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A Mathematical Model for Assessing the Reduce and Replace Strategy for Combating Dengue Transmission by *Aedes aegypti*

Traditional methods of controlling the primary vector of dengue fever, *Aedes aegypti*, have not been sufficient for controlling the disease itself. Despite an increase in surveillance as well as increased implementation of vector control strategies, dengue remains endemic in many parts of the world. In the last decade alone, a number of novel strategies, including those involving genetically modified mosquitoes (GMM), for controlling *Ae. aegypti* have been proposed and investigated. Strategies involving GMM typically have one of two general goals: Population replacement or population reduction. In the former, GMM would be released that carry an anti-pathogen gene so that mosquitoes that inherit the gene would not be able to transmit disease. In the latter, GMM would be released that pass on lethal genes to their offspring so that after many generations and continued releases, populations near extinction.

In this presentation, we propose and evaluate the potential of another novel strategy which combines the two general goals of GMM strategies. This strategy, henceforth known as Reduce and Replace (R&R), aims to introduce mosquitoes with a single genetic construct that causes female-specific lethality while simultaneously introducing anti-pathogen genes into that population. Using numerical simulations of an ordinary differential equation model, we explore the efficacy of the R&R strategy. We compare several strategies that involve the release of R&R mosquitoes in concert with GMM that confer lethal genes or those that carry only anti-pathogen genes.

We find that the continued release of R&R mosquitoes alone can successfully replace a wild population with one that cannot transmit dengue fever if there are no fitness costs associated with the transgenes involved. If there is a fitness cost associated with carrying the transgenes, continued release of R&R or anti-pathogen only mosquitoes would be required to maintain a low frequency of competent vectors. We find that introducing mosquitoes with lethal genes only before introducing R&R mosquitoes does not, in general, lead to a lower frequency of competent vectors than other strategies. Our model suggest that a release of R&R mosquitoes followed by a release of mosquitoes carrying only an anti-pathogen gene lowers the number of competent vectors more than any other single or combined strategy we consider; however, the R&R strategy on its own underperforms when compared to a combined strategy of R&R and anti-pathogen only mosquitoes.

We discuss the R&R strategy as a component of integrated pest control and motivate the need for further assessment of the utility of this strategy before testing of its efficacy begins.