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Master of Public Health Research Project

***Long-term Effects of West Nile
Virus in Virginia***

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TABLE OF CONTENTS

Abstract.....	3
Introduction.....	4
Objectives.....	7
Methods.....	7
Results.....	9
Discussion.....	13
Conclusion.....	16
Tables.....	17
References.....	32

Long-term Effects of West Nile Virus in Virginia

Diana Ocampo

ABSTRACT

Objective: The purpose of this investigation was to describe the long-term effects and functional outcomes of patients in Virginia who were reported to the Virginia Department of Health with West Nile virus (WNV) non-neuroinvasive and neuroinvasive disease. The study identified the duration of symptoms after initial illness, the number of persons who fully recovered versus the number who continue to be symptomatic and how patients' quality of life differed after illness.

Methods: The study population was drawn from 60 human cases that met the surveillance case definition for non-neuroinvasive and neuroinvasive WNV illness in Virginia between 2002-2004. Information was collected during personal interviews using a standard questionnaire. The questionnaire included questions on demographics, clinical signs and symptoms, existing medical conditions and the respondents' personal assessment of health. Statistical analysis were used to compare pre and post illness symptoms, respondents vs. non-respondents, and non-neuroinvasive respondents vs. neuroinvasive respondents.

Results:

Thirty-four patients were enrolled in the study. Five (14.7%) respondents had non-neuroinvasive disease and 29 (85.2%) had neuroinvasive disease. Thirty respondents (88.2%) reported being hospitalized. Respondents with non-neuroinvasive disease spent a median of 3.5 (range, 0-7) days in the hospital and were unable to resume normal activities for a median of 17 (range, 7-365) days. Respondents with neuroinvasive disease spent a median of 7.5 (range, 0-82) days in the hospital and were unable to resume normal activities for a median of 127.50 days (range, 0-1023). Two (40%) of the respondents that suffer from non-neuroinvasive illness were unable to resume normal activities for at least 90 days. Fifteen (51.7%) respondents with neuroinvasive disease were unable to resume normal activities for at least 90 days. At the time of the interview, 20% of respondents with non-neuroinvasive disease reported fatigue, tremors, arthralgia, paralysis and memory problems. Respondents with neuroinvasive disease reported fatigue (58.5%), weakness (51.7%), myalgias (37.9%), confusion (41.4%), and memory loss (55.2%).

Conclusion: WNV illness, including non-neuroinvasive illness, may be more serious and prolonged than generally thought. Neuroinvasive disease resulted in long-term morbidity and non-neuroinvasive disease resulted in work absenteeism and extended recovery periods. The mortality rates and potential long-term effects associated with non-neuroinvasive and neuroinvasive illness emphasizes the importance of continuing to develop effective methods of targeting preventive education to high-risk populations while continuing to pursue longer-term solutions such as vaccines to prevent emerging infection. Further research is needed to document the long-term effects of WNV, especially in areas with a high number of WNV human cases with more non-neuroinvasive patients. WNV is an emerging infectious disease with a wide clinical spectrum and variable long-term effects; thus a public health concern.

Introduction

West Nile virus (WNV) is a mosquito-borne pathogen that is indigenous to Africa, Asia, Europe, and Australia ^{1,2,21}. WNV belongs to the family *Flaviviridae* which also includes Saint Louis encephalitis (SLE) and Japanese encephalitis viruses. Although outbreaks have occurred from these viruses in the past, WNV was unique because it caused a national epidemic, unlike the other arboviruses ^{27,22}.

WNV was first discovered in the blood of a febrile woman from the West Nile province of Uganda in 1937 ^{4,20}. Human outbreaks occurred in Israel and Africa in the early 1950's, and humans with neuroinvasive disease were reported in Romania, Russia, and Israel in the late 1990's ^{5,6,25}.

The first North American human case of WNV infection identified in the United States was in Queens, New York, in the summer of 1999. The outbreak resulted in 62 clinical cases, including seven deaths ^{2,7}. Since that outbreak, WNV has spread rapidly south and west and in 2002 reached the Pacific Coast. WNV reached the West coast on September 2002 with one human case from Los Angeles County, in Southern California ²⁸.

Many states, including Virginia, detected human WNV infection for the first time in 2002 ²⁸. For the years 1999 through 2001, the total number of US human WNV infection cases reported from the Centers for Disease and Control and Prevention (CDC) was 149, including 18 deaths, from 27 states and the District of Columbia ^{28,8} (**Table 1**). The number of human WNV cases in the U.S. increased dramatically to a peak of 9,862 in 2003 and decreased to 2,539 in 2004 (**Table 1**) with 46 and 50 states reporting respectively in those years ³³.

Shortly after WNV was first detected in the U.S., the Virginia Department of Health established the Interagency Arbovirus Surveillance and Response Task Force, which developed a plan for detecting and responding to WNV and other arboviruses³². Surveillance activities aimed at detecting WNV infection in wild birds, mosquitoes, horses and humans began in 2000, which was the year WNV was first detected in Virginia in seven crows. The first WNV positive mosquito pool in Virginia was detected in 2001, the first horse in 2001, and the first human in 2002. Although all arbovirus infections are on the reportable disease list, many cases may have been undetected because of a low index of suspicion. With the advent of WNV, testing for all arboviruses increased. Because the state Division of Consolidated Laboratory Service (DCLS) utilizes an arboviral panel that includes eastern equine encephalitis, St. Louis encephalitis, WNV and the California group of arboviruses, specimens submitted for testing for any of those infections are tested for all. Although mild WNV disease is far more common than the severe diseases, mild cases are underrepresented in case counts because those persons are less likely to seek medical care, and testing of persons with mild WNV has traditionally been discouraged.

Birds are considered reservoirs of WNV and mosquitoes are vectors. Mosquitoes become infected after taking blood meals from birds that are infected with WNV and then passing the virus to other birds that they feed on. WNV is amplified in at least 100 different bird species and several mosquito species during the bird-mosquito-bird cycle which occurs in warm months. This results in an increased likelihood of infection late in the season when a maximum number of birds and mosquitoes are infected with high levels of the virus. WNV is transmitted to humans most commonly through infected *Culex* mosquitoes²². However, a variety of mosquito species have been implicated in transmitting the virus depending on the geographic area and the species' ability to transmit³⁴. Humans and domestic animals are considered dead-end-hosts to the virus

and therefore WNV is not transmitted from person to person by mosquitoes; there is not enough viremia for a long enough time to continue the cycle³⁷. Although human-to-human WNV infection is rare, it has occurred through blood transfusions, transplacental transfer, organ transplantation, and breast feeding³³.

WNV infection usually results in no symptoms (80%), mild symptoms (20%), or in a minority of infections serious neurologic disease³⁸. WNV surveillance conducted on humans in Connecticut and New York, during October-November in 2000, reported 1 in 5 infected persons had a febrile illness, and approximately 1 in 150 infected persons had severe illness^{7, 30, 31}. In most literature, common symptoms reported are fever, headache, malaise, fatigue, muscle aches and joint pains²⁶. WNV disease is classified as either neuroinvasive or non-neuroinvasive. Non-neuroinvasive infections are considered milder and lack neurologic manifestations.

Neuroinvasive disease results from the virus traveling via the blood to the brain and infecting the central and peripheral nervous systems. Symptoms used to define WNV neuroinvasive disease include fever and at least one of the following: acutely altered mental status such as disorientation or coma, acute signs of central or peripheral neurologic dysfunction, or pleocytosis³³. Neuroinvasive diseases can manifest as encephalitis, meningitis, or acute flaccid paralysis^{5, 7, 17}. The risk of developing neuroinvasive disease increases in patients over 50 years of age, while younger patients are more likely to develop non-neuroinvasive disease³¹.

Although numerous papers have described the clinical characteristics of hospitalized patients, the duration of symptoms has not been specifically addressed. The long-term consequences of WNV disease, both non-neuroinvasive and neuroinvasive, have not been well described for patients. An article by Sejvar et al. reports that persistent fatigue, headache, and myalgia are common long-term effects of neuroinvasive WNV disease. A recent article on neuroinvasive disease

reported that one third of cases were hospitalized and 60% were unable to return to pre-illness activity levels for a median of 150 days (range 90-180)³⁵. Clinical characteristics of hospitalized human cases have been described, but the duration of various signs and symptoms associated with initial signs and symptoms have not been specifically addressed^{26,33}. Further research is needed to document the long-term effects of both neuroinvasive and non-neuroinvasive illnesses to determine the individual and medical burdens that WNV infection represent.

OBJECTIVES

The purpose of this investigation is to describe the long-term effects and functional outcomes of patients in Virginia who were reported to the Virginia Department of Health with both types of WNV illness. The study identified the duration of symptoms after initial illness, the number of persons who fully recovered versus the number who continue to be symptomatic, and how patients' quality of life differed after illness.

METHODS

Data Collection

Although many suspected WNV cases were reported to VDH, cases were only counted if they met the surveillance case definition for probable or confirmed WNV illness. This included the clinical criteria in Figure 1 and positive laboratory test results from the Division of Consolidated Lab Services (DCLS) or another government public health laboratory. Specific laboratory tests were required to differentiate WNV infections from other flaviviruses and move cases from the probable to confirmed category.

Figure 1. Clinical Criteria

Neuroinvasive Disease: Requires the presence of fever and at least one of the following, as documented by a physician and in the absence of a more likely clinical explanation:

- Acutely altered mental status (e.g., disorientation, obtundation, stupor, or coma), or
- Other acute signs of central or peripheral neurologic dysfunction (e.g. paresis or paralysis, nerve palsies, sensory deficits, abnormal reflexes, generalized convulsions, or abnormal movements), or
- Pleocytosis (increased white blood cell concentration in cerebrospinal fluid [CSF]) associated with illness clinically compatible with meningitis (e.g., headaches or stiff neck).

Non-neuroinvasive Disease at minimum, the presence of documented fever, measured by the patient or clinician, the absence of neuroinvasive disease (above), and the absence of a more likely clinical explanation for the illness. Involvement of non-neuroinvasive organs (e.g., heart, pancreas, liver) should be documented using standard clinical-laboratory criteria.

After obtaining approval from Virginia Commonwealth University and the VDH's Institutional Review Board, persons who met the case definition of WNV infection were identified and existing records were retrieved. The state death registry was examined to determine whether any WNV patients were deceased. All cases under the age of 18 and pregnant women were excluded to expedite IRB approval. Demographic data, clinical data, information on initial diagnoses, and past health history that had been abstracted from medical records by VDH using a standard form were utilized by the investigator. Verbal consent was obtained from respondents during telephone interviews and all available respondents were

interviewed using a standard questionnaire. The questionnaire included questions on demographics, clinical signs and symptoms, existing medical conditions, health care and the respondents' own assessment of general health before and after the illness (**Table 2**).

Respondents were asked if they were acutely ill with any of 15 specific symptoms, how often they experienced the symptom before and after they became ill with WNV, and if they currently experience it (**Table 3**). Duration of symptoms was determined using self-reported illness information at the time of the interview and medical records. The Instrumental Activities of Daily Living Scale (IADLS) was used to evaluate patients' functional ability.

Statistical Analysis

Microsoft Office Excel 2003 and SPSS System for Windows, version 13.0 were used to analyze the collected data. Frequencies and percentages of demographics, underlying illnesses, clinical syndrome and discharge status were used to compare respondents and non-respondents. P-values were calculated using chi-square for correlated proportions between symptoms before and after the WNF infection. To calculate the p-values for the "before" and "after" symptoms, outcomes were split into dichotomous variables; never and sometimes were coded as one, and often and always were coded as two. Frequencies, medians and ranges were calculated for the duration of the symptoms.

RESULTS

In Virginia, for the years 2002 through 2004, 60 humans with WNV infection met the case definition as probable or confirmed cases. Of these, six were deceased, two were under the age of 18, and no contact information was available for seven. Of the 45 eligible for inclusion, 11 were lost to follow-up because one refused to participate, four could not be reached in at least four attempts, and six were not interviewed because current contact information was not

available. The remaining 34 patients were enrolled in the study. Medical information was available for all 60 cases.

Interviews were conducted from June 6 to June 29, 2005. Respondents with missing responses or responses of “do not remember” were not included in the calculations for that particular variable. Eleven of the 34 respondents had continuing symptoms they associated with their initial WNV illness. Table 4 shows the demographic and basic clinical information for the respondents and non-respondents. The two groups were similar in age. The median age of the respondents was 56.5 years (range 36-89). Over half of the respondents were men (64.7%) (**Table 4**) and only 8.8% of the respondents were black. There were over four times as many respondents with neuroinvasive disease (82.3%) than non-neuroinvasive disease, but only half of non-respondents had neuroinvasive diseases. Thirty respondents (88.2%) reported being hospitalized (median length of stay, 7 days [range, 0-82]) (**Tables 5 & 11**). Seven (20.6%) reported receiving occupational therapy, and 16 (47.1%) reported receiving physical therapy (**Table 5**). Seventeen (50.0%) respondents had hypertension prior to WNV, and seven (20.6%) had diabetes (**Table 5**).

Many respondents reported having physical and cognitive symptoms at the time of the interview (**Table 6**). When compared with symptoms that were present prior to their WNV illness, the largest changes before and after WNV illness were for memory loss (0 vs. 17), weakness (3 vs. 16), paralysis (0 vs. 9) and confusion (1 vs. 12). Four respondents experienced fatigue before WNV illness (11.3%), while 17 experienced fatigue at the time of the interview ($p < 0.001$). P-values could not be calculated for variables with any respondents with symptoms before WNV illness because there was nothing to compare the “after” variable to. No respondents reported memory loss before WNV illness, yet 17 (50.0%) respondents reported

having memory problems at the time of the interview. Weakness and myalgia followed with 16 and 11 respondents reporting problems, respectively (**Table 6**). Nine respondents reported still experiencing some form of paralysis after the WNV illness (26.5%). Lightheadedness was reported the least with 3 (8.8%) patients reporting symptoms at the time of the interview (**Table 6**).

The duration of physical and cognitive symptoms ranged from zero to 1095 days; it may be longer, but duration of illness was calculated as the time between the date of illness onset and the date of interview (**Table 7**). Weakness was the most frequently reported symptom and also had the longest duration (reported by all 34 respondents, lasting a median of 30 days). Fatigue was the second most common symptom (reported by 30 respondents, lasting a median of 30 days) (**Table 7**). More than half reported experiencing headaches, neck pain, myalgia, lower back pain, photophobia, difficulty concentrating, irritability, confusion and memory loss. Tremors, insomnia, arthralgia, and lightheadedness were reported by less than 20 respondents.

Twenty respondents missed work or school (58.8%) because of their illness (median duration of absence, 7 (range, 0 – 1023). Thirty-one (91.2%) respondents reported reductions in their household activities (e.g. cooking, cleaning, chores) and outside-of-home activities and 32 (94.1%) reported reductions in exercise due to WNV illness, 30 (88.2%) experienced difficulty walking because of their illness. Twenty-seven respondents reported that it took more than 90 days to “get back to normal” (79.4%) (**Table 8**). After the WNV illness 25 respondents reported needing no assistance for shopping (73.5%) and 31 (91.2%) respondents reported needing no assistance for managing money (**Table 9**).

The mean of the all the maximum symptom duration for each non-neuroinvasive patient was 222.40 days, while those with neuroinvasive disease had a mean of 272.21 days (**Table 10**). Among respondents with non-neuroinvasive disease (n=5), the median age was 50 (range, 41 to 68 years) (**Table 11**). Four were under the age of 65 years and one was over 65 years of age. Two out of five patients were hospitalized, with a median length of stay of 3.5 days (range, 0 to 7 days) (**Table 11**). Common acute symptoms included fatigue (100%), weakness (100%), myalgias (80%), headaches (60%), and neck pain (60%) (**Table 12**). Underlying diseases included one respondent (20%) with heart disease (**Table 11**). Symptoms reported at the time of the interview included weakness (20%), tremors (20%), arthralgia (20%), paralysis (20%) and memory loss (20%) (**Table 12**). One respondent reported fatigue for at least 90 days (median: 10, range, 7 to 998 days) and another respondent reported currently having memory loss (20%) (**Table 13**). Of the non-neuroinvasive respondents interviewed, 1 (20%) reported missing work for a median of 10 days (range, 0 to 180) (**Table 13**). Two respondents reported being “not normal” for a median of 17 days (range 7 – 365) (**Table 13**).

Respondents with neuroinvasive disease (n=29) had a median age of 57 (range, 36 to 89). Seventeen (58.6%) of the respondents were under the age of 65 and 12 (41.4%) were over the age of 65 (**Table 11**). Twenty-eight (96.6%) were hospitalized, with a median length of stay of 7.5 days (range, 0 to 82) (**Table 11**). Underlying health conditions included heart disease (51.7%) and diabetes (24.1%) (**Table 11**). Common symptoms during acute illness included fatigue (86.2%), weakness (100%), myalgias (79.3%), headaches (86.2%) and difficulty concentrating (58.6%). Symptoms reported at the time of the interview included fatigue (58.6%), weakness (51.7%), myalgias (37.9%), confusion (41.4%), and memory loss (55.2%) (**Table 12**). It took at least 90 days for 15 (51.7%) respondents to “get back to normal”

(mean: 127.5, range, 0-1023). For at least 90 days respondents reported weakness (37.9%, median: 30, range, 1 to 1095), and memory loss (34.5%, median: 9, range 0 to 1023). Other activities respondents reported having difficulty with included: shopping (31.0%), heavy chores (27.6%), light housekeeping (27.6%), and transportation (27.6%) (**Table 14**).

Of the neuroinvasive respondents interviewed, 12 (41.4%) reported their exercise being reduced after 90 days (**Table 13**). Fifteen (51.7%) respondents reported taking at least 90 days to get back to normal, with a median length of 127.5 (range, 0 to 1023) (**Table 13**). Eleven (37.9%) respondents reported experiencing weakness for at least 90 days, with a median length of 30 (range 1 to 1095) and ten (34.5%) respondents reported memory loss for at least 90 days, with a median of 9 days (range 0 to 1023).

DISCUSSION

The long-term effects described in our study were similar to those reported from the New York 1999 outbreak, a study describing the long-term outcomes of WNV in 2002 in Tennessee, and in patients from St. Tammany Parish, Louisiana in 2002^{12, 17, 35}. Similar to our study, approximately 40% of patients in the New York 1999 outbreak did not return to their own homes immediately after discharge. The common long-term signs and symptoms described in the New York 1999 study 18 months after initial illness included weakness (55.5%), fatigue (63.8%), and memory loss (44.5%)¹². Shopping (40.0%) and heavy chores (55.9%) were also found to be affected after initial illness¹². In Sejvar's article, WNV patients also reported fatigue, myalgias, headache and memory eight months after initial illness¹⁷. After one year, WNV patients from Tennessee reported fatigue (75%), weakness (58%), memory problems (25%) and headaches (25%) to be common long-term characteristics³⁵. In a case report study, four cases of WNV

neuroinvasive disease reported improvements in strength within the 6-month period, but no patient attained full recovery¹⁴.

The Tennessee study also reported that 60% of persons with non-neuroinvasive illness were unable to return to pre-illness level activities due to lingering symptoms³⁵. Although non-neuroinvasive illnesses are considered less severe than neuroinvasive illnesses, our findings also suggest that non-neuroinvasive illnesses can be associated with long-term symptoms (**Table 12 & 13**). Of non-neuroinvasive Tennessee patients, 80% reported having missed work for a median of 4 days and one person reported a decrease in income directly related to the illness³⁸. Our results also suggest that long-term effects of WNV include paralysis (**Table 6**). A study on recovery from paralysis found that after 18-months, previously paralyzed limbs in three patients had either poor or partial recovery³⁶. The study also found that paralysis was acute and plateaus within hours of infection. Regardless of the severity of acute paralysis, it did not predict recovery and effects were variable among affected limbs³⁶. In one case report, a 36-year-old woman had flu-like symptoms for one week and woke up to find herself paralyzed in the left leg³⁶. In comparison, a 44-year-old-man developed paralysis within 2-3 days, yet gained muscle strength in all limbs at nine months³⁶.

The results of our study indicate that the consequences of WNV illness may be more serious and prolonged than generally thought. The median time needed to recover “back to normal” was 180 days. Also, 88.2% of the patients in our study required hospitalization, over half missed school or work after the WNV infection and 67.7% reported that their exercise, household, and outside-of-home activities were reduced for more than 3 months (**Table 8**).

Advanced age (>50) is the greatest risk factor for severe neuroinvasive disease, long-term morbidity, and death from WNV⁴. As others have suggested, our study found that preexisting

health conditions were common among respondents with neuroinvasive disease and may be independent risk factors for severe illness and death^{3, 2, 25}. Although non-neuroinvasive disease is considered a milder form than neuroinvasive disease, our findings suggest that non-neuroinvasive disease can also be associated with long-term morbidity. Twenty percent of respondents with non-neuroinvasive disease reported fatigue, tremors, arthralgia, paralysis and memory problems at the time of the interview. Memory loss (20%) and fatigue (20%) was also experienced by non-neuroinvasive respondents for at least 90 days (**Table 13**). Non-neuroinvasive disease can result in work absenteeism, and extended recovery periods. Further study of person with non-neuroinvasive WNV illness is important to better understand the spectrum of potential morbidity from this disease.

Our findings have several limitations. First, interviews were conducted several months to years after the infection, and recall bias could have influenced responses. Those who were mentally affected with WNV illness may have over exaggerated or under attributed their symptoms to WNV illness. Second, in persons with continuing symptoms, duration of illness was calculated as the time between the date of illness onset and the date of interview and could have resulted in an under-estimate of actual duration. In addition, because persons with milder illnesses might have been less likely to seek medical care and therefore less likely to be tested, our study probably reflects the more severe characteristics of West Nile virus disease. Because WNV illness disproportionately affects older persons, the presence of underlying health conditions may have contributed significantly to the observed outcomes. Due to small sample size, our estimates may be inaccurate. Despite these limitations, the findings are similar to those in other studies and can contribute to our understanding of the impact of this disease on high risk populations.

CONCLUSION

WNV infection leads to persistent morbidity and prolonged recuperation periods. Long-term effects include weakness, fatigue, paralysis, and memory loss. Long-term symptoms were found to also affect activities such as shopping, heavy chores, and transportation. Everyday activities such as walking, exercise and household activities were also affected. Although non-neuroinvasive disease is considered less severe than neuroinvasive disease, our findings suggest non- neuroinvasive diseases can also have more serious long-term outcomes. All persons at risk, especially those over age 65 and those with underlying medical conditions, should take appropriate personal precautions to prevent WNV infection ³¹. Such measures include the use of insect repellents, wearing long, loose-fitting, and light-colored clothing when outside, and elimination of breeding habits near residences. Since there is no treatment for WNV infection, preventive measures should be taken to avoid mosquito exposure and eliminate mosquito breeding grounds.

Public health education about WNV infection and surveillance of WNV human cases, bird deaths, and mosquitoes is also critical for improving the control of the WNV. The mortality rates and potential long-term effects associated with WNV infections emphasizes the importance of continuing to develop effective methods of targeting preventive education to high-risk populations while continuing to pursue longer-term solutions such as vaccines to prevent emerging infection. Further research is needed to document the long-term effects of WNV, especially in areas with a high number of WNV human cases with more non-neuroinvasive patients. Overall, WNV is an emerging infectious disease in evolution, with a variety of clinical symptoms and long-term effects which makes it a public health concern.

Tables

Table 1. WNV human cases and deaths, U.S. and Virginia, 1999 through July 16, 2005

	1999	2000	2001	2002	2003	2004	2005
United States							
Human Cases	149	21	66	4156	9862	2539	41
Deaths	18	2	9	284	264	100	1
Virginia							
Human Cases	0	0	0	29	26	5	
Deaths	0	0	0	2	1	1	

Table 2. Survey characteristics and outcomes requested from WNV study respondents, Virginia, 2002-2004.

Demographics	History of Health	Health Care	Personal Assessment
Age	High blood pressure	Type of specialist used	General Health
Race	Diabetes	If hospitalized	Before WNV
Ethnicity	Seizure	Duration of hospitalization	After WNV
	Cancer	Where discharged	Overall
	Heart Disease	Occupational Therapy	
	Stroke/TIA	Physical Therapy	
	HIV infection	Medications prescribed	
	Tobacco use		
	Alcohol use		

* Cases were asked if they were ever diagnosed with the above diseases, when, and if any medications were prescribed. The personal assessment was scored 0-4 according to the following scale: 4 = Excellent, 3 = Very good, 2 = Good, 1 = Fair, 0 = Poor, 9 = Do not remember, 8 refused.

Table 3: Health outcomes assessed during telephone interviews of study respondents who met case definition of WNV disease, Virginia, 2002-2004

Physical Health	Cognitive Health	Functional Health	Lifestyle Impact
Fatigue	Confusion	Transportation	Work
Headache	Irritability	Telephone	Household Activities
Neck Pain	Lightheadedness	Meal Preparation	Outside-of-home activities
Myalgias	Difficulty Concentrating	Light Housekeeping	Exercise reduced
Tremors	Altered Mental Status	Heavy chores	Difficulty walking
Lower Back Pain		Laundry	Time to get back to "normal"
Weakness		Light chores	
Insomnia		Managing medications	
Photophobia		Managing money	
Arthralgia		Shopping	

* The Instrumental Activities of Daily Living (IADL) were scored 0-3 according to the following scale: With no assistance = 0, with some assistance = 1, cannot complete = 2, N/A = 3.

Table 4. Demographic and clinical characteristics of respondents vs. non-respondents, WNV cases, Virginia, 2002-2004

Characteristic	Total N (%)	Respondents N=34 (%)	Non-respondents N=26 (%)	Test Statistic	p-value
Age					
Median (range)	54.0 (4, 94)	56.5 (36, 89)	56.0 (7, 94)	t-test	0.837
Mean (SD)	57.1 (19.4)	59.24 (15.12)	58.23 (22.41)		
Sex					
Female	21 (35)	12 (35.3)	9 (34.6)	X ²	0.956
Male	39 (65)	22 (64.7)	17 (65.4)		
Race					
White	57 (95)	31 (31)	26 (100)	X ²	0.72
Black	3 (5)	3 (8.8)	0		
Ethnicity					
Non-Hispanic	37 (61.7)	29 (85.3)	8 (30.8)		
Hispanic	6 (10)	5 (5)	1 (3.8)		0.041
Unknown	17 (28.3)	0	17 (65.4)		
Clinical syndrome					
West Nile fever	16 (26.7)	6 (17.6)	10 (38.5)	X ²	0.035
Unknown	2 (3.3)		2 (7.7)		
West Nile neuroinvasive disease					
	42 (70.0)	28 (82.3)	14 (53.8)		
• Encephalitis	19 (45.2)	13 (46.42)	6 (42.9)		
• Meningitis	18 (42.9)	11 (39.3)	7 (50.0)		
• Meningoencephalitis	4 (9.5)	3 (10.7)	1 (7.14)		
• Myelitis	1 (2.4)	1 (3.6)	0		

Table 5. Conditions present prior to WNV and hospital discharge status of WNV study respondents, Virginia, 2002-2004

Characteristic	Respondents N=34	
	No.	%
Existing conditions prior to WNV		
Hypertension	17	50.0
Diabetes	7	20.6
Heart Disease	4	11.8
Cancer	3	8.8
Seizure	3	8.8
Stroke	1	2.9
Hospital Discharge status	30	88.2
Home	22	64.7
Required Physical Therapy	16	47.1
Required Occupational Therapy	7	20.6
Other	5	14.7
Rehabilitation	3	8.8
Skilled nursing facility	3	8.8
Unknown	1	2.9

* Responses of "do not remember" were excluded.

Table 6. Self-reported illness outcomes of WNV study respondents, Virginia, 2002-2004

Symptom	Number of patients reporting symptoms before illness n (%)	Number of patients currently with symptoms n (%)	p-value[†]
<i>Physical</i>			
Fatigue	4 (11.3)	17 (50.0)	<0.001
Weakness	3 (8.8)	16 (47.1)	<0.001
Myalgias	3 (8.8)	11 (32.4)	0.016
Headache	1 (2.9)	9 (26.5)	0.016
Neck pain	3 (8.8)	9 (26.5)	0.031
Lower back pain	5 (14.7)	9 (26.5)	–
Arthralgia	2 (5.9)	9 (26.5)	–
Paralysis	0	9 (26.5)	–
Insomnia	2 (5.9)	8 (23.5)	–
Photophobia	3 (8.8)	6 (17.6)	0.125
Tremors	1 (2.9)	6 (17.6)	0.125
Arthralgia	2 (5.9)	9 (26.5)	–
Paralysis	0	9 (26.5)	–
<i>Cognitive</i>			
Memory Loss	0	17 (50.0)	–
Confusion	1 (2.9)	12 (35.3)	–
Irritability	1 (2.9)	6 (17.6)	–
Difficulty concentrating	2 (5.9)	8 (23.5)	–
Lightheadedness	1 (2.9)	3 (8.8)	–

* Symptoms were scored 0-3 according to the following scale: never = 0, sometimes = 1, often = 2, always = 3, do not remember = 9. Reported include often, sometimes and always. Responses of "do not remember" or no response were excluded.

[†] To obtain p-values through the McNemar test, outcomes were recoded to dichotomous variables; never and sometimes = 0 and sometimes and often = 1.

Table 7. Type and duration of self reported symptoms, WNV study respondents, Virginia, 2002-2004

Symptom	Number of respondents with symptom while ill n (%)	Duration of Symptom		Median Days Duration (range)
		> 7 Days	> 90 Days	
Physical				
Weakness	34 (100)	13 (38.2)	11 (32.4)	30 (1, 1095)
Fatigue	30 (88.2)	12 (35.3)	9 (26.5)	30 (0, 1023)
Myalgias	27 (79.4)	9 (26.5)	9 (26.5)	10 (0, 1095)
Neck pain	23 (67.6)	6 (17.6)	8 (23.5)	9 (0, 1095)
Arthralgia	16 (47.1)	3 (8.8)	8 (23.5)	4 (0, 1023)
Lower back pain	22 (64.7)	8 (23.5)	8 (23.5)	9 (0, 1095)
Headache	28 (82.4)	10 (29.4)	7 (20.6)	9.5 (0, 23)
Insomnia	17 (50)	3 (8.8)	7 (20.6)	0 (0, 1022)
Photophobia	22 (64.7)	9 (26.5)	7 (20.6)	9 (0, 1023)
Tremors	15 (44.1)	6 (17.6)	5 (14.7)	0 (0, 1023)
Cognitive				
Difficulty concentrating	20 (58.8)	7 (20.6)	6 (17.6)	8 (0, 1095)
Irritability	19 (55.9)	6 (17.6)	6 (17.6)	7 (0, 1023)
Lightheadedness	15 (44.1)	5 (14.7)	3 (8.8)	0.5 (0, 1022)
Confusion	20 (58.8)	7 (20.6)	6 (17.6)	7 (0, 1095)
Memory loss	21 (61.8)	8 (23.5)	11 (32.4)	25.5 (0, 1095)

* Responses of "do not remember" or no response were excluded.

Table 8. Lifestyle impact, WNV study respondents, VA 2002-2004

	Total Patients, Number respondents while ill (%)	n (%) Patients Reporting Duration		Median days Duration (range)
		> 7 Days	> 90 Days	
Lifestyle Impact				
Missed work or school	20 (58.8)	4 (11.8)	9 (26.5)	7 (0, 1023)
Household activities limited	31 (91.2)	10 (29.4)	13 (38.2)	60 (0, 1023)
Outside-of-home activities reduced	31 (91.2)	10 (29.4)	13 (38.2)	60 (0, 1023)
Exercise reduced	32 (94.1)	10 (29.4)	13 (38.2)	60 (0, 1023)
Difficulty walking	30 (88.2)	10 (29.4)	13 (38.2)	60 (0, 1023)
Time to get "back to normal"	-	7 (20.6)	27 (79.4)	180 (0, 1023)

Table 9. Functional health outcomes of WNV study respondents, Virginia from 2002, 2004.

	Before illness no assistance n (%)	After illness no assistance n (%)	p-value
Functional Health			
Shopping	34 (100)	25 (73.5)	-
Heavy Chores	34 (100)	26 (76.5)	-
Light housekeeping	34 (100)	26 (76.5)	-
Transportation	34 (100)	26 (76.5)	-
Laundry	34 (100)	27 (79.4)	-
Meal preparation	34 (100)	28 (82.4)	-
Taking Medication	34 (100)	30 (88.2)	-
Telephoning	34 (100)	30 (88.2)	-
Managing Money	33 (97.1)	31 (91.2)	0.063

* Excluded some assistance and cannot complete

Table 10. Mean of maximum symptom duration between non-neuroinvasive vs. neuroinvasive WNV study respondents, Virginia, 2002-2004

	Non-Neuroinvasive N=5	Neuroinvasive N=29	p - value
<i>Patient's max symptom duration</i>			
Mean (SD)	222.40 (435.03)	272.21 (371.95)	0.789

Table 11. Characteristics of respondents of WNV neuroinvasive disease and non-neuroinvasive disease, Virginia, 2002-2004

	Total	Non-neuroinvasive	Neuroinvasive
	N (%)	N=5 (%)	N= 29(%)
All Cases (N=34)	34 (100)	5 (100)	29 (100)
Age median	56.5	50	57
Range	(36-89)	(41-68)	(36-89)
<65	21 (61.8)	4 (80)	17 (58.6)
≥65	13 (38.2)	1 (20)	12 (41.4)
Male (%)	22 (64.7)	2 (40)	20 (69)
Females (%)	12 (20.6)	3 (60)	9 (31)
Hospitalized	30 (88.2)	2(40)	28 (96.6)
Median days	7	3.5	7.5
Range	0-82	0-7	0-82
Underlying health conditions			
Heart disease	16 (47.1)	1 (2.9)	15 (51.7)
Diabetes	7 (20.6)	0	7 (24.1)
Seizure	3 (8.8)	0	3 (10.3)
Cancer	3 (8.8)	0	3 (10.3)
Stroke	1 (2.9)	0	1 (3.4)
Hospital Discharge Status			
Rehab	3 (8.8)	0	3 (10.3)
Skilled nursing facility	3 (8.8)	0	3 (10.3)
Home	22 (64.7)	5 (14.7)	17 (50)
Other	5 (14.7)	0	5 (17.2)
Physical Therapy	16 (47.1)	1 (3)	15 (51.7)
Occupational Therapy	7 (20.6)	0	7 (24.1)

Table 12. Self reported symptoms of WNV study respondents of non-neuroinvasive disease and neuroinvasive disease, Virginia, 2002-2004

Symptoms	Non-neuroinvasive N=5			Neuroinvasive N=29		
	Before	While	Currently	Before	While	Currently
Physical						
Fatigue	0	5 (100)	0	4 (13.8)	25 (86.2)	17 (58.6)
Weakness	0	5 (100)	1 (20)	3 (10.3)	29 (100)	15 (51.7)
Neck Pain	0	3 (60)	0	3 (10.3)	20 (69)	9 (31.0)
Myalgias	0	4 (80)	0	3 (10.3)	23 (79.3)	11 (37.9)
Headache	0	3 (60)	0	1 (3.4)	25 (86.2)	9 (31)
Tremors	0	3 (60)	1 (20)	1 (3.4)	12 (41.4)	5 (17.2)
Lower back pain	1 (20)	3 (60)	0	4 (13.8)	19 (65.5)	9 (31)
Insomnia	0	2 (40)	0	2 (6.9)	15 (51.7)	8 (27.6)
Photophobia	0	2 (40)	2 (40)	3 (10.3)	18 (62.1)	6 (20.7)
Arthralgia	0	1 (20)	1 (20)	2 (6.9)	15 (51.7)	8 (27.6)
Paralysis	0	2 (40)	1 (20)	0	8 (27.6)	8 (27.6)
Cognitive						
Difficulty concentrating	0	3 (60)	0	2 (6.9)	17 (58.6)	8 (27.6)
Irritability	0	3 (60)	0	1 (3.4)	16 (55.2)	6 (20.7)
Lightheadedness	0	2 (40)	0	1 (3.4)	13 (44.8)	3 (10.3)
Confusion	0	1 (20)	0	1 (3.4)	19 (65.5)	12 (41.4)
Memory loss	0	2 (40)	1 (20)	0	19 (65.5)	16 (55.2)

Table 13. Duration of lifestyle impacts and self-reported symptoms of WNV study respondents c, Virginia, 2002-2004

	> 7 days		> 90 days		Median day Duration (range)	
	Non-neuroinvasive	Neuroinvasive	Non-neuroinvasive	Neuroinvasive	Non-neuroinvasive	Neuroinvasive
	N=5	N=29	N=5	N=29	N=5	N=29
Lifestyle Impact						
Missed work or school	2 (40)	2 (6.9)	1 (20)	8 (27.6)	10 (0-180)	9 (0-1023)
Household activities limited	3 (60)	7 (24.1)	1 (20)	12 (41.4)	10 (0-180)	30 (0-1023)
Outside-of-home activities reduced	3 (60)	7 (24.1)	1 (20)	12 (41.4)	10 (0-180)	30 (0-1023)
Exercise reduced	3 (60)	7 (24.1)	1 (20)	12 (41.4)	10 (0-180)	30 (0-1023)
Difficulty walking	3 (60)	7 (24.1)	1 (20)	12 (41.4)	10 (0-180)	30 (0-1023)
Time to get "back to normal"	2 (40)	5 (17.2)	2 (40)	15 (51.7)	17 (7-365)	127.5 (0-1023)
Illness Outcomes						
Physical						
Weakness	3 (60)	10 (34.5)	0	11 (37.9)	10 (7-30)	30 (1-1095)
Fatigue	2 (40)	10 (34.5)	1 (20)	8 (27.6)	10 (7-998)	30 (0-1023)
Myalgias	2 (40)	7 (24.1)	0	9 (31.0)		10 (0-1095)
Neck pain	2 (40)	4 (13.8)	0	8 (27.6)	9 (0-10)	9 (0-1095)
Arthralgia	1 (20)	2 (6.9)	0	8 (27.6)	0	9 (0-1023)
Lower back pain	2 (40)	6 (20.7)	0	8 (27.6)	7 (0-10)	9 (0-1095)
Headache	2 (40)	2 (8)	0	7 (24.1)	9 (0-10)	9.5 (0-1023)
Insomnia	0	3 (10.3)	0	7 (24.1)	0 (0-0)	0
Photophobia	2 (40)	7 (24.1)	0	7 (24.1)	0	9 (0-1023)
Tremors	2 (40)	4 (13.8)	0	5 (17.2)	9 (0-10)	0
Cognitive						
Difficulty concentrating	2 (40)	5 (17.2)	0	6 (20.7)	7 (0-10)	8 (0-1095)
Irritability	1 (20)	5 (17.2)	0	6 (20.7)	7 (0-10)	7 (0-1023)
Lightheadedness	1 (20)	4 (13.8)	0	3 (10.3)	0	.50 (0-1022)
Confusion	1 (20)	6 (20.7)	0	6 (20.7)	0	7 (0-1095)
Memory loss	1 (20)	7 (24.1)	1 (20)	10 (34.5)	0	9 (0-1023)

Table 14. Self-reported illness outcomes of WNV study respondents of non-neuroinvasive disease and neuroinvasive disease, Virginia, 2002-2004

	Before		After	
	Non-neuroinvasive N=5	Neuroinvasive N=29	Non-neuroinvasive N=5	Neuroinvasive N=29
Functional Health				
Shopping	0	0	0	9 (31)
Heavy Chores	0	0	0	8 (27.6)
Light housekeeping	0	0	0	8 (27.6)
Transportation	0	0	0	8 (27.6)
Laundry	0	0	0	7 (24.1)
Meal preparation	0	0	0	6 (20.7)
Taking Medication	0	0	0	0
Telephoning	0	0	0	4 (13.8)
Managing Money	0	1 (3.4)	0	3 (10.3)

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