Journal of Pest Science
https://doi.org/10.1007/s10340-024-01787-w

ORIGINAL PAPER

Comparing the effectiveness of adulticide application interventions on mitigating local transmission of dengue virus

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Received: 31 January 2024 / Revised: 5 April 2024 / Accepted: 16 April 2024

Abstract

The southern US has a large presence of mosquito vector species for dengue virus (DENV) and experiences thousands of DENV importations every year, which have led to several local outbreaks. Adulticide spraying targeting active mosquitoes is one of the most common insecticide strategies used as a response to an outbreak. The aim of this study is to evaluate the effectiveness of adulticide spraying conducted at different times of the day to curb DENV transmission. Based on unique dataset of *Aedes aegypti* diel activity patterns in Miami-Dade County, Florida, and Brownsville, Texas, we developed a mechanistic model of DENV transmission, which simulates adulticide spraying interventions. We estimated that spraying adulticide for 14 consecutive days at 7am or 8 pm was highly effective in reducing DENV outbreak probability from 10% in the absence of interventions to 0.1% for Miami-Dade County, and from 7.8 to 0.1% for Brownsville. Moreover, in case of a local outbreak in Miami-Dade County, we estimated the median number of symptomatic infections after the identification of a local outbreak to be reduced from 67.0 (IQR: 25.5–103.0) in the absence of interventions to 1.0 (IQR: 0.0–2.0) when spraying adulticide for 14 consecutive days at 8 pm. In Brownsville, the same intervention is estimated to lead to a decrease from 15.0 (IQR: 7.0–33.0) cases to 1.0 (IQR: 0.0–2.0). Our study highlights the importance of considering diel activity patterns of vector mosquito species in arbovirus preparedness and response planning and provide quantitative evidence to guide the decision-making of mosquito control authorities.

Keywords *Aedes aegypti* · Diel activity · Arbovirus · Integrated vector management · Outbreak response

Introduction

Mosquito species acting as vectors of dengue virus (DENV), such as *Aedes aegypti* (L.) and *Aedes albopictus* (Skuse) (Diptera: Culicidae) are widespread throughout the southern US (Benelli et al. 2020; Monaghan et al. 2019), which experiences multiple importations of DENV every year (Centers for Disease Control and Prevention 2024). The large vector presence and continuous DENV importations have led to several outbreaks of local transmission in several states, including Florida (FL) and Texas (TX) (Centers for Disease Control and Prevention 2023, 2024). In both 2022 and 2023, outbreaks of 65 + locally acquired DENV infections were reported in Miami-Dade County, FL (Centers for Disease Control and Prevention 2024), highlighting the need for quantitative tools to improve arbovirus preparedness and response planning.

Mitigating the risks posed by DENV requires the allocation of considerable efforts and resources under the

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Communicated by Antonio Biondi.

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integrated vector management (IVM) framework (Lizzi et al. 2014), including understanding the relative effectiveness of different mosquito control interventions. Adulticide spraying is one of the most common insecticide strategies used in urban areas for controlling mosquito populations by targeting active host-seeking females (Giunti et al. 2023; Mundis et al. 2020). As mosquito activity varies through the day, diel activity patterns are essential for determining the effectiveness of adulticide spraying interventions in reducing the adult mosquito population (Mutebi et al. 2022).

Due to the scarcity of mosquito diel activity data, this important aspect is often overlooked in adulticide spraying planning and application. By accounting for mosquito diel activity patterns, (Wilke et al. (2023) have shown that adulticide spraying was substantially more effective in reducing the mosquito population during certain times of day compared to others. However, how this entomological effect translates into an epidemiological effect on DENV transmission is yet to be determined. The current study aims to identify the most effective adulticide spraying interventions for mitigating DENV spread through the analysis of a mathematical model of DENV transmission informed with empirical mosquito diel activity data, using Miami-Dade County, FL, and Brownsville, TX, as study sites.

Materials and methods

Study sites

The two study sites, Miami-Dade County, FL, and Brownville, TX, were selected due to their history of arbovirus outbreaks, large *Ae. aegypti* populations, and vulnerability to importation of DENV (Myer et al. 2020; Wilke et al. 2019a, b;; Wilke et al. 2021a, b). Miami-Dade County, FL is particularly vulnerable to importations of DENV, because it is a popular tourist destination that receives more than 120 million visitors on average each year, and it is the main port for cruise ships traveling through the Caribbean and the Gulf of Mexico (United States Bureau of Transportation Statistics 2016). Additionally, Miami-Dade County serves as a hub for freight cargo ships that transport goods between the US and several Caribbean countries where dengue is endemic such as Haiti, the Dominican Republic, and Cuba, which increases the risk of pathogen importation into the US (Wilke et al. 2022). Moreover, Miami-Dade County has a high percentage of foreign-borne individuals from DENV endemic areas (U.S. Census Bureau 2022). Brownsville is located in the southernmost county of Texas, Cameron, bordering Matamoros, Mexico, where dengue is endemic (Dzul-Manzanilla et al. 2021; Ramos et al. 2008). A seroepidemiologic survey conducted in Brownsville, has estimated an incidence of recent dengue infection of 4% (Ramos et al. 2008).

Data collection

***Aedes aegypti* diel activity patterns.** *Aedes aegypti* mosquitoes were collected by BG-Sentinel-2 traps (Biogents AG, Regensburg, Germany) baited with BG Lures and dry ice as a source of carbon dioxide. The BG-Lure and dry ice are highly attractive to female *Ae. aegypti* seeking blood meals (Wilke, et al. 2019a). Four traps were used for each study site and were monitored every hour for 96 consecutive hours (4 days) once every month from May to November 2019. More details on the data collection effort can be found in the reference (Mutebi et al. 2022).

Mosquito surveillance. We used mosquito surveillance data from January 1, 2021, to December 31, 2021, available for Miami-Dade County, FL, and from April 4, 2018, to November 4, 2018, for Brownsville, TX. In both study sites, mosquitoes were collected once per week using BG-Sentinel-2 traps baited with dry ice. During the study period, the mosquito surveillance system consisted of 307 and 152 traps in Miami-Dade County and Brownsville, respectively.

Temperature. Miami-Dade County, FL, we collected average daily temperature data between January 1, 2021, and December 31, 2021, from the Miami International Airport station (Miami International Airport Station 2021). For Brownsville, TX, temperature data between April 4, 2018, and November 4, 2018, was obtained from the Brownsville/South Padre Island International Airport station (Brownsville/South Padre Island International Airport Station 2021).

Estimation of temperature-dependent development and mortality rates

To determine the temperature-dependent development and mortality rates for *Ae. aegypti*, we used data collected in previous studies (Farnesi et al. 2009; Yang et al. 2009, 2011). Time for completion of embryogenesis (i.e., till egg hatching), the number of eggs laid, and the temperatures at which the observations occurred were obtained from Farnesi et al. (2009). Survival, mortality, at different temperatures for the larval and pupal stages were taken from Yang et al. (2011). Survival, mortality, oviposition rates, and the observed temperatures for adult female mosquitoes were obtained from Yang et al. (2009). Based on these data, we performed a polynomial regression analysis using temperature as a predictor for development or mortality for each mosquito life stage (see Supplementary Material for details).

Mathematical modeling analysis

We used a compartmental model to produce stochastic simulations of the *Ae. aegypti* population and DENV transmission dynamics. The model estimates the abundance of *Ae. aegypti* at a calendar date t through the four developmental stages of the mosquito lifecycle: egg (E), larva (L), pupa (P), and (female) adult (A). We assumed a 1:1 sex ratio for adult mosquitoes, considering only female adult mosquitoes because males are not epidemiologically important (Kojin et al. 2022; Lounibos and Escher 2008). Adult female mosquitoes were further classified as susceptible (A_S), latent (A_E), or infectious (A_I) to model DENV transmission through the mosquito population. We assumed a human host population where hosts move through a set of compartments where they are classified as susceptible (S_H), latent (E_H), symptomatic infectious (I^s_H), asymptomatic infectious (I^a_H), and recovered (R_H).

Transitions between compartments were simulated by sampling from binomial distributions with the appropriate rate (Abbey 1952) according to the following system of equations:

$$\mathrm{E}(t+\Delta t) \leftarrow n_E \cdot d_A\left(\mathrm{T}_t\right) \cdot \left[\mathrm{A}_S(t)+\mathrm{A}_E(t)+\mathrm{A}_I(t)\right] \cdot \left[1-\frac{\mathrm{E}(t)}{\mathrm{K}_E(t)}\right] - m_E\left(\mathrm{T}_t\right) \cdot \mathrm{E}(t) - d_E\left(\mathrm{T}_t\right) \cdot \mathrm{E}(t)$$

$$\mathrm{L}(t+\Delta t) \leftarrow d_E\left(\mathrm{T}_t\right) \cdot \mathrm{E}(t) - m_L\left(\mathrm{T}_t\right) \cdot \mathrm{L}(t) - d_L\left(\mathrm{T}_t\right) \cdot \mathrm{L}(t)$$

$$\mathrm{P}(t+\Delta t) \leftarrow d_L\left(\mathrm{T}_t\right) \cdot \mathrm{L}(t) - m_P\left(\mathrm{T}_t\right) \cdot \mathrm{P}(t) - d_P\left(\mathrm{T}_t\right) \cdot \mathrm{P}(t)$$

$$\mathrm{A}_S(t+\Delta t) \leftarrow \frac{1}{2} d_P\left(\mathrm{T}_t\right) \cdot \mathrm{P}(t) - m_A\left(\mathrm{T}_t\right) \cdot \mathrm{A}_S(t) - \lambda_v(t) \cdot \mathrm{A}_S(t)$$

$$\mathrm{A}_E(t+\Delta t) \leftarrow -m_A\left(\mathrm{T}_t\right) \cdot \mathrm{A}_E(t) + \lambda_v(t) \cdot \mathrm{A}_S(t) - \omega_V \cdot \mathrm{A}_E(t)$$

$$\mathrm{A}_I(t+\Delta t) \leftarrow -m_A\left(T_t\right) \cdot \mathrm{A}_I(t) + \omega_V \cdot \mathrm{A}_E(t)$$

$$\mathrm{S}_H(t+\Delta t) \leftarrow -\lambda_H(t) \cdot \mathrm{S}_H(t)$$

$$\mathrm{E}_H(t+\Delta t) \leftarrow \lambda_H(t) \cdot \mathrm{S}_H(t) - \omega_H \cdot \mathrm{E}_H(t)$$

$$\mathrm{I}^s_H(t+\Delta t) \leftarrow p_s \cdot \omega_H \cdot \mathrm{E}_H(t) - \gamma \cdot \mathrm{I}^s_H(t)$$

$$\mathrm{I}^a_H(t+\Delta t) \leftarrow \left(1-p_s\right) \cdot \omega_H \cdot \mathrm{E}_H(t) - \gamma \cdot \mathrm{I}^a_H(t)$$

$$\mathrm{R}_H(t+\Delta t) \leftarrow \gamma \cdot \mathrm{I}^s_H(t) + \gamma \cdot \mathrm{I}^a_H(t)$$

where

- The arrow ($\leftarrow$) represents the binomial transition;
- $\Delta t = 0.1$ days is the time step used to simulate binomial transitions;
- T_t is the temperature on calendar date t in the study site;
- n_E is the average number of eggs laid per oviposition, which was set to 100 eggs (Clemons et al. 2010);
- d_E, d_L, and d_P, are the temperature-dependent development rates for *Aedes aegypti* during each life stage, while d_A is the temperature-dependent oviposition rate (see Supplementary Material);
- m_E, m_L, m_P, and m_A are the temperature-dependent mortality rates for *Aedes aegypti* during each life stage (see Supplementary Material);
- $K_E(t)$ is the environments carrying capacity on calendar date t, which account for constraints in the availability of resources for the aquatic stage of the mosquito life cycle (namely, eggs, larvae, and pupae) throughout the year. Specifically, $K_E(t)$ was defined as a step function changing every 13 weeks for Miami-Dade County starting from January 25, and changing every 10 weeks for Brownsville starting from April 30;
- $\lambda_v = \frac{k \cdot \chi_V \cdot (\mathrm{I}^s_H(t)+\mathrm{I}^a_H(t))}{\mathrm{N}_H(t)}$ is the force of infection for vectors;
- k is the daily mosquito biting rate on human hosts, which is set to obtain the desired epidemic reproduction number (see section "Mosquito biting rate");
- χ_V is *Aedes aegypti* susceptibility to DENV infection per bite on an infected human host, which was set to 0.85 (Andraud et al. 2012);
- N_H is the number of human hosts in the population at time t, which was set to 2,662,777 for Miami-Dade County (*Miami-Dade* County 2021) and 181,844 for Brownsville (Brownsville 2018);
- ω_V is the inverse of DENV latent period for vectors (1/6.1 days) (Chan and Johansson 2012);
- $\lambda_H = \frac{k \cdot \chi_H \cdot \mathrm{A}_I(t)}{\mathrm{N}_H(t)}$ is the force of infection for human host;
- χ_H is the human host susceptibility to DENV infection per bite of an infected adult female of *Aedes aegypti*, which was set to 0.65 (Andraud et al. 2012);
- ω_H is the inverse of DENV latent period for human hosts (1/6.1 days) (Chan and Johansson 2012);
- γ is the inverse of DENV infectious period for human hosts (1/4.5 days) (Chao et al. 2012);

- p_s is the probability of developing symptoms for DENV-infected individuals, which was set to 0.2 (Sriprom et al. 2007).

Model calibration

To estimate the values of the carrying capacity for each period and study site, we defined the likelihood of observing the reported number of female adult *Ae. aegypti* given a negative binomial distribution with a mean given by the number of female adult *Ae. aegypti* estimated by the model (which depends on the carrying capacity) and a given over-dispersion. We then used a Markov chain Monte Carlo (MCMC) Metropolis–Hastings algorithm to explore this likelihood and estimated the joint posterior distributions of the carrying capacities, initial number of eggs, and the over-dispersion of the negative binomial distribution used in the likelihood (see Supplementary Material for details).

The estimated initial number of eggs is then multiplied by a scaling factor, $\psi = 50,000$, that accounts for the catchment radius of each trap (Zardini et al. 2024). It is important to stress that this scaling factor does not alter the results as, for a given value of the reproduction number, in the model it is equivalent to have a larger number of mosquitoes and a lower biting rate or a lower number of mosquitoes with a larger biting rate (see equation for the epidemic reproduction number in section "Mosquito biting rate") (Poletti et al. 2011).

Mosquito biting rate

To simulate DENV transmission, a further model parameter needs to be estimated: the mosquito biting rate. First, we derived the equation for the reproduction number on calendar date t, $R(t)$, as in Poletti et al. (2011):

$$\mathrm{R}(t) = k^2 \cdot \frac{\chi_H \cdot \chi_V}{\gamma \cdot m_A\left(\mathrm{T}_t\right)} \cdot \frac{\omega_V}{\omega_V + m_A\left(\mathrm{T}_t\right)} \cdot \frac{\mathrm{N}_V(t)}{\mathrm{N}_H}$$

Then, since all the terms of this equation are either known from the literature or the result of the simulation of the mosquito dynamic model, we solved this equation for k to obtain an estimate of the biting rate for any given value of the reproduction number. Specifically, in the baseline analysis, we set DENV reproduction number for both study sites at 1.5 during the week when mosquito abundance was the highest in each study site (i.e., July 26, 2021-August 1, 2021, for Miami-Dade County; August 20, 2018-August 26, 2018, for Brownsville) (Zardini et al. 2024). We refer to the average reproduction number during the week of highest mosquito abundance as R^*. Other values of R^* (i.e., 1.7 and 2.0) were explored as sensitivity analyses.

Simulation of adulticide application interventions

Our model considers a completely susceptible human and *Ae. aegypti* population at the first timestep. To initiate infection transmission, we assume an imported DENV asymptomatic infection into the population on April 1. Other dates to import the first infection were explored as sensitivity analyses. In baseline analysis, we defined the start of the adulticide application intervention as the day after the cumulative number symptomatic infections reached (or exceeded) 5. We refer to this as the outbreak identification threshold. Other definitions of the outbreak identification threshold were explored as sensitivity analyses.

For this analysis, we simulated truck-mounted ultralow volume (ULV) adulticide applications that reflect the standard application procedures used in Miami-Dade County, FL. This procedure is performed using DeltaGard (Deltamethrin 2% AI) (Bayer Environmental Science, Research Triangle Park, NC), where the Deltamethrin was applied using a Grizzly ULV Sprayer (Clarke, St. Charles, IL) at the label rate of 0.0009 lbs (André B. B. Wilke et al. 2021a, b). To simulate spraying Deltamethrin, our model assumes a diagnostic dose of 0.75 mg per 250-mL bottle and a 50% mortality of *Ae. aegypti*, consistent with a previous study (Parker et al. 2020). This spraying intervention was implemented in our model to target adult female mosquitoes that are active at the time of spraying throughout the entire study site. The proportion of active *Ae. aegypti* for each study site and time of day were estimated as $r_{ij}(h) = \frac{\mathrm{C}_i(h)}{\max[\mathrm{C}_i(h)]}$, where $C_i(h)$ is the estimated number of active adult female *Ae. aegypti* in study site i, at time of day h (Wilke et al. 2023). As described in (Wilke et al. 2023), uncertainty in the number of captured mosquito at each time of the day was accounted for by sampling $C_i(h)$ from a Poisson distribution with $\mu = \widetilde{\mathrm{C}}_i(h)$ – the observed number of captured *Ae. aegypti* in study site i at time of day h. We consider the adulticide spraying to reduce the *Ae. aegypti* adult female population on average by $\sigma r_i(h)$, where σ is the efficacy of the adulticide per application. We also assume that the adulticide application affects in the same way of susceptible, latent, and infectious mosquitoes. As such, we sampled the number of mosquitoes removed from the population from a Poisson distribution with mean $\mu = \mathrm{C}_i(h)\sigma r_i(h)A_x(t^*)$, where t^* represents the date of the adulticide application and $A_x(t^*)$ corresponds to the number of adult mosquitoes susceptible

($x = S$), latent ($x = E$), and infectious ($x = I$) mosquitoes at time t^*.

Adulticide spraying was conducted under multiple scenarios that differ by the time of day (i.e., 1 am, 7 am, 3 pm, and 8 pm) and the number of days the intervention was implemented (i.e., 14 and 28 days). To estimate the effectiveness of adulticide applications, for each analyzed scenario, we performed 1,000 stochastic model realizations. We calculated the effectiveness of the adulticide spraying application as described in Hladish et al. (2020):

$$\text{eff} = 1 - \frac{\sum_{t=0}^{365} \mathrm{I}_H^S(t)\text{with adulticide application}}{\sum_{t=0}^{365} \mathrm{I}_H^S(t)\text{with no intervention}}$$

Results

Estimated diel activity patterns

In Miami-Dade County, an average of 46.0 (95% CI: 24.0–55.6) *Ae. aegypti* females were collected between 12 and 5 am (Fig. 1). Then, we observed an increase in activity to an average of 253 (95% CI: 109.55–488.55) collected *Ae. aegypti* females between 6 am and 12 pm, with an initial peak at 7 am (504 females). Activity then declined between 1 and 4 pm to an average of 47.5 (95% CI: 42.1–54.6) collected *Ae. aegypti* before increasing to an average of 422.8 (95% CI: 142.4–885.7) between 5 and 9 pm, with a second peak at 8 pm (931 collected *Ae. aegypti*).

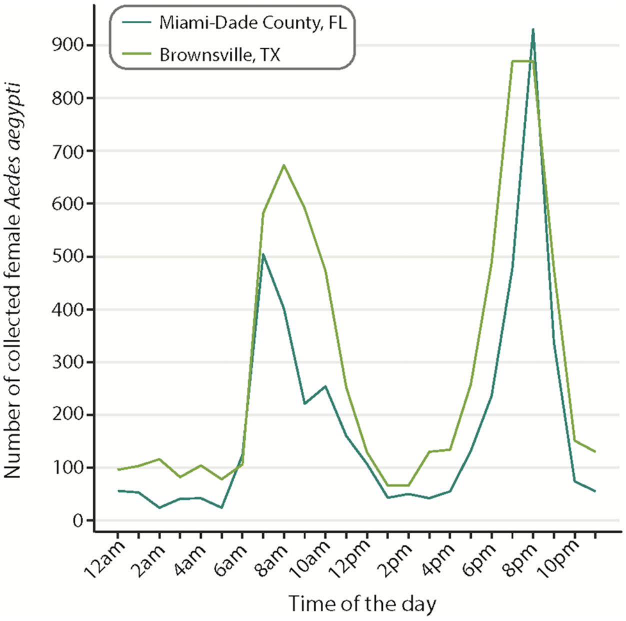

Fig. 1 Hourly number of *Ae. aegypti* females collected in Miami-Dade County, FL, and Brownsville, TX

Diel activity followed a similar pattern in Brownsville with an average of 97.8 (95% CI: 78.6–114.5) *Ae. aegypti* females collected between 12 and 6 am (Fig. 1). Then, we observed an increase in activity to an average of 514.2 (95% CI: 274.1–664.8) collected *Ae. aegypti* females between 7 am and 11 pm, with an initial peak at 8 am (673 females). Activity then declined between 12 and 4 pm to an average of 105.0 (95% CI: 66.0–133.6) collected *Ae. aegypti* before increasing to an average of 492.4 (95% CI: 279.8–870.0) between 5 and 9 pm, with a second peak from 7 to 8 pm (870 collected *Ae. aegypti*).

Estimated *Ae. aegypti* relative abundance

The estimated weekly number of *Ae. aegypti* reflected the observed number of weekly catches in both Miami-Dade County, FL, and Brownsville, TX (Fig. 2). For Miami-Dade County, FL, the model showed a gradual increase in *Ae. aegypti* abundance from an average of 293.2 (95% CI: 263.5–331.1) in January to an average of 2531.4 (95% CI: 2450.2–2610.2) July and declined through the rest of the year. For Brownsville, TX, there was an increase from an average of 91.9 (95% CI: 56.2–137.0) in April to an average of 198.4 (95% CI: 186.0–213.2) in June. We then estimated a slight decline in abundance through July and August and then increased to a maximum of 228.5 (95% CI: 148.0–337.0) in September.

Effectiveness of adulticide application interventions

Among the DENV outbreaks that were identified (here we assumed an outbreak identification threshold of 5), we estimated that, in the absence of interventions and for $R^* = 1.5$, an importation of an asymptomatic DENV-infected individual resulted in a 10.0% chance of having 40 or more total symptomatic infections in Miami-Dade County. In case of an outbreak (i.e., 5 + symptomatic cases are identified), we estimated the outbreak to have a median size of 72.0 symptomatic infections (IQR: 30.5–108.0) (Fig. 3a, b). Under the same assumptions, for Brownsville, we estimated a 7.8% chance of having more than 10 total symptomatic infections and a median outbreak size of 15.0 symptomatic infections (IQR: 7.0–33.0) (Fig. 3c, d).

For Miami-Dade County, when adulticide application is conducted at 1 am and 3 pm for 14 days, the probability of having 40 or more symptomatic cases was only slightly reduced (8.0 and 8.1%, respectively, as compared to 10.0% in the absence of interventions). However, we estimated a marked decrease in the probability of having 40 or more symptomatic cases when adulticide application is conducted

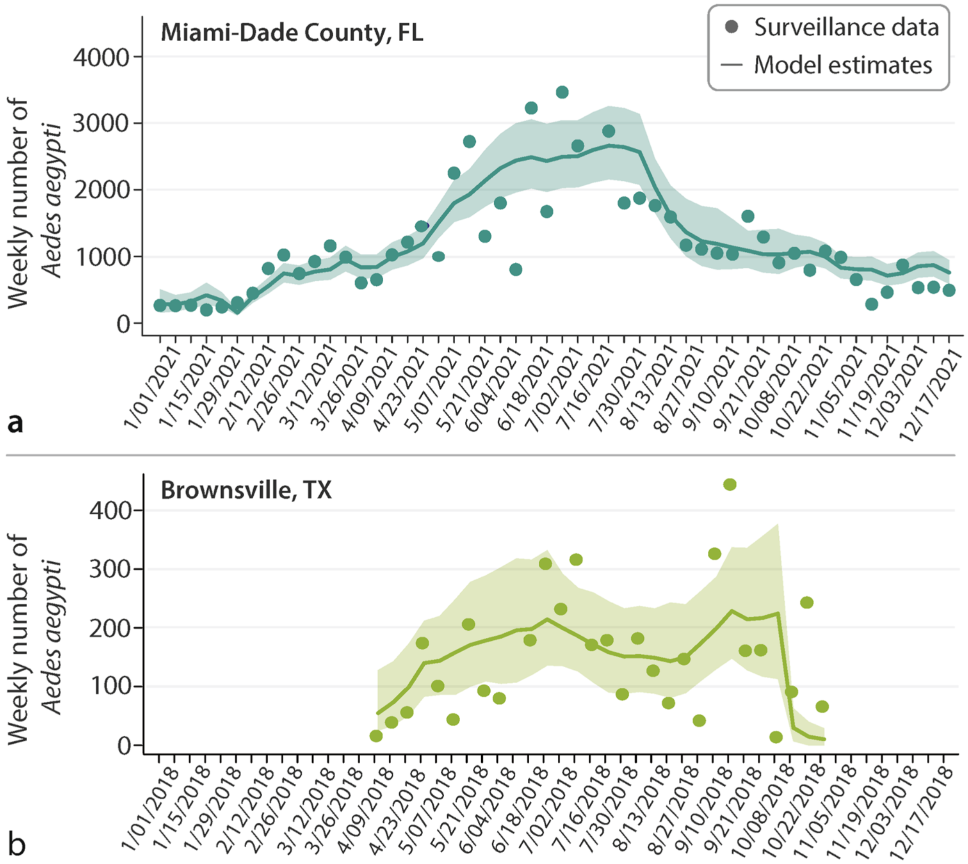

Fig. 2 **a** Weekly number of *Aedes aegypti* collected in Miami-Dade County, FL (dots) and as estimated by the model (mean and 95% CI) **b.** As a., but for Brownsville, TX

at 7 am (0.6%) and 8 pm (0.1%), when *Ae. aegypti* were highly active. Likewise, should an outbreak start to unfold and be identified (5 + identified symptomatic cases), we estimated a marked decrease in total symptomatic infections when adulticide application was implemented at 7 am (7.0, IQR: 6.0–11.8) and 8 pm (6.0, IQR: 5.0–7.0) for an estimated 90.3 and 91.7% reduction in the number of symptomatic cases, respectively, as compared to 72.0 symptomatic infections (IQR: 30.5–108.0) in the absence of interventions. For Brownsville, when adulticide application was conducted at 1 am and 3 pm for 14 days, the probability of having 10 or more total symptomatic infections was estimated at 5.3 and 4.2% (as compared to 7.8%, in the absence of interventions). Similar to Miami-Dade County, a remarkably larger decrease in outbreak probability was observed when adulticide application was conducted at 7 am (0.4%) and 8 pm (0.3%), reducing the number of symptomatic cases by 70% when conducted at either time. Should an outbreak take place and identified, its size is estimated to be reduced to 1.0 symptomatic infection (IQR: 0.0–3.0) and 1.0 symptomatic infection (IQR: 0.0–2.0) after outbreak identification when the intervention is conducted at 7 am and 8 pm, respectively, as compared to 15.0 symptomatic infections (IQR: 7.0–33.0) in the absence of interventions.

We conducted an extensive sensitivity analysis to determine the effect of DENV transmissibility, time of DENV importation, timeliness of outbreak identification, and duration of adulticide spraying. For Miami-Dade County, while the absolute values of the estimated outbreak probability and size were larger when setting R^* to 1.7 and 2.0, there was a marked decrease when the adulticide spraying intervention was implemented at 7 am for 14 days (Fig. 4a). Specifically, the probability of having 40 or more symptomatic cases was reduced from 11.5 to 1.5% for an $R^*=1.7$ and from 13.4 to 6.4% for an $R^*=2.0$. Excluding the 5 symptomatic cases considered to identify an outbreak, we estimated a 98.9% reduction in the outbreak size from 88.0 symptomatic infections (IQR: 28.0–198.3) to 1.0 (IQR: 0.0–6.5) and a 99.1% reduction in the outbreak size from 351 symptomatic infections (IQR: 115.0–623.0) to 3.0 (IQR: 1.0–37.5), when R^* is 1.7 and 2.0, respectively.

We estimate both the outbreak probability and size to be higher when an importation of an asymptomatic DENV-infected individual was imported in May (Fig. 4b). Both outbreak probability and size then decreased throughout the course of the season. Regardless of the time of importation, we estimated adulticide application at 7 am to be highly effective in reducing both outbreak probability and its eventual size.

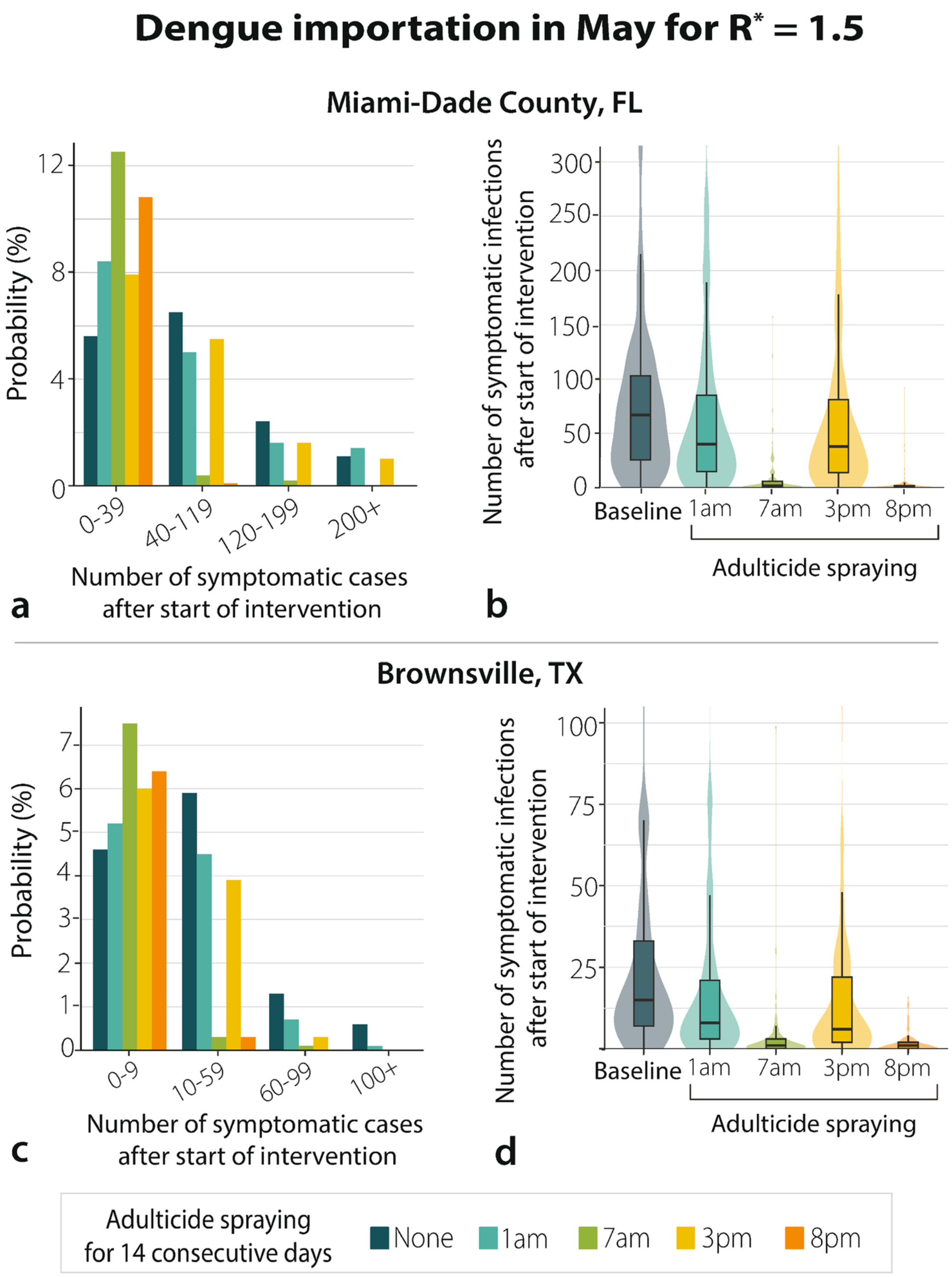

Fig. 3 **a** Estimated probability of observing an outbreak of a given size in Miami-Dade County, FL, after dengue importation in May assuming $R^* = 1.5$ in the absence of interventions and when the adulticide spraying for 14 consecutive days (adulticide efficacy 50%) is implemented at different times of day. **b** Estimated number of symptomatic infections after outbreak detection (i.e., 5 symptomatic cases) in Miami-Dade County, FL. Box plots represent quantiles 0.025, 0.25, 0.5, 0.75, 0.975, and shaded area represents the distribution of the number of symptomatic infections. **c** As a, but for Brownsville, TX. and **d** As b but for Brownsville, TX

When comparing different outbreak identification thresholds (Fig. 4c), we estimated similar outbreak probabilities, but different outbreak sizes. Specifically, when an adulticide spraying intervention was implemented at 7 am for 14 days, we estimated a reduction of 90.3% (7.0 symptomatic infections, IQR: 6.0–11.8), 81.9% (13.0 symptomatic infections, IQR: 11.0–17.0), and 65.3% (25 symptomatic infections, IQR: 21.0–30.0) in the number of symptomatic infections when the outbreak identification threshold was set to 5, 10, and 20, respectively.

Prolonging the duration of adulticide application from 14 to 28 days had the effect to decrease outbreak potential and size median outbreak size (Fig. 4d) only marginally.

Results for interventions carried out at other times of the day are reported in Tables S2-S9.

We estimated similar qualitative patterns also for Brownsville (Fig. 5), although some quantitative differences between the two locations existed. As compared to Miami-Dade County, in Brownsville DENV outbreaks were estimated to be smaller and less likely, with both metrics decreasing sharply as the season progresses. Like for Miami-Dade County, we estimated adulticide application

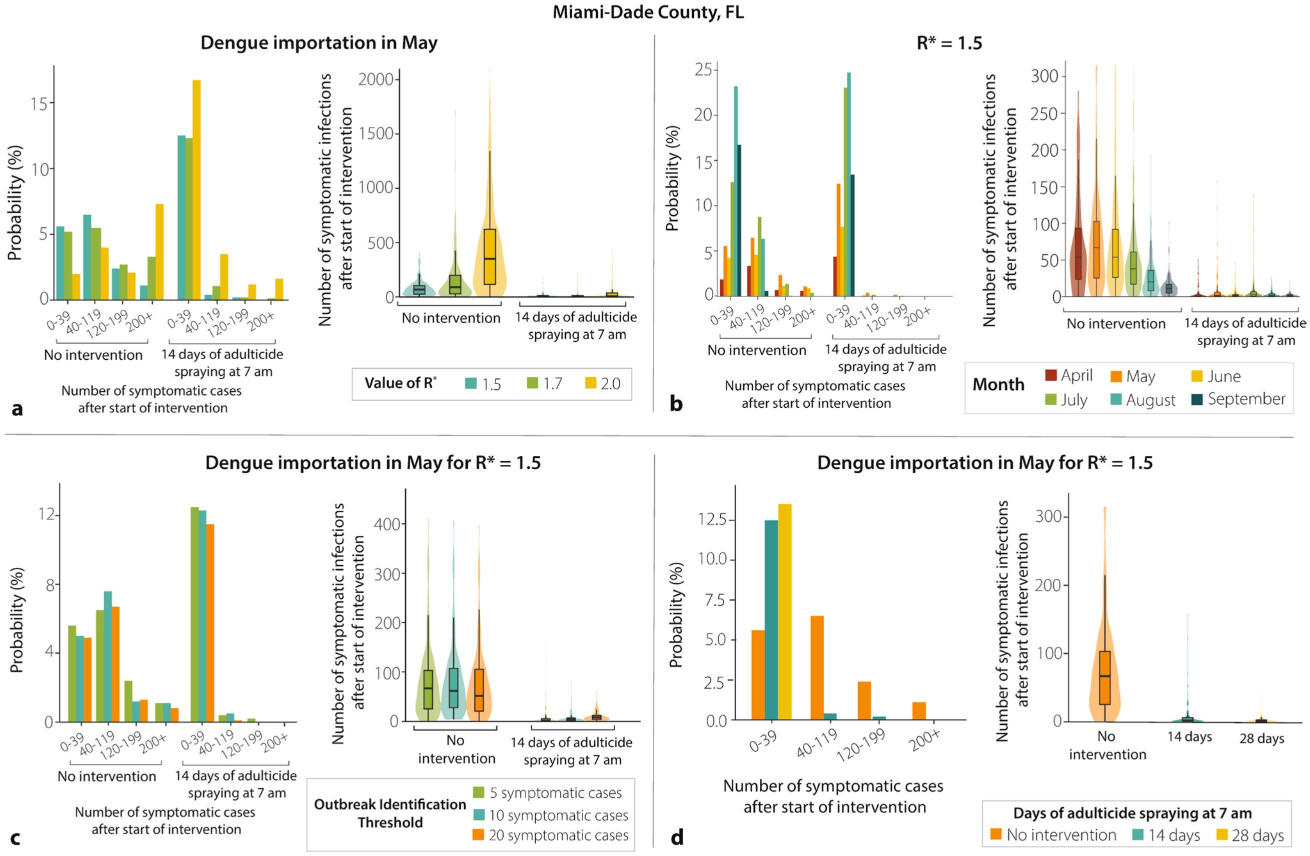

Fig. 4 **a** Estimated probability of observing an outbreak of a given size and the number of symptomatic infections after outbreak detection (i.e., 5 symptomatic cases) in Miami-Dade County, FL, after dengue importation in May in the absence of interventions and when the adulticide spraying for 14 consecutive days (adulticide efficacy 50%) is implemented at 7am for different values of R^*. Box plots represent quantiles 0.025, 0.25, 0.5, 0.75, 0.975, and shaded area represents the distribution of the number of symptomatic infections. **b** Same as a but for importations of DENV at different times of the year. **c** Same as a but for different thresholds for outbreak detection. **d** Same as a but for different durations of the intervention

from 14 days at 7 am to be highly effective. Results for interventions carried out at other times of the day are reported in Tables S10-S17 in the Supplementary Material.

We also conducted a sensitivity analysis to determine the effect of changes in mosquito activity during different times of the year in Miami-Dade County. This sensitivity analysis considers the differences between the overall proportion of active *Ae. aegypti*, the proportion of active *Ae. aegypti* in May, and the proportion of active *Ae. aegypti* in October. The findings of this sensitivity analysis reflected the trends we observed in the main analysis. Regardless of using the proportion of active mosquitoes for a single month, the slight decreasing trend in the outbreak potential and size remains when adulticide spraying is conducted at 1am or 3 pm (Fig. 6a, c). There was a marked decrease in the outbreak probability and size when considering the proportion of *Ae. aegypti* activity in May and October. When considering only activity in May, the probability of having 40 or more symptomatic cases was 0.7% with a 91.7% reduction in the number of symptomatic infections (6.0, IQR: 5.0–8.0) when adulticide spraying was conducted at 7am, whereas when we only consider the activity in October, the probability of having 40 or more symptomatic cases decreases to 2.3% with a 88.9% reduction in the number of symptomatic infections (8.0, IQR: 6.0–22.3) total symptomatic infections (Fig. 6b). However, when spraying at 8 pm and considering a proportion of active *Ae. aegypti* in October, the probability and size of the outbreak is larger compared to using the overall proportion or the proportion considering only *Ae. aegypti* activity in May (Fig. 6d). This suggests that during months with fewer daylight hours, adulticide may need to be sprayed during earlier hours.

Discussion

Among the many tools available to authorities under the IVM framework (Guzman et al. 2010; Saadatian-Elahi et al. 2021), adulticide spraying interventions are at the forefront to control mosquito vector populations during an

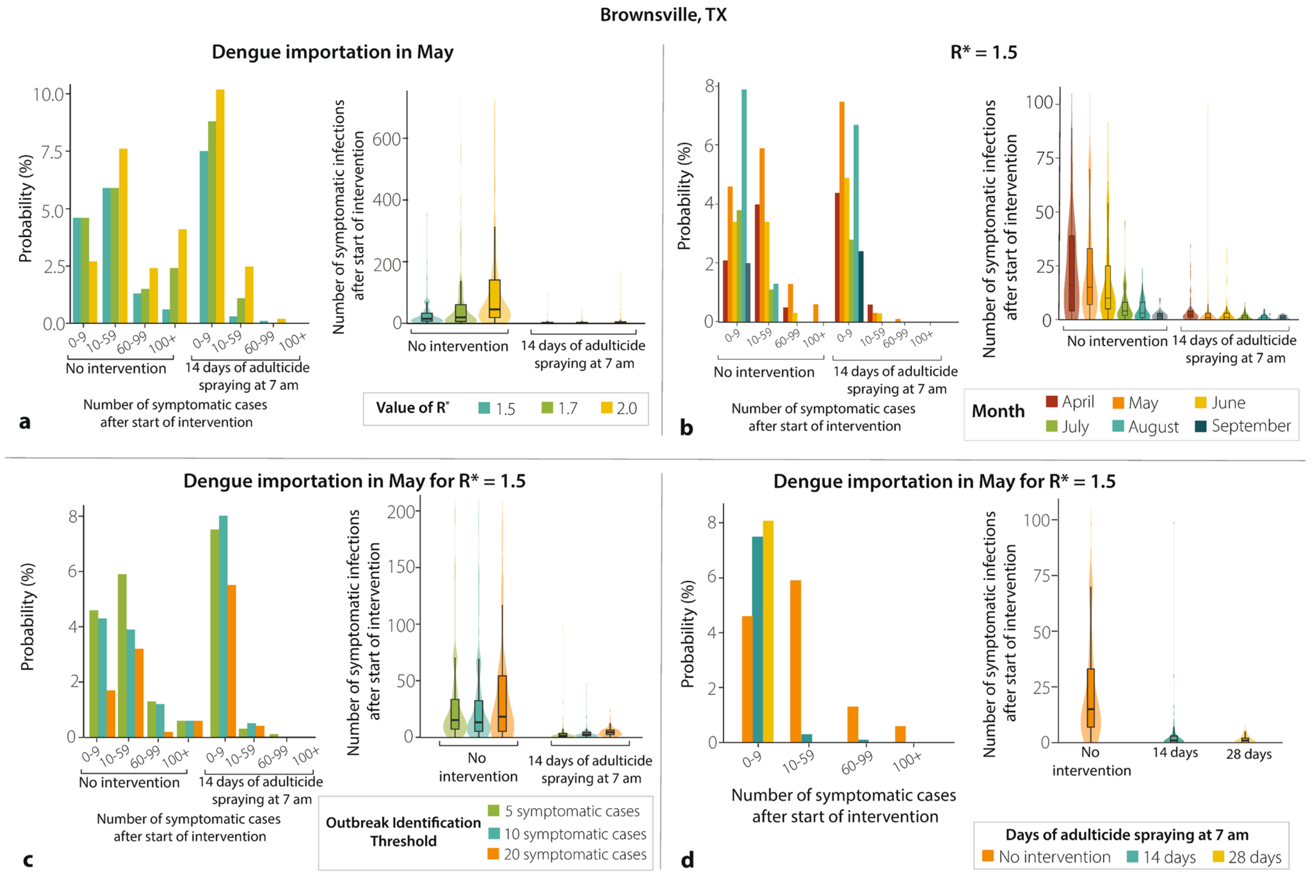

Fig. 5 **a** Estimated probability of observing an outbreak of a given size and the number of symptomatic infections after outbreak detection (i.e., 5 symptomatic cases) in Brownsville, TX, after dengue importation in May in the absence of interventions and when the adulticide spraying for 14 consecutive days (adulticide efficacy 50%) is implemented at 7am for different values of R^*. Box plots represent quantiles 0.025, 0.25, 0.5, 0.75, 0.975, and shaded area represents the distribution of the number of symptomatic infections. **b** Same as a but for importations of DENV at different times of the year. **c.** Same as a but for different thresholds for outbreak detection. **d** Same as a but for different durations of the intervention

outbreak, because they target active host-seeking female mosquitoes that sustain transmission. Wilke et. al. (2023), identified the entomological effects of adulticide spraying during different times of the day. The present study expands upon these findings to determine how the effects of adulticide spraying on the mosquito population impact local DENV transmission. We found that the effectiveness of adulticide spraying on mitigating DENV transmission differs widely depending on the time of day the intervention is implemented. Moreover, these patterns were consistent between the two study sites despite minor quantitative differences in the estimated effectiveness.

Our analysis, indicated that implementing adulticide spraying interventions at 7 am and 8 pm, when we estimated *Ae. aegypti* to be most active, significantly decreases the outbreak probability and the total number of symptomatic cases of dengue. On the contrary when implementing the intervention at 1 am and 3 pm (i.e., periods of low *Ae. aegypti* activity), the effectiveness of the intervention dramatically decreases. Our results demonstrate that the entomological effects of adulticide on the *Ae. aegypti* population found by Wilke et. al. (Wilke et al. 2023) do translate into an epidemiological effect for DENV transmission and support the relevance of collecting data on mosquito diel activity patterns.

Furthermore, our analysis showed that adulticide spraying for 28 consecutive days led to a slightly larger decrease in the probability and size of the outbreak compared to a 14 consecutive day intervention, in most cases. However, implementing an adulticide spraying intervention every day for 4 weeks may not always be feasible, as there are constraints in the amount of insecticide that can safely be sprayed in the environment to respond to an emergency (Silver et al. 2017; United States Environmental Protection Agency 2023). Moreover, indiscriminate spraying of insecticides can lead to increased levels of insecticide resistance (Mundis et al. 2020; Pridgeon et al. 2008).

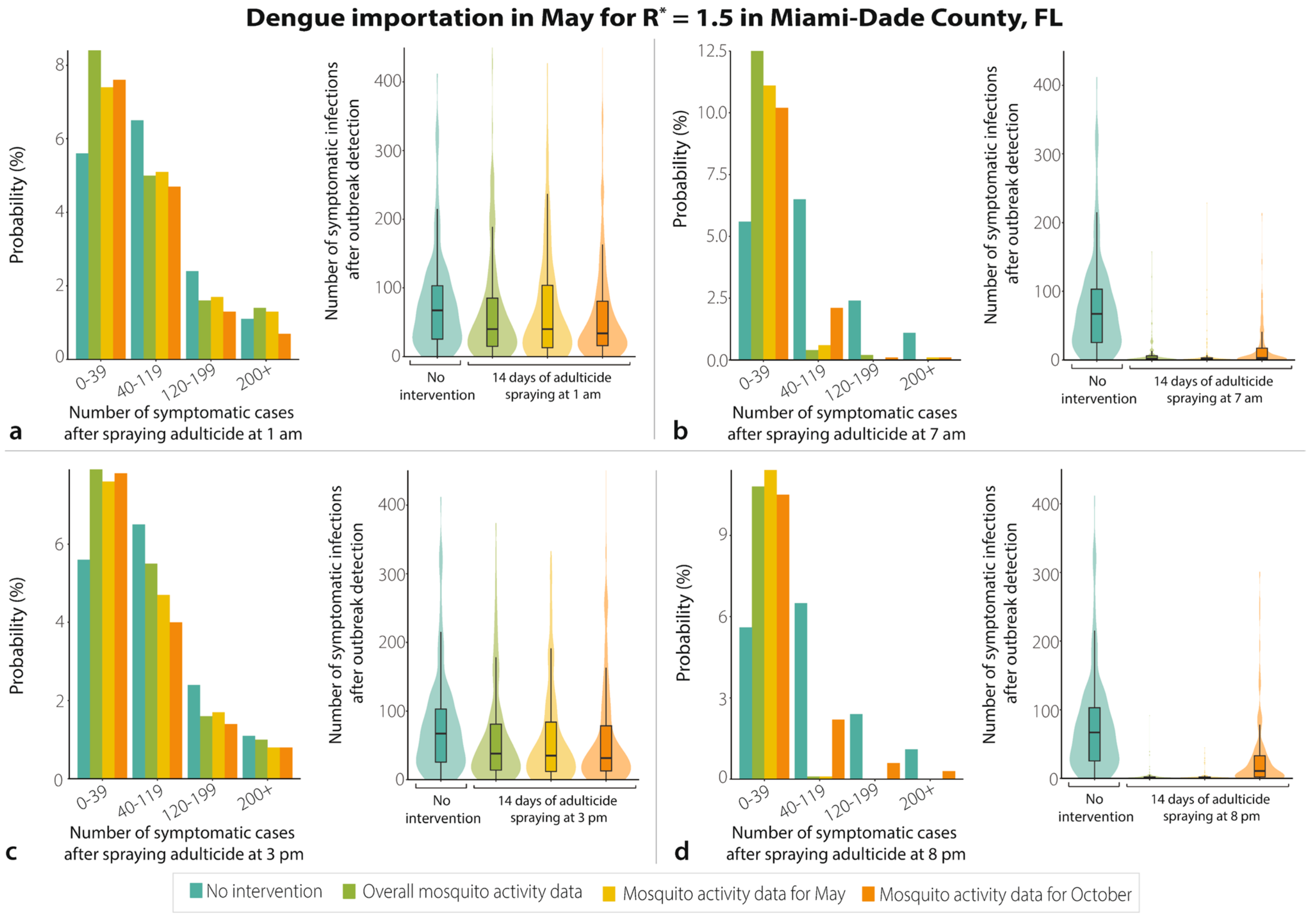

Fig. 6 **a** Estimated probability of observing an outbreak of a given size and the number of symptomatic infections after outbreak detection (i.e., 5 symptomatic cases) in Miami-Dade County, FL, after dengue importation in May in the absence of interventions and when the adulticide spraying for 14 consecutive days (adulticide efficacy 50%) is implemented at 1am for different proportions of *Ae. aegypti* activity. Box plots represent quantiles 0.025, 0.25, 0.5, 0.75, 0.975, and shaded area represents the distribution of the number of symptomatic infections. **b** Same as a but when the adulticide spraying intervention is implemented at 7am. **c** Same as a but when the adulticide spraying intervention is implemented at 3 pm. **d** Same as a but when the adulticide spraying intervention is implemented at 8 pm

Our sensitivity analysis of dengue importations at different times of the year demonstrated that outbreak probability and outbreaks size are higher when a DENV importation occurs during the early part of the season (i.e., April-June) compared to the later part of the season. While the absolute value of the outbreak probability and the outbreak size are much larger when a DENV importation occurs early in the season, the overall effectiveness of the adulticide spraying intervention is significantly reduced when implemented during times of the day when mosquitoes are highly active. Additionally, when we adjusted the outbreak identification threshold, our findings showed the importance of early identification of local transmission, thus supporting the importance of arbovirus and epidemiological surveillance.

We found that Brownsville had lower estimates for the outbreak probability and size for all tested interventions compared to Miami-Dade County, which agrees with the observations on locally acquired DENV infections (Centers for Disease Control and Prevention 2023). Despite the quantitative differences between the two study sites, there were qualitative similarities. *Aedes aegypti* activity followed similar patterns in both Brownsville and Miami-Dade County, with higher activity during the morning and evening and lower activity during the late night and afternoon. Consequently, adulticide spraying at 7 am and 8 pm was more effective in both locations. It is thus possible that our findings could be applied to other settings as well.

Our findings support the idea that diel activity patterns are an essential component in planning effective adulticide spraying interventions. However, despite being an integral part effective adulticide applications, diel activity data is not rarely part of the decision-making process. The majority of current mosquito control efforts rely primarily on mosquito surveillance data, detection of human cases or citizen complaints to inform decisions on when to spray adulticides (United States Department of Justice 2007; Wilke et al. 2019a, b). Interestingly, mosquito control interventions are conducted during the middle of the night to limit direct human exposure (Roiz et al. 2018). However, as demonstrated by this and previous studies (Wilke et al. 2023), *Ae. aegypti* is less active during the night, thus the effectiveness of the adulticide application interventions is dramatically reduced.

The present study has several limitations. First, in the baseline analysis, we considered a reproduction number of 1.5 during the week when mosquito abundance was highest. Although this estimate is in agreement with previous studies (Zardini et al. 2024), every outbreak follows a different trajectory and other values may be more appropriate to describe a specific outbreak. For this reason, we conducted a sensitivity analysis on the value of the reproduction number which shows large quantitative differences in outbreak size and probability. However, our main finding of the highest effectiveness of the adulticide application intervention at 7 am and 8 pm remained unaltered. Second, our analysis considers only adulticide spraying interventions. During a dengue outbreak in well-equipped vector control programs, it is very likely that a set of interventions including source reduction and larvicide applications would be conducted simultaneously (Beier et al. 2008; Poletti et al. 2011). Further research is needed to improve our understanding of the effectiveness of combined mosquito control interventions. Thirdly, our main analysis uses the same proportion of *Ae. aegypti* activity throughout the year without considering changes in times of peak activity as the number of daylight hours changes. The results of our sensitivity analysis considering *Ae. aegypti* diel activity data for May and October show similar results, but still noticeable quantitative differences on the effectiveness of adulticide spraying interventions. Future studies should consider the dynamic variation in mosquito activity over time as this deserves further exploration. Finally, our study is based on the analysis of data from two study sites and data collected over a single season. More evidence on *Ae. aegypti* dial activity patterns in other areas should be collected to further increase the translational impact of our findings.

In conclusion, the present study highlights the importance of including diel activity patterns data for the vector mosquito species in arbovirus preparedness and response planning. Specifically, we identified that conducting adulticide spraying interventions during periods of the day when mosquito activity is high can increase the effectiveness of the interventions to curb DENV transmission. While the present study focuses on dengue, our analysis can be adapted to other arboviral diseases with similar transmission dynamics, such as Zika and chikungunya. Overall, our modeling analysis provides valuable information to guide vector control authorities on the effectiveness of mosquito adulticide spraying interventions.

Author contributions

A.B.B.W., J.-P.M., and M.A. designed the research. C.V., J.M., I.U., Y.G., and J.-P.M collected the data. A.G.K. analyzed the data. A.G.K., A.B.B.W., P.C.V., C.V., J.M., I.U., Y.G., A.M., G.B., K.E., J.-P.M., and M.A. interpreted the results. A.G.K., A.B.B.W., and M.A. wrote the paper. P.C.V., C.V., J.M., I.U., Y.G., A.M., G.B., K.E., and J.-P.M. edited the paper.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s10340-024-01787-w.

Acknowledgements The authors would like to acknowledge Andrea Morrison (Florida Department of Health) for helpful comments on an earlier version of the manuscript. We would like to express our deepest gratitude to Jesus Rodriguez of Brownsville for his invaluable assistance with the data collection. His dedication and expertise greatly contributed to the success of this project. Jesus will be dearly missed, and his legacy in our work will always be remembered.

Funding This study was made possible by cooperative agreement CDC-RFA-FT-23-0069 from the CDC's Center for Forecasting and Outbreak Analytics. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the Centers for Disease Control and Prevention.

Data availability Data are provided within the manuscript or supplementary information files.

Declarations

Conflict of interest The authors declare that no competing interests.

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