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Initial and Long-Term Costs of Patients Hospitalized with West Nile Virus Disease

J. Erin Staples,* Manjunath Shankar, James J. Sejvar, Martin I. Meltzer, and Marc Fischer

Arboviral Diseases Branch, Centers for Disease Control and Prevention, Fort Collins, Colorado; Prion and Health Office, Centers for Disease Control and Prevention, Atlanta, Georgia; Division of Preparedness and Emerging Infections, Centers for Disease Control and Prevention, Atlanta, Georgia

* Address correspondence to J. Erin Staples, Arboviral Diseases Branch, Centers for Disease Control and Prevention, 3150 Rampart Road, Fort Collins, CO 80521. E-mail: AUV1@cdc.gov

Abstract.

There are no published data on the economic burden for specific West Nile virus (WNV) clinical syndromes (i.e., fever, meningitis, encephalitis, and acute flaccid paralysis [AFP]). We estimated initial hospital and lost-productivity costs from 80 patients hospitalized with WNV disease in Colorado during 2003; 38 of these patients were followed for 5 years to determine long-term medical and lost-productivity costs. Initial costs were highest for patients with AFP (median $25,117; range $5,385–$283,381) and encephalitis (median $20,105; range $3,965–$324,167). Long-term costs were highest for patients with AFP (median $22,628; range $624–$439,945) and meningitis (median $10,556; range $0–$260,748). Extrapolating from this small cohort to national surveillance data, we estimated the total cumulative costs of reported WNV hospitalized cases from 1999 to 2012 to be $778 million (95% confidence interval $673 million–$1.01 billion). These estimates can be used in assessing the cost-effectiveness of interventions to prevent WNV disease.

INTRODUCTION

West Nile virus (WNV), a mosquito-borne flavivirus, was first detected in the Western Hemisphere in 1999. Since then, it has become the leading cause of domestically acquired arboviral disease in the United States and is responsible for seasonal outbreaks of disease affecting all regions of the country.[1] Approximately 80% of WNV infections are asymptomatic.[2] Most symptomatic persons experience an acute systemic febrile illness, known as West Nile fever or non-neuroinvasive disease, that often includes headache, myalgia, arthralgia, or rash.[3,4] Less than 1% of infected persons develop neuroinvasive disease, which typically manifests as encephalitis, meningitis, or acute flaccid paralysis (AFP).[5] Most patients with WNV meningitis or non-neuroinvasive disease recover completely, but fatigue and malaise can linger for weeks or months.[6–8] Patients who recover from WNV encephalitis or AFP often have residual neurologic deficits.[9] Among patients with neuroinvasive disease, the overall case-fatality ratio is ?10%, but it is notably higher for patients with WNV encephalitis and AFP.[1]

From 1999 to 2012, over 36,000 cases and 1,500 deaths caused by WNV disease were reported to the Centers for Disease Control and Prevention (CDC).[1,10–12] Despite the large number of cases over the last 14 years, only two studies have estimated the initial cost of WNV disease.[13,14] There are no published data on the economic burden of the specific clinical syndromes seen with WNV infections or the longer term costs of WNV disease incurred several years after the initial illness. We present data on both initial hospital costs and 5 years of follow-up care costs for persons hospitalized with different clinical presentations of WNV disease. We then use the data to estimate the total costs of hospitalized WNV disease cases and deaths reported to CDC. The data can be used in assessing the cost-effectiveness of various interventions designed to lower WNV disease risk.

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METHODS

The analysis is divided into two parts. First, we estimate the direct and indirect medical costs of initial hospitalization and 5-year follow-up costs by WNV clinical syndrome among a cohort of hospitalized patients in Colorado. Second, we build a Monte Carlo simulation model using the findings from the cohort to estimate the costs incurred by all hospitalized WNV cases in the United States that were reported to CDC for 1999–2012.

For all cost estimates, we took a societal perspective (i.e., relevant costs regardless of who paid). We adjusted all costs to 2012 U.S. dollars (USD) using the Prescription Drugs part of the U.S. Consumer Price Index (CPI) for drug costs, the medical care part of CPI for medical costs, and the CPI inflation for productivity costs from the Bureau of Labor Statistics (http://www.bls.gov/). We used the productivity tables from Grosse and others[15] to derive the indirect (i.e., lost productivity) costs. Where appropriate, we discounted future costs at an annual rate of 3%.

Direct and indirect medical costs of WNV patient cohort.

Study participants and data collection.

In 2003, we enrolled a cohort of patients (original Colorado cohort) who were hospitalized with acute WNV disease at 17 institutions in northern Colorado ($N = 221$).[16] Participant's WNV clinical syndrome was classified as fever (i.e., non-neuroinvasive disease), meningitis, or encephalitis, with or without AFP based on their presenting signs and symptoms and a follow-up assessment completed by a neurologist (JJS). If a participant was diagnosed with > 1 clinical syndrome, we classified them as having the most severe presentation for the purpose of this report (severity: fever < meningitis < encephalitis < AFP).

A subset of survivors was followed prospectively to assess functional and neurocognitive outcomes.[17] Inpatient costs for the initial hospitalization were obtained from the respective hospitals (acute follow-up cohort). In 2008, we administered a questionnaire regarding outpatient medical and home care costs incurred during the 5 years following their initial hospitalization (long-term follow-up cohort). Participants were asked if after their initial hospitalization, they required any of the following related to their WNV illness: 1) subsequent inpatient hospitalization, rehabilitation, nursing home, assisted living, or home health care; 2) outpatient primary care, neurology, physical therapy, occupational therapy, or speech therapy visits; 3) new medications, equipment, or modifications of home or vehicle; or 4) missed work or school. The study was approved by the CDC Institutional Review Board and participants provided informed consent.

Cost data.

A. Initial costs.

1. Direct hospital costs. We obtained direct medical charges for the hospitalization in 2003 for acute follow-up cohort directly from the hospital finance department. To measure costs, we used actual health insurance reimbursements, if available, or multiplied the total hospital charges by the 2003 cost-to-charge ratio (0.42) for Colorado from the Center for Medicare Services (CMS NIS_CCR_2003 file of HCUP available at http://www.hcup-us.ahrq.gov/db/state/costtocharge.jsp) to derive an estimate of reimbursed costs. We did not collect any outpatient costs associated with hospital-based acute care.

2. Indirect costs. We assumed for hospitalized patients who missed work that they had a work schedule of 5 out of every 7 days. We valued time lost from work, by age and sex, using estimates from Grosse and others.[15] If a participant worked part-time, 50% daily production value was used. The lost productivity for persons who died

during their initial hospitalization was derived from the lifetime production at a 3% discount rate for their age and sex.[15] We did not assign any value to the days spent in hospital for those who died during their initial hospitalization.

B. Costs incurred in the 5 years after initial hospitalization.
1. Medical appointments and institutional care costs. To determine medical appointment and institutional care costs, we used data provided by participants in the long-term follow-up cohort regarding the type and number of outpatient medical and home care appointments they had during the 5 years after their initial hospitalization and multiplied this by type-specific cost estimates obtained from MarketScan Commercial Claims and Encounter databases (Truven Health Analytics, Sacramento, CA). The MarketScan databases are compiled from insurance claims filed by patients used by ?100 companies; they include information on persons < 65 years of age and their dependents and covered nearly 7 million lives in 2003. The databases contain both out-of-pocket payments and insurance reimbursements. Current Procedural Terminology, Fourth edition (CPT-4) service-based codes were used to extract cost data from MarketScan for medical appointments and institutional care (Table 1). Because all the costs were positively skewed and had a high variance, we used the median costs for the United States in the calculations. We excluded any future costs for the three participants who indicated, at the time of the survey, they were still receiving care related to their WNV illness from a neurologist.
2. Drug costs. We used the average wholesale price of drugs from MicroMedex 2.0 (Truven Health Analytics Red Book online) to determine the cost of drugs that survey participants indicated that they received post-hospitalization. Unless the dosage was indicated by the participant, we assumed they received a standard dose. For as needed (prn) medicines, we assumed a normal or maximum amount for the first 3 months; the frequency was then gradually decreased over time to once a week if they were still taking the medicine > 3 years after their initial hospitalization. We excluded future costs for the four participants who indicated they were still taking a medicine at the time of the survey.
3. Durable medical equipment. We used the CMS 2003 floor fee schedule (https://www.cms.gov/DMEPOSFeeSched) to determine durable medical equipment costs for participants in the long-term follow-up cohort who indicated on the questionnaire that they needed specific equipment after their hospital discharge. If a specific model was not provided by the participant, the equipment was assumed to be a new basic model with the least cost.
4. Indirect costs. We used the same methodology as described previously to assign a cost for the number of days of missed employment after their initial hospitalization for participants in the long-term follow-up cohort who were working at the time of their illness. For persons who retired early as a result of WNV, we valued their indirect costs as the number of potential years and months of lost employment (65 minus age at early retirement).[15] For persons who indicated they were retired or unemployed at the time of their illness, the survey tool did not capture the number of days they were unable to perform daily household tasks. We did not, therefore, value any such losses.

Data analysis.

Data were analyzed using SAS statistical software version 9.3 (SAS Institute, Cary, NC) or EpiInfo 7 (CDC, Atlanta, GA) to determine if there were differences between demographic and cost data between clinical syndrome. To assess representativeness of the follow-up cohorts, their demographics, clinical syndrome, and clinical outcomes were compared with the original Colorado cohort. Though the data came from a comprehensive cohort, we compared categorical variables using the Fisher's exact or χ^2 test and continuous variables using the Kruskal-Wallis test when the variance was not homogeneous (e.g., cost data) or analysis of variance when the variance was normally distributed (e.g., age). We did this to determine if there was sufficient difference in the variability of costs by syndrome and to inform if syndrome-specific costs were needed when extrapolating such cost to the national level (assuming such costs were representative at such level). The overall critical *P* value was chosen to be 0.05; however, when there were multiple tests performed, the *P* value was adjusted using the Bonferroni correction.[18]

Cost of hospitalized WNV cases and deaths in the United States.

We compared the background characteristics of patients from the follow-up cohorts to those reported nationally from ArboNET, the national arboviral surveillance system.[1] We extrapolated cost data collected from the follow-up cohorts described previously to the cumulative hospitalized WNV disease cases in the United States from 1999 to 2012 reported to CDC through ArboNET. We built a spreadsheet-based Monte Carlo simulation model using @Risk 5.7 software (Palisade Corporation, Ithaca, NY) to achieve this goal. The model used the following formula to determine the costs of WNV hospitalized cases:

Total costs of hospitalized cases from 1999 to 2012 = Σ (number of hospitalized cases by year and syndrome X cost distributed by syndrome from the Colorado cohort).

For acute costs, the number of hospitalized cases and deaths by year and clinical syndrome were obtained from ArboNET. Because hospitalization was only first reported to ArboNET in 2004, cumulative proportions for 2004–2012 were used to estimate the number of cases hospitalized for 1999–2003 by clinical syndrome. To approximate the proportion of hospitalized cases in the United States who would incur long-term cost, we used a uniform distribution with a minimum of zero and a maximum equivalent to the proportion of cases in the Colorado cohort who experienced any long-term costs by clinical syndrome.

We applied the "fit distribution to data" function of @Risk software to the costs incurred by patients in the follow-up cohorts to generate the cost distribution for the model. The best distribution that fit the participant's data was selected from those provided by @Risk software based on relative frequencies, quantile–quantile graphs, χ^2, Kolmogorov-Smirnov, and Anderson-Darling goodness-of-fit tests (Table 2). The distributions were assigned a lower bound of zero because all costs were positive. We ran the model for 10,000 iterations and results are presented as 1) mean (mean of 10,000 iterations) with 95% confidence interval (CI) (2.5th and 97.5th percentiles of 10,000 iterations), and 2) median with range.

All deaths reported to ArboNET were assigned a lifetime productivity loss (discounted at 3%) based on the patient's age and sex.[15] For case-patients who died and where the age or sex was missing, we assumed the person to be 80 years of age and/or female because this provided the smallest estimate of lifetime productivity loss.

RESULTS

Demographic and clinical characteristics.

Initial hospital cost data incurred in 2003 were obtained for 80 WNV disease cases in the acute follow-up cohort. When the demographic features, clinical syndromes, and outcomes were compared between the 80 patients in the acute follow-up cohort and those in the original Colorado cohort who were not followed prospectively ($N = 141$), there were no differences noted between the age, sex, number of days hospitalized, and the number of deaths between the groups. The acute follow-up cohort was less likely to include patients with meningitis (24%) than the original Colorado cohort (48%) ($P < 0.01$) and more likely to include patients who were originally discharged to a chronic care or rehabilitation facility, or needing home health assistance (51% versus 31%) ($P < 0.01$). The only difference that was observed when the acute follow-up cohort was compared with the original cohort by clinical syndrome was that patients with AFP in the acute follow-up cohort were more likely to be younger (median age 55 years,

interquartile range [IQR] 44–62 years) than those who were not followed prospectively (median age 69 years, IQR 52–80 years).

In the acute follow-up cohort (N = 80), 41 (51%) were male and their median age at hospital admission was 55 years (IQR 45–66 years) (Table 3). Twenty-two (28%) were 65 years of age or older. Case-patients were most commonly diagnosed as having AFP (34%), followed by meningitis (24%), fever (22%), and encephalitis (20%). There was no difference in the sex distribution of participants between various clinical presentations. However, median age at admission varied significantly by clinical syndrome, with encephalitis and fever patients being the older than AFP and meningitis patients ($P < 0.001$). Nine (50%) of the participants with fever were 65 years of age or older compared with 7 (44%) with encephalitis, 5 (19%) with AFP, and 1 (5%) with meningitis. Participants were hospitalized for a median of 5 days (IQR 3–11 days). The length of hospitalization was significantly different depending on the person's WNV clinical syndrome with AFP case-patients requiring longer hospitalization ($P < 0.001$).

Six (8%) case-patients died during the initial hospitalization caused by WNV disease. Two of the case-patients were diagnosed with AFP and four had encephalitis; none of the case-patients with fever or meningitis died during their initial hospitalization. Case-patients who died were older (median 76 years) than survivors (median 53 years) ($P < 0.01$). Duration of hospitalization was similar for fatal (median 7 days) and non-fatal cases (median 4 days) ($P = 0.2$).

Of the 80 participants in the acute follow-up cohort, 38 (48%) completed the follow-up survey of their subsequent direct and indirect medical care incurred 5 years after their hospitalization. When compared with those for whom no follow-up data were obtained (N = 141), participants in the long-term follow-up cohort were similar with regards to sex distribution, median age at hospital admission, length of hospitalization, proportions discharged to home versus a rehabilitation facility, and proportions with each clinical syndrome. The only difference was in the rates of death, where 12 (5%) of the 141 without long-term data died however no one in long-term cohort died. Furthermore, there were no differences between demographic and clinical outcomes by clinical syndrome between persons in the long-term cohort versus those with no follow-up data. When compared with those for whom only acute follow-up data were obtained (N = 42), participants in the long-term follow-up cohort (N = 38) were similar with regards to sex distribution, median age and the proportion of persons 65 years of age or older at hospital admission, and proportions with each clinical syndrome (Table 3). However, the 38 patients who provided long-term cost data had shorter hospitalizations (median 4 days; IQR 2–6 days) than the 42 patients for whom long-term costs were not available (median 7 days; IQR 4–16 days) ($P < 0.01$).

Initial direct or indirect medical costs.

Overall, persons with AFP or encephalitis had significantly higher total initial costs (i.e., initial hospital and lost productivity costs) than persons with meningitis or fever ($P < 0.001$) (Table 4). The median cost for a patient with AFP was $20,774 (IQR $10,749–$120,945) compared with a median cost of $4,467 (IQR $3,241–$8,433) for a patient with WNV non-neuroinvasive disease. The majority of the total costs were incurred as a result of hospital charges. However, lost productivity was also significantly higher in persons with AFP and encephalitis ($P < 0.001$); this was caused by the fact that several persons with AFP and encephalitis died and thus had lifetime lost productivity, which contributed to a higher total lost productivity.

Five-year follow-up costs.

Thirty-four (89%) of the 38 persons who provided long-term cost data reported incurring costs either through medical care (29 of 38, 76%) or lost productivity (27 of 38, 71%) (Table 5). The most commonly incurred medical care costs were receiving a new medication (53%), visiting a neurologist (42%), needing durable medical equipment (37%), and visiting a physical therapist (34%). There was variation in the median number of follow-up medical care visits by syndrome (0 to 104 visits). Patients with encephalitis needed the most follow-up medical care visits and meningitis patients needed the least number of visits. Three (8%) persons either retired early or lost their job because of their illness. Persons who returned to work or school were absent for a median of 42 days (IQR 19–66 days).

Case-patients with AFP incurred significantly higher median long-term medical care costs ($5,323; IQR $2,584–$9,882) than case-patients with fever or meningitis ($110; IQR $59–$762 and $138; IQR $0–$654, respectively) ($P = 0.002$); case-patients with encephalitis had intermediate long-term medical care costs ($2,459; IQR $1,425–$10,430). Medical care appointments contributed to the largest proportion of long-term medical care costs for most clinical syndromes.

The trends in lost productivity costs by clinical syndrome were different than the long-term medical care costs. Case-patients with meningitis incurred higher median lost productivity costs ($10,363; IQR $1,988–$15,709) than case-patients with AFP ($6,771; IQR $1,401–26,817), fever ($1,180; IQR $377–$4,220), or encephalitis ($0); however, no statistical difference was detected.

Overall, there was no significant difference in total long-term costs by syndrome (Table 4). Finally, there was no correlation found between initial hospital costs and any long-term costs.

Cost of hospitalized WNV cases and deaths in the United States.

From 1999 to 2012, 37,088 WNV disease cases, including 16,196 (44%) neuroinvasive disease cases, were reported to CDC. Of these, 1,529 (4%) died and an estimated 18,313 (49%) of the total cases were hospitalized. When all ArboNET cases were compared with WNV cases from the follow-up cohorts, the data were not significantly different in terms of age and sex by clinical syndrome. The follow-up cohorts did have a higher proportion of AFP patients in comparison to the U.S. national data.

The total mean cost of WNV hospitalized cases and deaths as reported to CDC for 1999–2012 was ?$778 million (95% CI $673 million–$1.01 billion) or an average of $56 million per year (95% CI $48–$72 million) (Table 6). Of the overall cumulative costs, $449 million (58%) are from lifetime lost productivity caused by deaths from WNV infection. Hospitalization during the acute illness accounted for an estimated $252 million (95% CI $158–$459 million). Long-term medical and long-term lost productivity costs total $54 million (95% CI $25–$104 million). The median values for cost categories were similar to the mean values (Table 6).

DISCUSSION

This study found that both acute and long-term costs varied between the different clinical presentations of WNV disease. Overall, a substantial proportion of case-patients in our long-term follow-up cohort incurred additional medical or lost productivity costs in the 5 years after their

hospitalization. We estimate that tens of millions of dollars are spent each year on WNV hospitalized cases and deaths.

Traditionally, WNV neuroinvasive disease (e.g., meningitis, encephalitis, and AFP) cases have been grouped together when looking at long-term outcomes and impact of the disease.[1,13,14,19] We found, however, that persons diagnosed with AFP incurred the most expense related to their WNV disease. This is not surprising given the severity of AFP, which often results in partial paresis to extensive paralysis, including neuromuscular respiratory failure, which are often permanent and similar high costs found with other conditions that can cause limb paralysis such as Guillain-Barré Syndrome.[9,20] Medical care costs, in particular the initial hospital costs, for case-patients with encephalitis were similar to that of AFP cases in our study and the costs for WNV encephalitis are similar to those previously published for other forms of encephalitis.[21] However, the lost productivity was notably lower for encephalitis cases because encephalitis tended to occur in older individuals who were retired at the time of their illness onset and thus incurred no lost productivity costs in our study. The hospitalization costs for case-patients with WNV meningitis in our study are similar to those for other causes of viral meningitis and were more similar to hospitalized fever or non-neuroinvasive cases than other neuroinvasive disease cases.[22] In fact, meningitis cases had some of the lowest medical care costs, in particular for long-term costs, which was typically associated with only requiring a new medication (e.g., analgesic) and a visit with their primary care doctor after their initial hospitalization. However, persons with WNV meningitis tended to be younger and experienced more time away from work than fever or encephalitis cases and thus they had the highest cost for long-term lost productivity. Finally, hospitalized fever patients incurred initial median costs of $4,600 and long-term median costs over $2,200. Given that one in five cases of WNV fever reported to CDC are hospitalized, we believe that previous costs associated with WNV fever cases have been substantially underestimated.[1,13]

Two previous studies have estimated the total cost of WNV disease outbreaks.[13,14] Zohrabian and others[14] focused on neuroinvasive disease cases during the early outbreak of WNV disease in Louisiana during 2002. They estimated an average cost per case of approximately $27,000. Even after adjusting to 2012 USD, this estimate is lower than the cumulative (initial and long-term) costs we have for most neuroinvasive disease syndromes, in particular AFP and encephalitis. The differences found in the costs between this and our study could be the result of the longer follow-up time in our study (5 years versus 1–8 months), inclusion of medication and home modifications costs in our study, and differences in the proportion of patients with various clinical syndromes (e.g., higher proportion of AFP patients in our study). Barber and others[13] examined the cost of the WNV outbreak in Sacramento County, California during 2005 and included the costs for WNV neuroinvasive disease cases, all assumed to be hospitalized, and for WNV fever cases, all assumed to not be hospitalized. The average cost per case in that outbreak was $13,971, which is lower than most of our cumulative costs for the various syndromes after adjusting to 2012 USD. In Barber's study, however, they included a large proportion of unhospitalized fever case-patients who had an average cost of $1,170/case that likely contributed to their lower cost estimates.

Extrapolating from hospitalized case data from Colorado, the total societal costs of WNV hospitalized cases and deaths as reported to CDC for 1999–2012 was estimated to be roughly $778 million dollars or ?$56 million per year. However, the annual cost of WNV disease varies substantially as the number of WNV disease cases has ranged from 21 cases in 2000 to 9,862

cases in 2003.[1] Our estimate of WNV costs is conservative as it does not account for costs incurred by non-hospitalized WNV cases or make any adjustment for the under diagnosis or underreporting of WNV disease cases.[1,23] To date, an estimated 18,775 non-hospitalized cases of WNV disease have been reported to CDC. If the cost estimate of a fever case (cost of one healthcare provider office visit, one diagnostic test, and 5 days off work) from Barber and others[13] is applied and adjusted to 2012 USD, the estimated total costs of non-hospitalized cases from 1999 to 2012 would be ?$28 million or 3.6% of the total direct or indirect medical costs incurred by WNV disease cases. The extrapolated costs do not include the costs that were incurred by public health or those related to mosquito control efforts, which are often 25% to 50% of the total cost during an outbreak response.[13,14] Finally, in the model we were conservative by 1) using a uniform distribution with a minimum of zero and a maximum equivalent to the proportion of cases in the long-term follow-up cohort who experienced any long-term costs to approximate the proportion of hospitalized cases in the United States who would incur long-term cost, and 2) selecting distributions from those short listed by @Risk for the Monte Carlo model that fit the data but had higher probability of picking lower costs than higher costs for the same Kolmogorov-Smirnov and Anderson-Darling goodness-of-fit.

There are several limitations to our study. Participants were interviewed about long-term care and costs 5 years after their disease onset, which may have led to recall biases. We used hospital charges directly from the hospitals in Colorado and adjusted care costs for the United States to estimate other medical expenditures. In general, hospital charges in Colorado tend to be lower than the national costs.[24] Medical care costs vary by type of service, provider, and insurance coverage from state to state and within a state[24]; thus, our cost data may not reflect the costs incurred by those in other states. As previously noted persons in the long-term cohorts represent a non-random sample and therefore may not be representative of persons with WNV disease in other areas. However, the long-term cohorts were similar in their age and sex distribution to both the original Colorado cohort and WNV disease cases in ArboNET and their cost data reflected the known clinical severity of the different disease presentations and cost data for like syndromes. Given this, we feel that our cost data is likely reflective of costs incurred by WNV disease cases in other locations in Colorado or the United States. By using the Bonferroni correction when multiple tests were being performed simultaneously, we took a conservative approach and may have underestimated the significance of potential differences between clinical syndromes. Patients with WNV infections often have signs and symptoms that overlap different clinical syndromes.[9] Given this, patients in the follow-up cohorts and national data could have been incorrectly categorized into one of four syndromes; this would impact the per syndrome costs and total cost estimates. There were relatively small numbers of patients with any one syndrome in the follow-up cohorts; this likely impacted the precision of the estimated costs. Some of the data (e.g., number of hospital cases for 1999–2003) used for estimating the total national cost of WNV disease was inferred, which likely impacts the precision of the total cost. Finally, we only included hospitalized patients and thus are unable to state anything about the acute or long-term costs for WNV disease case-patients who are not hospitalized; however, the economic impact of this group is likely to be of minimal significance overall.

We provided acute and long-term costs of WNV disease among hospitalized patients and estimate that tens of millions of dollars are spent each year on hospitalized WNV disease cases. We found that long-term direct and indirect medical costs after the initial illness and hospitalization are incurred by most patients and account for a proportion of the total costs of the disease. Therefore, long-term costs need to be figured into the cost of WNV disease. Additional

studies are warranted among larger cohorts of both hospitalized and non-hospitalized persons with various clinical WNV disease syndromes to better understand and estimate the long-term effects and costs associated with WNV disease. Results from this study can be used in assessing the cost-effectiveness of various interventions designed to lower WNV disease risk.

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Authors' addresses: J. Erin Staples and Marc Fischer, Arboviral Diseases Branch, Division of Vector-Borne Disease, Centers for Disease Control and Prevention, Fort Collins, CO, E-mails: auv1@cdc.gov and mxf2@cdc.gov. Manjunath Shankar and Martin I. Meltzer, Scientific And Program Services Branch, Division of Preparedness And Emerging Infections, Centers for Disease Control and Prevention, Atlanta, GA, E-mails: kiu8@cdc.gov and qzm4@cdc.gov. James J. Sejvar, Prion and Public Health Office, Division Of High-Consequence Pathogens and Pathology, Centers for Disease Control and Prevention, Atlanta, GA, E-mail: zea3@cdc.gov.

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TABLE 1

Current Procedural Terminology, fourth edition (CPT-4) codes and median costs from MarketScan databases by type of medical and home care

Health services	Variable	CPT4 codes*	Median cost per visit or per day in 2012 USD†
Physical therapy	Procedure	Initial visit CPT4 code 97001 Follow-up visit CPT4 code 97002	93.18 65.36
Occupational therapy	Procedure	Initial visit CPT4 code 97003 Follow-up visit CPT4 code 97004	97.35 72.32
Speech therapy	Procedure	Initial visit CPT4 code 92506 Follow-up visit CPT4 code 92507	126.55 97.35
Primary care physician	Type of provider	Medical doctor MD (NEC) code 200 or internal medicine (NEC) code 204 or family practice code 240	94.57
Neurologist	Type of provider	Neurology only code 260 (excludes neurosurgery)	123.77
Inpatient rehabilitation and nursing home	Place of service	All inpatient long-term (NEC) code 27 or comprehensive inpt rehab facility code 61 or skilled nursing or nursing facility codes 31 and 32	83.44
Home health	Place of service	Home health code 12	135.51

* CPT4 codes used to filter patients who received a particular type of medical or home care for all of the United States.

† Median cost data for each type of medical or home service obtained from MarketScan database for 2003 and then adjusted to 2012 using medical care part of Consumer Price Index (Bureau of Labor Statistics). Median costs were used to be more conservative as costs were positively skewed. These costs were used in conjunction with Table 4 to generate 5-year follow-up medical care costs.

TABLE 2

Input parameters for the Monte Carlo model

Cost categories by syndrome and cost type*	Distribution type†	Parameters‡	Parameter values	Range
Fever acute medical	Gamma	α (β)	1.7954 (3335.8)	0–∞
Meningitis acute medical	Weibull	α (β)	3.0039 (7791.2)	0–∞
Encephalitis acute medical	Pearson5	α (β)	2.161 (20129.3)	0–∞
AFP acute medical	Invgauss	μ (λ)	55931,22231.8	0–∞
Fever acute productivity	LogNorm	μ (σ)	416.17 (416.18)	0–∞
Meningitis acute productivity	Exponential	β	633.39	0–∞
Encephalitis acute productivity	Pearson5	α (β)	1.3097 (665.47)	0–∞
AFP acute productivity	LogNorm	β	2954.8 (4272.2)	0–∞
Fever LT medical	Exponential	β	789.66	0–∞
Meningitis LT medical	Exponential	β	314.07	0–∞
Encephalitis LT medical	Exponential	β	7601.4	0–∞
AFP LT medical	Weibull	α (β)	1.2628 (6182)	0–∞
Fever LT productivity	Exponential	β	2362.2	0–∞

Meningitis LT productivity	Exponential	β	9072.5	0–∞
Encephalitis LT productivity	Exponential	β	1119.2	0–∞
AFP LT productivity	Exponential	β	14757	0–∞

* Medical is defined as the initial inpatient hospital costs for acute costs and as subsequent medical care costs (e.g., medical appointments, rehabilitation, medicines, durable medical equipment) for long-term costs. Productivity is defined as the value of time lost from work, by age and sex, using estimates from Grosse and others[15] assuming a 5-of 7-day work schedule.

† Cost data from the Colorado cohort were fitted using "fit distribution to data" function of @Risk software. From the suggested distributions of @Risk, the best distribution for each cost type was selected based on relative frequencies, quantile–quantile graphs, χ^2, Kolmogorov-Smirnov, and Anderson-Darling goodness-of-fit (see text for further details).

‡ μ (σ) refer to the Mean (SD) of a logistic normal, α (β) refer to the alpha and beta of a Gamma, Weibull, or Pearson5 distribution, and β refers to the beta of an exponential distribution.

AFP = acute flaccid paralysis; LT = long-term.

TABLE 3

Demographic and clinical characteristics of patients hospitalized with West Nile virus disease by type of cost data and clinical syndrome

A. Participants providing initial hospital cost data (*N* = 80)					
	Fever	Meningitis	Encephalitis	AFP	Total
	N = 18	*N* = 19	*N* = 16	*N* = 27	*N* = 80
Sex Male no. (%)	9 (50)	11 (58)	7 (44)	14 (52)	41 (51)
Age in years* Median (range)	64 (37–86)	47 (16–67)	64 (37–86)	55 (15–84)	55 (15–86)
Days hospitalized* Median (range)	3 (1–12)	4 (2–7)	7 (2–56)	17 (2–68)	5 (1–68)
B. Participants providing long-term cost data (*N* = 38)					
	Fever	Meningitis	Encephalitis	AFP	Total
	N = 12	*N* = 11	*N* = 5	*N* = 10	*N* = 38
Sex Male no. (%)	7 (58)	6 (55)	2 (40)	4 (40)	19 (50)
Age in years Median (range)	52 (37–86)	47 (17–67)	64 (40–77)	60 (15–81)	52 (15–86)
Days hospitalized* Median (range)	3 (1–12)	4 (2–6)	6 (2–10)	14 (2–49)	4 (1–49)

* Test was statistically significant at an individual test critical *P* value < 0.0167 when comparing among clinical syndromes for that variable using analysis of variance for age and Kruskal-Wallis test for days hospitalized and adjusting for multiple tests using the Bonferroni correction.

AFP = acute flaccid paralysis.

TABLE 4

Total economic costs in 2012 USD for patients with West Nile virus disease by clinical syndrome

A. Initial costs				
	Fever *N* = 18	Meningitis *N* = 19	Encephalitis *N* = 16	AFP *N* = 27
Total inpatient hospital costs*				
Median (Range) Mean (SD)	$4,467 (419–23,374) $6,955 (6,282)	$7,261 (337–13,633) $6,961 (3,300)	$15,136 (3,734–207,303) $27,020 (49,012)	$20,774 (5,066–264,176) $70,186 (80,133)
Total lost productivity*†				
Median (range) Mean (SD)	$328 (92–2,729) $546 (659)	$682 (68–1,592) $684 (376)	$1,380 (113–307,871) $53,234 (97,583)	$2,136 (232–145,750) $12,357 (33,089)
Total initial costs*				
Median (range) Mean (SD)	$4,617 (538–24,010) $7,501 (6,762)	$7,942 (1,057–14,569) $7,644 (3,495)	$20,105 (3,965–324,167) $80,254 (104,785)	$25,117 (5,385–283,381) $82,542 (94,388)
B. Long-term costs				
	Fever *N* = 12	Meningitis *N* = 11	Encephalitis *N* = 5	AFP *N* = 10
Medical appointments‡				
Median (range) Mean (SD)	$109 (0–677) $193 (255)	$0 (0–851) $255 (329)	$495 (0–17,160) $3,727 (7,520)	$3,671 (452–12,093) $4,488 (4,007)
Additional care costs§				
Median (range) Mean (SD)	$0 (0–8,900) $742 (2,569)	$0 (0) $0	$334 (0–10,013) $3,371 (4,634)	$278 (0–6,119) $1,318 (1,965)
Medicines, equipment, or modifications¶				
Median (range) Mean (SD)	$72 (0–5,320) $601 (1,521)	$33 (0–1,305) $227 (440)	$109 (0–1,964) $503 (833)	$590 (106–427,028) $43,356 (134,810)
Subtotal of long-term medical costs‡				
Median (range) Mean (SD)	$110 (0–9,751) $1,536 (3,090)	$138 (0–2,156) $481 (726)	$2,459 (0–23,693) $7,601 (9,866)	$5,323 (624–439,945) $49,163 (137,379)
Lost productivity				
Median (range) Mean (SD)	$1,180 (0–39,760) $5,479 (8,974)	$10,363 (0–258,592) $31,756 (60,693)	$0 (0–5,596) $1,119 (2,010)	$6,771 (0–143,033) $27,585 (36,746)
Total long-term costs				
Median (range) Mean (SD)	$2,271 (0–41,401) $7,015 (12,099)	$10,556 (0–260,748) $32,238 (76,125)	$8,055 (0–23,693) $8,721 (9,445)	$22,628 (624–439,945) $76,747 (135,103)

* Test was statistically significant at an individual test critical *P* value < 0.0167 when comparing among clinical syndromes for that variable using Kruskal-Wallis test and adjusting for multiple tests using the Bonferroni correction.

† Lost productivity costs include the lifetime lost productivity costs for six case-patients that died during the acute hospitalization, including four encephalitis cases and two AFP cases. For these cases, no value was assigned to the days spent in the hospital prior to their death.

‡ Test was statistically significant at an individual test critical *P* value < 0.0083 when comparing among clinical syndromes for that variable using Kruskal-Wallis test and adjusting for multiple tests using the Bonferroni correction.

§ Additional care costs include costs experienced because of stay in an inpatient rehabilitation or nursing home facility and as a result of home care costs.

¶ Medication, medical equipment, or modifications include cost of new medications after hospitalization, new durable medical equipment, or any modifications that were needed to their home or car because of their West Nile virus disease.

AFP = acute flaccid paralysis; USD = United States dollars.

TABLE 5

Number and proportion of hospitalized patients with West Nile virus disease needing long-term medical services and care and median number of encounters or goods by clinical syndrome

	Fever		Meningitis		Encephalitis		AFP	
	N = 12		*N* = 11		*N* = 5		*N* = 10	
Physical therapy								
No. (%)	1	(8)	–*	(–)	2	(40)	10	(100)
No. visits (range)	8	(–)	–	(–)	11	(9–12)	34	(5–164)
Occupational therapy								
No. (%)	–	(–)	–	(–)	2	(40)	6	(60)
No. visits (range)		(–)	–	(–)	6	(3–8)	6	(1–48)
Speech therapy								
No. (%)	1	(8)	–	(–)	1	(20)	–	(–)
No. visits (range)	1	(–)	–	(–)	104	(–)	–	(–)
Primary care physician								
No. (%)	3	(25)	5	(45)	1	(20)	2	(20)
No. visits (range)	2	(1–2)	6	(2–9)	12	(–)	5	(3–6)
Neurologist								
No. (%)	4	(33)	1	(9)	3	(60)	8	(80)
No. visits (range)	3	(1–5)	2	(–)	4†	(1–36)	4†	(1–6)
Inpatient rehab or nursing home								
No. (%)	–	(–)	–	(–)	1	(20)	4	(36)
No. days (range)	–	(–)	–	(–)	30	(–)	25	(20–74)
Home health								
No. (%)	1	(8)	–	(–)	3	(60)	2	(20)
No. days (range)	8	(–)	–	(–)	36	(3–90)	6	(5–6)
New medication								
No. (%)	7	(58)	6	(55)	2	(40)	5	(50)
No. drugs (range)	1	(1)	1	(1–3)	1	(1)	2	(1–3)
Durable medical equipment								
No. (%)	1	(8)	1	(9)	2	(40)	10	(100)
No. equipment (range)	1	(–)	2	(–)	2	(1–2)	4	(1–6)
Modified home/car								
No. (%)	2	(17)	–	(–)	1	(20)	5	(50)
No. modifications (range)	1	(1)	–	(–)	1	(–)	2	(1–3)
Missed work or school								
No. (%)‡	9	(75)	10	(91)	1	(20)	7	(70)
No. days (range)§	23	(3–172)	65	(10–2277)	47	(–)	144	(22–1520)

* None reported.

† Three persons (encephalitis – 2, AFP – 1) were still seeing a neurologist at the time of the survey in 2008; number of visits does not reflect any additional visits past 2008.

‡ Includes persons who: missed work (*N* = 23); retired early or lost their job because of their illness (*N* = 3); and worked in the household but whose spouse took off work to care for them (*N* = 1).

§ Number of days worked assuming for every 7 days, 5 days of work, or school are missed. Persons working part-time were assumed to work 50% of a complete day.

Abbreviations: AFP = acute flaccid paralysis.

TABLE 6

Total estimated costs for United States hospitalized West Nile virus cases and death from 1999 to 2012 by cost category from simulation model in 2012 USD

Cost category	Mean*	95% CI	Median*	Range
Total acute medical care	$252,115,100	($158,022,000–$458,998,400)	$230,879,300	($115,644,400–$2,822,846,000)
Total acute lost productivity†	$22,081,260	($9,550,370–$63,069,700)	$16,144,050	($7,070,480–$2,643,251,000)
Total long-term medical care	$27,570,280	($11,566,780–$56,221,870)	$25,468,510	($6,087,800–$118,883,900)
Total long-term lost productivity	$26,866,800	($13,526,800–$48,279,320)	$25,416,720	($7,790,800–$85,567,700)
Total lifetime lost productivity caused by deaths‡	$449,464,800	(NA)	$449,464,800	(NA)

* Represents the mean and median of the 10,000 outputs from the Monte Carlo simulation model for 18,256 hospitalized West Nile virus (WNV) disease cases.

† Includes only survivors.

‡ Lifetime lost productivity was calculated directly from Grosse and others based on age and sex for the 1,524 WNV disease case-patients reported to Centers for Disease Control and Prevention (CDC) who died[15]; the data were not modeled and as such do not have 95% CI or range.

CI = confidence interval; USD = United States dollars.