Evaluating Field Trial Designs for Genetically Modified Mosquito Interventions: An In-Silico Simulation Approach

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Abstract

Mosquito control strategies based on the mass release of modified males, such as genetically modified mosquitoes (GMMs), aim to suppress wild populations by impairing reproduction. Evaluating these interventions requires resource-intensive field trials, but a lack of standardized implementation practices, particularly regarding release ratios of modified males to wild female mosquitoes and trial timing, has led to variable outcomes. This study's objective is to propose a modeling tool for the "in-silico" simulation of trial designs before field implementation. To this aim, we developed an agent-based model of mosquito population dynamics. As a case study, we calibrated the model using 2019-2023 *Aedes aegypti* surveillance data from Miami-Dade County, Florida, and compared two GMM trial designs: a "constant-release" design (fixed releases based on a baseline entomological survey) and an "adaptive-release" design (releases adjusted weekly to the population of the control arm). Our results show that the constant-release design's effectiveness is highly dependent on the trial's start date relative to mosquito seasonality, creating large outcome uncertainty. For a 6-month trial with a 4:1 GMM:wild ratio and constant-release, the median effectiveness across all start dates was 71.4%, with an interquartile range (IQR) spanning from 55.3% to 90.0%. In contrast, the adaptive-release design yielded similar median effectiveness but with a narrower IQR regardless of the start date, trial duration, and release ratio. Overall, effectiveness is closely linked to the total number of mosquitoes released but also dependent on the timing, frequency of releases, release ratio, mosquito fitness, and duration of interventions. Our findings suggest that "in-silico" simulation is a valuable tool for improving trial protocol design, allowing stakeholders to test strategies and reduce outcome uncertainty before committing to a fieldwork experiment.

Keywords: Genetically Modified Mosquitoes; *Aedes aegypti*; Agent-Based Modeling; Population Dynamics

Introduction

Traditional insecticide-based strategies are the cornerstone of mosquito control [1–4]. However, they have limitations such as insecticide resistance [5–7] and potential environmental impacts and effects on biodiversity, ecosystems, and human health, regardless of the effectiveness on mosquito control [8]. Therefore, in past decades, a new generation of interventions has emerged, which are based on irradiated sterile mosquitoes (SIT), *Wolbachia*-infected mosquitoes, or genetically modified mosquitoes (GMM) [9–18]. These strategies, here referred to as "*Next-generation*" mosquito control strategies, rely on inundative releases of adult male mosquitoes that are either sterile or carrying a modified gene or parasite, which impair reproduction [12,19]. However, implementing next-generation strategies still requires rigorous testing and evaluation to assess their effectiveness, ecological impact, and safety before large-scale implementation.

Field trials represent the gold standard in evaluating the effectiveness of mosquito control strategies. However, they require substantial financial resources, logistical support, and expert coordination to ensure proper implementation [20,21]. To date, trial results of next-generation mosquito control strategies have been deemed inconclusive, highlighting a major knowledge gap [9–18]. Pilot studies in Kentucky, Panama, Brazil, China, Cuba, and the Cayman Islands have yielded promising results [10,12–15,17]. On the other hand, trials in Florida, Mexico, Italy, and Malaysia had limited success [9,11,16,22]. The lack of standardized guidelines on how to implement field trials for next-generation mosquito control strategies has possibly contributed to these results. For instance, the ratio of sterilized, *Wolbachia*-infected, or genetically modified male mosquitoes to wild-type males varied widely [9,10,14]. Other trials did not consider the size of the wild-type mosquito population [13,15]. Additionally, variations between studies were observed in the start and end date of the trial, with some conducted during the low mosquito season [22], others during the high season [16], and some spanning most of the year [13,15].

Without clear and standardized guidelines in place, it is challenging to evaluate the effectiveness of these interventions and compare findings across different studies and settings. Mathematical models have been used to inform and guide the implementation of field trials [23], including those for Ebola [24] and dengue [25] vaccines, and SARS-CoV-2 antiviral therapies [26,27]. Furthermore, mathematical models have been developed to assess the effectiveness of next-generation mosquito control strategies [19,28–43], suggesting that model simulation represents a suitable tool to evaluate field trial designs for these strategies.

To overcome the lack of standardized guidelines, our study proposes "in-silico" simulations to investigate trial designs and estimate their effectiveness in reducing mosquito populations. As a case study, we investigate alternative designs for a GMM-based trial focusing on the control of the *Aedes aegypti* population in Miami-Dade County, Florida. Miami-Dade County is an ideal location as it has an abundant *Ae. aegypti* population, an archive of historical mosquito surveillance data, and a history of local transmission of arboviruses [44–46].

Methods

Data

We used mosquito surveillance data from January 1, 2019, to December 31, 2023, for Miami-Dade County, FL, which is collected and managed by the Miami-Dade County Mosquito Control Division. The surveillance system consists of about 300 BG-Sentinel-2 traps baited with dry ice that are deployed once per week for 24 hours. Collected mosquitoes are identified using taxonomic keys. Details on the data collection are reported in our previous publication [47]. Daily mean temperature data for Miami-Dade County, Florida, was retrieved from publicly available records from the Miami International Airport [48].

Model Formulation

In this study, we simulate GMM-based trials that aim at reducing the mosquito population. GMM population suppression strategies involve the release of homozygous adult male mosquitoes carrying a gene that impairs the fertility of female offspring [49]. Specifically, when a genetically modified male mosquito mates with a wild adult female mosquito, it will produce a heterozygous offspring carrying that gene. Heterozygous females are infertile, while heterozygous males have the possibility to mate with wild females, further propagating the gene in the wild mosquito population [19,49–52].

We developed an agent-based model to produce "in-silico" stochastic simulations of *Ae. aegypti* population dynamics through four stages of development: egg, larva, pupa, and adult (Fig. 1A). The model estimates the number of *Ae. aegypti* in each stage of their life cycle for each calendar date at a time step of 0.1 days. Each agent in the model represents a single mosquito in the population with a given sex (male or female), genetic makeup (genetically modified homozygous, genetically modified heterozygous, or wild type), and current stage of development (egg, larva, pupa, or adult). We assumed a 1:1 female-to-male ratio for eggs. At each time step of the simulation, each agent's transition into the next development stage or mortality and adult female oviposition are sampled from a Bernoulli distribution using the appropriate temperature-dependent rate [53–56]. Wild-type adult female mosquitoes lay eggs at a given temperature-dependent oviposition rate [54,56] with an average of 100 eggs laid during oviposition [57]. Newly laid eggs then become new agents in the model. Eggs' mortality is both temperature- and density-dependent to account for the carrying capacity of the environment (see section Model Calibration).

To simulate GMM-based trials, we periodically introduce a given number of new adult male agents that are genetically modified (homozygous) into the population. These mosquitoes continue through the life cycle in the same way as wild-type mosquitoes. When a wild-type female mates with a homozygous male, the offspring is heterozygous, and heterozygous females are infertile (i.e., their oviposition rate is set to 0). When a wild-type female mates with a heterozygous male, half of the offspring will be heterozygous for the transgene, and half will not carry the transgene. Moreover, we assume that female mosquitoes mate only once in their lifetime [58]. Finally, mosquitoes carrying the transgene have a different (generally lower) fitness than wild-type males, which reduces

Figure 1. A. Conceptual representation of the modeled mosquito life cycle. **B.** Conceptual representation of the GMM mechanisms of action and list of trial design variables that are investigated in this study.

the likelihood of successful mating [59]. A conceptual representation of the process is shown in Fig. 1B.

Model Calibration

Temperature-dependent development and mortality rates of mosquito lifecycle stages were taken from previous literature [53–55]. The model also considers seasonal changes in the carrying capacity to account for variations throughout the year [56]. We used a Markov chain Monte Carlo (MCMC) procedure to obtain estimates of the posterior distributions of the carrying capacity for the period May-July and the carrying capacity for the period August-April. MCMC explored the likelihood of observing the actual number of collected adult female *Ae. aegypti* specimens from Miami-Dade County, Florida, from a negative binomial distribution of the mean given by the model and the over-dispersion parameter, which is estimated as well [60]. Details are reported in the Supplementary Material.

Simulation Analysis of Trial Implementation

The calibrated model simulates *Ae. aegypti* population dynamics from January 2019 through December 2023 and provides estimates of the daily number of *Ae. aegypti* specimens for each life stage of development, sex, and genetic makeup. This allows us to simulate different trial designs and trial implementation variables "in silico". In our analysis, we simulated 2-arm trials where the control arm consists of the model realizations that are run without any GMM-based intervention, while the intervention arm consists of the model realizations simulating a GMM-based intervention.

We consider two types of trial designs:

- **Constant-release trial design.** The number of genetically modified (homozygous) male mosquitoes released per release in the intervention is set to obtain the desired ratio between the number of released male mosquitoes and the number of female mosquitoes per trap night collected during a baseline entomological survey. This baseline entomological survey is conducted before the start of the trial to assess the relative abundance of the mosquito population by monitoring traps for adult female mosquitoes (e.g., BG-Sentinel-2 traps). It is important to stress that in this design, the number of released male mosquitoes per release is constant for the entire duration of the trial; thus, in populations following seasonal trends and where control is effective, the actual ratio of released male mosquitoes as compared to the actual female mosquito population changes over time.
- **Adaptive-release trial design.** The number of genetically modified (homozygous) male mosquitoes released per release in the intervention is dependent on the number of mosquitoes estimated in the control arm. The idea of the adaptive-release trial design is to rely on the control arm to obtain an estimate of the actual target female population relative abundance at any time point. Then, this estimate is used at the time of each release as the denominator to calculate the number of male mosquitoes to be released to obtain a constant release ratio as compared to the actual female mosquito population at any given point in time. Specifically, the number of male mosquitoes released at time t, $G(t)$ is given by: $G(t) = r \cdot s \cdot \bar{C}(t - 7)$, where r is the target release ratio, s is the trap collection ratio estimated in the literature (which corresponds to the ratio between the collected adult female mosquitoes and the total number of adult female mosquitoes), and $\bar{C}(t - 7)$ is the mean estimated number of mosquitoes in the control arm over the past week. The one-week lag was incorporated to account for the time required for trap collection, mosquito identification, data entry, and release planning.

The effectiveness of a simulated trial (trial outcome) is defined as the reduction in the *Ae. aegypti* female population within the monitored area during the trial period as:

$$E_{ff} = 1 - \frac{T}{C}$$

where T is the sum of estimated adult female mosquitoes in the treatment arm from 2 months after the start of the trial until the end of the trial, and C is the same quantity but for the control arm.

Results for each simulated trial are based on 100 stochastic model realizations obtained by uniformly sampling 100 indexes of MCMC corresponding to the joint posterior distributions of the carrying capacity for the two periods. Then, for each sampled index, we run the control and the treatment arm for both trial designs.

Standardized guidelines for trial implementation of GMM mosquito control strategies encompass a wide range of aspects and cover different steps of the implementation of the trial, from laboratory protocols to field practices. Among them, we investigate four

variables: i) release ratio, ii) start date of the trial (which will allow accounting for temporal trends of the target mosquito population in the site of the trial), iii) the duration of the baseline entomological survey (only for the constant-release trial design), iv) release frequency, and v) trial duration. For the main analysis, we simulated 6-month trials with a release frequency of once per week, a 2-month baseline entomological survey, and that genetically modified mosquitoes have the same fitness as wildtype ones. We investigated release ratios from 0.1 to 9.0 by 0.1 steps, and we consider starting dates of the trial on the first day of the month for every month of the year in 2022. Regarding the release ratio, it is important to emphasize that an n:1 release ratio is relative to the collected female mosquitoes, which represents an underestimate of all female mosquitoes within the area. Specifically, we considered a 24.6% trap collection ratio within the study area [61].

To ensure the robustness of our findings, we conducted several sensitivity analyses varying the release frequency (every 3, 7, and 14 days), trial duration (90, 180, and 365 days), and duration of the baseline entomological survey (2, 6, and 12 months), and the fitness of the genetically-modified mosquitoes (set at 50% and 75% relative to the fitness of wild-type male mosquitoes). Moreover, we conducted a sensitivity analysis considering two alternative values for the collection ratio, 12.3% and 49.2%, encompassing the uncertainty reported in the reference study [61]. To ensure that our results do not depend on the analyzed year (i.e., on the mosquito surveillance and temperature data), we conducted a sensitivity analysis where the trials were carried out in 2020, 2021, and 2022. Finally, to assess the impact of temperature and carrying capacity on the effectiveness of the GMM-based trial, we performed an analysis where the temperature was set to a constant 25°C and the carrying capacity to the one estimated for April-August, while all other parameters remained the same as in the main analysis.

Code Availability

The code of the model used in this manuscript is openly available on GitHub at https://github.com/jagadeesh-chitturi/GMM-Interventions/tree/main.

Results

The estimated weekly number of adult female *Ae. aegypti* per trap night compares well with the observed data for Miami-Dade County over the entire study period (Fig. 2A). The data show a year-round presence of *Ae. aegypti* with a clear seasonal trend in its abundance, with peak activity taking place in July (about 10 collected adult female *Ae. aegypti* per trap night) and lower activity during the winter months, with about 2 collected specimens per trap night.

Figure 2B,C shows two illustrative examples of a constant-release and an adaptive-release GMM trial of a 6-month duration, weekly releases, a 4:1 release ratio, and two different start dates (March 1 and May 1). For the constant-ratio design, we considered a 2-month baseline entomological survey. As shown in the figure, the control arm and the two treated arms follow a similar trajectory for the first few weeks before diverging. Overall, for trials starting on March 1, we estimated an effectiveness of 46.1% (interquartile range, IQR: 41.6%-68.6%) and 90.9% (IQR: 71.7%-94.2%) for the constant-release ratio and adaptive-release ratio, respectively. For those starting on May 1, the

Figure 2. A. Number of collected adult female *Ae. aegypti* per trap night by month of the year as reported in the Miami-Dade mosquito surveillance system and as estimated by the model. **B.** Daily number of collected adult female *Ae. aegypti* per trap night estimated by the model in the control arm and in the treatment arm of constant-release trial and an adaptive-release trial. The trial duration is 6 months, releases are made weekly, the release ratio is 4:1, and the start date of the trial is March 1. For the constant-release trial, the duration of the baseline entomological survey is 2 months. **C.** As B but for trials starting on May 1.

estimated effectiveness is 47.3% (IQR: 37.5%-58.4%) and 81.3% (IQR: 71.3%-92.-0%), respectively.

By systematically analyzing the start date of the trial, while fixing the other trial implementation variables (weekly release, 6-month trial duration, and 2-month entomological survey duration), we found that the effectiveness is highly variable for constant-release trial design, especially for release ratios between 2:1 and 8:1 (Fig. 3A). The highest effectiveness is estimated for trials starting in August and the lowest one for trials starting in May. On the other hand, the adaptive-release trial design shows a narrower variability for any release ratio, suggesting that regardless of the trial start date the estimated effectiveness is approximately the same (Fig. 3B). In fact, regardless of the release ratio, we found a similar yearly median effective for the two trial designs but a wider variability in effectiveness depending on the trial start date for the constant-release trial design as compared to the adaptive-release design (Fig. 3C). It is important to stress that we found no evident difference in the efficiency between the two trial designs (Fig.

Figure 3. A. Estimated effectiveness of a constant-release trial as a function of the start date of the trial and release ratio. The other trial variables are set as follows: 6-month trial duration, weekly release, and 2-month baseline entomological survey. **B.** As A, but for an adaptive-release trial. **C.** Estimated median and IQR of the effectiveness of a constant-release and adaptive-release trial designs given a release ratio, for any possible trial start date. The other trial variables are set as in panel A. **D.** Estimated trial effectiveness as a function of the total number of genetically modified adult male mosquitoes released per trap over the entire duration of the trial. Each dot represents a single simulation; dashed lines represent the mean. The panel shows the results for 6-month trials with and weekly releases, any starting date, and any release ratio from 1:0.1 to 9:1. For the constant-release trial design, the duration of the baseline entomological survey is set to 2 months.

3D), where efficiency is defined as the ratio between trial effectiveness and the total number of genetically modified male mosquitoes released per trap over the entire trial duration.

Our results show that more frequent releases, longer trial durations, and greater fitness of transgenic mosquitoes increase the effectiveness of the trial (Fig. 4A-C). Regardless of the frequency of releases, trial duration, and fitness, the adaptive-release trial design is estimated to have slightly higher effectiveness and a considerably smaller variability in the outcome (Fig. 4A-C). To decrease the variability in the estimated effectiveness for the

constant-release trial design, a longer baseline entomological survey should be carried out (Fig. 4D).

We found that all our findings remain unchanged if trials are simulated using data from different years (see Fig. S8 in the Supplementary Material). However, in a hypothetical scenario where the temperature and carrying capacity do not change over the course of

Figure 4. A. Estimated median and IQR of the effectiveness of a constant-release and adaptive-release trial designs given the release frequency, for any possible trial start date. The release ratio is set to 4 and the trial duration to 6 months; for the constant-release design, the duration of the baseline entomological survey is set to 2 months. **B.** Estimated median and IQR of the effectiveness of a constant-release and adaptive-release trial designs given the trial duration, for any possible trial start date. The release ratio is set to 4 and the release frequency to once per week; for the constant-release design, the duration of the baseline entomological survey is set to 2 months. **C.** Estimated median and IQR of the effectiveness of a constant-release and adaptive-release trial designs given the fitness of genetically modified male mosquitoes, for any possible trial start date. The release ratio is set to 4, the trial duration is set to 6 months, and the release frequency to once per week; for the constant-release design, the duration of the baseline entomological survey is set to 2 months. **D.** Estimated median and IQR of the effectiveness of a constant-release and adaptive-release trial designs given the duration of the baseline entomological survey, for any possible trial start date. The release ratio is set to 4, the trial duration is set to 6 months, and the release frequency to once per week.

the year, we estimated that a much larger release ratio is needed to obtain the same effectiveness estimated for the simulated trials using data for Miami-Dade County, FL (Fig. S9 in the Supplementary Material). Given that no changes take place over time and thus the mosquito population is constant year-round, the variability in the estimated effectiveness drastically decreases. Finally, we estimated a higher effectiveness of the trails for higher collection ratios of the traps, but our main finding about the lower variability in the effectiveness estimated using the adaptive-release design remains unchanged (see Fig. S10 in the Supplementary Material).

Discussion

Our results showed that the trial start date has a remarkable impact on the estimated effectiveness, especially for the widely-adopted constant-release trial design. To maximize effectiveness, we estimated suitable trial start dates immediately following a rise in the mosquito population (e.g., June for *Ae. aegypti* trials in Miami-Dade County, Florida). By neglecting to consider the effect of the start date of the trial, our simulation results show that the estimated effectiveness would encompass a large variability. For example, our simulations show that for a 6-month trial with weekly releases at a 4:1 constant-release ratio, the estimated effectiveness is 71.4%, with an interquartile range spanning from 55.3% to 90.0%. Such a wide uncertainty on the intervention effectiveness has the potential to hamper the willingness of stakeholders to make the large-scale investment needed to implement GMM-based interventions. To reduce variability, we could conduct longer baseline entomological surveys that better capture the true seasonal variations in female *Ae. aegypti* populations, albeit at an increased logistic cost and overall trial duration. Finally, we conducted a wide range of sensitivity analyses confirming our qualitative findings. Nonetheless, these analyses have shown that the release frequency, trial duration, and fitness of genetically modified male mosquitoes do have a quantitative impact on the trial effectiveness. Specifically, longer trials and a higher release frequency would improve the effectiveness of the intervention but would also entail higher monetary and logistic costs. The reduction in fitness resulting from genetic modification remains a limiting factor in the effectiveness of population suppression strategies [42,59,62].

In this study, we also investigated an alternative trial design based on an adaptive-release ratio that is adjusted weekly based on the number of mosquitoes collected in the control arm during the preceding week. This weekly reassessment allows the intervention to respond dynamically to changes in the mosquito population, potentially improving effectiveness compared to a constant-release approach. Our simulations estimated a similar median effectiveness for this strategy, but a lower variability as well as a lower influence of the trial start date on the trial outcome. Our findings show that such a design would not increase the number of genetically modified mosquitoes required for a trial as compared to the classic constant-release trial design, supporting the potential for real-world implementation of this design. However, a key aspect of the adaptive-release design is the reliance on the control arm for weekly estimates of the relative abundance of the mosquito female population, which could introduce potential biases. Unexpected fluctuations in the control arm, due to localized environmental factors or stochastic events, could lead to inaccurate estimations of the required number of mosquitoes to be released

in the intervention arm. For instance, a localized increase in mosquito breeding sites in the control area, not mirrored in the intervention area, might trigger an overestimation of the necessary GMM release, potentially wasting resources. Conversely, an underestimation could compromise the effectiveness of the intervention. Such aspects should be carefully weighed against the seemingly lower uncertainty in the results of the adaptive-release trial design as compared to the constant-release design when planning a field trial. This lower uncertainty stems from the adaptive design's ability to adjust to temporal fluctuations in mosquito populations, which are not captured by a fixed release schedule.

The focus on a specific case study, simulating GMM-based interventions for *Ae. aegypti* in Miami-Dade County, is both a strength and a limitation of our study. While it allows for detailed analysis and context-specific recommendations, it also raises questions about the generalizability of the findings to other mosquito species or study sites. However, our primary contribution is to provide an inexpensive and flexible modeling tool to reduce trial outcome uncertainty during the crucial first step in a pipeline toward full-scale public health adoption: the small-scale, proof-of-concept trial. The outcomes of such initial trials are critical, as they determine whether stakeholders may commit resources to subsequent, larger-scale trials focused on optimizing long-term effectiveness (e.g., year-round release schedules). This optimization phase is, in turn, the prerequisite for the eventual, sustainable implementation of these strategies in real-world public health programs. Our model directly supports this first step by helping to design trials with higher likelihood of success. Furthermore, our agent-based modeling approach, openly available via GitHub, is inherently flexible and can be readily adapted to support both the design of larger-scale trials and the optimization of a wide range of other mosquito control interventions.

Our study is subject to the following limitations. First, our model simplifies certain biological, ecological, and environmental aspects. For example, it assumes a 1:1 sex ratio, female mosquitoes mating only once in their lifetime, and uniform mixing between male and female mosquitoes, as well as relying on specific temperature-dependent parameters derived from the literature on *Ae. aegypti* rather than on the specifics of the population in the study site. While these assumptions are standard in many mosquito population dynamic models, they may not fully capture the nuances of real-world dynamics. Second, our model was validated against historical mosquito surveillance data from Miami-Dade County, Florida, providing a good fit to observed population trends. However, it has not yet been validated against data from actual GMM field trials. Such validation would be crucial to confirm the model's predictive accuracy regarding the impact of GMM releases. Future work should prioritize obtaining and incorporating such data. Third, the current model does not account for spatial heterogeneity in breeding site availability, microclimatic conditions, etc., which may affect the outcome of a trial. Incorporating spatial factors into future model iterations would enhance the model's capability to test more nuanced factors affecting the outcome of a trial. For example, the model currently considers a fitness parameter that represents the (potentially) reduced ability of genetically modified male mosquitoes to successfully mate. A spatial model would allow the evaluation of different mechanisms driving such a reduction (e.g., shortened flight range, lower energy level) as well as boundary and spillover effects that are not considered here. Fourth, our analysis focuses solely on GMM-based interventions

and does not consider the potential for integrating other mosquito control methods. In practice, GMM releases might be combined with other interventions, such as the application of *Bacillus thuringiensis israelensis* (*Bti*) or other larvicides before the start of a trial.

In conclusion, this study presents a novel modeling tool designed for the "in-silico" simulation of field trials evaluating GMM-based mosquito control strategies. Grounded in empirical mosquito surveillance data and incorporating key environmental factors, such as temperature-dependent development and mortality rates and temporal variations in carrying capacity, this tool offers a platform for exploring different trial designs. While our analysis focused on *Ae. aegypti* in Miami-Dade County, the flexibility of the agent-based modeling approach allows for its adaptation to other mosquito species and geographic locations, making it a valuable asset in the broader field of vector control. By enabling the identification of trial implementations with the highest likelihood of success, our model can contribute to the development of standardized guidelines for field trial design, ultimately minimizing the need for extensive and costly real-world experimentation. This is particularly important considering the inherent risks to non-target species, humans, and the environment associated with any field release of genetically modified organisms. If field trials, guided by in-silico optimization, demonstrate the effectiveness of GMM-based strategies, these interventions could offer a powerful alternative to traditional vector control methods, which are often hampered by insecticide resistance and environmental concerns. By providing a more targeted and potentially more sustainable approach to mosquito control, GMM-based strategies could significantly enhance public health by reducing the burden of arboviral diseases. The insights gained from this study, coupled with future model refinements and validation with field trial data, could contribute to a more comprehensive understanding of the effectiveness and feasibility of GMM-based interventions, ultimately facilitating evidence-based public health decision-making to mitigate the risks of arbovirus transmission.

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Competing Interests

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