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Descriptive Epidemiology of West Nile Virus in Nebraska, 2005-2021

Luke Murphy
University of Nebraska Medical Center

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Luke Murphy, MPS

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Capstone Committee:
Kendra Ratnapradipa, PhD
Joseph Fauver, PhD
Jeff Hamik, MS

Abstract

Objectives: West Nile virus (WNV) is a mosquito-borne flavivirus that is naturally sustained in a *Culex* mosquito-bird-mosquito transmission cycle and can cause disease in birds, equines, and humans. Most human infections with WNV are asymptomatic; however, West Nile fever (WNF), or West Nile neuroinvasive disease (WNND) can develop and be fatal in some circumstances. Between 2005 and 2021 there have been over 1,800 cumulative cases of WNV in Nebraska, which currently ranks as fourth in the United States for reported cases. WNV cases are a mandatory reportable disease in Nebraska through an electronic reporting system managed by the Nebraska Department of Health and Human Services (NDHHS). This passive surveillance system has been in place since 2005; however, no analysis has been done on WNV surveillance data in Nebraska. The objective of this study is to examine trends in WNV infections in Nebraska from 2005-2021 and examine characteristics between WNF and WNND cases between 2005 and 2021.

Methods: To examine the burden of WNV disease in Nebraska, descriptive epidemiology using data reported in Nebraska Electronic Disease Surveillance System (NEDSS) from 2005-2021 was performed using the SAS analysis tool. WNF and WNND cases were compared using Chi Square analysis, and predictors for developing WNND were examined by logistic regression analysis. Finally, maps to visualize the cumulative incidence by local health department (LHD) jurisdictions were created using ArcGIS software.

Results: 1,822 cases met the inclusion and exclusion criteria for analysis. Case counts have varied every year between 2005-2021, with noticeable outbreaks occurring in 2006, 2013, and 2018. The average cumulative incidence for Nebraska between 2005-2021 was 5.86 cases per 100,000 people. Urban residence, people aged 65+, Hispanic ethnicity, and races other than white or black were significant predictors for developing WNND.

Conclusion: The overall burden of WNV in Nebraska remains higher than the national average. Continued surveillance and better understanding of the distribution of disease across Nebraska create the best opportunity for utilization of prevention and control resources.

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Abbreviations

Abbreviation	Definition
WNV	West Nile Virus
WNF	West Nile Fever
WNND	West Nile Neuroinvasive Disease
CDC	Centers for Disease Control and Prevention

Background

Origin and Emergence of WNV in Nebraska

West Nile virus (WNV) is an enveloped positive sense single-stranded RNA virus belonging to the *Flaviviridae* family, *Flavivirus* genus [1]. It was first discovered in 1937 in the West Nile region of northern Uganda and has subsequently spread across the world [2]. WNV was first identified in the United States in New York, New York in 1999 [3]. In the years following, WNV rapidly spread across the country causing significant disease burden and death.

WNV was first detected in Nebraska in 2002 and has resulted in 4,122 total cases as of 2021 [4]. WNV is the most frequently reported vector-borne disease in Nebraska, which consistently ranks among the top ten in the United States for reported human cases per year [4-5]. Large WNV disease outbreaks have occurred in Nebraska, most recently in 2018, where 251 WNV disease cases were reported, the most reported cases in the United States that year [4]. The largest outbreak in Nebraska to date was in 2003, when 1,942 cases were reported [4].

Transmission

WNV is driven by a continuous enzootic transmission cycle between mosquitoes and birds. Many different mosquitoes can transmit WNV, but several among the *Culex* species are thought to be the common mosquito vector of WNV [6]. The *Culex tarsalis* mosquito is the most common WNV vector in Nebraska [7]. Birds serve as the reservoir and amplifying hosts of WNV. Human, equines, and other vertebrate animals are considered "dead-end" hosts for WNV due to the low level of viremia, which is not sufficient for the virus to be transmitted to mosquitoes, thus ending the transmission cycle [8]. Transmission of WNV to humans is complex but occurs when significant viral amplification occurs in bird populations which allows bridging vector mosquitoes to transmit the virus to humans. WNV enters a mosquito through a bloodmeal of an infectious bird, where the virus eventually infects the mosquito's salivary glands, after which the mosquito becomes capable of transmitting the virus to susceptible hosts during future bloodmeals [2,9].

Corvids (e.g. American crows and blue jays) are particularly susceptible to WNV infection which can lead to an increase in bird mortality, an indicator that WNV is present in the area [2]. The magnitude of transmission to humans is dependent on several factors including the abundance of susceptible and infected birds and mosquitoes, human exposure, as well as environmental conditions such as vegetation and ground cover [10]. Climate is also thought to play role in WNV transmission, and a study in Nebraska that modeled climate, precipitation, human WNV cases and population found that warm temperatures and a dry year preceded by a wet year were the strongest predictors of cases of WNV [11].

Clinical Manifestation and Diagnosis

Most (approximately 80%) WNV infections are asymptomatic [12-13]. For symptomatic infections, the onset of symptoms typically follows an incubation period of 2-14 days [13]. An estimated 20% of WNV infections develop West Nile fever (WNF), which includes symptoms such as fever, headache, tiredness, body aches, nausea, vomiting, occasionally a skin rash and swollen lymph glands [12-13]. Approximately, 0.7% of people with a WNV infection develop more severe disease, West Nile neuroinvasive disease (WNND), which includes symptoms such as headache, high fever, neck stiffness, stupor, disorientation, coma, tremors, convulsions, muscle weakness, and paralysis [12-13].

Public Health Surveillance

Nebraska Department of Health and Human Services (NDHHS) has developed the West Nile Virus Surveillance Program, which is a statewide partnership between local health departments, local vector control agencies, the Nebraska Public Health Laboratory, and the

NDHHS Epidemiology Unit to test mosquitoes, dead birds, and human samples for WNV infection [14].

WNV is a mandatory reportable disease, in which positive diagnostic tests from hospitals, clinics, and laboratories are reported to NDHHS and to local health departments for case investigations. Reporting is done by telephone, facsimile, other secure electronic mail system, or automated reporting systems such as electronic laboratory reporting or electronic case reporting. Information collected during the investigation includes demographic information, clinical symptoms, hospitalization status and dates, and mortality, among other variables [14].

Current surveillance measures likely underestimate the total number of WNF cases in Nebraska, particularly for asymptomatic and mild-to-moderate infection. Previous research has suggested that for every WNND case there are 30-70 WNF cases, which would suggest that there has been anywhere from 24,000 – 56,000 WNF cases in Nebraska since 2002 [25].

Prevention

There are currently no available human vaccines for WNV, so the key to reducing the risk of WNV is reducing mosquito bites. Educating public health officials and the public more broadly regarding the seriousness of mosquito transmitted diseases like WNV and how they can prevent mosquito bites is crucial to reducing WNV disease burden. NDHHS serves as a resource for local health departments for information on mosquito surveillance, education, prevention, and control. Prevention measures for WNV transmission include reducing exposure through eliminating mosquito breeding habitats and using personal protective measures. Public education can encourage property owners to eliminate sources of standing water such as puddles in low-lying areas, bird baths, and gutters. Mosquito control aims to eliminate and prevent WNV transmission in areas using different chemicals to kill either adult mosquitos or larvae. Local communities or health departments make the final decision regarding mosquito control activities. Communities are responsible for developing, maintaining, and financing local mosquito control programs.

Economic Burden

There has been no economic burden analysis done on WNV cases in Nebraska to date. However, research has estimated that WNV disease cost nearly $780 million dollars between 1999-2012 in direct health care expenditures and indirect costs such as loss of productivity [28]. Individual estimated medical care and hospitalization costs vary from state to state but estimates found higher costs associated with WNND cases in both direct and indirect costs. Estimates from one study found that cases with encephalitis had health care costs ranging from approximately $4,000 to $325,000, while cases with acute flaccid paralysis had medical care costs ranging from $5,000 to $283,000. WNF cases had estimated costs ranging from $500 to $24,000 [32]. Other studies have found outbreaks of 175 or less cases have estimated costs anywhere from $1.7 million to nearly $10.9 million when considering both medical and non-medical costs [33-35]. WNV disease likely creates a considerable economic burden on Nebraska as well, however, more research is needed to get a better understanding of costs associated with the disease.

Project Aims

Specific Aim 1: Describe the burden of West Nile Virus (WNV) cases in Nebraska from 2005 - 2021. This aim utilized NDHHS WNV case surveillance data to perform descriptive statistics, as well as examine annual and cumulative incidence rates for Nebraska during that period.

Specific Aim 2: Compare the clinical characteristics between West Nile fever (WNF) and West Nile neuroinvasive disease (WNND) human cases in Nebraska between the years 2005-2021. This analysis explored significant differences by age groups, sex, and rural residence. This information contributed to the current knowledge of WNV disease and risk factors in Nebraska.

Methods:

Study Design

This project is a retrospective, epidemiological analysis using public health surveillance data among WNV infections among humans in Nebraska between 2005 -2021.

Data Sources

WNV case investigation data was obtained from NDHHS through their tracking system, Nebraska Electronic Disease Surveillance System (NEDSS). A dataset with all case investigations between 2005-2021 was provided for analysis. The NDHHS uses a standardized case history form to collect demographic and clinical information about cases that meet specific criteria for WNV disease. Variables collected through the surveillance system included race, gender, year of birth, date of onset, hospitalization status, and clinical symptoms. Population estimates were obtained from the US Census Bureau (http://www.census.gov) for annual and cumulative incidence calculations. Case investigations are assigned either a WNF or WNND designation depending on lab testing and clinical symptoms. The only asymptomatic cases included in the dataset were positive viremic blood donor cases, which will be excluded from analysis.

Rurality was defined for each case based on the Rural-Urban Commuting Area Codes (RUCA) coding system. The system has assigned every zip code in the US with a number between 1-10 based on population density, urbanization, and daily commuting [24]. Urban residency is defined as a code value between 1-3, and rural residency was defined as a code value between 4-10 [29].

Data Cleaning

The dataset was obtained from NDHHS which included surveillance data on WNV case investigations in Nebraska between 2005-2021. The dataset originally contained 2,972 case investigations. There were 1,847 cases that met the case definition requirement for analysis including 803 confirmed cases and 1,044 probable cases. The remaining 1,125 cases that were removed from the dataset consisted of 4 cases listed as "NULL", 1,060 cases listed as not a case, and 61 cases listed as suspect cases. The dataset also included 13 cases that were identified through blood donor screening. These cases were also removed due to the inability to determine when the infection may have occurred and which condition class they may have been.

Additional data was removed from the analysis. There were 4 cases in which the jurisdiction or residence of the person was not in Nebraska. This included 1 person with a jurisdiction listed as "310023", 2 cases with a jurisdiction listed as "Alpha DHD" (for Training Only), and 1 case with a jurisdiction listed as "Iowa." Additionally, there were 8 cases listed with "Sandhills District Health Department" which is no longer a health district in Nebraska. The final dataset included 1,822 cases that met the eligibility criteria for analysis.

Analysis

The data were analyzed using SAS Studio 3.8 (Enterprise Edition) software. Descriptive statistics included case counts (N) and percentages (%) between WNF and WNND cases. Included in the analysis were total cases, age groups (0-15, 16-24, 25-44, 45-64, 65+), gender, ethnicity, race, hospitalization, rural residence, clinical symptoms, and deaths.

An epidemiological curve of the cumulative case onset date by the epidemiologic week was created to help visualize and compare Nebraska WNV data to previous research. Each bar in the histogram was stratified by both WNV and WNND cases.

Annual incidence rates per 100,000 population were calculated using the case totals for each year divided by the annual Nebraska population estimate (http://www.census.gov) for each year between 2005-2021. Cumulative incidence rate per 100,000 population were calculated using the total number of cases between 2005-2021 divided by the multiplication of the 2010 Nebraska population (http://www.census.gov) and 17 years. Additionally, the cumulative incidence rate for each local health district in Nebraska were calculated and displayed on a map of Nebraska. This will be calculated by taking the number of cases between 2005 to 2021 in each district and divided by the multiplication of the sum of the county's population in each district based on the 2010 Nebraska census and 17 years.

There are 19 local health districts: Panhandle, North Central, West Central, Southwest, Loup Basin, Two Rivers, East Central, Central, South Heartland, Four Corners, Public Health Solutions, Northeast, Dakota, Elkhorn Logan Valley, Three Rivers, Douglas County, Sarpy/Cass County, Lincoln/Lancaster County, and Southeast. Finally, the average annual incidence rates per 100,000 population of WNF and WNND were calculated using case counts of WNF and WNND cases and the population estimate for the respective year.

To compare the characteristics between WNF and WNND, several analyses will be done. Categorical data (e.g. gender, rurality, age, hospitalization status) was analyzed using Chi-square test to determine if there a significant difference between WNF and WNND groups. Fisher's Exact test was used in instances where cell counts were 5 or less. Finally, to identify if gender, age group, and rurality were predictive factors for developing WNND versus WNF, a logistic regression analysis was performed. Odds ratios and 95% confidence intervals based on the logistic regression were calculated. An association was considered statistically significant when the p value was equal or less than 0.05 ($p \leq 0.05$).

Results

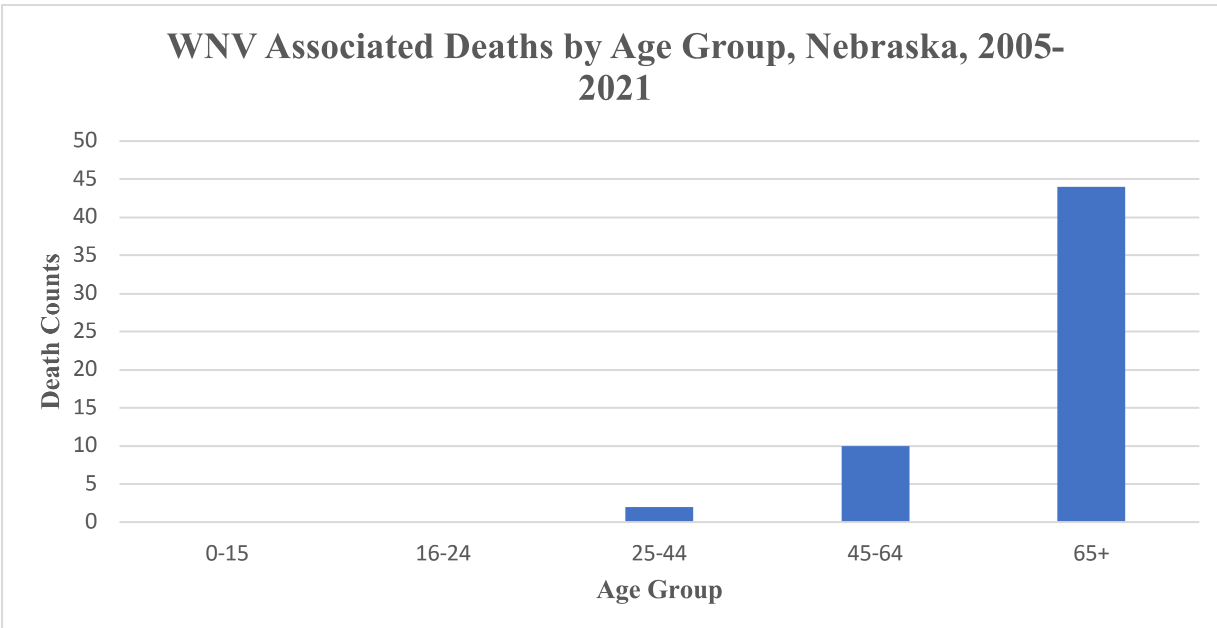
Table 1 presents the demographic and clinical characteristics of reported WNV cases in Nebraska. Median age of all cases was 51 years (range 1-94 years), while the median age of WNF cases was 48 years (range 1-94 years) and the median age of WNND cases was 55 years (range 6-92 years). There were 56 deaths (3.1%) in Nebraska associated with WNV infections, 9 WNF cases and 48 WNND cases. The median age of the cases that died was 75 years (range 30-92 years). For both WNF and WNND, the 45-64 age group comprised of the largest number of cases (41% and 39%, respectively). A majority (57%) of all WNV infections have occurred in males. For WNF, 744 (55%) of the cases were male compared to 301 WNND cases (61%; $p = 0.05$). As expected, a greater proportion of WNND (87%) cases were hospitalized compared to WNF cases (24%; $p < 0.0001$). Overall, cases were predominantly from rural residences (65%). WNF had a larger proportion of cases from rural residences (70%) compared to WNND (52%; $p < 0.0001$). A large portion of both the WNF and WNND cases had unreported or unknown ethnicity (63% and 48%, respectively). From the responses that were collected, WNND had a larger proportion of cases listed as not Hispanic or Latino (49%) compared to WNF (36%). Similarly, a large proportion of the WNF cases (56%) had race not reported or listed as unknown. Both WNF and WNND cases were predominately white (43% and 68%, respectively).

Table 1. West Nile Virus Case Characteristics, Nebraska, 2005-2021.

Variable	WNF (%)	WNND (%)	Total	P-Value*
Total Cases	1331 (73)	491 (27)	1822	
Age Group				
0-15	54 (4)	10 (2)	64	<0.0001
16-24	92 (7)	20 (4)	112	
25-44	380 (28)	103 (21)	483	
45-64	542 (41)	192 (39)	734	
65+	263 (20)	166 (34)	429	
Median	48	55	51	
Gender				
Male	744 (55)	301 (61)	1045	0.0519
Female	586 (44)	190 (39)	776	
Unknown	1 (0.1)	0 (0)	1	
Ethnicity				
Hispanic or Latino	12 (0.9)	16 (3)	28	<0.0001
Not Hispanic or Latino	490(36)	238 (49)	728	
Unknown/Not Reported	848 (63)	237 (48)	1085	
Race				
American Indian or Alaska Native	0 (0)	4 (0.8)	4	<0.0001
Asian	1 (0.07)	0 (0)	1	
Black or African American	9 (0.7)	15 (3)	24	
White	606 (43)	336 (68)	942	
Multiracial	0 (0)	1 (0.2)	1	
Unknown/Not Reported	741 (56)	137 (28)	878	
Hospitalization				
Hospitalized	327 (24)	428 (87)	755	< 0.0001
Not Hospitalized	965 (73)	59 (12)	1024	
Unknown/Not Reported	39 (3)	4 (0.8)	43	
Rural Residence				
Rural	932 (70)	258 (52)	1190	< 0.0001
Urban	350 (26)	231 (47)	581	
Unknown/Not Reported	49 (4)	2 (0.4)	51	
Clinical Symptoms				
Acute flaccid paralysis	0 (0)	2 (0.4)	2	<0.0001
Encephalitis - Including Meningoencephalitis	0 (0)	129 (26.3)	129	
Febrile Disorder	182 (13.7)	0 (0)	182	
Meningitis	0 (0)	101 (20.6)	101	
Other Neuroinvasive	0 (0)	5 (1.0)	5	
Other Clinical - Not Defined	45 (3.4)	0 (0)	45	
Unknown/Not Reported	1104 (82.9)	254 (51.7)	0	
Deaths				
Died	9 (0.7)	47 (9.6)	56	<0.0001
Survived	1139 (85.6)	372 (75.7)	0	
Unknown/Not Reported	183 (13.7)	72 (14.7)	0	
* Chi Square test				

Figure 1. shows the deaths associated with WNV were largely among the 65+ age group (78%) compared to the younger age groups. The two youngest age groups, 0-15 and 16-24, had no deaths reported between 2005-2021.

Figure 1. West Nile Virus Associated Deaths by Age Group, Nebraska, 2005-2021.



A total of 1,822 cases were included for the analysis, and the case counts ranged from 267 (2006) to 15 (2020). Figure 2. shows the case counts for all WNV cases reported in Nebraska between 2005-2021. Three years, 2006, 2012 and 2018 had a spike in cases with the preceding year being substantially lower. In 2006, the total case count for the year was over 11 times greater than the previous year. In 2012, there were 190 cases included for analysis, which was nearly 7 times greater than the cases reported in 2011. In 2013 and 2014 there continued to be elevated case counts with 229 and 141 cases reported, respectively. Finally, in 2018, a total of

251 cases were included in the analysis, which was over 3 times the number of cases reported in 2017.

Figure 2. West Nile Virus Disease Cases Reported by Year, Nebraska, 2005-2021

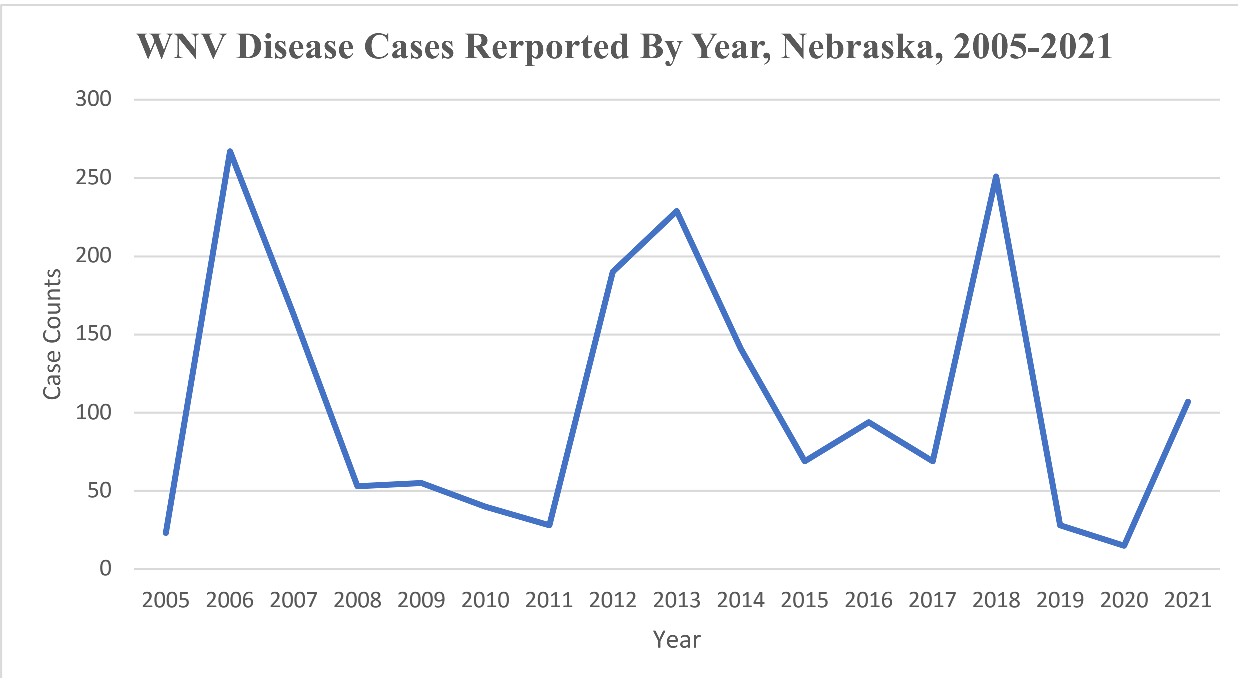
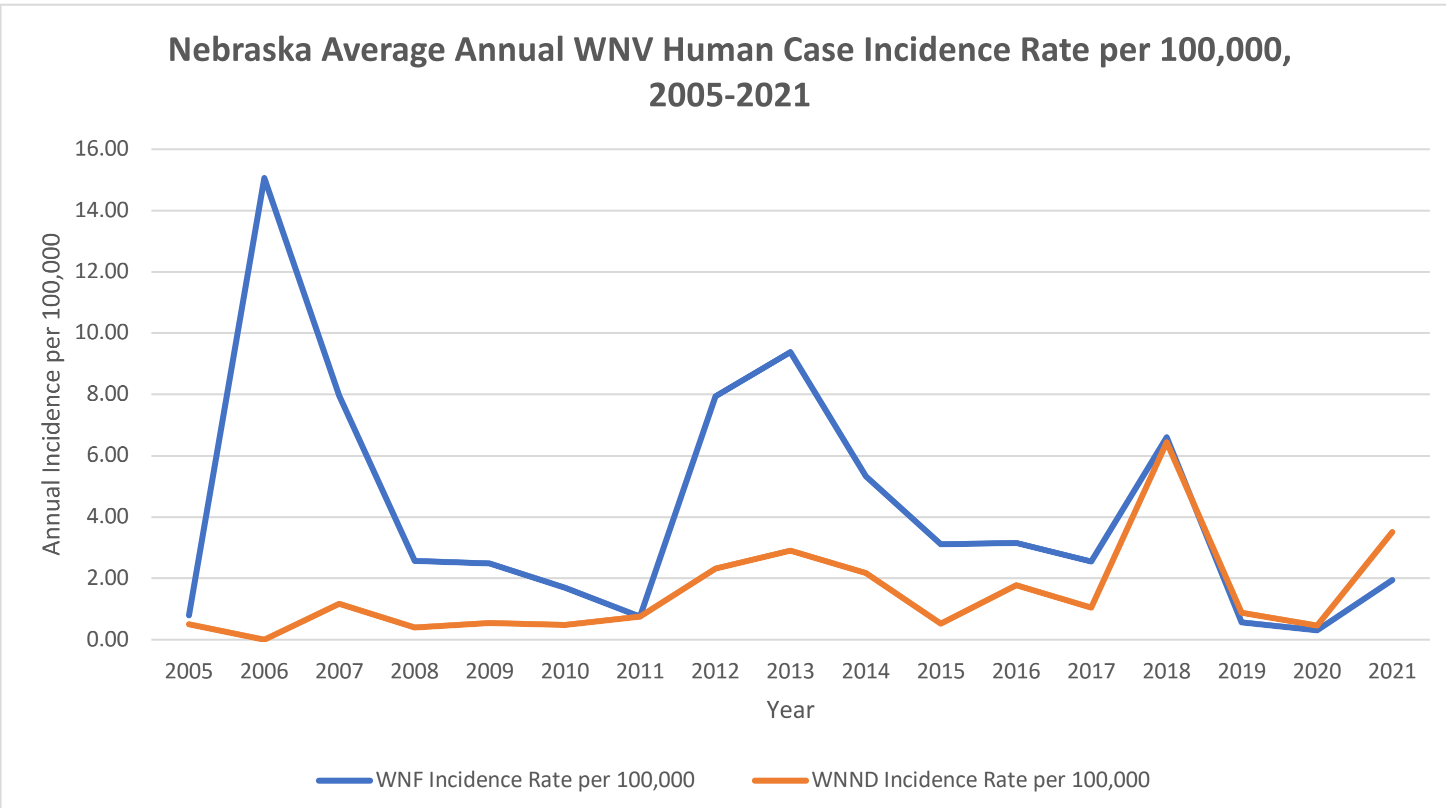


Figure 3. displays the annual incidence rates per 100,000 people of WNF and WNND cases in Nebraska between 2005-2021. The annual incident rates for WNF ranged from a low of 0.31 per 100,000 people in 2020 to the highest rate of 15.06 per 100,000 people in 2006. There have been three peak years for WNF incidence, as seen in Figure 3. The peak years were 2006, 2013 with an incident rate of 9.38 per 100,000 people, and 2018 with an incident rate of 6.60 per 100,000 people. The annual incidence rates for WNND ranged from a low rate of 0.00 per 100,000 people in 2006 to the highest rate of 6.44 per 100,000 people in 2018. As expected,

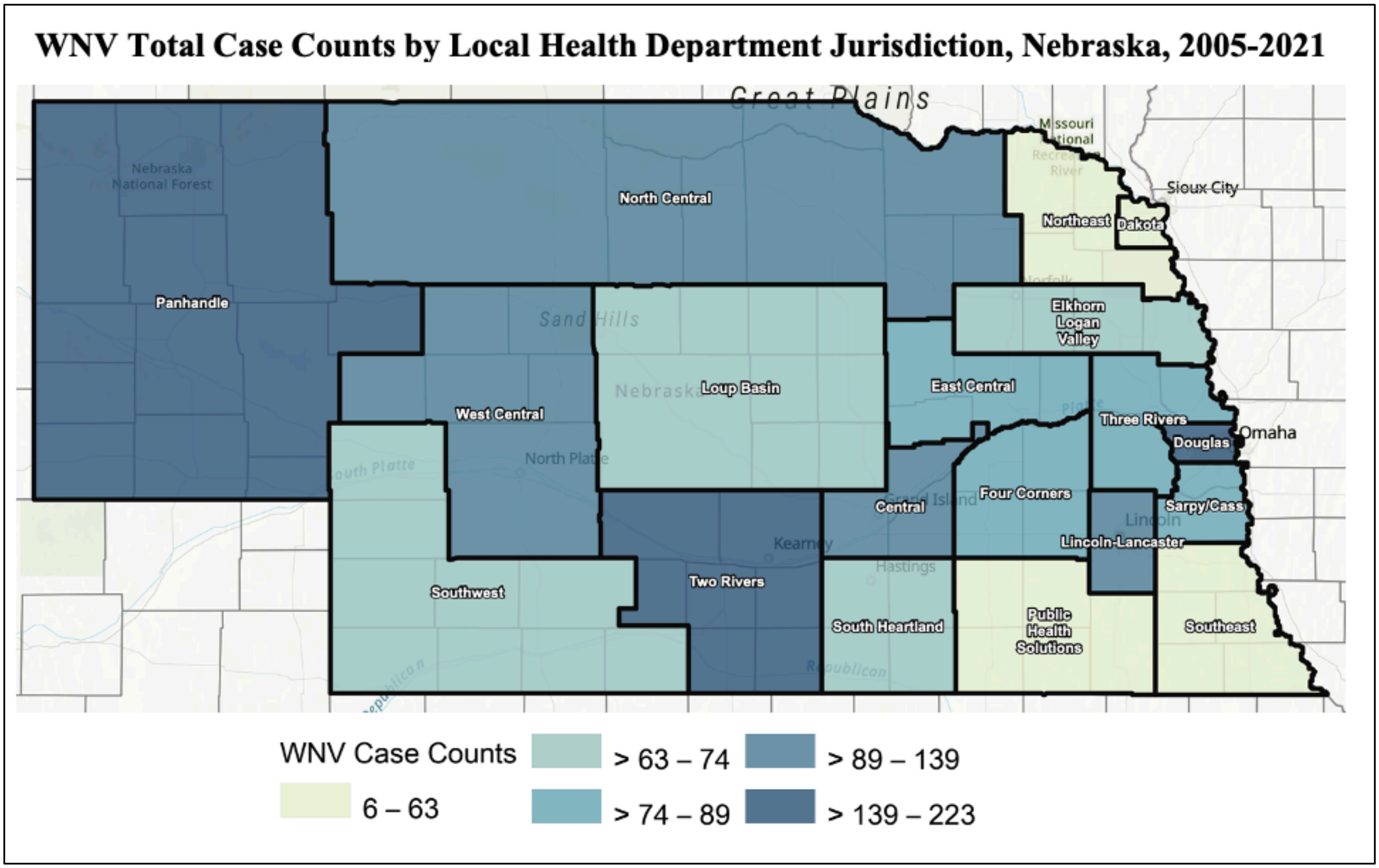
WNF incidence rates were more often higher than WNND incidence rates. However, in recent years, 2019-2021 has shown WNND to have slightly higher incidence rates than WNF.

Figure 3. **Annual WNF and WNND Case Incidence Rate per 100,000, Nebraska, 2005-2021**



In Figure 4, the cumulative WNV cases for each LHD jurisdiction from 2005-2021 are shown. The three LHD jurisdictions with the highest cumulative case counts were Douglas County with 223 cases, Panhandle Public Health District with 208 cases, and Two Rivers Public Health Department with 177 cases. The three LHD jurisdictions with the lowest cumulative case counts were Dakota County Health Department with 6 cases, Southeast District Health Department with 17 cases, and Northeast Nebraska Public Health Department with 31 cases.

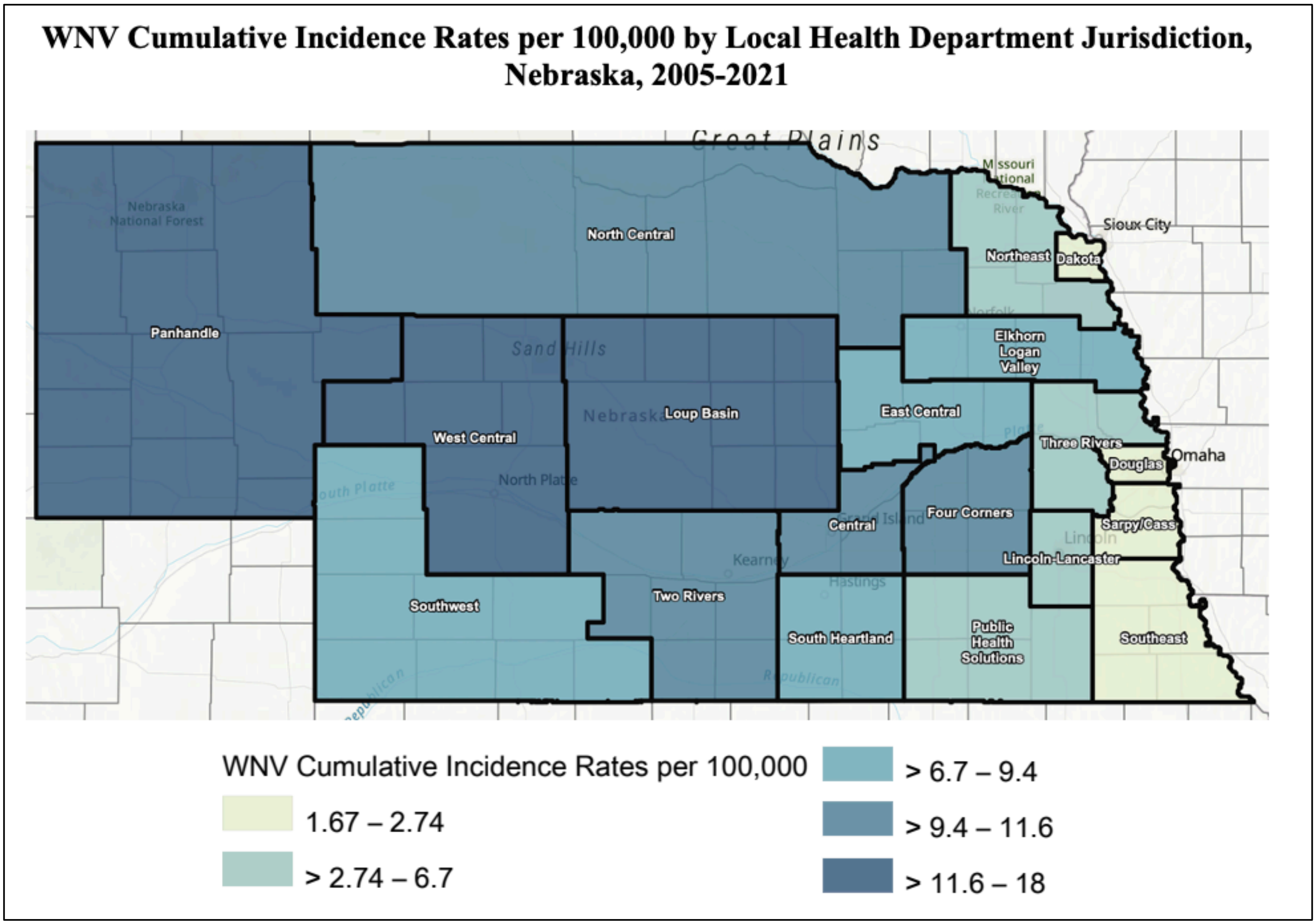
Figure 4. Total WNV Cases by Local Health Department Jurisdiction, Nebraska, 2005-2021.



Cumulative WNV incidence rates per 100,000 population by LHD are depicted in Figure 5. The West Central District Health Department jurisdiction had the highest incidence rate of all LHDs at 18.20. The other jurisdictions with high incidence rates included Panhandle Public Health District (13.84), Loup Basin Public Health Department (13.79), and North Central District Health Department (11.66). The jurisdictions with the lowest incidence rate were Dakota

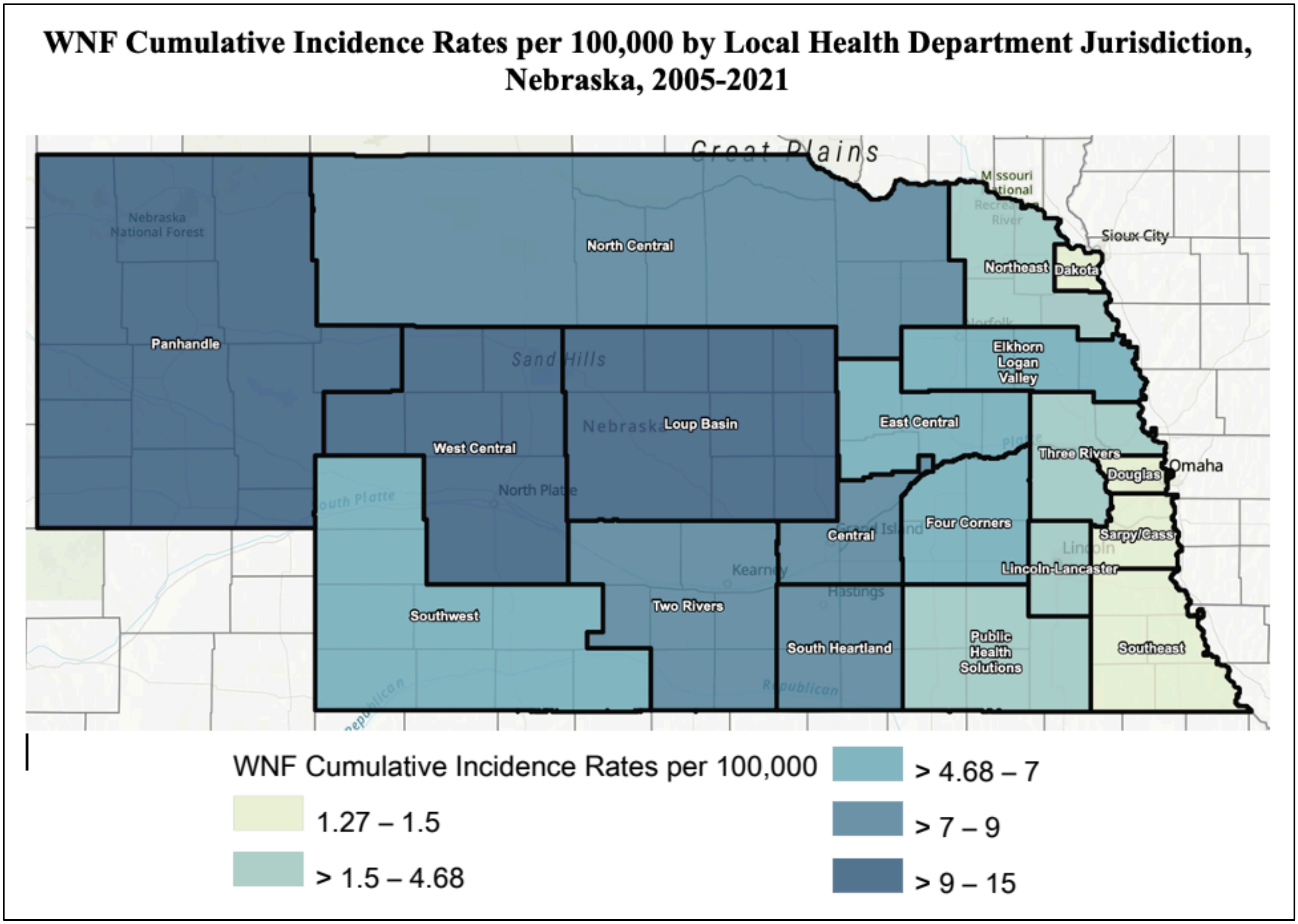
County Health Department (1.68), Douglas County Health Department and Southeast District Health Department each with a rate of 2.54, and Sarpy/Cass Health Department (2.75).

Figure 5. WNV Cumulative Incidence Rate per 100,000 by Local Health Department Jurisdiction, Nebraska, 2005-2021.



WNF cumulative incidence rates per 100,000 population for each LHD jurisdiction can be seen in Figure 6. The three LHD jurisdictions with the highest cumulative WNF incidence rates were West Central District Health Department (15.07), Panhandle Public Health District (11.71), and Loup Basin Public Health Department (11.52). The three LHD jurisdictions with the lowest cumulative WNF incidence rates per 100,000 were Sarpy/Cass Health Department (1.28), Dakota County Health Department (1.40), and Douglas County Health Department (1.43).

Figure 6. WNF Cumulative Incidence Rate per 100,000 by Local Health Department Jurisdiction, Nebraska, 2005-2021.



WNND cumulative incidence rates per 100,000 population for each LHD jurisdiction can be seen in Figure 7. The three LHD jurisdictions with the highest cumulative WNND incidence rates were Four Corners Health Department (3.73), West Central District Health Department (3.13), and North Central District Health Department (2.66). The three LHD jurisdictions with the lowest cumulative WNF incidence rates per 100,000 were Dakota County Health Department (0.28), South Heartland District Health Department (0.64), and Lincoln-Lancaster County Health Department (1.05).

Figure 7. WNND Cumulative Incidence Rate per 100,000 by Local Health Department Jurisdiction, Nebraska, 2005-2021.

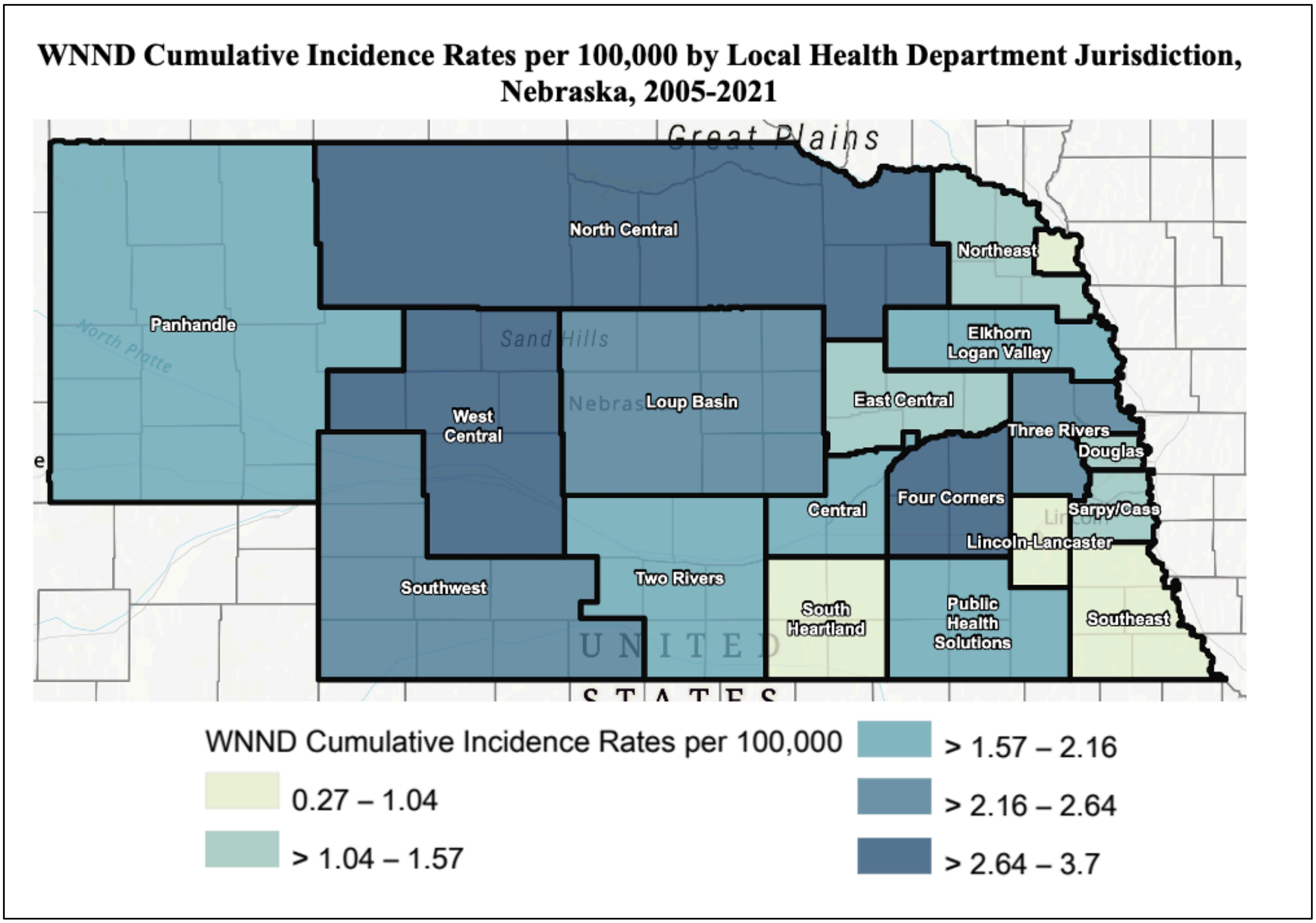


Figure 8 depicts an epidemiological curve depicting both WNND and WNF case onset dates based on the epidemiological calendar week. The graph illustrates that WNV disease onset begins to steadily increase beginning in epidemiological week 21 (late May to early June) until it peaks in week 36 (or early September). Case onset epidemiological weeks ranged from week 15 to week 52. WNND and WNF cases both follow a similar curve, peaking in week 36. WNND does continue to have a large number of cases in weeks 37 and week 38 before tapering off.

Figure 8. Epidemiological Curve of Reported Human WNV Disease Onset Date, Nebraska, 2005-2021.

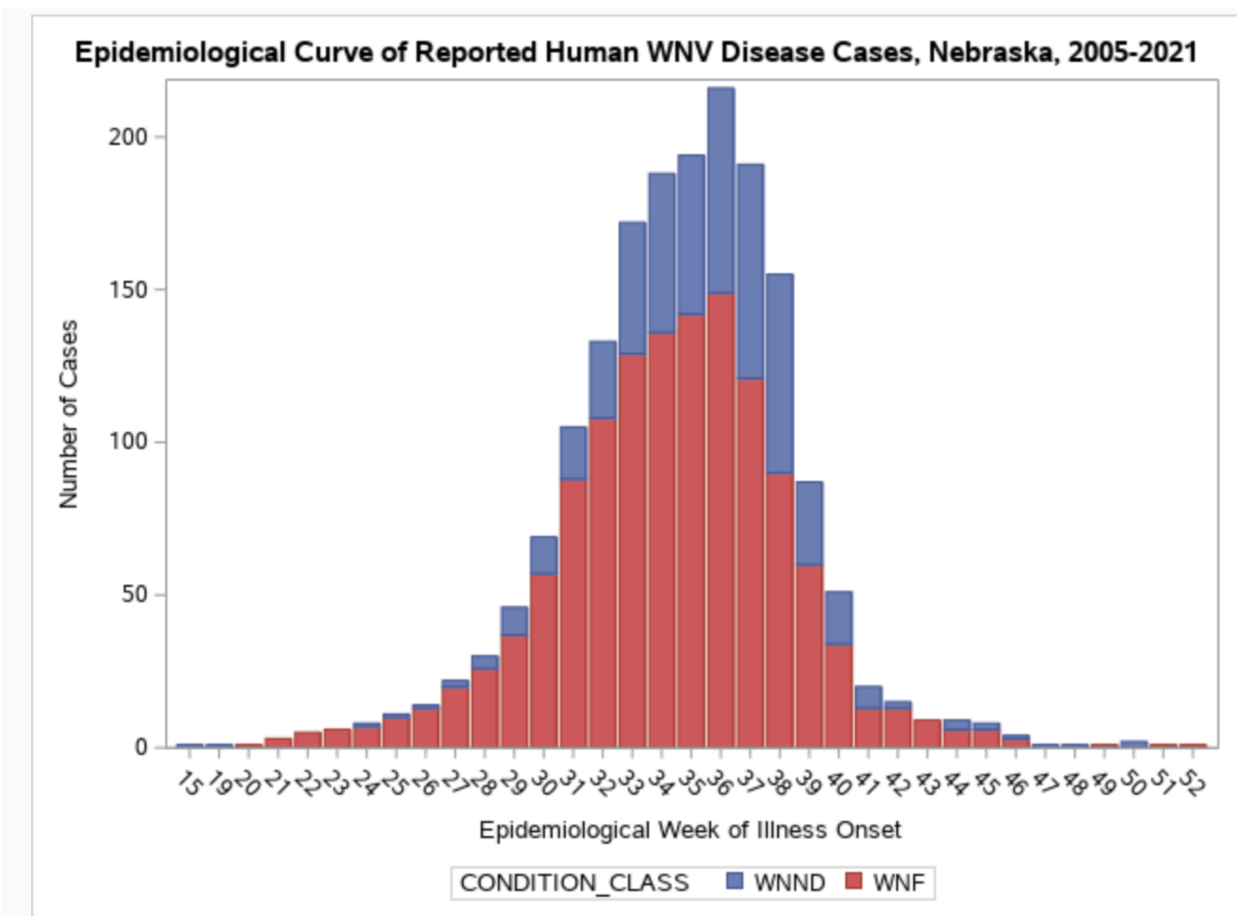


Table 2 displays the univariate analysis on the predictor variables to determine if they met a p-value cutoff of p<0.25 for entry into the multivariate logistic regression model. All variable effects were found to be significant and were entered into the full model.

Table 2. Univariate Analysis for WNND development, Nebraska, 2005-2021.

Variables	Crude P-Value
Gender	0.12
Age Group	<0.0001
Rural Status	<0.0001
Ethnicity	<0.0001
Race	0.006

Table 3 displays the adjusted odds ratios, 95% confidence intervals, and p-values from the logistic regression model for the development of WNND. During the stepwise selection process, gender was not entered into the model due to the effect being non-significant (p>0.05). The remaining predictors in the type 3 analysis of effects in this model were all significant. There were several predictors that were significant including the 65+ age group, urban residence, Hispanic ethnicity, and other race category. The estimated odds of developing WNND were 2.18 times greater for cases aged 65+ than the estimated odds of cases aged 45–64 (95% CI 1.55-3.06, p <0.0001). For cases with an urban residence, odds of developing WNND were 2.18 times more likely than the odds of cases with a rural residence (95% CI 1.64 – 2.89, p <0.0001). The estimated odds of cases with Hispanic ethnicity were 2.35 times the odds of non-Hispanic cases

(95% CI 1.00 – 5.52, p = 0.05). Finally, the estimated odds of cases with a race other than white or black was 9.59 times the odds of white cases (95% CI 1.06—86.48, p = 0.04).

Table 3. Multivariate Analysis for WNND development, Nebraska, 2005-2021.

Variables	Adjusted Odds Ratio Estimates	Adjusted 95% Confidence Interval	P-value
Age (year)			
Ages 0-15	0.35	0.12 - 1.06	0.06
Ages 16-24	0.88	0.45 - 1.72	0.7
Ages 25-44	0.73	0.51 - 1.05	0.09
Ages 45-64	Reference	Reference	Reference
Ages 65+	2.18	1.55 - 3.06	<0.0001
Rural Status			
Urban	2.18	1.64 - 2.89	<0.0001
Rural	Reference	Reference	Reference
Ethnicity			
Hispanic or Latino	2.35	1.00 - 5.52	0.05
Non-Hispanic or Latino	Reference	Reference	Reference
Race			
Black or African American	1.992	0.67 - 5.94	0.07
Other Race	9.59	1.06 - 86.48	0.04
White	Reference	Reference	Reference

Discussion

To my knowledge, this is the first report that summarizes the epidemiological characteristics of WNV cases in Nebraska. Additionally, this report data spanned 17 years, which incorporates some of the most recent data available and one of the longest time spans for analysis.

The epidemiological curve revealed results consistent with previous research, with most of the cases reporting illness onset between July – September [26]. Case counts varied widely from year to year in Nebraska between 2005-2021, including three major outbreak years (2006, 2012, and 2018) during this time. These events happened in other states where WNV is endemic as well; however, the etiology of outbreaks has yet to be determined.

Record low reported cases were seen as recently as 2020, which could possibly be explained by the COVID-19 pandemic. While many people were reportedly spending more time outdoors, thus increasing their potential exposure, healthcare utilization was also disrupted likely leading to fewer WNF cases being reported. Overall, the average incidence for WNV disease between 2005-2021 was 5.86 cases per 100,000 people. In comparison, research from the Centers for Disease Control and Prevention (CDC) found that the United States average incidence between 2009-2018, was 0.4 cases per 100,000 people [26]. North Dakota and South Dakota also had significantly higher average incidence rates during that time (3.16 cases per 100,000 and 3.06 cases per 100,000, respectively) compared to Iowa, Kansas, and Missouri (0.45, 0.51, and 0.22 cases per 100,000, respectively) [26]. Nebraska appears to have suitable conditions for greater transmission compared to some neighboring states. Firstly, Nebraska sits within a bird migration flyway and is a migration stopover site which increases the abundance of available hosts for potential WNV transmission. Secondly, Nebraska has the most acres of irrigated land in the US, over 8.5 million acres, which creates a suitable breeding environment for *Culex tarsalis* mosquitoes [30]. In comparison, Iowa, Kansas, and Missouri have significantly fewer acres of irrigated land at 200,000 acres, 2.5 million acres, and 1.5 million acres, respectively [30].

Additionally, differences in arboviral surveillance practices and funding makes it difficult to assess differences in arboviral activity in the states that surround Nebraska. For example, Kansas only recently (2017) expanded their mosquito surveillance from 1 county to 3 [31]. In Iowa, according to a yearly report from 2013, mosquitos were trapped in 5 counties across the state. Nebraska has 21 counties that trap mosquitos throughout the WNV season each year.

The annual incidence rates of both WNF and WNND in Nebraska overall appeared to follow the expected trend of WNF having a higher incidence rate and to increase and decrease at a similar rate. Most years, 2008-2017, this trend was observed. However, in 2005-2007, there were notable difference in WNF incidence rates and WNND. There was a significant surge in WNF annual incidence rate in 2006, with very little change or a decrease in the WNND incidence rate. There were no WNND cases included in the analysis for 2006, which could be the result of an outlier year in which no severe disease developed or the result of reporting bias where appropriate testing was not done to trigger a case investigation. More recently, 2018-2021 has seen WNND annual incidence rate that is greater than the WNF incidence rate during this time. This could be the result of fewer people seeking medical care for more mild symptoms, especially in the COVID-19 pandemic years 2020 and 2021.

The incidence rates among the different LHD jurisdictions varied across the state. Central and western Nebraska LHD jurisdictions (Panhandle Public Health District, Loup Basin Public Health Department, and West Central District Health Department) had some of the highest cumulative WNV incidence rates between 2005-2021. The eastern half of Nebraska, specifically the jurisdictions along the Missouri river, had some of the lowest cumulative incidence rates which can, in some instances, be attributed to larger populations. The WNF and WNND incidence maps also reflect that the western and central Nebraska LHD jurisdictions, which are largely rural, have some of the higher incidence rates in the state. Agriculture and irrigation use are likely contributors to the higher incidence rates in these areas of the state. Different mosquito species also prefer different breeding environments as well. Specifically, *Culex tarsalis*, the prominent vector for WNV in Nebraska, breeds primarily in irrigated agriculture areas [10]. Conversely, *Culex pipiens*, also capable of WNV transmission, favor urban areas and often breed in standing water (i.e., bird baths, tire piles, etc.) [10].

Males made up a larger proportion of cases for both WNF and WNND cases (55% and 61%, respectively), which was consistent with other research [15, 17-19, 21-23]. Interestingly, male sex was not found to be a significant predictor for developing WNND, which is in contrast to other research [15,22-23]. It is unclear if mosquito exposure for males and females is different in Nebraska compared to other states, suggesting that additional research is necessary. While a large portion of the race and ethnicity data was unknown or unreported, of the data that was collected, both WNF and WNND cases were predominantly non-Hispanic or Latino (36% and 49%, respectively) and white (43% and 63%, respectively). This can largely be explained by Nebraska's predominately non-Hispanic white population [27]. The 2021 Nebraska race and ethnicity estimated that 77.4% of the population was non-Hispanic white, 12% were Hispanic or Latino, and 5.3% were black [27]. Hispanic ethnicity and race other than white or black were found to be significant predictors for developing WNND. While this might suggest there is a potential ethnic or racial disparity in WNND case development, more complete data collection and additional research is needed to further support this finding.

Hospitalization, clinical symptoms, and deaths all represented expected findings with a larger proportion of WNND cases being hospitalized (87%), accounting for all of the neuroinvasive symptoms reported, and accounting for a majority of deaths (84%). Both WNF and WNND cases had larger proportions of cases with rural residency (70% and 52%, respectively). Urban residence was also found to be a predictor for the development of WNND, which is interesting considering Nebraska's large rural population [27].

There were several limitations in this study. One limitation of this study was that case reporting in Nebraska is a passive surveillance system and reported cases are dependent on health-care providers and laboratories. The result is a likely underestimation of true incidence, specifically for WNF cases. Another limitation of the study was that case history is obtained by LHD or in some instances NDHHS personnel. There are likely differences between jurisdictions and completeness of the case history forms. Certain sections of the case report forms, such as race and ethnicity as well as symptoms, lacked a significant amount of data. Additionally, no underlying disease is obtained in the case history, which could also be used to better identify predictors for the development of WNND.

Conclusion

WNV has been in Nebraska for 20 years, and throughout that time the state consistently reports some of the largest case counts in the country. Incidence rates for Nebraska are much higher than national averages and several surrounding states. Given how quickly WNV spread across the US, the devastation that was caused in both human and bird populations (specifically Corvid birds), and the recurrent outbreaks throughout the US, the need for WNV surveillance, prevention, and research continues to be necessary. This is certainly not without its challenges. Nebraska has a relatively small population dispersed over a large geographic area, which makes prevention efforts challenging [26]. In addition, vectors, hosts, environment, human behavior, and climate change all make predicting future WNV disease and disease prevention difficult. Continually monitoring and developing a better understanding of the geographic distribution of cases at a county or LHD jurisdiction level helps provide the best opportunity to direct the necessary resources for disease prevention and mosquito control.

This project helped identify LHD jurisdictions with high case counts, high incidence rates relative to jurisdictions within the state, and reveal demographic information. More complete data collection and collecting new information such as underlying health conditions would be beneficial for future analysis.

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Application of Public Health Competencies

Foundational Competency: MPHF19 Communicate audience-appropriate public health content, both in writing and through oral presentation. Competency MPHF19 was integrated into this capstone project through the capstone presentation and the capstone paper. These items provide public health content on WNV burden in Nebraska, and present epidemiological findings that can be understood by all public health students, faculty, and staff.

Concentration Competency: EPIMPH3 Analyze datasets using computer software. This competency was applied to this project in multiple ways. Firstly, the descriptive data analysis, univariate and bivariate analysis was done utilizing SAS Studio 3.8 (Enterprise Edition) software. Secondly, Microsoft Excel was utilized to display different information such as WNV case totals by year, cumulative disease onset date by month, and annual incidence trends.

Concentration Competency: EPIMPH4 Utilize analytical approaches to describe, summarize and interpret epidemiological data. Competency EPIMPH4 builds on the previous competency EPIMPH3, in that the data being analyzed, summarized, and interpreted for a capstone paper. The output from the analysis (i.e., graphs, tables, and maps) were used to help illustrate and describe the WNV burden in Nebraska.

Appendix A

LUKE MURPHY

16592 SW Sunshine Coast St | Tigard, OR 97224 | 402-659-5947 | lmurphy402@gmail.com

PROFESSIONAL EXPERIENCE

Clinical Study Coordinator

University of Nebraska Medical Center 09/2019 – Present

Omaha, NE

- Coordinate patient participation in clinical trials.
- Recruit and screen subjects; ensuring informed consent is obtained for assigned trials.
- Educate subjects regarding the study, schedule clinical visits and procedures under the direction of the Principal Investigator.
- Coordinate the collection and testing of laboratory samples, including shipping to off-site laboratories.
- Ensure compliance with protocol guidelines and requirements for regulatory agencies.
- Serve as liaison between internal departments and external entities for regulatory and protocol compliance.
- Assist other researchers, nurses, CRAs and Lead Nurses involved in research trials.
- Collect, document, and organize study related information.
- Design and develop data collection tools, complete case report forms, and various forms to use for screening, data collection, data entry, and data set management.
- Audit data and create reports.

Clinical Research Technician

University of Nebraska Medical Center 12/2018 – Present

Omaha, NE

- Process specimens collected for research according to the unique study protocol, and in compliance with all requirements of the study sponsor.
- Assist with specimen collection scheduling and ordering on an as-needed basis.
- Laboratory management, including lab processing coverage and supply management.

Clinical Perfusionist

Essentia Health 08/2016 – 12/2018

Fargo, North Dakota

- Operation and management of the Heart-Lung Machine during cardiopulmonary bypass surgery.
- Operation of mechanical support devices (ECMO, VAD).

SKILLS

Administrative

- Clinical study management

- Project management
- Laboratory management

Software

- Microsoft Office
- Electronic medical records systems (EPIC)
- Statistical software (SAS)

Communication

- Excellent verbal and written communication with physicians, staff, and patients

Problem-solving

- Ability to identify and adapt to potential problems in a timely manner.

EDUCATION

University of Nebraska Medical Center
Master of Public Health 2020-Present
Omaha, NE

- Concentration: Epidemiology
- Expected graduation: December 2022

University of Nebraska Medical Center
Certificate in Public Health 2019-2020
Omaha, NE

University of Nebraska Medical Center
Master of Perfusion Science 2014 - 2016
Omaha, NE

- Research Capstone Project:
  - "The Effect of Transfusion of Hemoconcentrated Salvaged Blood Compared to Cell Washed Salvaged Blood on the Thromboelastograph During Cardiopulmonary Bypass Simulation."

Rockhurst University
Bachelor of Science 2010 – 2014
Kansas City, MO

- Major: Biology
- Minor: Psychology