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THE IMPACT OF ADULTICIDE ON *CULEX* ABUNDANCE AND INFECTION RATE IN NORTH SHORE OF COOK COUNTY, ILLINOIS

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ABSTRACT. Mosquito surveillance is critical to reduce the risk of West Nile virus (WNV) transmission to humans. In response to surveillance indicators such as elevated mosquito abundance or increased WNV levels, many mosquito control programs will perform truck-mounted ultra-low volume (ULV) adulticide application to reduce the number of mosquitoes and associated virus transmission. Despite the common use of truck-based ULV adulticiding as a public health measure to reduce WNV prevalence, limited evidence exists to support a role in reducing viral transmission to humans. We use a generalized additive and fused ridge regression model to quantify the location-specific impact of truck-mounted ULV adulticide spray efforts from 2010 to 2018 in the North Shore Mosquito Abatement District (NSMAD) in metropolitan Chicago, IL, on commonly assessed risk factors from NSMAD surveillance gravid traps: *Culex* abundance, infection rate, and vector index. Our model also takes into account environmental variables commonly associated with WNV, including temperature, precipitation, wind speed, location, and week of year. Since it is unlikely ULV adulticide spraying will have the same impact at each trap location, we use a spatially varying spray effect with a fused ridge penalty to determine how the effect varies by trap location. We found that ULV adulticide spraying has an immediate temporary reduction in abundance followed by an increase after 5 days. It is estimated that mosquito abundance increased more in sprayed areas than if left unsprayed in all but 3 trap locations. The impact on infection rate and vector index were inconclusive due to the large error associated with estimating trap-specific infection rates.

KEY WORDS Adulticide application, fused ridge, generalized additive model, truck-mounted ULV, West Nile virus

INTRODUCTION

West Nile virus (WNV) is a mosquito-transmitted virus that was first reported in the USA in 1999 (Lanciotti et al. 1999). Since then, WNV quickly spread across the country, with 51,801 human cases and 2,390 fatalities reported between 1999 and 2019 (CDC 2020). Mosquitoes transmit the virus between hosts, with genus *Culex* comprising >95% of positive tests for WNV (Andreadis 2012). To monitor *Culex* spp. and the associated WNV risk to humans, many mosquito control programs routinely use a network of gravid traps placed throughout their operational areas. Gravid trap collections and subsequent WNV testing from these traps are used to determine when and where more intensive control efforts, specifically ultra-low volume (ULV) adulticide application, are to be used (CDC 2013). Despite the common use of aerial or truck-mounted ULV sprays, there is little evidence that they effectively reduce the risk of WNV (Nasci and Mutebi 2019). In the Chicago metropolitan area where truck-mounted ULV sprays are typically used in July and August, Clifton et al. (2019) observed that sprays reduced host-seeking mosquitoes by 65.3%, but rebounded above prespray levels (303.1%) 3 days after ULV treatment. A reduction and subsequent rebound in gravid mosquito abundance in the 3 days following a spray event was also observed, but was highly variable in magnitude possibly due to these mosquitoes' temporary physiological resistance to ULV sprays during the 24- to 72-h period following a blood meal. Similarly, in the city of Chicago, Mutebi et al. (2011) saw variable success from truck-mounted ULV treatments in reducing numbers of gravid *Culex* spp. and no reduction of WNV infections in mosquitoes.

Weather variables are important drivers of WNV transmission; higher than normal winter temperatures and lower than normal spring precipitation are associated with an increase in some mosquitoes (Walsh et al. 2008). Other key contributing factors such as demographic characteristics, management of sewer and drainage systems, mosquito abatement practices, and public health infrastructure also influence the risk of WNV infections (Brinton 2001). Identifying significant risk factors and variables allow models to predict weekly WNV infection rates or years in which WNV infection might be more prevalent. Historically, model development has been disjointed and tailored to specific regions due to a lack of collaboration. Keyel et al. (2021) explore a model comparison study of 13 models applied to data in varying regions across the USA in an attempt to unify and standardize WNV modeling efforts nationwide. The key models utilized in northern Illinois include that of Ruiz et al. (2010), Shand et al. (2016), and Karki et al. (2020). Ruiz et al. (2010) used linear

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regression to show that temporal and spatial patterns of precipitation and air temperature have a consistent and significant impact on timing and location of increased mosquito infections. Shand et al. (2016) further found that the interaction terms between precipitation and air temperature in a linear model provided a more accurate representation of the effect on infection rate. Karki et al. (2020) used multilevel modeling to find the fine-scale drivers of spatiotemporal variability of human WNV cases.

An important remedy measure when mosquito infection rate in a region is high is to conduct ULV adult mosquito control activities (i.e., adulticiding). The effectiveness of ULV adulticiding depends on a number of variables that include which species of mosquitoes are present, what active ingredients are used, volume applied, application timing and interval, weather conditions, and the density of homes and streets in a treatment area. In the Chicago area, ULV adulticide spraying for WNV is usually done late in the evening to reduce exposure to nontarget species and bystanders. Synergized and nonsynergized pyrethroid materials are most commonly employed at one-half the label rate. In general, mosquito abatement programs in the Chicago area lack an aerial adult control component and are limited to ground-based ULV treatments at weekly or greater intervals between treatments. Despite the importance of understanding the impact of adulticiding to help regulate mosquito populations and disease transmission, there have been limited studies on the topic. Carney et al. (2008) compared the proportion of WNV cases in regions treated with aerial spray effect versus untreated regions in California. It was found that treated regions had a decrease in the proportion of WNV cases. However, the impact on mosquito abundance and infection rate (IR) was not quantified. Holcomb et al. (2021) used generalized additive models (GAMs) accounting for spatial and temporal trends to model aerial insecticide treatments in California and found that aerial adulticide is effective in achieving short-term reductions in mosquito abundance. While these previous studies utilized mosquito collections and testing from aerial spraying, the use of consistent surveillance of gravid trap networks by mosquito abatement districts in the Chicago region provides an opportunity to assess the effectiveness of truck-mounted ULV sprays on mosquito abundance and infection over multiple seasons.

In this paper, we estimate the location-specific relationship between WNV risk factors and ULV adulticide spraying using a GAM in conjunction with a fused ridge regression model. A GAM is a semiparametric technique that allows for the relationship between the response variable and individual predictor variables to follow smooth functions that can be linear or nonlinear (Hastie and Tibshirani 1990). Generalized additive models are a common method used for modeling nonlinear relationships that are often present in environmental data and have previously been found effective in modeling mosquito abundance (Drexler and Ainsworth 2013, Holcomb et al. 2021). We chose the GAM function for its flexibility in capturing nonlinear mosquito dynamics with respect to time or in response to certain weather variables. The GAMs also have easily interpretable parameter estimates allowing us to quantify the impact of ULV adulticide spraying. After fitting our data to the GAM, we utilized a fused ridge regression penalty to model the effect of adulticide spraying. Fused ridge regression models are a power tool for estimating smoothly varying effects from covariates. The coefficients in the fused ridge regression model provide the 14-day impact of adulticide spraying. The fused ridge penalty enforces smooth estimates between sites, which is important to prevent overfitting at an individual site while still allowing for spatially varying estimates. The objective of this study is to quantify the reduction in population and the duration of the effect from routinely employed ground-based ULV mosquito adulticide applications on a natural population of gravid vector mosquitoes by retrospectively analyzing 8 years of trap surveillance data.

MATERIALS AND METHODS

Study region

The North Shore Mosquito Abatement District (NSMAD) was formed in 1927 and serves 13 municipalities in a 69-mi^2 area located north of the city of Chicago in Cook County, IL (Fig. 1). The southern portions of the district contain older and denser communities that contain a complex water management system exemplified by an antiquated combined sewer and stormwater system. The northern portion of the NSMAD contains suburban communities with more modern stormwater and sewage management infrastructure. Running through the center of the NSMAD, from north to south, is a series of preserves, forests, and other protected natural habitat along the North Branch of the Chicago River. The entire District can be characterized as having poor drainage, frequent standing water, and highly fragmented natural habitats integrated throughout. Larval habitat for *Culex pipiens* (L.) and *Cx. restuans* (Theobald) mosquitoes is abundant and diverse and includes aboveground sites such as abandoned pools, clogged gutters, household containers, and woodland pools, as well as the extensive underground water management infrastructure.

Collection methods

Since 2010 the NSMAD has maintained a series of Centers for Disease Control and Prevention (CDC) Gravid traps baited with alfalfa pellet infusion. The CDC Gravid traps are deployed in April of each year and collected in October. Generally, the traps are collected every Monday (M), Wednesday (W), and

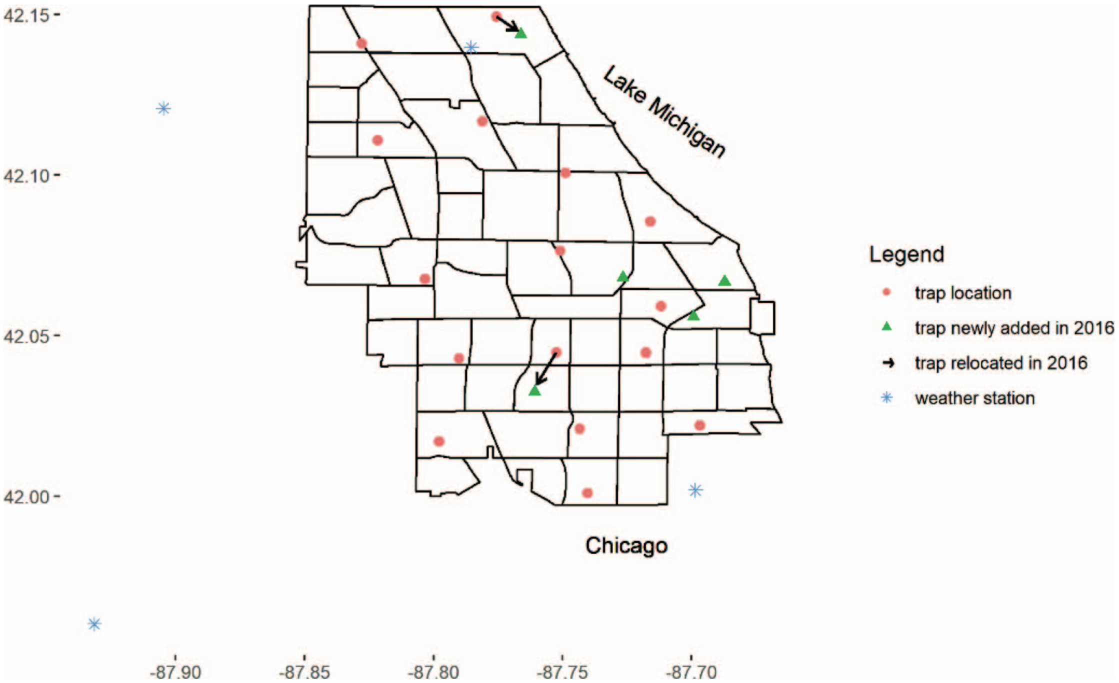

Fig. 1. Map of the gravid trap and weather stations in the North Shore Mosquito Abatement District (NSMAD).

Friday (F) from May through September annually (NSMAD 2021). Traps are set out for the entirety between collection days, meaning they are accumulating mosquitoes for 48 h to 72 h depending on the day. Mosquitoes are taxonomically sorted to the genus *Culex*, counted, pooled in groups of up to 50 mosquitoes, and tested via Rapid Analyte Measurement Platform (RAMP) (Response Biomedical Corporation, Vancouver, BC, Canada). Abundance and IR information is used to estimate the risk of WNV infection for human populations and to determine the timing of adult control ULV treatments. From 2010 to 2016, 16 gravid traps were placed throughout NSMAD. In 2016, 2 of the traps were relocated and an additional 3 were added (Fig. 1). Since the relocated traps changed geographic location, which could impact mosquito abundance and spray impact, we consider the old location and new location as 2 separate traps.

Mosquito data

The mosquito data collected from gravid traps during the years 2010 to 2018 were used for the analyses. This time period was chosen because all mosquitoes were tested for WNV using the same RAMP testing methodology, providing for the most reliable data. Beginning in 2019, mosquitoes were tested using reverse transcriptase–quantitative polymerase chain reaction and thus are excluded from our analysis. The RAMP test was used to determine if a pool of up to 50 mosquitoes was positive for WNV, scoring a RAMP value of 100 or more (Burkhalter et al. 2014). Due to the difficulty in morphologically differentiating the 2 primary vector species of WNV in the region, *Cx. pipiens* and *Cx. restuans* from trap collections, they will subsequently be referred to as *Cx. pipiens/restuans*.

Risks related to WNV are typically calculated in 3 ways from gravid trap collections: 1) abundance, 2) IR, and 3) vector index (VI). Abundance is the count of female mosquitoes collected in a trap. The true IR is 1,000 × the number of positive individual mosquitoes/number of mosquitoes tested. Due to the large number of mosquitoes collected, it is not practical to test every mosquito individually; therefore, the NSMAD tests mosquitoes in pools of 50. Then the proportion of infected mosquitoes can be estimated in 2 ways, minimum infection rate (MIR) or maximum likelihood estimate (MLE) as follows:

$$\mathrm{MIR} = (X/\text{total \# mosquitoes tested}) \times 1,000$$

$$\mathrm{MLE} = \left[1 - \left(1 - \frac{X}{n}\right)^{1/m}\right] \times 1,000,$$

where n is the number of pools tested, X is the number of positive pools, and m is the pool size. The underlying assumption of MIR is that there is just one infected individual within a pool of mosquitoes, while MLE is defined as the IR most likely observed given the testing results and an assumed binomial distribution (Gu et al. 2003). The MLE of IRs is more accurate and robust than the MIR when at least one

Table 1. The analyzed range of days in which the spray occurred before trap collections.

	Spray Occurred
$\mathbb{1}\{Spray_1\ (s,\ t)\}$	1–2 nights prior
$\mathbb{1}\{Spray_3\ (s,\ t)\}$	3–5 nights prior
$\mathbb{1}\{Spray_6\ (s,\ t)\}$	6–7 nights prior
$\mathbb{1}\{Spray_8\ (s,\ t)\}$	8–9 nights prior
$\mathbb{1}\{Spray_{10}\ (s,\ t)\}$	10–12 nights prior
$\mathbb{1}\{Spray_{13}\ (s,\ t)\}$	13–14 nights prior

pool is negative and requires no more data than that for calculation of MIR (Walter et al. 1980, Gu et al. 2003). We use the MLE of IR except in cases where all pools are positive, in which MIR was calculated instead of MLE (Gu et al. 2004). This is because when all pools are positive MLE estimates 1,000 per 1,000 mosquitoes are positive for WNV, which is unrealistic. The VI is calculated as the estimated IR × abundance/1,000. This unit measures the abundance of WNV-infected mosquitoes and therefore should provide a quantitative measure of the risk of human WNV infection.

An area within the NSMAD reaches a threshold for ULV adulticide application if one or more of the following occurs in a nearby trap: 1) average weekly abundance > 45/trap-night; 2) average weekly IR > 5/1,000; or 3) average weekly VI > 1. Common mosquito surveillance practices monitor WNV risk on a weekly basis. While modeling weekly data may provide better model fits, it can be less informative on the exact impact of spray given reductions in mosquitoes may last only a few days or less. Additionally, because a spray event can occur between M and Thursday, the impact will consequently be different on mosquitoes collected on M than those collected on W or F. Therefore, we analyze the impact ULV adulticide spraying has on the 3 risk measures on a collection-day basis. This allows us to better understand the effect of a ULV spray within a time period shorter than a week. In terms of abundance, the collection-day analysis uses the daily average abundance for the collection period rather than the total number of mosquitoes in the trap because the traps are set for varying time periods. For example, M traps have been collecting mosquitoes for 72 h, whereas W and F traps have been collecting for 48 h.

Adulticide data

From 2010 to 2013, NSMAD used Anvil 2 + 2® (2% d-phenothrin synergized with 2% piperonyl butoxide; Clarke, Roselle, IL) and from 2014 to 2018 used Duet® (5% d-phenothrin and 1% prallethrin as active ingredients synergized with 5% piperonyl butoxide; Clarke). Both control materials were employed at approximately one-half of the full label rate during the time period examined (Anvil 2 + 2 at 1.6 fl oz/acre and Duet at 0.64 fl oz/acre). Ultra-low volume adulticide applications generally occurred between 2000 h and 0100 h on weekdays except F. Due to the limited number of trucks available, the entire district cannot be sprayed in a single evening; therefore, the district is divided into 59, approximately 1-mi^2 sections (Fig. 1), with up to 8 sections being sprayed per night.

We evaluated the impact of ULV adulticide spraying up to 2 wk after the spray event occurred. We represent whether or not ULV adulticide spraying occurred l lags before trap $\boldsymbol{s}$ was collected on date t with an indicator function, where $\boldsymbol{s} = \{s_1, \ldots, s_{21}\}$ and $t \in T$ represents all collection dates in the 2010–18 mosquito seasons. Let $\mathbb{1}\{Spray_l\,(s_i,\ t)\} = 1$ if trap s_i collected on date t was sprayed l lags ago, and 0 otherwise. A lag l simply refers to a range of days in which the spray event occurred before the trap observation.

We represent the spray lags as $l \in \{1, 3, 6, 8, 10, 13\}$, such as shown in Table 1.

Essentially, the indicator tells us whether or not spraying occurred between each collection period.

For example, consider an observation that includes information collected from a trap on August 13. If in the prior 14 days there was only one ULV adulticide spraying on August 9, 3–5 nights prior, then $\mathbb{1}\{Spray_3\} = 1$ and all other indicator functions would equal 0 (i.e., $\mathbb{1}\{Spray_1\} = \mathbb{1}\{Spray_6\} = \mathbb{1}\{Spray_8\} = \mathbb{1}\{Spray_{10}\} = \mathbb{1}\{Spray_{13}\} = 0$). Table 2 demonstrates a 2-wk period prior to the collection day in which a spray event could have occurred and what the corresponding indicator function would be on each day.

Weather data

Daily maximum temperature, total precipitation, and average wind speed were retrieved from the National Oceanic and Atmospheric Administration.

Table 2. A 2-week calendar demonstrating the relationship between the indicator lags l and time between a spray event and collection date. An asterisk (*) indicates that the trap was collected in the morning of that day.[1]

August						
Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
1	2*	3	4*	5	6*	7
	$\mathbb{1}\{Spray_{10}\}$	$\mathbb{1}\{Spray_{10}\}$	$\mathbb{1}\{Spray_8\}$	$\mathbb{1}\{Spray_8\}$	$\mathbb{1}\{Spray_6\}$	
8	9* ULV spraying	10	11*	12	13*	14
	$\mathbb{1}\{Spray_3\}$	$\mathbb{1}\{Spray_3\}$	$\mathbb{1}\{Spray_1\}$	$\mathbb{1}\{Spray_1\}$	Trap collected	

[1] ULV, ultra-low volume.

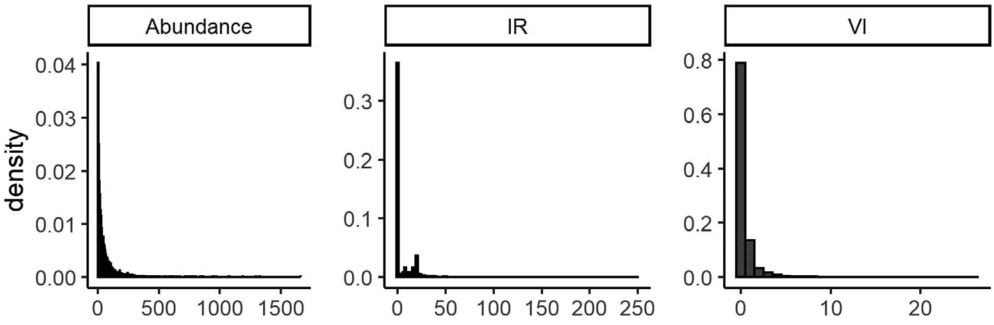

Fig. 2. The average daily density of abundance, infection rate (IR), and vector index (VI) for the years 2010–18 collected from the 21 trap locations in the North Shore Mosquito Abatement District (NSMAD).

The daily weather was collected from 4 weather stations (Fig. 1) and interpolated to each trap location using inverse distance weighting. Temperature data were used to calculate a variable called "degree day" (*DD*), calculated as:

$$DD = \begin{cases} T_{\text{day}} - T_{\text{base}}, & \text{if } T_{\text{day}} > T_{\text{base}} \\ 0, & \text{if } T_{\text{day}} \leq T_{\text{base}} \end{cases}$$

where T_{day} is the maximum daily temperature and T_{base} is the threshold temperature of 22°C. The threshold was calculated by Ruiz et al. (2010) such that the correlation between temperature and estimated IR was maximized. We calculated 30-year weekly normal degree day, precipitation, and wind speed using the averages from the 4 weather stations over the years 1989–2018. Weather variables were then calculated as the differences from the 30-year normals in order to remove the seasonal trend from the model.

For our model development, we consider the average weekly degree day (DD), precipitation (PRCP), and wind speed (AWND) for 0- to 4-wk lags, where 0 represents the current week up until the collection day. Let $\boldsymbol{Z} = \{DD_0, \ldots, DD_4, PRCP_0, \ldots, PRCP_4, AWND_0, \ldots, AWND_4\}$ represent the vector of weather variables considered.

Statistical analysis

We evaluated the impact that truck-mounted ULV adulticide spraying has on *Cx. pipiens/restuans* related to the 3 risk measures—abundance, IR, and VI—using GAMs. All GAMs were fit using the R package *mgcv* (R Core Team 2020). Let Y represent the response variable (either abundance, IR, or VI); the density of each is shown in Fig. 2. For count data, a negative binomial or Poisson distribution is the typical model choice. We chose to model abundance with a negative binomial GAM to account for the overdispersion in the Poisson distribution. The IR and VI have a large number of zeros in the data due to many incidences of zero positive pools. To account for the mass point at zero, we fit the IR and VI with a hurdle model (Cragg 1971). We did not fit abundance with a hurdle model because the amount of zeros were not excessive. A hurdle model fits the data in 2 parts, the 1st is the probability of attaining a zero value, and the 2nd models the positive values. Hurdle models are commonly used when accounting for zeros in entomology (Demétrio et al. 2014, Kassahun et al. 2014, Falk et al. 2015). We fit a hurdle model using binomial GAMs to predict the probability of zeros and gamma GAMs with a log-link to predict the positive value. The gamma distribution is a natural choice for a hurdle model with continuous data because its domain restricts all outcomes to be greater than zero. The hurdle model can be expressed as simply the multiple of the 2 distributions, $E(Y) = P(Y > 0)\ E(Y \mid y > 0)$, where $P(Y > 0)$ is the probability the binomial distribution is greater than zero and $E(Y \mid y > 0)$ is the expected value from the gamma distribution.

Due to varying geographic factors and placement locations of traps it is unlikely ULV adulticide spraying will have the same impact at each trap location. Therefore, we consider a model that allows for spatially varying spray coefficients regularized using a fused ridge penalty. The model is fit in 2 stages; first the risk factor, Y, is fit to temporal and weather covariates using a GAM, then the residuals of the GAM are used to model a spray indicator function with a fused ridge penalty. The fused ridge penalty promotes similarity between parameter estimates, which is beneficial to prevent overfitting at locations with limited observations (Goeman 2010).

The GAM is fit as follows:

$$f\{E(Y)\} = \text{factor}\{\beta_0(\boldsymbol{s})\} + \sum_{m=1}^{4} \beta_m \xi_m + s(\text{week}) + \sum_{j=1}^{15} s(Z_j) + \sum_{j \neq k} ti(Z_j, Z_k) \tag{1}$$

where $\text{factor}\{\beta_0(\boldsymbol{s})\}$ allows for spatial variation that could be contributing to varying mosquito activity in the different locations $\boldsymbol{s} = \{s_1, \ldots, s_{21}\}$, ξ_m are the vectors of scores with coefficients β_m associated with

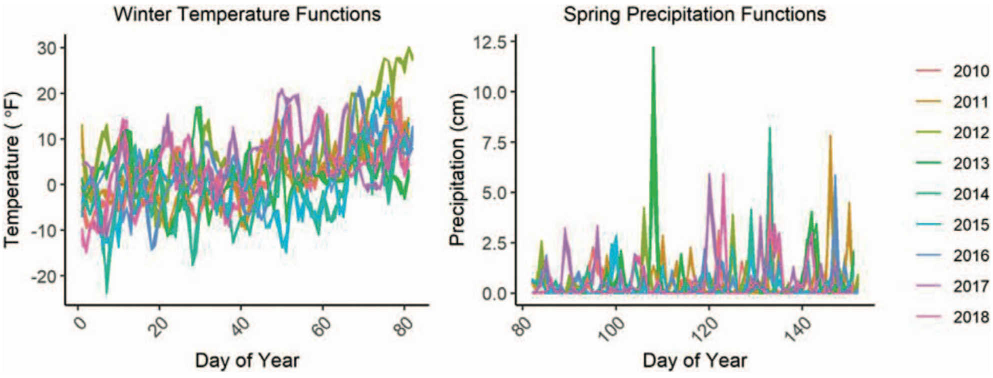

Fig. 3. The daily winter and spring functions for each trap location for the years 2010–18.

the winter temperature and spring precipitation, the derivation of which is described later in the Functional Covariates section, *week* represents the week in the year to account for any temporal variation, and $\boldsymbol{Z}$ is the vector of weather covariates described previously in the Weather Data section.

Next, *f*() represents the link function associated with the distribution: log link for the negative binomial and gamma distributions versus logit for the binomial distribution. Thin plate spline regressions were chosen for the functions *s*() because they avoid knot specification and have shown to be the optimal smoother in any given basis dimension with restricted MLE as the smoothing parameter estimation (Wood 2003). All weather covariates, $\boldsymbol{Z}$, were considered in the initial models along with choices of interactions between weather covariates using tensor product smooth functions, *ti*(), based on biological relevance. For example, the interaction between DD_2 and DD_3 was proven relevant in Shand et al. (2016) because 2 warmer than average weeks will have an increased impact compared to considering the 2 weeks separately. We consider dropping covariates based on Akaike Information Criteria (AIC) via backward selection. We also consider concurvity, a measure of collinearity, to remove redundant variables.

Let $\hat{Y}$ represent the fitted GAM estimates from Eq. 1. To quantify the spray impact we model the residuals, $(Y - \hat{Y})$ using a spray indicator and fused ridge penalty. To define the fused ridge penalty, consider an undirected graph G consisting of 21 vertices that represent the trap locations and edge set $\mathcal{E}$. An edge $(s_p, s_q) \in \mathcal{E}$ means that location s_p and s_q are neighbors. The fused ridge regression model to evaluate the spray impact is specified as:

$$(Y - \hat{Y}) = \theta_l(\boldsymbol{s})X_l + \lambda_l \sum_{(s_p,s_q)\in\mathcal{E}} |\theta(s_p) - \theta(s_q)|^2, \quad (2)$$

where $\theta_l(\boldsymbol{s})$ is the vector of coefficients associated with spray lag l for trap locations $\boldsymbol{s} = \{s_1, \ldots, s_{21}\}$, X_l is an $I \times 21$ indicator matrix associated with lag l where $X_l[i,j] = 1$ if spraying occurred at trap location j for observation $i = 1, \ldots, I$ and 0 otherwise, and λ_l is a tuning parameter for spray lag l.

The tuning parameter λ is optimized by searching along a sequence of values and choosing the λ with the smallest AIC (Tansey et al. 2018, Li and Sang 2019, Sass et al. 2021). To select the set of edges, $\mathcal{E}$, we use Delaunay triangulation. The coefficients for the spray lags $\theta_l(\boldsymbol{s})$ for $l = \{1, 3, 6, 8, 10, 13\}$ are estimated sequentially beginning with lag l. The residuals are then updated accounting for the estimated spray impact before estimating the next lag.

Functional covariates

We used the daily winter temperatures and daily spring precipitation to calculate the scores, ξ_m, associated with each trap in each year using multivariate functional principal component analysis (MFPCA) (R Core Team 2020). The scores are incorporated into the GAM as covariates. Let the time series for the daily winter temperatures be represented as a set of functions, $X^{\text{temp}}(t_1)$, where each function corresponds to a different trap and year with domain $t_1 \in \mathcal{T}_1$. Similarly, the time series for the daily spring precipitation can be represented as a set of functions, $X^{\text{prcp}}(t_2)$, where each function corresponds to a different trap and year with domain $t_2 \in \mathcal{T}_2$.

Then $X(t) = \{X^{\text{temp}}(t_1), X^{\text{prcp}}(t_2)\}$ is a bivariate functional data set. The functions are shown in Fig. 3.

The multivariate Karhunen–Loève theorem states that $X(t)$ can be represented by a linear combination of basis functions:

$$X(t) = \sum_{m=1}^{M} \xi_m \phi_m(t), \qquad t \in \mathcal{T} := \mathcal{T}_1 \times \mathcal{T}_2$$

where $\phi_m(t)$ are the principal components and ξ_m are the principal component scores. Single observations x_i of X can then be characterized by their score vectors $(\xi_{i,1}, \ldots, \xi_{i,M})$ with $\xi_{i,m} = \langle x_i, \phi_m \rangle$, where $\langle \, , \rangle$ is the inner product. We calculate 4 score components of each trap location for each year due to the

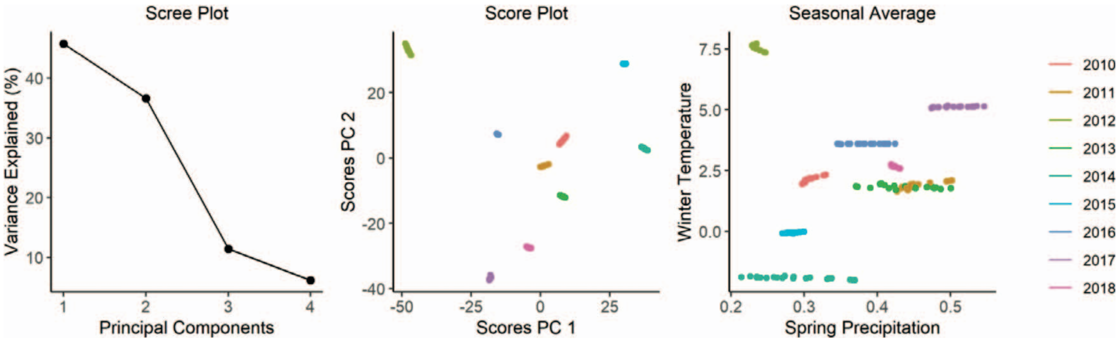

Fig. 4. The resulting scree plot and plot of the 1st 2 scores of each trap location from the multivariate functional principal component analysis (MFPCA). The seasonal average is the average winter temperature and average spring precipitation for each trap location each year.

large percent of variation explained by the 1st 4 eigenfunctions and incorporate the scores as covariates for each observation in the GAM using the *MFPCA* R package.

Figure 4 shows the score results for each trap location for the years 2010–18. The scree plot shows the amount of variance explained by each principal component, with the 1st 2 components accounting for 82.42% of the variance. The scores of the 1st 2 components are displayed in the score plot. The seasonal average plot shows the average winter temperature and average spring precipitation for each trap location each year. The differences between the score plot and the seasonal average demonstrates that using multivariate functional components accounts for more than simply the univariate average of the functions. Since July and August are the prime mosquito months and the daily spring precipitation for the functional covariates extends from March to May, there is no overlap between the variables X and $\boldsymbol{Z}$ causing concurvity.

RESULTS

Due to the limited number of trucks available and the large study region, not all sites are sprayed at the same time or at the same frequency. Table 3 shows the number of spray events that occurred each year for each of the traps. A blank entry in the table means that the trap was not collected that year. We fit the spatial spray model with the data to determine the trap-wise spray impact.

Figure 5 shows the estimated coefficients, $\boldsymbol{\theta}(\boldsymbol{s})$, for the abundance, IR, and VI analysis. Since the spatially varying coefficient model is fit with the residuals, the scale in the plots represent the direct

Table 3. List of the 21 trap locations and number of spray events that occurred in the North Shore Mosquito Abatement District containing the trap each year. A blank entry means no data were collected for that trap during that year.

Name	2010	2011	2012	2013	2014	2015	2016	2017	2018	Total
NSG2	4	2	2	1	1	1	1	1	3	16
NSG3	1	1	3	1	2	1	3	3	3	18
NSG5	2	2	2	2	1	2	3	2	5	21
NSG6	2	2	2	3	1	1	2	3	2	18
NSG9	3	2	1	1	1	1	2	1	2	14
NSG13	3	1	1	2	1	1	1	0	1	11
NSG14	1	2	1	2	2	1	4	2	3	18
NSG17	2	1	2	1	1	1	3	2	3	16
NSG21	1	1	1	1	2	0	2	3	3	14
NSG22	3	1	2	2	1	2		2	3	16
NSG23	1	1	2	2	1	1	2	1	2	13
NSG24	2	1	1	1	1	1	1	0	1	9
NSG25	1	2	1		2	0	2	3	3	14
NSG26	1	2	1	1						5
NSG28		2	2							4
NSG29					1	1	3	1	2	8
Skokie3		2	2				3	3	3	13
Skokie4							3	3	4	10
EV1							3	3	3	9
EV2							2	3	3	8
EV3							3	3	3	9

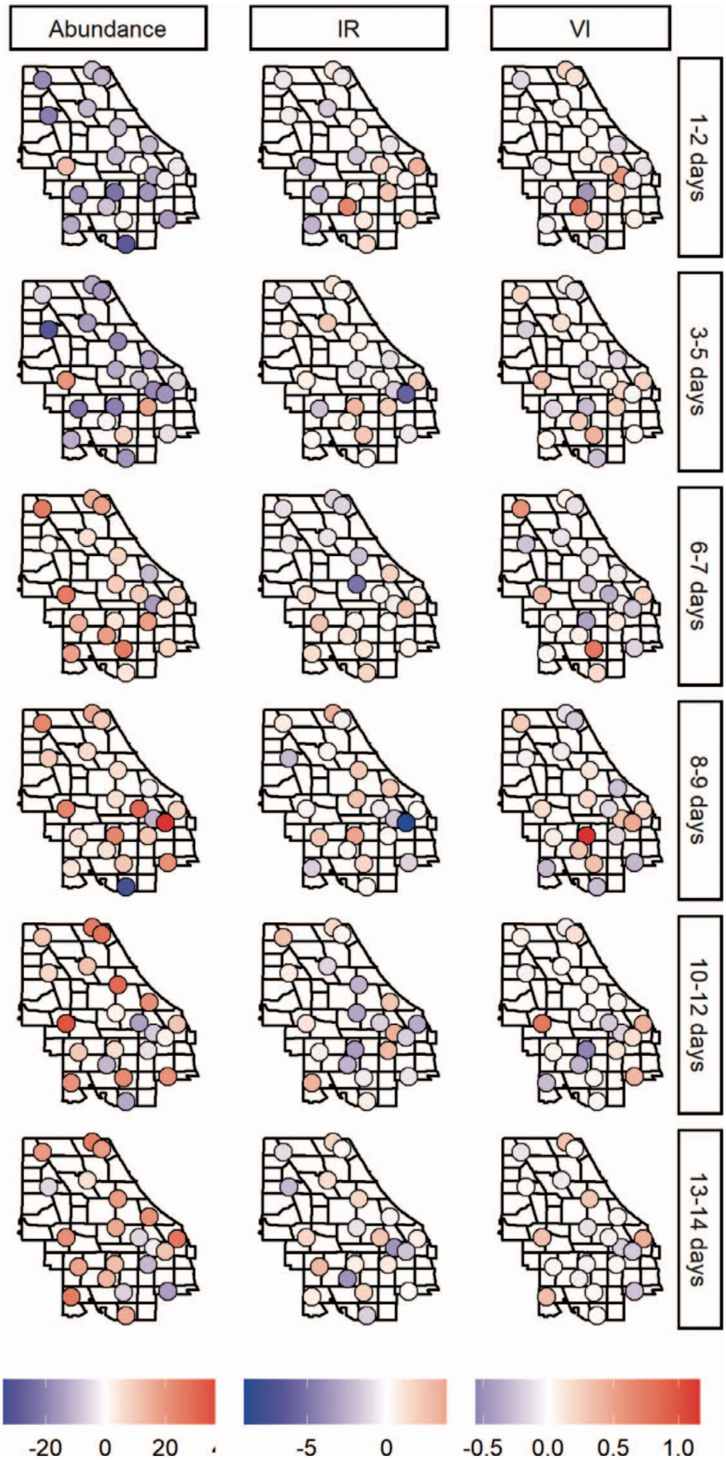

Fig. 5. Spatially varying coefficient estimates for the spray effect with collection day data. The day lags correspond to $\{\theta_1(\boldsymbol{s}),\ \theta_3(\boldsymbol{s}),\ \theta_6(\boldsymbol{s}),\ \theta_8(\boldsymbol{s}),\ \theta_{10}(\boldsymbol{s}),\ \theta_{13}(\boldsymbol{s})\}$.

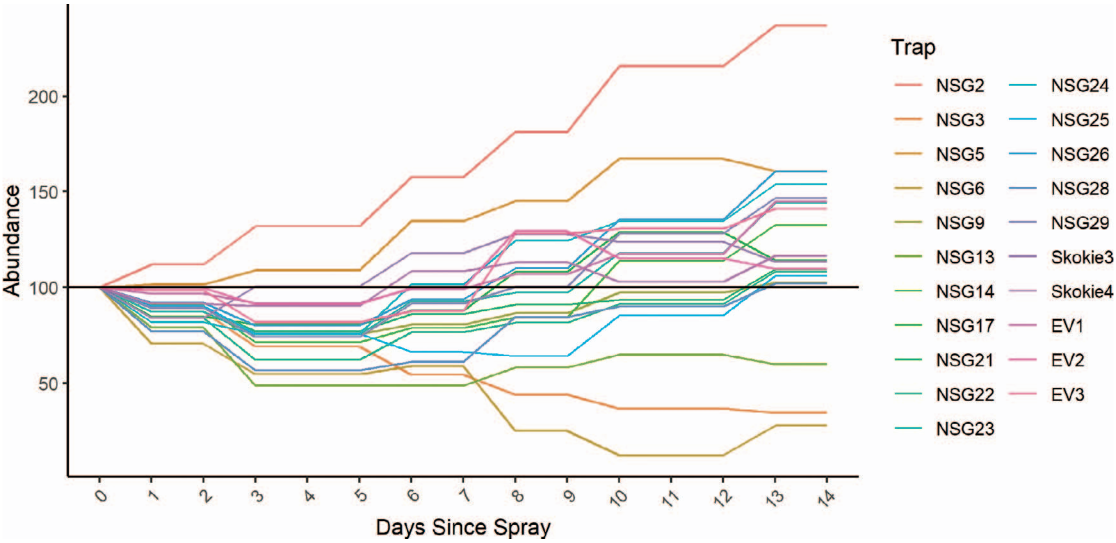

Fig. 6. Demonstration of the numerical representation of the abundance coefficients in Fig. 5, assuming each site has 100 mosquitoes and all other factors remain constant. A majority of the sites show an initial decline in abundance after spraying followed by a rebound.

impact on the change in value. Abundance shows predominantly a decrease for the 1st 5 days after spraying and an increase 6–14 days after spraying, although a few sites show contrary effects. To demonstrate how the coefficients in Fig. 5 are directly reflected in mosquito abundance, consider if each site had 100 mosquitoes and all other factors remained constant. Then Fig. 6 provides a quantitative representation of the spray effect on abundance over a 14-day period. After 14 days all but 3 trap locations have rebounded to above prespray levels.

The IR and VI analysis have roughly half of the sites increasing and half decreasing at each lag, suggesting that ULV adulticide spraying may not have a direct effect on these risk measures. However, the quality of IR estimation must also be considered when evaluating these results. The uninformative result for IR and VI is most likely due to the limited number of pools tested at each site. Considering we are analyzing data at each trap location individually and 91% of observations have 3 or fewer pools tested, there is simply not enough data to provide an informative enough IR estimate. Based on these data limitations, the impact adulticide spraying has on IR and VI is inconclusive.

To show an example of our analysis, Fig. 7 demonstrates the model fit of data collected at trap NSG14 after the region was sprayed in 2015. The model with no spray effect refers to the fitted GAM estimates, $\hat{Y}$, from Eq. 1. The spatial spray model is

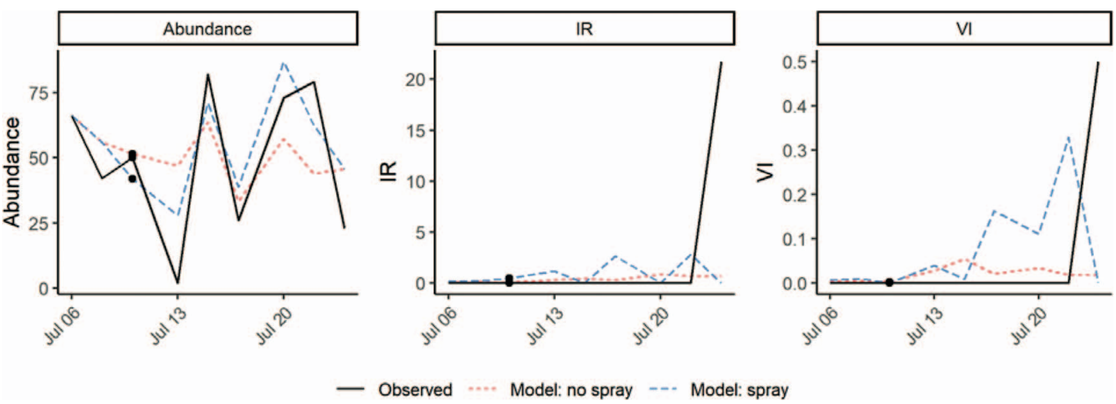

Fig. 7. Observed and estimated abundance, infection rate (IR), and vector index (VI) from July 6, 2015, to July 24, 2015, using no spray effect and the spatial spray effect model. The black dots on July 10 indicate that this was the 1st collection since the region was sprayed, i.e., $\mathbb{1}\{Spray_1(s)\} = 1$. The spatial spray model is better able to capture the initial decrease in abundance as well as the rebound in abundance compared to a model with no spray effect.

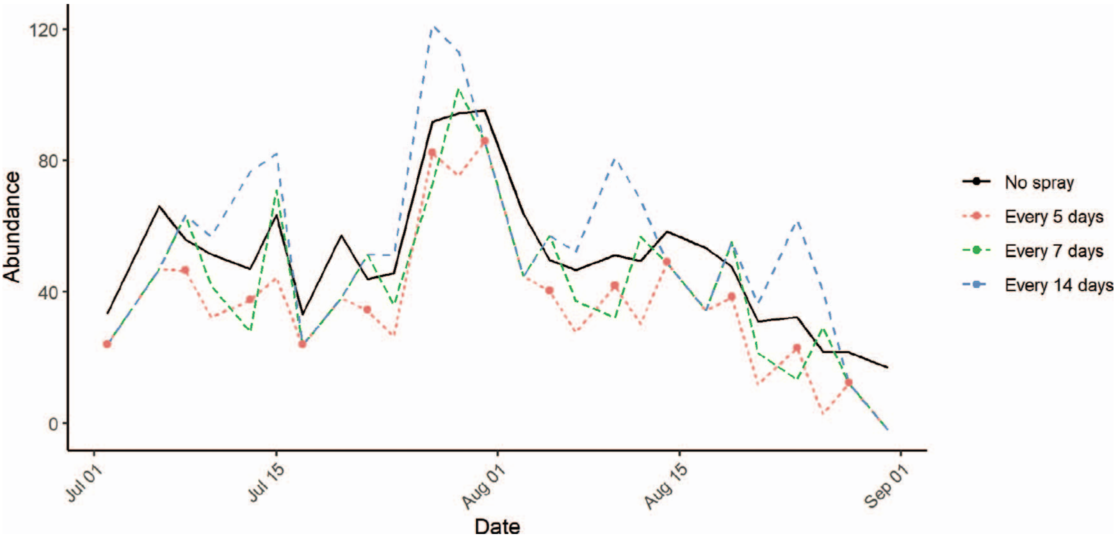

Fig. 8. Model fit of abundance at site NSG14 using 2015 data in the event of no spraying, spraying every 5 days, 7 days, or 14 days. The dots on the lines represent when adulticide spraying occurs. Serial spraying at least every 5 days maintains a lower abundance than nominal no-spray levels at all times.

better able to capture the drop in abundance on July 13 compared to when spray effect is not considered. More importantly, the spatial spray model demonstrates its ability to capture the rebound in mosquito abundance on July 20. The spatial spray model also recognizes that the VI is increasing around July 20 while the other model does not, displaying its flexibility when modeling IR and VI.

Our model can help to guide the adulticide spray scheduling. Since the reduction in abundance after adulticide spraying is short term, it could be of interest to consider serial spraying patterns for better control practices. Figure 8 shows the model fit of site NSG14 in the months of July and August of 2015 if spraying occurs every 5 days, 7 days, or 14 days beginning July 1. Spraying once every 7 days or once every 14 days does not seem to change the population abundance very much. The abundance rebound is most prevalent if spraying only occurs every 14 days, with abundance reaching above the nominal no-spray levels on multiple occasions. Whereas, if spraying were to occur every 5 days the predicted abundance remains below the nominal no-spray levels at all times, demonstrating that serial spraying at least every 5 days could provide long-term abundance reduction. This demonstration is applicable to a majority of our trap locations, based on Fig. 6 which shows most of the sites have an initial decrease in abundance followed by an increase to above nominal levels after approximately 6–7 days.

DISCUSSION

When WNV risk measures such as *Culex* spp. abundance, IR, and VI are high, ULV adulticide sprays are used to reduce the risk of virus transmission to humans. We quantified the relationship between ULV adulticide spraying and these 3 risk measures using GAMs in conjunction with fused ridge regression models based on data collected on M, W, and F of each week. Due to varying site-specific factors near each trap location, it is unlikely the impact of ULV adulticide spraying is identical at each location. We allowed for spatially varying spray coefficients by using a fused ridge penalty to enforce smoothness. This method returned a numerical change in abundance, IR, and VI, allowing for easy interpretation of the effect. The spatially varying abundance coefficients showed an initial decrease in abundance for most sites followed by a rebound after 5 days. It is estimated that gravid mosquito abundance increased more in sprayed areas than if left unsprayed in all but 3 trap locations.

The rebound in mosquito abundance indicates that a single spray event may not be enough to control vector mosquito abundance and serial spraying, weather permitting, every 5 days (or perhaps some other closer or more intense interval not examined here) should be evaluated. A postspray rebound was also observed within the NSMAD in 2018 when a more intensive trapping scheme was utilized (Clifton et al. 2019). Mitchell et al. (1970), Mutebi et al. (2011), Pawelek et al. (2014), and Holcomb et al. (2021) also documented a rebound in mosquitoes postspraying. Fox and Specht (1988) similarly concluded that one-time spraying was not effective against *Aedes aegypti* (L.), while Focks et al. (1987) discovered that sequential ULV spraying of malathion decreased the adult population by 75% during a 5-day study period, demonstrating the potential importance of serial spraying in maintaining a population reduction.

Although a rebound in adult population seems to be a predictable response to a single adult control ULV treatment, it is not entirely clear the mechanism for such a rebound. Some resurgence in adult population can be expected from reinfestation or migration from surrounding areas, and this possibility was identified in Mitchell et al. (1970) and Reddy et al. (2006). Other works have identified a transient physiological resistance to pyrethroid adult control materials in gravid female mosquitoes (Halliday and Feyereisen 1987, Eliason et al. 1990, Moore et al. 1990, Clifton et al. 2019). Bloodfed and gravid mosquitoes, less susceptible to control materials, would presumably be attracted to gravid traps in the days following a treatment, thus appearing as a rebound in population. Finally, olfactory or other excitatory effects on mosquito behavior may play a role. Cohnstaedt and Allan (2011) described a temporary inhibition of host-seeking olfaction after exposure to sublethal pyrethroid exposure that would manifest as a population decline in traps that are dependent on olfactory attraction to capture mosquitoes. Fox and Specht (1988) similarly attribute rebounds after spraying to excitatory behavior following exposure to a mosquito adulticide. Locomotor stimulation (also called excito-repellancy) clearly occurs when adult mosquitoes are exposed to adult control pesticides (Cooperband and Allan 2009) but as of yet, its impact on perceived ULV spraying effectiveness has not been well defined in field conditions.

While the existence or magnitude of mosquito tolerance to insecticides was not explicitly evaluated in this study, preliminary assessments using CDC bottle bioassays identified *Cx. pipiens* populations resistant and partially resistant to d-phenothrin, permethrin, and malathion throughout the NSMAD (Harbison, unpublished data, 2020). It is unknown when resistant populations developed, the full spatial or temporal distribution of resistance populations, or how resistance as detected in a CDC bottle bioassay relates to field effectiveness or rebounds in population. Notably, populations of *Cx. restuans* have not demonstrated resistance to any of the aforementioned adult control active ingredients. It is conceivable that almost every factor previously identified as contributing to population rebounds (migration/reinfection, gravid tolerance, olfaction changes, locomotor stimulation) could be enhanced or magnified by the existence of a heritable pesticide tolerance. Nonetheless, this paper highlights the importance of understanding the susceptibility of mosquitoes to adult control materials from a variety of perspectives, including pesticide susceptibility, application timing, application sequence, and gonotrophic state of vector mosquitoes.

The impact on IR and VI was not detectable due to the large error associated with estimating IR at individual trap locations. This is a result of the limited model sampling and pool sizes, not necessarily a reflection of ULV effectiveness. Chakraborty and Smith (2019) found that the error in estimated IR was wide when the density of traps was small. Additionally, Gu et al. (2004) found that estimated IR was most accurate when variable pool sizes are used rather than a constant size of 50. In order to evaluate the impact adulticide spraying has on IR and VI, there would need to be varying smaller pool sizes to provide a more accurate estimate of IR. An additional solution would be to group information from all the trap locations together and model a fixed spray effect; however, to do so all traps would need to be sprayed on the same day, which is impractical with available resources.

The spatially varying coefficient model showed which trap locations were more impacted by ULV adulticide spraying than others. In particular, site NSG2 showed no decrease in abundance after spraying and it could be of interest to look into the location placement. We employed covariates related to temperature, precipitation, wind speed, location, and week of the year to control the confounding effects from the risk factors that are known to be related to the nature of WNV when estimating the impact of adulticide spray. Many studies have found degree day to be a measure of the thermal environment related to insect development (Baker et al. 1984, Kunkel et al. 2006). In addition, we incorporated daily winter temperatures and daily spring precipitation as functions using MFPCA to account for long stretches of cold days in the winter or drought in the spring which are known to be associated with higher incidences of WNV outbreaks (Wong et al. 2019). It could be of further interest to consider more informative variables related to land coverage surrounding the trap and amount of ULV adulticide deployed to further improve the model fit. While our analysis is based on observational data, it could be of further interest to study the spray impact in a controlled setting to get a better understanding of the relationship between ULV adulticide treatments, IR, and VI.

Adult mosquito control for public health purposes is focused primarily on controlling the transmission of a virus through modification to the age structure of the vector mosquito population, which is not necessarily the same as widespread and sustained reductions in the gravid mosquito population (although it could be). It is unknown how the adult control treatments described here modified the age structure of the vector mosquito population or reduced transmission risk by killing the oldest and most likely to be infected mosquitoes. Further work is needed to separate the effect of adult control ULV treatments on the gravid population as a whole (as this study examined) from the effect of adult control ULV treatments on age structure or infection rates. Although we failed to detect sustained reductions in the gravid adult vector mosquito population and in most cases detected a resurgence of the population to above prespray levels, it remains unknown how the age structure, infection status, or risk to the human population changed. It is also unknown how spraying intervals of less than 5 d would impact mosquito populations or how aerial ULV treatments, unhindered by spatial and landscape features, would have compared. Finally, these treatments were all conducted with d-phenothrin as the main active ingredient. It is unknown how other chemistries or application rates would have differed in their effect. With these caveats highlighted, it is important to recognize that this work is describing a commonly employed and likely inadequate ULV adult control methodology (weekly or biweekly ground-based treatments with mosquitoes of unknown susceptibility) rather than a failure of adult control methods as a whole. Programs that utilize similar ground-based adult control ULV methods should strongly consider resistance to pesticides, active ingredient employed, dosage, and the timing and interval of applications as important factors in achieving adult mosquito population reductions.

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