DEVELOPMENT OF AN INDEX TO MEASURE WEST NILE VIRUS TRANSMISSION RISK IN NEW JERSEY COUNTIES

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ABSTRACT. We developed an index for use by New Jersey counties to measure West Nile virus (WNV) transmission risk to the human population. We used a latent profile analysis to develop the index, identifying categories of environmental conditions associated with WNV transmission risk to humans. The final model included 4 indicators of transmission risk: mosquito abundance and minimum field infection rate, temperature, and human case count. We used data from 2004 to 2018 from all 21 New Jersey counties aggregated into 11 2-wk units per county per year ($N = 3,465$). Three WNV risk classes were identified. The Low Risk class had low levels of all variables. The Moderate Risk class had high abundance, average temperature levels, and low levels of the other variables. The High Risk class had substantially above average human case likelihood, average temperature, and high mosquito infection rates. These results suggest the presence of 3 distinct WNV risk profiles, which can be used to guide the development of public health actions intended to mitigate WNV transmission risk to the human population.

KEY WORDS   Latent profile analysis, minimum field infection rate, mosquito abundance, risk index, West Nile virus

INTRODUCTION

West Nile virus (WNV) is a mosquito-borne arboviral flavivirus and is the leading cause of mosquito-borne disease in the USA (Fischer and Hills 2015, McDonald et al. 2019). About 70–80% of humans infected with WNV are asymptomatic (Murray et al. 2011, CDC 2018). Among symptomatic cases, most are non-neuroinvasive typically manifesting in fever, headaches, body aches, vomiting, rash, and joint pain (Staples and Fischer 2015). However, about 1 in 150 symptomatic cases develop neuroinvasive WNV, characterized by meningitis or encephalitis, and about 10% of those cases result in death (CDC 2018). Between 1999 and 2018, there were 50,830 total confirmed cases and 2,330 deaths reported in the USA (CDC 2019).

West Nile virus occurs in a zoonotic cycle in which birds are reservoirs and mosquitoes are the vectors. The virus can spill over into incidental hosts including humans and other animals (Staples and Fischer 2015). Extant research has demonstrated that spikes in mosquito abundance—the number of mosquitoes circulating in an area—precede spikes in mosquito infection (Bolling et al. 2009), and that both mosquito abundance (Bolling et al. 2009) and infections (Kilpatrick and Pape 2013, Karki et al. 2020) are positively associated with human cases. Additionally, positive associations have been identified between WNV infection in horses and the occurrence of human cases (Patnaik et al. 2006, Ward and Scheurmann 2008).

Moreover, temperature and precipitation appear to be associated with human infection and mosquito abundance and infection. Temperature has been found to be positively associated with mosquito abundance, mosquito infection, and human WNV occurrence (Reisen et al. 2006, Hahn et al. 2015, Paz 2015). Unpublished research using data from New Jersey (L. Reed, personal communication) as well as published research from the USA suggests that human WNV occurrence is positively associated with precipitation levels (Landesman et al. 2007, Soverow et al. 2009). Other findings from Suffolk County, New York, indicate that alternating periods of high precipitation and/or wetter land surfaces followed by extended dry periods with higher temperatures throughout the spring and summer are associated with increased mosquito infection rates (Little et al. 2016). Alternatively, a study from southern Florida indicated the opposite sequence: the likelihood of human WNV cases increased when preceded by periods of drought followed by wet conditions (Shaman et al. 2005).

The only known validated index of WNV transmission risk is the California Mosquito-Borne Virus Surveillance & Response Plan (CMBVSRP; California Department of Public Health 2020), which

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includes 6 variables scored on ordinal scales: mosquito abundance and infection rate, average daily temperature, human case count, infected dead bird count, and sentinel chicken seroconversion count. The risk index score is calculated by averaging the scores of the variables for which data are available (Barker et al. 2003).

Our model was based on the CMBVSRP but included important modifications. First, we included only the variables available for use in the New Jersey Department of Health (NJDOH) WNV surveillance program, by excluding sentinel chicken and dead bird data and including equine cases and precipitation. Second, rather than reducing variability and potentially hindering classification by applying ordinal transformations to some of our continuous variables, we preserved the variability in those indicators by retaining the interval structure.

Our index was intended to measure the current WNV transmission risk to the human population based on weather conditions, mosquito and horse infection, and human cases during the previous 2 wk. It was also intended for use by New Jersey county mosquito control personnel as a descriptive (rather than predictive) tool that integrates several sources of information to document current WNV risk to county residents, monitor changes in risk over time, and support requests for additional resources.

To address these objectives, we first needed to establish the presence of WNV transmission risk levels. As such, the current study was intended to answer the following questions: In data collected between 2004 and 2018, are there unique profiles of variables that suggest different levels of WNV risk in New Jersey counties? If so, how many profiles exist?

MATERIALS AND METHODS

Sample characteristics: Our sample consisted of all 21 New Jersey counties. There were no exclusion criteria. All data were aggregated to the county level in 2-wk intervals (i.e., half-months). Only the data collected from CDC weeks 21–42 (half-months 11–21, approximately late May through October) were analyzed because these are the times when mosquito trapping and testing typically occur in New Jersey. To obtain our sample of 3,465 county half-months, we took observations from 21 counties, across 11 half-months over 15 years.

The project received institutional review board approval as an exempted study because all human data were deidentified and aggregated to the county level.

A retrospective data analysis was conducted on data collected between 2004 and 2018 and obtained from several secondary data sources described below.

Climatologic data: For climatologic variables, we used data obtained in 2020 from the Rutgers NJ Weather Network weather stations (Office of the New Jersey State Climatologist at Rutgers University). We selected 27 stations from among the 66

stations that collected data used in our analysis during at least part of the study period. Additionally, we used data accessed in 2020 from the Global Historical Climatology Network—Daily database (National Oceanic and Atmospheric Administration—National Centers for Environmental Information). Of the 34 New Jersey stations in this network from which data were available during at least part of the study period, 26 were selected for analysis. Three stations were selected per county based on their spatial distribution to optimize spatial coverage of climatologic readings. In total, data from 53 weather stations were used in the analysis. For some counties, weather stations from adjacent counties were used because of an insufficient number or distribution of stations in the county. Thus, 10 stations were included twice in the analysis: once for their "home" county and once as a proxy station for an adjacent county.

Average temperature and total precipitation were used as the climatologic variables. County half-month average temperature was calculated by obtaining the daily average for each weather station and then calculating the mean of the daily averages across all stations during the half-month. Daily average temperature was calculated by taking the mean of the maximum and minimum daily temperatures in degrees Fahrenheit. Average temperature was included in the analyses as a continuous variable in raw units.

To obtain half-month total precipitation, all daily precipitation totals (in inches) from each day of the half-month were summed across all county stations. Because of a moderately positively skewed distribution, a square root transformation was performed on total precipitation values, which were then used in the analyses.

Mosquito abundance and infection rate: New Jersey's mosquito surveillance program involves the collection of mosquitoes by county mosquito control officials statewide, who set several types of traps and collect specimens daily during mosquito season. The specimens are sexed, speciated, and counted by county personnel. These data are sent for tabulation to the Rutgers University Center for Vector Biology, which prepares weekly reports on adult mosquito and vector surveillance for the mosquito research and control community, as part of a program funded by the New Jersey State Mosquito Control Commission.

Specimens used to measure mosquito infection are collected from all trap types besides New Jersey light traps and are submitted for arboviral testing. The specimens collected from New Jersey light traps are used to measure mosquito abundance because these traps are consistently run in the same location daily throughout the season, regularly maintained, and routinely calibrated for air flow to ensure sampling consistency. For both the mosquito infection and abundance estimates, only female mosquitoes—both gravid and nongravid—were used.

Mosquito abundance and minimum field infection rate were calculated for "*Culex* mix" mosquitoes, which includes 3 species that are difficult to visually differentiate: *Cx. salinarius* Coquillett, *Cx. pipiens* L., and *Cx. restuans* Theobald. In New Jersey, the last 2 species are most commonly found to be infected with WNV and, as such, were selected for use.

Mosquito abundance was defined as the sum of mosquito counts across all New Jersey light traps in the county during a half-month. Because of a severely positively skewed distribution and excessive variability, with a high proportion of zero values, a $\log_{10}(x + 2)$ transformation was performed, and the transformed values were included in the analyses.

Minimum field infection rate (MIR) was used to measure the rates of infection in mosquito populations and was calculated using the following formula (Reeves and Hammon 1962):

Minimum field infection rate

$$= \left(\frac{\text{Number of positive mosquito pools}}{\text{Number of mosquitoes across all tested pools}} \right)$$
$$\times 1,000.$$

MIR was calculated for each county half-month by summing all test results from pools—groups of homogenized (i.e., ground together) mosquitoes—obtained during that half-month, summing the number of mosquitoes within each tested pool, and then using the above formula. Because of a moderately positively skewed distribution and excessive variability, a square root transformation was performed on the raw MIR values prior to the analyses.

Human and equine cases: The New Jersey human and equine surveillance programs are both passive. New Jersey administrative code stipulates that human cases of arboviral diseases be reported to NJDOH within 24 h of diagnosis. For WNV, diagnosis is made on the basis of a positive test result (real-time polymerase chain reaction [RT-PCR] or serology). Upon report to NJDOH, cases are investigated by public health officials and classified according to Centers for Disease Control case definitions (CDC 2015). Cases are documented and stored in the New Jersey Communicable Disease Reporting and Surveillance System database, which is a web-enabled electronic communicable disease registry that accepts electronic and manual entry of lab results and case details. For equine surveillance, blood samples are extracted from horses by veterinarians if WNV is suspected. Specimens are sent to the New Jersey Department of Agriculture Animal Health Diagnostic Lab, which then determines case status based on test results, and positive results (RT-PCR or serology) are reported to NJDOH.

Human and equine cases were defined and processed similarly. All confirmed and probable cases with a date of symptom onset occurring during a half-month within the study period were included in the analysis. Number of human cases was recoded into 3 categories: 0, 1, and 2 or more cases. The equine cases variable was binary (0/1) because the maximum number of cases across all half-months was 1.

Data analyses: To identify different categories of risk, a latent profile analysis (LPA) was utilized. This technique is used to identify discrete, homogenous subgroups (e.g., WNV risk categories) within a larger population when the presence and number of these subgroups is unknown (Vermunt and Magidson 2002). Mplus 8.2 (Muthen and Muthen 2017) was used to estimate the LPA models and allows for the inclusion of continuous, count, nominal, and ordinal variables. SAS 9.4 for Windows (SAS Institute, Cary, NC) was used to perform descriptive analyses.

To control for the effect of within-county variability, county was specified as a clustering variable. Multiple measurement models were tested: a null model specifying 1 profile and 4 additional models specifying 2, 3, 4, and 5 risk profiles, respectively.

Model selection was based upon an evaluation of several model characteristics including profile interpretability, prevalence of profile groups, and model fit statistics. Profile group prevalence estimates of less than 5% of observations suggested the presence of a noninformative group, and any models containing a noninformative group were discarded. We also evaluated the Akaike information criteria (AIC), Bayesian information criteria (BIC), sample-size–adjusted BIC (SSA-BIC), and log-likelihood (LL) model fit statistics, with lower values on each indicating better model fit. To evaluate the separation across latent profiles, we used the entropy measure, which has values ranging from 0.0 to 1.0 with values closer to 1.0 indicating better class separation (Celeux and Soromenho 1996).

The maximum likelihood estimate with robust standard errors (MLR) estimator was used to account for the non-normal distributions of risk indicators. The MLR is appropriate for models containing categorical latent variables (i.e., mixture models) and is robust to nonindependence of observations (e.g., observations nested within counties) and non-normality of observed variables (Muthen and Muthen 2017). As part of the model estimation process in Mplus, full-information maximum likelihood estimation was used to handle missing values (3.7% of all values).

RESULTS

Summary statistics are reported for the 6 risk indicators in Table 1. The transformations performed on abundance, MIR, and precipitation reduced variability substantially and reduced skewness and kurtosis to within acceptable ranges ($\pm$ 2.0 for skewness and $\pm$ 7.0 for kurtosis; West et al. 1995).

Table 1. Means and standard deviations of variables: all New Jersey counties, 2004–2018.

Variable, unit	Untransformed	Transformed	N^1
Total *Culex* mix abundance (standard deviation [SD]), no.	245.9 (440.0)	1.9 (0.8)[2]	3,234
Cx. mix minimum field infection rate (SD), (no. positive mosquito pools/mosquito) × 1,000	4.4 (8.0)	1.4 (1.6)[3]	3,003
Total precipitation (SD), inches	5.4 (4.5)	2.1 (0.9)[3]	3,393
Average temperature (SD), °F	69.8 (6.6)	—	3,457
Human case count (% 1 case, ≥ 2 cases)	4.5, 0.9	—	3,465
Equine case count (% 1 case)	0.8	—	3,465

[1] *N* observations used in models = 3,465.
[2] $\log_{10}(x + 2)$ transformed.
[3] Square root transformed.

Although models with various variable operationalizations and specifications were conducted, the specification of risk indicators selected for the final model included total *Cx*. mix abundance ($\log_{10}[x + 2]$ transformed), *Cx*. mix MIR (square root transformed), average temperature, and human case count (percent of observations with 0, 1, and > 2 cases, respectively). Equine cases and total precipitation were removed from the model because their levels were similar across profile groups, thus failing to contribute to the interpretability of the profiles.

Fit indices for the 5 LPA models tested with the above variable specification are shown in Table 2. As each additional class was added to the model, the LL, AIC, BIC, and SSA-BIC all decreased, suggesting progressively better fit as classes were added. Moreover, latent class separation was similar across the 2–5 class models as evidenced by the entropy values all sitting near or above 0.80. We ultimately chose the 3-class model because it provided interpretable and practically applicable classes while also being the most consistent with previous research on the variables.

The parameter estimates provided by the 3-class model are shown in Table 3. The largest group was labeled Moderate Risk because mosquito abundance was high relative to the other classes, but both MIR and the probability of human cases were low. The Low Risk class was labeled as such because the estimated mean values of the continuous variables were below the full-sample means, and there was a very low estimated likelihood of human cases. The High Risk group was labeled as such due to the relatively high estimated proportion of half-months with 1 or more cases, and the elevated MIR. Notably, the Moderate and High Risk classes displayed

estimated temperature levels roughly in line with the full-sample mean temperature, while the temperature estimate for the Low Risk class fell well below average.

Figure 1 shows the distribution of risk categories over the course of the mosquito season across all years and counties. The bar to the left of the black line represents all county half-months combined (*N* = 3,465). Each bar to the right of the black line represents all observations across all years and counties during a specific half-month (*n* = 315 per half-month).

Visual inspection of Fig. 1 revealed that earlier in the season (late May–July), Moderate Risk was most likely to be present, with 67–98% of observations classified as such. Moving into August and September, High Risk became most common, with 53–63% of observations classified as High Risk. At the close of the season in late October, risk diminished substantially, as about 4 of 5 observations during this half-month were classified as Low Risk.

DISCUSSION

The current study was conducted by NJDOH to develop an index for use by counties that could classify the level of transmission risk to humans based on a county's current level of WNV activity. As such, we sought to identify patterns of WNV activity indicators that suggested different levels of current viral circulation. Our initial model included 6 variables: mosquito minimum field infection rate and total abundance; human and equine WNV cases; and average temperature and total precipitation. Our final model excluded equine cases and total precipitation.

Table 2. Model fit indices for 1–5 class solutions: all New Jersey counties, 2004–2018.[1]

Classes	LL	FP	AIC	BIC	SSA-BIC	Entropy
1	−21,714.7	8	43,445.5	43,494.7	43,469.2	—
2	−21,226.5	14	42,481.0	42,567.1	42,522.6	0.78
3	−20,857.3	20	41,754.6	41,877.6	41,814.1	0.75
4	−20,615.3	26	41,282.5	41,442.4	41,359.8	0.82
5	−20,284.3	32	40,632.6	40,829.4	40,727.7	0.82

[1] AIC, Akaike information criteria; BIC, Bayesian information criteria; FP, free parameters; LL, log-likelihood; SSA-BIC, sample-size–adjusted BIC.

Table 3.   Estimated means and probabilities by class: all New Jersey counties, 2004–2018.[1]

	Full sample (N = 3,465)	Low risk (14.4%; n = 499)	Moderate risk (54.5%; n = 1,888)	High risk (31.1%; n = 1,078)
Total *Culex* mix abundance,[2] mean (standard deviation [SD])	74.6 (4.0)	7.1	132.0	74.4
Cx. mix minimum field infection rate,[3] mean (SD)	1.8 (2.6)	0.1	0.2	10.9
Average temperature, mean (SD)	69.8 (6.6)	59.8	71.5	71.5
Human case count (% half-months with cases)				
0	94.6	98.8	98.5	85.8
1	4.5	1.2	1.4	11.5
2+	0.9	0.0	0.1	2.6

[1] Latent profile analysis performed to estimate means and probabilities reported above. Within class sample sizes are estimates and have been rounded to the nearest integer.
[2] Variable was $\log_{10}(x + 2)$ transformed in analysis; back-transformed $(10^x - 2)$ value shown.
[3] Variable was square root transformed in analysis; back-transformed (x^2) value shown.

We used LPA to develop a model that best represented the patterns of risk indicators collected from all 21 New Jersey counties from late May through October during 2004–2018, adjusting for the influence of county-level clustering on categorical latent class membership. Models ranging from 1 to 5 classes were tested, and it was determined that the best-fitting model contained 3 classes, which we labeled as Low, Moderate, and High Risk.

The analysis revealed that Moderate Risk was most common during late spring through mid-summer (May–July), when mosquito populations are rising due, in part, to increases in temperature that accelerate mosquito development (Ciota and Keyel 2019). However, mosquito infection rates during this time remain low; thus, the likelihood of human infections is quite low. That said, high abundance paired with temperatures similar to the High Risk class may create the conditions for rapid WNV amplification and possible spillover into humans and equines. Accordingly, Moderate Risk periods tend to precede High Risk periods, which is consistent with past research showing that high abundance predicts subsequent spikes in MIR and the onset of initial human cases about 4–7 wk later (Bolling et al. 2009). Moreover, adulticidal treatments early in the season, soon after initial detection of WNV infection in mosquitoes, have been found to reduce abundance levels and slow WNV transmission to humans (Lothrop et al. 2008). These data suggest that interventions intended to reduce mosquito populations will likely have the greatest impact if they are implemented during early-season Low and Moderate Risk time periods, as they may diminish
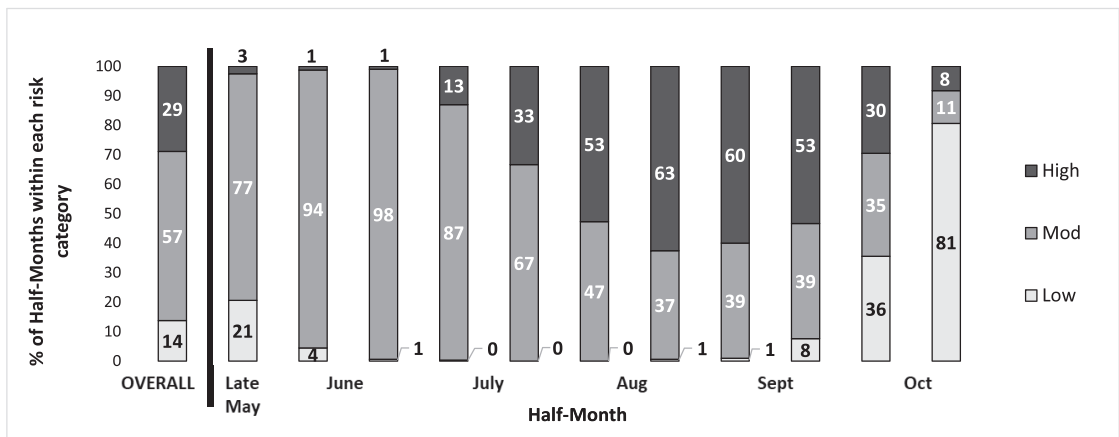

Fig. 1.   Risk category distributions across all half-months: all New Jersey counties, 2004–2018. N overall = 3,465 observations, across all 21 New Jersey counties; n per half-month = 315. There are slight differences between the class size estimates (i.e., proportions) shown in Table 3 and the overall proportions reported in this figure (see bar to left of black line labeled "OVERALL"). The reason for these differences is because the former accounts for measurement error in the estimates, while the latter does not. Table 1 includes the parameter estimates of class size generated by the latent profile analysis. The overall proportions reported in this figure are based on probabilities of membership within each class for individual observations. For the purposes of this figure, each observation was placed in the class in which the probability of membership was the highest. Thus, the OVERALL bar in this figure summarizes the *most likely* class membership of all observations in the sample.

the number of older females—which are more likely than younger females to be infected—later in the season. And the reduction of infected female mosquitoes may, in turn, curtail transmission to humans.

Interestingly, during the High Risk periods which predominate in late summer (August–September), mosquito populations decline in abundance while infections spike. Declining mosquito abundance may be influenced by the reduction in mosquito breeding grounds throughout the summer as the hot and dry conditions reduce the availability of standing water sources (Carrieri et al. 2014). Additionally, mosquito control actions such as ground and aerial larviciding as well as truck-mounted adulticide spraying typically intensify during periods of high abundance (G. Williams and J. Gruener personal communication, November 17, 2020) and contribute to reductions in mosquito abundance and mosquito infection rates (Elnaiem et al. 2008).

The high mosquito infection rates during High Risk periods may be influenced by the characteristics of both the mosquito and avian populations during the late summer months. Specifically, mathematical modeling points to an inverse relationship between mosquito population density and proportion of infected mosquitoes (Smith et al. 2004). Thus, the older mosquitoes that remain later in the season are more likely to be infected, while fewer young mosquitoes emerge because of the diminished availability of breeding sites. Additionally, human infection risk is elevated during High Risk periods due, in part, to human behavior patterns that increase the risk of interaction with infected mosquitoes, such as spending time outdoors in clothing that leaves skin exposed.

The Low Risk periods are most common in October when levels of all risk index indicators drop substantially. As temperatures fall and older mosquitoes that may be infected die off, most of the remaining population includes young mosquitoes programmed for diapause (Spielman 2001). The latter seek only nectar, rather than blood meals, to build fat stores in preparation for the winter (Denlinger and Armbruster 2014). Moreover, humans are less likely to engage in behaviors placing them at risk for infection.

Despite the associations with human WNV cases identified in previous research, we found minimal differences in the proportions of equine cases across classes. This finding suggests that equine cases are a poor indicator of WNV activity, likely due to the limited number of cases—equine cases were present in 26 of the 3,465 observations (0.8%). The low occurrence of WNV in horses may be the result of underreporting and/or high rates of natural immunity (from previous infections) or vaccine-induced immunity (Kilpatrick and Pape 2013).

The spatial resolution of the data is one limitation of this study. Specifically, aggregating data to the county level implies that WNV activity is the same throughout the county, but it likely varies substantially within counties. The relatively low spatial resolution may have contributed to the lack of variability in the precipitation variable, for which county-level aggregates are less informative. Previous research where the geographical location of interest was broken into spatial grids of 13 km^2 found that precipitation was a significant predictor of future mosquito abundance and infection rate (Little et al. 2016). Additionally, we excluded variables from the analysis for which associations with mosquito abundance and infection rate and human WNV occurrence have been identified. These variables include but are not limited to soil moisture (Little et al. 2016, Lockaby et al. 2016), dead bird clusters (Mostashari et al. 2003), and land cover and housing density (Lockaby et al. 2016). The variables were not collected or could not be compiled due to limited resource availability and because we sought to use only variables which would be convenient for local jurisdictions and NJDOH to access and track prospectively.

The profiles derived from our analysis suggest the presence of Low, Moderate, and High Risk periods of WNV transmission, each with a unique pattern of variable manifestation that can be used guide public health interventions. The Low Risk profile is characterized by relatively low levels of all variables. Thus, public health actions focused on integrated mosquito management strategies to reduce mosquito populations are advisable in these conditions.

The Moderate Risk profile shares features with both the High and Low Risk profiles; however, the very high abundance level is a clear differentiator. The presence of this feature points to the importance of intensified larval and adult mosquito population control measures and increased messaging to the public about protecting oneself from mosquitoes.

The distinguishing features of the High Risk profile are mosquito infection rates and probability of human infection well above the other risk classes during periods when temperatures are sufficient to facilitate more accelerated mosquito breeding and development. Thus, public health actions during High Risk periods should be focused on driving down adult mosquito populations and urging residents to modify behavior to reduce their infection risk.

Traditionally, mosquito control and public health officials have had to interpret each of these indicators of WNV risk separately to inform public health risk mitigation actions. Our risk index combines those variables and reveals unique profiles at each risk level that can aid officials in communicating the need for additional resources and applying the right intervention at the right time, thus optimizing those resources. It is important to note that our index represents current WNV transmission risk based on data collected in the previous 2 wk; thus, the index should not be used as a predictive measure of future risk.

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