Title

Cysticercosis in the United States: A Nationwide Hospitalization Study Assessing Burden of Disease, Fatality Risk Factors and Economic Impact of Infection

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Cysticercosis in the United States:
A Nationwide Hospitalization Study
Assessing Burden of Disease, Fatality Risk Factors
and Economic Impact of Infection

A dissertation submitted in partial satisfaction of the

requirements for the degree Doctor of Philosophy

in Epidemiology

by

Kaitlin Ashley O'Keefe

2013

ABSTRACT OF THE DISSERTATION

Cysticercosis in the United States:

A Nationwide Hospitalization Study

Assessing Burden of Disease, Fatality Risk Factors

and Economic Impact of Infection

by

Kaitlin Ashley O'Keefe

Doctor of Philosophy in Epidemiology

University of California, Los Angeles, 2013

Professor Frank J. Sorvillo, Chair

Background: Cysticercosis, an infection caused by the larval stage of the pork tapeworm *Taenia solium*, has become increasingly important both in the United States and globally in recent decades. Neurocysticercosis is one of the most common parasitic diseases of the human nervous system and a leading cause of acquired epilepsy worldwide. Despite its potential impact, there is a lack of comprehensive information on cysticercosis infection in the US. This study was designed to estimate the impact of cysticercosis nationwide, in terms of the number of people hospitalized and the economic burden of hospitalizations, as well as explore potential risk factors for cysticercosis in-hospital fatality. **Methods:** The Nationwide Inpatient Sample (NIS),

representing a 20% sample of annual hospital discharge records in the US, was used for analysis from 1998-2009. National estimates of cysticercosis-related hospitalizations and rates, patient and hospital stay characteristics, and hospitalization-related charges were calculated using NIS sample weights and US Census Bureau data. Risk factors for fatality were evaluated using bivariate and multivariate logistic regression. **Results:** There were 28,565 cysticercosis-related hospitalizations nationwide estimated during the study period, representing a hospitalization rate of 8.16 per million population. The highest proportion of cases were reported in males, Hispanic populations, hospitals in the West and among patients aged 18-44, consistent with previous studies. There were 364 total in-hospital deaths estimated, representing an overall case-fatality rate of 1.28% and a nationwide in-hospital mortality rate of 0.1 deaths per million population. National estimates of associated charges among cysticercosis-related hospitalizations amounted to approximately $996 million. Male sex, hospital location in the West, shunting procedures and diagnoses of obstructive hydrocephalus were associated with in-hospital fatality in bivariate regression analysis (OR: 1.18, 2.36, 1.79 and 2.85 respectively). **Discussion:** National estimates of cases, deaths and associated charges reinforce the importance of cysticercosis in the US. Despite improvements in management strategies, the burden of cysticercosis-related hospitalizations remains substantial, indicating the need for significant progress towards reducing infection nationwide. Increased surveillance and identification of cases can serve to better define the burden of disease, potentially allowing for targeted prevention and control campaigns in populations at greatest risk.

The dissertation of Kaitlin Ashley O'Keefe is approved.

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2013

DEDICATION

I dedicate this work to my family and friends. Without the overwhelming support and encouragement from my mom and dad, Lynn and John O'Keefe, I would not have been able to achieve my goals. They helped me from the beginning and always told me that anything I wanted to accomplish was possible. I wouldn't be the person I am today without them and could not have asked for more amazing parents. My fabulous sisters, Suzanne, Maggie and Jean were there whenever I needed a good laugh or support to keep me going.

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Bristow BN, O'Keefe KA, Shafir SC, Sorvillo FJ. Congenital cytomegalovirus mortality in the United States, 1990-2006. PLoS Negl Trop Dis. 2011 Apr 26;5(4):e1140.

Abstracts and Presentations

Arrington K, O'Keefe K, Kelley M, Shoaf K. Top factors for successful collaborations between local health departments and school districts. National Association of County and City Health Officials. 2013 Public Health Preparedness Summit. Poster Presentation. March 2013.

O'Keefe K, Kelley M, Prelip M, Arrington K, Shoaf K. Status of collaboration between local health departments and school systems for emergency preparedness and response: School district perspective. Poster Presentation. 140th American Public Health Association Annual Meeting, October 2012.

Kelley M, O'Keefe K, Prelip M, Arrington K, Shoaf K. Status of collaboration between local health departments and school systems for emergency preparedness and response: Local health department perspective. Poster Presentation. 140th American Public Health Association Annual Meeting, October 2012.

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Chapter 1 – Cysticercosis-related Hospitalizations in the United States, 1998-2009

INTRODUCTION

Cysticercosis is a parasitic infection caused by the larval stage of the pork tapeworm, *Taenia solium.* Neurocysticercosis (NCC), which occurs when larvae migrate to the central nervous system, is one of the most common parasitic diseases of the human nervous system and a leading cause of acquired epilepsy worldwide.[1, 2] Common in lower-income countries where the parasite is endemic, cysticercosis, particularly NCC, has become increasingly important in the United States in recent decades as well.[1, 2]

T. solium has an intricate lifecycle involving both humans and pigs.[1, 3] Humans are the natural definitive host, harboring the adult tapeworm in a condition known as taeniasis.[1, 3] Pigs serve as an intermediate host, harboring the larval form of the tapeworm known as a cysticercus, after ingesting viable eggs shed in the feces of a human infected with the adult form.[1, 4] The adult tapeworm will develop in the small intestine of the human host after the ingestion of raw or undercooked pork containing the cysticerci.[1, 3, 4] After 1-3 months of maturation, gravid proglottids, containing 40,000-60,000 fertile eggs, will begin to detach from the adult worm and eggs and proglottids will be shed in feces.[1, 4] Human cysticercosis occurs when viable eggs are ingested, typically in contaminated food or water.[1, 3] Taeniasis may be asymptomatic or present with mild symptoms, though usually produces no serious pathology.[3] Cysticercosis, on the other hand, can produce severe symptoms depending on the number, size and location of the cysticerci within the body, including loss of vision, meningitis, hydrocephalus and in some cases death.[4]

Cysticercosis cases have been reported in several case series and surveillance studies across the United States, with diagnosed and hospitalized patients identified in many states, hundreds within a small collection of hospitals and nearly 4,000 cases identified in a study examining California statewide hospital discharge records from 1991-2008.[2, 5-21] The increased frequency of neurocysticercosis diagnoses in the United States and other high-income countries has been attributed in part to an increase in migration of people from areas where the disease is endemic, as well as travel by US residents to endemic areas.[2, 22, 23] While the majority of cysticercosis cases reported in the United States are recognized to be imported from endemic countries, studies have also identified autochthonous cases reported in US-born persons, with no history of travel to a disease endemic area before the onset of symptoms.[2, 5-8, 13, 24]

These limited surveillance and case series studies conducted in the US highlight the nationwide importance of cysticercosis, as well as underscore the need for additional data. Although previous studies contribute vital information towards describing this devastating disease in the US, these studies reflect only a portion of actual cases, leaving the true impact of the disease in the national population largely unknown. Surveillance and education efforts for disease prevention and control cannot be efficiently targeted to areas and groups that are at increased risk of infection before these groups are identified on a national scale.

Given the potential severity and impact of cysticercosis, a lack of comprehensive data on the burden of cysticercosis in the US, and the opportunity for prioritizing prevention and control activities for populations most at risk, human cysticercosis warrants further analysis on a national scale. To help better define the burden of cysticercosis in the US, cysticercosis-related hospitalizations nationwide were analyzed for the 12 year period 1998-2009.[25]

METHODS

Data source

In-patient hospitalization records were examined using the Nationwide Inpatient Sample (NIS), part of the Healthcare Cost and Utilization Project (HCUP) sponsored by the Agency for Healthcare Research and Quality.[26] Yearly NIS data from 1998-2009 contain roughly 7-8 million hospital discharge records each from around 1,000 hospitals throughout the country, and are designed to approximate a 20% stratified sample of US community hospitals.[26] The NIS was chosen for this analysis in part because the large size of the NIS enables examination of the burden of cysticercosis in a way that smaller datasets would not, in addition to allowing for the calculation of national estimates of hospitalizations. Each dataset contains more than 100 clinical and nonclinical data elements for each hospital stay, including demographic, institutional and hospital stay characteristics, such as age, regional hospital location and up to 15 diagnostic and procedural codes (up to 25 diagnostic codes in 2009).[26] This allows for the detailed examination of said variables in patients diagnosed with cysticercosis. Further description of the NIS datasets can be found through the Agency for Healthcare Research and Quality.[25]

Case identification and inclusion

Cysticercosis-related hospitalizations were identified as any discharge record with an International Classification of Diseases, Ninth Revision, Clinical Modifications (ICD-9-CM) code of 123.1, defined as Cysticercosis (Cysticerciasis - Infection by Cysticercus cellulosae [larval form of *T. solium*]), listed for either primary or non-primary diagnoses.

Data analysis

Both the overall and annual numbers of cysticercosis-related hospitalizations were recorded and characteristics of those hospitalized were examined. Hospital and discharge weights provided with the NIS data and documentation, which account for the stratified sampling design employed, were used to produce national estimates of cysticercosis hospitalizations.[26] Primary demographic characteristics of interest included age at admission, gender and race/ethnicity (white, black, Hispanic, Asian or Pacific Islander, Native American and other). To aid in interpretation, "age at admission" was analyzed both by calculating mean age (in years) and by separating age into 5 categories of age group (1-17, 18-44, 45-64, 65-84, and 85+ years of age). Differences in age group, gender and hospital region between categories of race/ethnicity among all cysticercosis-related hospitalizations during the 12 year period were examined using χ^2 tests (with a significance level of 0.05), with techniques accounting for the sampling design of the NIS. Primary institutional and hospital stay characteristics examined included regional location of hospital (Northeast, Midwest, South and West), hospital teaching status (non-teaching vs. teaching), hospital location type (rural vs. urban), hospital bed size (small, medium and large) and average length of hospital stay (in days) per discharge for cysticercosis-related hospitalizations.[27] Estimates for the total number of national in-hospital deaths among cysticercosis-related hospitalizations for the overall study period were also calculated using NIS sample weights. Several of the variables in the NIS dataset included missing observations for a number of records, most notably for the variable race/ethnicity which was missing in approximately 18.3% of discharges over the entire study period. The proportion of missing data was reported separately for each variable.

Patient records were also broken down by those with primary and non-primary diagnoses of cysticercosis. Differences in demographic factors including age group, gender and race between those with and without a primary diagnosis of cysticercosis among all cysticercosis-related hospitalizations were tested using χ^2 tests with a significance level of 0.05, with techniques accounting for the sampling design of the NIS. Among patients with a listed primary diagnosis other than cysticercosis, the most common primary diagnoses were identified. Among patients with cysticercosis listed as the primary diagnosis, the most common secondary diagnoses were identified. For analysis of comorbidities, unweighted estimates from the NIS were used for ease of interpretability. Unless otherwise specified, all other data presented are based on national estimates of hospitalizations. Temporal trends in cysticercosis hospitalizations over the 12 year period under analysis were also described. Population estimates obtained from the US Census Bureau were used to calculate characteristic-specific estimates of rates of cysticercosis-related hospitalizations.[28, 29] Data analysis was completed using SAS version 9.2 (SAS Institute, Cary, North Carolina, USA). Analysis was performed using procedures designed to account for the complex stratified cluster sampling design of the NIS.

RESULTS

Cysticercosis hospitalizations

National estimates of cysticercosis-related hospitalizations are presented in Table 1. Over the entire 12 year study period from 1998-2009, there were an estimated 28,565 (95% CI [25,485.4 – 31,644.4]) hospitalizations with an included diagnosis of cysticercosis. Of these, an estimated 12,669 (95% CI [11,417.2 – 13,920.1]) discharges listed a primary diagnosis of cysticercosis. The number of cysticercosis-related hospitalizations varied but an increasing trend

over the study period was demonstrated, with a high of 2,753.1 nationally estimated hospitalizations in 2006 and a low of 1,998.1 hospitalizations in 1998 (Figure 1). The number of hospitalizations with a primary diagnosis of cysticercosis exhibited a more static trend ranging from a low of 913.3 in 1998 to a high of 1,211.6 in 2006. A total of 364.3 (95% CI [244.4 – 484.1]) in-hospital deaths were estimated to have occurred among cysticercosis-related hospitalizations throughout the 12 year study period.

Demographic characteristics of hospitalizations

Overall demographic characteristics of cysticercosis hospitalizations are presented in Table 2. Males constituted a larger proportion of nationally estimated cysticercosis hospitalizations when compared to females (55.0% compared to 44.2%). The race/ethnicity accounting for the largest proportion of nationally estimated hospitalizations were Hispanic individuals (60.6%), with white, black, and "other" race/ethnicity individuals accounting for 7.6%, 4.1% and 7.4% respectively. The age group ranging from 18-44 years held the largest proportion of national estimates (59.9%) with the smallest proportion of hospitalizations reported in the 85+ years age group. The mean age of patients with cysticercosis-related hospitalizations was 38.8 years of age (95% CI [37.8 – 39.8])). Demographic characteristics of nationally estimated hospitalizations stratified by year are presented in Table 3. National estimates across the 12-year period showed consistently larger proportions of males who had a cysticercosis-related hospitalization, ranging from the most similar proportions in 2004 (males 50.8% and females 48.0%) to the most dissimilar in 2001 (59.1% in males and 40.9% in females). For race/ethnicity, the largest proportion of cases were consistently Hispanic, from a low of 53.0% in 1998 to a high of 68.1% in 2007. The largest proportion of nationally estimated hospitalizations fell in the 18-44 years

age group across the entirety of the study period, accounting for the highest proportion of cases in 2001 (64.6%). The average age in years over the study period ranged from 35.9 years in 2000 to 42.6 years in 2009. Statistically significant associations were found between both age group and gender when compared with race/ethnicity for the overall study period ($p=0.022$ and $p<0.0001$ respectively). Statistically significant associations were also found when evaluating differences between discharges with primary vs. non-primary diagnoses of cysticercosis and the selected demographic variables of race ($p=0.044$), gender ($p<0.0001$) and age group ($p<0.0001$).

Institutional characteristics of hospitalizations

Overall institutional characteristics of cysticercosis hospitalizations are presented in Table 2. The largest proportion of nationally estimated cases came from hospitals located in the West region of the country (45.0%) followed by the South (28.1%), Northeast (13.6%) and Midwest (13.3%) regions. Nearly double the number of estimated cases were from teaching hospitals when compared with non-teaching hospitals throughout the country (61.2% vs. 38.6%). The vast majority of estimated cases were from hospitals located in urban regions vs. rural locations (97.6% vs. 2.2%). Overall proportions of cases from different sizes of hospitals (by bed size), fell in ascending order with 7.8%, 26.0% and 66% of cases coming from small, medium and large hospitals respectively. The average length of hospital stay for those with a cysticercosis diagnosis was 6.2 days (95% CI [5.9- 6.6]). A statistically significant association between hospital region and race/ethnicity for the overall study period was observed ($p<0.0001$).

National hospitalization rates for cysticercosis

Nationally estimated hospitalization rates for cysticercosis are presented in Tables 4 and 5. The overall cysticercosis-related hospitalization rate for the study period was 8.16 hospitalizations per million population, using nationwide population data from the US Census. The rate for hospitalizations with cysticercosis as a primary diagnosis was 3.62 cases per million population. The 18-44 years age group had the highest hospitalization rate of 12.69 per million population, with the lowest in the 1-17 year age group of 2.78 cases per million population. Hispanic individuals had the highest cysticercosis-related hospitalization rate of 35.68 cases per million population, with the lowest rate in those with white listed as race/ethnicity (0.93 cases per million). Males had a higher rate when compared to females of 9.15 vs. 7.09 per million population. The West region had the highest rates by far of 16.10 per million population, with the lowest occurring in the Midwest region (4.84 per million population). Yearly cysticercosis-related hospitalization rates are presented in Figure 2. The highest annual cysticercosis-related hospitalization rate was 9.23 hospitalizations per million population in 2006, with the lowest of 7.21 hospitalizations per million population in 2001.

Comorbid diagnoses

In all cysticercosis-related hospitalizations, cysticercosis was listed as the primary diagnosis in 44.2% of records, followed by “other convulsions”, “obstructive hydrocephalus”, “mechanical complication of nervous system device, implant or graft” and “cerebral artery occlusion, unspecified with cerebral infarction” listed as primary diagnosis in 8.2%, 3.5%, 2.6% and 1.3% of records respectively. In cases where cysticercosis was listed as the primary diagnosis, common secondary diagnoses included “other convulsions” (in 46.7% of records), “obstructive hydrocephalus” (in 8.0% of records), “epilepsy, unspecified, without mention of intractable

epilepsy" (in 2.5% of records), "headache" (in 2.2% of records) and "cerebral edema" (in 1.9% of records).

DISCUSSION

These findings indicate a substantial burden of cysticercosis-related hospitalizations in the US. Hispanics, males, younger adults and those living in the western states were more likely to be hospitalized with cysticercosis as a diagnosis. Cysticercosis-related hospitalizations and rates were observed to have increased between the period from 1998-2009, despite improvements in management strategies, indicating that there is significant progress that needs to be made in reducing rates of infection nationwide.[30, 31] Based on these estimates, as well as data from past studies, cysticercosis should be considered an important infection in the United States.[23]

Our results reinforce previous findings which describe frequent demographic features of those hospitalized with a diagnosis of cysticercosis.[2, 6, 9, 10, 13, 14, 16, 20, 21, 32] Estimated hospitalization frequencies and rates were highest for Hispanics. The high prevalence of Hispanic cases is consistent with previous studies, likely associated with immigration from endemic areas or contact with family and friends potentially harboring the adult tapeworm.[2, 6, 9, 10, 13, 14, 16, 20, 21, 32] It should also be noted that estimates on hospitalization rates in Hispanic population also have the additional obstacle of barriers to immigrant health, including a lack of access to health care or health insurance, potentially leading to substantial underreporting in these populations.[2] As the Hispanic population is projected to increase significantly in the United States in the coming decades, public health education, control and prevention campaigns for cysticercosis should be targeted to this demographic.[33] Though Hispanics accounted for the majority of hospitalizations, there were also significant numbers of cases in other race/ethnicity groups, including white and

black populations, with 2,182 (7.6%) and 1,161 (4.1%) estimated hospitalizations respectively. While not as frequent in other populations, physicians need to be trained to consider a diagnosis of cysticercosis in any individuals reporting symptoms consistent with illness, regardless of race/ethnicity or travel history. Autochthonous cases are routinely reported and studies such as the 1992 report of four cases of NCC in an Orthodox Jewish community illustrate that no population should be considered free from risk of contracting cysticercosis.[2, 5-8, 13, 24]

The gender distribution of hospitalizations is consistent with previous studies showing higher proportions of male cases than females with cysticercosis and NCC.[2, 10, 20, 32] The mean age and categorical age distribution of cases is also consistent with recent previous studies on NCC hospitalizations, showing the highest proportion of cases in early-mid adulthood.[2, 20] As the largest number of cases were of Hispanic race/ethnicity, this age and sex distribution can likely be attributed in part to higher rates of immigration of young adult males in search of employment.[18]

The majority of studies on cysticercosis in the United States have focused on the southwestern states, particularly Texas and California, with high populations of immigrants from endemic countries throughout Latin America, where numbers and rates of cysticercosis infection have been found to be particularly high.[6, 8-10, 17, 21] There have been several studies conducted in other regions of the United States which have also found substantial numbers of cysticercosis and NCC cases.[13-16] Results from this study are consistent with these previous findings, showing the highest number of hospitalizations and hospitalization rates in the West region of the country. Although the West region accounted for the largest proportion, there were considerable numbers of hospitalizations found in the South, Northeast and Midwest regions of the country during the

12 year study period. While the West region should be prioritized for allocation of resources for prevention and control efforts, education of physicians as well as surveillance for cysticercosis should not be overlooked in other regions not typically thought of as areas of high risk for disease occurrence.

Few other studies have examined institutional characteristics of hospitals most frequently reporting cysticercosis-related hospitalizations. The majority of nationally estimated cases came from hospitals in urban locations and those designated as teaching hospitals. Hospitals reporting the highest number of cysticercosis-related discharges during the study period tended to be classified as large in terms of bed size. Concentration of cysticercosis cases in hospitals with particular features suggest that the prioritization of education of physicians might be best aimed at those employed at such hospitals. As the largest estimated number of cases have come from large hospitals in urban areas, physician training on proper diagnostic tools and appropriate treatment strategies for various types of NCC and cysticercosis have the potential to impact greater relevant populations if targeted in these types of hospitals, as hospital physicians play critical roles in helping to control disease.[2]

A key factor in preventing transmission of cysticercosis is removing the adult tapeworm carrier source of infection.[5] As taeniasis usually causes no serious damage and results in mild, if any symptoms, patients are very seldom hospitalized for adult tapeworm infection.[3] Unfortunately, the asymptomatic nature of infection leads to high rates of underreporting of taeniasis, and the use of hospital data in particular does little to estimate true incidence of infection. Though a sensitive and specific serologic test exists that utilizes a simple finger-stick blood specimen collected procedure, implementation of this procedure and a comprehensive screening of

cysticercosis cases has been implemented in very limited areas.[5, 34] For each case of cysticercosis diagnosed, the case and case contacts should each be tested for taeniasis, which may help reduce further disease transmission.[2, 5]

There were several limitations to study analysis, many of which arose from the ways in which the original dataset was constructed and restrictions on utilization. The NIS does not record information about immigration from other countries, travel history, country of birth/residence, or behavioral characteristics, therefore, in using this data, it was not possible to directly examine if cysticercosis patients were immigrants from other countries or if they had a travel history which included travel to high prevalence areas, as has been seen in other studies.[2, 21, 32] ICD-9-CM coding used for disease diagnosis was not necessarily designed to track infection prevalence and has been previously criticized as clinically imprecise, potentially leading to erroneously classified cases and non-cases.[35] As the NIS contains no personal identification codes in the discharge records, it was also impossible to tell whether records were from hospitalization of different patients or multiple hospitalizations of the same patient within a year. If a person is hospitalized more than once for the same cysticercosis infection, estimates obtained from the NIS data might overestimate the true number of cysticercosis patients within the US. The lack of patient identifiers in records also prevents validation of the diagnosis and patient characteristic information listed.

Conclusions

This study was designed to provide further insight into the nationwide burden of cysticercosis in the United States.[23] Although results from this study show a sizeable number of hospitalizations each year, this is captures only a portion of the disease burden in the United States. Currently,

cysticercosis is not a reportable condition in most states and very few surveillance programs have been implemented.[5, 6] This lack of reportability, as well as the underreporting of less severe infections not requiring hospitalization, leads to the assumption that even national estimates from this study only provide a minimal approximation of the true number of infected individuals in the United States.[5, 14, 18] It has been stated that the first step in any control program for cysticercosis should be in developing and implementing an adequate surveillance system to comprehensively understand the scope of the disease.[38] Once appropriate surveillance systems are in place to detect cases of cysticercosis, limited resources can be prioritized to areas most in need for control efforts, including screening and treatment efforts for the adult tapeworm in cysticercosis cases and contacts preventing further transmission of cysticercosis.[5] In the absence of effective surveillance and adequate reporting of disease, the true burden of cysticercosis in this country is difficult, if not impossible to define. Previous studies have recommended routine public health efforts regarding cysticercosis, including the establishment of cysticercosis surveillance and required reporting of any cases of disease.[2, 5] There have been several reports specifically calling for the compulsory reporting of cysticercosis cases.[23, 36] Findings from this study reinforce regions and communities on a national scale where surveillance, education and control efforts might be particularly needed. Results also suggest that public health surveillance and prevention campaigns, while more heavily needed in certain places, should not be ignored in those groups and locations not commonly thought of as high risk. Cysticercosis can be found in a diverse array of populations and regions, and public health/health care professionals should diligently design and implement adequate surveillance and prevention strategies to plan for this case distribution in all areas of the United States. The results of this study will hopefully serve to emphasize the nationwide significance of this disease and help to establish cysticercosis as a

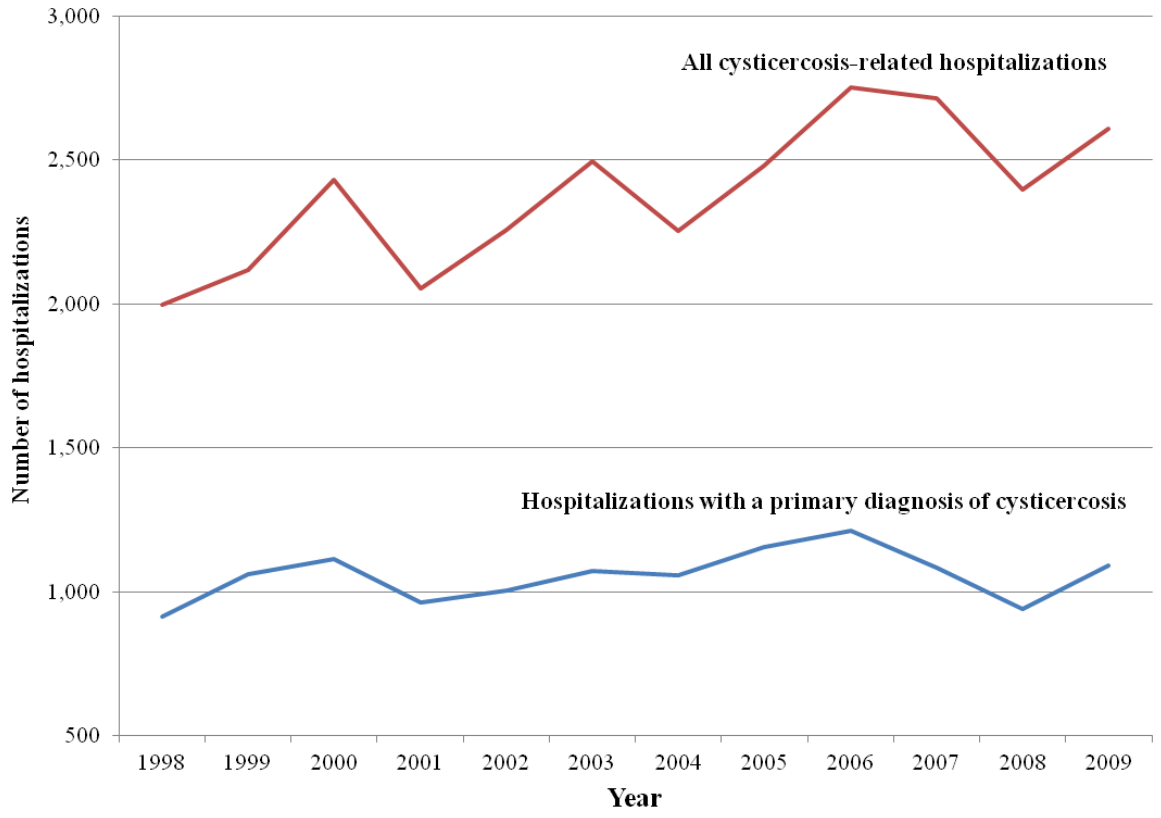
concern in the US. Health authorities should consider making cysticercosis reportable on a wider, if not national scale. Given that most of the cysticercosis cases in the US are identified among immigrants from endemic countries, additional support for cysticercosis elimination efforts in these areas should be provided.[2, 5]

Table 1. Annual national estimates of cysticercosis hospitalizations, 1998-2009

	Number of hospitalizations with cysticercosis listed as any diagnosis		Number of hospitalizations with cysticercosis listed as primary diagnosis	
	n	95% CI	n	95% CI
1998	1998.1	[1535.6 – 2460.6]	913.3	[673.8 – 1152.7]
1999	2118.8	[1669.0 – 2568.7]	1061.2	[854.5 – 1267.9]
2000	2429.9	[1837.9 – 3021.9]	1114.6	[823.8 – 1405.3]
2001	2053.8	[1676.7 – 2430.8]	962.6	[762.6 – 1162.5]
2002	2259.5	[1757.4 – 2761.5]	1004.8	[780.8 – 1228.8]
2003	2495.9	[1929.0 – 3062.9]	1070.8	[856.0 – 1285.7]
2004	2254.7	[1860.1 – 2649.2]	1056.8	[840.4 – 1273.2]
2005	2481.7	[1994.0 – 2969.4]	1155.3	[931.9 – 1378.7]
2006	2753.1	[2128.3 – 3377.9]	1211.6	[955.9 – 1467.3]
2007	2714.5	[2056.6 – 3372.4]	1085.1	[793.9 – 1376.3]
2008	2397.3	[1898.4 – 2896.1]	941.4	[736.1 – 1146.7]
2009	2607.8	[2118.8 – 3096.7]	1091.2	[866.1 – 1316.4]
Total	28565.0	[25485.4 – 31644.4]	12669.0	[11417.2 – 13920.1]

*National estimates based on NIS hospital and sample weights

Figure 1. Annual national estimates of cysticercosis hospitalizations



*National estimates based on NIS hospital and sample weights

Table 2. Demographic and institutional characteristics of nationally estimated cysticercosis-related hospitalizations, 1998-2009

	n	95% CI	%
Sex			
Male	15,718.0	[14,123.4 – 17,312.7]	55.0
Female	12,632.0	[11,016.3 – 14,247.2]	44.2
Missing			0.8
Race/ethnicity			
White	2,181.5	[1,884.6 – 2,478.5]	7.6
Black	1,161.2	[859.9 – 1,462.5]	4.1
Hispanic	17,321.0	[14,746.6 – 19,896.1]	60.6
Asian or Pacific Islander	496.2	[288.1 – 704.4]	1.7
Native American	60.9	[23.3 – 98.5]	0.2
Other	2,102.7	[1,498.2 – 2,707.1]	7.4
Missing			18.3
Region of hospital			
Northeast	3,896.0	[3,119.8 – 4,672.1]	13.6
Midwest	3,793.3	[2,856.6 – 4,730.0]	13.3
South	8,026.8	[6,387.5 – 9,666.0]	28.1
West	12,849.0	[10,543.1 – 15,154.6]	45.0
Missing			0.0
Hospital teaching status			
Non-teaching	11,037.0	[9,281.9 – 12,791.3]	38.6
Teaching	17,477.0	[14,947.0 – 20,007.3]	61.2
Missing			0.2
Hospital location			
Rural	639.1	[485.9 – 792.3]	2.2
Urban	27,875.0	[24,799.5 – 30,949.9]	97.6
Missing			0.2
Bed size of hospital			
Small	2,233.3	[1,734.8 – 2,731.9]	7.8
Medium	7,431.7	[6,230.6 – 8,632.7]	26.0
Large	18,849.0	[16,057.8 – 21,639.7]	66.0
Missing			0.2
Age group			
1-17	2,304.1	[1,891.4 – 27,16.8]	8.1
18-44	17,098.0	[15,329.4 – 18,866.1]	59.9
45-64	6,002.0	[5,117.1 – 6,887.0]	21.0
65-84	2,800.1	[2,271.7 – 3,328.5]	9.8
85+	332.1	[237.7 – 426.5]	1.2
Missing			0.1
Mean age (in years)	38.8	[37.8 – 39.8]	
Mean length of hospital stay (in days)	6.2	[5.9 – 6.6]	

*National estimates based on NIS hospital and sample weights. Estimates for age group <1 had too few estimated hospitalizations to report.

Table 3. Demographic characteristics of annual nationally estimated cysticercosis hospitalizations, 1998-2009

	1998		1999		2000		2001	
	n	%	n	%	n	%	n	%
Sex								
Male	1073.0	53.7	1143.1	53.9	1385.9	57.0	1213.7	59.1
Female	925.1	46.3	975.7	46.1	1044.0	43.0	840.1	40.9
Race/ethnicity								
White	93.7	4.7	209.0	9.9	132.3	5.4	172.2	8.4
Black	85.4	4.3	112.5	5.3	80.0	3.3	76.1	3.7
Hispanic	1059.3	53.0	1162.4	54.9	1570.7	64.6	1201.6	58.5
Asian or Pacific Islander	28.3	1.4	45.0	2.1	15.3	0.6	25.0	1.2
Native American	***	***	***	***	***	***	***	***
Other	160.8	8.0	161.1	7.6	117.8	4.8	131.4	6.4
Age group								
1-17	219.3	11.0	262.5	12.4	328.5	13.5	224.8	10.9
18-44	1183.1	59.2	1195.8	56.4	1440.2	59.3	1326.0	64.6
45-64	418.8	21.0	402.4	19.0	453.9	18.7	314.5	15.3
65-84	163.0	8.2	225.0	10.6	180.8	7.4	148.8	7.2
85+	13.9	0.7	33.2	1.6	26.5	1.1	34.1	1.7
Mean age (in years)	36.5		38.1		35.9		36.2	

*National estimates based on NIS hospital and sample weights. Estimates for age group <1 had too few estimated hospitalizations to report.
**Percentages account for missing data not shown in the above table.
***Cell sizes were too few to report.

Table 3. Demographic characteristics of annual nationally estimated cysticercosis hospitalizations, 1998-2009

	2002		2003		2004		2005	
	n	%	n	%	n	%	n	%
Sex								
Male	1318.8	58.4	1304.0	52.2	1146.3	50.8	1322.7	53.3
Female	940.6	41.6	1115.8	44.7	1083.1	48.0	1128.4	45.5
Race/ethnicity								
White	141.8	6.3	126.9	5.1	210.3	9.3	253.4	10.2
Black	77.8	3.4	112.8	4.5	139.3	6.2	58.3	2.3
Hispanic	1320.4	58.4	1586.4	63.6	1275.7	56.6	1389.7	56.0
Asian or Pacific Islander	32.3	1.4	83.9	3.4	60.4	2.7	51.8	2.1
Native American	13.1	0.6	***	***	***	***	***	***
Other	250.7	11.1	154.8	6.2	118.3	5.2	227.5	9.2
Age group								
1-17	235.6	10.4	223.1	8.9	230.5	10.2	161.0	6.5
18-44	1445.3	64.0	1493.3	59.8	1296.2	57.5	1577.9	63.6
45-64	377.8	16.7	506.5	20.3	437.0	19.4	498.1	20.1
65-84	188.9	8.4	235.9	9.5	254.0	11.3	222.0	8.9
85+	11.9	0.5	37.1	1.5	31.9	1.4	17.8	0.7
Mean age (in years)	36.1		39.0		38.9		38.2	

*National estimates based on NIS hospital and sample weights. Estimates for age group <1 had too few estimated hospitalizations to report.
**Percentages account for missing data not shown in the above table.
***Cell sizes were too few to report.

Table 3. Demographic characteristics of annual nationally estimated cysticercosis hospitalizations, 1998-2009

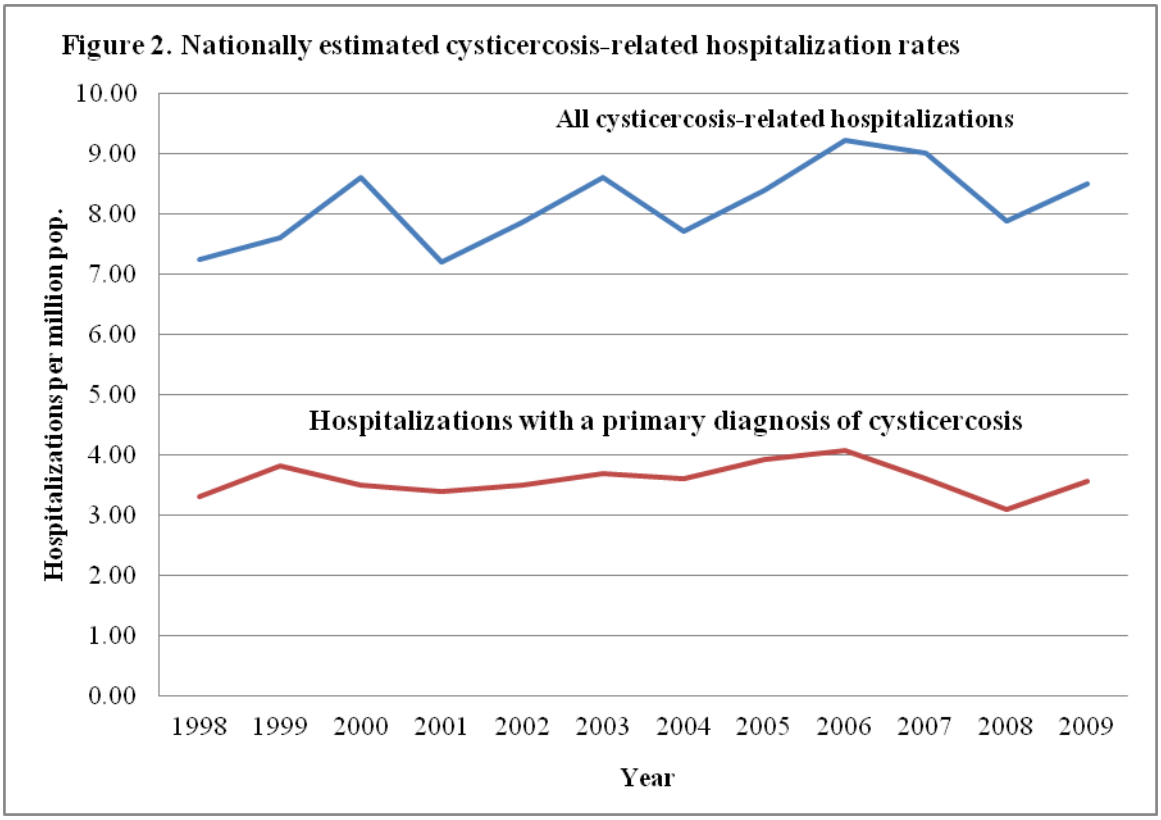
	2006		2007		2008		2009	
	n	%	n	%	n	%		
Sex								
Male	1503.7	54.6	1507.1	55.5	1307.7	54.6	1492.0	57.2
Female	1223.7	44.4	1189.6	43.8	1075.0	44.8	1090.7	41.8
Race/ethnicity								
White	129.6	4.7	172.7	6.4	305.3	12.7	234.3	9.0
Black	87.2	3.2	125.8	4.6	67.8	2.8	138.2	5.3
Hispanic	1790.4	65.0	1847.8	68.1	1396.9	58.3	1720.2	66.0
Asian or Pacific Islander	33.6	1.2	47.7	1.8	38.4	1.6	34.5	1.3
Native American	***	***	***	***	***	***	12.5	0.5
Other	201.3	7.3	130.9	4.8	174.0	7.3	274.1	10.5
Age group								
1-17	127.9	4.6	120.1	4.4	87.1	3.6	83.8	3.2
18-44	1737.2	63.1	1626.9	59.9	1337.9	55.8	1438.0	55.1
45-64	630.7	22.9	646.6	23.8	617.9	25.8	697.9	26.8
65-84	225.4	8.2	281.3	10.4	326.9	13.6	348.1	13.4
85+	28.0	1.0	35.1	1.3	27.5	1.1	35.1	1.3
Mean age (in years)	39.3		40.7		42.5		42.6	

*National estimates based on NIS hospital and sample weights. Estimates for age group <1 had too few estimated hospitalizations to report.
**Percentages account for missing data not shown in the above table.
***Cell sizes were too few to report.

Table 4. Nationally estimated hospitalization rates for cysticercosis for the period, 1998-2009

	Rate / million population
Cysticercosis hospitalizations, any diagnosis	8.16
Cysticercosis hospitalizations, primary diagnosis	3.62
Age Group	
1-17	2.78
18-44	12.69
45-64	7.18
65-84	7.33
85+	6.01
Sex	
Male	9.15
Female	7.09
Region	
Northeast	5.99
Midwest	4.84
South	6.34
West	16.10
Race/ethnicity	
White	0.93
Black	2.73
Hispanic	35.68
Asian or Pacific Islander	3.34
Native American	2.36

*National estimates based on NIS hospital and sample weights and calculated using data from the US Census Bureau[28, 29]



*National estimates based on NIS hospital and sample weights

Table 5. Nationally estimated hospitalization rates for cysticercosis, 1998-2009

	1998	1999	2000	2001	2002	2003
	Rate / million population	Rate / million population	Rate / million population	Rate / million population	Rate / million population	Rate / million population
Cysticercosis hospitalizations, any diagnosis	7.24	7.59	8.61	7.21	7.86	8.60
Cysticercosis hospitalizations, primary diagnosis	3.31	3.80	3.48	3.38	3.49	3.69
Age Group						
1-17	3.24	3.85	4.79	3.27	3.42	3.23
18-44	10.60	10.68	12.83	11.78	12.85	13.30
45-64	7.19	6.67	7.27	4.88	5.66	7.36
65-84	5.33	7.34	5.87	4.80	6.06	7.51
85+	3.45	7.98	6.21	7.92	2.73	8.31
Sex						
Male	7.94	8.36	10.01	8.68	9.34	9.16
Female	6.57	6.86	7.26	5.79	6.43	7.56
Region						
Northeast	5.45	7.43	3.95	4.11	4.08	3.66
Midwest	8.16	5.29	7.44	6.30	4.94	2.42
South	2.79	2.95	5.40	6.07	7.13	7.23
West	14.92	17.46	18.83	12.51	15.04	20.93
Race/ethnicity						
White	0.48	1.07	0.68	0.88	0.72	0.65
Black	2.61	3.40	2.33	2.19	2.22	3.18
Hispanic	35.02	37.09	44.04	32.35	34.19	39.61
Asian or Pacific Islander	2.87	4.42	1.41	2.21	2.75	6.87
Native American	**	**	**	**	6.14	**

*National estimates based on NIS hospital and sample weights acalculated using data from the US Census Bureau[28, 29]

** Indicates cell sizes too small to report

Table 5. Nationally estimated hospitalization rates for cysticercosis, 1998-2009

	2004	2005	2006	2007	2008	2009
	Rate / million population	Rate / million population	Rate / million population	Rate / million population	Rate / million population	Rate / million population
Cysticercosis hospitalizations, any diagnosis	7.70	8.40	9.23	9.01	7.88	8.50
Cysticercosis hospitalizations, primary diagnosis	3.61	3.91	4.06	3.60	3.10	3.56
Age Group						
1-17	3.33	2.32	1.83	1.72	1.24	1.19
18-44	11.54	14.06	15.48	14.49	11.88	12.76
45-64	6.16	6.81	8.38	8.39	7.86	8.69
65-84	8.02	6.95	6.98	8.58	9.73	10.16
85+	7.01	3.79	5.75	6.97	5.29	6.54
Sex						
Male	7.97	9.11	10.25	10.18	8.75	9.89
Female	7.27	7.51	8.06	7.77	6.95	6.99
Region						
Northeast	5.89	5.97	6.42	8.18	6.96	9.65
Midwest	3.07	5.43	4.25	2.97	4.59	3.39
South	7.73	7.94	7.19	7.29	7.38	6.33
West	13.66	13.94	19.47	18.16	12.51	15.85
Race/ethnicity						
White	1.07	1.29	0.66	0.88	1.55	1.19
Black	3.89	1.61	2.39	3.41	1.82	3.67
Hispanic	30.74	32.30	40.14	40.00	29.23	34.87
Asian or Pacific Islander	4.78	3.96	2.48	3.41	2.66	2.33
Native American	**	**	**	**	**	5.56

*National estimates based on NIS hospital and sample weights and calculated using data from the US Census Bureau[28, 29]

** Indicates cell sizes too small to report

References

1. García HH, Gonzalez AE, Evans CA, Gilman RH. *Taenia solium* cysticercosis. Lancet. 2003;362:547–56. doi:10.1016/S0140-6736(03)14117-7

2. Wallin MT, Kurtzke JF. Neurocysticercosis in the United States: review of an important emerging infection. Neurology. 2004;63:1559Y1564.

3. Craig, C., Faust, E., Russell, P., Craig and Faust's Clinical parasitology. 8th edition. 1976. Philadelphia Lea & Febiger.

4. Ash LR, Orihel TC. Parasites in human tissues. Chicago, IL: ASCP Press. 1995. 304-306.

5. Sorvillo, F., Wilkins, P., Shafir, S., Eberhard, M. Public Health Implications of Cysticercosis Acquired in the United States. Emerging Infectious Diseases. Vol. 17, No.1 January 2011.

6. Sorvillo FJ, Waterman SH, Richards FO, Schantz PM. Cysticercosis surveillance: locally acquired and travel-related infections and detection of intestinal tapeworm carriers in Los Angeles County. Am J Trop Med Hyg. 1992;47:365–71.

7. Schantz PM, Moore AC, Munoz JL, Hartman BJ, Schaefer JA, Aron AM, et al. Neurocysticercosis in an Orthodox Jewish community in New York City. N Engl J Med. 1992;327:692–5. DOI: 10.1056/ NEJM199209033271004

8. Richards FO Jr, Schantz PM, Ruiz-Tiben E, Sorvillo FJ. Cysticercosis in Los Angeles County. JAMA. 1985 Dec 27;254(24):3444-8.

9. del la Garza Y, Graviss EA, Daver NG, Gambarin KJ, Shandera WX, Schantz PM, White AC Jr. Epidemiology of neurocysticercosis in Houston, Texas. Am J Trop Med Hyg. 2005;73:766Y770

10. Serpa JA, Graviss EA, Kass JS, White AC Jr. Neurocysticercosis in Houston, Texas: an update. Medicine (Baltimore). 2011 Jan;90(1):81-6.

11. Sorvillo FJ, Portigal L, DeGiorgio C, Smith L, Waterman SH, Berlin GW, et al. Cysticercosis-related deaths, California. Emerg Infect Dis. 2004;10:465–9

12. O'Neal SE, Townes JM, Wilkins PP, Noh JC, Lee D, Rodriguez S, Garcia HH, Stauffer WM. Seroprevalence of antibodies against Taenia solium cysticerci among refugees resettled in United States. Emerg Infect Dis. 2012 Mar;18(3):431-8. doi: 10.3201/eid1803.111367.

13. Townes JM, Hoffman CJ, Kohn MA. Neurocysticercosis in Oregon, 1995–2000. Emerg Infect Dis. 2004;10:508–10.

14. O'Neal S, Noh J, Wilkins P, Keene W, Lambert W, Anderson J, Compton Luman J, Townes J. Taenia solium Tapeworm Infection, Oregon, 2006-2009.Emerg Infect Dis. 2011 Jun;17(6):1030-6.

15. Rosenfeld EA, Byrd SE, Shulman ST. Neurocysticercosis among children in Chicago. Clin Infect Dis. 1996;23:262–8.

16. Ong S, Talan DA, Moran GJ, Mower W, Newdow M, Tsang VC, Pinner RW; EMERGEncy ID NET Study Group. Neurocysticercosis in radiographically imaged seizure patients in U.S. emergency departments. Emerg Infect Dis. 2002 Jun;8(6):608

17. DeGiorgio C, Pietsch-Escueta S, Tsang V, Corral-Leyva G, Ng L, Medina MT, Astudillo S, Padilla N, Leyva P, Martinez L, Noh J, Levine M,del Villasenor R, Sorvillo F. Sero-prevalence of Taenia solium cysticercosis and Taenia solium taeniasis in California, USA. Acta Neurol Scand. 2005 Feb;111(2):84-8.

18. Sorvillo FJ, DeGiorgio C, Waterman SH. Deaths from cysticercosis in the United States. Emerg Infect Dis. 2007;13:230–5. DOI: 10.3201/eid1302.060527

19. Croker C, Reporter R, Mascola L. Use of statewide hospital discharge data to evaluate the economic burden of neurocysticercosis in Los Angeles County (1991–2008). Am J Trop Med Hyg. 2010;83:106–10. doi:10.4269/ajtmh.2010.09-0494

20. Croker C, Redelings M, Reporter R, Sorvillo F, Mascola L, Wilkins P. The impact of neurocysticercosis in california: a review of hospitalized cases. PLoS Negl Trop Dis. 2012 Jan;6(1):e1480. doi: 10.1371/journal.pntd.0001480. Epub 2012 Jan 24.

21. Shandera WX, White AC Jr, Chen JC, Diaz P, Armstrong R. Neurocysticercosis in Houston, Texas. A report of 112 cases. Medicine (Baltimore). 1994 Jan;73(1):37-52.

22. Garcia HH, Del Brutto OH; Cysticercosis Working Group in Peru. Neurocysticercosis: updated concepts about an old disease. Lancet Neurol. 2005;4:653–61. DOI: 10.1016/S1474 4422(05)70194-0

23. Del Brutto OH, García HH. Neurocysticercosis in nonendemic countries: time for a reappraisal. Neuroepidemiology. 2012;39(2):145-6. Epub 2012 Aug 22.

24. Kruskal BA, Moths L, Teele DW. Neurocysticercosis in a child with no history of travel outside the continental United States. Clin Infect Dis. 1993;16:290–2.

25. HCUP Databases. Healthcare Cost and Utilization Project (HCUP). Overview of the Nationwide Inpatient Sample (NIS). November 2011. Agency for Healthcare Research and Quality, Rockville, MD. http://www.hcup-us.ahrq.gov/nisoverview.jsp

26. Healthcare Cost and Utilization Project (HCUP). Introduction to the HCUP Nationwide Inpatient Sample (NIS) 2009. Agency for Healthcare Research and Quality, Rockville, MD. Issued May 2011. http://www.hcupus.ahrq.gov/db/nation/nis/NIS_Introduction_2009.jsp

27. Healthcare Cost and Utilization Project (HCUP). Description of Data Elements, Nationwide Inpatient Sample Hospital Weights File. Agency for Healthcare Research and Quality, Rockville, MD. May 2002.

28. US Census Bureau. Resident Population Estimates of the United States by Sex, Race, and Hispanic Origin: April 1, 1990 to July 1, 1999, with Short-Term Projection to November 1, 2000. Available at: http://www.census.gov/popest/data/national/totals/1990s/tables/nat-srh.txt

29. US Census Bureau. National Intercensal Estimates (2000-2010). Available at: http://www.census.gov/popest/data/intercensal/national/nat2010.html

30. Garcia HH, Del Brutto OH, Nash TE, White AC Jr, Tsang VC, Gilman RH. New concepts in the diagnosis and management of neurocysticercosis (Taenia solium). Am J Trop Med Hyg. 2005;72:3Y9.

31. Yancey LS, Diaz-Marchan PJ, White AC. Cysticercosis: Recent Advances in Diagnosis and Management of Neurocysticercosis. Curr Infect Dis Rep. 2005 Jan;7(1):39-47.

32. Ehnert KL, Roberto RR, Barrett L, Sorvillo FJ, Rutherford GW 3rd. Cysticercosis: first 12 months of reporting in California. Bull Pan Am Health Organ. 1992;26(2):165-72.

33. US Census Bureau. U.S. Census Bureau projections show a slower growing, older, more diverse nation a half century from now. Newsroom. December 12, 2012. https://www.census.gov/newsroom/releases/archives/population/cb12-243.html

34. Wilkins PP, Allan JC, Verastegui M, Acosta M, Eason AG, Garcia HH, et al. Development of a serologic assay to detect *Taenia solium* taeniasis. Am J Trop Med Hyg. 1999;60:199-204.

35. Noskin GA, Rubin RJ, Schentag JJ, Kluytmans J, Hedblom EC, Smulders M, Lapetina E, Gemmen E. The burden of Staphylococcus aureus infections on hospitals in the United States: an analysis of the 2000 and 2001 Nationwide Inpatient Sample Database. Arch Intern Med. 2005 Aug 8-22;165(15):1756-61.

36. Roman G, Sotelo J, Del Brutto OH, Flisser A, Dumas M, Wadia N, Botero D, Cruz M, Garcia H, de Bittencourt PR, Trelles L, Arriagada C, Lorenzana P, Nash TE, Spina-França A: A proposal to declare neurocysticercosis an international reportable disease. Bull WHO 2000;78:399–406.

Chapter 2 – Cysticercosis Mortality and Associated Risk Factors Among Hospitalized Patients in the United States

INTRODUCTION

Cysticercosis, caused by infection with the larval form of the pork tapeworm *Taenia solium*, is an important global public health problem.[1] Neurocysticercosis (NCC), the most severe form of disease, occurs when the larvae invade the central nervous system of a host.[2, 3] With improvements in diagnostic techniques in recent years as well as increased immigration from endemic areas, cysticercosis, especially NCC, has become much more frequently diagnosed in the United States, a country traditionally considered to be nonendemic.[3, 4]

Humans become infected with the adult tapeworm, a condition known as taeniasis, upon consumption of raw or undercooked pork containing the larval form, or cysticerci.[2, 5] Once the larva is digested out of the pork flesh in the stomach, it attaches to the wall of the small intestine and develops into a mature worm in approximately 1-3 months.[1, 2, 5, 6] Pigs become infected with the larval form after ingesting embryonated eggs, shed in the feces of a human carrier of the adult worm.[5] Humans acquire cysticercosis through consumption of food or water contaminated with *T. solium* eggs.[5] Cysticercosis outside the central nervous system typically does not produce major symptoms, though symptom severity and presentation of infection varies according to the number and location of cysticerci present.[1] Ocular cysticercosis, however, can lead to severe pain or loss of vision and NCC can cause seizures, meningitis, increased intracranial pressure, and hydrocephalus.[2]

Due to the severity of potential symptoms, NCC can often lead to hospitalization and can occasionally result in fatality, though less frequently. The WHO has previously reported worldwide estimates of over 50,000 deaths due to NCC each year.[7] Cysticercosis deaths have been identified in many different studies specifically throughout the United States, though few have utilized hospital records to study disease and those that have tended to focus analysis on a local or statewide level.[8-15] These studies help to describe the burden of cysticercosis fatalities, but further analysis on a comprehensive national scale is required to truly understand the impact of cysticercosis mortality in the United States, particularly given the lack of required reporting of cysticercosis cases in most states.[16] There are also very limited studies existing which attempt to describe potential risk factors associated with in-hospital fatality in the United States.[13] This study presents analyses aimed at expanding the pool of knowledge regarding cysticercosis fatality in the US by examining nationwide hospital discharge records for in-hospital fatality among patients diagnosed with cysticercosis. In addition, risk factors associated with in-hospital deaths among identified cysticercosis cases, including demographic, hospital stay and insurance characteristics, are also described.

METHODS

Data source

Hospital discharge records from yearly datasets of the Nationwide Inpatient Sample (NIS) were used for analysis. The NIS is the largest, publically available hospital inpatient database in the United States containing information on patients of all-payer types, and was developed as part of the Healthcare Cost and Utilization Project (HCUP), which is sponsored by the Agency for Healthcare Research and Quality.[17] The NIS is designed to represent a stratified sample of 20%

of US community hospitals, with each annual NIS containing 5-8 million hospitalization records from approximately 1,000 hospitals sampled around the country.[17] Stratification variables include geographic region, ownership, location, teaching status and bed size.[17] The datasets are drawn from states participating in HCUP, which most recently in 2009, was comprised of 44 states representing 96% of the US population.[17] The NIS contains demographic and institutional level variables for discharged patients, as well as hospital stay information including up to 15 diagnoses and procedures (expanded to 25 diagnoses in 2009), length of stay and in-hospital fatality outcomes.[17]

Case identification

This study examined hospitalization records contained in the NIS over the 12-year period 1998-2009. The first step of analysis was to extract cysticercosis hospitalizations from each yearly NIS, using the International Classification of Diseases, Ninth Revision, Clinical Modifications (ICD-9-CM) diagnostic code for cysticercosis (123.1) listed for either primary or non-primary diagnoses. In-hospital fatalities were identified from extracted records with a diagnosis of cysticercosis based on the variable recording in-hospital death.

Data analysis

Discharge weights which accounted for the complex stratified cluster sampling scheme of the NIS were used to produce national estimates of cysticercosis fatalities, including 95% confidence intervals (CIs). Demographic information for nationally estimated in-hospital fatality cases were summarized, although due to data use restrictions for the NIS designed to protect confidentially of patients, certain estimates could not be reported because of small size.[17] "Age at admission"

was summarized both by calculating average age (in years) and by separating age into 5 categories of age group (1-17, 18-44, 45-64, 65-84, and 85+ years of age) for interpretability. Case-fatality rates for the overall 12 year period, as well as year-stratified estimates, were calculated. Population estimates obtained from the US Census Bureau were used to calculate national rates of in-hospital mortality among cysticercosis-related hospitalizations.[18, 19] Bivariate and multivariate logistic regression techniques, accounting for the sampling design of the NIS, were used to calculate odds ratio (OR) and 95% confidence interval (CI) estimates of risk factors associated with in-hospital fatality among cysticercosis hospitalizations. Possible risk factors for in-hospital fatality included age, sex, region (Northeast, Midwest, South and West), primary payer, hospital teaching status (non-teaching vs. teaching), hospital location (urban vs. rural) and hospital bed size (small, medium and large). As previous studies have also found an association between surgical shunting procedures, hydrocephalus and fatality, a variable indicating whether or not "insertion, replacement, or removal of extracranial ventricular shunt" had been performed was created using the HCUP Clinical Classification Software (CCS) coding variables, as well as a variable identifying whether or not a patient record included a diagnosis of obstructive hydrocephalus using the ICD-9-CM code 331.4. [13, 20, 21] Both of these variables were used as a predictors in fatality regression models.

Bivariate analysis employed separate logistic regression models for each variable to produce unadjusted ORs. Multivariate logistic regression was then performed adjusting for age, sex, listed obstructive hydrocephalus diagnosis, hospital region, primary payer and year of hospitalization. Possible risk factors of interest and potential confounding variables included in

the models were chosen based on risk factors recognized from the published literature on cysticercosis and biologic plausibility.[13]

Data for one or more of the variables of interest were missing in approximately 20% of the study sample, most frequently for the variable of race/ethnicity. For descriptive statistics, all variables of interest were summarized. To minimize potential bias in analyses of in-hospital fatality risk factors, the complete-subject approach was used which completely excluded any records with missing predictor variables for regression modeling.[22] All data analysis was performed using SAS version 9.2 (SAS Institute, Cary, North Carolina, USA).

RESULTS

National estimates for the total number of in-hospital deaths in cysticercosis-related hospitalizations, both for the overall 12 year period and stratified by year, are presented in Table 1. The total number of national in-hospital deaths among discharge records including a diagnosis of cysticercosis from 1998-2009 was estimated to be 364 (95% CI [244.4 - 484.1]), ranging from 14.2 deaths (95% CI [-2.1- 30.5]) estimated in 2001 to 43.9 deaths (95% CI [6.5-81.3]) estimated in 2000. Case-fatality rates, presented in Table 1 and Figure 1, measuring the percentage of cysticercosis-related hospitalizations which ended with in-hospital death, varied throughout the study period ranging from a low of 0.69% in 2001 to a high of 2.58% in 2002, with an overall case-fatality rate for the 12-year period of 1.28%. In-hospital mortality rates for cysticercosis-related hospitalizations, based on population data from US Census estimates, are presented in Table 1. In-hospital mortality rates ranged from 0.05 deaths per million population in 2001 to 0.20 deaths per million population in 2002, with an overall mortality rate for the study period of 0.10 deaths per million population.

Demographic, institutional and hospital stay characteristics of cysticercosis-related hospitalizations are presented in Table 2. Results showed a higher proportion of males than females among cysticercosis related in-hospital deaths (59.3% vs. 40.7%). The largest proportion of deaths were Hispanic (56.3%), followed by white (11.4%), and black (5.1%). National estimates for the numbers of Asian or Pacific Islanders, Native American or "other" race/ethnicity categories could not be presented due to NIS data use restrictions on presentation of small counts. Most cases occurred in adults aged 18-44 and 45-64 (36.9% and 34.1% respectively), with a mean age at death of 53.0 years (range between 2 and 88 years). The largest number of fatal cysticercosis-related hospitalizations occurred in the West region of the country (59.1%), with the smallest proportion occurring in the Northeast (7.7%). More deaths occurred at teaching hospitals than in non-teaching hospitals (57.2% vs. 42.8%) and in hospitals with a bed size classification of large (70.8%). The highest proportion of cysticercosis deaths listed Medicaid as the primary payer (29.9%), followed by Medicare (23%) and private insurance (19.9%).

Bivariate and multivariate analyses estimating the unadjusted and adjusted ORs of in-hospital fatality among cysticercosis-related hospitalizations are presented in Table 3. In bivariate analyses of patient characteristics, male sex (OR: 1.18, 95% CI 0.74 – 1.87), Asian/Pacific Islander race/ethnicity (OR: 1.21, 95% CI 0.25 – 5.86), increasing age (OR per year: 1.04, 95% CI: 1.03 – 1.05) and a primary payer of Medicare (OR: 2.88, 95% CI: 1.45 – 5.72), likely due to the association of Medicare with age, were positively associated with in-hospital fatality. Institutional characteristics positively associated with in-hospital fatality included location in the West (OR: 2.36, 95% CI: 0.93 – 6.01) or Midwest (OR: 1.90, 95% CI: 0.64 – 5.62) regions. No

institutional characteristics were statistically significantly associated with in-hospital fatality. Increasing length of stay was positively associated with in-hospital fatality (OR per day: 1.02, 95% CI: 1.01 – 1.02), as were having had an "insertion, replacement, or removal of extracranial ventricular shunt" performed during hospital stay" (OR: 1.79, 95% CI: 0.88 – 3.61) and a listed diagnosis of obstructive hydrocephalus (OR: 2.85, 95% CI: 1.73 – 4.68).

In multivariate analysis, upon adjusting for age, year of hospitalization, sex, primary payer, hospital region and a listed diagnosis of obstructive hydrocephalus, age remained a statistically significant positively associated factor with in-hospital fatality (OR per year: 1.05, 95% CI: 1.03 – 1.06, p-value <0.0001), as did a listed diagnosis of obstructive hydrocephalus (OR: 3.14, 95% CI: 1.90 – 5.17, p-value <0.0001). Upon model inclusion of controlling variables including the highly related variable of age, Medicare was found to be negatively associated with in-hospital fatality, though the association was not statistically significant.

DISCUSSION

Male sex, increasing age and Asian/Pacific Islander race/ethnicity were each positively associated with increased odds of in-hospital fatality in bivariate analysis, though only the association with age was statistically significant. In multivariate analysis, adjusting for potential confounding variables noted above, the positive association with in-hospital fatality and male sex became stronger, and black race/ethnicity also appeared to be positively associated with in-hospital fatality. The higher proportion of males with cysticercosis-related in-hospital deaths is consistent with previous studies of cysticercosis mortality in the United States, though inconsistent with studies conducted using hospitalization records in California.[8-10, 15] This could possibly reflect greater exposure and higher inoculum for males. The mean age at death (53.0

years) found in national estimates was slightly higher than that seen in previous studies on fatal cysticercosis cases, most of which reported mean ages in the 30-50 years of age range.[8-10, 14, 15, 23] This supports previous assertions that cysticercosis is indeed a cause of premature death in the United States.[9] Reported race/ethnicity observed amongst fatal cysticercosis hospitalizations in this study had a more diverse distribution than that seen in other studies of fatal cysticercosis in the United States, which reported proportions of Latino populations above 80 or 90%.[8-10, 15] It is worthy of note that data for the race/ethnicity variable was missing in a large number of fatal cysticercosis-related hospitalization records. These results indicate that although the majority of cysticercosis deaths occur in Hispanic populations, it is important to recognize that members of other race/ethnicity categories are also at risk for both infection and fatality.

Recommended management and treatment strategies are very dependent on an individual's infection with cysticercosis, in particular NCC, and can vary depending on the size, location and number of cysts, as well as the host's immune response.[24, 25] Treatment of neurocysticercosis with anthelminthic medications can be potentially beneficial in certain cases of disease, and potentially harmful in others due to complications caused by host inflammatory response, which can lead to severe morbidity and death.[24, 25] Because treatment strategies for disease can be complicated, physicians must be aware of factors that put a patient at particular risk of fatal infection. [13] Physician education regarding the safest and most effective treatment course for each case of infection may lead to significant improvement in patient outcome, reducing both morbidity and mortality due to cysticercosis.

Though not statistically significant, the associations seen between fatality and both hospital teaching status and hospital location could reflect a lower number of resources and unfamiliarity

with disease inhibiting appropriate treatment procedures from being performed. The observed association between smaller bed size and decreased odds of fatality could possibly be attributed to the likelihood of patients with more severe disease, thus greater inherent risk of fatality, having a tendency to utilize larger hospitals. Upon adjustment, no primary payer categories were found to be significantly associated with fatality. This could potentially reflect limitations in calculation of more robust statistics due to a relatively low case-fatality rate of cysticercosis infection.

Regional associations with in-hospital fatality represent potential deficiencies in identification of disease and use of appropriate diagnostic and treatment methods. Unfamiliarity with disease in regions where physicians do not typically encounter large number of cases of disease can lead to misuse of diagnostic and treatment strategies that may be unnecessarily invasive and potentially risky.[3] Even in regions where disease is more commonly observed, controversy over the use of antihelminthic medications and the complexities of developing an appropriate treatment strategy for cases of cysticercosis may lead physicians to avoid use of treatment strategies that might be beneficial.[13, 24]

Symptomatic factors associated with case-fatality have been described in previous studies indicating a relationship between surgical procedures and fatality, potentially due to shunt-related infections.[13, 20] Though not statistically significant, results from bivariate analysis were consistent with previous findings indicating an association between in-hospital fatality and insertion, replacement, or removal of extracranial ventricular shunt. While this might be due to previously observed increased risks of shunt-related infections, results must be viewed with

caution, as shunt placement can be associated with more severe disease which inherently carries greater risk of fatality.

Despite improvements in treatment strategies for cysticercosis and NCC in recent years, results from this study have failed to show consistent improvements in the case-fatality rate of cysticercosis-related hospitalizations nationwide, remaining in the range of 1-2% for most years of the study period.[26] Case-fatality rates found in this study were consistent with those seen in previous studies of cysticercosis hospitalizations.[10] Study estimated in-hospital deaths and mortality rates found in cysticercosis-related hospitalizations add to the existing knowledge of cysticercosis mortality found in previous studies.[8, 9, 11-14] Reducing mortality represents a potential area for improvement in cysticercosis management in the United States.

Although the NIS records contain valuable data for describing nationwide disease burden and fatality, information taken from hospital records does contain inherent limitations. The possibility of demographic and institutional variable misclassification and miscoding of diagnostic codes exists, and a lack of patient identifiers in records and confidentiality restrictions in NIS data use prevent validation of diagnosis, treatment and patient characteristics. ICD-9-CM coding used for recording of diagnoses also does not contain a breakdown of different forms of cysticercosis and NIS coding does not provide for a comprehensive evaluation of diagnostic test results. Because of this, further analyses regarding type of cysticercosis infection or location/size of present cysts were not possible using data in this study. It is likely that most, if not all, hospitalized cases represent neurocysticercosis as this is well-regarded as the most severe manifestation of disease.[1] Other studies conducted in US hospitals have reported findings including further description of cyst size, location and type observed in patient records. [27, 28]

Use of hospitalization data could result in significant underreporting of less severe infection, leading to overestimates of true case-fatality, as less severe cases absent from the dataset cannot be included in calculations. In contrast, each record in the NIS is limited to the duration of the single hospital stay that the discharge record represents which prevents information regarding hospital readmission, transfer to other facilities or fatality following discharge from being obtained. Thus, true nationwide case-fatality including those that do not die in hospital could be underestimated when using in-hospital fatality estimates. Moreover, persons who die at home or in an emergency department, and may be more likely to lack health insurance and adequate access, would not be included in this data. It is unclear how these factors balance each other, but each should be taken into account when extrapolating overall nationwide case-fatality from in-hospital fatality estimates. Estimated patient characteristics found in this study will likely match more with patients experiencing more severe symptoms of disease.

Additionally, although an important infection in the United States, the relatively low case-fatality and numbers of deaths prevented the calculation of more robust statistics.

Conclusions

Although cysticercosis fatality is relatively infrequent in the United States, with the availability of prevention methods including diagnostic and treatment strategies for the adult worm carrier to prevent transmission, cysticercosis has the potential to be eliminated.[29] In 1993, the recommendations from the International Task Force for Disease Eradication, convened by the Carter Center of Emory University, declared cysticercosis potentially eradicable.[30] Despite this assertion, the number of deaths, case-fatality rates and hospital mortality rates have not been shown to decrease significantly in the US in the last decade. Much of this can likely be attributed

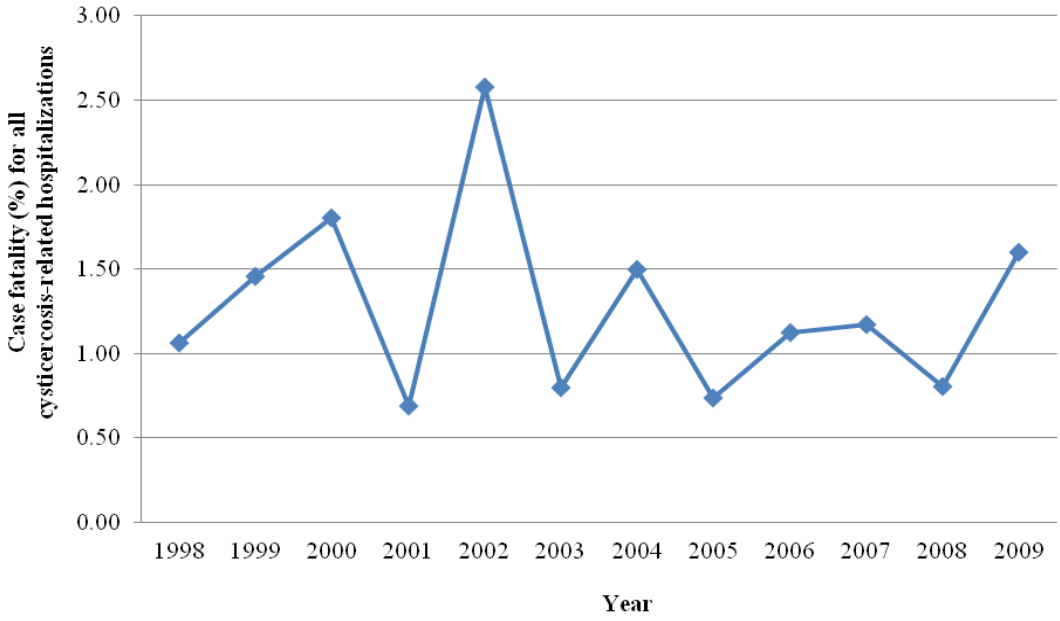
to the complex and various courses of cysticercosis and NCC infection and difficulties in choosing the most beneficial treatment strategy for each case.[24, 25] It has been recognized that physicians involved in deciding the course of treatment for affected patients would benefit from an increased awareness of the factors associated with cysticercosis case-fatality.[13] Results regarding demographic features of patients associated with fatality may provide further understanding to help physicians identify those patients that have the greatest risk of dying and using appropriate treatment methods accordingly.[13] Findings on associations between in-hospital death and institutional and payer characteristics highlight the possibility of existing disparities in effective treatment between hospitals with unequal resources available for disease management, inconsistent physician knowledge about cysticercosis, and limited treatment options for those who might not have the access or opportunity for newer procedures such as endoscopic removal of intraventricular cysts, and others. Further study on these factors among a larger number of cysticercosis deaths could enable the calculation of more robust statistics regarding associations. Striving to close the gaps in any existing institutional disparities by universally increasing physician awareness and education about proper diagnostic and treatment methods for different courses of cysticercosis infection will hopefully help in reducing the impact the disease has throughout the United States.

Table 1. Nationally estimated deaths, case-fatality and mortality rates for cysticercosis hospitalizations, 1998-2009

	n	95% CI	Case-fatality %	Mortality rate per million population
1998	21.3	[0.27 – 42.4]	1.07	0.08
1999	30.9	[6.4 – 55.5]	1.46	0.11
2000	43.9	[6.5 – 81.3]	1.81	0.16
2001	14.2	[-2.1 – 30.5]	0.69	0.05
2002	58.3	[23.8 – 92.8]	2.58	0.20
2003	20.0	[0.6 – 39.4]	0.80	0.07
2004	33.7	[8.9 – 58.5]	1.50	0.12
2005	18.2	[0.7 – 35.8]	0.73	0.06
2006	30.9	[6.1 – 55.8]	1.12	0.10
2007	31.8	[8.7 – 54.9]	1.17	0.11
2008	19.3	[0.4 – 38.3]	0.81	0.06
2009	41.7	[9.2 – 74.2]	1.60	0.14
Total	364.3	[244.4 – 484.1]	1.28	0.10

*National estimates based on NIS hospital and sample weights and calculated using data from the US Census Bureau[18, 19]

Figure 1. Nationally estimated cysticercosis in-hospital case-fatality rates, 1998-2009



*National estimates based on NIS hospital and sample weights

Table 2. Demographic, institutional and hospital stay characteristics of nationally estimated cysticercosis-related in-hospital deaths, all years 1998-2009

	n	95% CI	%
Total deaths	364.3	[244.4 – 484.1]	
Sex			
Male	216.2	[140.5 – 291.8]	59.3
Female	148.1	[80.3 – 215.9]	40.7
Race/ethnicity			
White	41.6	[14.4 – 68.7]	11.4
Black	18.6	[0.3 – 37.0]	5.1
Hispanic	205.1	[100.7 – 309.6]	56.3
Asian or Pacific Islander	*	* *	*
Native American	*	* *	*
Region of hospital			
Northeast	27.9	[3.5 – 52.3]	7.7
Midwest	51.0	[16.7 – 85.3]	14.0
South	69.9	[28.9 – 111.0]	19.2
West	215.4	[111.0 – 319.9]	59.1
Hospital teaching status			
Non-teaching	155.9	[58.0 – 253.9]	42.8
Teaching	208.3	[139.2 – 277.5]	57.2
Bed size of hospital			
Small	23.4	[2.8 – 43.9]	6.4
Medium	82.9	[44.3 – 121.5]	22.8
Large	258.0	[146.4 – 369.6]	70.8
Primary payer			
Medicare	83.7	[26.2 – 141.3]	23.0
Medicaid	108.8	[61.0 – 156.5]	29.9
Private insurance (including HMO)	72.5	[36.6 – 108.3]	19.9
Self-pay (uninsured)	63.4	[26.2 – 100.6]	17.4
Other	30.5	[2.6 – 58.3]	8.4
Age group			
1-17	*	* *	*
18-44	134.6	[75.0 – 194.2]	36.9
45-64	124.4	[66.7 – 182.0]	34.1
65-84	86.8	[44.4 – 129.2]	23.8
85+	*	* *	*

Mean age (in years)	53.0	[48.6	–	57.3]	Range: 2–88
Average length of hospital stay (in days)	13.5	[9.3	–	17.7]	

*Denotes values which were too small due report due to NIS data use restrictions.

+Percentages account for missing data not presented here.

Table 3. Predictors of in-hospital fatality among cysticercosis-related hospitalizations, 1998-2009

	Cysticercosis Hosp. in NIS 98-09 (n)	Unadj. OR	95% CI	Adj. OR*	95% CI
Year (per year)	--	0.98	[0.92 – 1.05]	0.97	[0.91 – 1.04]
Sex					
Male	2591	1.18	[0.74 – 1.87]	1.46	[0.88 – 2.41]
Female	3226	Ref.		Ref.	
Race/ethnicity					
White	448	Ref.			
Black	235	0.84	[0.25 – 2.77]	1.23	[0.36 – 4.18]
Hispanic	3593	0.62	[0.30 – 1.28]	0.64	[0.29 – 1.41]
Asian or Pacific Islander	103	1.21	[0.25 – 5.86]	1.19	[0.23 – 6.32]
Native American	**	**	** **	**	** **
Other	419	0.25	[0.05 – 1.19]	0.43	[0.09 – 2.02]
Region of hospital					
Northeast	750	Ref.		Ref.	
Midwest	739	1.90	[0.64 – 5.62]	1.81	[0.61 – 5.37]
South	1697	1.22	[0.44 – 3.40]	1.31	[0.46 – 3.69]
West	2675	2.36	[0.93 – 6.01]	1.64	[0.63 – 4.26]
Hospital teaching status					
Non-teaching	2307	1.19	[0.75 – 1.88]	0.96	[0.60 – 1.53]
Teaching	3543	Ref.		Ref.	
Hospital location					
Rural	128	1.20	[0.28 – 5.17]	1.36	[0.32 – 5.87]
Urban	5722	Ref.		Ref.	
Bed size of hospital					
Small	481	0.76	[0.30 – 1.94]	0.90	[0.34 – 2.36]
Medium	1555	0.81	[0.47 – 1.41]	0.88	[0.51 – 1.51]
Large	3814	Ref.		Ref.	
Primary payer					
Medicare	641	2.88	[1.45 – 5.72]	0.79	[0.34 – 1.81]
Medicaid	1644	1.41	[0.73 – 2.72]	1.26	[0.63 – 2.54]
Private insurance (including HMO)	1548	Ref.		Ref.	
Self-pay (uninsured)	1431	0.95	[0.45 – 2.00]	1.21	[0.56 – 2.61]
Other	578	1.13	[0.43 – 2.97]	1.20	[0.45 – 3.18]
Age (per year of age)		1.04	[1.03 – 1.05]	1.05	[1.03 – 1.06]

Length of stay (per day)	1.02	[1.01	–	1.02]	1.01	[1.00 – 1.02]
Insertion, replacement, or removal of extracranial ventricular shunt	1.79	[0.88	–	3.61]	0.85	[0.35 – 2.04]
Listed diagnosis of obstructive hydrocephalus	2.85	[1.73	–	4.68]	3.14	[1.90 – 5.17]

*Adjusted for age, sex, listed diagnosis of obstructive hydrocephalus, hospital region, primary payer and year of hospitalization

**Calculation of OR estimates not possible due to cell size

References

1. García HH, Gonzalez AE, Evans CA, Gilman RH. *Taenia solium* cysticercosis. Lancet. 2003;362:547–56. doi:10.1016/S0140-6736(03)14117-7

2. Ash LR, Orihel TC. Parasites in human tissues. Chicago, IL: ASCP Press. 1995. 304-306.

3. Del Brutto OH, García HH. Neurocysticercosis in nonendemic countries: time for a reappraisal. Neuroepidemiology. 2012;39(2):145-6. Epub 2012 Aug 22.

4. Schantz PM, Tsang VC. The US Centers for Disease Control and Prevention (CDC) and research and control of cysticercosis. Acta Trop. 2003 Jun;87(1):161-3.

5. Craig, C., Faust, E., Russell, P., Craig and Faust's Clinical parasitology. 8th edition. 1976. Philadelphia Lea & Febiger.

6. White Jr AC. Neurocysticercosis: updates on epidemiology, pathogenesis, diagnosis, and management. Annu Rev Med 2000;51: 187- 206.

7. Román G, Sotelo J, Del Brutto O, Flisser A, Dumas M, Wadia N, Botero D, Cruz M, Garcia H, de Bittencourt PR, Trelles L, Arriagada C, Lorenzana P, Nash TE,Spina-França A. A proposal to declare neurocysticercosis an international reportable disease. Bull World Health Organ. 2000;78(3):399-406.

8. Sorvillo FJ, Portigal L, DeGiorgio C, Smith L, Waterman SH, Berlin GW, et al. Cysticercosis-related deaths, California. Emerg Infect Dis. 2004;10:465–9

9. Sorvillo FJ, DeGiorgio C, Waterman SH. Deaths from cysticercosis in the United States. Emerg Infect Dis. 2007;13:230–5. DOI: 10.3201/eid1302.060527

10. Croker C, Reporter R, Mascola L. Use of statewide hospital discharge data to evaluate the economic burden of neurocysticercosis in Los Angeles County (1991–2008). Am J Trop Med Hyg. 2010;83:106–10. doi:10.4269/ajtmh.2010.09-0494

11. Sorvillo FJ, Waterman SH, Richards FO, Schantz PM. Cysticercosis surveillance: locally acquired and travel-related infections and detection of intestinal tapeworm carriers in Los Angeles County. Am J Trop Med Hyg. 1992;47:365–71.

12. Richards FO Jr, Schantz PM, Ruiz-Tiben E, Sorvillo FJ. Cysticercosis in Los Angeles County. JAMA. 1985 Dec 27;254(24):3444-8.

13. DeGiorgio CM, Houston I, Oviedo S, Sorvillo F. Deaths associated with cysticercosis. Report of three cases and review of the literature. Neurosurg Focus. 2002 Jun 15;12(6):e2.

14. Townes JM, Hoffman CJ, Kohn MA. Neurocysticercosis in Oregon, 1995–2000. Emerg Infect Dis. 2004;10:508–10.

15. Croker C, Redelings M, Reporter R, Sorvillo F, Mascola L, Wilkins P. The impact of neurocysticercosis in California: a review of hospitalized cases. PLoS Negl Trop Dis. 2012 Jan;6(1):e1480. doi: 10.1371/journal.pntd.0001480. Epub 2012 Jan 24.

16. Sorvillo, F., Wilkins, P., Shafir, S., Eberhard, M. Public Health Implications of Cysticercosis Acquired in the United States. Emerging Infectious Diseases. Vol. 17, No.1 January 2011.

17. Healthcare Cost and Utilization Project (HCUP). Introduction to the HCUP Nationwide Inpatient Sample (NIS) 2009. Agency for Healthcare Research and Quality, Rockville, MD. Issued May 2011. http://www.hcupus.ahrq.gov/db/nation/nis/NIS_Introduction_2009.jsp

18. US Census Bureau. Resident Population Estimates of the United States by Sex, Race, and Hispanic Origin: April 1, 1990 to July 1, 1999, with Short-Term Projection to November 1, 2000. Available at: http://www.census.gov/popest/data/national/totals/1990s/tables/nat-srh.txt

19. US Census Bureau. National Intercensal Estimates (2000-2010). Available at: http://www.census.gov/popest/data/intercensal/national/nat2010.html

20. Colli BO, Martelli N, Assirati JA Jr, Machado HR, de Vergueiro Forjaz S. Results of surgical treatment of neurocysticercosis in 69 cases. J Neurosurg. 1986 Sep;65(3):309-15.

21. HCUP Databases. Healthcare Cost and Utilization Project (HCUP). Clinical Classifications Software (CCS) for ICD-9-CM. Accessed May 2011. Agency for Healthcare Research and Quality, Rockville, MD. http://www.hcup-us.ahrq.gov/toolssoftware/ccs/ccs.jsp#download

22. Rothman, K.J., Greenland, S., Lash, T.L., Modern Epidemiology. Third Edition. 2008 Lippincott Williams & Wilkins.

23. Serpa JA, Clinton White A Jr. Neurocysticercosis in the United States. Pathog Glob Health. 2012 Sep;106(5):256-60. doi: 10.1179/2047773212Y.0000000028.

24. Nash TE, Singh G, White AC, Rajshekhar V, Loeb JA, Proaño JV, Takayanagui OM, Gonzalez AE, Butman JA, DeGiorgio C, Del Brutto OH,Delgado-Escueta A, Evans CA, Gilman RH, Martinez SM, Medina MT, Pretell EJ, Teale J, Garcia HH

Treatment of neurocysticercosis: current status and future research needs. Neurology. 2006 Oct 10;67(7):1120-7

25. Nash TE, Garcia HH. Diagnosis and treatment of neurocysticercosis. Nat Rev Neurol. 2011 Sep 13;7(10):584-94. doi: 10.1038/nrneurol.2011.135.

26. Garcia HH, Del Brutto OH, Nash TE, White AC Jr, Tsang VC, Gilman RH. New concepts in the diagnosis and management of neurocysticercosis (Taenia solium). Am J Trop Med Hyg. 2005;72:3Y9.

27. Shandera WX, White AC Jr, Chen JC, Diaz P, Armstrong R. Neurocysticercosis in Houston, Texas. A report of 112 cases. Medicine (Baltimore). 1994 Jan;73(1):37-52.

28. Rosenfeld EA, Byrd SE, Shulman ST. Neurocysticercosis among children in Chicago. Clin Infect Dis. 1996;23:262–8.

29. Wilkins PP, Allan JC, Verastegui M, Acosta M, Eason AG, Garcia HH, et al. Development of a serologic assay to detect *Taenia solium* taeniasis. Am J Trop Med Hyg. 1999;60:199–204.

30. Centers for Disease Control. Recommendations of the international task force for disease eradication. Morb Mortal Wkly Rep 1993;42:1–38.

Chapter 3 - Economic Impact of Cysticercosis Hospitalizations in the United States

INTRODUCTION

Infection with the larval form of the tapeworm *Taenia solium*, known as cysticercosis, causes appreciable morbidity both worldwide and in the United States, and can exact a significant financial toll on both infected individuals and health care systems.[1-3] Studies conducted worldwide have found considerable costs associated with symptoms of illness, loss of productivity and treatment associated in particular with the most severe form of disease, neurocysticercosis (NCC), when the larvae migrate to the human central nervous system.[4, 5] Neurocysticercosis is one of the main causes of acquired epilepsy globally, commonly resulting in debilitating symptoms which can require extensive medical management and treatment strategies.[3]

Humans are the definitive host for the adult *T. solium* tapeworm and acquire the infection through the consumption of raw or undercooked pork containing the larval form of the parasite, or cysticercus.[3, 6] The larva attaches to the intestinal wall, and is capable of producing eggs within 1-3 months.[3, 7, 8] The life cycle of *T. solium* is frequently able to continue in areas where human waste is improperly disposed, when the pig intermediate host comes into contact with and ingests feces containing infective eggs shed by a human carrier of the adult worm.[3] Humans usually acquire cysticercosis upon consumption of food or water contaminated with human fecal material containing the infective eggs of *T. solium.*[7] Once ingested, the shell of the egg disintegrates and the oncosphere is released, penetrates the intestinal mucosa and is transported via the bloodstream where it lodges in various tissues and continues to develop into a

cysticercus.[6, 9] Severe infection can occur when the larva migrates to the central nervous system, causing NCC.[3]

Detection and treatment of cysticercosis can be enormously expensive. Neuroimaging, utilizing magnetic resonance imaging (MRI) and computed tomography (CT), is one of the most important diagnostic tools for cysticercosis, though associated costs with these techniques can be prohibitive.[3, 10-12] Treatment strategies for cysticercosis, in particular NCC, can be complex and challenging, as well as exact a huge financial toll on infected individuals.[3, 13] Treating neurocysticercosis with antiparasitic drugs, such as albendazole, can lead to potential worsening of neurologic symptoms due to the perilesional inflammatory response, which has led to some contention about the use of these drugs in treatment.[3] In cases where patients might be at particular risk of complications from antiparasitic drugs, surgical techniques including cyst removal and ventricular shunt placement can be utilized, though these therapeutic methods can be quite expensive.[3, 13] Surgical treatment can also result in significant complications, which can be associated with additional costs and increased risk of mortality.[14, 15] In all cases of NCC, it is recommended that treatment strategies be adapted to each patient based on characteristics of individual infection, such as number, location and viability of cysticerci and clinical presentations of disease.[3, 13, 16, 17]

Studies conducted in endemic countries in South America, Africa and India found substantial treatment and diagnostic related costs per patient, in many cases translating to a significant proportion of both minimal wage salary and per capita gross national product (GNP).[4, 5, 18, 19-21] Though less prevalent in the United States, cysticercosis still can be associated with significant nationwide morbidity and associated costs.[22-24] In a study published in 1994, Roberts et al.

reported annual minimum estimates for cysticercosis hospitalizations in the United States at $8.8 million, based on rough estimates of average hospital stay costs and wage losses, though not taking into account treatment and diagnostic methods used.[20] In a study conducted using statewide hospital discharge data over the period from 1991 to 2008, overall hospitalization charges for neurocysticercosis patients for the entire time frame were calculated at $136 million in Los Angeles County alone, with a county annual charge averaging $7.9 million.[2] An examination of hospitalization discharge records in 2009 found that the total annual hospital charges associated with NCC diagnoses were greater than $17.1 million in California, with an average charge of $57,800 per hospitalization.[1] Results from the same study also reported the average length of a NCC hospitalization to be 6.5 days, representing a significant amount of potential days of work lost due to illness.[1] Neither of these state or local estimates attempted to account for additional fees preceding or post-hospitalization which likely significantly contribute to the total financial burden of the disease nationwide. Though these estimates serve as strong indicators of the potential economic impact of cysticercosis in the US, there has not been a comprehensive analysis using nationwide data to estimate the costs related with cysticercosis hospitalization in recent years. This study examines the financial burden of cysticercosis-related hospitalizations on a national scale, using data from the Nationwide Inpatient Sample for the years 1998-2009.

METHODS

Data Source

The Nationwide Inpatient Sample (NIS), sponsored by the Agency for Healthcare Research and Quality as a component of the Healthcare Cost and Utilization Project (HCUP), is the largest

publically available all-payer database of in-hospital discharge records in the United States.[25, 26] The NIS approximates a 20% sample of hospitalization stay discharge records from community hospitals across the country, and each year contains close to 8 million records from approximately 1,000 hospitals.[25] Though yearly NIS datasets are available beginning in 1988, due to significant changes in the design and sampling scheme of the dataset between 1997 and 1998, this analysis utilizes NIS data from the 12 year period 1998-2009.[26] The NIS is a comprehensive resource for hospital charge information, including charge, diagnostic and procedural data (up to 15 diagnostic and procedural codes, expanded to 25 diagnostic codes in 2009) for all discharges regardless of insured status or primary payer.[25, 26]

Identification of Cysticercosis Hospitalizations

A cysticercosis-related hospitalization was defined as any hospitalization record listing an ICD-9-CM code of 123.1, defined as Cysticercosis (Cysticerciasis - Infection by Cysticercus cellulosae [larval form of *T. solium*]) for either primary or non-primary diagnoses.

Hospital stay and procedural information

Variables of interest included cost-related hospital stay characteristics of payer information (Medicare, Medicaid, private insurance including HMO, self-pay/uninsured, no charge or other), average length of stay in hospital (mean, in days) and average number of procedures coded on the discharge record. The HCUP Clinical Classification Software (CCS) coding variables, available with NIS data, were used to evaluate procedural information. The HCUP CCS groups the ICD-9-CM coding listed elsewhere in hospital discharge records into a condensed list of categories, making procedural coding more interpretable.[27]

Data Analysis

Data analysis was performed with SAS version 9.2 (SAS Institute, Cary, North Carolina, USA). National estimates of charge-related variables were calculated using hospital and discharge weights provided with the data, with statistical techniques designed for complex, stratified cluster sampling methods, to account for the NIS sampling scheme.[26] Cost-related hospital stay variables, including payer information, average length of stay and average number of procedures were analyzed and summarized both annually and for the entire 12-year period, with means and 95% confidence intervals calculated where appropriate. Most frequently listed hospital procedures from discharge records were evaluated using HCUP CCS coding, stratified by cysticercosis-related hospitalizations with and without a primary diagnosis of cysticercosis. For all analyses of procedural information, NIS unweighted estimates were used for ease of interpretability. Overall hospital charge information, charge information from cysticercosis primary-diagnoses and charge information stratified by in-hospital death were calculated. Records with missing data for variables of interest were excluded from analysis. Hospital charges were evaluated over the study period after charge information was adjusted for inflation to year 2009 dollars using the general Consumer Price index (CPI), to allow for the interpretation of constant dollars.[28] Overall charges for additional selected infectious diseases for comparison purposes were calculated using the same techniques as were used for cysticercosis, with each including both primary and non-primary diagnoses and adjusting for inflation to 2009 dollars using the general CPI.

RESULTS

Hospital charges

All hospitalization charges presented have been adjusted to 2009 dollars using the Consumer Price Index as stated above. Summarized national estimates of annual charges associated with hospital stay for cysticercosis-related hospitalizations for the entire study period are presented in Table 1. The average annual charge per discharge record for selected hospitalizations was estimated at $37,140 (95%CI [34,224 – 40,056]). The adjusted total hospital charges for the 12 year study period for all cysticercosis-related hospitalizations was $996,008,596 (95% CI [851,016,951 – 1,141,000,241]). When examining hospitalizations with a primary diagnosis of cysticercosis, the nationally estimated annual charge per discharge was $30,366 (95%CI [27,581 – 33,151]) and the total charges for the study period was estimated at $362,444,565 (95% CI [309,664,175 – 415,224,955]). Nationally estimated averages of hospital charges per discharge were much higher among patients that died in-hospital versus patients who did not die in-hospital ($106,860 and $36,237 respectively).

Annual adjusted national estimates for charges associated with hospitalization are presented in Table 2. The adjusted average charge per discharge record for all cysticercosis hospitalizations ranged from a low of $22,053 in 2001 to a high of $46,825 in 2008. The annual adjusted total hospital charges for related hospitalizations ranged from a low of $43,594,519 in 2001 high of $121,332,262 in 2007. The adjusted average charges per discharge for hospitalizations with a primary diagnosis of cysticercosis were similar or lower than the total average charge per discharge for all cysticercosis-related hospitalizations for each year of analysis. National estimates of average hospital charges per discharge were consistently higher across all years among patients that died in-hospital versus patients who did not die in-hospital, except during

2001 ($14,649 vs. $22,087), although this was likely influenced by a low number of cysticercosis-related hospitalizations and in-hospital deaths in that year.

Trends of adjusted annual charges for all records are presented in Figure 1. Total adjusted estimated hospitalization charges were inconsistent prior to 2004, increased consistently from 2004-2007 and remained relatively similar from 2007-2009. Adjusted average hospital charges per discharge record were inconsistent from 1998-2001, decreased slightly from 2002-2004, made slight consistent increases from 2004-2008 and dropped slightly in 2009.

Data from select infectious diseases designated as nationally notifiable by the Centers for Disease Control and the Council of State and Territorial Epidemiologists were analyzed for comparison purposes.[29, 30] Calculated charges from select alternate infectious diseases are presented in Table 3. Calculating overall hospitalization charges for the 12-year period in the same manner for each of the selected alternate diseases yields important comparisons to cysticercosis.[29, 30] Cysticercosis-related CPI-adjusted hospitalization charges for the overall period approximated over a third of recorded Hepatitis A-related hospitalization charges, about 3 times the charges related with malaria diagnoses, and nearly double the charges associated with listeriosis.

Hospital stay characteristics

Total study period results of hospital stay characteristics for nationally estimated cysticercosis hospitalizations are presented in Table 4. Over the 12 year period from 1998-2009, there were 28,565 nationally estimated cysticercosis-related hospitalizations. The highest proportion of cysticercosis-related hospitalizations had Medicaid listed as the primary payer of hospital costs

(8,049.4, 28.2%), followed by private insurance including HMO (7,552.4, 26.4%) and self-pay or uninsured (6,968.2, 24.4%). Average mean length of hospital stay for the study period was 6.2 (95% CI [5.9 – 6.6]) days and the average number of procedural codes listed on the discharge records was 1.3 (95% CI [1.2-1.4]).

Annual estimates for hospital stay characteristics are presented in Table 5. Medicaid, private insurance including HMO and self-pay or uninsured consistently held the largest proportions, each representing approximately 20-40% of the primary payer listed on records annually. The average length of hospital stay for cysticercosis hospitalizations ranged from the lowest in 2001 (5.7 days, 95%CI [4.8 – 6.7]) to the highest in 1998 (7.1 days, 95%CI [5.3 – 8.9]). The average number of procedures coded on the discharge record for selected hospitalizations ranged from 1.2 to 1.7 (95%CIs [1.0-1.4] and [1.4-2.0] respectively).

Common procedures

Frequent procedures listed on discharge records of all patients with cysticercosis-related hospitalizations, and those with a hospitalization including a primary diagnosis of cysticercosis are presented in Tables 6 and 7 respectively. The most common procedures listed amongst cysticercosis-related hospitalizations included a diagnostic spinal tap, CT scan, MRI, insertion/replacement/removal of a ventricular shunt and incision and excision of the CNS. Listed procedures are consistent with previous studies on frequent diagnostic and treatment procedures used for patients with suspected or confirmed cysticercosis.[1, 2]

DISCUSSION

Results indicate that cysticercosis-related hospitalizations impose a substantial economic toll in the United States. Estimated total national cysticercosis-related hospitalization charges of nearly a billion dollars over the 12-year period, as well as total charges associated with discharges with a primary diagnosis of cysticercosis of over $360 million, reinforces the impact of cysticercosis in this country, particularly when compared to other diseases similar in terms of mechanism, prevalence or association to importation and travel.

Much of the costs associated with cysticercosis-related hospitalizations are falling to individuals who are not using insurance coverage (self-pay/uninsured 24.4%), likely overwhelming them or their health care provider with such considerable costs. The primary payers listed in the largest proportion of cases are state or federally funded programs such as Medicaid (28.2%). This suggests that not only individual patients, but the health care system on a statewide and national scale is being significantly impacted by cysticercosis-related hospitalizations. These figures demonstrate the need to raise awareness of cysticercosis on a national scale and underscore the sizeable effect this disease has on both the individual and societal level.

A serologic test developed to identify tapeworm carriers can significantly aid in helping to reduce costs associated both with detection and treatment of human cysticercosis.[24, 31] By identifying tapeworm carriers, techniques to treat infection can be used to eliminate these potential sources of transmission.[24] Identifying and treating carriers can help in reducing the transmission of cysticercosis, thereby reducing related diagnostic and procedural hospitalization costs from cysticercosis infection.[24, 32, 33]

A plausible first step in successfully reducing cysticercosis-related costs in the United States is the implementation of adequate reporting systems capable of efficiently identifying cysticercosis

cases, so cases and case contacts can be tested and subsequently treated for existing adult tapeworm infection. Two decades ago, the International Task Force for Disease Eradication declared cysticercosis potentially eradicable through surveillance and available interventions.[34] In 2000, a proposal by the World Health Organization (WHO) was put forth to declare cysticercosis an internationally reportable disease and in the 2005 Guidelines for the Surveillance, Prevention and Control of Taeniosis/Cysticercosis, the WHO called for the creation of a reporting system for cysticercosis at all levels of medical services.[35, 36] Even with numerous reports calling for cysticercosis to be made a notifiable condition on a wide-scale throughout the United States, only six states (Arizona, California, New Jersey, New Mexico, Oregon and Texas), currently require reporting of disease.[37] Without accurate identification of those with infection, control and prevention measures cannot be adequately implemented and the significant costs associated with cysticercosis infection could remain steady or grow unnecessarily in the coming years.

Using hospital charge information to represent the economic burden of disease does have inherent limitations.[38] Hospital charges reflect the total hospital bill for the entire hospital stay and the charge cited on the discharge record is generally more than the amount paid to the hospital by the payers, whether private or insurance, and is also generally more than the hospital's costs of care.[38] This factor in itself would likely lead to an overestimation of the true economic burden of disease when using hospital charge information. Conversely, the hospital charge information does not reflect any professional fees (e.g. physician's fees) accrued during a patient's stay, nor does the NIS data account for certain serology diagnostic information and other procedures used for diagnosis or treatment.[26] Moreover, the economic burden of

hospitalization, though considerable, does not capture the costs of treatment or management pre/post-hospitalization, use of outpatient and emergency department services, disability and lost productivity. These factors would likely lead to an underestimation of the true financial cost of cysticercosis using analysis results. Though the exact impact of these factors on true disease cost is unclear, it is important to note each aspect when drawing any conclusions regarding the economic burden of disease.

The NIS does not contain patient identifying information, and those utilizing the NIS for research are prohibited from attempting to link NIS data with any other source that identifies individuals.[26] This inhibits the ability to determine if records contained in the NIS are from hospitalizations of unique individuals, or represent multiple hospitalizations of the same patient in this study. If patients are hospitalized for infection multiple times, as has been seen in previous studies, results from this analysis will tend to underestimate the true financial impact on an individual with cysticercosis.[1] Estimates for overall hospital charges on a national scale should not be impacted by this possibility, nor should estimates per hospitalization of cysticercosis.

Conclusions

Little data exist on the economic impact of cysticercosis on a national scale within the United States. These findings, using one of the largest all-payer hospital discharge datasets in the country to produce comprehensive and representative national estimates of hospitalization charge information, underscore the substantial economic impact cysticercosis imposes in the United States and support previous studies' assertions that an increased emphasis on the importance of cysticercosis on a nationwide scale is needed.[1, 22-24] Primary payer information suggests that cysticercosis-related hospitalizations impose significant economic costs on both the individuals

infected, as well the overall healthcare system in this country through state and federally funded healthcare programs. Findings show that cysticercosis infection can be associated with prolonged hospital stay and can involve invasive, expensive and potentially risky surgical procedures. These costs to patients and society have the potential to be reduced through adequate prevention and control strategies. The vast national economic impact exemplified by these findings will hopefully serve to emphasize the need for increased surveillance and reporting of disease, so appropriate treatment and control procedures can be implemented in the future.

Table 1.Summary of annual charges associated with hospital stay for patients with a diagnosis of cysticercosis, 1998-2009, adjusted to 2009 dollars

	$	95% CI
Total charges		
Adjusted average annual charge per discharge record	37,140	[34,224 – 40,056]
Adjusted total charges for all discharge records, 1998-2009	996,008,596	[851,016,951 – 1,141,000,241]
Primary diagnosis of cysticercosis		
Adjusted average annual charge in subset per discharge record	30,366	[27,581 – 33,151]
Adjusted total charges in subset of all discharge records, 1998-2009	362,444,565	[309,664,175 – 415,224,955]
In-hospital fatality charges		
Adjusted average annual charge in subset per discharge record	106,860	[71,448 – 142,271]
Adjusted total charges in subset of all discharge records, 1998-2009	34,702,354	[17,106,246 – 52,298,462]
Non-inhospital fatality charges		
Adjusted average annual charge in subset per discharge record	36,237	[33,359 – 39,114]
Adjusted total charges in subset of all discharge records, 1998-2009	959,711,471	[822,607,696 – 1,096,815,246]

*National estimates calculated using NIS hospital and sample weights, adjusted to 2009 dollars using the Consumer Price Index.

Table 2.Charges associated with hospital stay for patients with a diagnosis of cysticercosis, 1998-2009, adjusted to 2009 dollars

	1998	1999	2000	2001	2002	2003
	$	$	$	$	$	$
Total charges						
Adjusted average annual charge per discharge record	27,869	24,901	37,480	22,053	37,147	35,142
Adjusted total annual charges for all discharge records	54,127,617	47,109,314	79,218,159	43,594,519	75,920,729	79,705,483
Primary diagnosis of cysticercosis						
Adjusted average annual charge per discharge record	25,989	19,820	26,036	18,832	29,444	29,316
Adjusted total annual charges for all discharge records	22,993,150	19,564,986	25,292,406	17,544,882	26,411,183	28,778,688
In-hospital fatality charges						
Adjusted average annual charge per discharge record	106,384	62,281	165,162	14,649	127,853	47,256
Adjusted total annual charges for all discharge records	1,722,512	1,615,532	7,250,665	128,158	6,894,349	448,964
Non-inhospital fatality charges						
Adjusted average annual charge per discharge record	27,208	24,382	34,773	22,087	34,189	35,091
Adjusted total annual charges for all discharge records	52,405,103	45,493,781	71,967,493	43,466,362	67,890,283	79,256,519

*National estimates calculated using NIS hospital and sample weights, adjusted to 2009 dollars using the Consumer Price Index.

Table 2.Charges associated with hospital stay for patients with a diagnosis of cysticercosis, 1998-2009, adjusted to 2009 dollars

	2004	2005	2006	2007	2008	2009
	$	$	$	$	$	$
Total charges						
Adjusted average annual charge per discharge record	33,475	39,224	43,459	46,704	46,825	42,548
Adjusted total annual charges for all discharge records	70,331,076	94,363,674	113,500,862	121,332,262	107,190,801	109,614,631
Primary diagnosis of cysticercosis						
Adjusted average annual charge per discharge record	28,979	36,667	43,521	32,347	29,186	39,209
Adjusted total annual charges for all discharge records	29,162,329	40,504,175	49,909,173	34,090,593	26,412,681	41,780,461
In-hospital fatality charges						
Adjusted average annual charge per discharge record	136,466	113,745	75,653	78,613	109,315	89,252
Adjusted total annual charges for all discharge records	4,600,245	2,072,832	1,985,799	2,149,648	2,113,116	3,720,552
Non-inhospital fatality charges						
Adjusted average annual charge per discharge record	31,797	38,655	43,131	46,365	46,186	41,780
Adjusted total annual charges for all discharge records	65,730,832	92,290,844	111,515,063	119,182,614	104,619,006	105,894,079

*National estimates calculated using NIS hospital and sample weights, adjusted to 2009 dollars using the Consumer Price Index.

Table 3.Summary of nationwide overall charges associated with hospital stay for patients with both primary and non-primary diagnoses of selected infectious diseases, 1998-2009, adjusted to 2009 dollars

Disease	ICD-9-CM codes	Total charges ($)	95% CI
Hepatitis A	070.0, 070.1	$2,966,605,654	[$2,764,121,001 – $3,169,090,306]
Listeriosis	027.0	$596,794,320	[$535,020,764 – $658,567,877]
Malaria	084.0-084.9, 647.40-647.44	$354,040,917	[$314,059,170 – $394,022,665]

*National estimates calculated using NIS hospital and sample weights, adjusted to 2009 dollars using the Consumer Price Index.

Table 4. Hospital stay characteristics for nationally estimated cysticercosis hospitalizations, 1998-2009

	n	95% CI	%
Number of cysticercosis hospitalizations	28,565.0	[25,485.4 – 31,644.4]	
Payer			
Medicare	3,092.5	[2,474.6 – 3,710.4]	10.8
Medicaid	8,049.4	[6,856.1 – 9,242.6]	28.2
Private insurance (including HMO)	7,552.4	[6,516.5 – 8,588.3]	26.4
Self-pay (uninsured)	6,968.2	[5,940.0 – 7,996.3]	24.4
No charge	634.9	[413.2 – 856.5]	2.2
Other	2,179.3	[1,653.1 – 2,705.4]	7.6
Average (mean) length of stay in hospital, in days	6.2	[5.9 – 6.6]	
Average (mean) number of procedures coded on the original record	1.3	[1.2 – 1.4]	

*National estimates calculated using NIS hospital and sample weights.

Table 5. Hospital stay characteristics for annual nationally estimated cysticercosis hospitalizations, 1998-2009

	1998		1999		2000		2001	
	n	%	n	%	n	%	n	%
Number of cysticercosis hospitalizations	1998.1		2118.8		2429.9		2053.8	
Payer								
Medicare	155.7	7.8	234.6	11.1	163.5	6.7	188.4	9.2
Medicaid	614.3	30.7	511.6	24.1	842.7	34.7	466.5	22.7
Private insurance (including HMO)	626.9	31.4	813.9	38.4	548.6	22.6	627.6	30.6
Self-pay (uninsured)	391.7	19.6	458.2	21.6	579.0	23.8	556.6	27.1
No charge	33.7	1.7	5.3	0.3	18.8	0.8	63.2	3.1
Other	175.8	8.8	85.2	4.0	262.9	10.8	137.8	6.7
Mean length of stay in hospital, in days [95% CI]	7.1	[5.3-8.9]	5.9	[4.6-7.3]	6.8	[5.6-8.0]	5.7	[4.8-6.7]
Mean number of procedures coded on the original record [95% CI]	1.5	[1.2-1.7]	1.3	[1.0-1.5]	1.5	[1.2-1.7]	1.2	[1.0-1.4]

*National estimates calculated using NIS hospital and sample weights.

Table 5. Hospital stay characteristics for annual nationally estimated cysticercosis hospitalizations, 1998-2009

	2002		2003		2004		2005	
	n	%	n	%	n	%	n	%
Number of cysticercosis hospitalizations	2259.5		2495.9		2254.7		2481.7	
Payer								
Medicare	246.8	10.9	243.0	9.7	269.7	12.0	273.8	11.0
Medicaid	638.9	28.3	785.5	31.5	609.4	27.0	653.0	26.3
Private insurance (including HMO)	582.5	25.8	688.9	27.6	630.8	28.0	703.9	28.4
Self-pay (uninsured)	620.2	27.4	529.2	21.2	598.8	26.6	581.8	23.4
No charge	34.7	1.5	37.7	1.5	38.7	1.7	101.0	4.1
Other	132.2	5.9	211.6	8.5	89.5	4.0	163.4	6.6
Mean length of stay in hospital, in days [95% CI]	6.4	[5.5-7.3]	6.1	[4.8-7.4]	6.0	[5.3-6.8]	6.1	[5.1-7.1]
Mean number of procedures coded on the original record [95% CI]	1.2	[1.0-1.4]	1.2	[1.0-1.4]	1.3	[1.1-1.5]	1.2	[1.0-1.4]

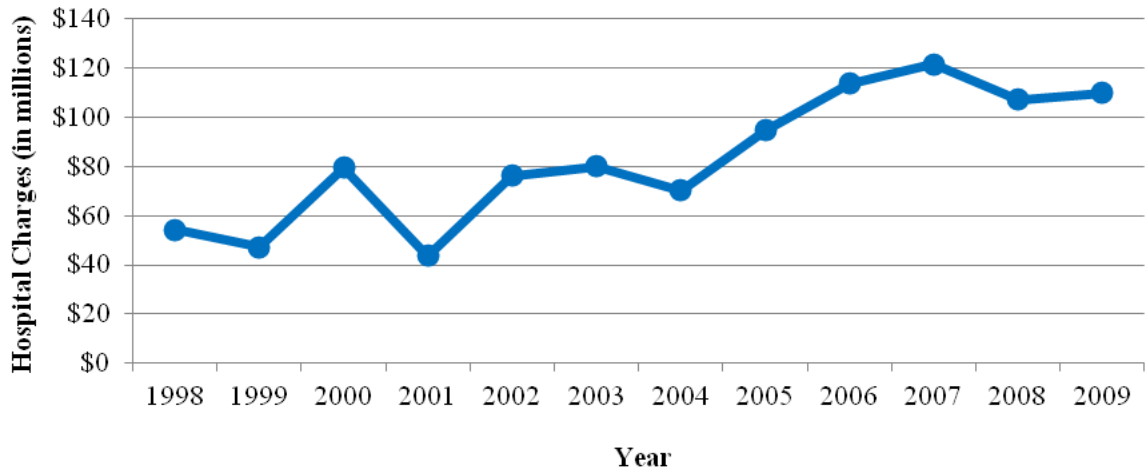
*National estimates calculated using NIS hospital and sample weights.

Table 5. Hospital stay characteristics for annual nationally estimated cysticercosis hospitalizations, 1998-2009

	2006		2007		2008		2009	
	n	%	n	%	n	%	n	%
Number of cysticercosis hospitalizations	2753.1		2714.5		2397.3		2607.8	
Payer								
Medicare	296.7	10.8	303.6	11.2	321.1	13.4	395.6	15.2
Medicaid	715.3	26.0	672.8	24.8	681.6	28.4	857.9	32.9
Private insurance (including HMO)	655.3	23.8	661.4	24.4	561.5	23.4	451.3	17.3
Self-pay (uninsured)	800.4	29.1	695.4	25.6	518.6	21.6	638.3	24.5
No charge	38.2	1.4	88.1	3.2	83.9	3.5	91.5	3.5
Other	238.0	8.6	288.1	10.6	221.4	9.2	173.3	6.6
Mean length of stay in hospital, in days [95% CI]	6.4	[5.5-7.3]	6.4	[5.5-7.2]	5.8	[5.1-6.6]	6.1	[5.2-6.9]
Mean number of procedures coded on the original record [95% CI]	1.3	[1.0-1.6]	1.7	[1.4-2.0]	1.5	[1.2-1.7]	1.2	[0.9-1.4]

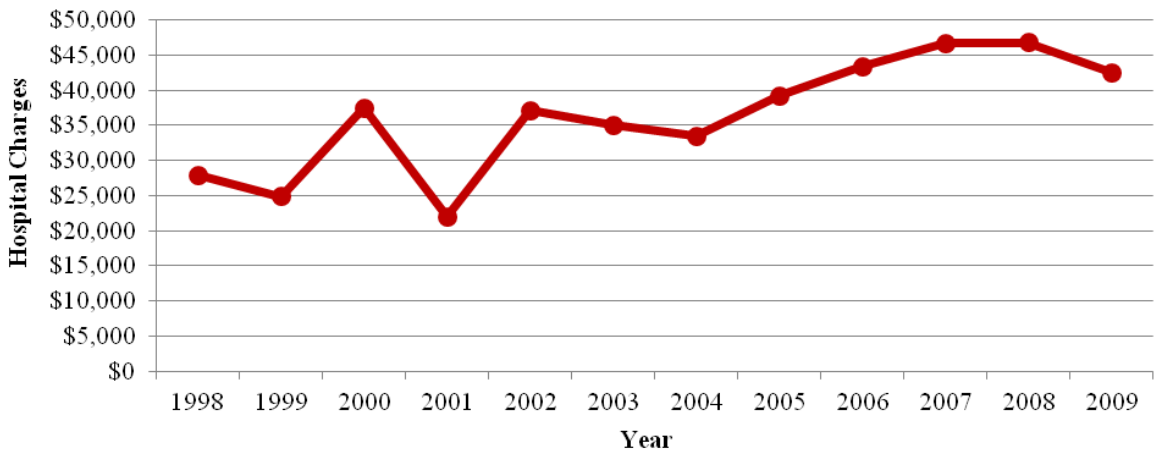
*National estimates calculated using NIS hospital and sample weights.

Figure 1. CPI adjusted annual charges associated with hospital stay for all records among cysticercosis hospitalizations



*National estimates calculated using NIS hospital and sample weights, adjusted to 2009 dollars using the Consumer Price Index (CPI).

Figure 2. CPI adjusted average annual charges associated with hospital stay per discharge record among cysticercosis hospitalizations



*National estimates calculated using NIS hospital and sample weights, adjusted to 2009 dollars using the Consumer Price Index (CPI).

Table 6. Most common procedures listed on all cysticercosis-related hospitalization records, 1998-2009, by HCUP Clinical Classification

Procedure	n	%
Diagnostic spinal tap	843	14.4
Computerized axial tomography (CT) scan head	635	10.8
Magnetic resonance imaging	614	10.5
Insertion; replacement; or removal of extracranial ventricular shunt	440	7.5
Incision and excision of CNS	365	6.2
Respiratory intubation and mechanical ventilation	322	5.5
Other OR therapeutic nervous system procedures	264	4.5
Other vascular catheterization; not heart	228	3.9
Electroencephalogram (EEG)	211	3.6
Other therapeutic procedures	170	2.9
Cerebral arteriogram	130	2.2

*Unweighted estimates from NIS records
** HCUP Clinical Classification Software (CCS) coding variables were used to group ICD-9-CM codes into categories

Table 7. Most common procedures listed on hospitalization records with a primary diagnosis of cysticercosis, 1998-2009, by HCUP Clinical Classification

Procedure	n	%
Diagnostic spinal tap	424	16.4
Magnetic resonance imaging	365	14.1
Computerized axial tomography (CT) scan head	306	11.8
Incision and excision of CNS	233	9.0
Respiratory intubation and mechanical ventilation	130	5.0
Other OR therapeutic nervous system procedures	112	4.3
Electroencephalogram (EEG)	102	3.9
Insertion; replacement; or removal of extracranial ventricular shunt	96	3.7

*Unweighted estimates from NIS records
** HCUP Clinical Classification Software (CCS) coding variables were used to group ICD-9-CM codes into categories.

References

1. Croker C, Redelings M, Reporter R, Sorvillo F, Mascola L, Wilkins P. The impact of neurocysticercosis in california: a review of hospitalized cases. PLoS Negl Trop Dis. 2012 Jan;6(1):e1480. doi: 10.1371/journal.pntd.0001480. Epub 2012 Jan 24.

2. Croker C, Reporter R, Mascola L. Use of statewide hospital discharge data to evaluate the economic burden of neurocysticercosis in Los Angeles County (1991–2008). Am J Trop Med Hyg. 2010;83:106–10. doi:10.4269/ajtmh.2010.09-0494

3. García HH, Gonzalez AE, Evans CA, Gilman RH. *Taenia solium* cysticercosis. Lancet. 2003;362:547–56. doi:10.1016/S0140-6736(03)14117-7

4. Murthy JM, Rajshekar G. Economic evaluation of seizures associated with solitary cysticercus granuloma. Neurol India. 2007 Jan-Mar;55(1):42-5.

5. Rajkotia Y, Lescano AG, Gilman RH, Cornejo C, Garcia HH; Cysticercosis Working Group of Peru. Economic burden of neurocysticercosis: results from Peru. Trans R Soc Trop Med Hyg. 2007 Aug;101(8):840-6. Epub 2007 May 15.

6. Craig, C., Faust, E., Russell, P., Craig and Faust's Clinical parasitology. 8th edition. 1976. Philadelphia Lea & Febiger.

7. Ash LR, Orihel TC. Parasites in human tissues. Chicago, IL: ASCP Press. 1995. 304-306.

8. White Jr AC. Neurocysticercosis: updates on epidemiology, pathogenesis, diagnosis, and management. Annu Rev Med 2000;51: 187- 206.

9. Markell, E., Voge, M., Medical Parasitology. 4th edition. Elsevier. 1976

10. Del Brutto OH. Diagnostic criteria for neurocysticercosis, revisited. Pathog Glob Health. 2012 Sep;106(5):299-304. doi: 10.1179/2047773212Y.0000000025.

11. Del Brutto OH, Rajshekhar V, White AC Jr, Tsang VC, Nash TE, Takayanagui OM, Schantz PM, Evans CA, Flisser A, Correa D, Botero D,Allan JC, Sarti E, Gonzalez AE, Gilman RH, García HH. Proposed diagnostic criteria for neurocysticercosis. Neurology. 2001 Jul 24;57(2):177-83.

12. Sotelo J. Neurocysticercosis: eradication of cysticercosis is an attainable goal. BMJ. 2003 Mar 8;326(7388):511-2.

13. Nash TE, Singh G, White AC, Rajshekhar V, Loeb JA, Proaño JV, Takayanagui OM, Gonzalez AE, Butman JA, DeGiorgio C, Del Brutto OH, Delgado-Escueta A, Evans CA, Gilman RH,Martinez SM, Medina MT, Pretell EJ, Teale J, Garcia HH. Treatment of neurocysticercosis: current status and future research needs. Neurology. 2006 Oct 10;67(7):1120-7.

14. DeGiorgio CM, Houston I, Oviedo S, Sorvillo F. Deaths associated with cysticercosis. Report of three cases and review of the literature. Neurosurg Focus. 2002 Jun 15;12(6):e2.

15. Colli BO, Martelli N, Assirati JA Jr, Machado HR, de Vergueiro Forjaz S. Results of surgical treatment of neurocysticercosis in 69 cases. J Neurosurg. 1986 Sep;65(3):309-15.

16. Garcia HH, Evans CAW, Nash TE, et al. Current consensus guidelines for treatment of neurocysticercosis. Clin Microbiol Rev. 2002; 15:74–56.

17. Garcia HH, Del Brutto OH, Nash TE, White AC Jr, Tsang VC, Gilman RH. New concepts in the diagnosis and management of neurocysticercosis (Taenia solium). Am J Trop Med Hyg. 2005;72:3Y9.

18. Carabin H, Krecek RC, Cowan LD, Michael L, Foyaca-Sibat H, Nash T, Willingham AL. Estimation of the cost of Taenia solium cysticercosis in Eastern Cape Province, South Africa. Trop Med Int Health. 2006 Jun;11(6):906-16.

19. Zoli A, Shey-Njila O, Assana E, Nguekam JP, Dorny P, Brandt J, Geerts S. Regional status, epidemiology and impact of Taenia solium cysticercosis in Western and Central Africa. Acta Trop. 2003 Jun;87(1):35-42.

20. Roberts T, Murrell KD, Marks S. Economic losses caused by foodborne parasitic diseases. Parasitol Today. 1994 Nov;10(11):419-23.

21. Praet N, Speybroeck N, Manzanedo R, Berkvens D, Nsame Nforninwe D, Zoli A, Quet F, Preux PM, Carabin H, Geerts S. The disease burden of Taenia solium cysticercosis in Cameroon. PLoS Negl Trop Dis. 2009;3(3):e406. doi: 10.1371/journal.pntd.0000406. Epub 2009 Mar 31.

22. Del Brutto OH, García HH. Neurocysticercosis in nonendemic countries: time for a reappraisal. Neuroepidemiology. 2012;39(2):145-6. Epub 2012 Aug 22

23. Wallin MT, Kurtzke JF. Neurocysticercosis in the United States: review of an important emerging infection. Neurology. 2004;63:1559Y1564.

24. Sorvillo, F., Wilkins, P., Shafir, S., Eberhard, M. Public Health Implications of Cysticercosis Acquired in the United States. Emerging Infectious Diseases. Vol. 17, No.1 January 2011.

25. HCUP Databases. Healthcare Cost and Utilization Project (HCUP). Overview of the Nationwide Inpatient Sample (NIS). November 2011. Agency for Healthcare Research and Quality, Rockville, MD. http://www.hcup-us.ahrq.gov/nisoverview.jsp

26. Healthcare Cost and Utilization Project (HCUP). Introduction to the HCUP Nationwide Inpatient Sample (NIS) 2009. Agency for Healthcare Research and Quality, Rockville, MD. Issued May 2011. http://www.hcupus.ahrq.gov/db/nation/nis/NIS_Introduction_2009.jsp

27. HCUP Databases. Healthcare Cost and Utilization Project (HCUP). Clinical Classifications Software (CCS) for ICD-9-CM. Accessed May 2011. Agency for Healthcare Research and Quality, Rockville, MD. http://www.hcup-us.ahrq.gov/toolssoftware/ccs/ccs.jsp#download

28. US Department of Labor, Bureau of Labor Statistics. Consumer price index. Available at: ftp://ftp.bls.gov/pub/special.requests/cpi/cpiai.txt. Accessed May 15, 2013.

29. Centers for Disease Control and Prevention. 2012 Case Definitions: Nationally Notifiable Conditions Infectious and Non-Infectious Case. Atlanta, GA (2012).

30. Council of State and Territorial Epidemiologists. CSTE List of Nationally Notifiable Conditions. August 2012. http://c.ymcdn.com/sites/www.cste.org/resource/resmgr/PDFs/CSTENotifiableConditionListA.pdf. Accessed: June 17, 2013

31. Wilkins PP, Allan JC, Verastegui M, Acosta M, Eason AG, Garcia HH, et al. Development of a serologic assay to detect *Taenia solium* taeniasis. Am J Trop Med Hyg. 1999;60:199–204.

32. Sorvillo FJ, DeGiorgio C, Waterman SH. Deaths from cysticercosis in the United States. Emerg Infect Dis. 2007;13:230–5. DOI: 10.3201/eid1302.060527

33. Sorvillo FJ, Portigal L, DeGiorgio C, Smith L, Waterman SH, Berlin GW, et al. Cysticercosis-related deaths, California. Emerg Infect Dis. 2004;10:465–9

34. Centers for Disease Control. Recommendations of the international task force for disease eradication. Morb Mortal Wkly Rep 1993;42:1–38.

35. Guidelines for the Surveillance, Prevention and Control of Taeniosis/Cysticercosis (WHO/FAO/ 2005) - http://www.oie.int/doc/ged/d11245.pdf

36. Roman G, Sotelo J, Del Brutto OH, Flisser A, Dumas M, Wadia N, Botero D, Cruz M, Garcia H, de Bittencourt PR, Trelles L, Arriagada C, Lorenzana P, Nash TE, Spina-França A: A proposal to declare neurocysticercosis an international reportable disease. Bull WHO 2000;78:399–406.

37. Serpa JA, Clinton White A Jr. Neurocysticercosis in the United States. Pathog Glob Health. 2012 Sep;106(5):256-60. doi: 10.1179/2047773212Y.0000000028.

38. Healthcare Cost and Utilization Project (HCUP). Statistical Brief #13 The National Hospital Bill: The Most Expensive Conditions, by Payer, 2004. Agency for Healthcare Research and Quality, Rockville, MD. September 2006. http://www.hcup-us.ahrq.gov/reports/statbriefs/sb13.pdf