


Figure 2.13. Total mean Impact of La Crosse Encephalitis Scale (ILCES) scores and overall percent burden resulting from La Crosse encephalitis for 24 case patients that were assigned to sequelae classes (NS = no sequelae, IS = intermediate sequelae, LS = lifetime sequelae). Total mean ILCES scores followed by different letters are significantly different at $\alpha < 0.05$ by a Wilcoxon rank sum test.

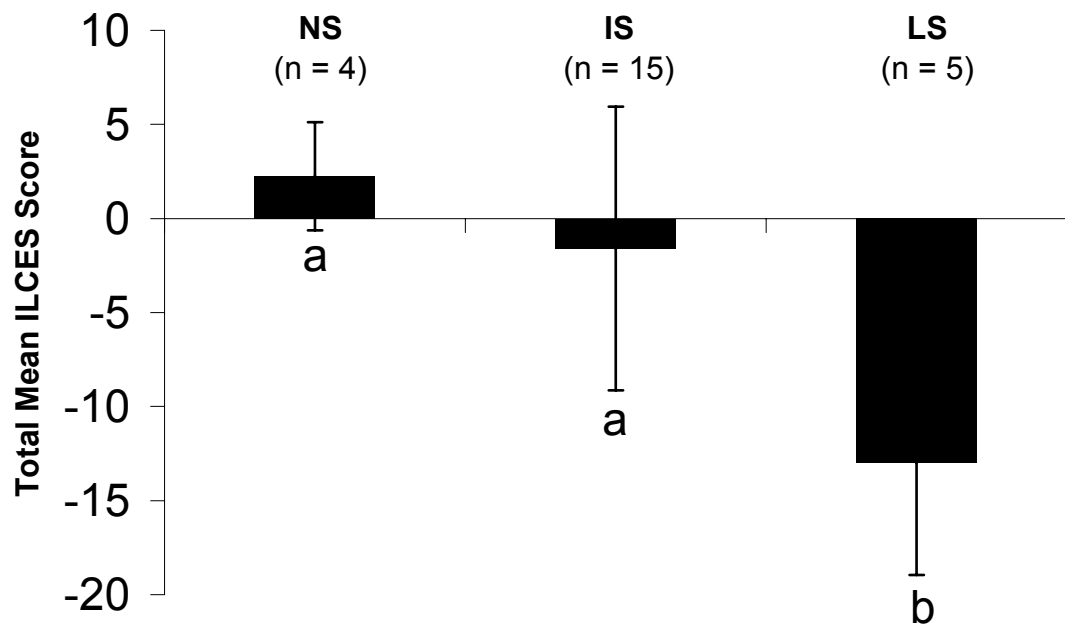


Figure 2.14. Mean scores for Impact of La Crosse Encephalitis Scale (ILCES) by quality of life category and La Crosse encephalitis sequelae class for 24 case patients (NS = no sequelae, IS = intermediate sequelae, LS = lifetime sequelae; * NS class sample size of n = 3; ** LS class sample size of n = 4). Mean ILCES scores for sequelae classes within each quality of life variable that are followed by different letters are significantly different at $\alpha < 0.05$) by a Wilcoxon rank sum test.

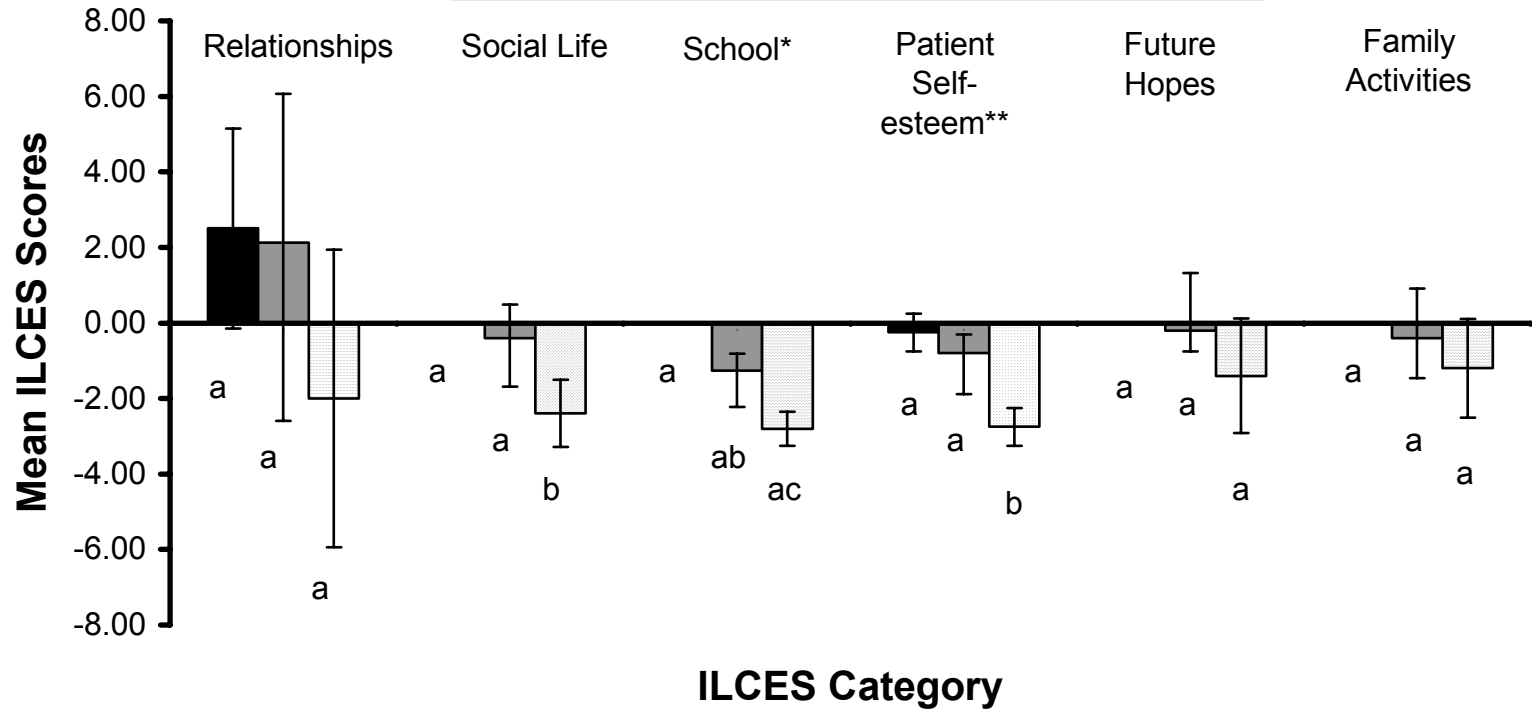
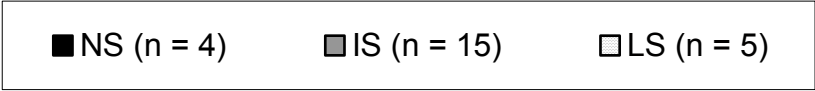
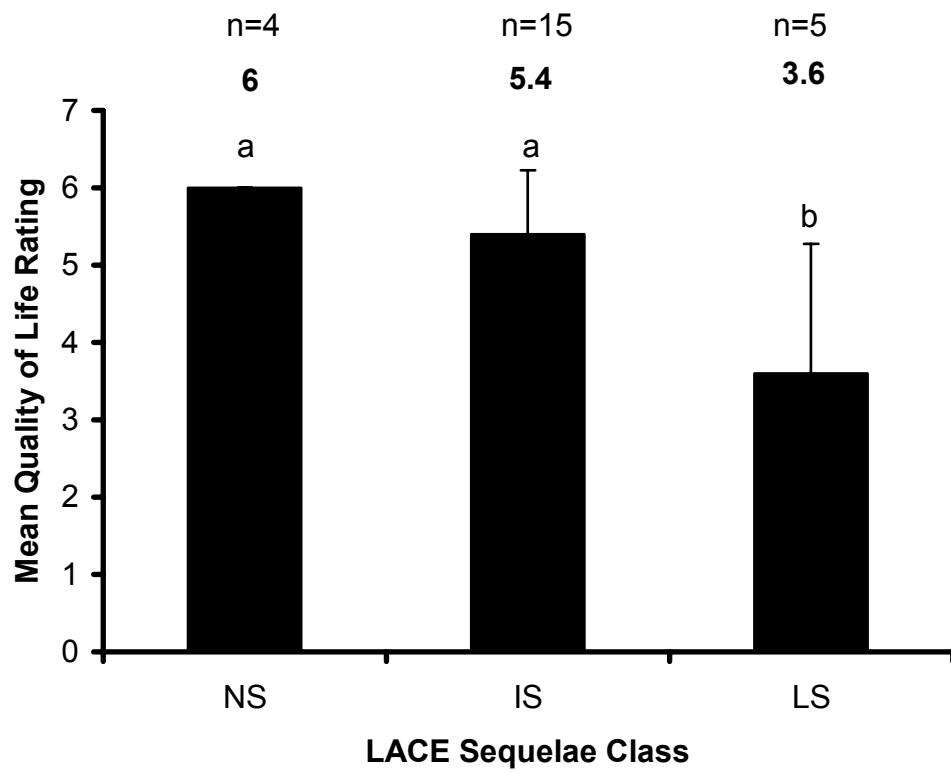


Figure 2.15. Mean quality of life ratings (QOL) for 24 La Crosse encephalitis (LACE) case patients assigned to sequelae classes (NS = no sequelae, IS = Intermediate sequelae, LS = lifetime sequelae). Mean QOL scores followed by the same letters are not significantly different at $\alpha < 0.05$ by a Wilcoxon rank sum test.



Appendix 1. Contact and confirmation of interviews

All LACE cases were identified from case cards and/or serology records supplied by the North Carolina Department of Health and Human Services (n = 63). All case patients contacted about the study experienced LACE between 1989 and 2001.

No. case patients	# Male (% of total)	Description of procedures
63	43 (68%)	Confirmed case patients were mailed an information packet containing a reply sheet and a return addressed/stamped envelope. Attempts were made to contact non-repliers by mailing them information packets, using the most current available addresses or they were contacted by telephone multiple times during the study period, using the most current available phone numbers available.
32	21 (62%)	Number of non-repliers.
31	22 (71%)	Number of completed reply forms returned (repliers).
2	2 (100%)	Number of repliers who did not wish to be interviewed. Reasons: Two subjects stated that they were not interested and did not have time for a face-to-face interview.
29	20 (69%)	Number of repliers agreeing to be interviewed
4	0 (0%)	Number of repliers who agreed to be interviewed but were not Reasons: 1 = Decided not to interview due to the emotional pain caused by the death of the patient of complications due to La Crosse encephalitis. 3 = Did not show up at prearranged interview site. ** Attempts were made to reschedule interviews with the participants who did not attend the prearranged interview, but were not successful.
25	20 (80%)	Number of repliers interviewed: 18 case patients from case cards; and 6 case patients from serology records. 1 from physician identification/retrospective reporting

Appendix 2: Disability Adjusted Life Years

In this paper, I report two different types of DALYs: SDALY and USDALY. For each type of DALY, I have made two calculations. One calculation uses the standard age weight function ($\beta=0.04$) and discount rate ($r=0.03$) and the other calculation does not use age weighting or a discount rate. DALY type explanations are as follows:

Standard DALYs (SDALYS) are calculated using standard life expectancy of 82.5 years for females and 80 years for males (Murray and Lopez 1994).^a

- SDALYS $[r,K,\beta]$: SDALYS $[0.03,1,0.04]$ and SDALYS $[0,0,0]$
- If $\beta =0$, then C and $K=0$

United StatesDALYs (USDALYS) are calculated using life expectancies from US life tables (Anderson and DeTurk 2002)^b.

- USDALYS $[r,K,\beta]$: USDALYS $[0.03,1,0.04]$ and USDALYS $[0,0,0]$
- *if $\beta =0$, then C and $K=0$

DALY Formula (Murray 1996)^c

$$D\{[KCe^{-ra}/(r+\beta)^2][e^{-(r+\beta)(L+a)}[-(r+\beta)(L+a)-1]-e^{-(r+\beta)a}[-(r+\beta)a-1]]+(1-K/r)(1-e^{-rL})\}$$

K =age weighting modulation factor (1 or 0)

D =disability weight (1 of 6 possible severities 0-1) 1=death

C =age weighting constant (0.16243 or 0)

r =discount rate (0.03 or 0)

β =parameter of age weight function (0.04 or 0)

L =duration of disability (in years)

a =age of onset (in years)

$e=2.72$ (approx) (Fox-Rushby and Hanson 2001)^d

- If discount rate ($r=0$) is set to 0 then;
DALYS $[0,K,\beta]=D\{(KC^{e^{-\beta e}}/\beta^2)[e^{-\beta L}(-\beta(L+a)-1)-(-\beta a-1)]+[(1-K)(L)]\}$
- If discount rate ($r=0$) equals zero and use uniform age weighting
DALYS $[0,0,0]=DL$

Disability class descriptions and weighting factors (D).^a

Class	Description	Weight (D)
1	Limited ability to perform at least one activity in one of the following areas: recreation, education, procreation or occupation.	0.096
2	Limited ability to perform most activities in one of the following areas: recreation, education, procreation or occupation.	0.220
3	Limited ability to perform activities in two or more of the following areas: recreation, education, procreation or occupation.	0.400
4	Limited ability to perform most activities in all of the following areas: recreation, education, procreation or occupation.	0.600
5	Needs assistance with instrumental activities of daily living such as meal preparation, shopping or housework.	0.810
6	Needs assistance with activities of daily living such as eating, personal hygiene or toilet use.	0.920

^a**Murray, C. J.L. and A. D. Lopez. 1994.** Global comparative assessments in health sector: Disease burden, expenditures, and intervention packages. Bull. W.H.O. Geneva, Switzerland. 196 p.

^b**Anderson, R. N. and P. B. DeTurk. 2002.** United States Life Tables, 1999. National Vital Statistics Reports, National Center for Health Statistics. 50:1 – 38.

^c**Murray, C.J.L. 1996.** Rethinking DALYs. Chapt. 1, pp. 1-98. *In: C.J.L. Murray and A.D. Lopez (eds.). The Global Burden of Disease: A Comprehensive Assessment of Mortality and Disability from Disease, Injuries, and Risk Factors in 1990 and Projected to 2020, (Global Burden of Disease and Injury series vol. I).* Harvard School of Public Health University Press. Boston, MA. 990 p.

^d**Fox-Rushby, J.A. and K. Hanson. 2001.** Calculating and presenting disability adjusted life years (DALYs) in cost effectiveness analysis. Health Policy Plan. 16:326 – 331.

Appendix 3: La Crosse Encephalitis Survey Questionnaire

La Crosse Encephalitis Survey

Interview Code Number:

Name of case patient/Race/Gender:

Date of Birth:

Street address:

Phone Number:

Email:

County of residence:

Date of interview:

Time of interview (begin/end):

Hospital where case patient was treated:

Attending physician:

Date of illness:

GPS reading:

Highest level of education completed by parent(s)/guardian(s):

Before the illness, had you heard about La Crosse encephalitis?

YES NO

Part 1. Background Information

- 1a. What are the ages and gender of members of your household? Please tell me how each relates to the patient (**record using Table 1**).
- b. What is the normal weekly activity of each person? I am interested in whether they work full time or part time, go to school or are a homemaker (**Table 1**).
- c. For those that work part or full time, about how many hours is that per week and what was their approximate hourly wage rate last year (**Table 1**)?
2. I am going to read a list of income categories. I am interested in recording your total household income including wages, tips and any interest you received last year (2000) before taxes. This information will be kept strictly confidential.
 - (1) 0-10,000
 - (2) 10,001-20,000
 - (3) 20,001-30,000
 - (4) 30,001-40,000
 - (5) 40,001-50,000
 - (6) 50,001-60,000
 - (7) 60,001-70,000
 - (8) 70,001-90,000
 - (9) 90,001-110,000
 - (10) 110,001 and above
- a. Now I would like you to think about the year before the patient in your family contracted LACE. Using this same scale, about what was your before tax income category in that year?
- b. What year was that?
- c. Now during the year of the illness, using the same income scale, what was your before tax income category?
- d. If higher, can you tell me why it was higher?
If lower, can you tell me why it was lower?
3. Provide a travel history 2 weeks prior to the illness and chronology of events leading up to and including the illness. (**Tape response**)
4. What, if any, are the residual effects of the illness that you have observed (list and describe using residual sheet)?
5. What residual effects have been diagnosed by a physician or other medical professional?

Part 2. Direct Medical Cost - What was the dollar cost of the following?

Primary Hospitalization expenses	Total \$ Cost
1. Cost of room per day: _____ Number of days hospitalized: _____ Dates of hospitalization: _____ Days in ICU: Days in Regular Room:	
2. Cost of inpatient drugs.	
3. Cost of medical procedures (please list them).	
6. Cost of transportation to and from the hospital. Method of transport (ambulance, private car, etc...): If private vehicle was used, what is the roundtrip mileage to and from the hospital? How many round trips were made during the case patient's illness?	
7. Emergency room cost:	
8. Total direct medical costs	

Rehospitalization expenses	Total \$ Costs
1. Cost of room per day: _____ 2. Total number of days rehospitalized: _____ 3. Dates of any rehospitalization: _____ 4. Number of times rehospitalized: _____	
5. Cost of transportation to and from hospital. Method of transport: _____ If private vehicle was used, what is the roundtrip mileage to and from the hospital? How many round trips were made during the case patient's rehospitalization?	
6. Cost of inpatient drugs.	
7. Cost of inpatient procedures.	
8. Total cost of rehospitalization	

Outpatient Expenses (including therapies)	Total \$ Costs
1. Average cost per visit: _____ Number of visits per year: _____	
2. Cost of transportation to and from hospital or medical office. Method of transport: _____ If private vehicle was used, what is the roundtrip mileage to and from the hospital or medical office? _____ How many round trips were made during the case patient's recovery?	
3. Cost of prescription or nonprescription drugs during the illness and recovery period.	
4. Cost of specialized medical equipment or home modifications. (List equipment or modifications)	
5. Cost of specialized childcare due to illness.	

Part 3. Indirect Medical Cost

Now I would like to discuss the other adjustments you or your household made during and after (patient's name) illness.

- 1a. During the hospitalization did any member have to take days off from work?
 - b. Who did this and how many workdays were missed?
 - c. Were these days paid leave or did you lose pay?
- 2a. In the first year after the hospitalization, can you tell me about how many days were required for different household members to help with responsibilities regarding the illness?

Were any of these lost workdays without pay or lost school days?

If yes, how many days were there?

- b. Do family members still have to miss school or work to help with responsibilities regarding the patient's illness?

If so, can you tell me the average number of days involved in care and whether there has been a need to miss work without pay or school days?

3. How many days of school did (patient's name) miss during hospitalization?
4. How many days of school did (patient's name) miss during the year following hospitalization due to the illness?
5. Does the patient still miss school due to illness related causes? If so explain the nature of these problems and how many days missed.
6. Were there requirements for any specialized daycare after the illness? If so, explain.
7. Please explain any specialized non-medical needs (special education, counseling for guardians, etc...).

**Part 4. Information needed to calculate Disability Adjusted Life Years
Primary Event**

1. Age at onset of La Crosse encephalitis: _____(a)¹

2. Severity of Disease

Mark one	Class	Description	Weight(D)
	Class 1	Limited ability to perform at least one activity in one of the following areas: recreation, education, procreation or occupation	0.096
	Class 2	Limited ability to perform most activities in one of the following areas: recreation, education, procreation or occupation	0.220
	Class 3	Limited ability to perform activities in two or more of the following areas: recreation, education, procreation or occupation	0.400
	Class 4	Limited ability to perform most activities in all of the following areas: recreation, education, procreation or occupation	0.600
	Class 5	Needs assistance with instrumental activities of daily living such as meal preparation, shopping or housework	0.810
	Class 6	Needs assistance with activities of daily living such as eating, personal hygiene or toilet use	0.920

3. Age at Death (if relevant) _____(a)²

4. Duration of disability or time lost due to premature death _____(L)

5. Life expectancy in geographical region _____(a)²

**Part 4. Information needed to calculate Disability Adjusted Life Years
Residual Effects**

1. Age at onset of La Crosse encephalitis: _____(a)¹

2. Severity of Disease

Mark one	Class	Description	Weight(D)
	Class 1	Limited ability to perform at least one activity in one of the following areas: recreation, education, procreation or occupation	0.096
	Class 2	Limited ability to perform most activities in one of the following areas: recreation, education, procreation or occupation	0.220
	Class 3	Limited ability to perform activities in two or more of the following areas: recreation, education, procreation or occupation	0.400
	Class 4	Limited ability to perform most activities in all of the following areas: recreation, education, procreation or occupation	0.600
	Class 5	Needs assistance with instrumental activities of daily living such as meal preparation, shopping or housework	0.810
	Class 6	Needs assistance with activities of daily living such as eating, personal hygiene or toilet use	0.920

3. Age at Death (if relevant) _____(a)²

4. Duration of disability or time lost due to premature death _____(L)

5. Life expectancy in geographical region _____(a)²

Section 5. Social Cost

Explain how having a child with La Crosse Encephalitis has affected your family. State the most frustrating aspect during the illness and after the illness. Give your thoughts on the quality of health care you received. Finally, make sure to add any information you feel people should know (include frustrating, emotional pain, stress, changes your family has endured due to the illness and any other feeling you wish to express **(Tape response)**)

Did you or any members of your family participate in a La Crosse Support group during and/or after the illness? **Yes** **No**

If yes, was a face to face support group or another type (describe)

If No, would your family have benefited from a La Crosse support group during/after the illness?

Yes

No

Did you have insurance that helped defray the medical costs of the disease? If so, what percent was paid by you and by the insurance?

Table 1. Background and household information on survey participants at time of illness.

RELATIONSHIP TO PATIENT	AGE	Gender	NORMAL WEEKLY ACTIVITY	WAGE RATE IF WORKING	USUAL WEEKLY HOURS WORKED	JOB LEAVE WITH PAY	TIME LOST TO WORK Paid / Unpaid

Appendix 4. Data obtained from interviews of families of 25 La Crosse encephalitis case patients from North Carolina between 1989 – 2001.

Appendix 4. Abbreviations

Abbreviations for variables used in multiple tables are defined in the table they first appear.

Background Information

c#	Case number
r	Race
g	Gender
age	Age at onset
p#	Parent number
ins	Family has medical insurance
% cov	Percent coverage of medical insurance
mchr	Medical

Direct Medical Days

dsv	Sequelae category
icu	Nights in intensive care unit
reg	Nights in a regular hospital room
trn	Total nights in a hospital room
dc	Days in coma
ov	Number of office visits
wm	Weeks on medication
atw	Weeks of alternative therapy
atm	Number of alternative therapy meetings
stw	Weeks of speech therapy
stm	Number of speech therapy meetings
otw	Weeks of occupational therapy
otm	Number of occupational therapy meetings
ptw	Weeks of physical therapy
ptm	Number of physical therapy meetings
nrh	Nights rehospitalized

Direct Medical Dollars

svw	Long-term DALY severity weight
gtc	Professional ground transportation costs
hc	Hospital costs
htc	Hospital and air lift costs
oc	Office costs
mc	Seizure medication costs
tc	Overall therapy costs
stc	Speech therapy costs
otc	Occupational therapy costs

ptp	Physical therapy costs
atc	Alternative therapy costs
edc	Educational costs
eqc	Equipment costs
rhc	Rehospitalization costs
rht	Rehospitalization professional transport costs
trhc	Total rehospitalization costs
tdmc	Total direct medical costs

Indirect Medical Days

flwdd	Father lost work days during hospitalization
flwda	Father lost work days after hospitalization
flwdt	Father lost work days total
mlwdd	Mother lost work days during hospitalization
mlwda	Mother lost work days after hospitalization
mlwdt	Mother lost work days total
olwdt	Other lost work days total
fflwd	Total family lost work days
plsdd	Patient lost school days during hospitalization
plsda	Patient lost school days after hospitalization
plsdt	Patient lost school days total
olsdt	Other lost school days total

Indirect Medical Dollars

mh	Miles accumulated during hospitalization
mo	Miles accumulated for office visits
mt	Miles accumulated for therapy visits
mtot	Total mileage accumulated
m\$	Total mileage costs
flw	Father lost wages
mlw	Mother lost wages
olw	Other lost wages
tlw	Total family lost wages
eqc	Equipment costs
timc	Total indirect medical costs

Total Dollar Cost

tdmc	Total direct medical cost
timc	Total indirect medical cost
gtmc	Grand total medical costs

Reported Symptoms

ha	Head ache
fv	Fever
ns	Nausea
vm	Vomiting
fg	Fatigue
bc	Change in behavior
cnf	Confusion
ssp	Slurred speech
fp	Facial palsy
sz	Seizure
gm	Grand mal seizure
pm	Petit mal seizure
dibh	Days ill before hospitalization
sh	Sent home after initial trip to doctor or emergency room
dibr	Days ill before rehospitalization

Reported Sequelae

rsz	Currently experiencing recurrent seizures
szm	Weeks of seizure medication
rw	Weeks of recovery
tpy	Required therapy of some type
cms	Change in motor skills
cep	Change in educational performance
edp	Experienced educational problems
dm	Difficulties in mathematics class
de	Difficulties in English class
ebc	Emotional or behavioral change
com	Difficulty with communication
wgt	Weight gain
trad	Total restricted activity days
tad	Total activity days possible
tot ryoti	Total restricted years due to LACE
tot yoti	Total years possible
%tr	Percent of time restricted due to LACE

Hospital and Recovery DALYs

US le	US life expectancy
US lyr	US life years remaining
S le	Standard life expectancy
S lyr	Standard life years remaining

Impact of La Crosse encephalitis Impact Scale (ILCES)

tot pos	Total possible on ILCES
% change	Percent change in family due to LACE based on ILCES score
ysill	Years since LACE onset
QOL	Quality of life rating (1-6)

ILCES category scores

-3	Great negative effect
-2	Some negative effect
-1	A little negative effect
0	No effect
1	A little positive effect
2	Some positive effect
3	Great positive effect
.	Does not apply

Yes No responses

hoi	Have heard of LACE before family member illness
psg	Participated in support group
wsg	Would have participated in support group
al	Air lifted
bt	Breathing tube
ft	Feeding tube
sm	Required seizure medication
tpy	Required therapy of some type
st	Required speech therapy
ot	Required occupational therapy
pt	Required physical therapy
hn	Required home nursing

Appendix 4.1. Background information

C#	r	g	Age	p#	ins	%cov	mdcr
001	C	M	15.39	1	y	100	y
002	C	M	6.13	1	n	.	n
003	C	M	56.01	.	y	80	n
004	C	M	11.72	2	y	80	n
005	C	M	76.97	.	y	100	n
006	C	M	3.03	2	y	80	n
007	C	M	5.09	2	y	80	n
008	C	M	2.34	1	y	100	y
009	C	M	5.66	2	y	60	n
010	C	M	9.45	2	y	80	n
011	H	M	5.67	2	y	80	n
012	I	M	11.85	1	y	100	y
013	I	M	0.25	1	y	100	y
014	I	F	9.40	1	y	100	y
015	I	F	9.78	1	y	100	y
016	I	M	13.45	2	y	100	y
017	I	M	8.17	2	y	80	n
018	I	M	10.92	2	y	100	y
019	C	M	15.13	2	n	.	n
020	C	F	4.89	2	y	95	n
021	B	F	7.63	2	y	80	n
022	C	M	12.19	2	y	100	y
023	C	M	2.80	1	y	100	y
024	C	F	11.01	2	y	85	n
025	C	M	1.35	1	y	90	n

Appendix 4.2. Direct medical days

c#	age	dsv	icu	reg	trn	dc	ov	wm	atw	atm	stw
001	15.39	is	2	4	6	3	2	14	4	20	6
002	6.13	ls	1	3	4	3	8	.	0	0	0
003	56.01	is	1	4	5	4	15	.	0	0	0
004	11.72	is	3	4	7	0	1	.	0	0	0
005	76.97	ns	0	10	10	1	2	.	0	0	.
006	3.03	ns	6	2	8	4	1	2	0	0	0
007	5.09	is	2	4	6	3	3	18	0	0	0
008	2.34	is	0	6	6	0	1	6	0	0	0
009	5.66	is	0	7	7	2	6	6	0	0	0
010	9.45	is	2	7	9	3	6	2	0	0	6
011	5.67	ns	0	7	7	1	1	12	0	0	0
012	11.85	ns	.	.	.	0	2	.	0	0	0
013	0.25	ls	2	6	8	.	8	98	98	.	0
014	9.40	ls	2	9	11	4	35	514	0	0	0
015	9.78	ls	0	4	4	1	8	98	0	0	0
016	13.45	is	2	5	7	3	2	1	0	0	0
017	8.17	is	2	5	7	8	4	4	0	0	4
018	10.92	is	0	4	4	0	2	52	0	0	0
019	15.13	is	1	18	19	4	8	26	0	0	0
020	4.89	is	4	3	7	5	10	1	0	0	0
021	7.63	is	2	38	40	.	2	8	6	12	0
022	12.19	is	3	8	11	6	3	6	3	21	0
023	2.80	is	3	6	9	7	7	6	0	0	.
024	11.01	is	3	6	9	3	14	6	0	0	0
025	1.35	ls	8	42	50	0	54	86	70	70	0

Appendix 4.2. Direct medical days continued

c#	stm	otw	otm	ptw	ptm	nrh
OO1	18	6	18	24	72	0
OO2	0	0	0	0	0	0
OO3	0	0	0	0	0	0
OO4	0	0	0	0	0	0
OO5	4	.	13	.	18	0
OO6	0	0	0	0	0	0
OO7	0	0	0	0	0	0
OO8	0	0	0	0	0	0
OO9	0	0	0	0	0	0
O10	6	0	0	6	1	0
O11	0	0	0	0	0	0
O12	0	0	0	0	0	0
O13	0	98	58	98	58	2
O14	0	0	0	0	0	0
O15	0	0	0	0	0	0
O16	0	0	0	0	0	0
O17	.	0	0	0	0	0
O18	0	0	0	0	0	0
O19	0	0	0	0	0	0
O20	0	0	0	0	0	0
O21	0	0	0	0	0	0
O22	0	0	0	0	0	0
O23	0	0	0	1	1	0
O24	0	0	0	0	0	0
O25	0	70	70	70	70	3

Appendix 4.3. Direct medical dollars

c#	age	dsv	svw	gtc	hc	htc	oc	mc	tc	stc
001	15.39	is	0.096	986.43	12,862.09	13,848.52	361.78	350	5,132.91	1,440.00
002	6.13	ls	0.096	0	12,317.47	12,317.47	1,162.00	.	0	0
003	56.01	is	0.4	536.75	17,771.23	18,307.98	1,126.86	.	0	0
004	11.72	is	0.096	548.05	14,365.02	14,913.07	314.86	.	0	0
005	76.97	ns	0	0	14,351.28	14,351.28	372.86	.	1,675.57	319.15
006	3.03	ns	0	590.25	18,729.81	19,320.06	314.86	50	0	0
007	5.09	is	0.4	0	12,176.49	12,176.49	496.02	450	0	0
008	2.34	is	0.096	0	5,750.32	5,750.32	314.86	150	0	0
009	5.66	is	0.22	583.00	8,615.25	9,198.25	630.50	150	0	0
010	9.45	is	0.096	594.23	13,792.71	14,386.94	604.86	50	720.00	480.00
011	5.67	ns	0	429.68	12,254.81	12,684.49	314.86	300	0	0
013	0.25	ls	0.4	986.43	17,955.61	18,942.04	1,243.05	2450	8,932.00	0
014	9.40	ls	0.4	1,141.15	18,690.73	19,831.88	4,776.22	12850	0	0
015	9.78	ls	0.4	1,082.07	8,391.08	9,473.15	1,425.87	2450	0	0
016	13.45	is	0.096	585.00	19,220.89	19,805.89	372.86	25	0	0
017	8.17	is	0.096	1,033.95	15,395.40	16,429.35	488.86	100	1,280.00	1,280.00
018	10.92	is	0.096	452.00	5,641.08	6,093.08	372.86	1300	0	0
019	15.13	is	0.096	1,640.42	27,819.33	29,459.75	720.86	650	0	0
020	4.89	is	0.4	0	17,616.18	17,616.18	836.86	25	0	0
021	7.63	is	0.4	6,080.40	52,618.46	58,698.86	1,868.54	200	0	0
022	12.19	is	0.4	1,082.07	19,169.27	20,251.34	2,959.26	150	0	0
023	2.80	is	0.096	562.90	14,964.39	15,527.29	662.86	150	2,572.38	2,412.80
024	11.01	is	0.4	929.18	30,832.65	31,761.83	1,068.86	150	0	0
025	1.35	ls	0.92	2,227.52	91,018.19	93,245.71	16,518.16	6755.56	13,311.00	0

Appendix 4.3. Direct medical dollars continued

c#	otc	ptp	atc	edc	eqc	rhc	rht	trhc	tdmc
001	720.00	2,880.00	92.91	0	310.00	0	0	0	20,003.21
002	0	0	0	0	0	0	0	0	13,479.47
003	0	0	0	0	0	0	0	0	19,434.84
004	0	0	0	0	0	0	0	0	15,227.93
005	598.42	758.00	0	0	0	0	0	0	16,399.71
006	0	0	0	0	0	0	0	0	19,684.92
007	0	0	0	0	0	0	0	0	13,122.51
008	0	0	0	0	0	0	0	0	6,215.18
009	0	0	0	0	0	0	0	0	9,978.75
010	0	240.00	0	0	0	0	0	0	15,761.80
011	0	0	0	0	0	0	0	0	13,299.35
013	0	0	0	0	0	4,733.52	590.00	5,323.52	36,890.61
014	0	0	0	1,260.00	0	0	0	0	38,718.10
015	0	0	0	0	0	0	0	0	13,349.02
016	0	0	0	750.00	0	0	0	0	20,953.75
017	0	0	0	0	0	0	0	0	18,298.21
018	0	0	0	0	0	0	0	0	7,765.94
019	0	0	0	3,223.80	0	0	0	0	34,054.41
020	0	0	0	0	0	0	0	0	18,478.04
021	0	0	0	0	0	0	0	0	60,767.40
022	0	0	0	3,492.45	0	0	0	0	26,853.05
023	0	159.58	0	0	0	0	0	0	18,912.53
024	0	0	0	0	0	0	0	0	32,980.69
025	0	0	0	0	6,920.00	4,491.20	0	4,491.20	141,241.63

Appendix 4.4. Indirect medical days

c#	age	dsv	flwdd	flwda	flwdt	mlwdd	mlwda	mlwdt	olwdt	tflwd	plsdd	plsda	plsdt	olsdt
OO1	15.39	is	.	.	.	8	53	61	.	61	8	46.25	54.25	0
OO2	6.13	ls	.	.	.	7	0	7	.	7	6	0	6	.
OO3	56.01	is	120	120
OO4	11.72	is	9	1	10	9	1	10	.	20	1	0	1	.
OO5	76.97	ns
OO6	3.03	ns	10	0	10	10	0	10	.	20	0	0	0	.
OO7	5.09	is	7	0	7	7	0	7	7	0
OO8	2.34	is	5	0	5	12	0	12	.	17	0	0	0	.
OO9	5.66	is	5	0	5	10	0	10	.	15	19	0	19	.
O10	9.45	is	0	0	0	10	20	30	.	30	10	10	20	0
O11	5.67	ns	1	0	1	8	4	12	.	13	2	13	15	0
O12	11.85	ns	.	.	.	14	16	30	.	30
O13	0.25	ls	.	.	.	0	18	18	.	18
O14	9.40	ls	.	.	.	6	20	26	.	26	5	125	130	.
O15	9.78	ls	.	.	.	6	4	10	.	10	6	30	36	.
O16	13.45	is	2	0	2	6	2	8	.	10	6	0	6	.
O17	8.17	is	5	0	5	.	.	.	10	15	12	78	90	.
O18	10.92	is	0	0	0	4	0	4	.	4	0	1	1	.
O19	15.13	is	10	0	10	10	0	10	.	20	3	87	90	.
O20	4.89	is	3	0	3	7	14	21	.	24	7	23	30	1.1
O21	7.63	is	10	0	10	0	365	365	.	375	40	50	90	90
O22	12.19	is	9	21	30	9	38	47	.	77	0	30	30	0
O23	2.80	is	.	.	.	15	40	55	83	138	11	40	51	.
O24	11.01	is	5	0	5	5	0	10	10	.
O25	1.35	ls	0	14	14	60	14	74	.	88	.	.	.	4

Appendix 4.5. Indirect medical dollars

c#	age	dsv	mh	mo	mt	mtot	m\$	flw	mlw
001	15.39	is	110	120	9,440	9,670	3,336.15	.	7,003.04
002	6.13	ls	100	160	0	260	89.70	.	446.46
003	56.01	is	20	120	0	140	48.30	.	.
004	11.72	is	496	4	0	500	172.50	1,260.92	869.60
005	76.97	ns	192	16	264	472	162.84	.	.
006	3.03	ns	155	35	0	190	65.55	884.00	663.00
007	5.09	is	314	628	0	942	324.99	1,338.40	0.00
008	2.34	is	800	100	0	900	310.50	382.68	612.29
009	5.66	is	360	180	0	540	186.30	992.70	882.40
010	9.45	is	300	360	180	840	289.80	0.00	2,669.51
011	5.67	ns	280	35	0	315	108.68	0.00	789.50
012	11.85	ns	60	8	0	68	23.46	.	2,926.80
013	0.25	ls	260	960	0	1,220	420.90	.	1,148.04
014	9.40	ls	300	4,200	0	4,500	1,552.50	6,760.00	0.00
015	9.78	ls	200	585	0	785	270.83	.	722.84
016	13.45	is	500	200	0	700	241.50	285.60	1,142.40
017	8.17	is	1100	280	40	1,420	489.90	750.03	195.66
018	10.92	is	120	150	0	270	93.15	0.00	220.88
019	15.13	is	1520	120	.	1,640	565.80	1,739.20	391.32
020	4.89	is	980	294	0	1,274	439.53	473.57	2,009.07
021	7.63	is	4800	280	0	5,080	1,752.60	1,734.14	16,935.00
022	12.19	is	360	330	1950	2,640	910.80	3,125.22	0.00
023	2.80	is	630	280	1560	2,470	852.15	.	4,677.20
024	11.01	is	292	56	0	348	120.06	22,500.00	0.00
025	1.35	ls	.	534	0	5,725	1,975.13	2,331.50	8,141.76

Appendix 4.5. Indirect medical dollars continued

c#	olw	tlw	eqc	time
001	.	7,003.04	0	10,339.19
002	.	446.46	0	536.16
003	20,870.40	20,870.40	0	20,918.70
004	.	2,130.52	0	2,303.02
005	0	0.00	0	162.84
006	.	1,547.00	0	1,612.55
007	.	1,338.40	0	1,663.39
008	.	994.97	0	1,305.47
009	.	1,875.10	0	2,061.40
010	.	2,669.51	0	2,959.31
011	.	789.50	0	898.18
012	.	2,926.80	0	2,950.26
013	.	1,148.04	0	1,568.94
014	.	6,760.00	0	8,312.50
015	.	722.84	0	993.67
016	.	1,428.00	0	1,669.50
017	.	945.69	0	1,435.59
018	.	220.88	0	314.03
019	.	2,130.52	0	2,696.32
020	.	2,482.64	0	2,922.17
021	.	18,669.14	0	20,421.74
022	.	3,125.22	0	4,036.02
023	7,857.70	12,534.90	0	13,387.05
024	.	22,500.00	0	22,620.06
025	.	10,473.26	21,895.05	34,343.44

Appendix 4.6. Total dollar costs

c#	age	dsv	tdmc	timec	gtmc
001	15.39	is	20,003.21	10,339.19	30,342.40
002	6.13	ls	13,479.47	536.16	14,015.63
003	56.01	is	19,434.84	20,918.70	40,353.54
004	11.72	is	15,227.93	2,303.02	17,530.95
005	76.97	ns	16,399.71	162.84	16,562.55
006	3.03	ns	19,684.92	1,612.55	21,297.47
007	5.09	is	13,122.51	1,663.39	14,785.90
008	2.34	is	6,215.18	1,305.47	7,520.65
009	5.66	is	9,978.75	2,061.40	12,040.15
010	9.45	is	15,761.80	2,959.31	18,721.11
011	5.67	ns	13,299.35	898.18	14,197.53
012	11.85	ns	.	2,950.26	.
013	0.25	ls	36,890.61	1,568.94	38,459.55
014	9.40	ls	38,718.10	8,312.50	47,030.60
015	9.78	ls	13,349.02	993.67	14,342.69
016	13.45	is	20,953.75	1,669.50	22,623.25
017	8.17	is	18,298.21	1,435.59	19,733.80
018	10.92	is	7,765.94	314.03	8,079.97
019	15.13	is	34,054.41	2,696.32	36,750.73
020	4.89	is	18,478.04	2,922.17	21,400.21
021	7.63	is	60,767.40	20,421.74	81,189.14
022	12.19	is	26,853.05	4,036.02	30,889.07
023	2.80	is	18,912.53	13,387.05	32,299.58
024	11.01	is	32,980.69	22,620.06	55,600.75
025	1.35	ls	141,241.63	34,343.44	175,585.07

Appendix 4.7. Reported symptoms

c#	age	dsv	ha	fv	ns	vm	fg	bc	cnf	ssp
001	15.39	is	y	y	n	n	y	n	y	y
002	6.13	ls	y	y	y	y	y	n	n	y
003	56.01	is	y	y	y	n	y	n	y	n
004	11.72	is	y	y	y	y	y	y	y	n
005	76.97	ns	y	y	y	n	y	n	n	n
006	3.03	ns	n	n	n	n	n	n	n	n
007	5.09	is	y	y	n	n	y	n	n	n
008	2.34	is	y	y	y	y	y	n	n	n
009	5.66	is	y	n	y	y	n	n	n	n
010	9.45	is	y	y	n	n	y	n	n	n
011	5.67	ns	y	y	y	y	y	n	n	y
012	11.85	ns	y	y	n	n	y	n	y	n
013	0.25	ls	y	y	y	y	y	n	y	n
014	9.40	ls	y	n	n	n	n	n	n	n
015	9.78	ls	y	y	n	n	y	n	n	n
016	13.45	is	y	n	n	n	n	n	n	n
017	8.17	is	y	y	n	y	y	y	y	y
018	10.92	is	y	y	n	n	y	y	y	y
019	15.13	is	y	n	n	n	n	n	n	n
020	4.89	is	y	y	y	y	y	y	n	y
021	7.63	is	y	y	y	y	n	n	n	n
022	12.19	is	y	y	y	n	y	n	y	y
023	2.80	is	y	y	y	n	y	n	n	n
024	11.01	is	y	y	y	n	y	n	y	n
025	1.35	ls	n	n	n	n	n	n	n	n

Appendix 4.7. Reported symptoms continued

c#	fp	sz	gm	pm	dibh	sh	dibr
001	y	y	y	n	6	n	.
002	y	y	n	y	3	n	.
003	n	n	n	n	4	n	.
004	n	y	y	n	4	n	.
005	n	n	n	n	1	n	.
006	y	y	y	y	0	n	.
007	n	y	y	y	4	y	1
008	n	y	n	y	3	y	1
009	n	y	n	y	2	n	.
010	n	y	y	n	4	y	4
011	y	y	n	y	4	n	.
012	n	n	n	n	2	y	1
013	n	y	n	y	3	y	1
014	n	y	y	n	1	n	.
015	n	y	y	n	2	n	.
016	n	y	y	n	0	n	.
017	y	y	y	n	5	n	.
018	n	y	y	n	6	y	1
019	n	y	y	n	0	n	.
020	n	y	y	y	3	y	.
021	n	y	n	y	0	n	.
022	n	y	y	y	2	n	.
023	n	y	y	y	4	n	.
024	n	y	y	y	2	n	.
025	n	y	y	n	0	n	.

Appendix 4.8. Reported sequelae

c#	age	dsv	rsz	szm	rw	tpy	cms	cep	edp	dm	de
001	15.39	is	n	14	26	y	y	y	y	y	y
002	6.13	ls	y	.	.	n	n	y	y	y	y
003	56.01	is	n	.	16	n	y	y	y	y	y
004	11.72	is	n	.	26	n	n	n	n	n	n
005	76.97	ns	n	.	0	y	n	n	n	n	n
006	3.03	ns	n	2	4	n	n	n	y	n	n
007	5.09	is	n	18	16	n	n	y	y	n	n
008	2.34	is	n	6	.	n	n	.	y	n	n
009	5.66	is	n	6	39	n	y	n	n	n	n
010	9.45	is	n	2	6	y	y	y	y	y	y
011	5.67	ns	n	12	4	n	n	n	y	n	n
012	11.85	ns	n	.	.	n	n	n	n	n	n
013	0.25	ls	y	98	.	y	y	.	y	.	.
014	9.40	ls	y	514	.	y	n	y	y	y	y
015	9.78	ls	y	98	12	n	y	y	y	y	y
016	13.45	is	n	1	.	n	n	y	y	y	y
017	8.17	is	n	4	.	y	y	y	y	n	y
018	10.92	is	n	52	.	y	y	y	y	n	n
019	15.13	is	n	26	26	y	y	y	y	n	n
020	4.89	is	n	1	8	n	y	n	n	n	n
021	7.63	is	n	8	8	y	n	y	y	y	y
022	12.19	is	n	6	16	y	n	n	y	n	n
023	2.80	is	n	6	.	y	n	y	y	.	.
024	11.01	is	n	6	4	y	y	y	y	n	y
025	1.35	ls	y	86	.	y	y	y	y	.	.

Appendix 4.8. Reported sequelae continued

c#	ebc	com	wgt	trad	tad	tot ryoti	tot yoti	%tr
001	y	y	n	640	640	1.752	1.752	100.00
002	y	n	n	629	629	1.722	1.722	100.00
003	y	y	n	192	1023	0.526	2.801	18.77
004	n	n	n	19	1057	0.052	2.894	1.80
005	n	n	n	16	648	0.044	1.774	2.47
006	y	n	n	10	3625	0.027	9.925	0.28
007	y	n	y	128	2500	0.350	6.845	5.12
008	y	y	n	673	673	1.843	1.843	100.00
009	y	n	n	29	1421	0.079	3.890	2.04
010	n	y	n	2493	2493	6.825	6.825	100.00
011	y	n	n	8	348	0.022	0.953	2.30
012	n	n	n	14	4017	0.038	10.998	0.35
013	y	y	n	684	684	1.873	1.873	100.00
014	y	y	n	3600	3600	9.856	9.856	100.00
015	y	y	y	684	684	1.873	1.873	100.00
016	n	n	n	4337	4342	11.874	11.888	99.88
017	y	y	n	1050	1050	2.875	2.875	100.00
018	n	n	n	1096	1096	3.001	3.001	100.00
019	n	n	n	146	1086	0.400	2.973	13.44
020	y	y	n	63	706	0.172	1.933	8.92
021	n	n	n	1831	1831	5.013	5.013	100.00
022	y	y	n	135	815	0.370	2.231	16.56
023	y	y	n	1013	1013	2.773	2.773	100.00
024	y	y	n	51	158	0.140	0.433	32.28
025	y	y	n	603	603	1.651	1.651	100.00

Appendix 4.9. Hospital DALYS

c#	Date of Birth	age	dsv	duration in days
001	04/15/84	15.39	0.92	15
002	07/30/93	6.13	0.92	5
003	08/24/42	56.01	0.92	7
004	11/07/86	11.72	0.92	5
005	09/30/22	76.97	0.096	16
006	07/15/88	3.03	0.92	10
007	07/26/89	5.09	0.92	6
008	05/16/97	2.34	0.92	7
009	12/31/91	5.66	0.92	8
010	04/11/85	9.45	0.92	10
011	12/07/94	5.67	0.92	8
012	09/14/78	11.85	0.92	14
013	06/07/99	0.25	0.92	8
014	04/19/82	9.40	0.92	14
015	11/28/89	9.78	0.92	6
016	03/24/76	13.45	0.92	5
017	07/10/90	8.17	0.92	12
018	08/24/87	10.92	0.92	4
019	06/18/83	15.13	0.92	20
020	09/28/94	4.89	0.92	7
021	12/11/88	7.63	0.92	50
022	07/17/87	12.19	0.92	12
023	08/11/96	2.80	0.92	7
024	09/29/90	11.01	0.92	9
025	04/08/99	1.35	0.92	603

Appendix 4.9. Hospital DALYs continued

cs nbr	US le	US lyr	S le	S lyr
O01	75.3	60.3	80	64.6105
O02	75.2	70.2	80	73.8700
O03	78	23.8	80	23.9945
O04	75.3	64.3	80	68.2820
O05	86	9	80	3.0335
O06	75.2	72.2	80	76.9692
O07	75.2	70.2	80	74.9076
O08	75.1	73.1	80	77.6646
O09	75.2	70.2	80	74.3354
O10	75.2	66.2	80	70.5489
O11	74.6	69.6	80	74.3326
O12	74.7	63.7	80	68.1451
O13	74	73.9	80	79.7454
O14	78.1	71.1	82.5	73.0955
O15	80.1	71.1	82.5	72.7204
O16	74.7	60.7	80	66.5517
O17	74.7	66.7	80	71.8330
O18	74.7	64.7	80	69.0787
O19	75.4	59.4	80	64.8679
O20	80.4	76.4	82.5	77.6075
O21	75.9	67.9	82.5	74.8669
O22	75.3	63.3	80	67.8138
O23	75.1	73.1	80	77.1964
O24	80.5	70.5	82.5	71.4856
O25	75.5	74.1	80	78.6530

Appendix 4.10. Recovery DALYs

c#	Date of Birth	age	Days at onset	dsv	Days Duration	still occurring
001	04/15/84	15.39	5,621	0.096	625	y
002	07/30/93	6.13	2,239	0.4	624	y
003	08/24/42	56.01	20,456	0.4	185	n
004	11/07/86	11.72	4,280	0.096	14	n
005	09/30/22	76.97	28,112	0	0	n
006	07/15/88	3.03	1,107	0	0	n
007	07/26/89	5.09	1,860	0.4	122	n
008	05/16/97	2.34	853	0.096	666	n
009	12/31/91	5.66	2,069	0.22	21	n
010	04/11/85	9.45	3,452	0.096	2,483	n
011	12/07/94	5.67	2,070	0	0	n
012	09/14/78	11.85	4,330	0	0	n
013	06/07/99	0.25	93	0.4	676	y
014	04/19/82	9.40	3,435	0.4	3,586	y
015	11/28/89	9.78	3,572	0.4	678	y
016	03/24/76	13.45	4,912	0.096	4,337	y
017	07/10/90	8.17	2,983	0.096	1,038	y
018	08/24/87	10.92	3,989	0.096	1,092	y
019	06/18/83	15.13	5,527	0.096	126	n
020	09/28/94	4.89	1,787	0.4	56	n
021	12/11/88	7.63	2,788	0.4	1,781	y
022	07/17/87	12.19	4,451	0.4	123	n
023	08/11/96	2.80	1,024	0.096	1,006	y
024	09/29/90	11.01	4,023	0.4	42	n
025	04/08/99	1.35	492	0.92	603	y

Appendix 4.10. Recovery DALYs continued

c#	US let	US lyr	S le	S lyr
001	75.3	60.3	80	64.61
002	75.2	70.2	80	73.87
003	78	23.8	80	23.99
004	75.3	64.3	80	68.28
005	86	9	80	3.03
006	75.2	72.2	80	76.97
007	75.2	70.2	80	74.91
008	75.1	73.1	80	77.66
009	75.2	70.2	80	74.34
010	75.2	66.2	80	70.55
011	74.6	69.6	80	74.33
012	74.7	63.7	80	68.15
013	74	73.9	80	79.75
014	78.1	71.1	82.5	73.10
015	80.1	71.1	82.5	72.72
016	74.7	60.7	80	66.55
017	74.7	66.7	80	71.83
018	74.7	64.7	80	69.08
019	75.4	59.4	80	64.87
020	80.4	76.4	82.5	77.61
021	75.9	67.9	82.5	74.87
022	75.3	63.3	80	67.81
023	75.1	73.1	80	77.20
024	80.5	70.5	82.5	71.49
025	75.5	74.1	80	78.65

Appendix 4.11. ILCES scores

c#	Interview date	Date of Onset	age	dsv	Score	tot pos	%change	ysill	QOL
OO1	06/06/01	09/05/99	15.39	is	-4	30	-13.33	1.75	5
OO2	06/06/01	09/16/99	6.13	ls	-14	33	-42.42	1.72	5
OO3	06/14/01	08/26/98	56.01	is	-19	30	-63.33	2.80	3
OO4	06/18/01	07/27/98	11.72	is			.	2.89	.
OO5	06/27/01	09/18/99	76.97	ns	0	39	0.00	1.77	6
OO6	06/29/01	07/27/91	3.03	ns	0	30	0.00	9.92	6
OO7	07/03/01	08/29/94	5.09	is	-4	33	-12.12	6.84	5
OO8	07/20/01	09/16/99	2.34	is	6	30	20.00	1.84	6
OO9	07/21/01	08/30/97	5.66	is	-1	30	-3.33	3.89	6
O10	07/21/01	09/23/94	9.45	is	3	30	10.00	6.83	5
O11	07/21/01	08/07/00	5.67	ns	3	30	10.00	0.95	6
O12	07/22/01	07/23/90	11.85	ns	6	30	20.00	11.00	6
O13	07/23/01	09/08/99	0.25	ls	-5	24	-20.83	1.87	3
O14	07/23/01	09/14/91	9.40	ls	-10	30	-33.33	9.86	5
O15	07/24/01	09/09/99	9.78	ls	-15	30	-50.00	1.87	4
O16	07/25/01	09/04/89	13.45	is	-2	36	-5.56	11.89	5
O17	07/25/01	09/11/98	8.17	is	-4	30	-13.33	2.87	6
O18	07/26/01	07/26/98	10.92	is	0	30	0.00	3.00	6
O19	07/26/01	08/05/98	15.13	is	-2	30	-6.67	2.97	6
O20	07/26/01	08/20/99	4.89	is	10	30	33.33	1.93	6
O21	08/04/01	07/30/96	7.63	is	-4	33	-12.12	5.01	5
O22	12/16/01	09/23/99	12.19	is	8	33	24.24	2.23	6
O23	03/10/02	06/01/99	2.80	is	-13	33	-39.39	2.77	5
O24	03/11/02	10/04/01	11.01	is	2	33	6.06	0.43	6
O25	04/07/02	08/12/00	1.35	ls	-21	30	-70.00	1.65	1

Appendix 4.11. ILCES scores continued

c#	1	2	3	4	5	6	7	8	9	10	11	12	13
O01	.	3	1	0	0	.	-1	0	-3	.	-2	-1	-1
O02	-2	-2	-1	-1	-2	.	-1	-1	-3	.	-2	-1	0
O03	-1	-2	.	-1	.	.	-2	-3	-2	-2	-3	-2	-2
O04
O05	0	0	0	0	0	0	0	0	0	0	0	0	0
O06	.	1	0	0	0	.	0	0	.	0	-1	0	0
O07	-1	0	0	0	0	.	0	-1	-1	.	-1	0	0
O08	0	3	-1	.	3	.	0	0	-1	.	0	0	2
O09	.	-1	0	0	0	.	0	0	0	.	0	0	0
O10	.	2	0	0	2	.	0	0	-1	.	0	0	0
O11	.	0	3	0	0	.	0	0	0	.	0	0	0
O12	.	3	3	0	.	.	0	0	0	0	0	0	0
O13	.	3	.	0	.	.	0	-3	-2	.	-3	0	0
O14	.	3	.	-2	-1	.	-1	0	-3	-2	-3	0	-1
O15	.	0	-1	0	0	.	0	-3	-3	.	-3	-3	-2
O16	.	0	0	0	0	0	0	0	-1	-1	0	0	0
O17	.	0	0	-2	0	.	0	-1	-1	.	0	0	0
O18	.	0	0	0	3	.	0	0	-3	.	0	0	0
O19	.	0	0	0	0	.	0	0	0	.	-2	0	0
O20	.	2	2	3	3	.	0	0	0	.	0	0	0
O21	0	0	1	0	1	.	0	0	-2	.	-2	0	-2
O22	-2	3	3	3	3	.	0	0	-1	.	0	0	-1
O23	0	-2	1	-2	-3	.	-1	0	-2	.	-2	0	-2
O24	0	2	0	0	2	.	0	-1	-1	.	0	0	0
O25	-3	-3	-3	-3	3	.	-2	-1	-3	.	.	-3	-3

Appendix 4.12. Awareness of illness and required procedure responses

C#	age	dsv	hoi	psg	wsg	al	bt	ft
001	15.39	is	n	n	y	n	n	n
002	6.13	ls	n	n	y	n	n	n
003	56.01	is	n	n	y	n	n	n
004	11.72	is	n	n	y	n	n	n
005	76.97	ns	n	n	n	n	n	n
006	3.03	ns	n	n	y	y	y	n
007	5.09	is	n	n	y	y	y	n
008	2.34	is	n	n	y	n	n	n
009	5.66	is	y	n	y	n	n	n
010	9.45	is	n	n	y	n	n	n
011	5.67	ns	n	n	y	n	n	n
012	11.85	ns	n	n	y	n	.	.
013	0.25	ls	n	n	y	n	n	y
014	9.40	ls	n	n	y	y	y	n
015	9.78	ls	y	n	y	n	n	n
016	13.45	is	n	n	y	y	y	y
017	8.17	is	y	y	y	n	n	n
018	10.92	is	n	n	y	n	n	n
019	15.13	is	n	n	y	n	n	n
020	4.89	is	n	n	y	y	n	n
021	7.63	is	n	n	y	n	y	n
022	12.19	is	n	n	n	n	n	y
023	2.80	is	n	n	y	n	n	y
024	11.01	is	y	n	y	n	y	n
025	1.35	ls	y	n	n	y	y	y

Appendix 4.12. Awareness of illness and required procedure responses continued

c#	sm	tpy	st	ot	pt	hn
001	y	y	y	y	y	n
002	y	n	n	n	n	n
003	n	n	n	n	n	n
004	y	n	n	n	n	n
005	n	y	y	y	n	n
006	y	n	n	n	n	n
007	y	n	n	n	n	n
008	n	n	n	n	n	n
009	y	n	n	n	n	n
010	y	y	y	n	y	n
011	y	n	n	n	n	n
012	n	n	n	n	n	n
013	y	y	y	y	y	y
014	y	y	n	n	n	n
015	y	n	n	n	n	n
016	n	n	n	n	n	n
017	y	y	y	n	n	n
018	y	y	n	n	n	n
019	y	y	n	n	n	n
020	y	n	n	n	n	n
021	n	y	n	n	n	y
022	y	y	n	n	n	y
023	y	y	y	n	y	n
024	y	y	n	n	n	n
025	y	y	y	y	y	y